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CONTROL ID: 3493050

SUBMITTER (NAME ONLY): Alejandro Navas

TITLE: Subconjunctival sirolimus-loaded liposomes for the treatment of moderate to severe dry eye disease

SESSION TITLE: Dry eye clinical treatments

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Navas, A. Córdoba, N.C. Zatarain Barrón, E.O. Graue-Hernandez, N. Morales, Y. Garfias, Instituto de Oftalmología Fundación Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|Y. Garfias, Biochemistry, Universidad Nacional Autónoma de México, Coyoacán, Distrito Federal, MEXICO|G.A. García-Sánchez, M.A. Linares-Alba, Laboratorios Santgar, MEXICO|R. García-Santisteban, Universidad Panamericana, Ciudad de México, Ciudad de México, MEXICO|

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ABSTRACT BODY:

Purpose: To determine the effectiveness of subconjunctival application of a novel sirolimus liposomal formulation for the treatment of signs and symptoms of patients with moderate to severe dry eye.

Methods: A randomized, triple-blind, phase II clinical trial. A total of 38 eyes of 19 patients were included. 9 patients (18 eyes) assigned to Sham group (Sham) and 10 patients (20 eyes) to Sirolimus-loaded liposomes group (Sirolimus). Methods: Treatment group received three doses of subconjunctival liposome-encapsulated sirolimus and sham group received three doses of liposomal suspension without sirolimus. Main Outcomes Measures: Subjective (Ocular Surface Disease Index, OSDI) and objective (corrected distance visual acuity, conjunctival hyperemia, tear osmolarity, Schirmer's test, corneal/conjunctival staining and matrix metalloproteinase-9) variables were measured pre- and post-treatment. Intragroup comparisons were performed (pre-treatment and post-treatment).

Results: Sirolimus-entrapped liposomes treated group OSDI scores changed from 62.19 (\pm 6.07) to 37.8 (\pm 17.81) (p = 0.0024), and conjunctival hyperemia from 2.0 (\pm 0.68) to 0.83 (\pm 0.61) (p < 0.0001); Sham group with OSDI scores from 60.02 (\pm 14.2) to 36.02 (\pm 20.70) (p = 0.01), and conjunctival hyperemia from 1.33 (\pm 0.68) to 0.94 (\pm 0.87) (p = 0.048). All the other evaluated outcomes only showed significant differences in the Sirolimus group: corneal/conjunctival staining score (p =0.0015), lipid layer interferometry (p =0.006), and inferior meibomian gland dropout (p =0.038). No local or systemic adverse effects regarding the medication itself were reported, and the administration route was well accepted.

Conclusions: Our findings suggest that sub-conjunctival sirolimus-loaded liposomes is effective in reducing both signs and symptoms of dry eye in patients with poorly controlled moderate-severe dry eye disease, while avoiding other topical administration adverse effects. Further investigation with a larger sample size is required to determine long-term effects.

CONTROL ID: 3493494

SUBMITTER (NAME ONLY): Bruno Ferreira

TITLE: ASSESSMENT OF PARAFOVEAL RETINAL VASCULATURE IN BEHÇET'S SYNDROME USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: OCT-Angiography (OCT-A) has a unique ability to analyze retinal vascular plexuses, providing additional information about ocular involvement in Behçet's syndrome (BS), which manifests mainly as an occlusive retinal vasculitis. We performed a cross-sectional quantitative and qualitative assessment of parafoveal retinal vascular plexuses in Behçet's uveitis (BU) patients, comparing them with non-ocular Behçet's syndrome (NOBS) patients and healthy subjects (HS).

Methods: Twenty-six patients that met the International Criteria for Behçet's Disease (2014), 16 with BU (age 43.4 ± 12.8 years) and 10 with NOBS (40.7 ± 9 years), and 10 sex-matched HS (42.2 ± 11.7 years) were evaluated with Spectralis® OCT-A (Heidelberg Engineering, Heidelberg, Germany) (Figure 1). Five eyes with poor fixation or media opacities were excluded. Foveal avascular zone (FAZ) area and circularity index (CI) were manually measured in superficial vascular plexus (SVP), intermediate capillary plexus (ICP), and deep capillary plexus (DCP), using ImageJ (NIH, Bethesda, Maryland, USA). Parafoveal vessel density (VD) was quantified for superior, nasal, inferior, and temporal quadrants. Perifoveolar arcade disruption frequency was also evaluated. All biomarkers were correlated with age of onset, duration of disease, and episodes in BU patients. Statistical analysis was performed using generalized estimating equations with a normal distribution.

Results: Variance analysis showed a statistically significant difference ($p < 0.05$) in global VD between BU and NOBS groups and between BU and HS groups in ICP (nasal and inferior quadrants) and DCP (all quadrants) (Figure 2). No differences for CI, temporal VD in SVP and ICP, and perifoveolar arcade disruption were found among the groups ($p > 0.05$). FAZ area and other VD parameters were significantly different only between BU and HS. In the BU group, the Pearson correlation coefficient showed the age of onset has an inverse correlation with the FAZ area ($r = -0.460$) and a positive correlation with VD in SVP ($r = 0.447$).

Conclusions: In patients with BU, the deeper the retinal vascular layer, the lower is the VD. Nasal and inferior quadrants are the most affected, while the temporal quadrant is relatively spared. The age of onset seems to be a predictor for parafoveal vascular changes in BS. None biomarker showed a statistically significant difference between NOBS patients and HS.

CONTROL ID: 3493605

SUBMITTER (NAME ONLY): Sarah Atta

TITLE: Serratia marcescens Keratitis: Clinical Features, Risk Factors, Treatment, and Outcomes

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Atta, R.P. Kowalski, V. Jhanji, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|C. Perera, Department of Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|R.P. Kowalski, The Charles T. Campbell Ophthalmic Microbiology Laboratory, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To provide an up-to-date clinical characterization of Serratia marcescens keratitis and to assess changes in the microbiological spectrum and clinical trends of the infection over time.

Methods: Forty-six culture-proven cases (46 eyes) of Serratia marcescens ocular infection diagnosed and treated at the University of Pittsburgh Eye Center between Feb 2002-Feb 2020 were included in this retrospective, observational case series and reviewed for clinical and microbiological characteristics. Data collected from patient records included demographics, ocular and systemic risk factors, follow-up length, initial and final visual acuity, symptom duration prior to presentation, infiltrate size and shape, medical management, adjunctive management, time to defect closure, duration of treatment, microbiological characteristics, and antibiotic susceptibilities.

Results: Mean presenting age was 46.8 years with mean follow-up time of 329 days. Prevalent ocular comorbidities were contact lens use (68.6%), history of corneal disease (52.9%), lid pathology (25.5%), and glaucoma (15.7%). Systemic comorbidities were present in 58.8% of patients, with systemic atopy (49.0%) and immunosuppression (37.3%) being most common. Average treatment duration was 152 days, with most common administration of fluoroquinolones (76.5%) and fortified antibiotics (60.8%). Visual outcomes generally improved with treatment, with an average initial visual acuity (VA) of 1.3 logMar and final VA of 0.86 logMar. Worse final VA was associated with glaucoma ($p=0.038$), hypopyon ($p=0.045$), older age (0.000), worse initial VA ($p=0.009$), longer time to defect closure ($p=0.020$), and larger infiltrate ($p=0.037$). All cases showed antibiotic sensitivity to ciprofloxacin (100%), and most showed resistance to cefazolin (80.4%). No significant changes in clinical profile or treatment were observed over the 18-year period.

Conclusions: S. marcescens keratitis is associated with contact lens use and poor ocular surface. Fluoroquinolones and fortified antibiotics have shown effective management and improved visual outcomes. Worse outcomes are associated with older age and worse severity at presentation. Microbiological and clinical trends of this ocular infection have remained constant over nearly 20 years.

CONTROL ID: 3493764

SUBMITTER (NAME ONLY): Mashael Al-Namaeh

TITLE: Parkinson's Disease and Convergence Insufficiency: A Meta-Analysis

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Al-Namaeh, School of Health and Social Care, Optometry Department, Oulu University of Applied Sciences, Oulu, FINLAND|

Commercial Relationships Disclosure (Abstract): Mashael Al-Namaeh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A key manifestation of Parkinson's disease (PD) is visual impairment. Cognitive impairment has been found to commonly overlap with convergence insufficiency (CI) in PD and is associated with significantly greater near point convergence (NPC) distance. Difficulty reading and diplopia were the most often reported symptoms of CI in PD. The prevalence of CI is greater among patients with PD. No meta-analysis examined this subject; therefore, our aim was to assess the relationship between PD and CI.

Methods: This meta-analysis study has followed the standards and guidelines of Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA). PubMed search was used with the terms "Parkinson's Disease" AND "Convergence insufficiency ". The results showed 1,563 articles, 11 articles met the inclusion criteria, 8 articles were used for the CI screening survey as the primary outcome and 3 articles were used for the NPC distance (cm) as the secondary outcome. The random effects meta-analysis was used. Heterogeneity was evaluated with I^2 statistics, publication bias with Funnel plot, Egger's and Begg's tests.

Results: The database search resulted in 8 studies with a total of 1,520 PD patients and 905 control subjects for the primary outcome and a total of 103 PD patients and 52 control subjects for the secondary outcome. Relative to the control group, the PD group has high odds ratio (OR(s)) of CI clinical diagnosis (ORs = 3.67, 95%CI [2.71, 4.95]; $P < 0.00001$). In addition, PD group showed a statistically significant increase in NPC distance using mean difference (MD) compared to the control group (MD = 4.97; 95%CI [1.33, 8.61]; $P = 0.007$). No evidence of publication bias was detected.

Conclusions: These data suggest that the PD group increased the likelihood of CI visual symptoms and increased NPC distance compared to control group. These findings indicate that regular eye exam is very important for patients with PD. In addition, patients with objective findings of CI, if symptomatic or not, may have a high risk of cognitive impairment. Eye clinicians should have a high assumption for cognitive impairment in CI patients.

CONTROL ID: 3493789

SUBMITTER (NAME ONLY): Vikas Khetan

TITLE: Involvement of lens in Retinoblastoma (RB)- Challenging the concept of lens immunity and proposal for lens features to be defined in classification systems

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Khetan, P. Maitra, Ocular Oncology and Vitreoretina, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|

Commercial Relationships Disclosure (Abstract): Vikas Khetan: Commercial Relationship: Code N (No Commercial Relationship) | Puja Maitra: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In Retinoblastoma (RB) the crystalline lens is believed to have hypothetic “tumorous immunity” and is usually unaffected and clear. We aim to highlight four cases of RB with lens involvement with a histopathological (HPE) correlation of the same after enucleation. We believe that lens features should be defined in classification systems of RB.

Methods: We report 4 eyes with lens involvement with RB at presentation in 4 children aged between 2 months to 2 years. 3 out of 4 children had bilateral RB. 3 out of 4 eyes had subluxation of clear lens out of which one eye also had tumor infiltrating into the lens. The mechanism of subluxation was hypothesized as secondary to ciliary staphyloma possible due to zonular stretching in one eye and zonular degradation secondary to orbital cellulitis in another, both confirmed on HPE. The subluxation was noted clinically in all 3 eyes and confirmed on imaging and HPE. 1 out of 4 cases had absent lens, also confirmed on imaging and HPE. 3 out of 4 cases received systemic chemotherapy before enucleation. All 4 eyes were ultimately diagnosed to have advanced RB, (3 out of 4 had group E tumors as per IIRC, and 1 eye had orbital RB) all requiring enucleation ultimately.

Results: 4 of 4 eyes needed Enucleation.

Unexplained anterior segment findings should raise suspicion and mass lesions must be ruled out before any planned interventions. RB presenting with a subluxated or absent lens is scarcely reported and most often the mechanisms are not clearly understood. Lens involvement may be a consequence of the clinical course of the tumor, possibly a surrogate marker suggesting advanced nature or chronicity. Visual rehabilitation is impossible in such eyes with active tumor and eye salvage is seldom possible due to advanced anatomical damage.

Conclusions: In our experience as these eyes ultimately require enucleation, we propose that lens features should be defined and considered in classification systems of retinoblastoma and lens subluxation and infiltration could be considered a feature of Group E.

CONTROL ID: 3494291

SUBMITTER (NAME ONLY): William Hogue

TITLE:

Axial length is associated with individual differences in ON- and OFF- pattern detection

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Hogue, C.P. Taylor, Vision Science, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): William Hogue: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Taylor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The ON and OFF visual pathways have different spatial tuning and cortical connectivity. The ON and OFF pathways may play a role in emmetropization. Currently, the literature on the mechanisms that control choroidal thickness and emmetropization is, at best, immature. We measured individual differences in two detection tasks to explore the role contrast polarity plays in emmetropization.

Methods:

39 observers completed four one-hour sessions of psychophysical testing. We screened for a history of ocular disease, refractive surgery, or the use of ortho-k lenses. Refractive error was measured with a wavefront aberrometer and axial-length with an ocular biometer. Psychophysical detection and identification thresholds for two tasks were measured. The stimuli were Sloan Letters and Difference of Gaussians (DoG). The contrast polarity of the stimuli was either positive (ON) or negative (OFF). In the identification task, contrast sensitivity for the ten Sloan letters was measured. The detection task measured contrast sensitivity via a two-interval forced-choice task with a DoG stimulus as the target and a blank foil interval. Sessions consisted of either positive ON- or negative OFF- contrast on a grey background and never both. The two tasks were interleaved randomly during a single session of sub-blocks of 150 trials.

Results:

We found the ratio of OFF/ON sensitivities defined as $ONOFF_{index} = (con - coff) / (con + coff)$ increased as axial-length increased with a Difference of Gaussian (DoG) target ($r=0.41$, $P<0.01$). The lack of effect for letters is curious because we did not replicate a previous study that found an effect in an ON/OFF letter identification task ($r=-0.017$, $P=0.92$). Sensitivity decreased with axial length for all conditions. DoG ON ($r=0.33$, $P<0.05$), DoG OFF ($r=0.48$, $P<0.001$), Letters ON ($r=0.47$, $P<0.01$), Letters OFF ($r=0.41$, $P<0.01$).

Conclusions:

Natural scenes contain more information in the OFF than ON visual channels. The altered balance of OFF/ON thresholds for DoG provides a conceptual link between altered retinal ganglion cell sensitivity and the evidence that time spent outdoors slows the progression or onset of myopia.

CONTROL ID: 3494908

SUBMITTER (NAME ONLY): Sarah Marie

TITLE: Determination of Quantitative Light Discomfort Thresholds in a Large Healthy Human Sample

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Marie, R&P Light & Life Science, Essilor International, Paris, Île-de-France, FRANCE|R. Montés-Micó, A. Cerviño, N. Martínez-Albert, J. García-Marqués, Department of Optics and Optometry and Vision Sciences, Optometry Research Group (GIO), University of Valencia, Valencia, SPAIN|

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ABSTRACT BODY:

Purpose: To determine light discomfort thresholds quantitatively using a new clinical device on a large sample of healthy adult humans, reliability and relationship with biometric and optical parameters.

Methods: A total of 489 healthy subjects with ages ranging from 20 to 70 years (241 men, 248 women), were examined with the LUMIZ™ 100 (Essilor Intl., France), a new handheld, portable, clinical device for the determination of light discomfort thresholds. Instructions were given by means of a recorded video to ensure homogeneity in the explanations. A mock-up test was carried out prior to measurement. Two thresholds, “just perceptible” and “really disturbing” discomfort, were determined for three light presentation protocols (Continuous warm, Continuous cold, and flashing warm), using two different LED sources (Warm:4000°K, and Cold:6500°K). Iris color and skin pigmentation level were classified, and subjective manifest refraction was also determined.

Results: Discomfort thresholds are well distributed across the range of intensities. Intrasection intraclass correlation coefficients were higher than 0.80 for all thresholds. First measurement was representative of the median of three. There was no effect of age on discomfort thresholds ($r^2 < 0.1$, $p = 0.30$), nor affected reliability of the measurements ($p = 0.368$). For the considered population, women have lower discomfort thresholds than men ($p < 0.001$). Subjects with high self-perceived light sensitivity tend to have lower discomfort threshold and vice versa ($p < 0.001$). No effect on discomfort thresholds was found for ametropia ($p = 0.45$), nor was any link with pupil size, axial length or wavefront aberrations in this sample. There was no significant representation of iris color or skin tone to allow for statistical significance of the effect, although a trend for green eyes to have lower thresholds was observed.

Conclusions: The new device is reliable for the clinical determination of light discomfort thresholds on healthy subjects. Nor age, refractive error, or biometric parameters seem to have an effect on discomfort thresholds. Women tend to have lower thresholds than men. The new device is useful for the quantitative determination of light discomfort in healthy subjects. Applications in diseased eyes and filter treatments are to be explored.

CONTROL ID: 3495127

SUBMITTER (NAME ONLY): Benjamin Meyer

TITLE: Significance of Incidental Imaging Signs of Intracranial Hypertension with Corresponding Fundus Photography: A Prospective Study

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.I. Meyer, B.S. Chen, B.B. Bruce, N.J. Newman, V. Biousse, Neuro-Ophthalmology, Emory Eye Center, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|A.M. Saindane, Radiology and Imaging Sciences, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: MRI signs suggesting intracranial hypertension are common in patients with idiopathic intracranial hypertension (IIH), but are also incidentally detected in asymptomatic patients and those with primary headache syndromes, prompting neuro-ophthalmology consultations and investigations. We aimed to prospectively identify the prevalence and significance of MRI signs of intracranial hypertension (MRI-IH) in patients imaged for any clinical indication.

Methods: Prospective study evaluating 296 consecutive patients undergoing outpatient brain MRI and non-mydratic fundus photography immediately following MRI. Photographs were reviewed for papilledema and MRIs read for MRI-IH. Univariate analysis with Fisher's exact test or t-test was performed.

Results: Indications for MRI were brain neoplasm (27.7%), multiple sclerosis (MS)/MS-mimics (18.6%), seizure (17.9%), headache (8.8%), and other non-headache neurologic symptoms (19.6%). Four patients (1.4%) had known IIH. MRI-IH (N, %) included: empty sella (98, 33.1%); enlarged Meckel cave (47, 15.9%); meningocele/cephalocele (4, 1.4%); transverse venous sinus stenosis (TSS) (7/198, 3.6%); cerebellar tonsillar ectopia (4, 1.4%); scleral flattening (2, 0.7%); increased perioptic CSF (32, 10.8%); and increased optic nerve tortuosity (23, 7.8%). Overall, 51% patients exhibited no MRI-IH, 32.8% one sign, 10.8% two signs, 3.7% three signs, and 1.7% had \geq four signs. Five patients (1.7%) had definite papilledema on fundus photographs; two (0.7%) had questionable papilledema. Patients with definite papilledema had significantly increased average BMI (37.6 vs 27.5 kg/m²; P=0.038), history of IIH (40% vs 1%; P=0.001), increased optic nerve tortuosity (60% vs 7%; P=0.004), TSS (50% vs 3%; P=0.006), and \geq four MRI-IH (40% vs 1%; P=0.002), compared to patients without papilledema. Other MRI-IH were not significant, nor were having one, two, or three signs.

Conclusions: MRI-IH were encountered in almost half the patients in this prospective study of outpatients undergoing brain MRI for various clinical indications. However, definite papilledema was only detected in 1.7% patients, questioning the need to perform systematic investigations for patients with incidentally detected MRI-IH.

CONTROL ID: 3495405

SUBMITTER (NAME ONLY): Clarissa Ng Yin Ling

TITLE: Obesity and Risk of Age-Related Eye Diseases: A Systematic Review of Prospective Population-based Studies

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ng Yin Ling, King's College London School of Medical Education, London, London, UNITED KINGDOM|S. Lim, National University Singapore Saw Swee Hock School of Public Health, Singapore, SINGAPORE|J. Jonas, Department of Ophthalmology, Heidelberg University, Heidelberg, Mannheim, GERMANY|C. Sabanayagam, Singapore Eye Research Institute, Singapore, SINGAPORE|C. Sabanayagam, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Obesity and visual impairment are public health challenges worldwide. The relationship between obesity and age-related eye diseases including cataract, glaucoma, age-related macular degeneration (AMD) and diabetic retinopathy (DR) have remained elusive. This report summarizes evidence from prospective studies evaluating the associations between obesity and age-related eye diseases.

Methods: We conducted a systematic review of three electronic databases for longitudinal population-based studies on adults which described associations between measures of obesity including body mass index (BMI), waist-circumference (WC), and waist-to-hip ratio (WHR), and age-related eye diseases. Study quality was assessed using an adapted Newcastle-Ottawa Scale. We compared results between Western, non-Western and specifically Asian populations.

Results: Our search yielded 1731 articles, of which 14, 10, 16 and 8 articles met our eligibility criteria for cataract, glaucoma, AMD and DR, respectively. Obesity was assessed by BMI (n=46), WC (n=8) and WHR (n=7). BMI-defined obesity was positively associated with incident cataract, incident any AMD and incident DR in Western populations, but in Asian populations associations for incident any AMD were not significant and associations for incident DR were inverse. WC-defined obesity was associated with incident glaucoma in non-Western populations. WHR-defined obesity but not BMI-defined obesity was associated with the incidence or progression of AMD in two Western studies.

Conclusions: Overall, we found strong evidence supporting associations between obesity and age-related eye diseases, although the results vary depending on the population studied and measure of obesity used. Further research on obesity, weight loss and physical activity as risk factors for age-related eye diseases is warranted to support clinical and public health recommendations.

CONTROL ID: 3496008

SUBMITTER (NAME ONLY): Eu Ddeum (Philip) Chung

TITLE: KNP-301, a dual inhibitor of the complement pathway and angiogenesis, effectively suppresses angiogenesis and atrophy

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Chung, D. Kim, S. Ryu, J. Chang, B. Lee, Kanaph Therapeutics Inc., Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Patients with neovascular age-related macular degeneration (nAMD) are currently treated with anti-vascular endothelial growth factor (anti-VEGF). However, the benefit of the anti-VEGF treatment is diminished in the long-term due to appearance of atrophy. We tested whether KNP-301, a dual inhibitor of C3b of the complement system and VEGF, could reduce the formation of choroidal neovascularization (CNV) and retinal degeneration using mouse models of nAMD and dry-AMD.

Methods: The binding kinetics of KNP-301 with C3b and VEGF165 were tested using surface plasmon resonance assay. The activation of the alternative complement pathway and the classical complement pathway was evaluated with human C1q-depleted serum and human factor B-depleted serum, respectively. Three laser lesions were executed on the right eye of C57BL/6JRj mice to induce CNV. Test compounds were administrated by intravitreal (IVT) injection (2 µl/eye) immediately after lasering. The CNV lesions were monitored using fluorescein angiography and spectral domain optical coherence tomography. NaIO₃ was injected intravenously to induce retinal degeneration in C57BL/6 mice. Test compounds were administrated by IVT injection (1.5 µl/eye). The outer nuclear layer (ONL) thickness was determined by immunofluorescent staining. The ocular pharmacokinetics (PK) of KNP-301 was determined in vitreous humor of New Zealand White Rabbits.

Results: KNP-301 demonstrated binding to both C3b (KD = 4.34 nM) and human VEGF165 (KD = 6.28 pM). KNP-301 selectively inhibited the alternative pathway in a dose-dependent manner (EC50 = 330 nM), whereas the classical pathway was not inhibited. Mice treated with either a mouse surrogate of KNP-301 (n=14) or aflibercept (n=10) had a significantly lower grading of CNV leak compared to vehicle treatment group (n=13; Fisher's exact test, p≤0.0045 for all). Moreover, mice treated with the mouse surrogate of KNP-301 (n=10) showed reduced ONL thickness compared to mice treated with vehicle control (n=10). Lastly, the half-life of KNP-301 in vitreous humor was 2.5 fold greater than aflibercept.

Conclusions: Our study showed that KNP-301 binds to C3b and VEGF, and selectively inhibits the alternative pathway of the complement system. Moreover, the mouse surrogate of KNP-301 significantly inhibits the formation of CNV and prevents retinal degeneration in mouse models of n-AMD and dry-AMD.

CONTROL ID: 3496330

SUBMITTER (NAME ONLY): Sila Bal

TITLE: Risk of Acquired Retinal Detachment in Children with Ocular Coloboma

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bal, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|S. Bal, M. Mills, L. Tomlinson, E. Meer, G. Binenbaum, Ophthalmology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|M. Mills, E. Meer, G. Ying, G. Binenbaum, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optic nerve (ONC) and chorioretinal (CRC) coloboma are associated with acquired retinal detachment. The risk during early childhood remains unclear. We determined the incidence and age at onset during childhood of acquired retinal detachment in children with coloboma.

Methods: Retrospective cohort study of children with ONC and/or CRC, examined prior to age 18 years between 2009 and 2020 at a pediatric ophthalmology outpatient clinic. Eyes with presumed congenital retinal detachment or retinal dysplasia were excluded. Primary outcomes were incidence and age at diagnosis of acquired retinal detachment.

Results: We studied 387 eyes of 258 children, median age 6.59 years (range 0.04-18 years). Colobomas were bilateral in 129 (50%) children; 288 (74.4%) eyes had ONC, 236 (61%) eyes had CRC, and 137 (35.4%) eyes had both. Among CRC, the macula and periphery were involved in 141 eyes (59.7%) and periphery only in 90 eyes (38.1%). Two eyes of two children had acquired retinal detachment at ages 7 and 14 years (0.52% per eye, 95% CI: 0.06%-1.85%), of which one eye had both ONC and CRC and both eyes had CRC involving the macula and periphery.

Conclusions: Acquired retinal detachment associated with coloboma occurs during childhood but the risk is lower than previously reported. Periodic screening fundus examinations should be performed. The utility of prophylactic laser retinopexy during childhood in eyes with ONC/CRC requires further investigation.

CONTROL ID: 3497161

SUBMITTER (NAME ONLY): Brian Nguyen

TITLE: Beyond BPES: A case series of non-BPES blepharophimosis syndromes

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this retrospective case series was to determine the incidence of patients and describe cases with different diagnoses than Blepharophimosis-Ptoxis-Epicanthus Inversus Syndrome (BPES) initially presenting with eyelid manifestations of blepharophimosis, suspected to have BPES.

Methods: A retrospective review of consecutive cases of blepharophimosis at the Children's Hospital of Philadelphia was performed over a 12 year period (2009-2020). Genetic diagnosis was considered for the differential diagnosis of BPES: Dubowitz, Schwartz-Jampel, Marden-Walker, Ohdo Blepharophimosis, Malpuech-Michels-Mingarelli-Carnevale, Smith-Lemli-Opitz, and Koolen de Vries syndromes. (Table 1) Furthermore, any genetic mutation that included FOXL2 but was associated with adjacent mutations were included.

Results: 137 consecutive patients with blepharophimosis were identified. 9 patients (7%) were diagnosed with systemic or other syndromic disorders other than BPES. Alternative diagnoses included Dubowitz syndrome (n=2), Ohdo syndrome (n=1), 22q11.2 duplication (n=1), and 3q22 deletion (n=2) which represented FOXL2 mutations with adjacent mutations. Three patients had multiple systemic abnormalities without a definite genetic diagnosis. Genetic evaluation was critical in all cases and allowed the patients to benefit from multi-disciplinary care such as immunology, oncology, endocrinology, gastroenterology, and cardiology. The clinical and genetic characteristics reflected among these 9 patients are in Table 2.

Conclusions: Although blepharophimosis is most commonly associated with BPES, genetic investigation into other alternative syndromes is often warranted in the presence of other systemic disorders to provide comprehensive patient care to this unique pediatric population.

CONTROL ID: 3497623

SUBMITTER (NAME ONLY): Sohee Jeon

TITLE: Risk factors for onset or progression of posterior vitreous detachment at the vitreomacular interface after cataract surgery

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Jeon, Keye Eye Center, KOREA (THE REPUBLIC OF)

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ABSTRACT BODY:

Purpose: To study the incidence and the risk factors for onset or progression of posterior vitreous detachment (PVD) at the vitreomacular interface (VMI) after cataract surgery.

Methods: Patients with a history of phacoemulsification from April 2018 to April 2019 at the KEYE Eye Center, Seoul, Korea, and postoperative monitoring for more than 2 months were retrospectively reviewed. Cox proportional hazard ratios for the onset or development of PVD after cataract surgery in the presence of selected risk factors and demographic data were calculated. To evaluate the ocular risk factors, various ocular metrics including spherical equivalent (SE), axial length (AXL), anterior chamber depth, lens thickness, central subfield thickness, PVD status at macular and optic nerve head (ONH), peripapillary retinal nerve fiber layer thickness, and ONH parameters from optical coherent tomography (OCT) scans were used for the analysis.

Results: Among 988 eyes without PVD at baseline, 174 eyes (17.6%) showed changes in the VMI. Univariate analysis showed that age, SE, AXL, PVD status at macular and ONH, and average and vertical cup-disc ratios (CDRs) were significantly associated with the PVD onset or development ($P = .046$, $P = .004$, $P = .040$, $P < .001$, $P < .001$, $P = .008$, and $P = .042$, respectively). In a multivariate analysis, PVD status at macular and ONH, and smaller CDR were associated with PVD onset or progression after cataract surgery after adjustment of age, SE, and AXL ($P < .001$, $P < .001$ and $P = .005$, respectively).

Conclusions: The risk of PVD onset or progression was dependent on PVD status and the CDR detected on OCT scans, not on age or AXL, in a large patient cohort. Patients who show risk factors on OCT should be monitored carefully during the postoperative period.

CONTROL ID: 3497829

SUBMITTER (NAME ONLY): Caberry Yu

TITLE: Pain control for corneal abrasions: a meta-analysis of six topical interventions

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Highly variable practice patterns exist with regards to management of pain and discomfort from corneal abrasions. This meta-analysis was conducted to evaluate the efficacy and safety of six topical pain therapies: topical anesthetics, non-steroidal anti-inflammatory drugs (NSAIDs), cycloplegics, steroids, pressure patching, and bandage contact lens (BCL).

Methods: The protocol followed PRISMA guidelines and was published on PROSPERO. MEDLINE, EMBASE, CENTRAL, and Web of Science were searched to December 2020. Primary studies comparing topical pain therapies to other therapy or control were included. Primary outcomes included percentage of abrasions healed and pain control at 24, 48, and 72 hours. Secondary outcomes included use of oral analgesia, and incidence of complications. Risk of bias was assessed using the Cochrane guidelines and the MINORS criteria. Quality of evidence for estimates was assessed by the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) tool. Subgroup analysis was conducted for heterogeneity.

Results: Overall, 31 RCTs and 2 cohort studies (4,167 patients) were analyzed. Risk of bias was low for most studies. Topical NSAIDs showed significantly reduced pain scores at 24 hours (RR -0.69, 95% CI [-0.98, -0.41]) and 48 hours (RR -0.56, 95% CI [-1.02, -0.10]), and lower oral analgesia use (RR 0.47, 95% CI [0.33, 0.66]) compared to control (Figure 1). Topical anesthetics, cycloplegics, patching, and BCL did not result in significant reduction in pain scores or oral analgesia use, although there were limited studies of high methodological quality. No studies examined topical steroids. No intervention resulted in significant healing delays or higher complication rates compared to controls. GRADE certainty of evidence ranged from low to moderate for outcomes (Figure 2).

Conclusions: Available evidence suggests that topical NSAIDs significantly reduce pain from corneal abrasions in the first 48 hours and led to lower oral analgesia use without increased rates of complications or delays in healing. There is limited evidence to support or refute the efficacy and safety of other therapies.

CONTROL ID: 3497995

SUBMITTER (NAME ONLY): Joshua Canavan

TITLE: Corneal and Scleral Biomechanical Differences Among Individuals of Sub-Saharan African, European, and Mixed-Race Descent

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The prevalence and severity of primary open-angle glaucoma is higher and worse in Black than in Caucasian populations. The mechanism for this disparity remains unknown, but differences in ocular biomechanics between the groups may contribute. We investigated corneal and scleral stiffness responses in the eyes of healthy individuals with Sub-Saharan African (SSA), European (EUR), and mixed-race (MIX) ancestry to determine baseline biomechanical data.

Methods: Adult subjects without a history of ocular disease were recruited and categorized into SSA (n = 40 eyes, mean age \pm SD = 37.3 \pm 13.1 years, 65.00% female), EUR (n = 84 eyes, age = 34.9 \pm 14.6 years, 59.52% female), and MIX (n = 36 eyes, age = 31.7 \pm 13.4 years, 61.11% female) cohorts based on self-reporting of ancestry. For each subject, corneal hysteresis (CH) was measured using the Ocular Response Analyzer. The CorVis ST was used to measure central corneal thickness (CCT) and biomechanically corrected intraocular pressure (bIOP), as well as to derive in vivo corneal (SP-A1) and scleral (SP-HC) stiffness parameters. Additionally, intraocular pressure (IOP) was measured using Goldmann applanation tonometry (GAT) and Pascal dynamic contour tonometry (DCT). For each device, three reliable measurements were taken and averaged in both eyes. ANCOVA was used for statistical analysis with bIOP and CCT as covariates and a significance threshold of $p < 0.05$.

Results: There was no significant difference ($p > 0.05$) between cohorts for measurements of CH, SP-A1, GAT IOP, DCT IOP, bIOP, or CCT. Mean SP-HC \pm SD was 14.37 \pm 4.07 mmHg/mm in the SSA cohort, 13.86 \pm 2.73 mmHg/mm in the EUR cohort, and 14.72 \pm 3.18 mmHg/mm in the MIX cohort. When adjusted for CCT and the greater IOP in the MIX cohort, mean SP-HC was significantly higher in the SSA cohort compared to both the EUR ($p = 0.0019$) and MIX ($p = 0.0404$) cohorts.

Conclusions: Our results suggest there is greater scleral stiffness in individuals of SSA descent than in individuals of EUR and MIX descent, independent of other ocular biomechanical parameters. It is possible that higher scleral stiffness in the SSA cohort could contribute to the pathophysiology of primary open-angle glaucoma. The ramifications of this finding warrant further investigation.

CONTROL ID: 3498025

SUBMITTER (NAME ONLY): Dominique Geoffrion

TITLE: Tear film cytokine profiles of Boston keratoprosthesis patients with and without glaucoma

SESSION TITLE: Corneal transplantation and surgery

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Glaucoma is the most important threat to vision after Boston keratoprosthesis (KPro) surgery. Although inflammatory cytokines are involved in glaucoma pathogenesis, their role in KPro-associated glaucoma is unknown. We performed a cross-sectional study to determine cytokine levels in the tear film of Boston keratoprosthesis (KPro) patients with and without glaucoma, relative to controls, and correlate levels with clinical parameters.

Methods: The study enrolled 58 eyes from 58 patients: 48 KPro eyes (mean age 67.2 years), including 41 with glaucoma and 7 without, and 10 healthy controls (mean age 68.0 years). Tears were collected by micropipette after saline instillation. 27 cytokines were measured by multiplex bead immunoassay. Clinical parameters assessed in all KPro eyes included intraocular pressure (IOP), cup-to-disk ratio (CDR), visual acuity, retinal nerve fiber layer, topical medications, and angle closure. Cytokine level differences between groups were analyzed by non-parametric tests, and correlations with clinical parameters by Spearman's test.

Results: Mean time from KPro to tear sampling was 7.9 ± 3.5 years. Levels of TNF- α , IL-1 β , FGF-2, IFN- γ were significantly higher in KPro with glaucoma compared to KPro without ($p=0.020$; 0.008 ; 0.043 ; 0.018 , respectively). Both KPro groups had similar characteristics, diagnoses, and topical antibiotic/steroid regimen. Levels of IL-1Ra, IL-15, VEGF, RANTES were significantly higher in KPro with glaucoma compared to controls ($p<0.001$; 0.034 ; <0.001 ; 0.001 , respectively). IL-1 β and IFN- γ levels were positively correlated with CDR ($r=0.309$, $p=0.039$ and $r=0.452$, $p=0.006$, respectively) and IOP ($r=0.292$, $p=0.047$ and $r=0.368$, $p=0.023$, respectively). TNF- α and FGF-2 levels were positively correlated with CDR ($r=0.348$, $p=0.022$ and $r=0.344$, $p=0.021$, respectively).

Conclusions: TNF- α , IL-1 β , FGF-2, IFN- γ are elevated in tear fluid of KPro patients with glaucoma and correlate with CDR and IOP. These results show, for the first time in humans, concordance with reported elevations of TNF- α and IL-1 β in murine KPro model. Ocular surface inflammation may reflect inflammatory processes of KPro glaucoma.

CONTROL ID: 3498105

SUBMITTER (NAME ONLY): Gemma Aragones

TITLE: Glyoxalase System as a Therapeutic Target against retinal diseases?

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Advanced glycation end products (AGEs) are toxic compounds resulting from the non-enzymatic modification of biomolecules by sugars or their metabolites. AGEs are pathologically linked to AMD and diabetic retinopathy and anti-AGEs detoxifying systems are proposed as therapeutic targets to fight pathological dysfunction associated with AGE accumulation. The primary mechanism for detoxifying the reactive intermediates of glycation is the glyoxalase system, the limiting reaction of which is the enzyme glyoxalase 1 (GLO1). Information about the glyoxalase system in ocular tissues is limited.

In this study we evaluate the role of glyoxalase system in retinal tissues and we hypothesize that high level of glyoxalase activity prevents AGE accumulation under non-stressed conditions, and thereby protects against toxicity derived from glycative stress.

Methods: We dissected retina, RPE/choroid and lens along with other non-ocular tissues from 2 month-old wild type C57BL/6J mice. We quantified the GLO1 activity in cytosolic extracts of tissues and carried out a comparative analysis. GLO1 activity was determined spectrophotometrically as the initial rate of formation of S-D-lactoylglutathione. As a positive control, a comparative analysis was also carried out in ocular tissues from transgenic mice overexpressing Glo1 on C57BL/6J (B6) background. Western blotting and immunohistochemistry, using antibodies that specifically recognize GLO1, were performed to quantify protein levels and location of GLO1 in retinal tissue.

Results: Glyoxalase activity was detected in all tissues. The relative order of GLO1 specific activity was retina> liver> kidney> brain> heart> RPE/choroid >lens. Glyoxalase activity is clearly tissue-dependent. When compared to non-ocular tissues, the retinal rate of detoxification was about 2-fold, 8.5-fold, 3.5-fold and 4.5-fold greater than liver, heart, kidney and brain, respectively. Regarding ocular tissues, neuroretinal activity was about 9-fold and 13-fold greater than in the RPE/choroid and lens, respectively. Biochemical and morphological examination of retinal tissues corroborate the highest level of GLO1 expression in neuroretina. GLO1 activity in transgenic mice overexpressing Glo1 was about 3.7-fold and 2.2-fold in retina and RPE/choroid, respectively.

Conclusions: The neuroretina has the highest level of retinal GLO1 activity, suggesting an important protective role against AGEs-derived damage in retina.

CONTROL ID: 3498684

SUBMITTER (NAME ONLY): Patrick Yu-Wai-Man

TITLE: Evaluation of the efficacy of rAAV2/2-ND4 gene therapy for Leber hereditary optic neuropathy compared with the natural history

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Two Phase 3 multicenter clinical trials, RESCUE (NCT02652767) and REVERSE (NCT02652780), showed unexpected sustained bilateral improvement of best-corrected visual acuity (BCVA) following unilateral injection of rAAV2/2-ND4 gene therapy in patients with Leber hereditary optic neuropathy (LHON). In this study, we compared the treatment effect of rAAV2/2-ND4 with an external control group of untreated patients.

Methods: The treated population consisted of 76 ND4-LHON subjects injected unilaterally with rAAV2/2-ND4 in the RESCUE and REVERSE trials, of which 62 subjects enrolled in a long-term follow-up study (NCT03406104). The untreated population included a total of 208 subjects: 23 ND4-LHON subjects enrolled in the REALITY LHON Registry (NCT03295071) and 185 ND4-LHON subjects with individual patient-level data collected from 10 natural history studies in the literature. To allow for comparison with the treated population, the untreated population included only patients who were at least 15 years old at onset of vision loss. A Locally Estimated Scatterplot Smoothing (LOESS), non-parametric, local regression model was used to represent the evolution of BCVA over time. Comparison of BCVA between treated and untreated patients was performed at 12, 18, 24, 36 and 48 months after onset of vision loss.

Results: BCVA evolution in the treated patients showed gradual, progressive, and sustained improvement from Month 12 to the last available observation (on average 51.5 months), whereas no recovery was observed in the untreated patients. At Month 48, mean BCVA was 1.26 LogMAR for treated patients and 1.59 LogMAR for untreated patients, which is a difference of 0.33 LogMAR or 16.5 ETDRS letters equivalent ($p < 0.01$ for Kruskal-Wallis and repeated

measures tests).

Conclusions: This indirect comparison of 76 treated patients with an external control group of 208 untreated patients showed a clinically meaningful effect of gene therapy on visual outcomes in ND4-LHON patients.

CONTROL ID: 3499123

SUBMITTER (NAME ONLY): Austin DeGroff

TITLE: Theoretical Analysis of an Unknown Change in Corneal Refractive Index Following Corneal Cross-Linking Introduces Artifact in Optical Measurements of Central Corneal Thickness

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Central corneal thickness (CCT) measurements vary following corneal cross-linking (CXL), depending on the instruments used. We sought to explain this discrepancy by investigating the consequences of a proposed unexpected change in corneal refractive index (n_c) on Scheimpflug imaging and optical coherence tomography (OCT) measurements of CCT.

Methods: We developed two theoretical models to test the effect of a change in n_c on CCT. Our Scheimpflug model used existing equations that utilize a side viewing angle of an optical section of cornea illuminated by a central slit to predict CCT. Similarly, our OCT model used existing equations that describe optical path length (OPL) to predict CCT. Predicted CCT was calculated for a range of n_c values in both models. CCT measurement error was defined as the difference between the CCT measurement at the instrument-assumed index of 1.376 ($CCT_{1.376}$) and the predicted CCT at other indices (CCT_n). This error was plotted versus n_c to analyze the effect a change in n_c would have on predicted CCT for both models. To quantify the effect, we calculated the percent error in predicted CCT measurements and plotted it versus percent increase of n_c for both models.

Results: Our Scheimpflug model produced a positive association between predicted CCT and n_c . It also suggested a negative association between CCT measurement error ($CCT_{1.376} - CCT_n$) and n_c , which was quantified as a 0.822% reduction in CCT for every 1% increase in n_c (Fig1). In contrast, our OCT model produced a negative association between predicted CCT and n_c with a positive association between CCT measurement error and n_c , resulting in a 0.983% increase in CCT for every 1% increase in n_c (Fig2).

Conclusions: Our models suggest that an unknown increase in n_c results in underestimation of CCT from Scheimpflug-based devices, and, conversely, overestimation of CCT from OCT devices. These results suggest that a change in n_c after CXL introduces artifact in optical CCT measurement techniques. Our predictions are consistent with literature reports of CCT 2 weeks after CXL that show a 9.7 μ m increase when measured with OCT yet a 16 μ m decrease when measured by Scheimpflug (Antonios et al. 2016).

CONTROL ID: 3499932

SUBMITTER (NAME ONLY): Frederik Pedersen

TITLE: Diabetic retinopathy independently predicts five-year risk of Alzheimer's disease

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetes is a risk factor of Alzheimer's disease (AD), however data on the association between diabetic retinopathy (DR) and AD is limited. Both DR and AD may be viewed as progressive neurovascular disorders and we therefore hypothesized that DR predicts risk of AD. The present study investigates DR as a risk marker of 5-year incident AD.

Methods: We performed a register-based national cohort study, including 134,327 persons with diabetes above 60 years of age, who had attended DR screening, and 651,936 age- and gender-matched persons without diabetes. We investigated the association between DR and AD, both cross-sectionally and prospectively with data collected between 2013 and 2018. AD was defined according to the International Classification of Diseases codes G30* or F00*, as given by the Danish National Patient Registry. To evaluate the risk of present and incident AD among persons with DR, a multivariable logistic regression model and a Cox proportional hazard model were used, adjusting for age, gender, civil status, use of antihypertensive and lipid lowering medication, depression and an adjusted Charlson comorbidity index.

Results: At baseline, the prevalence of AD was 0.7% and 1.3% among persons with and without diabetes respectively. In a multivariable regression model, persons with diabetes were less likely to have AD at baseline (adjusted OR 0.63, 95% CI 0.58-0.67). During follow up, incident AD was registered in 1,454 (0.40%) and 6,796 (0.39%) persons with and without diabetes, respectively. Compared to persons without diabetes, persons with diabetes and no DR had a lower risk to develop AD (adjusted HR 0.88, 95% CI 0.82-0.94), while persons with diabetes and DR had higher risk of AD (adjusted HR 1.24, 95% CI 1.08-1.43). Still, when persons with diabetes without DR were used as references, a higher risk of incident AD was observed in persons with DR (adjusted HR 1.34, 95% CI 1.17-1.52).

Conclusions: In the present nationwide cohort study individuals with diabetes without DR were less likely to develop AD compared to persons without diabetes. However, individuals with DR had a 34% higher risk of incident AD compared to persons with diabetes without DR. Identification of risk or early detection of AD may provide the opportunity to treat modifiable risk factors to slow or prevent disease progression, or provide adequate help at an earlier stage.

CONTROL ID: 3500328

SUBMITTER (NAME ONLY): Kimberley Yu

TITLE: Systemic conditions associated with the severity of dry eye signs and symptoms in the Dry Eye Assessment and Management (DREAM) Study

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.Y. Bunya, M.G. Maguire, G. Ying, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|V.Y. Bunya, M.G. Maguire, G. Ying, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|K. Yu, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|P.A. Asbell, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Certain systemic conditions are reported to be risk factors for dry eye disease (DED), but their associations with DED severity are not well studied. We evaluated whether systemic conditions reported to be DED risk factors are associated with the severity of DED signs and symptoms via secondary analysis of data from the DREAM Study, a large-scale multi-center randomized clinical trial of patients with moderate-to-severe DED.

Methods: 535 patients with moderate-to-severe DED from 27 US centers reported their medical history at baseline. At baseline, 6 months, and 12 months, patients were assessed for DED symptoms using the Ocular Surface Disease Index (OSDI) and for six DED signs: tear break-up time, Schirmer's test with anesthesia, corneal staining, conjunctival staining, tear osmolality, and meibomian gland dysfunction. A composite signs severity score with range 0 to 1, with 1 being most severe, was calculated from the six DED signs. We analyzed the associations of systemic conditions reported as potential DED risk factors with the severity of DED signs and symptoms using generalized linear regression models adjusted by age, sex, race, and visit. To be included, conditions had at least 25 patients.

Results: The mean±SD age was 58±13.2 years, and 81% were female. More severe DED signs were significantly associated with Sjögren's syndrome (composite mean±SD: 0.52±0.17 with disease vs. 0.43±0.13 without disease, $p<0.001$), facial rosacea (0.47±0.13 vs. 0.43±0.13, $p=0.002$), rheumatoid arthritis (0.47±0.14 vs. 0.42±0.12, $p=0.002$), peripheral artery disease (0.50±0.14 vs. 0.43±0.13, $p<0.001$), and daily smoking history (0.45±0.13 vs. 0.43±0.13, $p=0.047$) (Table 1). Thyroid dysfunction, osteoarthritis, diabetes, irritable bowel syndrome, hypercholesterolemia, hypertension, and hypertriglyceridemia were not significantly associated with DED signs. No conditions were significantly associated with OSDI (Table 2).

Conclusions: In this large, well-characterized cohort of DED patients assessed under standardized procedures, the presence of certain systemic diseases and smoking were associated with more severe DED signs. The profile of significant DED signs varied by systemic condition, reflecting different DED etiologies. Understanding the systemic conditions and underlying etiologies that predispose some patients to more severe DED can improve management.

CONTROL ID: 3500650

SUBMITTER (NAME ONLY): Soshian Sarrafpour

TITLE: A Review of Commonly Accessed YouTube Videos about Glaucoma Treatments

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sarrafpour, J. Lee, J. Liu, C. Teng, Ophthalmology, Yale University, New Haven, Connecticut, UNITED STATES|B.K. Young, Ophthalmology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients are increasingly seeking information about treatment options for diseases including glaucoma from the internet. Sites like YouTube are easily accessible, though remain largely unregulated. This study evaluated the quality and accuracy of YouTube videos on glaucoma treatment.

Methods: A comprehensive search of “glaucoma” and “eye pressure” combined with “treatment” or “cure” was done on YouTube. To best approximate videos patients are viewing, we included only videos with at least 20,000 views and 15 views per day. Videos were excluded if they were not in English or about humans. Videos were categorized as educational, testimonial, or advert and reviewed by a two reviewers using a modified Currency, Relevance, Authority, Accuracy, and criteria. IRB exemption was obtained from Yale University.

Results: Overall, 61 videos met the inclusion criteria and 36 were excluded (30 because of language). Of those included, 80% were educational, 13% were testimonials, and 7% were adverts. The inter-rater reliability was acceptable after kappa values were calculated. 28% of videos were graded as misinformation or misleading. Average scores for each category are shown in Table 1. Audio and video quality scores were similar between categories. Higher accuracy and comprehensiveness scores were seen for educational videos. Although 64% of videos addressed the question of what is glaucoma, less than 50% discussed the course of untreated disease or the goals of treatment and only 8.2% discussed the risks of the proposed treatment options.

Conclusions: Patients are increasingly using YouTube for medical information. This study found that many videos lack useful information and some actually provide information that may be detrimental. Physicians should be aware of this risk and educate patients appropriately.

CONTROL ID: 3501039

SUBMITTER (NAME ONLY): Danny Diaz

TITLE: A Smartphone-Based Application to Support Recovery from Retinal Detachment Repair

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Diaz, A. Kunkler, L.J. Haddock, J. Townsend, H.W. Flynn, Bascom Palmer Eye Institute, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the design and development of a novel smartphone-based application aimed at helping patients maintain correct post-operative head positioning following retinal detachment repair.

Methods: An application to assist patients in recovering from retinal detachment repair was developed for the iPhone (Apple, Cupertino, CA) operating system (iOS). The application was written using the Swift programming language within the Xcode developer toolset and iOS software development kit (SDK). The Core Motion framework as part of the iOS SDK was utilized in order to capture motion- and environment-related data from onboard sensors (i.e gyroscope and accelerometer) on the iOS device. An algorithm was developed that processed and saved raw motion-related data including device orientation in three-dimensional space. The gyroscopic data is processed prior to use in order to remove bias from other factors, such as gravity. This user-initiated and refined data is then used to guide patients into the correct head position for optimal recovery.

Results: This user-friendly smartphone application consists of tutorial as well as physician and patient specific sections. Within the physician tab the provider is allowed to set the desired postoperative head position by moving the smartphone in three-dimensional space. The obtained gyroscopic positional data (primarily in the Z and X axes) is then parsed and translated into a series of stepwise instructions for patients to follow. By accurately following the outlined steps, patients can reliably be redirected into the desired position.

Conclusions: Correct post-operative positioning following retinal detachment repair facilitates recovery. The ability to precisely and accurately save the desired postoperative head position allows patients and providers previously unavailable control over recovery following retinal detachment repair. Smartphone-based mobile ophthalmic applications are increasingly being developed and, if evidence-based, are poised to offer tremendous clinical value in daily practice. Clinical studies aimed at validating the reliability and utility of this application in retinal detachment repair are underway.

CONTROL ID: 3501976

SUBMITTER (NAME ONLY): Lichun Zhong

TITLE: Electroretinography (ERG) Amplitude Changes in A Rat Retinal Ischemia Model

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zhong, Ocular, Toxikon Corporation, BEDFORD, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lichun Zhong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To demonstrate the functional changes of the retina monitored by ERG in a rat retinal ischemia model, which is for screening new therapies of retinal degeneration.

Methods: 12 Brown Norway male rats were randomized by body weight into 2 groups, 6 animals per group. After animals were sedated on Day 0, lateral conjunctival peritomy and disinsertion of the lateral rectus muscle were performed on the right eye per animal in Group 2 and the optic nerve sheath was exposed by blunt dissection and ligated with a 6-0 nylon suture until retinal vessel blood flow ceases (ischemia), as visualized by the operating microscope. After 60 minutes, the suture was removed. The same procedure was performed on the right eyes in Group 1 without ligation of the optic nerve sheath. The left eyes in all groups had no procedure and as the contralateral eyes. On Day 28, Dark and Light adapted ERG was performed on both eyes at all eyes at all animals.

Results: In the Group 2, the mean b-wave of 32.61 (μV) in the right eyes was reduced compared to 155.27(μV) in the left eyes in the Dark Rod Response; the mean b-wave of 45.57 (μV) in the right eyes was reduced compared to 238.80 (μV) in the left eyes in the Dark Maximal Response; the mean Peak-wave of 12.66 (μV) and the mean Trough-wave of -7.29 (μV) in the right eyes were reduced compared to 88.64 (μV) and -35.54 (μV), respectively, in the left eyes in the Dark Oscillatory Potential; the mean b-wave of 23.66 (μV) in the right eyes was reduced compared to 129.47 (μV) in the left eyes in the Light Single White Flash; and the mean Peak-wave of 4.82 (μV) in the right eyes was reduced compared to 22.70 (μV) in the left eyes in the Light 30 Hz Flicker. In the right eyes, the mean b-wave of 32.61 (μV) in Group 2 was reduced compared to 172.12 (μV) in Group 1 in the Dark Rod Response; the mean Peak-wave 12.66 (μV) in Group 2 was reduced compared to 62.09 (μV) in Group 1 in the Dark Oscillatory Potential; the mean b-wave of 23.66 (μV) in Group 2 was reduced compared to 92.43 (μV) in Group 1 in the Light Single White Flash; and the mean Peak-wave of 4.82 (μV) in Group 2 was reduced compared to 22.68 (μV) in Group 1 in the Light 30 Hz Flicker.

Conclusions: The ERG Amplitude Changes indicated that the ischemia procedure caused damage of the retinal cells and resulted in the retinal disfunction.

CONTROL ID: 3502370

SUBMITTER (NAME ONLY): Carolina Susanna

TITLE: Intraocular Pressure Peak Time During the Water Drinking Test and its Relationship with the Severity of Glaucoma Damage

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.N. Susanna, B. Susanna, Ophthalmology, Faculdade de Medicina do ABC, Santo Andre, SP, BRAZIL|F. Susanna, R. Susanna, Universidade de Sao Paulo Faculdade de Medicina, Sao Paulo, São Paulo, BRAZIL|G. De Moraes, Columbia University Vagelos College of Physicians and Surgeons, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the association between time of occurrence of intraocular pressure (IOP) peaks during the water drinking test (WDT) and the level of visual field damage in a cohort of primary open-angle glaucoma patients.

Methods: Medical records of 98 eyes from 49 consecutive primary open-angle glaucoma patients followed in a referral clinical practice were included in the study. The relationship between the time when IOP peaks occurred during the WDT and the visual field mean deviation (MD) assessed with 24-2 visual field was tested with mixed-effects linear regression models. The within-patient analysis was performed in patients with asymmetric visual fields (>3dB difference), using a binomial probability test.

Results: The time IOP peaks occurred was significantly associated with the MD value when adjusting for the number of medications in the cohort ($P<0.01$), but not between eyes of the same patient ($P=0.89$). The higher the IOP peaks and the later they occurred (interaction, IOP x Time) was also statistically significant both between ($P<0.01$) and within patients ($P<0.01$). No significant association was found between IOP peak values alone and visual field severity between patients ($P=0.07$), but it was significant within patients ($P<0.01$).

Conclusions: The time of occurrence of IOP peaks measured during the WDT was associated with glaucoma severity among treated primary open angle glaucoma patients. Both magnitude and time of peak should be taken into account when performing this stress test.

CONTROL ID: 3502973

SUBMITTER (NAME ONLY): Shinji Kakiyara

TITLE: Pathophysiological roles of adrenomedullin-2 in mouse model of ocular neovascularization

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kakiyara, M. Tanaka, K. Hirabayashi, A. Imai, Y. Toriyama, Y. Iesato, T. Murata, Ophthalmology, Shinshu University, Matsumoto, Nagano, JAPAN|S. Kakiyara, M. Tanaka, K. Hirabayashi, A. Imai, Y. Toriyama, Y. Iesato, T. Sakurai, A. Kamiyoshi, H. Kawate, Y. Ichikawa-Shindo, M. Tanaka, T. Shindo, Cardiovascular Research, Shinshu University, Matsumoto, Nagano, JAPAN|

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ABSTRACT BODY:

Purpose: Adrenomedullin-2 (AM2) (or intermedin), a member of the calcitonin gene-related peptide family, is a peptide which possesses a variety of physiological functions. Previously, we reported the therapeutic possibility of intravitreal injection of AM2 by using laser-induced choroidal neovascularization model (LI-CNV) and oxygen-induced retinopathy model (OIR) in mice (ARVO 2020). In the present study, we further investigated the pathophysiological roles of AM2 in ocular neovascularization by systemic administration of AM2 in mice and using AM2 knockout mice (AM2^{-/-}).

Methods: Wild-type mice (WT) were subjected to LI-CNV and the effect of systemic administration of AM2 using osmotic pump was investigated. Next, we established AM2 knockout mice (AM2^{-/-}) by genome editing. LI-CNV was compared between AM2^{-/-} and WT. To establish OIR, 7-day-old (P7) neonatal mice were subjected to hyperoxia (75% oxygen) for 5 days and returned to room air from P12 to 17. OIR was compared between AM2^{-/-} and WT.

Results: In LI-CNV, AM2-administration significantly reduced the CNV area and α SMA immunostaining-positive fibrosis area, and significantly suppressed the expression of genes encoding VEGF-A, VEGF-R2, CD68, CTGF, and p22phox in the choroid. Contrary to AM2-administration, CNV area and fibrosis area were increased in AM2^{-/-}. No apparent difference was observed in the retinal vessels of P7 and P12 between WT and AM2^{-/-}. There was no difference in the pathogenic angiogenic area of P17, however, the avascular area was reduced in AM2^{-/-} compared to WT.

Conclusions: AM2 is expected as a therapeutic target of ocular neovascular diseases. AM2 may affect both retinal and choroidal neovascularization, but the effect may be more pronounced in the choroidal neovascularization.

CONTROL ID: 3503518

SUBMITTER (NAME ONLY): Michael Dattilo

TITLE: Comparison of Optic Nerve Sheath Material Properties in male and female rhesus macaque

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Dattilo, C.R. Ethier, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|M. Dattilo, D. Brown, C.R. Ethier, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although optic nerve sheath (ONS) changes have been described in several ophthalmic disorders, such as idiopathic intracranial hypertension (IIH), ONS biomechanical properties remain poorly understood, particularly in humans. Recently, inverse finite element modeling (iFEM) of human ONS has estimated that males have stiffer ONSs than females. Although several prior studies have described ONS biomechanical properties, the effect of gender was not assessed in those studies.

Methods: In preparation for testing human tissue, the ONS from one male and one female rhesus macaque (rONS) was dissected from the ON and placed in 1X PBS. A cylindrical sample of rONS (1 mm diameter), obtained using a biopsy punch, was placed on a MicroTester platform (CellScale, Ontario, Canada) in a temperature-controlled fluid bath (PBS at 37°C). Samples were pre-loaded with a compressive tare load of 500 uN, allowed to equilibrate, and then subjected to a 3-step stress relaxation protocol (5-15% compressive strain). Data from each step were analyzed independently using poroelastic theory to determine rONS through-plane compressive modulus and in-plane tensile modulus.

Results: Female rONS compressive modulus was 4.7 kPa at 5% strain and increased to 8.8 kPa at 15% strain; tensile modulus was 35.1 kPa at 5% strain and increased to 116.9 kPa at 15% strain. Male rONS compressive modulus was 11.5 kPa at 5% strain and increased to 13.6 kPa at 15% strain; tensile modulus was 78.9 kPa at 5% strain and increased to 237.6 kPa at 15% strain.

Conclusions: Female rONS showed lower compressive and tensile moduli compared to male rONS, consistent with recently published iFEM data in humans. Although based on small sample numbers, this data suggests that human ONS biomechanical properties may also exhibit a gender difference. Further understanding of this difference may provide insights into the pathophysiology of IIH and may lead to the development of novel IIH treatments.

CONTROL ID: 3503547

SUBMITTER (NAME ONLY): Michael Belkin

TITLE: First-in-Human clinical study to establish the safety and efficacy of automated non-contact translimbal Direct Selective Laser Trabeculoplasty: 6-months results

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Belkin, S. Alon, A. Leshno, M. Goldenfeld, Golgdschleger Eye Institute, Tel Aviv University, Tel Hashomer, ISRAEL|Z. Sachs, M. Dobkin-Bekman, D. Lemann Blumenthal, Y. Solberg, Belkin Laser Ltd, Gan Yavne, ISRAEL|S. Alon, A. Leshno, Tel Aviv University, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: The purpose of this study was to preliminarily determine the safety and efficacy of Direct Selective Laser Trabeculoplasty (DSLTL) applied automatically without a gonioscope at various energies to the limbus overlying the trabecular meshwork in lowering intra ocular pressure (IOP) in open angle glaucoma (OAG).

Methods: Fifteen eyes of 15 patients (1 eye with exfoliative glaucoma, 4 with normal tension glaucoma and 10 with OAG) were treated by the DSLTL device. The mean age was 66.2 ± 8.2 years and 66% were males. Pre-medicated patients were washed out from their glaucoma medications for two weeks. The DSLTL treatment included 100-120 sequential non-contact 532 nm, Q-switched laser shots applied automatically directly on the limbus using image analysis of the limbus location and an eye tracking system monitoring both eye and laser beam location. Before each laser was spot was applied, multiple safety checks were automatically performed. Laser energies between 0.8 to 1.4 mJ/shot were used. The total duration of the irradiation was 2.3 seconds.

Results: In the six patients who were treated with 1.0 mJ/shot, the IOP was reduced from a baseline of 26.8 ± 2.0 mmHg by $26.6 \pm 15.1\%$, $18.8 \pm 11.5\%$ & $16.2 \pm 23.5\%$ at 1 month, 3 months & 6 months respectively.

In the six patients treated with 1.4 mJ/shot, the equivalent IOP percent reduction from a baseline of 26.7 ± 3.2 mmHg was $20.6 \pm 11.7\%$, $25.6 \pm 12.9\%$ & $26.9 \pm 7.1\%$ respectively.

One case of transient reduction in visual acuity and four cases of minor sub-conjunctival hemorrhages occurred. All side effects resolved spontaneously without sequelae within one day to one week. There were no serious adverse events.

Conclusions: This early experience shows the automated non-contact rapid DSLTL as a promising new modality in the treatment of POAG. Higher energy gave better-sustained results. Randomized Controlled studies with more patients are being conducted in order to validate these initial results in POAG patients

CONTROL ID: 3503928

SUBMITTER (NAME ONLY): Richard Hertle

TITLE: Demographic and Clinical Characteristics of 600 Children With Nystagmus

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.W. Hertle, B. McRitchie, A. Juric De Paula, I. Ricker, Ophthalmology, Akron Children's Hospital, Akron, Ohio, UNITED STATES|F. Evliyaoglu, Emory University, Atlanta, Georgia, UNITED STATES|B. McRitchie, The Ohio State University, Columbus, OH, US, academic, Columbus, Ohio, UNITED STATES|R.W. Hertle, Summa Health System, Akron, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the demographic and clinical characteristics of a large, international cohort of childhood patients with nystagmus.

Methods: This is a prospective, cohort analysis of demographic and clinical characteristics in 600 patients with nystagmus in infancy and childhood. Data collected included: 1) demography, 2) nystagmus type, 3) clinical characteristics, 4) associated ophthalmic conditions, 5) associated non-ophthalmic conditions, 6) special testing findings and 7) treatments.

Results: Between 2010-20 1,774 patients from 35 states and 26 countries with nystagmus were evaluated at Akron Children's Hospital. We are reporting on 600 infants and children (<18 years of age) whose data were collected prospectively as part of an IRB approved registry. Age ranged from birth to 18 yrs (mean 15.2 yrs), 58% were female, 35% were other than Caucasian, 75% had infantile nystagmus syndrome, 18% had acquired nystagmus, 6% had fusion maldevelopment nystagmus syndrome, 81% had strabismus, 52% had an anomalous head posture, 92% had a significant refractive error, 74% of patients had an associated ophthalmic abnormality (excluding ametropia), 63% had an associated systemic condition (most commonly albinism 35%). Targeted, genetic testing for inherited eye disease was positive in 76 of 156 (49%) tested patients. Special testing showed abnormalities of electrophysiological testing and/or imaging (other than eye movement recordings (EMR), in 67%. EMR's were an essential part of classifying nystagmus types and clearly differentiated infantile from acquired forms of nystagmus as well as characterizing (a) periodicity and gaze, monocular and vergence changes. Optical, medical or surgical treatments were performed together or in part in 95% of patients.

Conclusions: The prevalence of nystagmus in the general population is estimated to be 24/10,000 and in infancy 14/10,000. Although nystagmus can result from a variety of conditions, eye movement recordings provide a path towards accurate diagnosis and classification. There is a high prevalence of underlying genetic, ocular and/or systemic conditions requiring special testing as part of a diagnostic routine. Clinical treatments are available and of benefit to the vast majority of patients.

CONTROL ID: 3503989

SUBMITTER (NAME ONLY): Mohammad Yazdanie

TITLE: Pars Plana Ahmed Valve with Vitrectomy and Endolaser versus Anterior Chamber Ahmed Valve with Pan Retinal Photocoagulation: A Comparison of Two Treatments for Neovascular Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Yazdanie, S. Nimmagadda, H. Sadhra, B. Johnson, D. Harrington, S. Idrees, D.A. DiLoreto, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ahmed glaucoma valve (AGV) implant placement in conjunction with pan retinal photocoagulation (PRP) is frequently used in the management of neovascular glaucoma (NVG). AGV can be placed either in the pars plana (PP) or anterior chamber (AC). PRP can be performed in the office or intraoperatively with pars plana vitrectomy (PPV). This study compared the outcomes between PP AGV with PPV and endolaser (EL) versus AC AGV with in office PRP.

Methods: This is a retrospective study that investigated all AGV implants in patients with NVG at the University of Rochester Medical Center between 1/2010 and 1/2020. We performed a chart review to compare the outcomes between patients who underwent AGV in the setting of NVG: group 1 (PP AGV + PPV/EL) and group 2 (AC AGV + PRP). The outcome measures were intraocular pressure (IOP, mmHg) and visual acuity (VA, LogMar). The change in IOP and VA between these two groups, adjusted for preoperative lens status, was compared at 6-month and 1-year intervals using the analysis of variance.

Results: Both groups consisted of 15 subject eyes at baseline. Eleven (73%) eyes were pseudophakic in group 1 while 3 (20%) eyes were pseudophakic in group 2. The mean baseline IOP (38.6 ± 6.6 vs. 43.0 ± 8.9 mmHg) and VA (1.4 ± 0.7 vs. 1.3 ± 0.8 LogMar) were similar between groups 1 and 2. The adjusted change in IOP between groups 1 and 2 was not statistically significant at 6 months (-20.5 ± 6.1 vs. -25.6 ± 9.5 mmHg, $p = 0.11$) and 1 year (-23.8 ± 10.3 vs. -27.9 ± 11.0 mmHg, $p = 0.38$). The adjusted change in VA between groups 1 and 2 was also not statistically significant at 6 months (-0.04 ± 0.60 vs. -0.28 ± 0.66 LogMar, $p = 0.32$) and 1 year (0.12 ± 0.68 vs. -0.40 ± 0.72 LogMar, $p = 0.10$). In group 1, 2 eyes had foveal macular edema, 1 developed a retinal detachment, and 1 had rapid cataract progression. In group 2, 1 eye required a tube revision, 1 required further transscleral laser therapy, and 2 had cataract surgery.

Conclusions: PP AGV + PPV/EL and AC AGV + PRP were both effective in lowering IOP, and there was no significant difference between them. There was a trend toward better VA at 1 year in group 2, but this was not statistically significant. A prospective study and larger sample size is needed to address this question and further evaluate the outcomes of both treatment modalities.

CONTROL ID: 3504181

SUBMITTER (NAME ONLY): Ariel Gore

TITLE: Long-term outcome of aflibercept subconjunctival treatment for chemical induced corneal neovascularization in the rabbit model

SESSION TITLE: Corneal immunology and neovascularization II

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Gore, T. Kadar, M. Cohen, H. Gutman, L. Cohen, R. Gez, S. Dachir, V. Horwitz, Pharmacology, Israel Institute for Biological Research, Ness Ziona, ISRAEL|

Commercial Relationships Disclosure (Abstract): Ariel Gore: Commercial Relationship: Code N (No Commercial Relationship) | Tamar Kadar: Commercial Relationship: Code N (No Commercial Relationship) | Mayyan Cohen: Commercial Relationship: Code N (No Commercial Relationship) | Hila Gutman: Commercial Relationship: Code N (No Commercial Relationship) | Liat Cohen: Commercial Relationship: Code N (No Commercial Relationship) | Relli Gez: Commercial Relationship: Code N (No Commercial Relationship) | Shlomit Dachir: Commercial Relationship: Code N (No Commercial Relationship) | Vered Horwitz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The dynamic course of sulfur mustard (SM) induced ocular insult is characterized by an acute phase, which may be continued to a chronic phase or a quiescent period followed by a late pathology. The aim of this study was to evaluate the efficacy of ziv-aflibercept (Zaltrap) or aflibercept (Eylea) in preventing or ameliorating the corneal insult specifically the late phase induced neovascularization following ocular exposure to SM in the rabbit model.

Methods: Chemical SM burn was induced in the right eyes of NZW rabbits by vapor exposure. Zaltrap (2mg) was applied once by subconjunctival injection at 2h, 9 days or at 4 weeks post exposure. Eylea (2mg), the ocular specific preparation, was administered 4 weeks post SM exposure and following an initial one week treatment with 0.1% dexamethasone.

Non-treated exposed eyes served as controls. A clinical follow-up was performed for up-to 5-12 weeks following exposure and digital photographs of the cornea were taken for measurement of blood vessel length using an image analysis software. Eyes were taken for histological evaluation and extent of NV was determined by using H&E and Masson Trichrome staining.

Results: A single subconjunctival treatment of VEGF-trap 2h or 9 days post exposure presented a slight benefit in reducing the severity of the injury and in postponing the late induced NV growth. However in the group receiving treatment at 4 weeks following exposure, a significant reduced extent of existing NV was already seen at one week following injection, an effect which lasted for at least 8 weeks. The extensive reduction in existing corneal NV in the VEGF-trap treated group was confirmed by histological evaluation. Finally, eyes receiving the steroidal treatment during the first week and the ocular preparation of VEGF-trap following NV detection presented a significant reduction in corneal NV as compared to the steroid only treated group.

Conclusions: Subconjunctival Zaltrap or the combination of dexamethasone followed by Eylea treatment presented a long-term significant benefit in corneal NV reduction following ocular chemical exposure when used against existing NV rather than as a post exposure prophylactic treatment. These findings show the robust anti-angiogenic efficacy of both Eylea and Zaltrap and demonstrate the advantage of this treatment, in ameliorating corneal NV and protecting the ocular surface.

CONTROL ID: 3504541

SUBMITTER (NAME ONLY): Michael Wormstone

TITLE: Assessing intraocular lens/capsular bag biomechanical interactions over time in a human capsular bag model

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Wormstone, J.A. Eldred, School of Biological Sciences, University of East Anglia, Norwich, UNITED KINGDOM|N.B. Damm, M. Kelp, Ophthalmic Devices, Carl Zeiss Meditec AG, Berlin, GERMANY|

Commercial Relationships Disclosure (Abstract): Michael Wormstone: Commercial Relationship(s);Carl Zeiss Meditec AG:Code F (Financial Support);Carl Zeiss Meditec AG:Code C (Consultant) | Niklas Damm: Commercial Relationship(s);Carl Zeiss Meditec AG:Code E (Employment) | Martin Kelp: Commercial Relationship(s);Carl Zeiss Meditec AG:Code E (Employment) | Julie Eldred: Commercial Relationship(s);Carl Zeiss Meditec AG:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Stable positioning of an intraocular lens (IOL) in the capsular bag following cataract surgery is important for successful visual outcomes. Wound-healing events modify the capsular bag and can affect IOL stability. We therefore conducted a study to assess IOL/capsular bag interactions in a human in vitro capsular bag model over a three-month experimental period.

Methods: Capsulorhexis and lens extraction performed on human donor eyes generated suspended capsular bags (5 match-paired experiments). Preparations were secured by pinning the ciliary body to a silicone ring and maintained in 6 mL of medium for 84 days: days 1–3, 5% human serum and 10 ng/mL transforming growth factor β (TGF β 2); days 4–7, 2% human serum and 1 ng/mL TGF β 2; days 8–14, 1% human serum and 0.1 ng/mL TGF β 2; days 15–84, serum-free EMEM. A CT LUCIA 611PY IOL was implanted in all preparations. Quantitative measures were determined from whole bag images captured weekly. Images were registered and analysed in ImageJ to determine capsular bag area; distortion; angle of contact; and a fusion footprint associated with connection between the anterior and posterior capsules.

Results: Following surgery and IOL implantation, capsular bags appeared distorted, such that a long axis formed between the haptics relative to the non-haptic regions (short axis). The angle of contact between the haptics and the bag periphery inversely correlated to capsular bag area. Growth on the peripheral posterior capsule was observed 1 week after surgery and behind the IOL within 1 month. As coverage of the posterior capsule progressed matrix contraction/wrinkles were observed. Fusion footprints formed in non-haptic regions of the peripheral bag. Refractive structures formed in fusion footprint regions in the latter months of culture. Over time, the capsular bag area reduced, while the long/short axis ratio and angle of contact increased. End-point analysis revealed strong interaction between the CT LUCIA 611PY optic edge and the capsule. An indent in the posterior capsule was evident and cell density was greater peripheral to this mark.

Conclusions: The three-month graded model presents features of fibrotic and regenerative posterior capsule opacification and allows IOL/capsular bag interactions to be quantified and compared over time. The CT LUCIA 611PY IOL is stable within the bag and exhibits a strong optic barrier effect.

CONTROL ID: 3504731

SUBMITTER (NAME ONLY): Kamal Das

TITLE: Spectral Properties of Glare or Positive Dysphotopsia for Different Types of Intraocular Lenses

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Das, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|A. Kalapala, The University of Texas at Arlington College of Engineering, Arlington, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kamal Das: Commercial Relationship(s);Alcon Research Ltd:Code E (Employment) | Akhil Kalapala: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The wavelength dependence of positive dysphotopsia (PD) or glare due to light emitting diodes (LEDs) for intraocular lenses (IOLs) has not been found in the literature. The increased prevalence of LED light sources introduces new concerns for the spectral effects of PD or glare for IOLs. This study compares the glare for four commercially available IOL models with different material types and design features using an optical bench with LED sources.

Methods: Four separate monofocal IOL models (Alcon Clareon CNA0T0, Alcon AcrySof SN60WF, JNJ Tecnis ZCB00, and Hoya Vivinex XY1) of mid-diopter power were used to measure PD or glare-type photic phenomenon. Three LED sources of 480 nm, 555 nm and 640 nm wavelengths and a white light source were used for over a range of off-axis angles of illumination at 5 mm pupil to measure the glare from each IOL. Non-sequential ray trace simulation analysis and Fresnel based reflection and transmission coefficients were obtained to characterize the off-axis glare for these IOLs.

Results: For any given off-axis angle of incidence, the reflection and transmission properties of IOL glare may change as a function of wavelength. Both the measured reflected and transmitted glare for ZCB00 and XY1 are higher than CNA0T0 and SN60WF for white light and at 480, 555 and 640 nm from LEDs. While the transmitted reflection angle theoretically decreases with increasing wavelength, the transmitted glare for ZCB00 and XY1 increases when increasing the wavelength. This is explained by optical properties of the Fresnel reflection and transmission coefficients.

Conclusions: This is the first reported study that evaluates the wavelength dependence of PD or glare type photic phenomenon in IOLs. The reflected glare decreases with wavelength, while transmitted glare, which is an order of magnitude higher than the reflected glare, increases with wavelength. The measured reflected and transmitted glare spectra are observed to be in close agreement with Fresnel's equations. Both the transmitted and reflected glare for Clareon CNA0T0 and AcrySof SN60WF resulting from white light and at 480, 555 and 640 nm LEDs are lower compared to Tecnis ZCB00 and Vivinex XY1 IOLs.

CONTROL ID: 3504823

SUBMITTER (NAME ONLY): Fernanda Susanna

TITLE: Treatment Outcomes in the Susanna Glaucoma Drainage Device after 1 Year of Follow-up

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Susanna, R. Susanna, Universidade de Sao Paulo Faculdade de Medicina, Sao Paulo, São Paulo, BRAZIL|B. Susanna, C.N. Susanna, Ophthalmology, Faculdade de Medicina do ABC, Santo Andre, SP, BRAZIL|M. Nicolela, Ophthalmology, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, CANADA|

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ABSTRACT BODY:

Purpose: To determine the efficacy and complications of the Susanna glaucoma drainage device (SGDD) implant in refractory glaucoma.

Methods: Retrospective study. Medical records from consecutive glaucoma patients followed in a private clinical practice were included in the study. All patients that had undergone SGDD implant surgery from the period of September 2016 to July 2019 were included. All surgeries were done by the same surgeon (RSJ). Primary outcome was surgical failure, defined as IOP>18 mmHg and/or less than 20% IOP reduction from baseline, IOP less than 5 mmHg, reoperation for glaucoma need of implant removal or loss of light perception vision. Secondary outcomes included mean IOP, use of supplemental medical therapy, and complications.

Results: 22 eyes were analyzed. Mean patient age was 63 ± 15 (range: 27 to 87) years. Mean IOP decreased from 23 ± 7 mmHg to 11 ± 8 mmHg ($P<0.001$, paired t-test) at an average of 18 ± 9 months after the tube implant. The mean SD number of glaucoma medications was reduced from 3.3 ± 1 to 1.5 ± 1.2 at the last postoperative visit ($P<0.01$, paired t-test). No early postoperative complications occurred. There was one case of persistent hypotony that was solved with tube ligation. Failure due to high IOP occurred in two cases. There was no extrusion or erosion of the tube or the plate.

Conclusions: The SGDD presented a 13.6% failure rate with very few complications, being an efficient and safe alternative for refractory glaucoma.

CONTROL ID: 3504889

SUBMITTER (NAME ONLY): Matthew Parvus

TITLE: Effect of PDGF-BB on Human Retinal Pericytes

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Parvus, A.T. Tsin, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|C. Mercado, F. Elisarraras, The University of Texas Rio Grande Valley, Brownsville, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The majority of ocular pathologies seen in patients with diabetic retinopathy are a result of damage to the retinal vasculature, which leads to microaneurysms, hemorrhage, and eventually neovascularization. The first step in the pathogenesis of these conditions is derived from the loss of Human Retinal Pericytes (HRPs), which are cells essential to the preservation of the integrity of the retinal vasculature. Platelet-derived growth factor BB (PDGF-BB) is the primary promotor of growth and recruitment for HRPs.

Patients with non-proliferative diabetic retinopathy (NPDR) produce lower levels of PDGF-BB than in normal conditions, which could contribute to the loss of pericytes early in diabetic retinopathy. The purpose of this study is to evaluate the effect of PDGF-BB on HRPs in vitro to determine whether or not the longevity of the HRPs can be preserved with the intent of contributing to development of therapeutic interventions for patients with diabetic retinopathy.

Methods: Three groups of HRPs were treated with three different concentrations of PDGF-BB which correlate to concentrations found in patients with proliferative diabetic retinopathy (PDR), NPDR, and normal conditions. The control group was not treated. After 24 and 48 hours the viable cells were counted by tripan blue measurements. The results were reported by evaluating viable cells at 24 and 48 hours, growth of each group between these time periods, and significant growth differences between groups at each time period. Each group was grown in triplicates and an average from these triplicates was used during analysis.

Results: Pertaining to viability, the NPDR group was the only one with a significant result at 24 hours. Growth difference analysis was significant for the PDR group at the 24-hour period. Growth difference between all groups was significant at the 24 hours mark but not at 48.

Conclusions: Significant results were only seen at the 24 hours period which is thought to be a result of the well space not being large enough to accommodate growth beyond the 24-hour time frame. The finding of a statistically significant difference at 24 hours but not 48 hours further suggests this as a possible complication as well. That being said, significant growth difference was seen with the PDR group, which was treated with high levels of PDGF-BB. This finding is consistent with the hypothesis that PDGF-BB levels encourage the growth of HRP cells.

CONTROL ID: 3504987

SUBMITTER (NAME ONLY): Grant Justin

TITLE: Ocular Surface Microbiome: Simple methods to analyze Samples with low amounts of DNA and Effect of Different Sequencing Techniques

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Justin, Walter Reed National Military Medical Center, Bethesda, Maryland, UNITED STATES|H. Xia, T. Gibbons, Wilford Hall Ambulatory Surgical Center, Lackland AFB, Texas, UNITED STATES|H.H. Wang, Naval Medical Research Unit San Antonio, Fort Sam Houston, Texas, UNITED STATES|A. Johnson, US Army Brooke Army Medical Center, Fort Sam Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Characterize the differences in conjunctival microbiome profiles based on two minor variations in a standard next generation sequencing (NGS) library preparation technique to facilitate production of 16S rRNA metagenomics data from extremely low yield specimens. Results were analyzed with three different 16S bioinformatics pipelines. In addition, DNA shotgun sequencing was also performed and results were compared with the 16S analysis.

Methods: Seven subjects were enrolled. Conjunctival samples were taken bilaterally and combined into a single vial with DNA preservative for sequencing. After extraction, the DNA yield was insufficient for typical 16S rRNA NGS processing according to standard protocols. Given the low DNA yield, the 16S rRNA library preparation was altered to enable analysis of the specimens. Two separate methods were tried, and both produced metagenomics profiles for all of the samples. One involved following the library prep protocol as directed with the modification of loading as much sample possible even when no DNA was detected. The second involved an additional round of index PCR with the products from the first round utilized in the second so that sufficient DNA for preparation of the NGS library for sequencing was produced.

Results: The additional round of PCR produced an average of over 500,000 reads per sample but required removal of contaminant taxa based on results from the negative control. Without the additional round of PCR contaminant taxa was far less prevalent in the negative control but there was only an average of a little over 12,000 reads per sample. Both 16S methods and all three bioinformatics pipelines utilized produced similar results. Shotgun sequencing results correlated to the extent expected with the 16S results.

Conclusions: There was very little variability between the different 16S sequencing techniques in regards to the most common bacteria. Even though there were only subtle differences in the 16S metagenomics profiles of the specimens, additional studies are needed before definitive recommendations regarding the use of a second round of PCR to increase read or utilizing the costlier shotgun sequencing approach provides an optimal assessment of the ocular surface microbiome.

CONTROL ID: 3505117

SUBMITTER (NAME ONLY): john yan

TITLE: Epidemiology of Welding-Associated Ocular Injuries

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. yan, A. Uppuluri, M.A. Zarbin, N. Bhagat, Rutgers New Jersey Medical School
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ABSTRACT BODY:

Purpose: To analyze trends in ocular injuries related to usage of welding equipment from 2010 to 2019.

Methods: Using the Consumer Product Safety Commission's National Electronic Injury Surveillance System (NEISS) Database, we queried data from January 1st 2010 to December 31st 2019 using the corresponding product code for welding equipment (896). Results were stratified by year, and standard descriptive statistical methods were applied to components including gender, age, diagnoses, and ED disposition. Circumstances leading up to the injuries were reviewed as well.

Results: Between 2010 and 2019, NEISS estimated a total of 109,127 welding-associated ocular injuries in the United States (95% CI, 86937-131316). The estimates show a decreasing trend in cases from 13,415 (95% CI, 9979-16851) in 2010 to 6,944 (95% CI, 4868-9020) in 2019. The overwhelming majority of cases occurred in men (98.2%) and predominantly in the 10-49 year age range (83.8%). Overall, 3.3% of cases involved spectators. The top three ocular injury diagnoses were flash burns from welding arc UV radiation emissions (62.1%), foreign body implantation (19.6%), and contusions/abrasions (11.1%). Notably, the number of radiation injuries trended down from 9,286 (69.2% of injuries) in 2010 to 4023 (27.9% of injuries) in 2019 while injuries due to foreign bodies did not show a clear trend. 16.2% of patients diagnosed with foreign body injury reported using protective eyewear, while 15.3% of patients with radiation burn injuries reported wearing eye protection. Interestingly, 44.2% of welding-associated ocular injuries involved both eyes. Radiation injury contributed to 90.1% of cases with bilateral injury, while a majority of unilateral injuries were due to foreign bodies. With respect to a documented location, 38.9% occurred at home and 4.5% occurred in a school setting. Most patients (99.9%) were treated in the emergency department and discharged; only 0.1% were admitted to the hospital for further management. No open globe injuries were reported.

Conclusions: The data suggests that number of ocular injuries related to welding has decreased significantly over the past 10 years. The most common injuries were radiation burns, foreign body disruption, and contusions/abrasions of the eye. Patients were predominantly men and between the ages of 10 and 49. Of note, almost half of all ocular injuries due to welding were bilateral, and 3% of ocular injuries were seen in spectators.

CONTROL ID: 3505659

SUBMITTER (NAME ONLY): kento watanabe

TITLE: Relationship between ocular blood flow and systemic organ blood flow in white rabbits with hemorrhagic shock

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. watanabe, T. Shiba, Ophthalmology, International University of Health and Welfare Narita Hospital, Funabashi, Chiba, JAPAN|T. Komatsu, Y. Hori, Ophthalmology, Toho Daigaku, Ota-ku, Tokyo, JAPAN|A. Takahara, Pharmacology, Toho Daigaku, Funabashi, Chiba, JAPAN|

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ABSTRACT BODY:

Purpose: Shock is defined as the progression of organ disorder ; however, the evaluation method has not been established. We tested the hypothesis that ocular blood flow reflects the systemic organ blood flow, such as that in the kidneys and intestines, using an experimental rabbit model of hemorrhagic shock.

Methods: We used ten New Zealand white rabbits and administered general anesthesia. A catheter was placed in the brachial artery to measure their mean arterial blood pressure (MAP). Blood flow in the intestines and kidneys was measured using an ultrasonic blood flow meter at the mesenteric artery and the renal artery exposed on laparotomy. For the measurement of ocular blood flow, laser speckle flowgraphy that can evaluate the ocular blood flow non-invasively, was used. The mean blur rate (MBR) that is a blood flow index specific to laser speckle flowgraphy, was measured in the retinal vessels (RV) and choroid (CH). To create a shock state, blood was removed at a rate of 1 mL/min for 30 min. After an observation time of 20 min, blood was returned over a period of 15 min. Each parameter was evaluated as per the rate of change from the reference value before blood removal.

Results: MBR in RV and CH, intestinal and renal blood flow, and MAP were significantly decreased by the blood removal operation and recovered nearly to the reference value by the blood return operation. The rate of change at the end of blood removal was MAP, 69.4%; kidney, 43.5%; intestine, 54.8%; MBR-RV, 42.3%; and MBR-CH, 55.5%. The rates of change between MBR-RV and kidney and between MBR-CH and intestine were similar, and no significant difference was observed. MBR-RV and MBR-CH showed a significant positive correlation with MAP ($r = 0.87, 0.73$), with renal blood flow($r = 0.66, 0.59$) and with intestinal blood flow($r = 0.84, 0.61$).

Conclusions: Ocular blood flow reflected the renal and intestinal blood flow during the progression and recovery of hemorrhagic shock in white rabbits.

CONTROL ID: 3507108

SUBMITTER (NAME ONLY): Xiang-Run Huang

TITLE: The contribution of axonal cytoskeleton to retinal nerve fiber layer reflectance

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Huang, Y.Z. Spector, W. Kong, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Xiang-Run Huang: Commercial Relationship: Code N (No Commercial Relationship) | Ye Spector: Commercial Relationship: Code N (No Commercial Relationship) | Wei Kong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal nerve fiber layer (RNFL) reflectance is often assessed in clinical diagnosis of glaucoma. This study investigated the relationships between RNFL reflectance and axonal cytoskeleton, including microtubules (MTs), F-actin and neurofilaments (NFs).

Methods: Whole-mounted rat retinas were imaged at 500 nm by means of imaging reflectometry. Reflectance (R) of nerve fiber bundles was measured in normal retinas and retinas treated with colchicine. After the measurements, retinas were fixed for immunohistological staining. Confocal images were used to measure bundle thickness (T) and count the strings of MTs, F-actin and NFs within bundles (Fig. 1A-C). Reflectance per unit thickness ($\sigma = R/T$) and string density (d) were calculated.

Results: In normal RNFL, σ was correlated with d_{MT} ($r = 0.85$) and $d_{F-actin}$ ($r = 0.53$) but not d_{NF} ($r = 0.03$) (Fig. 1D-F). By assuming incoherent scattering of cytostructure, linear regression was used to describe the relationship between d and σ . The σ -intercept for d_{MT} vs. σ was 0.046 (%/ μm) which was 66% of the mean σ of normal bundles. The σ -intercept for $d_{F-actin}$ vs. σ was 0.055 (%/ μm) or 81% of the mean. In colchicine treated retinas σ , d_{MT} and $d_{F-actin}$ decreased significantly ($p < 0.001$); however, d_{NF} did not change ($p = 0.08$). The mean σ was reduced to 0.043 (%/ μm) which was a 38% reduction from the normal σ . With the linear model for d_{MT} (Fig. 1D), the reduction was estimated to contain a 22% reduction due to loss of MTs (solid black circle) and 16% due to change of scattering components other than MTs. For F-actin (Fig. 1E), the reduction was estimated to contain a 6% reduction due to loss of F-actin and 32% due to loss of MTs and changes of other unknown components.

Conclusions: Colchicine, a MT depolymerizing agent, also damages F-actin and other unknown structures. In normal retinas the contributions of MTs and F-actin to RNFL reflectance are not more than 34% and 19%, respectively. There are other structures contributing significantly to RNFL reflectance.

CONTROL ID: 3507327

SUBMITTER (NAME ONLY): Woo-Kuen Lo

TITLE: Epithelial-Mesenchymal Transition (EMT) induced by AQP0-deficiency during cataractogenesis

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Lo, S.K. Biswas, Neurobiology, Morehouse School of Medicine, Atlanta, Georgia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Woo-Kuen Lo: Commercial Relationship: Code N (No Commercial Relationship) | Sondip Biswas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The water transport is conducted by AQP0 for fiber cells and AQP1 for epithelium in the lens. We have previously shown that AQP0 deficiency in fiber cells causes significant upregulation of AQP1 in the epithelium. The increase in water influx from the epithelium caused further damage to the underlying fiber-cell mass. Enlarged anterior lens suture spaces and swollen fiber cells were frequently observed. Here, we report that AQP0-deficiency also induces EMT and connexins (Cx43 & Cx50) changes in lens epithelium.

Methods: EMT markers (α -actin, fibronectin, vimentin), AQP1, and Cx43 & Cx50 antibodies were used to examine lenses from WT, AQP0^{-/-}, and AQP0^{+/-} mice (P4-16wks old) in this study.

Results: By confocal immunolabeling on frozen sections, all WT lenses showed negative labeling for α -actin, fibronectin, and vimentin antibodies. In contrast, α -actin (α -SMA) was strongly labeled in the entire epithelial layer in AQP0^{-/-} lenses at P8 and older. Several distinct clusters of labeled epithelial cells with multiple layers were seen overlying the anterior lens sutures. However, strongly labeled fibronectin was mainly found in the detached clusters of EMT cells in the fiber-cell mass. At 2 weeks old, the migrated clusters of mesenchymal cells have reached the lens nucleus, seemingly via the enlarged lens sutures. The migrated mesenchymal cells in the lens nucleus showed positively labeled α -actin, fibronectin, and AQP1 antibodies. A similar pattern of EMT also occurred in the AQP0^{+/-} lenses, suggesting that partial deficiency of AQP0 was able to induce EMT in lens epithelium. By TEM analysis, 5-7 nm F-actin and 10 nm vimentin filaments were seen extensively distributed in EMT cells. Furthermore, since EMT causes epithelial structural changes, we examined possible alterations of Cx43 and Cx50 in epithelial whole mounts. While Cx43 labeling showed only a slight decrease, the labeling of Cx50 was dramatically reduced in the epithelium in AQP0^{-/-} lenses with age, suggesting that cell-cell communication between the epithelium and fiber cells at the interface was significantly reduced during the EMT process.

Conclusions: This study uncovers for the first time that AQP0 deficiency in lens fibers can induce EMT in anterior epithelial cells. As a result, some epithelial-mesenchymal cells can migrate into damaged nuclear fiber cells in the lens core, apparently through the enlarged anterior lens suture spaces.

CONTROL ID: 3507483

SUBMITTER (NAME ONLY): Yohei Tomita

TITLE: Single-cell analysis reveals a compensatory role of Muller glia in a mouse retinitis pigmentosa model

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Qiu, Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, UNITED STATES|Y. Tomita, E. Bull, W. Allen, Y. Kotoda, Z. Fu, Ophthalmology, Harvard Medical School, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|Z. Fu, The Manton Center for Orphan Disease, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is a set of >60 hereditary retinal diseases characterized by degeneration of rod, then cone photoreceptors. It is typically diagnosed in adolescence and patients lose vision during adulthood. Gene therapy has been approved for only one gene in RP and developing gene therapies for >60 genetic causes is time consuming and costly. Therefore, we investigated retinal cellular responses to photoreceptor abnormalities in a mouse RP model to find a potential generic target to treat RP.

Methods: Cellular responses in each major retinal cell type in RP model (P23H; mutation of rhodopsin) and wild-type mice were analyzed using single-cell transcriptomics. Morphological changes were examined in P23H and wild-type mice retinas with OCT and immunohistochemistry (IHC) staining.

Results: OCT analysis showed thinning of the outer nuclear layer (ONL) and IS/OS layer in P23H versus wild-type mice at one-month old ($p < 0.001$). Genes involved in IS/OS segments, photoreceptor cell cilia, and photoreceptor development were significantly decreased in both rod and cone clusters, in line with the structural changes seen with immunohistochemistry. The genes involved in energy production and metabolic pathways associated with this loss were notably decreased in both rods and cones. Furthermore, in the Müller glia/astrocyte cluster, there was a remarkable up-regulation in pathways responsible for photoreceptor maintenance, which was decreased in rods and cones.

Conclusions: Enhancing photoreceptor metabolism and modulating Müller glial responses may potentially serve as a generic approach to protect against retinal degeneration in RP.

CONTROL ID: 3510766

SUBMITTER (NAME ONLY): Zhongjie Fu

TITLE: Fibroblast growth factor 21 protects against phase I retinopathy of prematurity

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Fu, Y. Tomita, B. Cakir, Y. Kotoda, E. Bull, W. Allen, L.E. Smith, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|Z. Fu, Y. Tomita, B. Cakir, L.E. Smith, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S. Talukdar, Merck Research Laboratories Boston, Boston, Massachusetts, UNITED STATES|A. Hellström, Goteborgs Universitet, Goteborg, SWEDEN|

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ABSTRACT BODY:

Purpose: The primary cause of retinopathy of prematurity (ROP) is delayed retinal vascularization of immature retinas after preterm birth (phase I ROP). Neonatal metabolic dysfunction (hyperglycemia and dyslipidemia) occurring in the first few weeks of life is a very important but understudied (and potentially treatable) risk factor for phase I ROP. In term infants, blood fibroblast growth factor 21 (FGF21) levels increase beginning 2 days after birth and FGF21 levels positively correlate with postnatal growth. However, in preterm infants, FGF21 levels are very low, detectable in only 69% of preterm infants at postnatal week 1. We investigated if FGF21 promotes retinal vessel growth in phase I ROP utilizing a recently developed phase I ROP mouse model.

Methods: Neonatal metabolic dysfunction was induced with intraperitoneal (i.p.) injection of streptozotocin in mice from postnatal (P) day 1 to 9. At P10, retinal vessel growth was evaluated in FGF21- (i.p. from P7 to P9) vs vehicle-treated C57BL/6J (n=14-16), FGF21-knockout vs FGF21 wild-type mice (n=15-22). Co-treatment of FGF21 with intravitreal siRNA Acaca (the key enzyme in de novo fatty acid synthesis) or control (n=8-9), or i.p. etomoxir (CPT1A inhibitor) or control (n=8-9) in C57BL/6J mice was also conducted. Retinal metabolic enzyme levels were measured with quantitative proteomics and retinal lipid levels were analyzed with lipidomics. Both male and female mice were used. Littermate controls were used for drug treatment. Unpaired t test was used for statistical analysis.

Results: In mice modeling phase I ROP, FGF21 administration promoted ($P<0.001$) and FGF21 deficiency ($P<0.01$) worsened retinal vessel growth. Blocking retinal Acaca expression partially attenuated ($P<0.05$), while inhibiting CPT1A with etomoxir greatly decreased ($P<0.01$) FGF21 protection in retinal vessel growth. FGF21 did not change the protein levels of retinal metabolic enzymes. FGF21 reduced retinal lipid levels.

Conclusions: FGF21 protects against retinal vascular developmental delay in phase I ROP, possibly through modulating retinal lipid metabolism.

CONTROL ID: 3511844

SUBMITTER (NAME ONLY): Parth Patel

TITLE: Epidemiologic Trends in Pediatric Ocular Injury from 2010-2019 in the U.S

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.S. Patel, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|P.S. Patel, A. Uppuluri, M.A. Zarbin, N. Bhagat, Ophthalmology & Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe epidemiologic trends in consumer product-related pediatric ocular injuries from 2010-2019.

Methods: This retrospective epidemiological study utilizes data from the National Electronic Injury Surveillance System. Inclusion criteria for this study were: eye injury in patients aged between 1 and 20 years separated into 4 groups: 1-5, 6-10, 11-15 and 16-20 and injury occurring between 2010-2019.

Results: There were an estimated 636,582 ocular injuries in children ages 1-20 with an average age of 9.7 years (SD=5.92) presenting to US EDs; 416,378 (65.4%) were males with a male-to-female ratio of 1.9:1. The incidence of injury in males showed a downward trend over the span of the study while the rate in females remained the same. The greatest number of injuries occurred in the 1-5 age group (31.2%) followed by 6-10 (25.0%), 16-20 (22.4%) and 11-15 years (21.4%). The total number of injuries trended down from 65,724 in 2010 to 56,895 in 2019 as shown in Figure 1. Similarly, the incidence of ocular injury per 1 million persons across the same time period also trended downward.

The incidence and frequency of open globe injury displayed a positive trend over this time span. Ocular contusion was the most common diagnosis (45.7%) for the entire group. The most common location of injury was at home (41.7%). Most patients (96.2%) were released from the ED. Fewer than 1% of all ocular injuries were admitted to the hospital. Most ocular injuries occurred in the summer months (May, June and July) and were higher on the weekend compared to a weekday. In all pediatric patients, 27.7% of injuries were sports-related followed by detergents/chemicals (15.9%), toys (11.2%), home workshop equipment (7.5%), kitchenware (5.0%) and home furniture (4.4%), comprising the top 70% of consumer product categories in the entire population. Detergents/chemicals accounted for the most common cause of injury in the youngest age group (Figure 2).

Conclusions: The frequency and rate of pediatric ocular injuries trended downwards nationally over the last decade. Sports and non-powder guns caused the greatest amount of eye injuries in the older pediatric cohorts (11-15 and 16-20 age groups), while detergents/chemicals accounted for nearly 1/3 of all injuries in younger children (0-5).

CONTROL ID: 3512568

SUBMITTER (NAME ONLY): Mallika Somayajulu

TITLE: C57BL/6 and BALB/c mice: Microbiome composition and colonic cell population analysis.

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Somayajulu, S.A. McClellan, D. Bessert, A. Pitchaikannu, S. Suvas, L.D. Hazlett, Department of Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|M. Angoa-Perez, B. Zagorac, D. Kuhn, Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, Michigan, UNITED STATES|M. Angoa-Perez, B. Zagorac, D. Kuhn, John D. Dingell VA Medical Centre, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To validate the richness, heterogeneity and composition of the gut microbiome and colonic monocytic populations in C57BL/6 and BALB/c mice locally housed.

Methods: Female (8-9 weeks) C57BL/6 and BALB/c mice were housed in separate cages, 3-5 mice/cage and acclimatized in our animal facility for one week. Then, caeca were removed, DNA isolated from their contents and 16S rRNA gene sequencing of the V4 region done. Differences in microbial α - and β -diversity were evaluated for each group. Flow cytometry analyzed populations of colonic macrophages and inflammatory monocytes between the two mouse strains before and after ($n=3/\text{group/time}$) corneal infection with 1×10^6 CFU *Pseudomonas aeruginosa* (ATCC strain 19660).

Results: No differences in microbial richness were observed between the two mouse strains. However, bacterial heterogeneity and evenness were significantly reduced in the C57BL/6 vs BALB/c strain. The two groups also differed significantly in the composition and structure of their gut microbiomes. Data indicated increases in the relative abundance of Firmicutes and Verrucomicrobia specific to the BALB/c strain. In contrast, Bacteroidetes were increased in C57BL/6 mice. We also observed increased relative abundance in two species, *B. thetaiotaomicron* and *L. johnsonii* in C57BL/6 mice, agreeing with previous work by other research teams. Flow cytometry of colonic cells revealed no intrastrain differences in inflammatory monocytes between ocularly infected and uninfected mice. However, a significant increase in the number of colonic inflammatory monocytes was detected when comparing C57BL/6 with BALB/c infected mice.

Conclusions: We confirmed that two genetically different strains of mice show differences in the composition and structure of their gut microbiome. We provide evidence that ocularly infected C57BL/6 vs BALB/c mice have an increased number of inflammatory monocytes in the colon which may hold relevancy for their disparate response to corneal infection with *Pseudomonas aeruginosa*.

CONTROL ID: 3514743

SUBMITTER (NAME ONLY): Justin Karlin

TITLE: Upper eyelid weighting for facial palsy results in contralateral upper eyelid elevation

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Karlin, C. Le, D. Rootman, Orbital and Ophthalmic Plastic Surgery, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We examine the effect of eyelid weighting on the position of the ipsilateral and contralateral upper eyelid.

Methods: This cross-sectional cohort study included patients with unilateral facial palsy who underwent surgical upper eyelid weight implantation. Photographs were obtained in primary position parallel to the plane of the camera. The primary outcome measures were ipsilateral and contralateral margin to reflex distance 1 (MRD1), preoperatively and postoperatively. Postoperative MRD1 difference (symmetry) was assessed as a secondary outcome measure. Weight mass was examined as a covariate in predicting the magnitude of the effect.

Results: Twenty-two patients (16 female, 6 male) met inclusion criteria. Following eyelid weight implantation, contralateral (unweighted) MRD1 increased (mean 0.61 mm, standard deviation [SD] 1.23 mm, $p < 0.05$). Ipsilateral (weighted) MRD1 decreased, although not significantly (mean -0.41 mm, SD 0.94 mm, $p = 0.06$). Preoperatively, there was no significant MRD1 difference between the weighted and unweighted sides (mean difference -0.27, SD 1.94 mm, $p = 0.52$). Postoperatively, there was a significant difference in MRD1 between the weighted and unweighted eyelids (mean -1.29, SD 1.87 mm, $p < 0.05$). Weight mass was not a significant predictor of change in ipsilateral or contralateral MRD1 ($p = 0.54$, $p = 0.96$, respectively) following surgery.

Conclusions: Patients with facial nerve palsy undergoing unilateral insertion of an eyelid weight experience contralateral eyelid elevation, and demonstrate decreased postoperative upper eyelid height symmetry. These data highlight a heretofore undescribed manifestation of Hering's law, and add to the overall understanding of how eyelid height is regulated.

CONTROL ID: 3514749

SUBMITTER (NAME ONLY): Edward Lu

TITLE: Predicting Diabetic Vitreous Hemorrhage Using Neovascularization Features on Widefield Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA)

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.S. Lu, Y. Cui, Y. Zhu, R. Le, I. Lains, I. Garg, J. Wang, R. Katz, Y. Lu, D.M. Wu, D. Elliott, D.G. Vavvas, D. Husain, J.W. Miller, L.A. Kim, J. Miller, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Risk factors for the development of vitreous hemorrhage (VH) in patients with proliferative diabetic retinopathy (PDR) are not completely understood. We performed a prospective, observational clinical study to investigate the association between neovascularization features on WF SS-OCTA and the development of VH in eyes with PDR.

Methods: Patients with type 1 or type 2 diabetes mellitus and PDR without VH at baseline were included. All patients were imaged with WF SS-OCTA (Montage 15mm×15mm and HD-51 Line scan) at baseline. Images were independently evaluated by two graders for WF SS-OCTA metrics defined a priori. Mixed effects logistic regression models (outcome: occurrence of VH) and mixed effects Cox proportional-hazards models (outcome: time to occurrence of VH) were used for statistical analyses.

Results: Fifty-five eyes of 45 subjects were included. Over a median follow-up of 280 days (range: 28-534 days), 7 of 55 PDR eyes (12.73%) developed VH during the follow-up period. Presence of forward neovascularization (NV), defined as NV that traverse the posterior hyaloid face into the vitreous (odds ratio [OR]=2.56, P=0.007), larger flow area of NV (OR=1.36, P=0.039), and intraocular pressure greater than 21 mmHg (OR=31.20, P<0.001) were significantly associated with the occurrence of VH. Similarly, number of forward NV (hazard ratio [HR]=2.71 per 1 forward NV increase, P=0.01) and larger flow area of NV (HR=1.39 per mm² increase, P=0.02) were associated with time to occurrence of VH.

Conclusions: The number of forward NVs and NV flow area as measured by WF SS-OCTA were associated with the development of diabetic vitreous hemorrhage. Larger sample sizes with a greater duration of follow-up along with an examination of systemic factors and ophthalmic interventions (e.g. PRP, anti-VEGF) are needed to validate imaging biomarkers for the prediction of diabetic VH.

CONTROL ID: 3514769

SUBMITTER (NAME ONLY): Amy Chen

TITLE: Ethnic differences in the prevalence of ocular disease among hospitalized older adults with obesity

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chen, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|A. Uppuluri, M.A. Zabin, N. Bhagat, Department Of Ophthalmology & Visual Science, New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify ethnic differences in the prevalence of ocular diseases (non-traumatic) in obese patients over age 65.

Methods: Inpatients ≥ 65 years of age and diagnosed with ≥ 1 non-traumatic ocular disease between 2012-2014 were identified from the National Inpatient Sample (NIS), a nationally representative database of US hospitalizations. Demographics, ethnicity, duration and cost of hospital stay, comorbidities, and insurance status were recorded. Chi-squared analysis was used to calculate the prevalence of ocular disorders in obese vs. non-obese patients for each ethnic group using $p < 0.05$ as being significant. Cases were defined as obese patients with ocular diseases; the age and sex-matched control group consisted of non-obese patients with ocular diseases. The ratio of cases to controls was 1 to 5. The primary outcome was the prevalence of ocular disorders.

Results: 1,160,400 inpatients with non-traumatic ocular diseases were identified in the 3-year period; 193,615 (16.7%) were obese and had complete racial demographic information for categorization as non-Hispanic White, Hispanic, African American, Asian/Pacific-Islander, or Native American. With respect to ethnicity, prevalence of the following ocular diseases was higher in obese than non-obese patients: diabetic retinopathy (DR) in all ethnicities, ocular hypertension (OHTN) in all except Native Americans ($p < 0.03$); primary open-angle glaucoma (POAG) in all except Asian/Pacific-Islanders ($p < 0.001$); age related macular degeneration (AMD) in all except non-Hispanic Whites ($P < 0.001$); retinal vein occlusion (RVO) only among non-Hispanic Whites ($P < 0.001$); retinal artery occlusion (RAO) in all except African Americans ($p < 0.002$). Across all ethnicities, obese patients were more likely than non-obese patients to have hypertension ($p < 0.001$), hyperlipidemia ($p < 0.001$), and diabetes mellitus with or without chronic complications ($p < 0.001$). Among all obese patients, POAG was most prevalent in African Americans, DR was most prevalent in Asian/Pacific-Islanders and Native Americans, and AMD and RAO were most prevalent in Non-Hispanic Whites.

Conclusions: Within most ethnic groups, higher prevalence of DR, OHTN, POAG, AMD, RVO and RAO was found among obese adults ≥ 65 years old compared to non-obese controls. Within this NIS inpatient cohort, significant ethnic disparities were observed in the prevalence of ocular diseases in obese elderly patients.

CONTROL ID: 3514777

SUBMITTER (NAME ONLY): Jon Hammer

TITLE: Computerized analysis of retinal vascular growth following intravitreal bevacizumab monotherapy in retinopathy of prematurity until the age of three years

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Hammer, S. Agarwal-Sinha, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|H. Nguyen, J. Palmer, S. Rowlinson, Biomedical Engineering, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure retinal vessel growth post-intravitreal bevacizumab monotherapy (IVB) for retinopathy of prematurity (ROP) over time on serial fluorescein angiographic (FA) sessions until three years of age.

Methods: Serial angiographic images taken post-IVB on 4 serial examinations were analyzed starting at average 66 weeks post-menstrual age (PMA) with repeat imaging every 8 months until 3 years of age. The retinal vessel length was manually measured in ImageJ software from the temporal margin of the optic disc through the foveal center to the temporal vascular-avascular junction and vascular length at the different time points were compared.

Results: Seventy eyes in 35 infants treated for type-1 ROP were included, 63 eyes were treated with IVB and 7 eyes untreated. The mean retinal vessel length was 14.177 mm at time point #1 (66.2 weeks PMA) and 13.761 mm including all 4 FA sessions (range 44-234 weeks PMA). Paired t-tests compared the retinal vascular length of each individual eye over time and showed no statistically significant growth from the first FA at 66.2 weeks PMA until 3 years of chronological age. From time point #2 to #1 (N=30) the difference was -0.117 ± 0.785 mm (95% CI -0.416 to +0.176, $p=0.42$), from #3 to #1 (N=15) the difference was $+0.060 \pm 0.854$ mm (95% CI -0.413 to +0.533, $p=0.79$), and from #4 to #1 (N=7) the difference was -0.404 ± 1.32 mm (95% CI -1.628 to +0.820, $p=0.45$). Even the eyes with recurrence (n=6) and untreated eyes (n=7) showed no significant change in vascular growth over time.

Conclusions: Retinal vascular length measured angiographically post-IVB monotherapy treatment in ROP showed no significant vascular growth on serial examinations from 66 weeks PMA until three years of age. The persistent chronic vascular arrest and the inhibition of normal angiogenesis post-treatment with anti-VEGF monotherapy accounts for a longitudinal study in infants with ROP for dose titration and longer follow-up to study the vascular growth and recovery in the infants until adulthood.

CONTROL ID: 3514892

SUBMITTER (NAME ONLY): Tzu-Chen Lo

TITLE: Association between uveitis and an increased risk of inflammatory bowel disease

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Lo, Department of Medical Education, Taichung Veterans General Hospital, Taichung, TAIWAN|T. Lo, Y. Chen, School of Medicine, National Yang-Ming University, Taipei, TAIWAN|Y. Chen, Department of Ophthalmology, Taichung Veterans General Hospital, Taichung, TAIWAN|

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ABSTRACT BODY:

Purpose: To investigate the potential association between uveitis and an increased risk of developing Inflammatory bowel disease (IBD).

Methods: The whole population cohort was collected retrospectively from the Taiwan National Health Insurance Research Database between January 1, 2001, and December 31, 2013. A total of 198,923 subjects with uveitis were enrolled in the uveitis group, and 397,846 subjects without uveitis were enrolled in the comparison group. The two groups were matched on age, gender and index date. They were compared in the cumulative incidence of subsequent IBD during the study period. Adjusted hazard ratio (HR) of IBD corresponding to uveitis was generated by multivariate cox regression model after adjustment of hypertension, diabetes, hyperlipidemia, obesity and smoking. Furthermore, the HRs of Crohn's disease (CD) and ulcerative colitis (UC), which are subtypes of IBD, were calculated separately.

Results: The mean age of the cohort was 47.7 years. Uveitis patients had significantly higher proportions of hypertension, diabetes, hyperlipidemia, obesity and smoking than the comparisons. A significantly higher cumulative incidence of IBD was found in the uveitis group than in the non-uveitis group (4.13% vs. 1.48%, $p < 0.0001$). Under the univariate cox regression analysis, patients with uveitis had a significantly higher risk of IBD compared to those without uveitis (HR=1.47; 95% confidence interval [CI]: 1.43-1.52, $p < 0.0001$). The result remains significant in the multivariate regression model, with an adjusted HR of 1.44 (95% CI: 1.39-1.49, $p < 0.0001$). Moreover, when analyzed separately, uveitis was significantly associated with an increased risk of Crohn's disease (adjusted HR=1.49; 95% CI: 1.44-1.54), but not significantly associated with ulcerative colitis (adjusted HR=1.03; 95% CI: 0.92-1.15).

Conclusions: People with uveitis are at significantly greater risk of developing IBD than individuals without uveitis.

CONTROL ID: 3514896

SUBMITTER (NAME ONLY): Hongmin Zhang

TITLE: Role of AMP-activated protein kinase (AMPK) in corneal epithelial cells stimulated by fungi

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Zhang, C. Wang, J. Wei, W. Si, J. Yue, Y. Xie, Zhengzhou University People's Hospital, Henan Provincial People's Hospital, Henan Eye Institute, CHINA

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ABSTRACT BODY:

Purpose: To investigate the role of AMP-activated protein kinase (AMPK) in corneal epithelial cells stimulated by fungi.

Methods: The non-toxic concentration range of AMPK phosphorylation agonist AICAR and inhibitor Compound C on corneal epithelial cells was screened by real-time marker-free multifunctional analyzer. Western Blot method was used to detect the expression of p-AMPK in corneal epithelial cells induced by AICAR and Compound C, and to screen the optimal concentration and time of drug action. The epithelial cells were divided into the corneal epithelial cell (C) group, corneal epithelial cell + spore (C+S) group, corneal epithelial cell + spore + AICAR (C+S+A) group, corneal epithelial cell + spore + Compound C (C+S+CC) group. Western Blot method was used to detect the expression of AMPK and p-AMPK in corneal epithelial cells. ELISA method was used to detect the expression of IL-6 in the culture supernatant of corneal epithelial cells.

Results: The cell index of 100μM, 300μM, 500μM, 1000 μM AICAR group and 10μM, 12.5μM Compound C group were not increased statistically than that in the corneal epithelial cells group at 24h, 36h, 48h, 72h time point ($P > 0.05$). The AICAR 1000μM group at 4h time point had the highest AMPK phosphorylation level in all AICAR concentration and time point groups ($P < 0.05$). The AMPK phosphorylation level in the Compound C 10μM group was higher than that in the other Compound C concentration groups ($P < 0.05$). Therefore, 1000μM and 4h was selected as the optimal concentration and time point for AICAR and 10μM group for Compound C. The AMPK phosphorylation level was higher in C+S group than that in group C ($P < 0.01$). The AMPK phosphorylation levels were higher in the C+S+A group than that in the C+S group ($P < 0.05$). The AMPK phosphorylation levels were lower in the C+S + CC group compared than that in the C+S group ($P < 0.05$). The IL-6 expression in group C+S was higher in C+S group than that in group C ($P < 0.01$) and C+S + CC group ($P < 0.05$).

Conclusions: Corneal epithelial cells had AMPK phosphorylation expression, and the AMPK phosphorylation and IL-6 secretion were increased after fungal spores stimulate. AMPK phosphorylation and IL-6 may play an important role in corneal antifungal infection.

CONTROL ID: 3515145

SUBMITTER (NAME ONLY): Timothy Gawne

TITLE: Hyperspectral refractomics and the spatial frequency sweet spot for emmetropization

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Gawne, T.T. Norton, Optometry and Vision Science, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|R. Grytz, Ophthalmology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: A feedback mechanism in the post-natal developing eye uses visual cues to control its axial elongation to achieve and maintain good focus, a process termed emmetropization. Here we present a model of how the human retina could use chromatic cues to determine the magnitude and sign of defocus in complex visual scenes integrated across the entire visual spectrum, that is, using hyperspectral images.

Methods: We extended a model based on tree shrews (Gawne and Norton 2020) to the human eye, assuming that the activities of human medium- and long-wavelength sensitive cones ("M+LWS") are added together as a single value. We applied this model to 26 hyperspectral images of real-world scenes (Chakrabarty and Zickler 2011). For each hyperspectral image we calculated the radially averaged spatial frequency spectra for both SWS and M+LWS cone classes at several levels of simulated defocus. We define a "hyperspectral drive" as the difference between the averaged signal amplitude of the two cones classes, SWS - (M+LWS), at different spatial frequencies.

Results: Fig.1 illustrates the hyperspectral drive as a function of image defocus for six representative spatial frequencies. At 0.25 and 0.5 cycled per degree (CPD), the drive is highly variable and not very accurate (drive not consistently zero at 0 D defocus). At 1 CPD the drive function is less variable across scenes and more accurate. At 2 CPD the drive is even less variable and still accurate, but loses effectiveness beyond about ± 2 D of defocus. At 10 CPD, the range of the drive function shrinks to less than ± 1 D.

Conclusions: Emmetropization likely uses multiple visual cues, and even for chromatic ones, likely integrates them across some range of spatial frequencies. However, this analysis suggests that there is a "sweet spot" for the use of chromatic signals in emmetropization roughly in the range of 1-2 CPD, within the resolution of the widely-spaced SWS cones.

CONTROL ID: 3515173

SUBMITTER (NAME ONLY): Wijak Kongwattananon

TITLE: Changes in Choroidal Vascularity Index in Intermediate Uveitis

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Kongwattananon, A. Kumar, H. Sen, S. Kodati, NEI, National Eye Institute, Bethesda, MD, US, academic/medres, Bethesda, Maryland, UNITED STATES|W. Kongwattananon, Ophthalmology, King Chulalongkorn Memorial Hospital, Bangkok, THAILAND|

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ABSTRACT BODY:

Purpose: Choroidal vascularity index (CVI) is the proportion of luminal area to total choroidal area, and has been shown to be a sensitive parameter for detecting choroidal vascular changes in a range of ocular and systemic diseases. The purpose of this study is to evaluate the longitudinal changes in CVI in active and inactive patients with intermediate uveitis (IU).

Methods: Enhanced-depth optical coherence tomography (EDI-OCT) images of IU patients were retrospectively reviewed. The subfoveal choroidal area within the central 1500 μm of the macula was segmented into luminal area and stromal area using an image binarization tool (ImageJ software; Bethesda, MD USA). Choroidal parameters including subfoveal choroidal thickness (SCT), total choroidal area (TCA), luminal area (LA), stromal area (SA) and CVI were compared between baseline and follow-up visits among patients with active and inactive IU.

Results: Twenty patients with active IU (36 eyes; mean age 32.75 ± 17.00) and twelve patients with inactive IU (21 eyes; mean age 34.3 ± 22) were included. At baseline, no difference of CVI, LA, SA, TCA, and SCT was noted between two groups. After follow-up, CVI and LA in active IU eyes significantly increased from $66.80 \pm 3.36\%$ to $68.36 \pm 4.32\%$ ($P = 0.02$), and 0.93 ± 0.21 to $0.99 \pm 0.21 \text{ mm}^2$ ($P = 0.001$) while SCT did not significantly change (325.50 ± 68.07 to $331.03 \pm 63.05 \mu\text{m}$, $P = 0.335$). In patients with inactive IU, CVI did not significantly change after follow-up ($66.49 \pm 4.03\%$ to $66.78 \pm 3.90\%$, $P = 0.690$).

Conclusions: Our results show that in eyes with active intermediate uveitis, the CVI increased significantly on follow up following resolution of inflammation, which may be the result of increased vascularization of the choroid after treatment. Further studies are needed to evaluate the role of CVI as a biomarker for monitoring treatment response in uveitis patients.

CONTROL ID: 3515345

SUBMITTER (NAME ONLY): Ana Janic

TITLE: Values of Retinoblastoma Survivors and Parents Regarding Treatment Outcomes: A Qualitative Study

SESSION TITLE: Advances in Diagnosis and Management of Retinoblastoma and Congenital Eye Diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The purpose of this study was to uncover which treatment outcomes retinoblastoma survivors and their parents' value. Retinoblastoma is an aggressive pediatric eye cancer. Patient-reported outcome measures – instruments that measure any outcome related to health that are directly reported by patients themselves – reveal important insights on how patients perceive their own health. Currently, no widely used or validated measure for the assessment of retinoblastoma outcomes exists.

Methods: This qualitative, cross-sectional study included Canadian retinoblastoma survivors aged 6 years and older, and parents of retinoblastoma survivors. Participants who did not demonstrate fluency in English were excluded. Study subjects participated in semi-structured interviews or focus groups, either in person at The Hospital for Sick Children, Toronto, Canada, or through secure videoconference, between March 3, 2019, and January 25, 2020. Iterative rounds of opening coding, codebook development, and co-researcher analysis, were utilized to identify key emergent themes and subthemes.

Results: Seventeen adults (8 survivors, 9 parents) participated in 6 focus groups. Nine pediatric survivors participated in individual interviews, five children aged 6-9, and 4 adolescents, aged 11-16. Four common themes emerged from all participant groups: (1) Definition of treatment success, (2) Enucleation – acceptance and challenges, (3) Treatment outcomes to measure, and (4) Need for outcome reporting. An additional, unique theme was identified in all pediatric discussions: (1) Worries and coping mechanisms. Treatment outcomes deemed valuable were related to the following domains: psychosocial outcomes, daily functioning, functional vision, retinoblastoma education, cosmetic outcomes, and secondary eye conditions.

Conclusions: This study represents the first stage in the development of a retinoblastoma-specific patient-reported outcome measure. Further, this work represents the first study of its kind for the retinoblastoma population and is novel in its inclusion of pediatric survivors as young as 6 years of age. The findings reveal insight into what outcomes are valued by survivors after treatment and offers promise to improve outcomes assessment for retinoblastoma.

CONTROL ID: 3515354

SUBMITTER (NAME ONLY): Jing Jin

TITLE: Associations between hematologic value with ocular and brain findings in children with sickle cell disease

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Jin, Surgery/Ophthalmology, Nemours A. I. duPont Hospital for Children, Wilmington, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: A critical knowledge gap exists in how systemic disease markers relate to the clinical manifestations of sickle cell retinopathy (SCR). This prospective observational study investigated the link between hematologic values and retinal injury on OCT and cerebrovascular disease (CVD).

Methods: 73 patients (38 males), aged 5-20 years with sickle cell disease (SCD) (68 SS and 5 S β 0 thalassemia) underwent funduscopy and SD-OCT imaging. 52 of these patients had brain MRI, 49 of the 52 also had MRA. Data on CVD include history of stroke, silent cerebral infarct (SCI) by MRI, cerebral arteriopathy by MRA and abnormal transcranial Doppler (TCD). Hematologic values and markers of hemolysis were collected. X^2 and Fisher's exact tests of proportions were used to compare frequency of abnormal findings across subpopulations. For continuous variables, 2-tailed, unpaired t tests were used for age and Mann-Whitney test were used for blood tests results. P values of <.05 were considered statistically significant.

Results: While funduscopy findings in our cohort showed no correlation with CVD, 20/21 patients with CVD had evidence of SCR by OCT (p=0.008). The outcome of OCT detecting retinal injury from SCD had 95.24% sensitivity (95% CI 76.18% to 99.88%) and 38.71% specificity (95% CI 21.85% to 57.81%) of showing SCI by MRI. There was no significant correlation between OCT findings and abnormal TCD. Correlations of hematologic values with OCT and CVD are demonstrated in the table.

A logistic regression model was statistically significant (p = 0.000). The model explained 58.0% of the variance in SCI and correctly classified 84.6% of cases as with or without SCI. For each unit increase of reticulocyte, there was 1.43 times increase in the odds of SCI. Subjects with abnormal OCT were 11.5 times more likely to exhibit SCI on MRI. Increasing WBC, higher indirect bilirubin and AST were associated with an increased likelihood of having SCI.

Conclusions: A correlation between abnormal OCT and CVD strongly suggesting that retinal OCT may aid in detection and monitoring SCD related CVD. A significant correlation between higher reticulocyte percentage, higher AST and abnormal OCT, stroke and SCI suggests that retinopathy may be another component of the hemolytic sub-phenotype of SCD and that patients with higher levels of hemolysis may benefit from closer monitoring for the development of SCR and brain damage.

CONTROL ID: 3515455

SUBMITTER (NAME ONLY): Nedda Sanayei

TITLE: Patient satisfaction with ophthalmic telemedicine visits during the COVID-19 pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Sanayei, M. Albrecht, A. Baker, F. Vavrek, M.G. Fiorello, Ophthalmology, Boston Medical Center, Boston, Massachusetts, UNITED STATES|M. Desai, Ophthalmology, Glaucoma Service, Boston Medical Center, Boston, Massachusetts, UNITED STATES|N. Siegel, M.L. Subramanian, S. Ness, X. Chen, Ophthalmology, Retina Service, Boston Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare patient satisfaction for telemedicine visits to traditional in-person clinical visits during the COVID-19 pandemic in the Ophthalmology Department at Boston Medical Center (BMC), the largest academic safety-net hospital in New England.

Methods: Patient satisfaction surveys using the NRC Health platform were sent to all patients in their preferred language following eye clinic visits at BMC from June to October 2020. Three visit types were studied: 1) virtual visits via telephone or video conferencing, 2) hybrid visits with protocol-driven set of undilated imaging (e.g. OCT, fundus photos, visual fields), visual acuity, and intraocular pressure obtained by a trained technician, followed by a virtual visit with the physician within 1-2 weeks, and 3) traditional in-person visits. Two-tailed Student's t-test was used to compare survey responses of telemedicine to traditional visits in 4 questions: 1) trust in provider (4-point scale, "trust"), 2) felt provider listened (4-point scale, "listened"), 3) satisfied with amount of time spent with provider (4-point scale, "time"), and 4) recommend provider to other patients (10-point scale, "recommend"). Additionally, responses between English and non-English speakers, requiring trained interpreter services, were compared.

Results: A total of 793 visits were included (44 virtual, 56 hybrid, 693 traditional). The majority of telemedicine visits were from the retina and optometry services (Figure 1). There was no statistically significant difference in "trust", "listened", "time", or "recommend" when comparing virtual or hybrid visits to traditional visits (Table 1a). Non-English speakers had statistically significant lower scores in "trust", "listened", and "time" with no difference in "recommend" when compared to English speakers (Table 1b). When stratified by visit type, non-English speakers had a trend towards a lower score in "trust" for both virtual and hybrid groups.

Conclusions: Telemedicine provides patients access to clinical care with decreased risk of infection during the COVID-19 pandemic. Non-English speakers tended to have less trust in the physician for all visit types, which should be considered when communicating with patients. Overall, we found that patients were equally satisfied with telemedicine visits as with traditional in-person visits in a hospital-based academic eye clinic.

CONTROL ID: 3515833

SUBMITTER (NAME ONLY): Jacqueline Chua

TITLE: Choriocapillaris microvasculature dysfunction in systemic hypertension

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chua, B. Tan, E. Lamoureux, T.Y. Wong, L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|T. Le, C.W. Chin, National Heart Research Institute Singapore, SINGAPORE|B. Tan, L. Schmetterer, Nanyang Technological University, Singapore, Singapore, SINGAPORE|J. Chua, E. Lamoureux, C.W. Chin, T.Y. Wong, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: The choriocapillaris layer in the eye is one of the densest layers of capillary vasculature in humans and may be affected by early microvascular changes as a result of uncontrolled systemic hypertension. To examine the choriocapillaris microvasculature using a non-invasive swept-source optical coherence tomography angiography (SS-OCTA) in healthy controls and hypertensive patients and determined possible correlations with BP and renal parameters.

Methods: A prospective study of 41 healthy controls and 71 hypertensive patients with varying blood pressure (BP) control. BP levels, serum creatinine and urine microalbumin/creatinine ratio (MCR) specimens were collected. The estimated glomerular filtration rate (eGFR) was calculated based on CKD-EPI Creatinine Equation. The main outcome was choriocapillaris flow deficits (CFD) metrics (density, size and numbers).

Results: The CFD occupied a larger area and were fewer in number in the hypertensive patients with poor BP control ($407 \pm 10 \mu\text{m}^2$; 3260 ± 61) compared to the hypertensives with good BP control ($369 \pm 5 \mu\text{m}^2$; 3551 ± 41) and healthy controls ($365 \pm 11 \mu\text{m}^2$; 3581 ± 84). Higher systolic BP ($\beta=9.90$, 95% CI, 2.86 to 16.93), lower eGFR ($\beta = -0.85$; 95% CI, -1.58 to -0.13) and higher urine MCR ($\beta=1.53$, 95%CI, 0.32 to 2.78) were associated with larger areas of CFD. Similar significant associations with systolic BP, eGFR and urine MCR were found with number of CFD.

Conclusions: These findings highlight the potential role of choriocapillaris imaging using SS-OCTA as an indicator of systemic microvascular abnormalities secondary to hypertensive disease.

CONTROL ID: 3516090

SUBMITTER (NAME ONLY): Elliot Choi

TITLE: An inducible Cre mouse for studying roles of the RPE in retinal physiology and disease

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) provides vital metabolic support for photoreceptor cells. Many RPE proteins thought to be important for the maintenance of retinal health. For these reasons, there is great interest in studying gene function in the RPE through conditional knockout experiments using the Cre-LoxP system. Mouse lines reported to date that have been engineered to express Cre specifically in the RPE suffer from various inadequacies, most notably mosaic Cre expression, lack of tissue specificity, and long-term toxicity to the RPE. In this study, we aimed to overcome these challenges by generating a novel inducible Cre mouse line that exploits the endogenous promoter of the RPE-specific 65 kDa protein (RPE65).

Methods: A P2A-CreER^{T2} coding sequence was fused in frame with the endogenous Rpe65 gene by homologous recombination for bicistronic gene expression. Following removal of the neomycin selection cassette and backcrossing onto the C57BL/6J background, the Rpe65^{CreERT2} mice were bred with the mT/mG reporter mouse line to assess Cre recombinase activity as well as 129s and C57BL6/J mice expressing the L450 variant of Rpe65 to assess retinal morphology and visual cycle kinetics.

Results: The Rpe65^{CreERT2} mice were fully viable and had no gross morphological abnormalities. Mice heterozygous for the RPE65^{CreERT2} allele were able to recombine the mT/mG reporter with an efficiency of ~99% upon tamoxifen induction at both P21 and P50. Cre activity was found exclusively within the RPE as assessed by retinal cryo-sections. Tamoxifen-independent activity was negligible with < 1% of RPE cells converted at both P21 and P50. RPE65 expression from the knock-in allele was minimal. Dark-adapted ERG responses were normal in these mice. Also, visual chromophore recovery was normal in Rpe65^{CreERT2/Wt(M450)} and Rpe65^{CreERT2/Wt(L450)} mice. Heterozygous mice did not display any signs of RPE pathology following treatment with tamoxifen.

Conclusions: This study demonstrates that CreER^{T2} expression via cotranslational cleavage from the native Rpe65 locus overcomes previously reported difficulties with RPE-directed Cre mice. The mice we report here exhibit highly efficient, tamoxifen-inducible Cre activity specifically in the RPE and do not display evidence of RPE toxicity. These mice will be useful for future studies of gene function specifically in the RPE.

CONTROL ID: 3516595

SUBMITTER (NAME ONLY): Pochen Tseng

TITLE: Intraoperative Intravitreal Injection of Anti-VEGF During Phacoemulsification Surgery to Prevent the Incidence of Diabetic Macular Edema and Enhance Postoperative Visual Outcome

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tseng, C. Yen, Ophthalmology, Taipei City Hospital, Taipei, TAIWAN|P. Tseng, University of Taipei, Taipei, TAIWAN|C. Yang, National Taiwan University College of Medicine, Taipei, Taipei, TAIWAN|C. Yang, Ophthalmology, National Taiwan University Hospital, Taipei, TAIWAN|

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ABSTRACT BODY:

Purpose: The DRCR.net implicated cataract surgeries increased the risk of postoperative diabetes macular edema (DME) in 16 weeks and worsening of postoperative visual outcome. Whether concurrently anti-VEGF injection in cataract surgery in diabetic patients decrease the risk of DME has not been investigated.

Methods: A retrospective observational study was conducted from 2016/01/01 to 2020/10/31. All patients were diagnosed with diabetic mellitus prior to the operation. DME was defined as central subfield thickness (CST) 300 μ m or more. Epiretinal membrane or tractional maculopathy were excluded. All the cataract surgeries were done by a single surgeon with phacoemulsification and posterior chamber intraocular ocular lens implantation in the capsular bag without any posterior capsular tear or any other intra- or post-operative complications. We concurrently perform cataract surgery and intravitreal injection of 2 mg aflibercept (0.05 mL) in 43 eyes. The control group only received cataract surgery without intravitreal injection in 65 eyes. We analyzed the post-operative visual acuity, CST changes and the incidence of post-operative DME. CST was measured by spectral domain optical coherence tomography (Optovue, Inc, Fremont, California) prior and three months after surgery.

Results: 108 eyes in 74 patients were included. 43 eyes received cataract surgery and intravitreal injection concurrently, in which 8 eyes were found pre-operation DME (group A) and 35 eyes not (group C). 65 eyes received cataract surgery only, and 11 of which were found pre-operation DME (group B) and 54 not (group D).

CST was decreased in patients with DME in group A but increased in group B (-3.3 ± 47.3 μ m versus 28.0 ± 35.2 μ m) (fig 1.). The visual acuity improved significantly in group A than group B ($p < 0.01$) (fig 2.). There was no significantly different in CST changes, incidence of postoperative CME (8.5% and 9.2 % respectively) and visual acuity between Group C and D.

Conclusions: This study showed that if diabetic patients were diagnosed as DME postoperatively, concurrently intravitreal injection of anti-VEGF in cataract surgery may be beneficial in decreasing postoperative CST and improving visual acuity. If there is no preoperative DME initially, the role of anti-VEGF may not be highlighted.

CONTROL ID: 3516654

SUBMITTER (NAME ONLY): Wei Si

TITLE: Platelets enhance the antifungal activity of neutrophils

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Si, H. Zhang, S. Liu, Zhengzhou University People's Hospital, Henan Provincial People's Hospital, Henan Eye Institute, CHINA | F. Zhang, People's Hospital of Dezhou, CHINA |

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ABSTRACT BODY:

Purpose: In the previous experiment, platelet, neutrophil aggregation were observed in the focus area of fungal keratitis in mice, but the relationship between platelet and neutrophil was not clear. Therefore, the effects and mechanisms of the antifungal activity of neutrophils enhanced by platelets were studied.

Methods: All fungi used for experiments was the standard strain of *Fusarium solani*. Neutrophils and platelets were drawn from human peripheral venous and purified from whole blood respectively. Three groups were divided in this experiments: spore (S) group, spore + neutrophil (S+N) group co-incubated spores and isolated neutrophils together and spore + neutrophil + platelet (S+N+PL) group co-incubated spores, isolated neutrophils and platelets. The growth of fungi or neutrophils or platelets was observed and the pictures were took at specified time points used by a spinning disk confocal microscope. The rate of phagocytosis, spore germination, hyphae length and apoptosis in each group were calculated.

Results: The rate of phagocytosis of neutrophils in S+N+PL group were higher at 1h, 2h and 4h compared with that in S+N group ($P < 0.05$). The rate of spore germination was lower in S+N+PL group compared with that in S+N group ($P < 0.05$). In addition, with longer incubated time, the apoptosis of neutrophils grown higher. Until 18h, the apoptosis rate of N group was grown as high as 74.56%. The highest apoptosis rate of neutrophils was in N group, followed by S+N group and S+N+PL group at each time point ($P = 0.000$). The apoptosis rate in S+N group was significantly higher than that in S+N+PL group at 6h, 10h, 14h and 18h ($P < 0.01$).

Conclusions: Platelets could enhance neutrophils to engulf fungal spores, restrict fungal germination, delay the hyphae growth and reduce apoptosis of neutrophil. These results indicated that the platelets play an important role in anti-fungal field.

CONTROL ID: 3516661

SUBMITTER (NAME ONLY): Ivan Seah

TITLE: A micropulse laser-induced non-human primate photoreceptor injury model for the study of retinal degenerations

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Seah, Department of Ophthalmology, National University Hospital Department of Ophthalmology, Singapore, SINGAPORE|Z. Liu, V.A. Barathi, G. Lingam, X. Su, Department of Ophthalmology, National University Singapore Yong Loo Lin School of Medicine, Singapore, SINGAPORE|Z. Liu, Institute of Molecular and Cell Biology, Singapore, SINGAPORE|G. Tan, V.A. Barathi, G. Lingam, X. Su, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Retinal degenerations are a heterogenous group of conditions which differ in pathophysiology but are characterised by the demise of photoreceptors. The non-human primate (NHP) model is important for such studies due to the presence of an anatomical macula, which is not seen in other animals. While there have been attempts to create NHP models using systemic or intravitreal delivery of retinotoxic agents, these are associated with increased systemic complications and uncontrollable distribution of retinal lesions.

Ophthalmic lasers are useful for creating animal models of retinal diseases. As compared to the traditional argon laser, the micropulse (MP) laser delivers lower energy but repetitive series of short pulses. This may allow selective and consistent destruction of photoreceptors without damaging the Bruch's membrane. Thus, it may avoid choroidal neovascularisation (CNV) which has a different pathogenesis. In this abstract, we investigate the utility of the MP laser in creating a NHP model of degenerative retinal diseases.

Methods: A *Macaca fascicularis* was used to create the RD model using the IQ 532 Micropulse Laser (Iridex) with a TxCell scanning laser delivery device and a Volk HR centralis contact lens (Volk Optical Inc) with a 74° degree field of view. 4 settings were tested for their ability to cause selective photoreceptor damage:

A: 66J/m^2 Fluence: Duty cycles of 2% (0.2ms pulse "on", 9.8ms pulse "off"), Power 2000mW

B: 33J/m^2 Fluence: Duty cycles of 1% (0.1ms pulse "on", 9.0ms pulse "off"), Power 2000mW

C: 49.5J/m^2 Fluence: Duty cycles of 1.5% (0.15ms pulse "on", 9.8ms pulse "off"), Power 2000mW

D: 37.125J/m^2 Fluence: Duty cycles of 1.5% (0.15ms pulse "on", 9.8ms pulse "off"), Power 1500mW

Optical coherence tomography and autofluorescence of the macula were done on Day 0, 7 and 20 from the initial procedure. Histological analysis was done after 20 days.

Results: Of the 4 settings, Settings A, C and D were able to achieve photoreceptor damage reflected on imaging. Only Setting A was associated with CNV development after 20 days. Photoreceptor damage was not achieved with Setting B.

Conclusions: At specific settings, the MP laser can potentially be used for the creation of a NHP model of RD. Further investigations including electroretinography and transcriptional analyses are required for validation of this model.

CONTROL ID: 3516783

SUBMITTER (NAME ONLY): Aniket Ramshekar

TITLE: Elucidating the role of EPOR signaling in an experimental model of neovascular age-related macular degeneration

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ramshekar, E. Kunz, C.A. Bretz, M. Hartnett, Department of Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|B. Chaqour, Department of Ophthalmology, SUNY Downstate Health Sciences University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Erythropoietin (EPO) signaling through its receptor (EPOR) is believed to exacerbate neovascular age-related macular degeneration (AMD) pathology, but it is unknown if EPOR signaling has a direct effect on either endothelial cells (ECs) or macrophages (MΦs) recruited to the choroid that release angiogenic factors. We addressed the hypothesis that EPOR signaling increases choroidal neovascularization (CNV) by direct effects on endothelial cells (ECs). We used the murine laser-induced CNV model comparing tamoxifen-inducible EC- or MΦ-specific EPOR knockout mice.

Methods: Offspring from $Cdh5-CreERT2^{+/+}$ or $Cx3cr1-CreERT2^{+/+}$ crossed with $Rosa26-tdTomato^{flox/flox}$ mice were bred with $EpoR^{flox/flox}$ mice to generate $Cdh5-CreERT2^{+/-};Rosa26-tdTomato^{flox/flox};EpoR^{flox/flox}$ (EPOR^{iΔEC}) or $Cx3cr1-CreERT2^{+/-};Rosa26-tdTomato^{flox/flox};EpoR^{flox/flox}$ (EPOR^{iΔMΦ}), respectively, and appropriate Cre-negative littermate controls (EPOR^{fl}). 4-week old EPOR^{iΔEC}, EPOR^{iΔMΦ}, and EPOR^{fl} received intraperitoneal tamoxifen treatment every other day for one week. Two weeks later, laser injury was performed with the Phoenix Micron IV laser module. One week after laser, choroids were dissected and stained with isolectin-B4 to label CNV. Z-stacks of CNV lesions were captured using a confocal microscope, and CNV volumes were calculated using IMARIS software and verified by a masked reviewer. Data were analyzed using a multilevel linear regression model with laser spots nested within the same eye and normalized to the EPOR^{fl} mice.

Results: EPOR^{iΔEC} mice had 20% smaller lesions than EPOR^{fl} mice ($p=0.37$), whereas EPOR^{iΔMΦ} mice had similar sized lesions as EPOR^{fl} mice ($p=0.76$). Stratification based on sex revealed a 47% reduction in average CNV volume in male EPOR^{iΔEC} compared to male EPOR^{fl} mice ($p=0.03$), but not in female EPOR^{iΔEC} compared to female EPOR^{fl} mice ($p=0.62$). Male EPOR^{iΔMΦ} compared to male EPOR^{fl} mice ($p=0.35$) or female EPOR^{iΔMΦ} compared to female EPOR^{fl} mice ($p=0.18$) did not have significant changes in CNV volume.

Conclusions: EPOR^{iΔEC} with reduced EPOR signaling in ECs developed smaller lesions in males, whereas EPOR^{iΔMΦ} with reduced EPOR signaling in MΦs had no difference. These results support the hypothesis that EPOR signaling in ECs is important in CNV. Further study is required to determine mechanisms involved in choroidal ECs and address potential tamoxifen effect on laser-induced CNV in female mice.

CONTROL ID: 3516796

SUBMITTER (NAME ONLY): Chung-Jung Chiu

TITLE: Exposure to Porphyromonas gingivalis and Modifiable Risk Factors Modulates Risk for Early Diabetic Retinopathy

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Chiu, A. Kantarci, T.E. Van Dyke, W. Shi, The Forsyth Institute, Cambridge, Massachusetts, UNITED STATES|M. Chang, The Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We hypothesized that exposure to Porphyromonas gingivalis (P. g.) increases the risk for early diabetic retinopathy (DR) and that the risk can be modulated.

Methods: 116 early DR cases were identified, and 116 non-DR controls were selected randomly by frequency matching for age, sex, race, and education from the US Third National Health and Nutrition Examination Survey. DR was assessed using non-mydratic fundus photographs and graded by trained graders using the Modified Airlie House Classification scheme and the Early Treatment for Diabetic Retinopathy Study severity scale. Serum P. g. immunoglobulin G (IgG) antibody (Ab) was measured in enzyme-linked immunosorbent assay units. Logistic regression was used to relate serum P. g. IgG Ab levels to the risk for early DR.

Results: Per tenfold increase in P. g. IgG Ab levels, there was an over 60% increased risk for early DR (odds ratio=1.64; 95% confident interval: 1.36 – 1.97) and a linear trend was noted for the estimated probabilities of early DR at various P. g. IgG Ab levels (p for trend=0.0053). The analysis also suggested that moderate alcohol consumption (less than 12 drinks in the past 12 months; p for interaction=0.0003) and maintaining a normal serum glycated hemoglobin level (HbA1c≤5.7 %; p for interaction<0.0001) helped reduce the P. g.-related DR risk.

Conclusions: The increased P. g.-related DR risk could be alleviated by managing alcohol consumption and maintaining a normal blood glucose level. Findings from this study provide new directions for developing novel therapeutics and prevention strategies for DR.

CONTROL ID: 3516837

SUBMITTER (NAME ONLY): Kenkichi Baba

TITLE: Environmental circadian disruption alters rod signaling and bipolar cell structure in mice

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Baba, I. Roberts, H. Duong, G. Tosini, Morehouse School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The circadian clock plays important roles in the regulation of retinal functions and physiology. Previous study has indicated that removal of the clock gene, Bmal1, from the neural retina alters photosensitivity, spectral identity and cone viability during aging in mice. Environmental circadian disruption (ECD, e.g. shift work, jet lag, living in Arctic etc.) has been shown to be deleterious for the health, but no study has investigated the effect of ECD in the retina. In this study we investigated the effect of ECD on the retina functioning and circuitry.

Methods: PER2::LUC and C57BL/6 mice were placed in a light tight isolated chamber and expose to ECD light cycles by advancing the time of light-on at 6 hours/week for 4 weeks. For control group, mice were exposed to a 12/12 Light/Dark cycle without any shifts. After 4 weeks of ECD, PER2::LUC mice (4-5 mo. old) were sacrificed and the retina, the retinal pigment epithelium (RPE) and the cornea were isolated and cultured for bioluminescence measurement. C57BL/6 mice (3 mo. old) were also exposed to ECD and subjected to both scotopic and photic electroretinogram (ERG) recording at the end of the fourth week. Retinal circuitry and morphology of C57BL/6 mice was evaluated by immunostaining (peanut agglutinin for cone photoreceptors, anti-PKC α for rod bipolar cell, anti-PSD95 for postsynaptic density).

Results: The circadian rhythm in PER2::LUC bioluminescence revealed that ECD altered circadian phase and period in retina and RPE but not in cornea. The amplitude of scotopic b-wave was significantly decreased in the mice subject to ECD. Consistently with this observation the dendric branching of rod bipolar cells was also reduced. The amplitude of photic ERG and the viability of the cone photoreceptors were not affected by ECD.

Conclusions: Our data indicate that the ECD affect the retinal circadian system, the retinal functioning and circuitry. Our results suggest that disruption of circadian rhythms may induce visual impairment.

CONTROL ID: 3516881

SUBMITTER (NAME ONLY): Toshihiro Kawai

TITLE: The sustained release of genipin with a Drug Delivery System inhibit an axial length elongation in the guinea pigs for 21 days

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kawai, T. Nakamura, Y. Kato, M. Nakatani, T. Ueno, Bioengineering Institute, R&D Div, Nidek Co., Ltd, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: We evaluated an inhibitory effect of axial length (AL) elongation on form deprivation (FD) model in guinea pigs after a natural collagen crosslinker, genipin sustained release formulation (GSRF) injection.

Methods: Thirty-seven 3-week-old pigmented guinea pigs underwent monocular FD with diffusers for 21 days. Genipin solution was injected into Tenon capsule on FD eyes. Experimental design was assigned to 4 groups: Control Group (n = 9) , Single dose Group (100 μ L of 0.5% genipin solution at the 0th day, n = 10) , Multiple dose Group (100 μ L of 0.5% genipin solution at days 0, 7, and 14, n = 8) , and GSRF Group (30 μ L of 1.4% GSRF at the 0th day, n = 10) .

AL was measured before and after FD by A-scan ultrasonography (NIDEK US-4000). Two-tailed Student's t-test was used for statistical analysis.

Results: The AL elongation was 0.38 ± 0.10 mm, 0.37 ± 0.12 mm, -0.02 ± 0.13 mm, and -0.03 ± 0.09 mm in the Control Group, Single dose Group, Multiple dose Group, and GSRF Group, respectively (mean \pm SD).

GSRF Group significantly inhibited the AL elongation compared to Control Group ($p = 0.005$) and Single dose Group ($p = 0.012$).

Furthermore, there was no significant difference in AL elongation between GSRF Group and Multiple dose Group ($p = 0.942$).

Conclusions: In the FD guinea pig model, single injection of GSRF showed an inhibitory effect on AL elongation for at least 21 days.

Further studies are needed to examine the safety and stability of GSRF.

CONTROL ID: 3516988

SUBMITTER (NAME ONLY): Phuoc-Hanh Le

TITLE: Growth of geographic atrophy in non-neovascular age-related macular degeneration measured using sub-RPE illumination on optical coherence tomography

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Le, S. Sharma, A. Babiuch, P.K. Kaiser, K. Baynes, C. Chen, M. Ramos, K. Barekatin, M.A. McDonald, D. Burton, J.P. Ehlers, S. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Geographic atrophy (GA) growth in patients with non-neovascular age-related macular degeneration (NNAMD) is often measured from color fundus photography (CFP) and fundus autofluorescence (FAF). There is limited research on using the native sub-RPE (retinal pigment epithelium) illumination on the Zeiss Cirrus system to estimate GA area. In this study we assessed the ability to measure progression of geographic atrophy using sub-RPE illumination as measured on optical coherence tomography.

Methods: This is a retrospective review of NNAMD patients and at least 2 year follow-up. One follow-up visit was chosen yearly throughout follow-up for analysis. GA area was measured using sub-RPE illumination area (IA) from the Advanced RPE Analysis feature of FORUM Viewer (Carl Zeiss Meditec, Inc.). This feature measures the area (mm²) exhibiting sub-RPE hyper-reflectance within a 2.5 mm radius from the fovea. Central subfield thickness (CST, µm) and logMAR visual acuity (VA) were also obtained for each visit.

Results: 1051 eyes of 529 patients were included in the study. 383 eyes (36.4%) converted to neovascular AMD. 790 NNAMD eyes were analyzed with a mean follow-up length of 5.4 years and a mean age of 77. Mean baseline

measurements for IA, CST, and logMAR VA were 1.81 mm^2 , $252.1 \text{ }\mu\text{m}$, and 0.34, respectively. The mean GA growth as measured by IA was $0.42 \text{ mm}^2/\text{year}$. The mean change in CST was $-3.48 \text{ }\mu\text{m}/\text{year}$, and the mean worsening of logMAR VA was 0.06/year.

Eyes were categorized into 5 subgroups by initial presentation of IA in mm^2 : 0-2 (n=575), 2-4 (n=88), 4-6 (n=45), 6-12 (n=65), and 12-18 (n=16). The mean growth rate of each subgroup was $0.37 \text{ mm}^2/\text{year}$ (± 0.55), $0.73 \text{ mm}^2/\text{year}$ (± 0.85), $0.53 \text{ mm}^2/\text{year}$ (± 1.06), $0.50 \text{ mm}^2/\text{year}$ (± 1.14), and $0.06 \text{ mm}^2/\text{year}$ (± 0.67), respectively. Those exhibiting the highest IA growth rate (top 10%, n=79) had a mean growth rate of $1.88 \text{ mm}^2/\text{year}$ (± 0.49).

Conclusions: Sub-RPE illumination area as measured on OCT can be used to estimate the growth of geographic atrophy in NAMD. IA growth correlates with worsening in logMAR VA and reduction in CST. These measurements should be compared to the current gold standards of GA measurement to determine if it can be used as an outcome measure of clinical research.

CONTROL ID: 3516992

SUBMITTER (NAME ONLY): Rozemarijn Verhoeven

TITLE: Nonclinical Development of AG-920, A Topical Ocular Anesthetic for Analgesia During Intravitreal Injection

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Verhoeven, Little Creek Research, North Carolina, UNITED STATES|M. Uram, American Genomics, New Jersey, UNITED STATES|A. Schupp, CMC Turnkey Solutions, New Jersey, UNITED STATES|G.D. Novack, PharmaLogic Development Inc, San Rafael, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: While topical anesthetic agents achieve excellent anesthesia on the external surface of the eye, they do not numb the internal aspect of the pars plana, which is extremely sensitive. Patients often report moderate to severe discomfort during intravitreal injections with currently available analgesics. Articaine is an amide local anesthetic that blocks the generation and conduction of nerve impulses and was selected because of its ability to penetrate soft tissue and bone. Articaine is approved for dental injection. Nonclinical IND-enabling studies were conducted with articaine ophthalmic solution (AG-920) to support clinical development.

Methods: AG-920 was evaluated in pharmacodynamic, ocular distribution, and ocular toxicity and toxicokinetic studies in rabbit, and articaine was evaluated for melanin binding in vitro. Animals received a single bilateral topical ocular administration of two 35 µL drops of AG-920 with a 30-second dosing interval. Efficacy was assessed by Cochet-Bonnet esthesiometry, plasma and ocular matrices were analyzed with LC-MS/MS methods, and ophthalmic exams, intraocular pressure (IOP), pachymetry, and ocular histopathology were included in the toxicity studies.

Results: Ocular anesthetic effect was observed for 20 minutes post-dose. Articaine did not significantly bind melanin, and ocular distribution data showed that AG-920 penetrated the globe following topical administration, delivering articaine to the target tissue and rapidly metabolizing to the inactive metabolite. Systemic exposure was minimal, peaked at 15 minutes, and declined quickly. AG-920 was well tolerated in the rabbit, with no tolerability or toxicity findings noted in any ocular or systemic toxicology endpoint. The No Observed Adverse Effect Level was the highest dose administered, 5.6 mg/eye (11.2 mg/animal or 6.6 mg/kg).

Conclusions: These data demonstrate that AG-920 induces ocular anesthesia, delivers articaine to the target ocular tissues, and was well tolerated in nonclinical studies. The ocular anesthetic activity and safety of AG-920 is currently being evaluated in human subjects (NCT04513652).

CONTROL ID: 3517039

SUBMITTER (NAME ONLY): Maria Parker

TITLE: Grading Criteria for Intraoperative Subretinal Surgical Imaging

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Subretinal injection is a commonly used method to deliver retinal gene therapy. Recording and evaluating parameters of the surgical procedure including the site of the injection(s), bleb locations, duration of injection and other parameters could compliment the understanding of treatment efficacy and safety. The goal of this study is to use our surgical experience with post FDA-approval voretigene neparvovec gene therapy to develop a grading procedure of the surgical steps using surgical videos and intra-operative optical coherence tomography (iOCT) that may be applied by the Casey Reading Center (CRC).

Methods: 12 eyes of six patients underwent pars plana vitrectomy with subretinal injection of voretigene neparvovec-rzyl (Luxturna®) in patients diagnosed with RPE65 mutation-associated retinopathy. The grading procedure was developed by reviewing intra-operative images and iOCT surgical videos. The following sequential steps of the surgery were carefully reviewed and analyzed: core vitrectomy, pre-bleb placement, vector injection, post-injection posterior pole exam and air-fluid exchange. A surgery evaluation grading form was developed in collaboration with vitreoretinal surgeons and utilized by an experienced grader for each surgical procedure.

Results: Video interpretation was useful in delineating bleb location, number of injections and total bleb injection time. Critical features of the procedure and dynamic intraoperative events could be identified and catalogued using the surgical videos (Table 1). Figure 1 shows representative still images captured from iOCT videos.

Conclusions: This standardized analysis of the surgical procedure with intraoperative video and iOCT is useful to study and understand the variability associated with subretinal surgery. This pilot study demonstrated that pre-blebs and blebs were visualized in all cases without apparent loss in volume, that a wide range of subretinal injection times could be accurately measured, and that foveal detachment could be confirmed in 64% of cases. Implementation of the CRC intraoperative surgical grading procedures may contribute to an improved understanding of efficacy and safety of other subretinal delivery of gene and cell-based therapies.

CONTROL ID: 3517045

SUBMITTER (NAME ONLY): Valerie Huang

TITLE: Qualitative Impact of Recycle Eyeglasses: Results from a Los Angeles County Department of Health Services Survey

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.P. Huang, M.E. Kim, S. Mohan, J.L. Berry, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|L.P. Daskivich, Los Angeles County Department of Health Services, Los Angeles, California, UNITED STATES|J.L. Berry, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cost of eyeglasses is variably covered by medical insurance and thus is a significant barrier for patients in lower socioeconomic classes. This study seeks to evaluate the efficacy of Recycle Vision (RV) at Los Angeles County + University of Southern California (LAC+USC) Medical Center Eye Clinic, a monthly clinic run by volunteer medical students that provides free donated eyeglasses, through patient quality surveys of RV clinic attendees.

Methods: A convenience sample of 30 patients were surveyed upon initial visit between August 1, 2019 to December 31, 2019 on their perceived level of ease in completing daily tasks prior to visiting RV clinic, level of satisfaction with previous glasses, and reasons why they previously did not seek eyeglasses. Patients' prescriptions were matched with available eyeglasses based on spherical equivalent and axis of astigmatism using Winglasses software algorithm; patients selected their glasses from these presented options based on subjective improvement of visual acuity. They then completed a phone follow-up survey 1 month after initial visit to gauge satisfaction with the services of RV and perceived changes in ease of completing daily tasks after visiting RV clinic.

Results: Of the 30 study participants, 90% received eyeglasses from RV, with average reported improvement in ease of daily activities of 3.96 (SD 1.13) on a scale of 1 to 5. 67% responded that if RV clinic did not exist, they would not have obtained glasses elsewhere. Cost was the most commonly cited barrier (70%); other barriers cited by patients are listed in Figure 1. On follow-up survey, on a scale of 1 to 5 (5 being greatest), the average likelihood of patients referring a friend/family member to RV was 4.07 (SD 1.14).

Conclusions: The majority of patients who visited RV received free eyeglasses and had subsequent improvement in their quality of life. This study demonstrates that programs offering free eyeglasses are effective at correcting refractive error and can offer a practical public health solution to improving functional visual acuity for underserved populations.

CONTROL ID: 3517061

SUBMITTER (NAME ONLY): Jyoti Khadka

TITLE: Trends in prevalence of eye diseases, utilisation of eye health care services and medications after entering residential aged care in Australia

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Eye diseases and visual impairment are common in older people accessing aged care services. Once admitted into a residential aged care facility, older people are less likely to have access to an eye health care service. The objective was to evaluate the burden of eye diseases, utilisation of eye health care services and ophthalmic medications among older people living in residential aged care facilities in Australia

Methods: A retrospective cross-sectional study was conducted using linked national aged care and health care data from the Registry of Senior Australians; a national cohort of people who entered permanent residential aged care facilities between 2008 and 2015. The prevalence (95% confidence interval (CI)) of eye diseases by year, eye health care services and ophthalmic medication use within a year of entry into the service were evaluated. Poisson regression models were used to estimate crude and adjusted prevalence ratio (PR) to evaluate change in prevalence of eye diseases over the study period.

Results: Of 409,186 people aged ≥ 65 years included in the study, 43.8% (95%CI, 43.7%-44.0%) had an eye condition. Among those 32.9% (95%CI, 32.7%-33.0%), 19.7% (95%CI, 19.6%-19.8%), 13.6% (13.5%-13.7%) and 8% (7.9%-8.1%) had a chronic eye disease, acute eye disease, glaucoma and cataract, respectively. Prevalence for any eye disease (PR: 0.99, $P < 0.001$), chronic (PR: 0.99, $P < 0.001$) and acute eye diseases (PR: 0.97) slightly decreased over the study period but remained stable for glaucoma (PR: 1.01, $P < 0.001$) and cataract (PR: 1.00, $P < 0.001$). Among those with any eye disease, less than half (46.5%) used at least one eye health service and more than two thirds (70.5%) used one ophthalmic medication. The most accessed eye health care service was optometric services (41.7%) and the most used ophthalmic medication was anti-infective eye drops (37.2%).

Conclusions: The burden of people with an eye disease accessing residential aged care service in Australia was high, however the use of eye health care services was low. Understanding the profile of older people with an eye disease in residential aged care facilities and their access to eye health care services and medications can provide evidence for appropriate resource allocation and evaluation of future eye health care needs in this population.

CONTROL ID: 3517122

SUBMITTER (NAME ONLY): Carla Lanca

TITLE: Rapid Myopic Progression in Early Childhood is Associated with Teenage High Myopia

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the association of early childhood progression of spherical equivalent (SE) with high myopia (HM) in teenagers in the Singapore Cohort of Risk factors for Myopia (SCORM).

Methods: We included 1051 SCORM children followed over a mean follow-up of 6.9 ± 1.0 years from baseline (6-11 years-old) until their teenage years (12-19 years-old). Cycloplegic autorefractometry and AL measurements were performed yearly. Three-year SE and axial length (AL) progression in childhood, baseline SE and AL, and parental myopia were evaluated using multivariable logistic or linear regression models, with predictive performance of risk factors assessed using the area under the curve (AUC). The outcomes in teenagers were HM ($SE \leq -5$ D), $AL \geq 25$ mm, SE and AL.

Results: At the last visit, 20% of teenagers had HM and 35% had $AL \geq 25$ mm. In multivariate regression analyses, every -0.3 D/year increase in 3-year initial SE progression and every 0.2 mm/year increase in 3-year initial AL progression were associated with a -1.14 D greater teenage SE and 0.54 mm greater teenage AL ($p < 0.001$). The AUC (95% CI) of a combination of 3-year SE progression, baseline SE and parental myopia for teenage HM was 0.98 (0.98-0.99). The AUC for 3-year AL progression, baseline AL and parental myopia for teenage $AL \geq 25$ mm was 0.95 (0.94-0.97).

Conclusions: Three-year myopia progression in early childhood combined with baseline SE or AL, and parental myopia, were good predictors of teenage HM. Clinicians may use this combination of factors to guide timing of interventions, potentially reducing the risk of HM later in life.

CONTROL ID: 3517220

SUBMITTER (NAME ONLY): Sarah Miller

TITLE: Global Preferred Practice Patterns for the Management of Ophthalmic Trauma

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Miller, M. Fliotsos, A. Chen, S. Zafar, F. Woreta, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite ocular trauma being an important cause of vision loss worldwide, there is currently a lack of consensus on the optimal management for traumatic injuries.

Our objective is to summarize global preferred practice patterns for the management of ophthalmic trauma.

Methods: An online survey was distributed to 42 trauma centers throughout 6 continents to assess institutional management practice patterns for eye emergencies including open globe injuries, hyphema, and orbital fractures.

Results: Responses were collected from 32 institutions (response rate 32/42, 76.2%) that were distributed across Asia (37.5%), North America (34.4%), South America (12.5%), Africa (9.4%), and Europe (6.3%). The respondents practiced ophthalmology for a median of 15.5 (IQR 9, 20) years after residency. The majority of institutions (n=24, 75.0%) have ophthalmology coverage 24 hours per day each day; of those that do not, 8 (100%) have on-call ophthalmology coverage available within one hour of notification. Most institutions (n=25, 78.1%) routinely administer pre-operative systemic antibiotics for open globe injuries, while 31.3% (n=10) administer pre-operative topical antibiotics. Oral ciprofloxacin was most preferred for systemic antibiotics (n=5, 15.6%), while moxifloxacin was most popular for topical (n=6, 18.8%), but respondents lacked consensus. Around half of the institutions also administer intraoperative antibiotics during the time of open globe injury repair (n=17, 53.1%), while many (n=29, 87.9%) administer topical steroids post-operatively. Regarding hyphema management, 93.8% (n=30) of responding institutions administer topical steroids, with prednisolone as the preferred medication for many (n=29, 90.6%). Respondents also disagreed on the routine disposition for hyphema patients, with 25.0% (n=8) admitting all hyphema patients to the hospital. For patients presenting with orbital fractures, 18 centers (56.3%) give systemic antibiotics to prevent infection, while 9 (28.1%) administer systemic steroids to quell inflammation.

Conclusions: Preferred management practices for ocular trauma-related eye emergencies vary widely. Evidence-based consensus guidelines for the management of ophthalmic trauma are needed to ensure the highest quality of management for all ophthalmic trauma cases.

CONTROL ID: 3517228

SUBMITTER (NAME ONLY): Ashley Zhou

TITLE: Retinal Characteristics in Eyes with Pathologic Myopia Among Individuals Self-Identifying Race as Black

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zhou, O. Nanegrungsunk, S.B. Bressler, T.Y. Liu, M. Sachdeva, A. Scott, A. Wenick, N.M. Bressler, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The neovascular form of age-related macular degeneration has been reported to be less frequent among individuals self-identifying as Black, suggesting that darker fundus pigmentation due to increased concentration of melanin within uveal melanocytes may affect retinal abnormalities. Whether this association is found in other retinal conditions, such as pathologic myopia (PM), has not been evaluated to our knowledge. Therefore, we investigated retinal characteristics of PM among patients who self-identified as Black.

Methods: Retrospective review of medical records was performed of adult patients who self-identified as Black with ICD codes consistent with PM followed by retina specialists at the Retina Division, Department of Ophthalmology, Johns Hopkins Hospital, Baltimore, MD. For a comparison group, a similar review was done for only one of the retina specialists, among patients with PM who did not self-identify as Black. Data collection included central subfield thickness (CST) on optical coherence tomography (OCT) based on the most recently obtained OCT between January 2005 and December 2019.

Results: Among 7 retina specialists, 428 patients were ICD coded for PM and 60 of those patients (14%) self-identified as Black. In comparison, 2,026 (22%) of all 10,012 patients seen in the Retina Division self-identified as Black in 2014. Of the 368 patients who did not self-identify as Black, 63 patients from a single retina specialist were used as a comparison group. OCT images were available for 35 (58%) of the 60 black patients and 46 (73%) of the 63 patients in the comparison group. Mean (\pm SD) CST in the right eye was 260 ± 77 μ m in the Black patients and 296 ± 98 μ m in the comparison group, while median (25th, 75th quartiles) CST in the right eye was 259 μ m (218, 280) in black patients and 281 μ m (256, 319) in the comparison group.

Conclusions: While the retrospective design and multiple confounding factors that can affect CST—such as retinal detachment, choroidal neovascularization, or retinal atrophy—preclude formal statistical analyses, these preliminary investigations suggest there may be differences in CST among patients with PM who self-identify as Black and those who do not. A prospective cross-sectional study is planned to characterize PM in these patient populations in greater detail.

CONTROL ID: 3517256

SUBMITTER (NAME ONLY): Aneesha Ahluwalia

TITLE: Influence of the Topographic Location of Geographic Atrophy on Vision-related Quality of Life in Nonexudative Age-related Macular Degeneration

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vision-related quality of life (VRQoL) is a patient-centered metric that is utilized to examine the impact of geographic atrophy (GA) in patients with age-related macular degeneration (AMD). However, little is known about the relationship between VRQoL and functional and structural GA biomarkers such as lesion area, and prior work has not accounted for GA lesion location. Thus, we examined the influence of the topographic distribution of GA on VRQoL.

Methods: We manually segmented GA lesions on color fundus photographs of 161 Age-Related Eye Disease Study (AREDS) participants with nonexudative AMD. For each participant, we calculated the total area of atrophy in the better eye (eye with least atrophy) and the worse eye (eye with most atrophy), as well as the area of atrophy in each of the nine subfields of the Early Treatment for Diabetic Retinopathy Study (ETDRS) grid for each eye. VRQoL had been measured using the National Eye Institute Visual Function Questionnaire (NEI-VFQ). We assessed associations between VRQoL and area of atrophy in each topographic region of the better and worse eye utilizing linear mixed-effects models while controlling for age, gender, and the presence of bilateral disease.

Results: There was no significant association between VRQoL and total area of atrophy in the better eye (β , -0.22; 95% confidence interval [CI], -0.84 to 0.40; $p = 0.49$) or worse eye (β , -0.27; 95% CI, -0.73 to 0.19; $p = 0.25$). When examining the topographic distribution of GA in the better eye, lower VRQoL was significantly associated with greater area of atrophy in the central 1-mm-diameter zone (β , -3.65; 95% CI, -6.85 to -0.45; $p = 0.026$), but not with area of atrophy in any of the other eight ETDRS subfields. In the worse eye, VRQoL was not significantly associated with area of atrophy in any topographic subfield.

Conclusions: In this cohort, area of atrophy in the central 1-mm-diameter zone of the better eye was the only measure of atrophy that was significantly associated with VRQoL. Although GA area in the worse eye is often used as a structural endpoint in clinical trials, this measure was not associated with VRQoL and, thus, may not fully capture the effects of disease progression or interventions on VRQoL in patients with GA secondary to nonexudative AMD.

CONTROL ID: 3517263

SUBMITTER (NAME ONLY): Jaime Tejedor

TITLE: Atropine in intermittent exotropia

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tejedor, Neuroscience, Universidad Autonoma de Madrid, Madrid, Madrid, SPAIN|J. Tejedor, F. Gutiérrez-Carmona, Ophthalmology, Hospital Universitario Ramon y Cajal, Madrid, Madrid, SPAIN|F. Gutiérrez-Carmona, Surgery, Universidad Alfonso X El Sabio, Villanueva de la Canada, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To investigate the effect of atropine on the evolution, control, deviation angle, suppression, and stereoacuity of intermittent exotropia (IXT)

Methods: In a pilot study, twenty-three patients with basic or simulated divergence excess (proximal convergence excess) IXT, aged 3-6 years old, and fair to poor control (≥ 3 by revised Newcastle Control Score, NCS) were randomly assigned to atropine once a week ($n=13$) or 2h of occlusion daily ($n=10$) in the eye preferred for fixation. Deviation angle (PD) by prism and alternate cover test (APCT) at distance and near after 45 minutes of occlusion, followed by +3.00 D lens at near, stereoacuity (log arcsec), suppression by Bagolini and Worth 4 dot test (WFD), were measured before and after 6 months of treatment. Deterioration in control (NCS), angle or stereoacuity were the outcome variables studied. Variables were compared using nonparametric tests (Mann-Whitney, Wilcoxon, Fisher exact test), and the influence of potential confounding variables was studied (including age, initial deviation and degree of deviation control, and initial stereoacuity) using nonparametric tests and bootstrap multiple regression.

Results: Amblyopia was not observed in this cohort. Deterioration, defined as 3-point increase in the revised NCS, impairment of 2-octave or more in stereoacuity or 8-PD increase in distance deviation by APCT, was not observed in any case during the study period. Change in APCT at distance (-3.07 vs -3 PD, $p=0.9$) and near (-2.30 vs -1.50 PD, $p=0.4$), change in stereoacuity at near (-0.04 vs -0.02 log arcsec, $p=0.7$), and in revised NCS (-1.3 vs -1.9, $p=0.2$) were not significantly different between the two groups. Although suppression was more frequently detected in the atropine than occlusion group by Bagolini (6/13 vs 2/10, $p=0.3$) and WFD at distance (5/13 vs 3/10, $p=0.6$) at near (4/13 vs 1/10, $p=0.3$), differences did not reach significance. Age, initial deviation, revised NCS, and stereoacuity were not significant confounding variables ($p=0.2$; 0.4; 0.1; 0.6, respectively).

Conclusions: Although these are preliminary data of a pilot study that require confirmation, atropine is not different from occlusion in the control of basic or simulated divergence excess IXT at short or middle term.

CONTROL ID: 3517279

SUBMITTER (NAME ONLY): Eleanor Nche

TITLE: OCCURRENCE OF HERPES VIRUSES IN MORPHOLOGICALLY NORMAL CORNEAL GRAFTS

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.N. Nche, A. Katzir, A. Solomon, I. Lavy, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|A. Solomon, Ophthalmology, Hebrew University of Jerusalem Faculty of Medicine, Jerusalem, Jerusalem, ISRAEL|D. Wolf, Virology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|A. Panet, Biochemistry, Hebrew University of Jerusalem Faculty of Medicine, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: To discover the occurrence of Herpes Simplex Virus type 1 and 2 (HSV) and Varicella Zoster Virus (VZV) DNA in transplanted corneas using polymerase chain reaction (PCR), and to determine the relationship between latent HSV-1 and VZV with the occurrence of herpetic eye disease in recipients and graft failure.

Methods: Eighty-eight (88) corneas were morphologically evaluated before surgery by slit-lamp examination and CellChek® specular microscopy. Excluded corneas were tested for HBV, HCV, and HIV by donor serological assessment, a low cell count (under 2,300 cells /mm³), corneal scars, and abnormal endothelial cell morphology. Transplanted corneas were sampled for HSV 1,2 and VZV DNA by PCR. All eyes transplanted with the donor corneas were evaluated and followed for corneal transparency, endothelial cells morphology, and number by specular microscopy signs for ocular inflammation, intraocular pressure, and anterior segment optical coherence tomography (OCT).

Results: HSV-1 DNA was detected in five transplanted corneas out of the 88 that were examined (5.7%). HSV-2 was not detected in any cornea, and VZV in one cornea out of 82 examined (1.2%). Four of the positive corneas were used in descemet membrane endothelial keratoplasty (DMEK) surgeries. One for a combined DMEK/anterior vitrectomy/ iridoplasty surgery and one as a tectonic graft. One recipient (16.7%) developed herpes dendritic epitheliopathy and keratouveitis 12 months after transplant though the graft remained clear after treatment. One cornea was used for a tectonic graft and stayed edematous at 20 months follow - up. The rest of the corneas stayed clear.

Conclusions: Herpes viruses, especially HSV-1, may be PCR DNA positive in morphologically normal donor corneas. Recipients of herpes positive corneal grafts are at risk for herpetic eye disease. Further evaluation with a bigger sample size and a longer follow-up time is needed to establish a clinical correlation to donor graft survival and to recipient ocular infection with HSV. Positive samples will be evaluated for reverse transcriptase PCR (RT-PCR) to evaluate HSV latency and infectivity.

CONTROL ID: 3517296

SUBMITTER (NAME ONLY): Dominic Grisafe

TITLE: The Association of Traffic-Related Air Pollution and Perfusion of the Peripapillary Retina in African Americans

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Grisafe, M. Franklin, D. Noursome, R. McKean-Cowdin, B. Burkemper, Preventive Medicine, University of Southern California, Los Angeles, California, UNITED STATES|M. Torres, R. Varma, Southern California Eye Institute, CHA Hollywood Presbyterian Medical Center, Los Angeles, California, UNITED STATES|R. Chang, J. Lee, G. Richter, Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: African Americans have a greater prevalence of open angle glaucoma (OAG) and exposure to traffic-related air pollution (TRAP). We investigated whether glaucomatous vascular changes were related to exposure of nitrogen dioxide (NO₂) and particulate matter with aerodynamic diameter < 2.5 µm (PM_{2.5}) in the African American Eye Disease Study (AFEDS).

Methods: The AFEDS is a cross-sectional, population-based cohort study conducted from 2014–2018 of 6,347 self-reported African Americans aged 40 years or older residing in 32 US census tracts of Inglewood, California. Participants completed in-home interviews and detailed eye exams including optical coherence tomography angiography (OCTA) imaging. Perfusion of radial peripapillary capillaries in healthy eyes was measured as vessel area density (VAD) calculated over 6x6 mm images centered on the optic nerve head. Exposures to NO₂ (ppb) and PM_{2.5} (µg/m³) were estimated from spatiotemporal generalized additive models created using the EPA's Air Quality System data. Hierarchical linear regression models of VAD on NO₂ and PM_{2.5} were progressively adjusted for (1) sex and age; (2) education, employment, and income; (3) body mass index, glycated hemoglobin, duration of diabetes, systolic blood pressure, ever-smoking, and health insurance; and (4) axial length, OCTA signal strength, and vision insurance.

Results: AFEDS participants (n = 1,009) were on average 58.3 years old, 64.2% female, 50% employed, 61% earned ≥ \$40,000, and had 14.3 years of education. In the first three hierarchical models, lower VAD was associated with mean NO₂ and PM_{2.5} exposure (P < 0.05). Associations in the fully adjusted models were not significant, but in the expected direction; VAD was -0.160 (95% CI: -0.377, 0.056) percent lower per 10-ppb increase in NO₂, and -0.271 (95% CI: -0.588, 0.045) percent lower per 10 µg/m³ increase in PM_{2.5}. Differences in VAD equated to an increased age of 1.6 years for NO₂ and 2.7 years for PM_{2.5}.

Conclusions: We found an inverse relationship between peripapillary perfusion and TRAP after adjusting for sociodemographic and clinical covariates. Associations further adjusted for ophthalmic measures were not significant, which may be due to a small true effect and overadjustment. These findings complement an emerging body of evidence that TRAP may be related to eye disease and could contribute to disparities in OAG for African Americans.

CONTROL ID: 3517440

SUBMITTER (NAME ONLY): Christopher Santilli

TITLE: Change in Hemoglobin A1c Levels After Cataract Surgery.

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Santilli, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|J. Murray, K.R. Armbrust, Ophthalmology and Visual Neurosciences, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|K.R. Armbrust, Eye, Minneapolis VA Health Care System, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Impaired visual function may contribute to suboptimal glycemic control in diabetes mellitus. However, since prior studies examining changes in hemoglobin A1c (HbA1c) after cataract surgery have shown mixed results, it is unclear whether visual dysfunction from a clinically significant cataract affects glycemic control. We performed a retrospective, observational study to evaluate whether HbA1c levels change after cataract surgery.

Methods: As a pilot study we evaluated HbA1c in all patients who underwent cataract surgery at our institution in 2019 with HbA1c levels drawn both 0-90 days prior to and 90-180 days after cataract surgery. The primary outcome measure was the difference in HbA1c before and after cataract surgery for all study subjects. We performed subgroup analysis by age, based on the average, and in those with a pre-operative HbA1c ≥ 8 . The pre-operative HbA1c cut off ≥ 8 was selected before analysis of data. HbA1c levels before and after cataract surgery were compared using a paired, two-tailed t-test in SPSS. We then expanded this study to include all patients who underwent cataract surgery from 2015-2019 with the same inclusion criteria as the pilot study in addition to HbA1c levels 690-780 days after surgery, if available.

Results: In the pilot study the mean and median ages of 102 study subjects was 71 years. There were 97 males and 5 females. Pairwise comparison of pre- versus post-operative HbA1c showed significantly lower post-operative HbA1c, with more reduction in older subjects and those with higher pre-operative HbA1c (Table 1). In the expanded study the mean and median ages of 436 subjects were 71.8 and 71 years, respectively. There were 424 males and 12 females. Pairwise comparison of pre- versus post-operative HbA1c showed a trend toward HbA1c reduction at 90-180 days, with a significant reduction in older subjects and those with higher pre-operative HbA1c, and this effect was sustained 690-780 days after surgery (Table 2).

Conclusions: Glycemic control improved after cataract surgery, with more improvement in older subjects and subjects with higher pre-operative HbA1c values.

CONTROL ID: 3517483

SUBMITTER (NAME ONLY): Yujia Zhou

TITLE: Survival in patients with neovascular glaucoma following tube shunt implant or cyclodestructive procedures

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhou, S. Coleman, J. Boysen, M.L. Pansegrau, M. Wright, E.F. Carpel, K.R. Armbrust, University of Minnesota System, Minneapolis, Minnesota, UNITED STATES|M.L. Pansegrau, M. Wright, E.F. Carpel, K.R. Armbrust, Minneapolis VA Health Care System, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the survival of patients with neovascular glaucoma (NVG) after tube shunt implant or cyclodestructive procedure, and to assess whether clinical factors are predictive of survival.

Methods: A retrospective chart review was performed of patients with NVG who underwent tube shunt implant and/or cyclodestructive procedures (cyclophotocoagulation and cyclocryotherapy) between January 2002 and December 2019 at the Minneapolis Veterans Affairs Medical Center (VAMC). Patient survival was compared to the age and gender matched Minnesota population. Univariate and regression analyses were used to evaluate the correlation of specific clinical parameters with survival.

Results: A total of 39 patients and 41 eyes were included. Tube shunt alone was implanted in 30 (73.2%) eyes, cyclodestruction alone was performed in 9 eyes (22%), and 2 eyes (4.9%) underwent both procedures. The mean (median) age at first operation was 70.2 (70) years. The most common etiology of NVG was diabetic retinopathy (DR) in 20 eyes (48.8%), followed by central retinal vein occlusion in 14 eyes (34.1%). Diagnoses of cardiovascular diseases and diabetes were found in 38 patients (97.4%) and 33 patients (84.6%), respectively. At post-operative 5-year follow-up, survival rate of the NVG patients was 56% compared to 80% in controls. There was no difference in survival between patients with NVG secondary to DR and those from other etiologies, although patients with NVG caused by DR had their first procedure at a younger age ($p = 0.036$). Preoperative visual acuity, maximum intraocular pressure (IOP), creatinine, HbA1c, and postoperative IOP at 6 months were not associated with survival.

Conclusions: In the Minneapolis VAMC population, NVG patients had a lower survival rate than the matched Minnesota population. Most patients had vasculopathic risk factors. The etiology of NVG was not associated with survival. Ophthalmologists should consider the shorter survival when planning surgery for NVG patients and recommend a multi-disciplinary approach to optimize their care.

CONTROL ID: 3517497

SUBMITTER (NAME ONLY): Rodrigo Carlos De Oliveira

TITLE: Perlecan-associated defective epithelial basement membrane regeneration in rabbit corneas after fibrosis-inducing epithelial-stromal injury

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. De Oliveira, G. Tye, L. Sampaio, T.M. Shiju, S.E. Wilson, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|M.R. Santhiago, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|J. DeDreu, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|A. Menko, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study epithelial basement membrane (EBM) regeneration after photorefractive keratectomy (PRK) injuries that healed with and without stromal fibrosis.

Methods: One hundred sixteen rabbits had either no surgery, -4.5 diopter (D) PRK, or -9D PRK. Immunohistochemistry (IHC) was performed on cryofixed corneas at time points from unwounded to eight weeks, with four corneas at each time point in each group. Multiplex IHC was performed for laminin alpha 5, laminin beta 3, perlecan, and/or nidogen-1, keratocan, vimentin, and alpha-smooth muscle actin (SMA). Corneas at the one month peak for myofibroblast and fibrosis development were evaluated using Imaris 3D analysis.

Results: Laminin alpha-5, laminin beta 3, and nidogen-1 were incorporated into nascent EBMs. Defective perlecan incorporation in the nascent EBM was noted in corneas that developed large numbers of myofibroblasts and fibrosis in the anterior stroma.

Conclusions: Defective incorporation of transforming growth factor (TGF)-beta-modulating perlecan into the regenerating EBM by subepithelial myofibroblasts, and likely their precursor cells, underlies the development of stromal fibrosis after corneal injury.

CONTROL ID: 3517522

SUBMITTER (NAME ONLY): Jianhua Wang

TITLE: Improvement of retinal tissue perfusion after circuit resistance training in healthy older adults

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Wang, J. Zhang, Q. Chen, H. Jiang, Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|J. Zhang, Q. Chen, School of Ophthalmology and Optometry, Wenzhou Medical University, CHINA|K. Strand, M. Totillo, J. Signorile, Department of Kinesiology and Sports Science, University of Miami, Coral Gables, Florida, UNITED STATES|H. Jiang, Department of Neurology, University of Miami Miller School of Medicine, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the retinal tissue perfusion (RTP) and its relation to cognitive function in healthy older people after an 8-week high-speed circuit resistance training program (HSCT).

Methods: Eleven subjects in the HSCT group and seven age-matched non-training controls (CON) were recruited. The HSCT group trained 3 times per week for 8 weeks, while CON performed no formal training. One eye of each subject in both groups was imaged at baseline and at an 8-week follow-up, using a Retinal Function Imager to measure retinal blood flow (RBF). Retinal tissue perfusion (RTP) was calculated as RBF divided by the corresponding tissue volume. Cognitive function was assessed during both visits using the NIH Toolbox Fluid Cognition Battery.

Results: RTP was $2.99 \pm 0.91 \text{ nl s}^{-1} \text{ mm}^{-3}$ (mean \pm SD) at baseline and significantly increased to $3.77 \pm 0.86 \text{ nl s}^{-1} \text{ mm}^{-3}$ after training ($P < 0.001$) in the HSCT group, reflecting an increase of 26%. In the HSCT group, the Pattern Comparison Processing Speed Test (PAT) and Fluid Cognition Composite Score (FCS) were significantly increased after HSCT ($P = 0.01$). Furthermore, the changes in Flanker Inhibitory Control and Attention Test (FLNK) were positively correlated to increases in RTP ($r = 0.80$, $P = 0.003$).

Conclusions: This is the first prospective study to demonstrate that the increased RTP after HSCT was related to improved cognition in cognitively-normal elders, indicating RTP could be an imaging marker for monitoring cognitive changes due to physical activity in the elderly.

CONTROL ID: 3517526

SUBMITTER (NAME ONLY): Etienne Schönbach

TITLE: Changes of Fixation Stability and Fixation Location over 24 Months in Stargardt Disease: the ProgStar Study

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Stargardt Disease type 1 (STGD1) is the most common inherited macular degeneration. Several treatment approaches including pharmacotherapy, gene therapy, and stem cell therapy are in clinical trials. Fixation stability (FS) and location (FL) describe important dimensions of visual function but there is limited data on how they are affected by disease over time. Here, we present longitudinal changes of FS and FL over 24 months in STGD1 from the international, prospective, multicenter ProgStar study (NCT01977846).

Methods: Over 5 study visits every 6 months, patients with a molecular diagnosis of STGD1 completed separate fixation exams of roughly 30 seconds using the MP-1 Microperimeter (Nidek). FS was expressed through the 68.3 %-Bivariate Contour Ellipse Area (BCEA), FL through the distance of the barycenter of all fixation events from the fovea as determined on OCT images.

Results: At baseline, 239 patients (105 males, 44 %) and 459 eyes with a median age of 32 years (mean \pm SD, 33.8 \pm 15.2 years) were included. The baseline mean log BCEA was $0.75 \pm 1.29 \log \text{deg}^2$ and the mean FL was $6.45 \pm 4.52 \text{ deg}$. Although the mean log BCEA did not monotonically increase from visit to visit, the overall yearly increase in log BCEA was $0.124 \log \text{deg}^2$ (99% CI, 0.063-0.185). It was not different during the first year compared to the second year. The increase was faster in eyes without flecks outside of the vascular arcades and depended on baseline BCEA. Looking at the subset of the better of two eyes resulted in a yearly increase in log BCEA of $0.138 \log \text{deg}^2$ (99% CI, 0.045, 0.230) and confirmed the observed association with baseline BCEA.

Conclusions: Fixation parameters may serve as useful secondary endpoints to longitudinally describe visual dysfunction.

CONTROL ID: 3517553

SUBMITTER (NAME ONLY): Sachin Phakey

TITLE: Effect of zoster vaccination on rates of herpes zoster ophthalmicus and herpes zoster in Australia

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Phakey, S. Rogers, L.L. Lim, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|A.J. Hall, Department of Ophthalmology, Alfred Health, Melbourne, Victoria, AUSTRALIA|A.J. Hall, Department of Surgery, Monash University, Clayton, Victoria, AUSTRALIA|L.L. Lim, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Few population-based studies examine the effect of zoster vaccination on rates of herpes zoster ophthalmicus (HZO) and herpes zoster (HZ). The aim of this retrospective time-trend analysis was to examine rates of HZO and HZ in Australia over time, both in the immunocompetent and immunocompromised. We hypothesised HZO and HZ rates would decrease in immunocompetent individuals following the introduction of the live-attenuated zoster vaccine (Zostavax[®]) on Australia's National Immunisation Program (NIP) in 2016. The NIP allows 70-79-year-olds to receive Zostavax[®] for free. The recombinant subunit zoster vaccine (Shingrix[®]) is not available via Australia's NIP.

Methods: We analysed all antiviral prescriptions dispensed for the treatment of HZO and HZ in Australia from 1994 to 2019, as recorded by the Australian Pharmaceutical Benefits Scheme and Repatriation Pharmaceutical Benefits Scheme. We calculated annual prescription rates to descriptively explore HZO and HZ incidence over time.

Results: Amongst immunocompetent individuals, rates of HZO and HZ increased 1.90-fold in the period 1998-2015, before decreasing 0.48-fold between 2016-2019 (Figure). Amongst immunocompromised individuals, rates of HZ increased throughout the study period, rising 8.50-fold between 2006 (year data first available) and 2019.

Conclusions: The introduction of Zostavax[®] on Australia's NIP coincided with reduced rates of HZO and HZ in immunocompetent individuals, highlighting the likely beneficial effect of zoster vaccination within the Australian population. Ophthalmologists should remain alert to HZO in immunocompromised patients, whose immune status may be a contraindication to live zoster vaccination, with zoster rates rising amongst the immunocompromised, even after the introduction of Zostavax[®].

CONTROL ID: 3517560

SUBMITTER (NAME ONLY): Vered Horwitz

TITLE: Different mRNA expression patterns in cornea and limbus during the clinical course of sulfur mustard induced ocular injury in the rabbit model

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Horwitz, I. Egoz, M. Cohen, H. Gutman, R. Gez, T. Kadar, S. Dachir, A. Gore, Department of Pharmacology, Israel Institute for Biological Research, Ness Ziona, ISRAEL]

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ABSTRACT BODY:

Purpose: The sight threatening sulfur mustard (SM) induced ocular injury presents specific symptoms for each clinical stage. While the acute injury is characterized by erosions and severe inflammation, the chronic or late pathology that develops only in part of the eyes, is clinically expressed by corneal epithelial defects and neovascularization (NV). The pathological mechanisms underlying this injury are still under research and treatment is insufficient. Based on the results of RNA sequencing of corneas at 4 weeks post exposure, 5 mRNAs that were significantly elevated and were not studied previously in the context of SM-induced ocular injury were selected for further research. The expression pattern in both the cornea and the limbus at additional time points during the course of the injury was studied in the rabbit model.

Methods: Rabbit eyes were exposed to SM vapor and a clinical follow-up was carried out up to 4 weeks. Corneal and limbal tissues were collected at 48h, 1w and 4w post exposure and MMP-1, MMP-10, IRS-1, NGF and IL-33 mRNA levels were measured using real time PCR.

Results: Typical SM-induced ocular injury developed, including an acute injury that was partially resolved within a week in all of the exposed eyes, followed by an irreversible late pathology in 50%-80% of the eyes, beginning at 2w. Significant elevations were seen in the mRNA levels of the studied factors, however each factor presented a unique expression pattern. At the peak of the acute injury, at 48 h, significantly higher levels of corneal and limbal MMP-1, MMP-10 and NGF and corneal IRS-1 were found. At 1w, corneal and limbal MMP-1 and MMP-10 and corneal NGF, IRS-1 and IL33 levels were significantly elevated compared to naïve. During the late pathology, at 4w, significantly higher levels of corneal MMP-1, MMP-10, NGF and IRS-1 were found, with no change in the limbal levels.

Conclusions: The mRNA levels of the studied factors changed throughout the dynamic clinical course of the ocular injury and between the cornea and the limbus, mainly during the late pathology. The results suggest a possible involvement of these factors in the pathological processes in different ocular tissues at specific stages of the injury and may point out towards stage-specific therapeutic options.

CONTROL ID: 3517620

SUBMITTER (NAME ONLY): Peter Zhao

TITLE: Factors Affecting Rates of Genetic Testing for Inherited Retinal Degenerations

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.Y. Zhao, K.E. Branham, D. Schlegel, A.T. Fahim, T. Jayasundera, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Factors affecting rates of genetic testing for inherited retinal degenerations have not been characterized. We analyzed effect of launch of the My Retina Tracker Genetic Testing Study (MRT-GTS) research registry and associations with patient characteristics.

Methods: We performed retrospective chart review of new patients evaluated at an eye center between July 2016 and June 2018, analyzing rates of genetic testing 12 months pre- and post-launch of MRT-GTS, which launched locally in June 2017. We determined odds ratios (ORs) of association between patient characteristics and rates of obtaining genetic testing. We examined the proportion of test results returned within 90 days of the initial clinic evaluation.

Results: Among 369 patients (age 39.5 years, SD 20.8), 144 were evaluated in the pre-MRT-GTS period and 225 in the post-period. The pre-MRT-GTS rate of successfully obtaining testing was 51.4% (95% CI, 42.6–60.2%). Post-launch, the testing rate increased by 28.9 percentage points (95% CI, 16.7–41.1%; $P < .001$). Patient factors that increased odds of testing were eligibility for MRT-GTS (OR, 14.15; 95% CI, 7.36–27.24; $P < .001$) and worse visual acuity (logMAR +1.0) in the better-seeing eye (OR, 1.92; 95% CI, 1.27–2.91; $P < .01$). Odds were decreased for those identifying as African-American (OR, 0.10; 95% CI, 0.04–0.24; $P < .001$) or other race (OR, 0.37; 95% CI, 0.15–0.91; $P < .05$), and when the primary language was not English (OR, 0.13; 95% CI, 0.03–0.55; $P < .01$). The proportion of test results reported within 90 days was 81.5% (95% CI, 74.8–86.4%) when eligible for MRT-GTS and 48.1% (95% CI, 35.6–58.1%) when not eligible ($P < .001$).

Conclusions: Demographic and clinical factors affect decisions to pursue genetic testing. There was an increase in testing rates after launch of MRT-GTS. Collaborations between non-profit organizations, industry, and the public sector to fund testing help to identify the genetic cause of disease, a critical stepping stone to developing therapies.

CONTROL ID: 3517647

SUBMITTER (NAME ONLY): Cody Lo

TITLE: Risk of Requiring Glaucoma Surgery following Intravitreal anti-VEGF Injections: A Case-Control Study

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lo, B. Zack, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: It has been suggested that intravitreal anti-VEGF injections (IVIs) can accelerate progression of glaucoma but the risk of any IVI exposure on needing glaucoma surgery is not clear. This case-control study determines the increased risk associated with IVIs and the need for glaucoma surgery.

Methods: Participants were collected from a glaucoma specialist practice in British Columbia, Canada with a diagnosis of glaucoma, glaucoma suspect, or ocular hypertension and seen between January 1, 2017 – December 31, 2019. Cases were defined as having at least one glaucoma procedural intervention (not combined with cataract surgery) within this timeframe. Controls had no surgical interventions for their glaucoma and were recruited in a 2:1 ratio to cases with age and sex matching. Clinical data was collected for each participant's most recent follow up visit within the timeframe including whether the participant had any previous exposure to IVIs. Rates of previous IVI exposure amongst surgical glaucoma cases were compared to non-surgical controls to calculate an odds ratio. Ethics approval was obtained from the University of British Columbia ethics board.

Results: A total of 133 surgical glaucoma cases and 266 non-surgical glaucoma controls were recruited with no significant difference in demographic information. The average age in years being 71.9 in cases and 73.8 in controls. The cohort was 57% male in cases and 53% in controls. The distribution of glaucoma diagnoses and retinal indications for IVIs were similar amongst both cases and controls. Cases used a significantly ($P < 0.001$) larger number of topical medications (3.54) compared to controls (2.27). There was also a significant ($P < 0.001$) difference in average IOP between cases (25.69 mm Hg) and controls (15.03 mm Hg). The crude odds ratio for glaucoma surgery amongst those with any IVI exposure was 6.69 (95% CI 3.52-12.73). The adjusted odds ratio using multivariate logistic regression for this association was 8.49 (95% CI 4.20-17.18) when adjusting for age, sex, and medical comorbidities such as hypertension and diabetes.

Conclusions: This study demonstrates that any previous exposure to IVIs is associated with a significantly higher risk of glaucoma surgery amongst patients with glaucoma. As the use of IVIs continues to increase, it is important for providers to be aware of this risk particularly in those with pre-existing glaucoma.

CONTROL ID: 3517648

SUBMITTER (NAME ONLY): Monika Grudzinska Pechhacker

TITLE: Natural history study of visual function in patients with BBS1- and BBS10-related retinal degeneration.

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Grudzinska Pechhacker, A. Vincent, E. Heon, Ophthalmology, The Hospital for Sick Children, Toronto, Ontario, CANADA|M. Grudzinska Pechhacker, Paediatric Ophthalmology, St Erik Eye Hospital, SWEDEN|S.G. Jacobson, T.S. Aleman, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|A.V. Drack, Institute for Vision Research, University of Iowa, Iowa, UNITED STATES|M. Di Scipio, E. Tavares, E. Saleh, Genetics and Genome Biology, The Hospital for Sick Children, Toronto, Ontario, CANADA|I. Stubbe, B. Leroy, Ophthalmology, Ghent University Hospital, Ghent, BELGIUM|J.L. Duncan, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|H. Dollfus, INSERM, Universite de Strasbourg, Strasbourg, FRANCE|A.L. Vincent, Ophthalmology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|B. Leroy, Children's Hospital of Philadelphia, Pennsylvania, UNITED STATES|J. Maynes, The Hospital for Sick Children, Toronto, Ontario, CANADA|F. Munier, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Knowing the natural history of vision loss is key to select the appropriate endpoints and best interpret response to treatments. The purpose of this study was to compare the natural history of visual function change in a cohort of patients affected with retinal degeneration due to biallelic variants in BBS1 and BBS10 genes.

Methods: Design: Global, multicenter, retrospective chart review.

Patients were recruited from 9 participating academic centers from 6 countries (Belgium, Canada, France, New Zealand, Switzerland and USA). Inclusion criteria were: 1) female or male subjects with a clinical diagnosis of retinal dystrophy, 2) molecularly confirmed biallelic disease-causing variants in BBS1 or BBS10 and 3) measures of visual function for at least one visit. Retrospective data collected included age, onset of symptoms, visual acuity (VA) and genotypes. When possible we also collected data on refractive error, optical coherence tomography (OCT), kinetic perimetry (VF), electroretinography (ERG), and the systemic phenotype.

Results: 67 individuals had biallelic pathogenic variants in BBS1 (n=38; 20 females and 18 males); or BBS10 (n=29; 14 females and 15 males). Overall, the mean follow-up period was 10 years (range 0-33.9 years). Missense variants were the most common for BBS1-patients, and frameshift for BBS10. Extraocular signs were documented in 97% of BBS1-patients and in 92% of BBS10-patients. When ERGs were recordable, rod-cone dystrophy (RCD) was observed in 82% (23/28) of BBS1- and 73% (8/11) of BBS10-patients; cone-rod dystrophy (CORD) was seen in 18% of BBS1 only, and cone dystrophy (COD) was only seen in three BBS10-patients. ERGs were non-detectable earlier in BBS10-patients than in BBS1-patients. Similarly, VA and VF declined more rapidly in BBS10-compared to BBS1-patients.

Conclusions: Retinal degeneration appears earlier and is more severe in BBS10-patients compared to those with BBS1 variants. Non syndromic retinal degeneration was observed in both groups. The course of change of visual function appears to be related to genetic subtypes of BBS.

CONTROL ID: 3517665

SUBMITTER (NAME ONLY): Aaron Brown

TITLE: Automated Machine Learning vs. Inception for the Autonomous Detection of Disc Hemorrhage

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Brown, N. Chadha, K. Vinod, L.R. Pasquale, Department of Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|A. Harris, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|H. Cousins, Stanford University School of Medicine, Stanford, California, UNITED STATES|M. Coote, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|C. Cousins, Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|F. Topouzis, V. Kilintzis, Laboratory of Research and Clinical Applications in Ophthalmology, Aristoteleio Panepistemio Thessalonikes Tmema Iatrikes, Thessaloniki, Central Macedonia, GREECE|

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ABSTRACT BODY:

Purpose: To compare automated machine learning (AutoML) to transfer learning (Inception) for disc hemorrhage (DH) identification.

Methods: This study was a retrospective analysis of fundus photographs obtained from the Ocular Hypertension Treatment Study, New York Eye and Ear Infirmary of Mt. Sinai, Massachusetts Eye and Ear, Thessaloniki Eye Study, and GONE datasets. High magnification fundus photographs of different resolutions and sources centered on the optic disc were included. Ground truth was established by the consensus of grades from two masked glaucoma specialists. Images were graded independently and disagreements in grading were resolved via adjudication, ungradable images were excluded. The complete dataset was split into training (80%), validation (10%), and test (10%). An automated machine learning model (AutoML), which tunes model hyperparameters without user engagement, was trained to distinguish disc hemorrhage (DH) positive and DH negative images. After training and validation, AutoML evaluated the model against a subset of test images, providing Precision and Recall data for each confidence threshold from 0 to 1. This process yields a binary classification model that predicts DH based on the returned probability at a given confidence threshold. A hard-coded convolutional neural network model based on the widely used InceptionV3 architecture was trained on the same data set. The performance of each model on an identical test set was then evaluated.

Results: A total of 897 images were included, 314 DH positive and 583 DH negative. The AutoML model achieved an area under the precision-recall curve (AUPRC) of 0.923, a sensitivity of 85% and specificity and 86%. For the hard-coded deep learning model, AUPRC was 0.82 with a sensitivity and specificity of 83% and 60%, respectively. The Inception model attention maps help visualize what parts of an image contributed most to a prediction (Fig 1).

Conclusions: The AutoML algorithm performance was high and showed good concordance with a traditional hard-coded algorithm. AutoML offers a low clearance method for clinicians without programming expertise to develop and deploy deep learning solutions.

CONTROL ID: 3517678

SUBMITTER (NAME ONLY): Daniel Roberts

TITLE: Smoking, Lung Disease and Other Factors Associated with the Long Anterior Zonule (LAZ) Trait

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.K. Roberts, T.L. Newman, J.M. McMahon, C.E. Morettin, M.F. Roberts, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The long anterior zonule (LAZ) trait is characterized by anomalous zonule-like fibers present on the anterior lens capsule central to the normal zonule insertion zone. At least two varieties have been described. One rare type is associated with late-onset retinal degeneration (L-ORD) and caused by a S163R mutation in the C1q tumor necrosis factor-related protein 5 gene (C1QTNF5/CTRP5). The other variety is idiopathic, may have prevalence near 2%, and has predilection for hyperopic females with age >50 years. Both varieties may exhibit pigment dispersion, and there is potential association with glaucoma. With an ongoing study, we report further on potential health associations with LAZ.

Methods: Several practitioners in an urban, academic primary eye care center in Chicago, IL, USA evaluated consenting patients for LAZ from 2011 to 2018. To supplement clinical findings, questionnaires were used to obtain information related to lifestyle and demographics. Variables assessed included ocular and general health status, education, smoking, alcohol use, and height/weight for calculation of body mass index. Multivariate logistic regression was used to assess relationships to LAZ presence.

Results: The analysis included 3,494 total subjects (65.0% female, 82.3% African American), with mean age of 50.6 ± 15.4 years (18-98 years). Subjects with >trace LAZ in either eye (N=131, 80.2% female, 90.8% African American) with mean age of 63.4 ± 11.7 years (35-92 years). Mean sphere-equivalent refractive error of LAZ subjects was $+0.48D \pm 2.28D$ (-10.44D to 7.69D) vs. $-0.94D \pm 2.8D$ (-28.38D to 7.56D) for those without LAZ. Controlling for age, female gender, and hyperopic refractive error, strongest associations occurred with elevated body mass index, hypertension, and smoking in packyears ($P < 0.05$). In addition, there was strong association with non-asthma-related lung disease, with LAZ subjects being 2.5x (OR=2.52; 95% CI=1.35 to 4.72, $P=0.004$) more likely to exhibit lung disease than people without LAZ.

Conclusions: In addition to strong associations with age, female gender, and hyperopic refractive error, this analysis further suggests LAZ has relationship to adverse health factors including elevated body mass index, hypertension, history of smoking and non-asthma-related lung disease.

CONTROL ID: 3517725

SUBMITTER (NAME ONLY): Ruy Missaka

TITLE: Intraretinal cystoid spaces in acute Vogt–Koyanagi–Harada disease

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.F. Missaka, M. Goldbaum, C.G. Machado, F. Silveira Souto, M.M. Lavezzo, P.F. Nóbrega, M.K. Oyamada, C.E. Hirata, J.H. Yamamoto, Ophthalmology, University of São Paulo, São Paulo, São Paulo, BRAZIL|V.M. Sakata, Ophthalmology, Universidade Federal do Parana, Curitiba, PR, BRAZIL|

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ABSTRACT BODY:

Purpose: To present intraretinal cystoid spaces observed in spectral-domain optical coherence tomography (SD-OCT) images of eyes with acute Vogt-Koyanagi-Harada disease (VKHD).

Methods: Retrospective and descriptive study with VKHD patients who presented intraretinal cystoid spaces in the acute phase. All patients were followed for a minimum of one year from disease onset with predefined treatment protocols and systematic evaluation. We reviewed conventional OCT images, enhanced depth SD-OCT images (HRA+OCT, Heidelberg), including serial sections through the macula obtained at the initial visit and during the follow-up until complete resolution of serous retinal detachment.

Results: Twenty-nine patients (58 eyes) were evaluated. Of these, 8 patients (7 women, 12 eyes [20%]; mean age 34.6 ± 10.2 years) had intraretinal cystoid spaces (IRCS) at baseline (M0) and/or at first month of follow-up (M1) (Table 1). In this group, the mean time to start treatment was 29.2 ± 13.5 days. All these patients were treated with high-dose corticosteroid; six patients (75%) received additional early azathioprine until the second month of follow-up. In the group with cystoid spaces, the mean visual acuity (VA) at M0 was $1.70 \pm 0.5 \log \text{MAR}$ and at M1 was $0.55 \pm 0.65 \log \text{MAR}$. In 9 eyes, VA improvement was observed at M1, while in 3 eyes VA did not ameliorate. With 1 year of follow-up, VA was $0.07 \pm 0.2 \log \text{MAR}$. At M0/M1, on SD-OCT, all eyes with cystoid spaces had concomitant serous retinal detachment (SRD), and in 3 eyes there was a split in the inner photoreceptor myoid zone (bacillary detachment). We observed a slight increase in the density of the IRCS compared to the subretinal fluid in the SRD (Figure 1), with a significant variation in the mean optical density ratio (ODR) among them (0.36 ± 0.14 and 0.21 ± 0.09 , respectively; $P = 0.008$).

Conclusions: Even though cystoids spaces have been described in early SD-OCT literature in acute VKHD, detailed and better definition of SD-OCT findings relocated previous findings as serous retinal detachment or more recently as bacillary detachment. Intraretinal cystoid spaces, affecting inner and/or external nuclear layers, as described here, have not been reported till far. We hypothesize that our findings may be due to the action of inflammatory mediators, but studies are needed to understand its relevance since all patients had good VA during the follow-up.

CONTROL ID: 3517741

SUBMITTER (NAME ONLY): Ahmad Al Moujahed

TITLE: Proteomic identification of candidate biomarkers that distinguish lens-induced uveitis from infectious endophthalmitis

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Al Moujahed, G. Velez, J. Vu, V.B. Mahajan, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|G. Velez, P. Ferguson, A. Bassuk, University of Iowa, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lens-induced uveitis (LIU) is an intraocular inflammatory condition that occurs following aggravation of the lens capsule and release of lens proteins into the eye. The diagnosis of LIU can be challenging and distinguishing it from other causes of intraocular inflammation, including postoperative endophthalmitis, can be difficult. The purpose of this study is to profile vitreous protein expression of LIU and infectious endophthalmitis patients.

Methods: Liquid vitreous biopsies were collected from 3 groups: control subjects (n = 4) undergoing pars plana vitrectomy to repair an idiopathic macular hole (IMH), test subjects with lens-induced uveitis (n=9), and test subjects (n = 6) with infectious endophthalmitis. Vitreous samples were analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) and proteins were identified and quantified using a data-independent approach (DIA). Protein expression changes (i.e., relative intensities) were evaluated by analysis of variance (1-way ANOVA; significant p-value <0.05), gene ontology, and pathway analysis, to identify candidate biomarkers and pathways for prospective studies.

Results: We identified a mean of 399 proteins in control (IMH), 385 in LIU, and 419 in endophthalmitis vitreous. In LIU vitreous, 45 proteins were significantly differentially expressed proteins (20 upregulated and 25 downregulated) compared to controls, including lens-specific proteins (i.e. crystallins). Endophthalmitis vitreous exhibited 149 significantly differentially expressed proteins (87 upregulated and 62 downregulated) compared to controls and was characterized by the presence of elevated neutrophil specific markers. A total of 134 proteins were differentially expressed between LIU and endophthalmitis samples (55 upregulated and 79 downregulated) and lens-specific proteins were the greatest unregulated proteins in LIU samples.

Conclusions: The LIU vitreous proteome is characterized by the upregulation of crystallins while endophthalmitis samples are distinguished by the presence of proteins related to neutrophil degranulation and microbial antigen presentation. This is the first proteomic study to identify possible biomarkers in the vitreous for diagnosing LIU and differentiating it from infectious endophthalmitis.

CONTROL ID: 3517778

SUBMITTER (NAME ONLY): Poonam Mudgil

TITLE: Biophysical interactions of essential fatty acids with human tears

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Mudgil, Western Sydney University School of Medicine, Penrith South DC, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure (Abstract): Poonam Mudgil: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Dietary intake of essential fatty acids (EFAs) is recommended for relieving symptoms of dry eye disease as it is thought to reduce inflammation at the ocular surface, although conflicting reports also exist. Topical application of EFAs to the ocular surface is also being investigated. Fatty acids are surfactants and their topical delivery into tears can alter the tear stability which plays an important role in dry eye. While previous studies investigated interactions of EFAs with meibomian lipids, this study aimed at investigating the biophysical interactions of EFAs with human tears to determine the efficacy of EFAs for topical ocular application.

Methods: Human tears from asymptomatic volunteers were collected with informed consent. Pressure-area profiles and rheology of surface films of human tears, EFAs (LA - linoleic acid and ALA - α -linolenic acid), and mixtures of EFAs with tears were studied using Langmuir trough technology on an artificial tear solution at the physiological pH and temperature. The compressibility and elasticity of surface films were determined from pressure-area profiles.

Results: Pressure-area profiles indicated that tears formed a highly compressible, non-collapsible surface film with a maximum surface pressure of 35mN/m. The surface film of LA was also highly compressible, comparable with that of tears, with a maximum surface pressure of 30mN/m but the surface film of ALA was very expanded and showed very low surface pressure with a maximum of 5mN/m. The elasticity of surface films of tears and LA increased with the compression of the films till phase transition followed by a decrease. Elasticity of ALA remained very low. LA and ALA when mixed with tears did not increase the surface pressure or elasticity of the mixed films in comparison with that of tears alone.

Conclusions: Whole tears possess surface active properties better than those reported for meibomian lipids. This is likely due to the contribution from surfactant proteins in addition to the lipids in tears. Addition of small amounts of EFAs does not give a profound effect on the biophysical properties of tears because whole tears have their own robust surface active characteristics. Future studies with tears from dry eye patients, higher amounts of EFAs, and interactions of EFAs with tear proteins will help in determining possible benefits of topical application of EFAs to the ocular surface.

CONTROL ID: 3517862

SUBMITTER (NAME ONLY): Gulgun Tezel

TITLE: NF- κ B-regulated Cross-talk between Astroglia and Microglia for Neuroinflammation in Experimental Glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Tezel, X. Yang, Q. Zeng, Ophthalmology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Astroglia and microglia play synchronic/complementary roles during neuroinflammation in glaucoma; however, how they interplay and regulate each other's phenotype and immune functions is not fully understood. To improve the understanding of astroglia-microglia intersignaling for neuroinflammation in experimental glaucoma, this study analyzed microglia responses to astroglial NF- κ B inhibition.

Methods: Ocular hypertension was induced by anterior chamber microbead injections in mice with conditional deletion of p65 in astroglia (crossbreds of p65^{f/f} and GFAP-cre/ERT2) and controls (p65^{f/f}), and astroglia and microglia responses were analyzed through a 12-weeks period. Morphological responses were determined in retinal whole mounts and optic nerve sections by analyzing the intensity and coverage of immunolabeling for specific markers (GFAP or Iba1). Inflammatory responses, and A1/A2 and M1/M2 phenotypes, were evaluated by cytokine/chemokine profiling in isolated astroglia and microglia samples and immunolabeling of retina and optic nerve tissues.

Results: Besides decreased inflammatory activity of p65-deleted astroglia, a prominent decrease was detectable in microglia responses. The morphological response of microglia to ocular hypertension (a shift from ramified morphology to reactive morphology) was less prominent, and the intensity and coverage of Iba1 immunolabeling were over 30% less in ocular hypertensive eyes of GFAP/p65 mice than ocular hypertensive p65^{f/f} controls (P = 0.001, P = 0.01, respectively). In addition, similar to p65-deleted astroglia (that were C3- with lower titers of NF- κ B-regulated pro-inflammatory cytokines, such as ILs, TNF- α , IFN- γ), the pro-inflammatory cytokine response of microglia was significantly lower in ocular hypertensive GFAP/p65 mice than ocular hypertensive p65^{f/f} controls (P < 0.02). The reduced microglial response to experimental glaucoma should not be related to decreased neuron injury in GFAP/p65 mice, since parallel studies of RGC-protective treatments did not detect a similar response.

Conclusions: These findings support the importance of astroglia-derived factors to shape microglia responses during glaucomatous neurodegeneration. Astroglial NF- κ B-regulated cytokines/chemokines appear to critically modulate direct communication, and the amplifying relay effects, between astroglia and microglia during neuroinflammation in experimental glaucoma.

CONTROL ID: 3517893

SUBMITTER (NAME ONLY): wing yip

TITLE: Accuracy of self-selected magnifiers amongst patients with vision impairment

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. yip, A.L. Softing Hataye, M. Schornack, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision rehabilitation involves evaluation of individual patient visual needs, prescription of specific level of magnification to meet these needs, and training on how to use prescribed devices. Although magnification devices are commercially available without prescription, there is no standardized method of labeling such devices, nor are there guidelines to help consumers select the appropriate level of magnification for their visual needs and level of visual impairment. We performed a retrospective study to compare magnification power of patients' self-selected magnifier (SSM) and their level of satisfaction with the SSM to the device prescribed by a low vision specialist.

Methods: Retrospective record review of patients who brought in their own SSM's to their initial low vision consultations between January 1, 2019 and March 30, 2020. The following information was abstracted from the medical record: age, gender, ocular history, source of SSM, visual acuity, visual goals, power of SSM, prescribed magnification and patient preference of self-selected compared to prescribed magnifier. Descriptive statistics are presented.

Results: A total of 50 patients were identified. Average patient age was 83 ± 10 years (range: 51-100); male/female distribution was 12/38 (24%/76%). The average visual acuity in the better seeing eye was 0.51 logMAR, average visual acuity in the worse seeing eye was 0.22 logMAR. Eight (16%) patients had more than one magnifier. In 48 patients (96%), SSM power was incorrect based upon clinical examination and evaluation of patients' visual needs. Forty eight (96%) patients preferred the doctor-prescribed magnifier compared to the device that they had procured on their own. In 45 patients (90%), power of the SSM was less than what the doctor prescribed; SSMs were an average of 5 diopters less than what was prescribed by the low vision specialist. Only 16 (32%) of the SSM incorporated a light source into the device.

Conclusions: Magnification provided by a majority of patients' SSM's was not sufficient to meet the patients' visual needs. A majority of patients preferred the doctor-prescribed power over that which was provided by their SSM. These findings suggest that patients may be more likely to achieve success with prescribed low vision aids compared to over-the-counter devices obtained without a prescription.

CONTROL ID: 3517910

SUBMITTER (NAME ONLY): Leah Metzger

TITLE: Virulence assessment of the L -2-amino-4-methoxy-trans3-butenoic acid producing keratitis associated *Pseudomonas aeruginosa*

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.M. Metzger, M. Kovach, Biology & Geology, Baldwin Wallace University, Berea, Ohio, UNITED STATES|R. Bouhenni, Ophthalmology, Akron Children's Hospital, Akron, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously reported that the keratitis associated *Pseudomonas aeruginosa* produces the toxin L-2-amino-4-methoxy-trans-3-butenoic acid (AMB). In this study we sought to investigate the virulence of the AMB producing strain (E3) compared to the AMB mutant strain (PA3202), its parent strain (PAO1) and the non-virulent lab strain (ATCC 10145).

Methods: *Pseudomonas aeruginosa* strains (E3, PAO1, PA2302 and ATCC 10145) were grown in Luria-Bertani (LB). Overnight cultures were diluted 1:100 in LB and grown to an optical density of 0.3 to 0.4 at 600 nm, washed 1X with sterile PBS and diluted to an $A_{600} = \sim 0.05$ (0.046 – 0.048). A 10- μ l aliquot of each dilution was then injected into *G. mellonella* larvae (n=25/strain) via the hindmost left proleg. PBS was used as the negative control. The Health Index Score (HIS), which determines virulence, was calculated at 8 hours and 20 hours post infection. The time to death of the larvae was determined and used to create Kaplan-Meier survival curves. One-way analysis of variance (ANOVA) was used for statistical analysis to determine significance in differences in virulence between strains.

Results: At 8 hours post infection, the health index scores for all strains was similar and ranged from 7.8 ± 1.08 to 8.48 ± 0.5 . At 20 hours post infection, the health index score was significantly lower for the larvae injected with the keratitis associated *P. aeruginosa* E3 compared to those injected with the AMB mutant strain PA2303 and its parent strain PAO1 (0.48 ± 1.4 vs. 6.0 ± 1.5 and 1.76 ± 2.04 , $p > 0.001$). Larvae injected with ATCC 10145 and PBS had the highest health index scores (6.72 ± 1.17 and 7.28 ± 1.45 respectively), which were similar to those recorded at 8 hours post infection.

Conclusions: Results from this study confirm that the keratitis associated *P. aeruginosa* strain is highly virulent compared to the other strains tested, possibly due to its ability to produce AMB. This study will add more insight into the pathogenesis of *Pseudomonas* associated keratitis and will help develop novel antimicrobial agents for the treatment of ocular infections caused by *P. aeruginosa* such as those that result from the wear of contact lenses.

CONTROL ID: 3517920

SUBMITTER (NAME ONLY): Daniel Kiernan

TITLE: Effect of Dexamethasone Intracameral Drug-Delivery Suspension on Macular Thickness after Vitreoretinal Surgery

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.F. Kiernan, The Eye Associates of Manatee, Sarasota, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Daniel Kiernan: Commercial Relationship(s);Eyepoint Pharmaceuticals:Code F (Financial Support);Eyepoint Pharmaceuticals:Code C (Consultant);Eyepoint Pharmaceuticals:Code R (Recipient)

ABSTRACT BODY:

Purpose: To analyze the effect of treatment with an anterior chamber intracameral dexamethasone drug-delivery suspension (Dexycu; EyePoint Pharmaceuticals, Watertown, MA) on optical coherence tomography-measured macular thickness (OCT MT) in patients undergoing retinal surgery compared to post-operative treatment with topical corticosteroids.

Methods: Post Hoc analysis of a retrospective case-matched comparison of patients undergoing initial retinal surgery by a single surgeon. 27 eyes of 27 patients received intracameral dexamethasone at the time of surgery and were compared to 27 eyes of 27 patients who received daily post-operative corticosteroid eye drops over 4 weeks. The primary outcome was change of OCT MT before and 8 weeks after surgery. Secondary outcomes were changes of OCT MT before and 4 and 12 weeks after surgery. A paired T-test was used for statistical analysis.

Results: Baseline OCT MT was 317 um in the topical steroid-treated group and 332 um in the intracameral dexamethasone treatment group ($p=0.839$). Post-operatively at 8 weeks the average OCT MT change was +43.7 um ($p=0.0003$) in the topical steroid treated group and -22.4 um ($p=0.0082$) in the intracameral dexamethasone treatment group. At post-operative weeks 4 and 12, the topical steroid-treated group had increased OCT MT compared to baseline (36.3 and 4.67 um, $p=0.0002$ and 0.579) whereas the intracameral dexamethasone treatment group had decreased OCT MT (-18.78 and -22.61 um, $p=0.027$ and 0.007). Patients treated with topical steroids for 1 month after surgery had an average OCT MT that was 51 and 53 um greater ($p=0.0175$ and 0.019 respectively) at 4 and 8 weeks post-operatively than those who received the intracameral dexamethasone suspension at the time of surgery.

Conclusions: Intracameral dexamethasone drug-delivery suspension placed in the anterior chamber after vitreoretinal surgery was associated with a significant reduction in macular thickness up to 12 weeks following vitreoretinal surgery, whereas patients receiving daily topical corticosteroids demonstrated significantly more OCT MT at 4 and 8 weeks post-operatively. These results indicate a greater benefit of intracameral dexamethasone drug-delivery suspension for preventing post-operative causes of increased macular thickness including cystoid macular edema compared to topical anti-inflammatory treatment among patients undergoing vitreoretinal surgery.

CONTROL ID: 3517950

SUBMITTER (NAME ONLY): Daniel Olivieri

TITLE: Characterizing transnational ophthalmic surgical partnerships by engagement and training

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Partnerships represent an important yet under-researched modality in global eye care. We investigated ophthalmic partnerships between high-income country (HIC) and low- and middle-income country (LMIC) stakeholders and characterized them by 'Training' and 'Engagement' to better understand and address disparities in global ophthalmic surgical care.

Methods: A web search was conducted to identify stakeholders participating in the delivery and/or capacity building of ophthalmic services from 2010 - 2019 based on publicly available data. Partnerships were defined through clinical activities, education and training, and/or research support. Descriptive data on current ophthalmic partnerships was collected from published reports, literature reviews, and information on stakeholder webpages. Individual partnerships were separately classified by the extent of engagement and training patterned off criteria from a similar study in global neurosurgery; grade I represented the least and grade III the most extensive engagement and training. Data were analyzed using descriptive statistics and geospatial mapping.

Results: In total, 209 unique HIC - LMIC partnerships encompassing 92 unique countries were described. The most common HIC partners were from North America (123; 59%) and Europe (75; 36%); the most common LMIC partners were from Africa (103; 49%) and the Asia-Pacific (54; 26%). Partnerships most frequently provided services in cataract (48%), glaucoma (25%), and diabetic retinopathy (25%). The most common engagement classifications were grade I (35%) or II (39%) and training classifications were grade I (60%) or II (23%). A majority of partnerships utilized a coordinating agency (147; 70%). Finally, LMIC-based researchers first- or co-authored 61% of all peer-reviewed publications documented in the data set.

Conclusions: Transnational ophthalmic partnerships exist with varying degrees of both engagement and training. Research collaboration and direct services are two current areas of partnership strength in global ophthalmology, while LMIC-directed training programs need improvement relative to other surgical fields.

CONTROL ID: 3517981

SUBMITTER (NAME ONLY): Robert Baratta, MD

TITLE: Neuroprotective properties of collagen mimetic peptides

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.O. Baratta, MD, B.J. Del Buono, E. Schlumpf, D.J. Calkins, Research, Stuart Therapeutics, Inc, Stuart, Florida, UNITED STATES|S. Pasini, D.J. Calkins, Ophthalmology, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Robert Baratta, MD: Commercial Relationship(s);Stuart Therapeutics, Inc:Code I (Personal Financial Interest);Stuart Therapeutics, Inc:Code E (Employment);Stuart Therapeutics, Inc:Code P (Patent) | Brian Del Buono: Commercial Relationship(s);Stuart Therapeutics, Inc:Code E (Employment);Stuart Therapeutics, Inc:Code I (Personal Financial Interest);Stuart Therapeutics, Inc:Code P (Patent) | Silvia Pasini: Commercial Relationship: Code N (No Commercial Relationship) | Eric Schlumpf: Commercial Relationship(s);Stuart Therapeutics, Inc:Code I (Personal Financial Interest);Stuart Therapeutics, Inc:Code E (Employment);Stuart Therapeutics, Inc:Code P (Patent) | David Calkins: Commercial Relationship(s);Stuart Therapeutics, Inc:Code C (Consultant)

ABSTRACT BODY:

Purpose: Extracellular matrix in the central nervous system comprises a complex macromolecular combination of proteins and polysaccharides that provides a substrate for maintenance of neurons and their axons. Glaucoma and other optic neuropathies involve degradation of the extracellular matrix in the retina and optic nerve head, through which unmyelinated retinal ganglion cell axons pass in forming the optic nerve proper. This degradation also affects collagen fibers, which are a major constituent of the matrix. Here we tested whether collagen mimetic peptides (CMPs), which repair damaged collagen, promote (1) survival and neurite outgrowth of neurons in vitro stressed by collagen degradation and (2) ganglion cell axon function in an inducible mouse model of glaucoma.

Methods: For in vitro studies, we compared neurite outgrowth of dorsal root ganglion cells (DRGs) plated on partially digested type 1 collagen and treated either with CMP or vehicle. For in vivo testing of efficacy, we elevated ocular pressure unilaterally in mice using microbead occlusion and measured anterograde axonal transport of cholera toxin B to the superior colliculus following topical CMP treatment vs. vehicle.

Results: In vitro, DRG neurons on damaged collagen treated with CMP demonstrated increased dendritic field area ($p \leq 0.03$) and neurite length ($p \leq 0.02$) compared to untreated, while neurite length in treated collagen also exceeded by 70% length in naïve collagen ($p = 0.002$). In vivo, following three weeks of elevated ocular pressure (+35%), treatment with CMP's significantly protected axon transport vs untreated ($p < 0.01$).

Conclusions: Our results emphasize the critical role intact collagen plays in maintaining ECM and neuronal function. CMPs offer therapeutic potential for use in neuroprotective or reparative regimens designed to promote neurite growth and axon function in glaucoma and other optic neuropathies

CONTROL ID: 3517986

SUBMITTER (NAME ONLY): Patrice Hicks

TITLE: Blinding eye disease and associated genetic and epidemiological factors in a Mayan population of Guatemala

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Hicks, B. Haaland, M. Murtaugh, M.M. DeAngelis, Population Health Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|L. Owen, W. Self, A.S. Crandall, Ophthalmology and Visual Sciences, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|E. Au, S. Sieminski, A. Siedlecki, A. Reynolds, J. Lillvis, M.H. Farkas, M.M. DeAngelis, Department of Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|M. Feehan, Kantar, LLC, New York, New York, UNITED STATES|J.P. Shulman, Ophthalmology, New York Medical College, Valhalla, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Mayan population in Guatemala is understudied within vision research. This observational cohort of individuals seeking eye care may help identify unique clinical, demographic, environmental, and genetic factors for blinding eye disease. This study will serve to (a) identify the ocular health needs within this population and (b) any possible modifiable risk factors.

Methods: We conducted a cross-sectional study with 126 participants. Each received an eye exam, provided a blood sample, and were administered a standardized epidemiological questionnaire at the Lion's Eye Hospital in Salama, Guatemala. Interpreters were available for translation to the patients' native dialect. We also performed a genome-wide association study using Illumina's HumanOmni2.5-8 chip to examine SNPs. We used quality control measures and performed a logistic regression analysis to determine which genetic components were associated with eye disease.

Results: The population was 46% male, and the average age was 65.2. We found that the most prevalent eye conditions were cataracts (54.8%), followed by pseudoexfoliation syndrome (PXF) (24.6%). The population with both conditions was 22.2%. We conducted multivariate analyses to determine which epidemiological factors were significantly associated with the population's eye conditions at $p < .05$. In our epidemiological analysis, including 121 participants for completeness, we found that eye disease was significantly more likely with advanced age. Cataracts were significantly more common among those living in the 10 districts with the least resources. Furthermore, having cataracts was associated with a greater likelihood of PXF after adjusting for age and sex. In our genetic analysis, the SNP most significantly associated with PXF is within the gene KSR2 ($p < 1 \times 10^{-5}$). Several SNPs were associated with Cataracts at Genome-Wide significance adjusting for covariates ($p < 5 \times 10^{-8}$). Almost three-quarters of these SNPs lie within 13 genes, with the majority of genes having only one significant SNP.

Conclusions: To the best of our knowledge utilizing PhenGenI, these SNPs and genes have not been previously associated with cataracts, glaucoma, or PXF. This study can aid in understanding the prevalence of eye conditions in this population but may also inform public health planning and delivering of quality, accessible and relevant health and preventative care within Guatemala.

CONTROL ID: 3518007

SUBMITTER (NAME ONLY): Ahmed Soliman

TITLE: Incidence of periocular pain following intravitreal injections: which factors really matter?

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.Z. Soliman, J. De La Torre, M. Ellman, Southwest Eye Institute, El Paso, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the different factors correlating with pain severity following intravitreal injections.

Methods: All injections were performed by the same doctor (AZS). Patients were anesthetized either with drops only or with a subconjunctival injection of 0.1 cc of lidocaine 2%. The injections were performed with either a 30 or 32 gauge needle. Patients were randomly assigned into four groups: topical with 30 G needle (group A), topical with 32 G needle (group B), subconjunctival with 30 G (group C) and subconjunctival with 32 G (Group D). The visual analog scale (VAS) was used to assess pain. Primary study variables were the relationship between pain severity and anesthesia type, needle size, number of previous injections, age, sex, lens status and indication for injection. Secondary variables included best-corrected visual acuity (BCVA) and central macular thickness (CMT) changes 1 month post injection.

Results: 100 eyes of 100 patients were included in the study. Each group included 25 eyes. Sixty two patients were females (62%) and 38 were males (38%). Overall mean pain score was 2.73 ± 1.89 . Indications for injection were diabetic macular edema (81%), neovascular age-related macular degeneration (6%), and macular edema secondary to retinal vein occlusion (13%). The mean VAS scores in groups A, B, C and D were 4.1 ± 2 , 2.9 ± 2.3 , 1.9 ± 1.7 and 1.7 ± 2.1 , respectively. Pain severity was significantly correlated with anesthetic type ($p < 0.001$) and needle size ($p < 0.001$); A negative correlation existed between pain score and number of previous injections ($p = 0.03$). Pain severity was not associated with age ($p = 0.59$), sex ($p = 0.45$), lens status ($p = 0.48$), vitreous reflux ($p = 0.65$) or indication for injection ($p = 0.37$). No significant complications were observed.

Conclusions: Using subconjunctival anesthesia and a smaller needle size were associated with less pain during intravitreal injections. These results need to be validated in larger studies. However, adopting these changes can help increase patient comfort during the injection.

CONTROL ID: 3518076

SUBMITTER (NAME ONLY): Rusdeep Munda

TITLE: Idiopathic Orbital Inflammation Refractory to Rituximab but Sensitive to Methotrexate

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Munda, A. Harrison, A. Mokhtarzadeh, S.R. Montezuma, D. Koozekanani, M.S. Lee, C. McClelland, J.H. Hou, K.R. Armbrust, J. Yamanuha, Ophthalmology, University of Minnesota System, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Idiopathic orbital inflammation (IOI) represents a spectrum of non-infectious orbital processes that are managed with corticosteroids and/or steroid sparing immunosuppressive therapies in refractory or recurrent cases. We present two patients with IOI who were resistant to rituximab infusions but subsequently responded to oral methotrexate (MTX).

Methods: Case series

Results: Patient #1: A 73-year old man with a 16-year history of biopsy-proven recurrent left IOI involving the inferior rectus (Fig. 1a) presented with diplopia and persistent optic disc edema (ODE) (Fig. 2a) first noted 5 months prior. Previous treatments included prednisone up to 80 mg daily, orbital triamcinolone injections, and two rituximab infusion courses without improvement. He was started on oral MTX 15 mg weekly with a taper of prednisone. His ODE and diplopia improved at 6 weeks; however, treatment was discontinued after six months due to his concerns related to COVID-19. All findings resolved three months after stopping MTX.

Patient #2: A 67-year old woman presented with a 3-year history of a right orbital mass involving the lacrimal gland and extraocular muscles (Fig. 1b) causing proptosis and diplopia. Orbital biopsy showed chronic inflammatory changes and was negative for IgG4 or lymphoma. Systemic inflammatory and infectious workup was unremarkable. She had minimal improvement in proptosis and diplopia after two courses of rituximab with intermittent oral prednisone. She later presented with ODE, cystoid macular edema, and an inferotemporal exudative retinal detachment (RD) (Fig. 2b). The ocular manifestations improved with a 10 day course of prednisone 40 mg/day but recurred on prednisone taper. All findings resolved after 2 months of MTX 20 mg weekly.

Conclusions: While anti-metabolites are typically used early in the course of recurrent IOI with rituximab reserved for more recalcitrant disease, this study demonstrates that MTX may provide benefit for IOI refractory to rituximab with secondary ocular manifestations. This may be due to more gradual suppression of the immune system with MTX.

CONTROL ID: 3518087

SUBMITTER (NAME ONLY): Cynthia Roberts

TITLE: Corneal/Scleral Stiffness and Structural/Functional Status in Treatment with Prostaglandin Analogs

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Roberts, A.M. Mahmoud, P.A. Weber, G. Fleming, Ophthalmology & Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|C.J. Roberts, A.M. Mahmoud, P.A. Weber, G. Fleming, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare corneal/scleral stiffness from air puff deformation in Normal (NL), Primary Open Angle Glaucoma (POAG) without history of prostaglandin analog (PGA) treatment and with current/former PGA treatment (POAG-PGA), as well as Ocular Hypertension with (OHT-PGA) and without PGA treatment (OHT).

Methods: A prospective crosssectional study of 253 subjects was conducted: 387 eyes of 194 NL, 54 eyes of 29 POAG-PGA, 19 eyes of 11 POAG, 12 eyes of 6 OHT-PGA, and 26 eyes of 13 OHT subjects. Ganglion Cell Complex (GCC) from Optical Coherence Tomography was measured on all subjects. Cup/disc ratio (C/D) and mean deviation (MD) from visual field exams were extracted from the medical records of both OHT and both POAG cohorts. Biomechanical response from Corvis ST was evaluated with corneal parameters, Integrated Inverse Radius (IntInvRad) and stiffness parameter (SP) at first applanation (SP-A1). Scleral stiffness at highest concavity (SP-HC) was included. MANCOVA was performed with IOP from Dynamic Contour Tonometry (DCT), pachymetry and age as covariates for biomechanical parameters. GCC, C/D, and MD were compared with age as a covariate. Statistical significance threshold was set to $p < 0.05$.

Results: SP-A1 was not different between any group. NL showed a less stiff corneal response in IntInvRad than OHT ($p=0.0030$) and OHT-PGA ($p=0.0059$), which were not different than each other. OHT had a significantly stiffer scleral response in SP-HC ($p < 0.0001$) than all other cohorts, including OHT-PGA ($p=0.0003$) which was stiffer than NL ($p=0.0152$) and POAG ($p=0.0053$). NL, POAG and POAG-PGA were not different than each other. GCC was thickest ($p < 0.0001$) in NL than all cohorts except OHT, which was thicker than OHT-PGA ($p=0.0085$) and both POAG cohorts ($p < 0.001$). C/D was not different between POAG and POAG-PGA, but greater than both OHT cohorts ($p < 0.0005$) which were not different from each other. MD was significantly worse in POAG-PGA than POAG ($p=0.0029$). No other cohorts were different.

Conclusions: PGA treatment resulted in a less stiff scleral response in OHT with thinner GCC, consistent with site of action of PGA and reports of greater response in stiffer eyes at baseline. Although there was no difference in scleral stiffness with PGA in POAG, MD was worse with PGA treatment. It is not clear whether PGA resulted in thinner GCC in OHT and worse MD in POAG, or if these eyes were more advanced at baseline.

CONTROL ID: 3518099

SUBMITTER (NAME ONLY): Alison Chan

TITLE: Associations between healthcare utilization and access and diabetic retinopathy complications

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chan, J. McDermott, T. Lee, G. Ye, B. Shahrini, B. Radha Saseendrakumar, S.L. Baxter, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|A. Chan, J. McDermott, T. Lee, G. Ye, B. Shahrini, B. Radha Saseendrakumar, S.L. Baxter, Department of Biomedical Informatics, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess whether variations in healthcare utilization and access are associated with increased risk of developing proliferative diabetic retinopathy (PDR) or related complications.

Methods: We identified 1,882 adult participants in the NIH All of Us Research Program data repository with diabetic retinopathy (DR) based on diagnostic billing codes. Electronic health record data regarding comorbidities, laboratory values, and procedures were extracted. Healthcare utilization and access were assessed using participant responses to surveys on frequency of medical care, ability to afford care, and reasons for delaying medical care. Multivariable logistic regression with bi-directional stepwise variable selection was performed from a wide range of predictors to assess whether social determinants were associated with increased risk of developing PDR or related complications (e.g. neovascular glaucoma). Statistical significance was defined as $p < 0.05$.

Results: The mean (standard deviation) age of 1882 adults with DR enrolled in All of Us was 63.7 (11.0) years. The majority (57.3%) were female. 36.9% identified as Hispanic or Latino. 13.1% of DR patients had not spoken to an eye doctor in the past 12 months, and 10-20% of patients endorsed several reasons for avoiding or delaying care, including financial concerns and transportation (Figure 1). The number of eye doctor visits (odds ratio [OR] 1.46, 95% confidence interval [CI] 1.07-1.99, $p=0.02$) and diabetic kidney disease (OR 3.88, 95% CI 1.37-11.07, $p=0.01$) were associated with increased odds of developing PDR and related complications. Significant social determinants included healthcare coverage not accepted by provider (OR 3.48, 95% CI 1.35-12.10, $p=0.02$) and inability to afford general healthcare provider (OR 8.42, 95% CI 1.12-74.3, $p=0.04$) (Table 1).

Conclusions: Understanding the social determinants that influence risk for developing complications can help inform population health interventions. Nationwide data with diverse enrollment demonstrate that some DR patients face substantial barriers to healthcare access.

CONTROL ID: 3518131

SUBMITTER (NAME ONLY): Sheetal Shirke

TITLE: To compare the accuracy of intraocular lens calculation formulas in the prediction of postoperative refraction in eyes with short axial length (<22mm)

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shirke, N. Gupta, S. Ahmed, Ophthalmology, Northern health, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Accurate intraocular lens (IOL) power calculation in cataract surgery is very important to achieve the postoperative target refraction and high patient satisfaction. For short eyes, the IOL power calculation formulas are less accurate than normal, which presents challenges for cataract surgeons. In this study, we aim to compare the refractive outcome using different IOL calculation formulas (Barrett Universal II, Haigis, Hoffer Q, Holladay 1, Olsen, and SRK-T, Hill BRF II, Kane and EVO 2.0)

Methods: This was a retrospective chart review conducted for adult patients who underwent uncomplicated cataract surgery with implantation of monofocal posterior chamber intra ocular lens at Broadmeadows hospital during Jan 2012- Jan 2020. All patients received implantation of an Acrysof IQ SN60WF. Post op refraction was done at minimum 4 weeks post operatively. In patients whose both eyes satisfied the inclusion criteria, only one eye as randomly selected. Post op mean refractive error (ME) and mean absolute refractive error (MAE) were calculated, before and after adjusting the mean to zero, for each formula and compared.

Results: Total 129 eyes were included. Mean post op refraction was - 0.61D. Olsen formula had least ME (-0.13D). Mean MAE was minimal for EVO formula before and after adjusting mean to zero (0.47 and 0.46 respectively). EVO formula also had maximum number of eyes within 0.25D and 0.5D. There was no statistically significant difference in absolute predictive error after adjusting the mean to zero among these formulas.

Conclusions: The refractive outcome was significantly myopic than expected. EVO formula gave least absolute error after adjusting to zero though there was no statistical difference among the formulae.

CONTROL ID: 3518167

SUBMITTER (NAME ONLY): Ana Navarrete

TITLE: Safety Margins of Anti-VEGF Therapy using Treat and Extend Treatment Protocol – Lessons from the COVID-19 Pandemic

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Navarrete, B. Vofo, K. Matos, A. Rivera, J. Levy, I. Chowers, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL]

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ABSTRACT BODY:

Purpose: To analyze the consequences of delaying intravitreal (IVI) anti-vascular endothelial growth factor (VEGF) therapy in patients under treat-and-extend (TAE) protocol.

Methods: A retrospective review of medical records of a consecutive group of patients receiving IVI using TAE protocol before and during the COVID-19 pandemic. Data collected included diagnosis, demographics, treatment schedule, compound used and anatomical outcome according to spectral-domain optical coherence tomography (SD-OCT).

Results: A total of 923 eyes (691 patients) were included; 58.8% (543 eyes) were treated for neovascular age-related macular degeneration (nvAMD), 25% (231 eyes) had diabetic macular edema (DME), and 16.2% (149 eyes) with retinal vein occlusion (RVO). The average patient age (\pm SD) was 74.5 ± 11.7 years. The Female/male ratio was 1.08:1. Delayed therapy during the pandemic (≥ 7 days) occurred in 56.3% of the eyes. This included 56.2%, 61.5%, 49.0% of nvAMD, DME and RVO patients respectively. The overall average delay (\pm SD) was 15.3 ± 23.4 days. RVO patients were on average less late (9.3 ± 16.1 days) compared to nvAMD (15.8 ± 23.8) and DME (18.2 ± 25.6) eyes ($P=0.002$). Multivariate analysis showed that in nvAMD duration of the disease and type of anti-VEGF were predictors of the number of days late ($P=0.011$ and 0.019). In eyes ≥ 7 days late, 45.7%, 58.5%, and 58.9% of nvAMD, DME, and RVO eyes respectively showed an increase in central subfield thickness (CST). Worsening was related to absolute numbers of days late, and not to the percentage of delay of the recommended interval. A positive correlation was found between delay to treatment and an increase in CST.

Conclusions: Delaying IVI in eyes under TAE regimen was common during the COVID-19 pandemic. These delays were associated with macular thickening having potential visual consequences.

CONTROL ID: 3518220

SUBMITTER (NAME ONLY): Derek Nankivil

TITLE: A pilot study on the effect of high pass spectral filters on chromatic contrast sensitivity

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Nankivil, N. Franklin, J. Xu, J. Buch, Research & Development, Johnson & Johnson Vision, Florida, UNITED STATES]

Commercial Relationships Disclosure (Abstract): Derek Nankivil: Commercial Relationship(s);Johnson & Johnson Vision Care Inc.:Code E (Employment);Johnson & Johnson Vision Care Inc.:Code I (Personal Financial Interest);Johnson & Johnson Vision Care Inc.:Code P (Patent);Johnson & Johnson Vision Care Inc.:Code R (Recipient) | Nicole Franklin: Commercial Relationship(s);Johnson and Johnson Vision Care Inc.:Code E (Employment);Johnson and Johnson Vision Care Inc.:Code I (Personal Financial Interest) | Jie Xu: Commercial Relationship(s);Johnson & Johnson Vision Care Inc.:Code E (Employment);Johnson & Johnson Vision Care Inc.:Code I (Personal Financial Interest) | John Buch: Commercial Relationship(s);Johnson & Johnson Vision Care Inc.:Code E (Employment);Johnson & Johnson Vision Care Inc.:Code I (Personal Financial Interest);Johnson & Johnson Vision Care Inc.:Code P (Patent);Johnson & Johnson Vision Care Inc.:Code R (Recipient)

ABSTRACT BODY:

Purpose: Some patients express a preference for visual aids that include a high pass spectral filter (HPSF) (Clark, 1969). Although not demonstrated directly, research suggests that a filter, such as that provided by macular pigment, may improve chromatic contrast (Hammond, Fletcher & Elliott, 2013). We hypothesize that some HPSFs enhance chromatic contrast sensitivity.

Methods: To test this hypothesis, a single-site, subject-masked, 6x6 crossover, controlled, randomized, non-dispensing study was conducted. Heterochromatic flicker photometry (HCFP) was utilized to ensure that the stimuli were isoluminant. Results from the HCFP experiment were used to adjust the intensity of one component of the Gabor stimulus so that the stimuli were individualized for each subject. Each color axis was set at the nominal values, representative of the standard observer. Binocular chromatic contrast sensitivity functions (CCSFs) were measured along both the Protan (red-green) and Tritan (blue-yellow) axes with six different filters: UV control, ND control, 419nm HPSF, 437nm HPSF, 456nm HPSF, 476nm HPSF. Sensitivity thresholds were determined at seven spatial frequencies: 0.2, 0.4, 0.6, 1, 2, 4 and 6cpd. Both HCFP and CCSF experiments were conducted with a commercial visual function assessment system utilizing a 32in display located 1.5m from the subject (Metropsis, Cambridge Research Systems Ltd., Kent, UK). In total, 20 subjects completed the study per-protocol. The ratio of the area under the curve (AUC) of the CCSFs (test:control) were computed.

Results: With Protan stimuli, AUC CCSF ratios were 1.07, 1.10, 0.93 and 0.92 for the 419nm, 437nm, 456nm, and 476nm HPSFs, respectively. With Tritan stimuli, AUC CCSF ratios were 0.87, 0.97, 0.74 and 0.73 for the 419nm, 437nm, 456nm, and 476nm HPSFs, respectively. Results demonstrate that HPSFs blocking components nominally below 440nm appear to improve CCSF along the Protan axis. Other, more aggressive, HPSFs decrease CCSF along the Tritan axis.

Conclusions: Thus, we provide evidence that supports the notion that patient reported preferences for certain HPSFs are, at least in part, motivated by an improvement in chromatic contrast sensitivity.

CONTROL ID: 3518236

SUBMITTER (NAME ONLY): Luminita Tarita-Nistor

TITLE: Perceptual grouping during binocular rivalry in mild glaucoma

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Tarita-Nistor, G. Issashar Leibovitzh, Krembil Research Institute, Toronto, Ontario, CANADA | Y. Buys, G. Trope, Ophthalmology and Vision Science, University of Toronto, Toronto, Ontario, CANADA |

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ABSTRACT BODY:

Purpose: Studies on binocular rivalry point to a dysregulation in inter-hemispheric transfer in patients with mild glaucoma. During binocular rivalry, spatially separated stimuli with common features tend to group together; the grouping is mediated by lateral connections of the cortical hypercolumns. In this observational, case-control study we tested perceptual grouping during intra- and inter-hemispheric binocular rivalry to probe the strength of neural connectivity involved in early visual processing in patients with mild glaucoma.

Methods: Eight patients (4F/4M) with glaucoma with a visual field mean deviation better than -2dB and 9 (5F/4M) age-matched healthy controls participated. The 2 groups were equivalent in visual acuity and stereo-acuity. Rivalry stimuli were 1.8 deg-diameter discs, containing horizontal or vertical sine wave gratings (spatial frequency of 4 cpd), viewed dichoptically. In a control condition, the stimuli were presented centrally. To test grouping, 2 spatially separated adjacent rivalry stimuli were presented eccentrically to the same or different eyes and to the same or different hemifields. The outcome measures were time of exclusive dominance of the percept with synchronized orientations (i.e., both horizontal or both vertical) and rivalry rate.

Results: Mixed factorial ANOVAs showed that for both groups, synchronized dominance was longer when identical stimuli were presented to the same eye (i.e., both horizontal to one eye and both vertical to the other eye) than to different eyes irrespective of the hemifield ($p < .001$, partial $\eta^2 = 0.85$). Rivalry rates were significantly lower in the glaucoma group than in the control group across all conditions ($p < .001$, partial $\eta^2 = 0.27$). For the control group, rivalry rates for the central, same eye/same hemifield, and same eye/different hemifields conditions were identically high, but for the glaucoma group, the highest rivalry rate was observed for the same eye/same hemifield condition where no inter-hemispheric transfer was involved.

Conclusions: In addition to an inter-hemispheric transfer dysfunction, the results show impairment in perceptual grouping during rivalry in patients with mild glaucoma, suggesting that the strength of the lateral connectivity of the hypercolumns in the primary visual cortex is diminished. These deficits may have implications for higher levels of visual processing such as object recognition and scene segmentation.

CONTROL ID: 3518241

SUBMITTER (NAME ONLY): Rachida Bouhenni

TITLE: Cytochrome P450 1B1 binds to all trans retinal and affects p53 Expression and Growth Arrest in Human Trabecular Meshwork Cells

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Bouhenni, T. Rowe, Ophthalmology, Akron Children's Hospital, Akron, Ohio, UNITED STATES|R. Bouhenni, W. Shin, Pharmaceutical Sciences, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|I. Benmerzouga, West Virginia School of Osteopathic Medicine, Lewisburg, West Virginia, UNITED STATES|D.P. Edward, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cytochrome P450 1B1 (CYP1B1) mutations are the most frequent cause of Primary Congenital Glaucoma (PCG) globally; however, the mechanism/s by which the mutations cause glaucoma has not been yet elucidated. The purpose of this work was to investigate the binding ability of CYP1B1 to all trans retinal (t-RAL) and its effect on p53 protein levels and downstream pathways in human trabecular meshwork (HTM) cells.

Methods: Protein-ligand binding studies were performed using molecular docking where Alpha naphthoflavone and 17 β estradiol were used as positive controls, and microscale thermophoresis (MST) using wild type and G61E mutant CYP1B1. Expression of p53 and GADD45 was assessed by western blot in triplicate using protein extracted from primary HTM cells (from an 11-month-old donor) treated with different concentrations of t-RAL. Relative band densities were determined by densitometry and differences between control and each of the treatment groups were determined by using ANOVA. $p \leq 0.05$ was considered significant.

Results: Molecular docking showed a binding affinity of CYP1B1 for t-RAL that was 1.5 and 2-fold higher than Alpha naphthoflavone and 17 β estradiol respectively. With MST, the binding affinity of CYP1B1 to t-RAL was 3.5-fold greater in the wild type CYP1B1 compared to the mutant. t-RAL bound to wild type CYP1B1 with an average KD of 3338.75 ± 115.18 nM and to the mutant CYP1B1 with an average KD of 11608.05 ± 2289.5 nM ($p=0.036$). The average EC50 was 2764.55 ± 139.5 and 4313 ± 41.5 for wild type and mutant respectively. Treatment of HTM cells with t-RAL increased p53 and GADD45 expression in a dose-dependent manner. When compared to the control, p53 increased significantly by 1.92 and 3.3-fold in the 1 μ M ($p=0.03$) and 5 μ M ($p=0.01$) of t-RAL treatments respectively, whereas GADD45 increased by 1.25 and 3.48-fold in the 1 μ M ($p=0.03$) and 5 μ M ($p=0.001$) of t-RAL treatments respectively.

Conclusions: These results suggest that CYP1B1 binds to t-RAL and may be involved in retinoic acid synthesis, and that mutations in CYP1B1 lead to t-RAL accumulation in the trabecular meshwork. The latter induces cellular stress and activates p53 resulting in the subsequent growth arrest phenotype like that seen in PCG. This study will help in shedding light on the pathophysiology of PCG and other diseases caused by mutations in CYP1B1.

CONTROL ID: 3518274

SUBMITTER (NAME ONLY): Gang Luo

TITLE: What objects do people use a smartphone magnification app to help with viewing?

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Luo, A. Shubham, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Gang Luo: Commercial Relationship: Code N (No Commercial Relationship) | Anurag Shubham: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Many visually impaired people are using smartphone magnification apps to help see the fine details. The visual tasks performed with the vision assistance apps in their daily lives are largely unknown. Analytics studies on the visual targets viewed by the users can provide valuable insights into their visual demands.

Methods: The SuperVision Magnifier iOS app, which is free to the public, was used to collect data from people using the app in their daily lives. The images captured by the phone cameras were processed by Azure computer vision cloud service for object recognition. Only one image was processed for each app launch. The images were neither saved nor visually reviewed. The app received the object tags (e.g. text, person, child art), and uploaded the data to the Umeng analytics server for tallying in an aggregated manner, without any individually identifiable information being saved. Data across 31 days were downloaded and analyzed offline. More than 1000 types of object tags were grouped into 10 categories- Text, Indoor, Art, Human, Electronics, Outdoor, Food, Animal, Plant, and Others. The data collection and analysis were conducted separately for app users with at least one iOS vision accessibility option (e.g. voiceover, color inverted) toggled on. It is assumed these accessibility users had more severe vision loss than the other users.

Results: In total, 152,819 images from about 25,000 users were successfully processed by the Azure server. Textual targets appeared in 41.1% of the images for the accessibility users, and 29.8% for non-accessibility users. Among the non-textual targets, the top 4 categories were Indoor scene (31.3% and 37.7%), Art (7.4% and 7.4%), Human (6.5% and 10.3%), Electronics (5.7% and 6.0%) for accessibility users and non-accessibility users, respectively. Examining if one non-textual category was more than another non-textual category, it was found that the two groups of users were different in only 2 out of 36 category comparisons. According to the proportion test, the difference was not statistically significant ($p=0.08$, $z=1.43$).

Conclusions: The vision assistance app was used for reading text in about 30 to 40 percent of cases. People with more severe vision loss more frequently needed help with text reading. The majority of visual targets were non-textual, for which the visual demands may be similar for users with different severity of vision loss when grouping broadly.

CONTROL ID: 3518275

SUBMITTER (NAME ONLY): Ghulam Mohammad

TITLE: Mitochondria fission and diabetic retinopathy: Role of Drp1

SESSION TITLE: Mitochondria in ocular diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: In the pathogenesis of diabetic retinopathy, retinal capillary cells undergo accelerated apoptosis, and mitochondria dysfunction is considered as one of the mechanisms underlying in their death. Mitochondria are dynamic structures, and depending on the energy demand, they continuously fuse and divide. Mitochondrial fission is mediated by GTPase dynamin-related protein 1 (Drp1), and Drp1 activity is modulated by posttranslational modifications including phosphorylation and S-nitrosylation. While phosphorylation at Ser616 of Drp1 facilitates its recruitment to the surface of the mitochondria, S-nitrosylation facilitates phosphorylation at Ser616. Mitochondrial fission protein 1 (Fis1) and mitochondrial fission factor (Mff) serve as key receptors for Drp1 to promote mitochondrial fission. The aim of this study was to investigate the putative mechanisms underlying the activation of Drp1 in the development of diabetic retinopathy.

Methods: Drp1 S-nitrosylation and phosphorylation and Fis1 expression were quantified in the human retinal endothelial cells (HRECs), incubated in normal (NG) or high (HG) glucose for 96 hours by immunofluorescence microscopy and by Western blotting. Role of Drp1 in the regulation of mitochondrial fission, ROS generation and membrane depolarization, respectively, were detected using Mitotracker green, MitoSox and JC1 assays. To transition to the in vivo model, gene and protein expressions of Drp1, Fis1 and Mff were quantified by qRT-PCR and Western blotting in the retinal microvessel from streptozotocin induced-diabetic rats.

Results: Hyperglycemia elevated Drp1 S-nitrosylation and Ser616 phosphorylation, and also increased its co-localization in the mitochondrial outer membrane. Regulation of nitrosylation prevented glucose-induced phosphorylation of Drp1, and Drp1-siRNA ameliorated fragmentation of the mitochondria, superoxide production and membrane potential. Consistent with the in vitro model, retinal microvasculature from diabetic rats, compared to the age-matched nondiabetic rats, had increased Drp1-Ser616 phosphorylation and Fis1 and Mff expressions.

Conclusions: Due to posttranslational modifications of Drp1 in hyperglycemia, its translocation inside the mitochondria is increased, and mitochondrial integrity is disturbed. Thus, targeting Drp1 may serve as a potential therapy to halt the development of diabetic retinopathy.

CONTROL ID: 3518288

SUBMITTER (NAME ONLY): Terrence Lee

TITLE: Social Determinants of Health Data for Patients with Eye Conditions in a Nationwide Data Repository

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lee, A. Chan, J. McDermott, B. Shahrivini, G. Ye, B. Radha Saseendrakumar, S.L. Baxter, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|T. Lee, A. Chan, J. McDermott, B. Shahrivini, G. Ye, A.M. Sitapati, B. Radha Saseendrakumar, S.L. Baxter, UCSD Health Department of Biomedical Informatics, University of California San Diego, La Jolla, California, UNITED STATES|A.M. Sitapati, Department of Medicine, University of California San Diego, La Jolla, California, UNITED STATES|C. Nebeker, Herbert Wertheim School of Public Health and Human Longevity Science, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Social determinants of health (SDoH) have been shown to be important in the management of eye diseases, yet these data are frequently missing in electronic health record (EHR) data derived from routine clinical care. We queried a large national database to quantify and characterize SDoH data coverage to inform future research efforts.

Methods: We queried the NIH All of Us data repository, the product of a nationwide prospective cohort study that includes EHR and survey data. Adults with diabetic retinopathy (DR), glaucoma, cataracts, or age-related macular degeneration (AMD) were identified using ICD diagnosis codes and survey responses. The primary outcome of interest was SDoH data coverage, characterized by the proportion of each disease cohort with available data regarding general demographics and socioeconomic factors (Table 1). Variations in SDoH data coverage across cohorts were analyzed with chi-squared testing. Statistical significance was defined as $p < 0.05$.

Results: We identified 23,806 unique adult patients of which 2246 had DR, 13,448 had glaucoma, 6634 had cataracts, and 1478 had AMD. Survey completion rates were high (99.5%-100%) across all cohorts for demographic information, overall health, income, education, and lifestyle. However, healthcare access (12.7%-29.4%), housing (0.7%-1.1%), social isolation (0.2%-0.3%), and food security (0-0.1%) showed significantly lower response rates (Figure 1). Additionally, the proportion of patients reporting healthcare access varied significantly across different disease cohorts ($p < 0.001$), with the lowest in DR patients at 12.7% vs. AMD patients at 29.4%.

Conclusions: SDoH data play a significant role in understanding the risk factors and management for common eye conditions, yet data coverage is highly variable in All of Us. This highlights the need for researchers and clinicians to be proactive about gathering these data in order to assemble complete data sets. Further research is needed to identify barriers to collecting patient data and examine the availability of SDoH data in local EHRs to understand the impact on direct clinical care.

CONTROL ID: 3518318

SUBMITTER (NAME ONLY): Elena Pacella

TITLE: Efficacy and safety of intravitreal Fluocinolone Acetonide micro implant (ILUVIEN®) in patients with chronic diabetic macular edema: one-year follow-up

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pacella, E. Trovato Battagliola, F. Pacella, A. Pistone, M. Malvasi, E. Vingolo, E. Pino, M. Salducci, Department of Sense Organs, Universita degli Studi di Roma La Sapienza, Roma, Lazio, ITALY|S. Scalinci, DIMEC, Universita di Bologna, Bologna, Emilia-Romagna, ITALY|P. Turchetti, National Institute for Health, Migration and Poverty, Rome, ITALY|

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ABSTRACT BODY:

Purpose: evaluate the efficacy and safety of intravitreal 0.19 mg fluocinolone acetonide (FAC) micro implant (ILUVIEN®) in patients with chronic diabetic macular edema (cDME). This is defined as edema that persists or recurs despite treatment.

Methods: observational prospective study recruiting subjects with cDME. Inclusion criteria: cDME for at least 2 years documented with OCT imaging, pseudophakia, previous treatments with laser photocoagulation, intravitreal injections of anti-VEGF and/or dexamethasone. Exclusion criteria: phakia, ocular hypertension, glaucoma, previous vitrectomy. Outcome measures included best-corrected visual acuity (BVCA), intraocular pressure (IOP), and central macular thickness (CMT), measured one, three (T3), six (T6), and twelve (T12) months post-injection. Data was compared with the Friedman test and significance was set at $p < 0.05$.

Results: 18 eyes with a median duration of cDME of 45 months [25 - 118 months]. 77% of subjects either maintained or improved their BVCA (Fig. 1 and 2). 17% and 33% of subjects showed an improvement of 15 ETDRS letters or more at 3 and 12 months respectively (Fig. 3). 17% and 28% of subjects showed a CMT < 250 microns at 3 and 12 months respectively (Fig. 4). The median change in CMT thickness was of -370 and -373.5 microns at 3- and 12-months post-injection respectively (p -value is .025). Changes in median IOP at 3- and 12-months post-injection were not statistically significant (p -value is .210). Ocular hypertension (OHT) was detected in 2 eyes (11%) one-week post-injection.

Conclusions: the FAC micro implant has proved efficacy in improving and/or maintaining BVCA in 77% of patients with cDME up to 12 months post-injection. Ocular hypertension is the most common side effect in pseudophakic patients but generally responds well to topical pressure-lowering medications.

CONTROL ID: 3518320

SUBMITTER (NAME ONLY): Ahmed Abdelhady

TITLE: The Prevalence of Retinal Detachment and Associated Comorbidities Over a 5-year Period

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abdelhady, Lehigh Valley Health Network, Allentown, Pennsylvania, UNITED STATES|J. Gaughan, C. Schorr, Cooper University Health Care, Camden, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal Detachment (RD) has a modest incidence with a lifetime risk of 3% by age 85 and is classified as a true ophthalmic emergency. Left untreated, RD frequently leads to blindness in the affected eye. This is unfortunate and sometimes inevitable, as patients often present to their general practitioner after their central vision has been compromised. Studies have demonstrated that RD is associated with events such as myopia, cataract surgery and trauma. The purpose of this descriptive study is to describe the demographics, comorbidities and socioeconomic factors associated with retinal detachment. These results will guide further research comparing identified factors to patients without retinal detachment.

Methods: We used the Healthcare Cost and Utilization Project, National Inpatient Sample database, to identify patients with a discharge diagnosis of RD (ICD-9/10 codes, 36.1, H33) between 2012-2016. The Elixhauser Comorbidity Index was used to identify comorbid conditions and the comorbidity burden. Demographic, geographical, socioeconomic factors and incidence of blindness were evaluated. Continuous data are reported as mean (SD), descriptive statistics are presented as frequency and percentage.

Results: A total of 6985 patients with RD were identified. The mean age was 59 (SD, 19.69) years, 56% (n=3,788) were male, and 60% (n=3,909) were of white race. Most patients (73%, n=4,970) were discharged from urban teaching hospitals and 33% (2,240) were from the southern US region. Thirty percent of RD patients had an annual income lower than \$42K and 52% (3,544) had Medicare insurance. The most frequent comorbidities were hypertension (59%), diabetes mellitus (36%), anemia (24%), and renal disease 23%. Blindness was present in 6.5% of RD patients.

Conclusions: In this study, the incidence of retinal detachment is low. Blindness occurred in less than 7% of patients. RD patients present most often to urban teaching hospitals with common chronic health conditions. Clinicians should understand the influence that these comorbid conditions, demographic and socioeconomic factors have in the emergent treatment of RD to avoid adverse outcomes.

CONTROL ID: 3518324

SUBMITTER (NAME ONLY): Ali Fard

TITLE: Correlation of macula thickness parameters in healthy subjects acquired using SDOCT structural-only and angiography all-in-one scans

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Fard, K. Makedonsky, A. Kolli, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: With the introduction of optical coherence tomography angiography (OCTA) in clinical OCT devices, one must acquire two separate scans (structural OCT and OCTA) in order to access both the wealth of angiography information and structural metrics such as macula thickness. This is also required to be able to compare the macula thickness parameters with prior scans of the same eye. The purpose of this study is to demonstrate that an all-in-one OCTA scan can provide comparable structural metrics to those acquired using the structural-only scan.

Methods: In this study we designed and implemented a prototype all-in-one OCTA 6x6 mm scan (490 A-scans/B-scan, 490 B-scans, 2 repetitions) in CIRRUSTM 6000 AngioPlex (ZEISS, Dublin, CA). B-scans acquired using this prototype OCTA scan were down-sampled to 200x200 A-scans per cube using nearest neighbor interpolation method, in order to compare with structural B-scans acquired using Macula Cube 200x200.

Ten healthy subjects (N=10) were scanned using the prototype scan and Macula Cube 200x200 under an IRB-approved study. The macula thickness analysis was applied on both datasets and the resultant values were compared using Bland-Altman plots.

Results: Figure 1 shows examples of angiography en face, structural en face, and OCT B-scans acquired using these two scan types. The all-in-one OCTA 6x6mm scan provides superior angiography en face and OCT B-scan image quality compared with Macula Cube 200x200 scan. Figure 2 shows the Bland-Altman plots for four inner quadrants (superior, nasal, inferior, temporal) and the central region of the ETDRS grid. The analysis shows good correlation ($r^2 > 0.92$) and low coefficient of variance ($CV < 1.3\%$) in all regions.

Conclusions: Our results demonstrate good correlation between macula thickness parameters acquired using a structural OCT scan and an all-in-one OCTA scan. This finding can potentially eliminate the need for acquiring multiple OCT/A scans in order to obtain both angiography and structural metrics, while maintaining data equivalency with prior scans of the same eye.

CONTROL ID: 3518330

SUBMITTER (NAME ONLY): Chris Cho

TITLE: In-clinic vs. Free-living Ambulatory Cadence in Patients with Glaucoma

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Visual impairment is a major risk factor for gait disturbances in glaucoma. Previously reported gait changes obtained in the laboratory setting may not accurately reflect one's free-living ambulatory behavior. The objectives of this study were to: 1) compare lab-measured and real-world cadences in glaucoma patients, and 2) explore the relationship between each cadence metric with visual field (VF) damage.

Methods: Demographics and health data were acquired on 242 participants of the Falls in Glaucoma Study. Visual field testing results on each eye were combined into an integrated visual field (IVF) sensitivity to judge glaucoma severity. Cadence was defined as the average number of steps taken per minute. Lab-measured (gait mat) cadence was obtained using a GAITRite electronic walkway at the baseline clinical evaluation. Real-world cadence was estimated as the peak 1-min cadence using 7-day GPS and accelerometer data. Peak 1-min cadence was calculated as the highest cadence value for a single minute on each individual day, averaged over all valid days of the 7-day accelerometer trial. Average peak at-home and away from home cadences were calculated in the same fashion, with subject location determined by GPS data. Negative binomial regression models were used to determine the association between cadence metrics and VF damage.

Results: Study participant characteristics are described in Table 1. Mean gait mat cadence was greater than the mean real-world cadence (107 vs. 91 steps/min; $P < 0.001$), with intra-person gait mat and real-world cadences demonstrating only weak positive correlation ($r = 0.29$; $P < 0.001$). VF damage showed no association with gait mat cadence ($RR = 1.01$; 95%CI, 0.99-1.02; $P = 0.50$), but each 5-dB decrement in IVF was associated with a 6% slower real-world cadence ($RR = 0.94$, 95%CI, 0.90-0.97; $P = 0.001$) (Table 2). Associations of real-world cadence with IVF sensitivity persisted for both at-home ($RR = 0.94$; 95%CI, 0.89-0.99; $P = 0.03$) and away from home cadences ($RR = 0.96$; 95%CI, 0.92-0.99; $P = 0.02$) (Table 2).

Conclusions: Lab-measured cadence largely overestimates and poorly correlates with real-world cadence in patients with glaucoma. Greater VF damage was found to be associated with slower real-world cadence. Our findings indicate that gait metrics that are obtained in a controlled environment may not accurately reflect the free-living ambulatory behaviors of glaucoma patients.

CONTROL ID: 3518344

SUBMITTER (NAME ONLY): Yanhui Ma

TITLE: In Vivo Approach to Estimate Ocular Rigidity and to Compare Biomechanical and Biometry Characteristics in Humans

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Our purpose was to use dynamic optical coherence tomography (OCT) video to estimate ocular rigidity. Furthermore, we evaluated the relationship between ocular rigidity and the biomechanical and biometry characteristics of the human eye.

Methods: Ocular rigidity was calculated using Friedenwald's empirical equation which estimates the change in intraocular pressure (IOP) produced by volumetric changes of the eye due to choroidal pulsations with each heartbeat. High-speed OCT video was utilized to noninvasively measure changes in choroidal volume through time-series analysis. A control-case study design was based on 23 healthy controls and 6 glaucoma cases. Multiple diagnostic modalities were performed during the same visit including Spectralis OCT for nerve head video, Pascal Dynamic Contour Tonometry for IOP and ocular pulse amplitude (OPA) measurement, Corvis ST for measuring dynamic biomechanical response, and Pentacam for characterizing biometry dimensions of the eye.

Results: Ocular rigidity in glaucoma was significantly larger than in healthy eyes ($p=0.039$). Negative correlations of ocular rigidity were found with axial length ($n=29$, $p=0.003$), and anterior chamber volume ($p=0.0002$). A stronger correlation of ocular rigidity was observed with the stiffness parameter at the highest concavity (SP-HC; $R=0.62$, $p=0.0005$) quantifying scleral stiffness, than at the first applanation (SP-A1; $R=0.41$, $p=0.033$) quantifying corneal stiffness. In addition, there was a positive correlation between the ocular rigidity and the static pressure-volume ratio (P/V ratio) ($p<0.0001$) (see Fig.1).

Conclusions: Ocular rigidity was noninvasively assessed using OCT video and OPA in a clinical setting. The strong correlation of ocular rigidity with biomechanical parameters, SP-HC and P/V ratio, demonstrated the validity of the ocular rigidity estimation. These in vivo methods offer an important approach to investigate the role of ocular biomechanics in glaucoma. Higher ocular rigidity in glaucoma offers evidence that the scleral stiffness is a contributing factor to the pathogenesis of glaucoma.

CONTROL ID: 3518375

SUBMITTER (NAME ONLY): Hong Jiang

TITLE: Longitudinal study of retinal structure, vascular and neuronal function in patients with relapsing-remitting multiple sclerosis: 1-year follow-up

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To quantify retinal structural, vascular, and functional changes in patients with relapsing-remitting MS (RRMS) over 1 year.

Methods: Eighty-eight eyes of 44 patients with RRMS underwent assessments of low contrast letter acuity (LCLA), retinal ganglion cell function detected by the steady-state Pattern Electroretinogram (PERG), axonal microstructural integrity measured as birefringence, intraretinal layer thicknesses by ultra-high resolution optical coherence tomography (OCT), volumetric vessel density (VVD) by OCT angiography, and retinal tissue perfusion (RTP) by the Retinal Function Imager (RFI). All measurements were performed at baseline and 1-year follow-up. The impacts of disease activities and a history of optical neuritis (ON) were analyzed.

Results: Compared to baseline, there were no significant differences in all variables ($P > 0.05$), except for the axonal birefringence and RFI measurements. The birefringence's of retinal fiber layer at the temporal and superior quadrants was significantly decreased at follow-up ($P < 0.05$). The retinal blood flow and RTP were significantly increased at follow-up ($P < 0.05$). In the sub-group with ON, significantly longer PERG latency and decreased VVD in the retina were observed at follow-up ($P < 0.05$). In patients with improved LCLA, significantly increased RTP and decreased VVD ($P < 0.05$) were also observed.

Conclusions: This is the first longitudinal study that assessed the RTP and VVD, along with other retinal structural and functional parameters in MS. The recovery of retinal vascular function occurred with the improved LCLA, suggesting that these measurements may be associated with disease progression and therapeutic efficacy.

CONTROL ID: 3518379

SUBMITTER (NAME ONLY): Glenn Yiu

TITLE: Unsupervised deep learning for grading age-related macular degeneration using retinal fundus images

SESSION TITLE: AI in the retina: Clinical Applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Yiu, K. Snyder, Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|B. Yellapragada, S. Hornauer, S. Yu, Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many diseases such as age-related macular degeneration (AMD) are classified based on human-defined rubrics that are prone to bias. Supervised neural networks are trained using human-generated labels that require labor-intensive annotations and are restricted to the specific trained tasks. Here, we employ unsupervised learning which organizes fundus images based only on visual similarity to determine AMD severity and identify ocular features without the confines of human definitions or labels.

Methods: We trained an unsupervised deep neural network with Non-Parametric Instance Discrimination (NPID) using 100,848 human-graded fundus images from 4757 participants from the Age-Related Eye Disease Study (AREDS) to grade AMD severity using 2-step, 4-step, and 9-step classification schemes. We compared balanced and unbalanced accuracies of NPID against published supervised networks and ophthalmologists, explored network behavior using hierarchical learning of image subsets and spherical k-means clustering of feature vectors, then searched for ocular features that can be identified without labels.

Results: Unsupervised NPID demonstrated versatility across different AMD classification schemes without re-training, and achieved balanced accuracies comparable to supervised networks or human ophthalmologists in classifying advanced AMD (82% vs. 81% or 89%), referable AMD (87% vs. 92% or 96%), or on the 4-step AMD severity scale (65% vs. 63% or 67%), despite never directly learning these labels. Drusen area drove network predictions on the 4-step scale, while depigmentation and geographic atrophy (GA) areas correlated with advanced AMD classes. Unsupervised learning identified grader-mislabeled images and revealed susceptibility of some classes within the more granular 9-step AMD scale to misclassification by both ophthalmologists and neural networks. Importantly, unsupervised learning enabled data-driven discovery of AMD features such as GA and other ocular phenotypes of the choroid (e.g. tessellated or blonde fundi), vitreous (e.g. asteroid hyalosis), and lens (e.g. nuclear cataracts), that were not pre-defined by human labels.

Conclusions: Unsupervised learning enables automated AMD severity grading comparable to ophthalmologists and supervised networks, reveals biases of human-defined AMD classification systems, and allows unbiased, data-driven discovery of AMD and non-AMD ocular phenotypes.

CONTROL ID: 3518401

SUBMITTER (NAME ONLY): Abdelrahman Elhusseiny

TITLE: Is MIGS cost effective?

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To quantify and to analyze the relative cost of various glaucoma surgical procedures and selective laser trabeculoplasty (SLT) per mm Hg intraocular pressure (IOP) reduction (\$/mmHg).

Methods: Published glaucoma treatment studies were reviewed to quantitate the reduction of mean IOP and glaucoma medications for a given treatment modality. Medicare allowable costs were used to calculate a newly introduced parameter - cost per mmHg IOP reduction- at 1,2,3,4 and 5 years postoperatively. Medicare-allowable fee data for 2020 were obtained from Centers for Medicare and Medicaid Services to calculate the costs (in 2020 US dollars) associated with each treatment assuming it was administered a hospital-based (facility) practice. Our calculations included all professional fees including anesthesia and facility fees. The dollars per relative value unit (RVU) conversion factor was \$37.89, the estimated rate for 2020. Reimbursement was adjusted for the geographic modifier for Miami, Florida.

Results: The relative cost per mmHg IOP reduction was highest in year 1 as it included both the surgical cost and cost of anti-glaucoma medications needed postoperatively. Most efficient as SLT (\$66/mmHg at year 1) was substantially lower than all other glaucoma surgical interventions for the first 3 years. The most cost-efficient glaucoma surgery in the first year was trabeculectomy (\$215/mmHg) and least was iStent (\$1420/mmHg). Intermediate cost-efficiency modalities were for CPC \$(446/mmHg) and BGI (\$469/mmHg). The most cost-efficient MIGS procedure was Trabectome (\$505/mmHg) followed by GATT (\$748/mmHg).

Conclusions: There is a wide variation in the costs to lower the IOP and reduce dependence on nonsurgical modalities. While there may well be a role for a more costly modality in individual cases, the high costs of some of the existing therapies should be considered when designing a treatment strategy.

CONTROL ID: 3518465

SUBMITTER (NAME ONLY): Robin Hodges

TITLE: Resolvins D3, D4, and D5 activate phospholipase C and D to increase intracellular $[Ca^{2+}]_i$ in rat conjunctival goblet cells

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Resolvins (Rvs) D3, D4, and D5 are specialized proresolving mediators in inflammation-resolution biosynthesized from the w3 fatty acid docosahexaenoic acid. The purpose of this study was to determine if RvD3, RvD4, or RvD5 interact with rat conjunctival goblet cells and determine the signal transduction pathways utilized to increase intracellular $[Ca^{2+}]_i$ ($[Ca^{2+}]_i$).

Methods: Conjunctiva from male Sprague-Dawley rats was removed and placed in organ culture with RPMI media. Goblet cells were allowed to grow out of the tissue plug. First passage cells were used for all experiments. To measure $[Ca^{2+}]_i$, cells were trypsinized and transferred to 35-mm glass bottom dishes. The cells were incubated at 37°C for 1 hour with the calcium indicator fura2/AM with 250 mM sulfinpyrazone and 8 mM Pluronic acid F127. $[Ca^{2+}]_i$ was measured with a ratio imaging system (InCytIm2; Intracellular Imaging, Cincinnati, OH) using wavelengths of 340 and 380 nm and an emission wavelength of 505 nm. Cells were stimulated with RvD3, RvD4, and RvD5 from 10^{-12} - 10^{-8} M. Inhibitors were added 10-30 minutes prior to stimulation.

Results: RvD3, RvD4, and RvD5 each increased $[Ca^{2+}]_i$ in a concentration dependent manner with peak concentrations of 10^{-9} M for each resolvin. Only RvD5-stimulated increase in $[Ca^{2+}]_i$ was inhibited by BOC2, an inhibitor of the ALX/FPR2 receptor. $[Ca^{2+}]_i$ stimulated by all three of these D-series resolvins was blocked by inhibition of phospholipase (PL) C and D but not A2. Absence of extracellular Ca^{2+} also blocked the increase in $[Ca^{2+}]_i$ stimulated by RvD3, RvD4, and RvD5. Only RvD3-stimulated increase in $[Ca^{2+}]_i$ was blocked by H89, an inhibitor of protein kinase A.

Conclusions: RvD3, RvD4, and RvD5 activate PLC and D, but not A2. Only RvD3 uses cAMP and protein kinase A. Thus RvD3, RvD4, and RvD5 play a role in the physiologic regulation of conjunctival goblet cells.

CONTROL ID: 3518468

SUBMITTER (NAME ONLY): Juno Cho

TITLE: Effect of the Support, Educate, Empower (SEE) personalized glaucoma coaching program on patient-centered outcome measures

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Cho, L.M. Niziol, P.P. Lee, D.C. Musch, P. Newman-Casey, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|M. Heisler, Internal Medicine, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|K. Resnicow, University of Michigan School of Public Health, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Motivational Interviewing (MI), a type of counseling, has improved medication adherence, health outcomes, and patient-centered outcomes in many chronic diseases. The 7-month MI-based Support, Educate, Empower (SEE) personalized glaucoma coaching program improved medication adherence by 21-percentage points in a sample of non-adherent glaucoma patients. The goal of this study was to assess the impact of the SEE program on patient-centered outcome measures.

Methods: Glaucoma patients (≥ 40 years old, taking ≥ 1 medication) self-reporting poor medication adherence were recruited from the University of Michigan. Patients completed 10 validated surveys both before and after their 7-month coaching program. Five of these surveys measured the participants' skills in managing their glaucoma (Perceived Competence Scale, Glaucoma Knowledge Scale, Glaucoma Medication Self-Efficacy Scale, Goal Setting Scale, Confidence Asking Question Scale). The Treatment Self-Regulation Questionnaire measured participants' motivation for health behavior change. The Healthcare Climate Questionnaire measured the program's support for patient autonomy. Three other scales explored satisfaction with care (Satisfaction with Information Scale), glaucoma related distress (Diabetes Distress Scale adopted for glaucoma), and perceived benefit of treatment (Perceived Benefits Scale). Surveys were scored according to official documentation. Pre- and post-intervention scores were compared using paired t-tests and Wilcoxon signed-rank tests. P-values were adjusted for multiple comparisons using Holm's method.

Results: 39 patients completed the SEE program. Significant positive changes were noted in 8/10 patient centered outcome measures (perceived competence, autonomy support, intrinsic motivation, disease related distress, self-efficacy, satisfaction with information, confidence asking questions, and goal setting). There was no effect on perceived benefits of glaucoma treatment or glaucoma knowledge.

Conclusions: The SEE Program improved a large number of patient-centered outcome measures such as overall glaucoma related distress, motivation to be adherent, and confidence to ask their ophthalmologist questions. These positive changes will hopefully help participants maintain engagement with glaucoma treatment over their lifetime.

CONTROL ID: 3518470

SUBMITTER (NAME ONLY): Jian-Yu E

TITLE: Global Positioning System (GPS)-tracked physical activity in glaucoma

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. E, A. Mihailovic, C. Garzon, S.K. West, P.Y. Ramulu, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|J. Schrack, Johns Hopkins Bloomberg School of Public Health, Maryland, UNITED STATES|T. Li, University of Colorado Denver Anschutz Medical Campus, Colorado, UNITED STATES|D.S. Friedman, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L.N. Gitlin, Drexel University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Physical activity is a central feature of well-being and an essential component of quality of life in older adults, particularly those with vision loss. To optimize physical activity and safety, it is important to understand where persons with visual impairment perform their activities and which activity locations are safe. We performed a prospective cohort study to examine the association of visual field (VF) damage on physical activity away-from-home, per away-from-home excursion, and at home in glaucoma patients.

Methods: We analyzed three years (2013-2015) of data from a well-established cohort of community-dwelling older people with glaucoma (N=229, Table 1). The severity of VF damage was defined as average sensitivity within the integrated VF (IVF). Participants wore accelerometers and GPS trackers for seven days to measure physical activity and characterize activity location. Multivariable negative binomial regressions were used to test whether away-from-home activity per day, activity per away-from-home excursion, and at-home activity per day varied by the severity of VF damage. Covariates included age, race, sex, living arrangement, employment, education, comorbidity, polypharmacy, and cognitive function.

Results: Each 5-dB decrement in IVF sensitivity was associated with a lower amount of away-from-home activity per day [18% less Moderate & Vigorous Physical Activity (MVPA) minutes/day, 16% less active minutes/day (95% CI, 0.75, 0.93) and 17% fewer steps/day (95% CI, 0.74, 0.93)] (Table 2), and physical activity per away-from-home excursion [20% less MVPA minutes/excursion (95% CI, 0.65, 0.98), 19% less active minutes/excursion (95% CI, 0.71, 0.92) and 20% fewer steps/excursion (95% CI, 0.72, 0.90)]. However, worse IVF sensitivity was not associated with measures of at home activity (MVPA minutes/day, active minutes/day, and steps/day), time spent at or away from home, or excursions/week ($p>0.1$ for all).

Conclusions: Restriction of physical activity in more severe glaucoma patients results mostly from activity restriction outside home environment. These findings highlight the importance of maintaining a safe home environment and increasing confidence to perform activity, particularly high-intensity activity, when leaving the home amongst patients with glaucoma. Further research is warranted to define specific environmental features that may improve safety and functionality in visually impaired population.

CONTROL ID: 3518471

SUBMITTER (NAME ONLY): James Kwan

TITLE: The Effect of Systemic Immunomodulatory Therapy on Acute Outcomes of Stevens-Johnson Syndrome

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Systemic immunomodulator (SI) use in the acute phase of Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is controversial. Cyclosporine a (CsA) has been of particular recent interest. It is unknown if SIs affect acute ocular disease severity in SJS. Our study investigated the relationship of choice of SI and acute ocular severity (AOS) in SJS. We additionally observed the relationship between use of these regimens and rates of hospital service utilization including but not limited to intensive care unit (ICU) admission, ICU length of stay (LOS), and 30-day readmission.

Methods: We performed a retrospective, observational chart review of all patients in our system with confirmed SJS by biopsy or exam by dermatology. Patients were divided by treatment regimen including: steroids; intravenous immunoglobulin; CsA; combined CsA and steroids; and supportive care. Exclusion criteria included no documentation of the acute episode. Sixty-eight patients and 130 eyes were included. Statistics were performed in R version 4.0.2. The primary outcome was post-SI AOS score. Means with standard deviations are presented for continuous and ordinal variables and frequencies for categorical variables. Generalized estimating equations and Fisher's exact test were used to compare SI therapies on acute ocular disease (reference group was supportive care).

Results: No significant difference in greatest AOS score post-SI administration was seen between treatment groups after controlling for initial disease severity. Significant differences in presence of toxic epidermal necrolysis and ICU admission were noted across treatment groups. Significance did not persist when comparing those receiving any SI combination that included CsA vs no CsA in the aforementioned variables. Additionally, differences in ICU LOS and 30-day readmission rates were not observed.

Conclusions: No relationship was found between the treatment groups and mean AOS scores post-SI administration. Frequency of ICU care was significantly different across groups but not between CsA vs non-CsA groups, suggesting that CsA, versus other SIs, is more readily used across services and in varying degrees of systemic disease severity. SI regimen does not appear to correlate with acute ocular disease outcomes in this cohort. Next steps include studying the timeline and dosage of SI administration in relation to acute and chronic ocular disease in SJS.

CONTROL ID: 3518477

SUBMITTER (NAME ONLY): Johannes Birtel

TITLE: Occult retinopathy in patients with severe kidney disease: NPHP1-associated ciliopathy

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Birtel, P. Charbel Issa, Oxford Eye Hospital, Oxford University Hospitals NHS Foundation Trust and Nuffield Laboratory of Ophthalmology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UNITED KINGDOM|J. Birtel, M. Book, P. Herrmann, Department of Ophthalmology, University of Bonn, Bonn, GERMANY|G. Spital, Eye Center at St. Franziskus-Hospital Münster, Münster, GERMANY|S. Habbig, S. Bäumner, Department of Pediatrics, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, GERMANY|V. Riehmer, B. Beck, H. Bolz, Institute of Human Genetics, University of Cologne, University Hospital of Cologne, Cologne, GERMANY|B. Beck, Institute of Human Genetics, Center for Molecular Medicine Cologne, Center for Rare Diseases Cologne, Cologne, GERMANY|D. Rosenkranz, H. Bolz, Senckenberg Centre for Human Genetics, Frankfurt, GERMANY|M. Dahmer-Heath, J. König, Department of General Pediatrics, University Children's Hospital, Münster, GERMANY|

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ABSTRACT BODY:

Purpose: Nephronophthisis (NPH) is the leading cause of hereditary end-stage kidney disease in children and young adults. Biallelic NPHP1 deletions are the most frequent molecular defect found in NPH patients. Nephrocystin 1, the gene product of NPHP1, is also expressed in photoreceptors where it plays an important role in the intraflagellar transport between the inner and outer segments, but the retinal phenotype has never been investigated in detail. Here, we comprehensively characterized retinal changes in patients with biallelic NPHP1 deletions.

Methods: This cross-sectional, multicenter study included 16 patients with a homozygous deletion of the NPHP1 gene. Subjects underwent ophthalmic examination including best-corrected visual acuity (BCVA) testing and retinal imaging.

Results: Median age at examination was 17 years (range, 6-53 years). Fundoscopy and fundus autofluorescence (AF) imaging showed no obvious abnormalities. However, optical coherence tomography (OCT) imaging revealed a distinct retinal phenotype with mild thinning of the outer nuclear layer, reduced reflectivity of the ellipsoid zone, fading or loss of the interdigitation zone, but a preservation of the retinal pigment epithelium. Median visual acuity was 20/20 (range, 20/80-20/20) with a para-central sensitivity loss on visual field testing. Retina-wide function measured with full-field electroretinography revealed either normal responses or a mild cone-dominant dysfunction. Nine patients were asymptomatic, whereas those with visual symptoms mainly reported reduced night vision as initial vision problem. One patient with more severe retinal degeneration carried an additional heterozygous variant in CEP290.

Conclusions: These data suggest that homozygous NPHP1 gene deletions result in a mild retinal ciliopathy that predominantly affects cones, but with relative sparing of the fovea. The distinct retinal phenotype is visible on OCT and usually remains without obvious correlates on clinical examination and AF imaging ("occult retinopathy"). Despite the predominant cone dysfunction on ERG testing, night vision problems may be an early symptom. The identified additional CEP290 variant in the patient with the more severe retinopathy may indicate a potential role for genetic modifiers, although this requires further investigation.

CONTROL ID: 3518523

SUBMITTER (NAME ONLY): Brice Vofo

TITLE: Ten year outcome of neovascular age-related macular degeneration: association of functional and anatomical treatment outcomes with major risk allele for the disease

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.N. Vofo, G. Beykin, J. Levy, I. Chowers, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL]

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ABSTRACT BODY:

Purpose: To evaluate the long-term functional and anatomical outcomes of neovascular age-related macular degeneration (nvAMD) eyes treated with intravitreal anti-vascular endothelial growth factors (VEGF) compounds for up to 10 years and to identify associated factors.

Methods: Retrospective evaluation of consecutive nvAMD naïve eyes initially treated with intravitreal bevacizumab and switched to ranibizumab or aflibercept if required using a treat and extend protocol. Data were collected from the electronic medical records including demographics, clinical, and optical coherence tomography findings. Genotyping for the CFH (rs1061170), HTRA1 (rs1200638), and C3 (rs2230199) major risk single nucleotide polymorphisms for AMD were collected.

Results: A total of 206 patients (n=276 eyes) commenced anti-VEGF therapy ≥ 8 years, and 66 (32.0%) patients (n=80 eyes, 29.0%) remained in follow-up ≥ 8 years and were included in this study. The mean number of anti-VEGF injections (\pm SD) was 73.3 ± 28.0 over 10 years. Mean best-corrected visual acuity (BCVA) (LogMAR \pm SD) improved from 0.55 ± 0.53 at baseline to 0.42 ± 0.41 ($p < 0.0005$) at 24 months, but deteriorated to 0.81 ± 0.71 at 8 years ($p < 0.03$) and 1.00 ± 0.73 at 10 years ($p < 0.0005$, compared with baseline). Baseline central point thickness (CPT) and central subfield thickness (CST; microns \pm SD) were 410.9 ± 208.1 and 415.8 ± 162.1 , respectively. Both values decreased to 294.7 ± 135.9 and 323 ± 113.6 ($p < 0.0005$ in each case), respectively, after 3 monthly injections, and remained lower than baseline values until the end of follow-up. BCVA and intraretinal fluid at baseline, macular atrophy and thinning at end of follow-up were associated with the visual outcome after 10 years. Carriers of the CFH and C3 risk alleles had a smaller reduction of CST at follow-up compared with none-carriers. Thinning of CST correlated negatively with the number of CFH/C3 risk alleles borne by a patient. (Pearson rho= -0.246, and -0.608; $p=0.040$, and 0.003 at 8 and 10 years, respectively).

Conclusions: nvAMD patients under anti-VEGF therapy for over 10 years encounter a substantial mean vision loss that is influenced by the presence of IRF at baseline and by atrophy rather than re-thickening of the macula at follow-up. Major complement risk alleles for AMD are associated with a lesser reduction in baseline macula thickness in the long-term.

CONTROL ID: 3518546

SUBMITTER (NAME ONLY): Tal Sharon

TITLE: The Effect of Hypotensive drugs on Intraocular Lens Clarity

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sharon, L. Naftali Ben Haim, Y. Ton, E.I. Assia, A. Belkin, Ophthalmology, Meir Medical Center, Kfar Saba, ISRAEL|T. Sharon, L. Naftali Ben Haim, Y. Ton, A. Lifshitz Einan, E.I. Assia, A. Belkin, Sackler School of Medicine, Tel Aviv University, Tel Aviv, ISRAEL|A. Lifshitz Einan, Ophthalmology, Yitzhak Shamir Medical Center Assaf Harofeh, Zerifin, Center, ISRAEL|

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ABSTRACT BODY:

Purpose: To assess the effect of hypotensive drugs on light absorbance, discoloration, opacification and precipitate formation of IOLs

Methods: In this laboratory study, four types of IOLs (hydrophilic and hydrophobic acrylic) were soaked in solutions containing Brimonidine-tartrate 0.2%, Brimonidine-tartrate/Timolol-maleate 0.2%/0.5%, Dorzolamide 2%, Dorzolamide/Timolol-maleate 2%/0.5%, Latanoprost 0.005% and Timolol-maleate 0.5%. Non-treated IOLs and IOLs soaked in Balanced Salt Solution (BSS) served as controls. All Treated lenses were sealed in glass containers and placed in an oven at 82 degrees Celsius for 120 days (approximating 10 years in 37 degrees according to The Arrhenius equation).

Each IOL underwent four examinations: gross inspection by light microscopy, light absorbance by a photo-spectrometer, Scanning Electron microscopy and an Energy-dispersive X-Ray spectrometry.

Results: A total of 98 acrylic IOLs of 4 different models, were included in the study. 49 hydrophilic and 49 hydrophobic. All BSS-soaked IOLs appeared clear with no significant discoloration or precipitates formation and light absorbance in these lenses was comparable to that of non-soaked, non-heated IOLs ($P>0.05$).

Gross examination revealed brown discoloration of IOLs Soaked in solutions containing Dorzolamide and a yellow discoloration of IOLs soaked in solutions containing Brimonidine. Precipitates of different size, morphology and distribution were seen on hydrophilic and hydrophobic IOLs soaked in solutions containing Latanoprost, Timolol and Brimonidine. Opacification was noted in both hydrophilic and hydrophobic IOLs. Glistening was formed in one IOL model soaks in 6 different solutions, including BSS.

Significant difference in light absorbance was documented between IOLs soaked in Brimonidine/Timolol, Dorzolamide, Dorzolamide/Timolol and latanoprost as compared to control ($P<0.03$).

In most areas of precipitated, spectrometric signatures of Calcium and phosphor was obtained. Brown discolored IOLs contained sulfur.

Conclusions: Interactions between different hypotensive drugs and different IOLs exist in manner of change in light absorbance, discoloration and precipitate formation in-vitro

CONTROL ID: 3518557

SUBMITTER (NAME ONLY): RAKESH RADHAKRISHNAN

TITLE: Role of mitochondrial encoded long non-coding RNA in diabetic retinopathy

SESSION TITLE: Mitochondria in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. RADHAKRISHNAN, R.A. Kowluru, Kresge Eye Institute, Detroit, Michigan, UNITED STATES|

Commercial Relationships Disclosure (Abstract): RAKESH RADHAKRISHNAN: Commercial Relationship: Code N (No Commercial Relationship) | Renu Kowluru: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the pathogenesis of diabetic retinopathy, mitochondrial DNA (mtDNA) is damaged, compromising the electron transport chain (ETC) system, and accelerating retinal capillary cell death. The proteins, encoded by mtDNA have an important role in the proper functioning of the ETC system, and cytochrome B (CYTB) is one of the 13 mtDNA-encoded genes critical in the functioning of complex III. Diabetes also alters the levels of many nuclear DNA transcribed long non-coding RNAs (LncRNAs; RNAs with more than 200 nucleotides with no open reading frame for translation), and these LncRNAs have been implicated in diabetic retinopathy. However, mtDNA also transcribes three LncRNAs, but their role in diabetic retinopathy remains to be elucidated. Our aim was to investigate the role of mitochondrial encoded LncRNA Cytochrome B (LncCytB) in diabetic retinopathy.

Methods: Human retinal endothelial cells, incubated in 5mM (normal) or 20mM (high) D-glucose were analyzed for LncCytB expression by qRT-PCR and its mitochondrial localization by RNA fluorescence in situ hybridization. The interactions between LncCytB and CYTB were evaluated by Chromatin isolation by RNA purification method. The role of LncCytB in the regulation of CYTB expression was determined in HRECs overexpressing LncCytB using full-length LncCytB, synthesized by T7 promoter based in-vitro transcription.

Results: Compared to normal glucose, high glucose decreased LncCytB transcripts, and also attenuated its levels in the mitochondria. The interactions of LncCytB with CYTB were compromised and the activity of the complex III was reduced. Restoration of LncCytB ameliorated glucose-induced decrease in CYTB.

Conclusions: Decreased interactions of LncCytB-CYTB in hyperglycemic milieu attenuate the processing of mtDNA-encoded CYTB, resulting in its decreased expression, and the ETC system is compromised. Thus, regulation of LncCytB could prevent ETC-mediated self-propagation of the vicious cycle of free radicals, and protect mitochondrial integrity in diabetic retinopathy.

CONTROL ID: 3518565

SUBMITTER (NAME ONLY): Cecile Truong

TITLE: Characterizing Long-term Vision Change and Intravitreal Anti-VEGF Treatment Pattern Among Neovascular Age-Related Macular Degeneration (nAMD) Patients in the US: Analysis of the Vestrum Database

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Truong, S. Chang, J. Willis, K. Asik, P. Kulkarni, Genentech Inc, South San Francisco, California, UNITED STATES|G. Yiu, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|N. Boucher, F. Ishii, Vestrum Health, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study investigates the impact of anti-VEGF treatment frequency and pattern on long-term VA outcomes in real-world nAMD patients in the U.S..

Methods: A retrospective cohort study was conducted using the de-identified Vestrum Health EHR database. Patients who were newly diagnosed with nAMD between Jan 2015-Mar 2019, ≥ 50 years old, had ≥ 12 -month follow-up, and received ≥ 1 anti-VEGF treatment were included. The primary outcome was change in VA over 48 months. Changes in VA were evaluated across subgroups defined by: baseline VA, first year treatment frequency, and anti-VEGF induction, defined as first 3 injections within 4 months of diagnosis. VA scores were converted from Snellen to ETDRS equivalent letters.

Results: We identified 40,094 patients with newly diagnosed nAMD. Mean age was 80 years and 62.7% were female. The mean baseline VA (SD) was 50.2 (23.9) ETDRS letters; 28% had baseline VA ≤ 35 letters ($\leq 20/200$), 22% had 57-36 letters (20/70-20/200), 29% had 69-58 letters (20/70-20/40), and 22% had ≥ 70 letters ($\geq 20/40$). At 12, 24, 36, and 48 months, patients received an average of 7.7, 6.0, 5.7 and 5.5 injections each year and had a mean VA change from baseline of +4.5, +3.4, +1.7, and +1.1 letters respectively.

VA change was associated with a greater number of injections. Given similar injection frequency, patients with worse baseline VA had larger VA gain compared to those with better baseline VA (Figure 1). Additionally, patients who underwent induction with 3 monthly anti-VEGF doses had higher annual treatment frequency over time and corresponding better short- and long-term visual outcomes (Figure 2).

Conclusions: In the US, based on a large real-world dataset of treatment naive nAMD patients, better short- and long-term VA outcomes are associated with lower baseline VA, higher treatment frequency, and anti-VEGF induction with 3 injections within 4 months of diagnosis.

CONTROL ID: 3518589

SUBMITTER (NAME ONLY): Christine Sanfilippo

TITLE: Interim Analysis of Antibiotic Resistance from Bacterial Pathogens Collected in the 2020 ARMOR Study

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.M. Sanfilippo, H.H. DeCory, Medical Affairs, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|P.A. Asbell, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: When treating bacterial infections of the eye, knowledge of the antibiotic resistance profile of causative bacteria may aid in selection of the most suitable treatment. Now in its twelfth consecutive year, the ongoing Antibiotic Resistance Monitoring in Ocular microorganisms (ARMOR) study is the only nationwide surveillance study focused exclusively on common ocular pathogens. This interim analysis reports on the antibiotic susceptibility of ocular isolates collected to date in 2020.

Methods: Clinically relevant isolates of *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae* cultured from ocular infections were submitted to a central laboratory for in vitro antibiotic susceptibility testing as part of ARMOR. Minimum inhibitory concentrations (MICs) were determined per Clinical and Laboratory Standards Institute broth microdilution methods for up to 16 antibiotics (from 10 drug classes), and isolates were classified as susceptible or resistant based on established interpretative criteria.

Results: A total of 366 isolates from 20 US sites were analyzed. Staphylococci exhibited high levels of in vitro resistance to azithromycin (57-62%), oxacillin/methicillin (36-46%), and ciprofloxacin (25-33%); trimethoprim resistance (28%) was also observed among CoNS. Multidrug resistance (MDR; ≥ 3 antibiotic classes) was common among *S. aureus* (39%) and CoNS isolates (43%), with a substantial proportion of methicillin-resistant isolates exhibiting MDR (78% and 75%, respectively). Although *S. pneumoniae* isolates demonstrated resistance to azithromycin (47%) as well as oral penicillin and tetracycline (both 41%), no resistance to fluoroquinolones was detected. Resistance to polymyxin B and the fluoroquinolones was low (<2%) among *P. aeruginosa*, and no resistance to tested drugs was observed among *H. influenzae* isolates.

Conclusions: Preliminary results from the 2020 ARMOR study indicate continued high levels of in vitro antibiotic resistance among staphylococci, with considerable MDR especially in methicillin-resistant strains. Combined with other clinical information, these surveillance data can help guide the selection of antibiotics for empiric management of ocular infections.

CONTROL ID: 3518593

SUBMITTER (NAME ONLY): Tinh Le

TITLE: A novel, online platform for tracking amblyopia patients: cohort description and initial results

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Le, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|B. Can, A. Peiffer, H. Klein, M. Kohen, F. Orge, Ophthalmology, University Hospitals, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Amblyopia is a leading cause of childhood blindness. Although multiple effective treatment methods exist, patient compliance remains a major hurdle to successful outcomes. We assessed the outcomes of patients enrolled in a novel, online amblyopia tracking platform.

Methods: Inside Out Medicine (Seattle, WA) is an online, HIPAA-compliant platform that enhances monitoring of amblyopia patient treatment. The platform let parents create a virtual “log” in which they record their child’s daily treatment (hours patched per day, patches used per day, which eye was patched, etc.) and allows providers to view the logs. The platform also gives instructions for parents to assess and record their child’s near visual acuity (VA). Providers at an urban academic center enrolled eligible patients (amblyopia patients age 1-12 years undergoing occlusion or penalization therapies) by sending an email invitation to parents to create an account on the platform. Parents were instructed to log all amblyopia treatment prescribed by their ophthalmologist/optometrist in the platform. Baseline characteristics, treatment compliance and outcome measures (change in visual acuity) were collected for patients who had presented for a follow up clinic visit at least 60 days after enrollment in the platform.

Results: Since the integration of the program in our clinics on 7/14/20, 65 patients have been enrolled in the platform. The cohort has an average age of 4.95 years (std = 2.55) and is 51% female. For patients whose amblyopia can be graded, 44% have mild amblyopia, 48% have moderate amblyopia, and 10% have severe amblyopia. The right eye is amblyopic in 51% of patients.

Of the 65 enrolled patients, 12 had a follow up visit after at least 60 days of platform enrollment (average 101 days). 7 patients had mild amblyopia, 4 had moderate, and 1 had severe. Average change in visual acuity at first follow up was an improvement of .055 logMAR units (from .300 to .245).

Conclusions: We report the use of a novel, online, HIPAA-compliant platform to provide daily data on patients’ amblyopia treatment compliance. Patients enrolled in the platform for at least 60 days experienced an average VA improvement of .057 logMAR units in the amblyopic eye. This pilot study shows the potential of this online, easy-to-use platform to improve amblyopia patient outcomes by improving compliance monitoring and oversight.

CONTROL ID: 3518626

SUBMITTER (NAME ONLY): Jackie Tan

TITLE: Chitosan film adhesive for sutureless corneal surgery

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Tan, L.J. Foster, S.L. Watson, Corneal Research Group, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|L.J. Foster, Bio/Polymer Research Group, The University of Alabama in Huntsville, Huntsville, Alabama, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jackie Tan: Commercial Relationship: Code N (No Commercial Relationship) | Leslie Foster: Commercial Relationship: Code N (No Commercial Relationship) | Stephanie Watson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the efficacy of a novel laser activated, thin-film chitosan adhesive technology for sealing penetrating corneal incisions against self-sealed or sutured incisions in an in vivo rabbit model.

Methods: Central penetrating corneal incisions of 2mm were created on the right eyes of 135 albino rabbits. These incisions were closed using either the adhesive technology, 10-0 nylon sutures or left to self-seal (n=45 per group). Wound integrity was quantified by measuring the highest fluid pressure prior to wound leak (burst pressure). At timepoints of up to 14 days post-operatively, 5 rabbits from each group were euthanized and their corneoscleral rim dissected for the burst pressure testing using a modified Barron chamber. Statistical significance was determined at $p < 0.05$.

Results: Average burst pressure from corneal incisions sealed using the chitosan technology were persistently higher than both the suture and self-sealed groups from timepoints 0 to 72 hours ($p < 0.05$). At 3 hours post-operatively, the average burst pressures (\pm standard deviation) were 169.3 (± 100.1), 10.6 (± 6.8) and 5.3 (± 3.8) mmHg, respectively, $p = 0.0023$. At 24 hours, burst pressures were 233.8 (± 83.2), 6.4 (± 2.9), 45.2 (± 16.6) mmHg, respectively, $p = 0.000019$. Burst pressures 72 hours post-operatively were 229 (± 120.1), 12.4 (± 6.6), 36.4 (± 21.6) mmHg, respectively, $p = 0.000696$. After 7 days, burst pressures between all groups no longer showed any statistical difference. The chitosan group recorded an average burst pressure of 307.0 (± 106.0) and 360.0 (± 0.0) mmHg on day 7 and day 14 respectively.

Conclusions: Chitosan adhesive technology can seal full thickness corneal incisions in a living rabbit model, tolerating high burst pressures and accelerating healing.

CONTROL ID: 3518687

SUBMITTER (NAME ONLY): Sanjoy Bhattacharya

TITLE: Phospholipid composition and their interconversion enzymes differences in glaucomatous human trabecular meshwork compared to controls.

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.K. Bhattacharya, G. Edwards, R.K. Lee, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|S.K. Bhattacharya, G. Edwards, N. Ziebarth, R.K. Lee, Miami Integrative Metabolomics Research Center, University of Miami School of Medicine, Miami, Florida, UNITED STATES|Y. Liu, Augusta University, Augusta, Georgia, UNITED STATES|N. Ziebarth, Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine differences in phospholipid profiles, their interconversion enzymes and steady state precursors between human glaucomatous trabecular meshwork and normal controls. To establish whether phospholipid containing vesicles are different in glaucomatous aqueous humor (AH) compared to controls.

Methods: Trabecular meshwork (TM) and AH samples were obtained from human cadaveric donors [control, primary open angle glaucoma (POAG) (each n=24, equal distribution of gender, all Caucasian age 68±5.0 and 69.0± 7.5, respectively)]. The samples were analyzed using a Q-Exactive orbitrap mass spectrometer after chromatography on an Acela 600 HPLC for Lipids after extraction using Bligh and Dyer method. All enzymes in the phospholipid conversion pathway were determined for protein level using Western blot and ELISA, and their activities at 15 minutes interval using established assays. The cadaveric TM and AH were collected under NIH category 4, IRB exempted provisions without identifiers. Extracellular vesicles (EVs) were prepared using established centrifugation and 101Bio P100L isolation kit. The EVs were characterized using nanotracker, electron microscopy (EM), atomic force microscopy (AFM) imaging and dynamic light scattering methods. Steady state pre-phospholipid metabolites entering and exiting interconversion cycle were measured using a stop flow apparatus as well as individual metabolite chase methods. All measurements were performed with samples identities masked to the estimators. Data were subjected to statistical analysis using MetaboAnalyst 4.0/STATA14.2 with recommended settings.

Results: Significant differences in phospholipid composition and their interconversion enzymes were found between control and POAG groups. POAG TM and AH was characterized by significant lower levels of phosphatidylserine (PS) and higher phosphatidylethanolamine (PE) levels. We also found significant up-regulation of phosphatidylserine decarboxylase in POAG TM. POAG AH demonstrated smaller lipid containing EVs compared to normal controls using nanotracker and EM, which was corroborated by other methods.

Conclusions: We found significant differences in phospholipid levels and their interconversion enzymes in glaucoma compared to control eyes. Consistent with these lipid changes, we found decreased size of lipid containing vesicles in the POAG AH.

CONTROL ID: 3518738

SUBMITTER (NAME ONLY): Sravya Veligandla

TITLE: A Spectroscopic Approach to Measuring Meibum Lipid Composition and Conformation in Donors with Sjogren's Syndrome

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Veligandla, J. Swindel, D. Clark, D. Borchman, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|A. Ewum, Chemistry, University of Louisville, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sjogren's syndrome (SS) is a chronic autoimmune rheumatic disease affecting 3 million individuals in the United States. About 80 % of people with SS have dry eye, keratoconjunctivitis sicca. We measured the composition and conformation of meibum in donors with SS and donors without SS or dry eye since meibum lipid has been associated with dry eye and meibomian gland dysfunction.

Methods: Meibum was collected using an ILUX instrument (Alcon, Fort Worth, TX). Infrared spectroscopy was used to measure meibum lipid conformation (structure). ¹H-NMR spectroscopy was used to measure meibum composition.

Results: Meibum was collected from 35 donors without dry eye (Mn) and without SS and eight donors with dry eye and with SS (Mss). The cholesterylester/wax ester ratio was significantly, $P = 0.003$, higher for Mss 0.51 ± 0.02 compared with Mn, 0.70 ± 0.06 . Mss contained significantly, $P = 0.02$, more straight chains, 67 ± 5 %, compared with Mn, 57 ± 1 %. No statistical difference was apparent, $P > 0.05$, between the Anteiso Branched, 20 ± 1 , 15 ± 1 or Iso Branched chains 23 ± 1 , 19 ± 4 of Mn or Mss, respectively. There was no statistical difference, $P > 0.05$, between the eight phase transition parameters measured for Mss or Mn.: Transition Temperature ($^{\circ}\text{C}$), Mn : 30.3 ± 0.4 , Mss: 29.9 ± 0.9 ; Cooperativity, Mn : 7.9 ± 0.4 , Mss: 7.6 ± 0.6 ; Order 36.0°C (% trans), Mn : 35 ± 1 , Mss: 38.4 ± 3.6 ; Order 33.4°C (% trans), Mn : 40 ± 1 , Mss: 43.3 ± 3.7 ; Δ enthalpy (kcal/mol), Mn : 142 ± 6 , Mss : 135 ± 25 ; Δ entropy (kcal.mol/degree), Mn : 0.48 ± 0.02 , Mss: 0.45 ± 0.03 ; Minimum Frequency (cm^{-1}), Mn : 2849.71 ± 0.06 , Mss: 2849.5 ± 0.1 ; Maximum Frequency (cm^{-1}), Mn : 2853.69 ± 0.09 , Mss: 2853.3 ± 0.1 .

Conclusions: In spite of having a higher cholesterylester/wax ester ratio and more straight chains, the compositional differences between Mss and Mn did not affect their phase transition parameters. A higher CE/WE ratio and straight chain composition of Mss compared with Mn, could be a marker for SS and/or contribute to dry eye in patients with SS. Studies are planned to measure the rheology of Mss to test this idea.

CONTROL ID: 3518763

SUBMITTER (NAME ONLY): Sandra Jose

TITLE: Determination of the effects of extracellular acidosis on ARPE19 cells using whole transcriptome analysis

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Jose, W. Yanqun, L. Fan, T. Burks, C. Huang, T. Walshe, Novartis Institutes for BioMedical Research Inc, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Metabolic adaptations and perfusion abnormalities lead to extracellular acidosis in atherosclerosis, neurodegeneration, and cancer. We speculate that this also occurs in Age Related Macular Degeneration (AMD) and examined the role of acidosis on ARPE19 cells in culture. We previously observed that extracellular acidosis decreases ARPE19 cell glycolysis, mitochondrial respiration, ATP and NAD/NADH. These data suggest that metabolic/mitochondrial dysfunction could be an important component in AMD pathology. We examined the acute and chronic effects of extracellular acidosis on transcriptional changes in ARPE19 using RNA sequencing.

Methods: Fully confluent 14 day cultures of ARPE19 cells were exposed to pH 7.4 or pH 6.5 for 12, 24 or 48 hours. Total RNA was extracted and analyzed on the Illumina NovaSeq 6000 platform with polyA selection library. The fastq files were aligned to human genome (GRCh38.p10) using STAR 2.4.1a. The transcript abundance was estimated using RSEM 1.2.22. The normalization and differential expression (DE) analysis were performed using edgeR and limma-voom R packages to identify the DE genes between pH 7.4 and pH 6.5 at different time points. The enriched pathways at each time point were obtained using GSEA.

Results: We identified 326, 243 and 138 DE genes (absolute log2 fold change ≥ 1 and adjusted p-value < 0.05) at 12 hours, 24 hours and 48 hours, respectively, demonstrating the highest acidosis-induced gene expression changes occur at the earliest time point. The follow up gene set enrichment analysis showed ARF6 pathway, lysophospholipid pathway and TNF-Alpha signaling via NFkB were significantly altered in ARPE19 cell lines exposed to pH 6.5 at 12hrs (p-value < 0.05). Pathways associated with cell cycles were consistently down-regulated at all three time points.

Conclusions: The results demonstrated that extracellular acidosis reprograms ARPE19 cell gene expression within 12 hours. The gene set enrichment analysis showed that the low pH environment interferes with multiple pathways related to AMD. Further study is required to determine how extracellular acidosis affect those pathways and to validate their potential role in macular degeneration.

CONTROL ID: 3518768

SUBMITTER (NAME ONLY): Joannah Vaughan

TITLE: Effects of demographics on the dilation of preschool children during the eye exam

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Vaughan, T. Dale, D. Herrera, Oregon Elks Children's Eye Clinic, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Upon review of 4,722 charts of eye exams performed by Oregon eye doctors over the last decade, analysis revealed that one third of exams were completed without dilation. The goal of this study is to identify any potential demographic bias that may affect the practice of dilation in low-income children ages three to five.¹

1. FitzGerald, Chloë, and Samia Hurst. 'Implicit bias in healthcare professionals: a systematic review.' BMC medical ethics vol. 18,1 19. 1 Mar. 2017, doi:10.1186/s12910-017-0179-8

Methods: In 2017, after IRB permission, chart notes and demographics were collected from vision screening referrals. Results were analyzed to determine if any bias was involved in the usage of cycloplegic drops during the eye exam.

Results: Chart notes were analyzed from 591 Head Start children who went to an eye doctor. Dilation occurred in 65.5% of the eye exams. Chi-square tests revealed that the population size of the child's location did have an impact on dilation. There were no statistically significant differences in the use of cycloplegic drops when looking at age (range between 3, 4, and 5 years-old), ethnicity, gender, or language.

Conclusions: The Oregon Elks Preschool Vision Screening Program found a demographic bias against dilation among children living in a population size less than 50,000. No bias was found regarding age, ethnicity, gender, or language. It is difficult and time consuming to encourage parents to seek eye care for preschool school children who have been referred by a vision screening. More public education is needed to create awareness about the importance of dilation during a pediatric eye exam, especially in rural areas with less access to quality eye care.

CONTROL ID: 3518797

SUBMITTER (NAME ONLY): Elizabeth Dugan

TITLE: TNF- α Inhibitors and Risk of Age-related Macular Degeneration in Patients with Rheumatoid Arthritis

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Dugan, H. Sandhu, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|A. Nakamura, Dr. Bing Zhang Department of Statistics, University of Kentucky College of Arts and Sciences, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the hazard of age-related macular degeneration (AMD) in rheumatoid arthritis (RA) patients on TNF- α inhibitors to RA patients on methotrexate, the first-line therapy for RA.

Methods: A retrospective cohort study was performed on data from 2010-2015 within a large US commercial insurance database, using a weighted Cox proportional hazards model of three groups: 1) methotrexate alone, 2) TNF- α inhibitor alone, and 3) TNF- α inhibitor and methotrexate. Inclusion criteria were a diagnosis of RA and age ≥ 50 years of age. Exclusion criteria were use of hydroxychloroquine, prior history of inherited retinal degeneration, or a prior diagnosis of AMD within a six-month lead-in time. Covariates included age, sex, and a propensity score consisting of the following: hypertension, smoking (COPD and chronic bronchitis used as surrogates), stroke, uveitis or scleritis, diabetes, coronary artery disease, history of colonoscopy, history of endoscopy, history of GI imaging series, peptic ulcer disease, chronic liver disease, hepatitis C, congestive heart failure, hyperlipidemia, cox-2 inhibitors, renal failure, obesity, osteoporosis and fractures, and intra-articular injections. The end point was any diagnosis of AMD.

Results: Group 1 had 118,562 patients, group 2 had 10,711 patients, and group 3 had 18,657 patients. After controlling for age and sex, there was no significant difference in the hazard ratio in developing AMD between groups 1 and 2 (HR = 1.05, 95% CI 0.89-1.18, $p = 0.39$), or groups 1 and 3 (HR = 0.98, 95% CI 0.92-1.06, $p = 0.66$) or groups 2 and 3 (HR = 0.93, 95% CI 0.84-1.04, $p = 0.20$). A diagnosis of uveitis or scleritis in RA patients was the single largest risk factor for developing AMD (HR = 2.26, 95% CI 1.94-2.626, $p < 0.00001$). Stroke (HR = 1.49, 95% CI 1.35-1.65, $p < 0.00001$) and hypertension (HR = 1.44, 95% CI 1.32-1.57, $p < 0.00001$) were also strong risk factors.

Conclusions: In this sample of patients with RA, immune modulation via TNF- α inhibition did not change the hazard of developing AMD. Interestingly, there was an increased hazard for developing AMD in patients with uveitis or scleritis. This further suggests that an aberrant immune response is implicated in AMD, though therapeutic targets of these pathways remain elusive.

CONTROL ID: 3518811

SUBMITTER (NAME ONLY): Yi-Jen Hsueh

TITLE: Long-term Survival of Cultivated Oral Mucosal Epithelial Cell Sheets in post-COMET Patients

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Hsueh, H. Chen, H.D. Ma, Department of Ophthalmology, Chang Gung Memorial Hospital, Taoyuan, TAIWAN|

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ABSTRACT BODY:

Purpose: The purpose of this study is to verify that collagenase-based spheroidal suspension culture is a promising technique for cultivated oral mucosal epithelial transplantation (COMET).

Methods: Patients with limbal stem cell deficiency who received COMET to promote wound healing were studied retrospectively. Immunoconfocal microscopy was performed on corneal specimens from the patients after COMET, as well on normal corneas, conjunctiva, and oral mucosa for Keratin 3, 4, 13, p63 and p75^{NTR}.

Results: A biopsy taken two years after COMET showed stratified epithelium with small, compact basal epithelial cells. The epithelium was positive for Keratin 4, 13, and 3 in the suprabasal layer but universally negative in the basal layer. Staining for p63 and p75^{NTR} were both positive in the basal layer. The graft remained clear up to post-OP 4 years, and his best corrected vision remained above 20/120.

Conclusions: Both clinical observations and histological examination confirmed the long-term survival of the transplanted OMECs, suggesting that collagenase-based spheroidal suspension culture is a promising technique for COMET.

CONTROL ID: 3518812

SUBMITTER (NAME ONLY): Cristina Arruza

TITLE: Characteristics at Presentation of Patients with Scleritis in Puerto Rico

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Arruza, J. Colón, E. Ramírez, G. Puebla, E. Rivera Grana, F. Marrero, C. Santos, A.L. Oliver, Department of Ophthalmology, Universidad de Puerto Rico Escuela de Medicina, San Juan, PUERTO RICO|E. Báez, Department of Ophthalmology, San Juan Bautista School of Medicine, Caguas, PUERTO RICO|

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ABSTRACT BODY:

Purpose: Patients with scleritis may have an associated systemic disease, which is often autoimmune and seldom infectious in origin. The data regarding patient demographics and systemic disease associations for scleritis in the Puerto Rican population is scarce. Herein, we evaluated the demographics, scleritis types, ocular complications, and disease associations in a cohort of patients with scleritis living in Puerto Rico.

Methods: A retrospective review of medical records from January 1990 to July 2020 of 2 private uveitis practices in Puerto Rico was performed. Charts of patients with a diagnosis of scleritis were selected for analysis. Demographic and clinical data from the review of medical records were entered into a new database, and a descriptive statistical analysis was performed. The University of Puerto Rico, Medical Sciences Campus Internal Review Board reviewed and approved this protocol.

Results: A total of 116 eyes of 95 patients with a diagnosis of scleritis were identified. The median age was 54 (range 13-80), 69% were female, and all Hispanics. The disease was unilateral in 77.89% of patients. Diffuse anterior scleritis was present in 73.28%, nodular anterior scleritis in 13.79%, necrotizing scleritis in 6.90%, and posterior scleritis in 6.03% of eyes. Uveitis was present in 16.38%, glaucoma in 13.80%, and keratitis in 6.03% of eyes. The presenting visual acuity was better than 20/50 in 77% of eyes, while 9% had a visual acuity of less than 20/200. An associated autoimmune disease was present in 32.63% of patients (rheumatoid arthritis 15.79%, relapsing polychondritis 4.21%, Sjögren's syndrome 5.33%, sarcoidosis 3.16%, systemic lupus erythematosus 2.17%, and systemic vasculitis 1.05%). An associated infectious disease was present in 6.32% of patients (4.21% syphilis, 1.05% Herpes zoster, and 1.05% Lyme disease).

Conclusions: As in other cohorts, scleritis in Puerto Rico was most common in females and had a median age in the sixth decade. The majority of patients presented with unilateral and diffuse anterior scleritis. Rheumatoid arthritis was the most common autoimmune systemic disease association, while syphilis was the most common infectious cause.

CONTROL ID: 3518832

SUBMITTER (NAME ONLY): Afua Asare

TITLE: Material Deprivation and Eye Exams in Ontario Children: A Population-based Cohort Study.

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Asare, D. Maurer, A.M. Wong, W. Ungar, N. Saunders, Institute of Health Policy Management and Evaluation, University of Toronto, Toronto, Ontario, CANADA|D. Maurer, Neuroscience and Behaviour, McMaster University, Hamilton, Ontario, CANADA|A.M. Wong, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|A. Asare, W. Ungar, N. Saunders, Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Despite universal recommendations for comprehensive eye exams (CEE), uptake has been poor, with as few as 14% of children receiving a CEE in Ontario – Canada, despite coverage through provincial health insurance (PHI). Poor access to or use of vision care services may exacerbate health inequities. We performed a population-based, longitudinal, repeated measures study to test the association between material deprivation and receiving a CEE before age 7 years in Ontario using health administrative d

Methods: We followed 128,091 members of a birth cohort from birth until each child's 7th birthday. Children were included if they were born in Ontario, Canada on or between January 1st and December 31st 2010, and eligible for PHI. Children were excluded if: they became eligible for PHI more than 6 months after birth, were without insurance for more than 6 months during follow up, moved out of the province, did not access the health care system for more than 5 years during follow up, and/or had invalid encoded insurance identification numbers. Also excluded were children who died. Descriptive and logistic regression methods were employed.

Results: Sixty-five percent (82,833/128,091) of children had at least one CEE (56.9% and 70.5% in the most and least deprived neighbourhoods, respectively). Most children had their first CEE at 4 to 5 years of age representing 16.4% (20961/128091) of the cohort. After adjusting for clinical and demographic variables, low material deprivation was associated with a higher odds of receiving an eye exam (AOR 1.43; 95%CI 1.36, 1.51). The association was greatest in the 1st (AOR 1.73; 95%CI 1.55, 1.55) and 4th year of life (AOR 1.67; 95%CI 1.59, 1.59).

Conclusions: Uptake of CEEs is poor, with inequities in care delivery. Universal school-based vision screening could identify children at risk for vision impairment and facilitate the provision of referrals for diagnosis and treatment. Public education on the importance of CEEs for children 1 to 3 years is key.

CONTROL ID: 3518842

SUBMITTER (NAME ONLY): DAIKI SAKAI

TITLE: Factors associated with the development of ocular candidiasis and ocular prognosis with echinocandin therapy for candidemia

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. SAKAI, Ophthalmology, Kobe City Eye Hospital, Kobe, Hyogo, JAPAN|D. SAKAI, W. Matsumiya, S. Kusuhara, M. Nakamura, Ophthalmology, Kobe University Graduate School of Medicine, Kobe, Hyogo, JAPAN|W. Matsumiya, Ophthalmology, Byers eye institute at stanford university, PaloAlto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the factors associated with the development of ocular candidiasis (OC) and ocular prognosis with echinocandin therapy for candidemia.

Methods: The medical records of 56 consecutive patients with a positive blood culture for *Candida* species between November 2016 and October 2019 were retrospectively reviewed. Information on patient characteristics, isolated *Candida* species, treatment details for candidemia, and ocular findings were extracted to identify factors associated with OC development.

Results: The leading pathogen of candidemia was *Candida albicans* (41.1%). Of 56 patients, 18 (32.1%) were diagnosed with chorioretinitis, categorized as either probable (8 patients) or possible OC (10 patients). There was no case of endophthalmitis with vitritis. The incidence of probable OC was not significantly different between the groups treated with echinocandins and other antifungal drugs (15.2% vs. 11.1%, $p = 1.00$). In all probable OC cases, systemic antifungal therapy was switched from echinocandins to azoles, and no case progressed to endophthalmitis. A multivariate logistic analysis revealed that female sex (adjusted odds ratio [aOR], 8.93; 95% confidence interval [CI], 1.09–72.9) and *C. albicans* (aOR, 23.6; 95% CI, 1.98–281) were independent factors associated with the development of probable OC.

Conclusions: One-seventh of patients with candidemia developed probable OC. Given the evidence of female and *C. albicans* as the factors associated with OC development, careful ophthalmologic management is required especially in candidemia with these factors. Although echinocandins had no correlation with OC development and did not lead to the deterioration of ocular prognosis, further investigation is required.

CONTROL ID: 3518847

SUBMITTER (NAME ONLY): Ritvij Singh

TITLE: Exploring the What-If-Tool as a solution for machine learning explainability in clinical practice

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As machine learning (ML) algorithms become more common in the clinical setting, so does the importance of explainable AI. The aim of this study was to explore the use of the What-If Tool (WIT) to help clinicians understand how an ML algorithm makes decisions.

Methods: A supervised deep learning model was trained using Google AutoML Tables to predict visual acuity (VA) in diabetic macular oedema patients receiving anti-VEGF injections. It was trained on a public dataset consisting of 2614 eyes of 1964 patients at a tertiary referral centre in London and optimised for mean absolute error (MAE).

The model was interrogated using the WIT via a jupyter notebook extension. To see how it treated different subgroups, the WIT was used to slice the data by the input features gender and ethnicity. The mean absolute error (MAE) was reported for each of these. To individually explore the data, 10 male patients were chosen at random and had their gender hypothetically changed using the WIT's partial dependence plots. These are able to vary an input and report how a model's prediction changes with it.

Results: The MAE of the model in predicting VA was 8.060 letters. Slicing the data in the WIT by male and female eyes showed that it treated both broadly equally with a MAE of 7.510 and 8.855 respectively. Further slicing by both gender and ethnicity found the largest difference in MAE was between white males (6.888) and white females (10.400).

Partial dependence plots of the randomly chosen points showed a mean change in VA prediction of +0.952 letters when gender changed hypothetically from male to female (range: -8.676 to +10.906). In this sample, changing gender from male to female caused the predicted VA to increase 6 out of 10 times. This was investigated further with a global partial dependence plot, which demonstrated that the average change when changing gender from male to female was -0.57.

Conclusions: Our results show two ways the WIT can scrutinise an ML model. Firstly, the freedom to slice the data by any chosen feature allows us to see deeper than overall performance metrics. Secondly, the use of partial dependence plots to observe the model's behaviour in response to hypothetical scenarios offers a more granular understanding than the basic explainable AI features on the Google Cloud Platform. Overall, the WIT presents a novel method for clinicians to understand how ML algorithms make decisions.

CONTROL ID: 3518902

SUBMITTER (NAME ONLY): Zesemayat Mekonnen

TITLE: Early Nutritional Source and Retinopathy of Prematurity in Latin American Infants

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z.K. Mekonnen, School of Medicine, University of California San Francisco, San Francisco, California, UNITED STATES|J.E. Navarro, Department of Ophthalmology, Hospitales Angeles, Mexico City, MEXICO|L.C. Zepeda-Romero, Hospital Civil "Fray Antonio Alcalde", Universidad de Guadalajara Centro Universitario de Ciencias de la Salud, Guadalajara, Jalisco, MEXICO|M.M. Galan, Department of Ophthalmology, Hospital de Niños S. Ma. Ludovica de La Plata, La Plata, ARGENTINA|G. Binenbaum, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|A.G. de Alba Campomanes, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early nutritional status and nutritional source type has been reported to be associated with the prevention of retinopathy of prematurity (ROP) in high-income countries. We sought to determine if nutritional source within the first two weeks of life is associated with the development or regression of ROP in a Latin American cohort.

Methods: Secondary analysis of data from a prospective study of premature infants in La Plata, Argentina, and Guadalajara, Mexico between 2012-2014. Primary outcomes were the associations between the nutritional source in the first 2 weeks of life (predominantly total parental nutrition (TPN) or formula, or exclusive breastmilk) and presence, severity (treatment-requiring), and time to spontaneous regression of ROP or IGF-1 levels (ng/mL), adjusting for gestational age (GA) and birth weight (BW), using multivariable regression and ANOVA.

Results: One-hundred infants were studied, with mean (\pm SD) GA 31.3 (\pm 2.7) weeks, median BW was 1395 g (range 620-2250), and 52% female. Most common nutritional source was predominantly TPN in postnatal weeks 1 (74%) and 2 (45%). Forty-three infants developed ROP, 19 were treated, while 21 children had documented full spontaneous regression at time of discharge. Median time to regression was 5 weeks (range 1-9 weeks). No associations were found between the nutritional source in the first 2 weeks of life and presence, severity, or time to spontaneous ROP regression and vascular maturation. No association was found between mean IGF-1 levels and ROP status by nutritional source.

Conclusions: We did not find an association between sources of nutrition during the 1st two weeks of life and ROP development, severity, or spontaneous ROP regression in this cohort of Latin American infants at risk for ROP.

CONTROL ID: 3518909

SUBMITTER (NAME ONLY): Zdenka Haskova

TITLE: Efficacy and safety of satralizumab in neuromyelitis optica spectrum disorder (NMOSD): Results from open-label extension periods of SAKuraSky and SAKuraStar

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Satralizumab, a humanized, monoclonal recycling antibody that targets the interleukin-6 receptor, reduced patients' risk of NMOSD relapse in the double-masked (DM) periods of two randomized, phase 3 clinical trials: SAKuraSky (satralizumab in combination with baseline immunosuppressants; NCT02028884), and SAKuraStar (satralizumab monotherapy; NCT02073279). We assessed the efficacy and safety of satralizumab over a longer period of treatment, using data from the SAKura studies' open-label extension (OLE) periods.

Methods: Patients entering SAKuraSky/Star were randomized to receive satralizumab 120 mg or placebo at Weeks 0, 2, 4, and Q4W thereafter. After completing the DM period or experiencing a relapse, patients could enter the OLE period. Time to first investigator-assessed protocol-defined relapse (PDR) and safety were evaluated in the combined DM+OLE periods, using a pooled population from both studies. Data were analyzed through the clinical cut-off date

(June 2019).

Results: Overall, 179 patients were randomized to treatment (satralizumab n=105; placebo n=74), of whom 166 received ≥ 1 dose of satralizumab in the combined DM+OLE period. The median (range) satralizumab exposure in the DM period was 96.1 (8–224) weeks, and in the combined DM+OLE was 131.9 (13–276) weeks. In the combined DM+OLE, patients originally randomized to satralizumab had a 51% lower risk of investigator-assessed PDR vs those originally randomized to placebo (HR [95% CI] 0.49 [0.31–0.79]; $P=0.002$); the risk reduction was more pronounced in AQP4-IgG seropositive patients (66% risk reduction; HR [95% CI] 0.34 [0.19–0.62]; $P<0.001$). Patients who switched from placebo to satralizumab upon entry into the OLE period were included in the placebo group, which likely reduced the observed treatment difference between satralizumab and placebo compared with the DM period. No patients randomized to satralizumab withdrew from the OLE period due to a relapse, vs four patients who were originally randomized to placebo. Safety profiles in the combined DM+OLE were consistent with those in the DM period (Table). No deaths were reported.

Conclusions: In the DM and OLE periods of the SAKura studies, patients receiving satralizumab had a significantly reduced risk of relapse vs placebo. Satralizumab was well-tolerated and showed a favorable safety profile.

CONTROL ID: 3518946

SUBMITTER (NAME ONLY): Hailey Robles-Holmes

TITLE: A prospective survey assessing patient experiences and understanding of advertised stem cell therapies for retinal disease.

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Misinformation regarding non-Food and Drug Administration (FDA) sponsored, largely unproven, stem cell therapies (SCTs) for retinal disease may pose significant risks to patients. A survey was administered to patients with retinal disease to ascertain their baseline knowledge of SCTs.

Methods: A prospective survey was administered to patients presenting to a retina clinic for dry age-related macular degeneration (AMD) or a variant of diagnoses requiring anti-VEGF therapy. Before clinical evaluation, patients completed a survey evaluating their knowledge about SCTs for retinal disease. Demographics, visual acuity (VA), and clinical diagnoses were also recorded. Visual impairment was classified in accordance with guidelines defined by the World Health Organization (WHO). Pearson chi-square tests for independence were used for gender and ethnicity comparisons.

Results: There were 58 participants, 31 (53.4%) of whom believed there were FDA-approved and commercially available SCTs for retinal disease (95% CI= 39.9%-66.1%). Thirty-eight (65.5%) patients believed all clinical trials found online were regulated by the FDA (95% CI= 51.9%-77.5%). A chi-square test of independence showed no significant association between patient responses and gender. However, Hispanic patients were more likely than non-Hispanic patients to believe there were current FDA approved SCTs commercially available ($p=0.048$) and to believe that all clinical trials found online are approved by the FDA ($p=0.0006$). Only 9 (15.8%) respondents were aware of risks associated with non-FDA approved SCTs for retinal disease (95% CI=7.3%-27.4%). Twenty-two (37.9%) respondents said they would consider SCT not approved by the FDA (95% CI=25.5%-51.6%).

Conclusions: Confusion exists regarding the federal regulation of SCTs for retinal disease and Hispanic patients may be a population more vulnerable to misinformation regarding these unapproved therapies.

CONTROL ID: 3518959

SUBMITTER (NAME ONLY): Joseph Demer

TITLE: Comparing Hypertropia (HT) in Upgaze and Downgaze Does Not Distinguish Congenital From Acquired Superior Oblique Palsy (SOP)

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.L. Demer, Ophthalmology, University of California Los Angeles, University of California Los Angeles, Los Angeles, CA, US, academic, Los Angeles, California, UNITED STATES|J.L. Demer, Neurology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ivanir & Trobe claimed that HT greater in up than downgaze, or equal to it, is characteristic of decompensated congenital & never present in ischemic, traumatic, or tumorous SOP (J. Neuro-Ophthalmol. 37:2017). This claim was tested in SOP confirmed by MRI demonstration of subnormal superior oblique (SO) size.

Methods: Quasi-coronal, surface coil MRI was performed in target-controlled central gaze to identify patients with unilateral SO hypoplasia indicative of SOP. Nine subjects had unequivocal congenital onset (mean age 38 ± 16 yrs, standard deviation, SD); 7 subjects had unequivocal acquired onset (age 47 ± 14 yrs, symptom duration 5.4 ± 4.8 yrs), including 2 with trochlear Schwannoma and 5 with severe head trauma; and 15 subjects had progressive onset unequivocally not congenital (age 52 ± 19 yrs, symptom duration 13 ± 14 yrs).

Results: Results: Maximum SO cross section averaged $8.6 \pm 3.9 \text{ mm}^2$ in congenital & $11.3 \pm 3.5 \text{ mm}^2$ in acquired SOP ($P=0.08$), significantly less than 19 mm^2 identically in both groups contralesionally ($P < 10^{-4}$). Although mean central gaze HT was greater at $20.6 \pm 8.0 \Delta$ in 9 cases of congenital than 22 acquired cases at $11.4 \pm 6.8 \Delta$ ($P=0.002$), HT was $8.4 \pm 16.3 \Delta$ less in up than down gaze in congenital SOP, and $3.7 \pm 11.2 \Delta$ less in acquired SOP. In congenital SOP, 33% of subjects had HT greater in up than downgaze, while in 67% HT was greater in down gaze (by up to 42D). In acquired SOP, HT was greater in up than downgaze, or equal to it in 8 cases (36%, $P=0.87$, χ^2); the similar proportions contradict Ivanir & Trobe's claim. In acquired SOP, HT was greater in up than down gaze in 37%, & greater in down than up gaze in 59% of cases. HT was equal in up & central gazes in 3 acquired and no congenital SOP cases. Trends were similar in unequivocal acquired & progressive acquired (non-congenital) SOP ($P > 0.4$).

Conclusions: HT is not characteristically greater in up than down gaze in congenital SOP proven by SO atrophy on MRI. In fact, average HT is greater in down than up gaze in both acquired & congenital SOP, sometimes strikingly so in the latter. The finding of HT greater in up than downgaze, or equal to it, does not reliably indicate that SOP is congenital.

CONTROL ID: 3518965

SUBMITTER (NAME ONLY): Young Hyun Kim

TITLE: Effect of Soft-Contact-Lens Wear on Post-Lens Tear-Film Osmolarity

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Despite correlation between tear hyperosmolarity and dry eyes (Tomlinson et al. [2006]), no correlation has been found between tear osmolarity and soft-contact-lens (SCL) wear discomfort. This is likely because clinical instruments measure meniscus osmolarity rather than that in the post-lens tear film (PoLTF) where tear interfaces corneal nerve endings. We quantify the time-periodic differences in osmolarities between various tear-compartment during SCL wear.

Methods: Pre-lens tear-film (PrLTF), PoLTF, pre-conjunctival tear-film (PrCjTF) (i.e., the tear film on the bulbar conjunctiva), and meniscus osmolarities are determined based on water and salt conservation balances. The physical model simulates tear-film deposition, black-line formation, interblink period, and eyelid closure following Cerretani and Radke (2014). Lens ion diffusivity (D), ion partition coefficient (k), and thickness are varied to assess the effect of lens properties on various tear-compartment osmolarities. Similarly, tear production and evaporation rates are varied to ascertain the differences in tear osmolarity between normal and dry eyes. All tested parameters are obtained from commercially available SCLs and published studies.

Results: Figure 1 provides various tear-compartment periodic osmolarities during normal eye SCL wear for low and high D s. Increasing lens thickness, decreasing D , and decreasing k all reduce PoLTF osmolarity. However, the effect of k is small for commercially available SCLs. For hypertonic dry eyes, osmolarities of all compartments are elevated depending on the severity of the dry eye. Tested parameters show PoLTF and meniscus osmolarities vary between 303 to 340 mOsM and 310 to 325 mOsM, respectively. Meniscus osmolarity depends on dry-eye conditions and not on lens parameters.

Conclusions: We devised a numerical tool to determine PoLTF osmolarity during SCL wear for the first time. PoLTF osmolarity changes significantly with lens parameters but not the meniscus osmolarity. Tear osmolarity of dry eye is more sensitive to changes in lens parameters than the normal eye. Understanding correlation between SCL wear discomfort and PoLTF osmolarity requires further investigation as the corneal nerves interact with the PoLTF and not with meniscus tear.

CONTROL ID: 3519007

SUBMITTER (NAME ONLY): Mami Kusaka

TITLE: Elucidation of neuroprotective mechanism of valosin-containing protein modulators against retinal ganglion cell damage

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kusaka, T. Hasegawa, H. Ikeda, S. Iwai, A. Tsujikawa, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, JAPAN|K. Iida, Medical Research Support Center, Kyoto Daigaku, Kyoto, JAPAN|A. Kakizuka, Functional Biology, Kyoto Daigaku, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: Glaucoma is characterized by retinal ganglion cell damage, leading to visual field defects and even blindness. Currently, the only established treatment for glaucoma is reduction in intraocular pressure, but new neuroprotective treatment methods are being developed. We have previously shown that Kyoto University Substances (KUSs), which are valosin-containing protein (VCP) modulators, suppress cell death in animal models of glaucoma, retinitis pigmentosa, retinal ischemia, and age-related macular degeneration. The purpose of this study was to elucidate the precise neuroprotective mechanisms of KUSs by focusing on gene expression in mouse with acute retinal ganglion cell damage.

Methods: We administered KUSs orally for 7 days to Thy1-CFP mice, which express cyan fluorescent protein (CFP) in the retinal ganglion cells. Acute retinal ganglion cell damage was induced by an intravitreal injection of N-methyl-D-aspartic acid (NMDA). Four hours after NMDA injection, CFP-expressing retinal ganglion cells were isolated using a fluorescence-activated cell sorter. RNA was purified from the collected retinal ganglion cells and analyzed using next-generation RNA-sequencing to evaluate gene expression profiles. We focused on two genes, endothelin-1 (Edn1) and endothelin receptor type B (Ednrb), whose expression was upregulated by NMDA injection and downregulated by KUS treatments. The mRNA expression levels of the genes in the neural retina were examined by real-time PCR, and protein levels in the neural retina were confirmed by western blotting and immunostaining.

Results: The mRNA expression of both Ednrb and Edn1 was higher in the NMDA-injected group than in the control group ($p < 0.0001$ and $p = 0.005$, respectively). In contrast, mRNA expression of Ednrb in the NMDA-injected-KUS121-treated group and the NMDA-injected-KUS187-treated group did not significantly differ from that of the control group ($p > 0.05$). Expression of EDN1 was significantly higher in the NMDA-injected group than in the control group ($p = 0.007$) as observed in western blot analysis. Immunohistochemical staining showed that EDNRB and EDN1 proteins were strongly expressed in the retinal ganglion cell layer in the NMDA-injected group than in the control group.

Conclusions: These results suggested that KUSs protect retinal ganglion cells by suppressing the upregulated Edn1 and Ednrb expression.

CONTROL ID: 3519015

SUBMITTER (NAME ONLY): Esther Hoffmann

TITLE: National registry for childhood glaucoma in Germany: feasibility, clinical care and research (pilot study)

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Hoffmann, F. Aghayeva, H. Diel, A.K. Schuster, F.M. Wagner, F. Grehn, Dept. of Ophthalmology, Universitätsmedizin der Johannes Gutenberg-Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|F. Aghayeva, Dept. of Ophthalmology, National Centre of Ophthalmology, Baku, AZERBAIJAN|F. Grehn, Dept. of Ophthalmology, Würzburg, GERMANY|

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ABSTRACT BODY:

Purpose: The aim is to investigate epidemiological data, risk factors and treatment of childhood glaucoma in Germany. For this purpose, an initial database to register patients diagnosed with different types of childhood glaucoma was established from 2017 until 2019 as part of a prospective clinical cohort study. The intention is to create a national registry for childhood glaucoma in Germany

Methods: Twenty-eight children with different types of childhood glaucoma, who were admitted and treated at the Childhood Glaucoma Center of the University Medical Center Mainz, Germany, were included. Documents and questionnaires for the acquisition and storage of epidemiological and clinical data were developed and checked for feasibility and practicability in the clinical routine. Furthermore, each child and their parents were offered a genetic testing for known genes that cause childhood glaucoma. The test was carried out in cooperation with the Institute of Human Genetics of the University Medical Center in Mainz and was paid for by the statutory health insurance.

Results: The individual documents and questionnaires included: Informed consent form from the parents, medical history form of the child, patient's gestational history questionnaire and examination form of the examination under general anesthesia (EUAF). Primary congenital glaucoma (PCG) and secondary childhood glaucoma (SCG) were revealed in 11 (39.3%) and 17 (60.7%) patients, respectively. The most common cause of SCG was Peters anomaly (41.2%). Bilateral glaucoma was diagnosed in 81.8% (PCG) and 58.8% (SCG) of all patients. In 33.3% of the children mainly these four genes, which are associated with childhood glaucoma, were found: CYP1B1, FOXC1, LTBP2 and TEK.

Conclusions: This pilot study showed good feasibility of data acquisition of glaucoma children and their parents including individually developed documents and questionnaires to provide detailed unique baseline data for a national registry on different types of childhood glaucoma in Germany. In near future, registry data will provide valuable information to identify new risk factors for childhood glaucoma and to evaluate different treatments under real-life condition in Germany

CONTROL ID: 3519019

SUBMITTER (NAME ONLY): Sharon McClellan

TITLE: Effects of Topical Glycyrrhizin Application on the Normal Ocular Surface

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. McClellan, M. Somayajulu, D. Bessert, A. Pitchaikannu, B. Nguyen, L.D. Hazlett, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test whether topical glycyrrhizin (GLY) alters the cytoarchitecture, physiological and/or immunological parameters of the normal mouse cornea and conjunctiva.

Methods: Both normal corneas of C57BL/6 mice were treated topically with GLY (100µg/5µl) or PBS twice daily for 5 days and tested at 0, and/or 3 and 5 days. Slit lamp photography was used to assess bulbar conjunctival hyperemia and fluorescein staining was used to detect epithelial defects. Scanning electron microscopy (SEM) interrogated cell surface morphology, microvillar integrity and cell exfoliation. Phenol treated cotton threads were used to measure tear levels and a Cochet and Bonnet Esthesiometer was used before and after treatment to measure corneal sensitivity. Immunohistochemistry was used to examine corneal nerves (beta tubulin staining) and a phycoerythrin (PE) conjugated anti-langerin monoclonal antibody was used to stain and enumerate langerin positive cells. Intraocular pressure was measured with a tonometer before and after treatment. RT-PCR was used to compare mRNA levels of various TLRs and inflammatory molecules and ELISA assays were employed to compare protein levels of selected toll-like receptors (TLRs), cytokines, and neuropeptides [Substance P (SP) and Vasoactive Intestinal peptide (VIP)].

Results: GLY vs PBS controls showed no evidence of bulbar hyperemia, epithelial defects nor changes in surface cell morphology after 5 days of treatment. However, GLY vs PBS treatment transiently reduced the density of corneal nerves significantly (7%) only at 3 days, yet neither tear production nor corneal sensitivity were changed. No differences in the number of langerin positive cells nor mRNA levels of TLR2, 4, 5 and 9 were affected by GLY vs PBS. In contrast, levels of IL-1β, HMGB1, and TNF-α mRNA were significantly reduced, but protein levels of these molecules, other cytokine and neuropeptides did not differ between groups.

Conclusions: GLY transiently reduced corneal nerve density, but had no other measurable deleterious effect on the ocular surface that would preclude its therapeutic use.

CONTROL ID: 3519021

SUBMITTER (NAME ONLY): Sohil Bhagat

TITLE: Risk Factors for Central Retinal Artery Occlusion in Older Adults with Atrial Fibrillation and Flutter

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bhagat, A T Still University, Kirksville, Missouri, UNITED STATES|A. Uppuluri, M.A. Zarbin, N. Bhagat, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Several risk factors have been identified for central retinal artery occlusion (CRAO) in older populations. Its underlying pathophysiology is similar to that of a non-hemorrhagic ischemic cerebrovascular accident and includes a multitude of prothrombotic systemic risk factors. This observational study uses the National Inpatient Sample (NIS) Database to evaluate the systemic and ocular risk factors associated with developing CRAO in the senior population (age > 65 years) with atrial fibrillation and flutter (AFF).

Methods: We conducted a retrospective cross-sectional case-control analysis using the NIS Database, 2002-2014, to evaluate systemic risk factors for CRAO in seniors with AFF. Cases were comprised of inpatients over 65 years of age who were admitted for CRAO and had AFF. The age and gender matched control group included inpatients over 65 years of age with AFF but without CRAO. The ratio of cases to controls was 1:5. Chi square analysis and logistic regression analyses were performed with a Bonferroni correction (alpha significance of 0.0029). An odds ratio was obtained for every significant variable.

Results: We identified 740 weighted cases of AFF with CRAO and 3689 weighted controls of AFF without CRAO. The mean ages of the case and control groups were 79.2 and 79.4 years, respectively ($p=0.452$). Men comprised of 55.6% of the cases and 55% of the controls ($p=0.759$). Systemic comorbidities that significantly ($p<0.0029$) increased the risk of CRAO in these subjects included carotid stenosis ($OR=23.38$), history of stroke ($OR=2.56$), hypertension ($OR=1.80$), and hyperlipidemia ($OR=1.75$). A decreased risk was noted with bleeding diathesis ($OR=0.26$), and diabetes mellitus ($OR=0.54$); also, Hispanic ethnicity had a much lower risk of CRAO compared to Whites ($OR=0.18$).

Conclusions: The risk of CRAO in seniors with AFF increased 24 fold with carotid stenosis. Concurrent medical history of either hyperlipidemia, hypertension, or stroke doubled the risk of CRAO in this population, whereas, having a bleeding diathesis, or uncomplicated diabetes mellitus had a protective effect on developing central retinal artery occlusion.

CONTROL ID: 3519034

SUBMITTER (NAME ONLY): Kanjapat Temahivong

TITLE: Developing a computational model of the retina for evaluating structure-function relationships in glaucoma

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Temahivong, C. Bradley, R.W. Massof, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|K. Temahivong, Chulalongkorn University, Bangkok, THAILAND|

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ABSTRACT BODY:

Purpose: To develop a computational model for predicting contrast thresholds of localized spatial patterns across the visual field based on a model of the eye that includes retinal ganglion cell (RGC) responses, and to apply the model towards evaluating known structure-function relationships in glaucoma.

Methods: Our model is developed by modifying the retina-V1 (RV1) model (Bradley et al., 2014; J. Vis.), which includes a model of parvocellular (P) ganglion cell responses and predicts contrast thresholds of 43 different stimuli in the ModelFest dataset (Watson & Ahumada, 2005; J. Vis.) at the fovea. We extended the RV1 model to include magnocellular (M) ganglion cell responses because the RV1 model in its original form does not predict standard automated perimetry (SAP) thresholds well. In SAP, a stimulus is presented with an abrupt onset and offset suggesting that M cells, which are sensitive to high temporal frequency stimuli, are important for detection performance. M cell parameters in the modified retina-V1 (mRV1) model are estimated by fitting the central 30° of Hermann's hill of vision (HoV) (Hermann et al., 2008; Acta Ophthalmol.). Different types of RGC damage were simulated, including axonal loss and dendritic field (DF) loss, based on the pathophysiology of glaucoma.

Results: The mRV1 model predicts contrast thresholds for both the ModelFest dataset (RMSE = 1.18 dB) and for the central 30° of Hermann's HoV (RMSE = 0.82 dB) well. Without modifying any parameters, simulated RGC damage predicts a well-known but poorly understood structure-function relationships in glaucoma: a large initial decrease in retinal nerve fiber layer (RNFL) thickness is accompanied by only a relatively small sensitivity loss (Hood & Kardon, 2007; Prog. Retin. Eye Res.). Simulated axonal and DF loss predicts the data in Hood & Kardon (2007) better than simulated axonal loss alone (RMSE = 0.23 vs. 0.26 on a linear scale of sensitivity).

Conclusions: The mRV1 model is grounded in the known anatomy and physiology of the eye and predicts SAP thresholds well within the central 30° of visual field. Different types of RGC damage simulated with the mRV1 model may help explain known structure-function relationships in glaucoma that are currently not well understood.

CONTROL ID: 3519039

SUBMITTER (NAME ONLY): Giovana Rosa Gameiro

TITLE: Donor profile and causes of corneal discard in an eye bank in Southern Brazil

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Rosa Gameiro, L. Brust Osiak, D.G. Correia, Medical School, Universidade Estadual de Londrina, Londrina, PR, BRAZIL|G. Gameiro, Department of Ophthalmology and Visual Sciences, Universidade Federal de Sao Paulo Escola Paulista de Medicina, Sao Paulo, SP, BRAZIL|A. Miyagusko Taba Oguido, A.M. Casella, Department of Surgery, Ophthalmology, Universidade Estadual de Londrina, Londrina, PR, BRAZIL|

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ABSTRACT BODY:

Purpose: To evaluate cornea donor demographics and determine the number of discarded donated corneas and the causes associated with discard in an eye bank in Southern Brazil.

Methods: This retrospective, cross-sectional study analyzed the medical records of all cornea donations between January 2016 and December 2018 at the Londrina University Hospital Eye Bank. Variables analyzed included donor demographics, donor cause of death, enucleation time, endothelial assessment, tissue contamination, quality of the donated cornea and causes of discards.

Results: A total of 1418 donor corneas were identified from 712 donors. Mean age of the donors was 53.54 ± 13.82 years, and 38.2% of the donors were over 60 years old. The main cause of donor death was cardiovascular or neurovascular disease (60.8%), followed by external causes of death (18%). Overall, 739 corneas (52.1%) were discarded. The main causes of discard were positive hepatitis B serology (35.1%), corneal tissue expiry date (28.9%) and corneal tissue contamination (12%). *Acinetobacter baumannii* and coagulase-negative *Staphylococci* were the most frequently isolated bacteria. The discard rate was significantly higher in the over 60 year-old donor age group compared to the 60 year-old and under age group (chi-square: $p < 0.001$). In these groups, 64.4% and 44.5% of the donated corneas were discarded, respectively. Endothelial cell density (ECD) was found to be inversely correlated with the donor age ($r: -0.435$, $p < 0.001$). The ECD average of the discarded corneas was of 2118 ± 452 cells/mm², significantly lower than the average of 2492 ± 382 cells/mm² found in the corneas that were utilized for transplantation ($p < 0.001$). External causes of death had a higher ECD average when compared with cardiovascular or neurovascular diseases, respiratory system diseases and gastrointestinal diseases ($p < 0.001$).

Conclusions: A high corneal discard rate was observed in the present study, with positive serology, tissue expiry date and contamination being the main causes of discard. Discards were significantly more prevalent in older age groups (>60 years), and discarded corneas had lower endothelial cell density. The identification of significant trends in donor demographics could help with a more efficient assessment process of potential cornea donors in eye banks.

CONTROL ID: 3519042

SUBMITTER (NAME ONLY): Johnson Huang

TITLE: Thyroid Hormone Treatment Reveals Plasticity of Gene Expression in Cone Photoreceptors of Adult Zebrafish

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|J. Huang, A.A. Farre, A.M. Duncan, D.L. Stenkamp, University of Idaho, Moscow, Idaho, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vertebrate color vision requires the differential expression of specific cone opsins in separate cone populations. One model for the regulation of the human long and medium wavelength sensitive (LWS/MWS) opsin tandem array suggests an upstream regulatory region interacts with replicated opsin genes at random, resulting in mutually exclusive expression of a specific opsin. However, our prior investigations into the orthologous long wavelength sensitive (*lws1/lws2*) array in zebrafish suggest that thyroid hormone (TH) and retinoic acid serve as trans regulators of this gene array in larvae/juveniles (Mitchell et al., 2015, PLOS Genetics; Mackin et al., 2019, PNAS). This study investigates whether cone opsin expression remains plastic to TH treatment in adult zebrafish, where cone distribution is considered stable.

Methods: Adult zebrafish (both sexes) were treated with NaOH (0.01%, control) or TH (386 nM) for 1 or 5 days (n=3). Left eyes were harvested for qPCR analysis and right eyes for cryosectioning. A set of *lws* reporter transgenic adults (*lws*:PAC(H); *lws1* reported by GFP and *lws2* reported by RFP) were also treated for 5 days with NaOH or TH (n=3). Whole retinas and cryosections were analyzed by confocal imaging.

Results: In adult zebrafish, exogenous TH drastically increased *lws1* expression in both 1 and 5 day-treated groups (p=0.003, 0.0006, respectively) while decreasing *lws2* expression (p=0.002, 0.005). Other phototransduction-related transcripts that were shown to decrease in embryos and juveniles exposed to TH showed a similar response in adults: *gnat2b* (p=0.09, 0.003), *rh2-1* (p=0.05, 5 day treatment). TH treated transgenic *lws* reporter line revealed a clear switch from *lws2* to *lws1* in dorsal retina, consistent with the qPCR data. Whole retinas of transgenic reporters demonstrate an expansion of *lws1*-expressing cones nasally and dorsally as well.

Conclusions: Exogenous TH induced a drastic shift from *lws2* to *lws1* in adult zebrafish, consistent with previous studies of larvae and juveniles. This shift occurs as rapidly as 1 day when exposed to TH, which shows that cones remain highly plastic even into adulthood. Plasticity in spectral sensitivity (to be sensitive to higher wavelengths) in response to TH suggests a role in visual system function well into adulthood.

CONTROL ID: 3519051

SUBMITTER (NAME ONLY): Tina Xia

TITLE: Intraoperative MMC concentrations and surgical outcomes in XEN gel implantation for glaucoma

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Xia, A. Sheybani, Ophthalmology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|I. Conner, D. Rooney, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|E. Lagouros, Illinois Eye Center, Peoria, Illinois, UNITED STATES|L. Seibold, Ophthalmology, University of Colorado Health, Aurora, Colorado, UNITED STATES|J. Huecker, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the surgical outcomes of XEN gel implant at 12-month follow-up, including post-operative intraocular pressure (IOP), glaucoma medications, rate of needling and secondary surgery intervention for 3 intraoperative MMC concentrations ranges

Methods: Retrospective study of consecutive XEN gel implantation with MMC for treatment of glaucoma. Total MMC amount were divided into 3 ranges: $\leq 20\text{mcg}$ (n = 55), (20-40mcg] (not including 20mcg, n = 177) and $>40\text{mcg}$ (n = 15). The change in intra-ocular pressure and number of glaucoma medications at 12 months were compared among the three MMC groups. The rate of needling and additional surgical interventions were also compared.

Results: The three MMC groups had similar distribution of sex, glaucoma severity, visual acuity, pre-operative IOP, and number of glaucoma medications. There was a difference in the average patient age ($P < 0.01$). XEN implantation was combined with phacoemulsification in 13.5% of patients in the $\leq 20\text{mcg}$ group, 22.7% in the 20-40mcg group, and 33.1% in the $>40\text{mcg}$ group ($P < 0.05$). There were no significant differences in rates of prior tube or trabeculectomy surgeries among the three groups. 50.6% of patients had follow-up at month 12.

At 1 year, the average IOP significantly decreased by $10.8 \pm 8.5\text{mmHg}$ (-38.4%, n=29) for the $\leq 20\text{mcg}$ group, by $7.5 \pm 8.8\text{mmHg}$ (-26.3%, n=92) for the 20-40mcg group, and by $12.8 \pm 11.3\text{mmHg}$ (-55.5%, n=4) in the $>40\text{mcg}$ group. The IOP change was not statistically different among the 3 groups ($P = 0.72$). The average number of medications also decreased in all 3 groups, by -1.4 (-53.2%), -1.6 (-56.5%) and -1.8 (-46.7%), respectively. The rate of needling was 39.5% in the $\leq 20\text{mcg}$ group, 33.1% for the 20-40mcg group, and 22.2% in the $>40\text{mcg}$ group ($P = 0.44$). The rates of secondary surgeries were similar among the three groups, 10.26%, 15.34%, and 16.67%, respectively ($P = 0.69$). Common adverse events included transient hypotony (n=74), choroidal effusion (n=13), bleb leaks (n =10) and hyphema (n =8).

Conclusions: The total amount of MMC used intra-operatively during XEN gel implantation were grouped into 3 ranges: $\leq 20\text{mcg}$, (20-40mcg] and $>40\text{mcg}$. At 1 year, there were no significant difference in post-op IOP change, glaucoma medication, needling rate, and rate of secondary surgeries when comparing among the three MMC groups.

CONTROL ID: 3519052

SUBMITTER (NAME ONLY): Kristine Kalnica-Dorosenko

TITLE: Crowding effect in children with and without amblyopia

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kalnica-Dorosenko, Eye Diseases Clinic, Bernu kliniska universitates slimnica, Riga, Riga, LATVIA|K. Kalnica-Dorosenko, A. Svede, Department of Optometry and Vision Science, Latvijas Universitate Fizikas matematikas un optometrijas fakultate, Riga, LATVIA|

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ABSTRACT BODY:

Purpose: Amblyopia - reduction of visual acuity in one or both eyes, caused by abnormal binocular interaction during the critical period of visual development. One of the most used classifications of amblyopia is related to visual acuity. Amblyopia is most often associated with early onset strabismus, anisometropia or combined (strabismic anisometropic amblyopia). The aim of this study was to evaluate the effect of crowding and age on visual acuity in a sample of young children with and without amblyopia.

Methods: A total of 200 participants (3-9 years old) whose visual acuity was tested monocularly, using the entire open optotype line, isolating one optotype line and separating each optotype separately, participated. The results were analysed in four groups: children with and without amblyopia (younger (3 to 6 years) and older (7 to 9 years)).

Results: In the younger (3 to 6 years) group of children with strabismic and anisometropic amblyopia, the crowding effect was observed ($p < 0.05$) by checking visual acuity (with amblyopic and health eye) isolating the optotype line and showing the optotypes separately, but in the older (7 to 9 years) group the crowding effect was not observed ($p > 0.05$). In the younger (3 to 6 years) and older (7 to 9 years) groups of children without amblyopia, the crowding effect was not observed ($p > 0.05$) by checking visual acuity isolating the optotype line but was observed ($p < 0.05$) by showing the optotypes separately.

Conclusions: Young amblyopic patients up to 7 years old have better visual acuity readings from a single optotype or isolating one optotype line than from entire open optotypes in a row. By demonstrating the optotypes separately, there is a greater risk of overestimating the visual acuity of the amblyopic patient, thereby failing to diagnose amblyopia, and starting therapy in time. This is important because the earlier amblyopia is diagnosed – the better the chance of improving visual acuity.

CONTROL ID: 3519060

SUBMITTER (NAME ONLY): Azza El-Remessy

TITLE: Modulation of p75^{NTR} on Mesenchymal Stem Cells Improves Angiogenic Secretome and Vascular Protection in Retinal Ischemia-Reperfusion.

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.B. El-Remessy, H. Park, Surgery, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|H. Park, University of Chicago, Chicago, Illinois, UNITED STATES|A.B. El-Remessy, S. Elshaer, L. Pearson, W. Hill, Research Service, Augusta VA Medical Center, Augusta, Georgia, UNITED STATES|W. Hill, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|F.M. Longo, Neurology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mesenchymal stem cells (MSCs) are promising therapy to improve vascular repair, yet their role in ischemic retinopathy is not fully understood. The aim of this study is to investigate the impact of modulating the neurotrophin receptor p75^{NTR} on vascular protection of MSCs in an acute model of retinal ischemia-reperfusion (IR).

Methods: WT and p75KO mice were subjected to IR injury by increasing intraocular pressure to 120mmHg for 45 minutes followed by perfusion. Murine GFP-labeled MSCs (100,000cells/eye) were injected intravitreally 2days post-surgery and vascular homing was assessed 1-week later. Acellular capillaries were counted using trypsin digest 10-days post-IR. In vitro, MSC-p75^{NTR} was modulated either genetically using siRNA or pharmacologically using LM11A-31, and conditioned media were co-cultured with human retinal endothelial (HREs) to examine the angiogenic response.

Results: IR significantly increased the number of acellular capillaries (3.2-fold) in WT mice, but not in p75KO compared to sham-controls. GFP-MSCs were successfully engrafted into retinal vasculature and decreased the number of acellular capillaries in all groups, yet IR maintained a 2-fold increase in WT but not in p75KO mice. Silencing p75^{NTR} on GFP-MSC coincided with a higher homing of GFP-MSC to retinal vasculature in WT-IR and normalized number of acellular capillaries to control level when compared to scrambled-GFP-MSC in WT-IR. Silencing p75^{NTR}-MSCs enhanced their secretome including SDF-1, VEGF, and NGF as well as paracrine angiogenic response, where HREs showed enhanced migration (1.4-fold) and tube formation (2-fold) compared to controls. In parallel, modulating MSC-p75^{NTR} using LM11A-31 exerted similar effects on improving the secretome and its paracrine angiogenic effects on HREs. Further, intervention with LM11A-31 significantly improved the decline in visual acuity post-IR-injury.

Conclusions: Silencing p75^{NTR} from MSCs surface potentiates their vascular protective effect in vivo and in vitro. The underlying mechanism can involve, at least in part, increases in SDF-1α NGF and VEGF. LM11A-31, an orally bioavailable p75^{NTR} modulator that exerted vascular and neuro-behavioral protective effects. Thus, a combination of MSCs injection and p75^{NTR} inhibitor can serve as a potential therapeutic strategy to harness greater vascular repair in ischemic retinopathy diseases.

CONTROL ID: 3519076

SUBMITTER (NAME ONLY): Liang Wang

TITLE: Validation of a novel deep learning algorithm to segment geographic atrophy in spectral domain and swept source OCT en face images

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Wang, Y. shi, P.J. Rosenfeld, Department of Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|Z. Chu, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|Z. Yu, Department of Mechanical Engineering, University of Washington, Seattle, Washington, UNITED STATES|Z. Yu, Department of Statistics, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To validate a novel deep learning algorithm (DLA) to segment and measure the size of geographic atrophy (GA) in eyes with non-exudative age-related macular degeneration (neAMD) based on the presence of choroidal hyper-transmission defects (HTDs) applicable to both spectral domain (SD-OCT) and swept source (SS-OCT) en face images.

Methods: The DLA for GA segmentation is a deep convolutional neural network modified from U-net where average pooling, rather than max pooling, is used in the encoder stage to tolerate noise and a two-step non-linear transformation employing convolution and residual connections are applied in the skip connections to propagate the encoder features to the corresponding decoder features. Subjects with normal eyes without any evidence of retinal disorders and patients diagnosed with GA secondary to neAMD were enrolled in a prospective OCT study and underwent both SD-OCT and SS-OCT imaging using 6x6 mm scan patterns. The DLA was trained with the OCT images with and without GA accurately annotated by professional graders. For validation, manual gradings were compared to automatic algorithm segmentations to assess the algorithm's classification and segmentation performance.

Results: A total of 160 OCT en face images, including 48/32 SS-OCT images with/without GA, 48/32 SD-OCT images with/without GA, were used to train the DLA algorithm. Another independent series of 80 SD-OCT and SS-OCT en face images made of two balanced sets of 40 eyes (20 with GA, 20 without GA) were used for validation. The DLA achieved a 100% sensitivity and 100% specificity for SD-OCT and a 100% sensitivity and 95% specificity for SS-OCT, respectively. The average Jaccard Index was 0.83 for SD-OCT and 0.80 for SS-OCT. A strong positive correlation was established for the manual and automatic measurements of the GA square root areas for SD-OCT ($R = 0.996$, $P < 0.001$) and SS-OCT ($R = 0.985$, $P < 0.001$). The Bland Altman plots had a bias of -0.01 mm for SD-OCT and 0.05 mm for SS-OCT with no obvious trends.

Conclusions: The DLA had an excellent sensitivity and specificity for identifying and measuring GA in both SD-OCT and SS-OCT images. This algorithm should be useful clinically in providing quantitative measurements of GA and tracking the appearance and enlargement of GA in patients diagnosed with neAMD.

CONTROL ID: 3519093

SUBMITTER (NAME ONLY): Conor Leahy

TITLE: Feasibility of fast measurement of macular pigment optical density using a slit-scanning ophthalmoscope

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Leahy, A. Covita, Carl Zeiss Meditec Inc, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Conor Leahy: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Angelina Covita: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Objective, non-invasive measurement of the optical density (OD) of human macular pigment (MP) can be performed in vivo using fundus autofluorescence (FAF) imaging. Depending on the protocol used, the exam duration may be lengthened by the need for pupil dilation, repeat image acquisitions, and/or separate calibration for crystalline lens fluorescence. In this study, we investigate the feasibility of quantifying macular pigment optical density (MPOD) using a slit-scanning ophthalmoscope with a single-flash measurement protocol.

Methods: A slit-scanning ophthalmoscope (CLARUSTM 500, ZEISS, Dublin, CA) with prototype software was used to perform non-mydratic measurements of MPOD, derived from pairs of FAF images obtained with blue ($\lambda_{\text{peak}} = 459\text{nm}$, well-absorbed by MP) and green ($\lambda_{\text{peak}} = 520\text{nm}$, much less absorbed) excitation sources. The illumination rapidly alternates between the sources during a single scan, completing in under 0.2 seconds. The image sensor records separately the partial images of stripes of illuminated retina. Retinal autofluorescence appears only within the illuminated stripe, but unwanted crystalline lens fluorescence appears nearly uniformly across the partial image (allowing it to be removed). A fluorescent phantom, incorporating a yellow-colored filter of known OD, was used to test the implementation. MPOD measurements were performed on 5 human subjects.

Results: The manufacturer specified OD for the test phantom is shown in Figure 1A. From the FAF images (Figure 1B-C), the 2-D spatial MPOD profile for the test phantom is derived (Figure 1D). The mean MPOD was within 2.5% of the specified value. For human subjects, we present FAF images and the derived MPOD profiles (an example is shown in Figure 2) for the central 5° around the fovea.

Conclusions: A slit-scanning ophthalmoscope can perform objective FAF measurements of MPOD in a single perceived flash, through non-dilated pupils. This gives encouragement that such a method can be practical for screening, for example for risk of age-related macular degeneration. Validation of such an approach for in vivo use will require careful consideration of confounding effects, such as secondary fluorophores and photobleaching.

CONTROL ID: 3519098

SUBMITTER (NAME ONLY): Paul Steptoe

TITLE: Proposing a Neurotropic Etiology for Acute Posterior Multifocal Placoid Pigment Epitheliopathy and Relentless Placoid Choroidopathy

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.J. Steptoe, S. Sreekantam, B.R. Mohammed, R. Barry, Birmingham and Midland Eye Centre, Birmingham, Birmingham, UNITED KINGDOM|I. Pearce, N.A. Beare, St Paul's Eye Unit, Royal Liverpool Hospitals, Liverpool, UNITED KINGDOM|N.A. Beare, Institute of Ageing and Chronic Disease, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Merseyside, UNITED KINGDOM|L.R. Steeples, Manchester Royal Eye Hospital, Manchester, Manchester, UNITED KINGDOM|B.R. Mohammed, R. Barry, Institute of Clinical Sciences, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|A.K. Denniston, Centre for Translational Inflammation Research, Institute of Inflammation and Aging, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UNITED KINGDOM|A.K. Denniston, University Hospital Birmingham NHS Foundation Trust, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Controversy currently exists over the underlying pathology in acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and the related condition, relentless placoid chorioretinitis (RPC). We performed a retrospective case series imaging evaluation to reassess the clinical signs and current etiological hypotheses for these conditions.

Methods: Cases were identified from three tertiary uveitis centers in the UK between 2016 and 2020. We defined APMPPE using the following criteria: 1) The appearance of >1 creamy chorioretinal lesion; and 2) Evidence of choriocapillaris hypoperfusion, and; 3) An OCT appearance in keeping with the two described phenotypes. We defined RPC as fulfilling criteria 1-3 but with a clinical course exceeding 60 days and greater than 50 lesions. Qualitative comparative analysis of available multimodal imaging modalities was conducted. Serial imaging afforded the opportunity to analyse preclinical changes in eyes with sequential involvement.

Results: A total 14 patients (9 with bilateral disease) met the diagnostic criteria. 10 patients (17 eyes) had features consistent with APMPPE. 4 patients (6 eyes) had features consistent with RPC. 7/14 patients were female. Median age at presentation was 26.5 years (range, 20-57 years). Changes within the retinal nerve fiber layer precede the occurrence of clinical lesions and associated choriocapillaris hypoperfusion. Optic disc edema occurs proportionally to the extent of retinal lesions, and mirrors the sectoral distribution, suggesting an associated disruption of axoplasmic flow. Areas of choriocapillaris hypoperfusion correspond to zones of separation of the overlying retinal pigment epithelium (RPE) from Bruch's membrane (BM). Transient, hyperreflective foci occur within the outer nuclear layer above the area of RPE/BM separation during acute lesions, and follow the neurons which constitute the Henle's fiber layer orientation. Pathological disruption of retinal layers (following the initial RPE/BM separation) occurs in a descending sequence with ONL/ellipsoid zone disruption preceding the loss of RPE structure.

Conclusions: Our evidence suggests a primary neuronal pathogenesis with a descending progression through the retina, as opposed to a primary disorder of the choriocapillaris.

CONTROL ID: 3519111

SUBMITTER (NAME ONLY): Takeshi Kimura

TITLE: Clinical characteristics of and treatment trends for submacular hemorrhage: a retrospective multicenter survey in Japan

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the current clinical characteristics and the trends in treatment for submacular hemorrhage (SMH) in Japan.

Methods: The inclusion criteria were subfoveally involved SMH more than 2 optic discs in area, followed for at least 2 months. One hundred eighty-four (184) eyes of 184 patients (104 men and 80 women) were enrolled from 10 hospitals. The characteristics of SMH were classified by the FLATCAPS classification. Causes, selected treatments, and pre- and post-treatment best-corrected visual acuity (BCVA) were analyzed.

Results: The patients' mean age was 76.1 ± 9.2 . SMH was caused by retinal arterial macroaneurysm (RAM) in 52 eyes (28%), and by age-related macular degeneration (AMD) in 127 eyes (69%): typical age-related macular degeneration in 26%, polypoidal choroidal vasculopathy (PCV) in 73%, and retinal angiomatous proliferation (RAP) in 1%. SMH was observed in more than two retinal layers in 60% of the RAM group and in the subretinal and sub-RPE spaces in 106 eyes (83%) of the AMD group. The mean period between onset and treatment was 10.9 days in all cases, and more cases underwent vitrectomy in the RAM group than in the AMD group ($P < 0.0001$). Subretinal tissue plasminogen activator injection was selected for 49% of the vitrectomy cases. Mean BCVA in the AMD group was significantly better than in the RAM group at baseline, 1 month after treatment, and the final visit ($P > 0.0001$, $P > 0.0026$, $P > 0.0163$).

Conclusions: PCV was about twice as frequent as RAM as the cause of SMH. The RAM group included more cases with vitrectomy than the AMD group and showed poor BCVA.

CONTROL ID: 3519138

SUBMITTER (NAME ONLY): Arjan Dhoot

TITLE: Factors Affecting the Time to Publication in Ophthalmology Journals: A Comprehensive Bibliometric Analysis

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Bibliometrics is an understudied topic in ophthalmology. The purpose of this study is to provide comprehensive data on the duration from submission to various stages of the publication process and assess factors influencing time to publication.

Methods: A list of ophthalmology journals was obtained from the 2019 Web of Science Journal Citation Report. For each journal, characteristics such as journal acceptance rate and impact factor were collected. All articles published in 2019 from included journals were extracted and an independent review was conducted to determine dates of article submission, acceptance, electronic and print publication.

Results: In total, 56 journals and 8835 research articles were included. Of these articles, 3591 (40.6%) were open access and 4837 (54.7%) were multi-institutional. In 2019, most publications came from the United States of America (n=1973). For articles that reported relevant data, the median number of days from submission to acceptance was 128 (range across journals: 71-222), acceptance to electronic publication was 30 (range: 2-199) and acceptance to print publication was 146 (range: 27-448). Significant associations were found between the following predictors and a reduced mean number of days from submission to electronic publication: increased journal five-year impact factor (p=0.026), increased immediacy index (p=0.008), increased article influence score (p=0.032), more authors (p=0.028), publishing in a hybrid journal (i.e. both open-access and subscription articles) versus an open-access journal (p=0.021), and a reduced proportion of multi-institutional articles in a journal (p=0.030).

Conclusions: There is a wide variation in the time to acceptance and publication in ophthalmology journals. Authors can expect a shorter time to publication when publishing in high-impact journals. Reducing the time from acceptance to electronic publication for journals is a reasonable first step to improve article exposure and citation volume.

CONTROL ID: 3519151

SUBMITTER (NAME ONLY): Richmond Woodward

TITLE: Selective laser trabeculoplasty in Western Tanzania

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Woodward, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|G. Rodriguez, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|J. Joseph, Ophthalmology, Bugando Medical Centre, Mwanza, TANZANIA, UNITED REPUBLIC OF|G. Sun, Ophthalmology, Weill Cornell Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Selective laser trabeculoplasty (SLT) may represent a cost-effective treatment for glaucoma care in low-resource regions. To explore this we performed a retrospective chart review to learn about short-term intraocular pressure (IOP) results in the first group of patients in Western Tanzania to receive SLT for chronic primary open angle glaucoma (POAG) or isolated ocular hypertension (OHT) unresponsive to pressure lowering drops.

Methods: Patients at Bugando Medical Center (BMC) in Mwanza, Tanzania who underwent SLT with a Lumenis Selecta II laser over a one-week period and presenting six-weeks later for follow-up were included. Data collected included age, gender, IOP before SLT, central corneal thickness (CCT), energy and number of applications, and IOP within two hours of SLT and six-weeks later. Visual acuity (VA) was obtained before SLT and at the six-week follow-up. IOP was measured using an Icare tonometer (Icare, USA).

Results: A total of 14 eyes of 12 patients (mean age 60.2 years, 83% male) were treated. Mean IOP prior to SLT was 22.1 ± 9.4 mmHg. CCT was <555 μ m in all patients where CCT was measured. All eyes received laser over 360° of the trabecular meshwork at energy levels ranging from 0.7-1.2 mJ per pulse except for one eye treated 180° due to limited patient tolerance. No pressure spikes were observed immediately after treatment. Nine patients (eleven eyes) returned for the six-week follow-up. The mean IOP drop six-weeks post-SLT was 8.5 ± 7.0 mmHg. Five patients (six eyes) had a greater than 30% decrease and three patients (four eyes) had an 11-30% decrease in IOP compared to baseline. The IOP in the fellow eye of five patients six-weeks post-SLT was lower compared to pre-SLT, with a mean IOP drop of 8.0 ± 4.8 mmHg. No patients experienced a decrease in VA at the six-week follow-up.

Conclusions: Selective laser trabeculoplasty of twelve patients with POAG or OHT at BMC resulted in a notable pressure lowering effect in eight of nine patients evaluated at the six-week follow-up. No adverse effects were noted. Results showing one patient who did not have a pressure lowering effect may be attributed to challenges achieving a full treatment of 360°. Our data suggests additional studies of the long-term efficacy of SLT for POAG and OHT in Western Tanzania is warranted in light of the high cost of IOP lowering medication and limited access to specialist care in the region.

CONTROL ID: 3519171

SUBMITTER (NAME ONLY): Sol La Bruna

TITLE: Understanding patterns of glaucomatous progression in the macula using OCT thickness change maps

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To identify and understand patterns of progressive thinning in the macular ganglion cell layer (GCL) using spectral domain OCT thickness change maps of the GCL and retinal nerve fiber layer (RNFL).

Methods: 114 glaucoma, glaucoma suspect, and healthy (HC) eyes from 114 individuals had OCT scans and 24-2 and 10-2 visual fields (VFs) as part of a longitudinal, prospective study. Based upon an evaluation of all available OCT and 24-2 and 10-2 VF information, 12 eyes were classified as definite Progressors (P), and 67 as definite non-progressors (NP). OCT thickness change maps of the RNFL and GCL were generated from manually corrected OCT volume scans (30°x25°), by comparing the most recent follow-up to the baseline test (avg. 3.1 yrs apart).

Results: In 6 of the 12 P eyes arcuate shaped regions of progression (Fig. 1A) were visible on GCL, as well as RNFL, thickness change maps. In the other 6 eyes, diffuse regions of progression (Fig. 1B) were visible on GCL, while the RNFL, thickness change maps showed a combination of diffuse and arcuate regions of progression. Healthy controls showed little or no consistent arcuate or diffuse patterns on the RNFL or GCL change maps. (See comparison of maps for HC and P with diffuse changes in Fig. 2.)

Conclusions: Macular progression involves both deep local and shallow widespread thinning in the GCL. Change maps of the RNFL and the GCL can aid in the identification of glaucomatous progression.

CONTROL ID: 3519209

SUBMITTER (NAME ONLY): Edmund Khong

TITLE: Determining the course of diabetic retinopathy from pregnancy to the postpartum in women with pre-existing diabetes in metropolitan Melbourne

SESSION TITLE: DR: Epidemiology and service provision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The effect of the postpartum on diabetic retinopathy (DR) remains unknown. Understanding this can inform whether sight-threatening DR (STDR) is best treated during pregnancy or can be deferred till after delivery. This study explores the prevalence, typical DR course and risk factors for DR progression in the postpartum.

Methods: Subgroup analysis of a prospective longitudinal cohort study of pregnant women with type 1 (T1DM) or type 2 diabetes (T2DM) attending two tertiary maternity hospitals in Melbourne, Australia (Nov 2017 – Sept 2020) who had at minimum one eye examination in pregnancy and one up to 12 months postpartum. DR severity was determined either through grading of 2-field retinal photographs or clinical assessment when fundus photographs were unavailable. Progression was defined as worsening by ≥ 1 step on the Airlie House classification, development of diabetic macula edema (DME) or the need for laser treatment.

Results: This analysis included 87 pregnancies from 86 women; 48 had T1DM and 38 had T2DM (median duration 18.0 and 4.0 years respectively). Mean age was 33.4 years (range 21-47). DR prevalence at ≥ 27 weeks postpartum was 26.3 (CI 16.6, 39.0) per 100 eyes. Between late pregnancy and 12 months postpartum, progression occurred in 20/160 (13%) eyes while 10/160 (6%) regressed. Progression was more common in the latter 6 months postpartum and associated with existing DR at enrolment, T1DM (RR 5.03, CI 1.52-16.70) and duration of diabetes >10 years (RR 3.52, 1.38-8.21). Of the 13 eyes that progressed during pregnancy, 5 (38%) regressed in the postpartum. Regression was seen in 4/5 (80%) eyes that developed new DR in pregnancy, 1/5 (20%) eyes with pre-existing non-proliferative DR and 0/5 (0%) eyes with proliferative DR (PDR). Eyes with DME had good vision (20/40 or better) at the majority of their exams (92%, 49/53), with 53% (9/17) resolving in the postpartum.

Conclusions: The postpartum prevalence of DR was comparable to the non-pregnant diabetic population.

Progression in the postpartum was twice as common as regression, highlighting the need for adequate postpartum

eye screening. In eyes that progressed during pregnancy, most did not regress in the postpartum, especially eyes with PDR. Treatment for PDR thus cannot be delayed in anticipation of resolution post-delivery. However, DME treatment can be safely delayed in most cases.

CONTROL ID: 3519210

SUBMITTER (NAME ONLY): Se Joon Woo

TITLE: Analytical Similarity Assessment of a Ranibizumab Biosimilar SB11 to Reference Product

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: SB11 is a proposed biosimilar to reference ranibizumab, which is currently being reviewed for the marketing authorization, developed for the treatment of ocular diseases. The objective of this study was to assess the structural and functional similarity between SB11 and reference products obtained from United States (US-ranibizumab) and European Union (EU-ranibizumab).

Methods: A comprehensive structural and functional characterization was performed utilizing state-of-the-art analytical methods. Comparisons included the following: primary structure related to amino acid sequence and post-translational modifications; higher order structure; product-related substances and impurities including size and charge variants; and protein concentration. In addition, biological characterization included a series of bioassay such as vascular endothelial growth factor (VEGF)-A binding assay, cell-based VEGF-A neutralization assay, and human umbilical vein endothelial cells (HUVEC) anti-proliferation assay.

Results: The amino acid sequence of SB11 was identical to that of US- and EU-ranibizumab. SB11 was shown to be indistinguishable from the reference products with respect to post-translational modification profiles and higher order structures. Product-related size and charge variants and aggregates were also similar. Functionally, SB11 could not be distinguished from US- and EU-ranibizumab by using a set of bioassays and binding assays covering a broad range of VEGF-related functional activities. The relative binding activity or potencies were calculated relative to the reference standard prepared from one lot of reference product. The binding activity of SB11 representative batches analyzed using VEGF-A binding assay were evaluated as 98% (RSD=2%). The potencies of SB11 representative batches analyzed using HUVEC anti-proliferation and VEGF-A neutralization assay were evaluated as 101% (RSD=5%) and 99% (RSD=4%), respectively.

Conclusions: Based on the comprehensive analytical similarity assessment, SB11 is highly similar to the US- and EU-ranibizumab with respect to structural, physicochemical, and biological properties.

CONTROL ID: 3519338

SUBMITTER (NAME ONLY): Tyler Ogden

TITLE: Treatment of cystoid macular edema secondary to infectious uveitis with anti-vascular endothelial growth factor agents

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ogden, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|H. Sandhu, Ophthalmology/Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|T. Ogden, San Antonio Uniformed Services Health Education Consortium, Fort Sam Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal anti-vascular endothelial growth factor (VEGF) agents have not been well studied in treatment of cystoid macular edema (CME) secondary to infectious uveitis (IU) and may prove to be an effective alternative to steroids without the risk of reactivation of latent infection. The purpose of this retrospective case series was to evaluate anti-VEGF agents as a treatment of CME secondary to IU.

Methods: This retrospective case series included patients treated for CME secondary to inactive IU. Mean change was calculated for central macular thickness (CMT), intraocular pressure (IOP), and best corrected visual acuity (BCVA) between initiation of treatment and final follow up appointments. BCVA was converted into logMAR values for analysis. A paired t test was used to evaluate for statistically significant difference.

Results: 5 eyes of 3 patients were included with underlying diagnoses of syphilitic uveitis in 2 patients (4 eyes) and herpes simplex uveitis in 1 patient (1 eye). The mean treatment course was 11 months with an average of 6 treatments per eye. Mean change in CMT after treatment was -120 μm ($p=0.28$). There was no statistically significant difference in BCVA before and after treatment ($p=0.40$). Mean IOP was 17.4 prior to treatment and 17.2 after treatment ($p=0.86$). Recurrence of uveitis was not observed in any eye during treatment.

Conclusions: Anti-VEGF agents are safe in eyes with inactive IU. Although statistically insignificant in this small series, there was a trend towards improved anatomical outcomes with this treatment.

CONTROL ID: 3519378

SUBMITTER (NAME ONLY): Hugang Ren

TITLE: Optimizing inference performance of a fundus image quality neural network model for edge computing using TensorFlow Lite

SESSION TITLE: AI in the retina: Algorithms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Ren, S. Bello, M.N. Alam, N. Manivannan, T. Shagam, N. D'Souza, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acquiring good quality images is crucial for disease screening and diagnosis using fundus cameras. A quality indicator after image capture allows recapture of the low-quality ones while the patient is still available. However, running a deep learning image quality algorithm on low-cost fundus cameras can be slow. TensorFlow Lite (TFL) is a deep learning framework designed for inference on the device, also known as edge computing. In this study, we investigated methods to optimize the inference performance using TFL.

Methods: A VGG-16 neural network was trained using fundus images captured with VELARATM 200 (ZEISS, Dublin, CA), a fully automated non-mydriatic fundus camera with a 45 degree field of view centered around the macula. 4574 images, including 3158 good and 1416 bad quality ones were used for training; 597 images, consisting of 353 good and 244 bad quality ones, were used for testing. The grading of the images was performed by a majority vote among 3 subject matter experts. First, the floating-point (FP) TensorFlow model was converted and saved as a tflite file. Then, post-training dynamic range quantization was applied using TFL. The weight of the trained model was quantized into 8-bit integer. To test the accuracy, both the FP and quantized TFL models were evaluated using the same test set. To test the speed, an Android app was built and installed on the fundus camera tablet that comes with a Qualcomm Snapdragon 439 APU.

Results: The sensitivity, specificity and AUC score of the TensorFlow model were 85.7%, 99.2% and 0.976. For FP and quantized TFL models, they were 85.7%, 99.2%, 0.976 and 85.2%, 99.4%, 0.977. 95% confidence intervals and detailed comparison can be found in Figure 1. The sensitivity ($p=0.5$) and specificity ($p=0.5$) are not statistically different after TFL optimization. For inference speed, the FP and quantized TFL models ran at 4808ms and 3008ms per image using the tablet CPU with 1 thread. The inference time reduced to 1847ms and 783ms when using 8 threads. Inference time changed to 1263ms and 1261ms when running on the tablet GPU. For model size, the FP model is 67.3MB and the quantized one is 17.8MB.

Conclusions: In this study, we demonstrated a method to optimize the inference performance of a fundus image quality neural network model for edge computing using TFL.

CONTROL ID: 3519422

SUBMITTER (NAME ONLY): Dena Ballouz

TITLE: Assessing North American Native Eye Health and Care Needs

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The North American Native (NAN) population has been shown to face significant health disparities in the United States (US) across a spectrum of diseases. However, population-level studies are limited. We performed a retrospective, database analysis of Medicare Fee-for-Service (MFFS) claims to identify disparities in eye health and eye care services between NANs and White Non-Hispanics (WNH) in the US and in the state of Michigan (MI).

Methods: A retrospective analysis from the 2017 100% sample of MFFS claims in the Vision and Eye Health Surveillance System was completed. Mean claims rates in all age groups in all primary diagnoses and selected service categories were extracted. Claims were extracted for categories comprised of individual eye conditions and associated selected eye-care-related services. Logistic regression models were used to obtain age-adjusted claim rates of the cohorts' condition and selected service, and to test for directional patterns between NAN and WNH age-adjusted claims rates for conditions and services to make inferences about possible disparities.

Results: Medicare claims were identified for 177,100 NANs and 24,438,000 WNHs in the US and for 4,500 NANs and 865,400 WNHs in Michigan. Seventeen major categories of eye conditions were paired with their related eye care services (Figure 1). Five eye conditions in the US had significantly higher claims rates for NANs than WNHs, representing potentially higher prevalence in NANs than WNHs. Two of these five conditions, refractive error and diabetic eye diseases, also had significantly higher claim rates among MI NANs. Conversely, these two conditions had lower or on par related services rendered (Figure 2), representing a significant disparity between condition and service claims for NANs versus WNHs for two of the most common eye conditions leading to low vision and blindness.

Conclusions: Refractive error and diabetic eye diseases represent the greatest unmet eye health/care needs for US and MI NANs with MFFS coverage. Because of high Medicare coverage rates among NANs, MFFS claims are useful in examining and understanding disparities in eye health and services in the NAN population in the US.

CONTROL ID: 3519456

SUBMITTER (NAME ONLY): Lisa Hark

TITLE: Manhattan Vision Screening and Follow-Up Study in Vulnerable Populations:
1-Month Pilot Results

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Hark, Y.S. Kresch, C. De Moraes, J.D. Horowitz, L. Park, J. Auran, J.M. Liebmann, G.A. Cioffi, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose/Aim: In the United States, high rates of vision impairment and eye disease disproportionately impact those who lack access to eye care, specifically vulnerable populations. The objective of our study was to test instruments, implement protocols, and collect preliminary data for a larger 5-year study, which aims to improve detection of eye diseases and follow-up eye care in vulnerable populations using community health workers and patient navigators.

Methods: Methods: Eligible individuals age 40-and-older were recruited from the Riverstone Senior Center in upper Manhattan, New York City. Participants underwent on-site vision screening (visual acuity, intraocular pressure measurements, and fundus photography). Individuals who failed the vision screening (i.e., visual acuity worse than 20/40 in either eye with correction, 2) IOP 23-29 mmHg, or 3) unreadable fundus images, were scheduled with an on-site optometrist for a non-dilated eye exam, either the same day or within two weeks of initial screening; those with ocular pathologies were referred to an ophthalmologist. All images were read and graded by two study ophthalmologists. Participants were also administered the National Eye Institute Visual Function Questionnaire-9 (NEI-VFQ-9) by community health workers.

Results: Results: Participants (n=42) were predominantly older adults, with a mean age of 70.0 ± 9.8 , female (61.9%), and Hispanic (78.6%). Most individuals (78.6%, n=33) failed vision screening. Of those who failed, 84.8% (n=28) attended the on-site eye exam with the optometrist. Ocular diagnoses: refractive error 13/28 (46.4%), glaucoma/glaucoma suspect 9/28 (32.1%), cataract 7/28 (25.0%), retina abnormalities 6/28 (21.4%); 13 people required eyeglasses. Of the 35 participants who had fundus images taken, 40% (n=14) had a normal image with no significant findings, 37.1% (n=13) had an abnormal image with significant ocular findings, and 22.9% (n=8) had unreadable images. There was 100% agreement between the glaucoma and retinal specialists regarding referral for follow-up eye exam based on the fundus images.

Conclusions: Conclusion: Community-based vision screening using community health workers and optometrist-based eye exams in vulnerable populations may minimize barriers to eye care, improve early detection of eye disease, and patient navigators can link subjects to additional eye care appointments.

CONTROL ID: 3519464

SUBMITTER (NAME ONLY): Shawn Hanks

TITLE: Aged mice with AMD-associated genetic mutations in complement or extracellular matrix do not exhibit slow dark adaptation

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hanks, I. Arellano, E. Lima, J. Vrouvlianis, Y. Qiu, N.M. Buchanan, S. Shen, G. Klokman, M. Crowley, C. Bigelow, S. Poor, Ophthalmology, Novartis Institutes for BioMedical Research Inc, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of blindness in elderly patients. Genetic mutations in complement and extracellular matrix pathways are associated with AMD risk. Slow dark adaptation (DA) is a key functional defect observed in AMD patients. AMD mouse models do not develop structural hallmarks of clinical disease (e.g., drusen). We investigated whether aged wild type mice (WT) or mice with genetic mutations in complement (Cfh) or extracellular matrix (Efemp1) have slow DA.

Methods: Cfh^{+/-} and Efemp1^{R345W/R345W} mice were generated to induce overactive complement or extracellular matrix defects, respectively. Genetic mouse lines listed above were evaluated and compared to WT littermate controls at 2-18 months of age. C57BL/6J mice were assessed between 2-24 months of age to characterize the natural history of age-related dark adaptation decline. Rod-mediated DA was assessed by electroretinography (ERG) using a two day testing protocol: (i) baseline ERG response in fully dark adapted mice using a 2.7 log scot cd s m⁻² probe flash, (ii) DA ERG response using the same probe flash 4 hours after a photobleach (10 minutes @ ~10,000 lux white light). The DA ERG was compared to the baseline ERG to calculate % recovery after photobleach. Statistics: one-way ANOVA with Dunnett's posttest (3 or more groups) or unpaired t test (2 groups). All error bars are standard error of the mean.

Results: DA recoveries from 24 month old C57BL/6J mice range from normal to severely delayed (mean=68%±8.6, n=14) with 8/14 falling below the 95% confidence interval for 2-4 month old mice (mean=82%±4.6, n=29). Compared to WT littermate controls, Cfh^{+/-} and Efemp1^{R345W/R345W} mice do not have significant DA deficits at 18 and 16 months of age, respectively.

Conclusions: Age-related DA deficits in C57BL/6J mice are highly variable, with a change of -14% at 24 months of age. Aged mice (16-18 months old) with AMD-associated genetic mutations in complement (Cfh^{+/-}) or extracellular matrix (Efemp1^{R345W/R345W}) do not exhibit DA deficits compared to WT littermate controls.

CONTROL ID: 3519470

SUBMITTER (NAME ONLY): Tongalp Tezel

TITLE: IMPACT OF SUBSTRATE FLEXURAL MODULUS AND VERTICAL STABILIZATION ON PHOTORECEPTOR OUTER SEGMENT PHAGOCYTOSIS OF HUMAN IPS-DERIVED RETINAL PIGMENT EPITHELIAL CELLS

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.H. Tezel, Q. Zeng, Ophthalmology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the impact of flexural modulus and vertical stabilization of the scaffolds on the ability of the human iPS-derived retinal pigment epithelial cells (hiPS-RPE) to phagocytose photoreceptor outer segments.

Methods: RPE cells from five different hiPS-RPE lines and ARPE-19 cells were cultured to confluence on human Bruch's membrane (hBM; flexural modulus: 1.6-2.44 Mpa) explants and tissue culture inserts with a 10 µm-thick transparent polyester (PET; flexural modulus: 2.8-3.5 Gpa) membrane. One week after the confluence, 6.0 mm grafts were cut and transferred to another dish. These circular grafts were either stabilized on a photopolymerizable biogel or left unstabilized within the culture medium. Grafts were maintained within a culture medium for 4 hours in the presence of FITC-labeled human photoreceptor outer segments (10^8 per/ml). At the end of the incubation period, cells were collected after trypsinization. Flow cytometric analyses were carried out to determine the number of DRAQ5-stained viable cells that phagocytosed FITC-labelled human photoreceptor outer segments.

Results: hiPS-RPE exhibited better phagocytosis of photoreceptor outer segments compared to ARPE-19 cells on both substrates regardless of the graft stabilization ($15.6 \pm 4.4\%$ vs $6.8 \pm 2.4\%$ on stabilized hBM, $p=0.004$; $24.1 \pm 5.5\%$ vs $5.8 \pm 2.0\%$ on unstabilized hBM, $p=0.0001$; $56.8 \pm 16.0\%$ vs $5.7 \pm 1.6\%$ on stabilized PET membranes, $p=0.008$ and $78.4 \pm 9.8\%$ vs $29.2 \pm 8.7\%$ on unstabilized PET membranes, $p=1.5 \times 10^{-6}$). Phagocytic ability of the hiPS-RPE cells was better if hBM ($p=0.008$) and PET membrane ($p=4.6 \times 10^{-6}$) were not stabilized. hiPS-RPE demonstrated better phagocytosis on PET membranes compared to hBM regardless of the stabilization of the substrate. ($p<0.001$)

Conclusions: Flexural modulus of the hiPS-RPE graft can modulate the function of the grafted RPE cells. hiPS-RPE cells exhibit better phagocytosis on PET membranes compared to hBM grafts.

CONTROL ID: 3519519

SUBMITTER (NAME ONLY): Kelsey Chen

TITLE: Characterizing Content and Performance of Ophthalmology-Related Content on Social Media

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chen, Midwestern University Arizona College of Osteopathic Medicine, Glendale, Arizona, UNITED STATES|A.S. Huang, Augusta University, Augusta, Georgia, UNITED STATES|A.S. Huang, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|D. Zhu, Hyperspeed LASIK, NVISION Rowland Heights, Rowland Heights, California, UNITED STATES|A. Abdullah, University Hospital of Wales, Cardiff, Cardiff, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Social media is a powerful source of ophthalmologic information for the public. Ophthalmology-related content is especially pervasive on Instagram (IG), the most popular photo-sharing platform with over 112 million monthly active users. The objective was to identify top-performing ophthalmology posts on IG and characterize their content and features.

Methods: A 36 term hashtag list was curated composed of common ophthalmic diagnoses and procedures (e.g. #LASIK, #cataract, etc.). Related posts were searched on IG from Sept 1 to Oct 1, 2020. IG uses an engagement-based algorithm to rank posts based on the number of likes and comments, giving high-ranking posts greater reach. The top 9 posts for each term were identified. Posts unrelated to ophthalmology were excluded. Each post was analyzed for engagement level (e.g. total likes), media format (e.g. picture, video), content type (e.g. education, self-promotion, etc.), and the poster's background (e.g. credentials, country, seniority, etc.). Engagement level ratios (ER) for each post were calculated as the number of likes to number of followers per poster account. ANOVA analyses were performed.

Results: This was a cross-sectional epidemiological study where 1,763,898 posts were identified. 324 posts met the inclusion criteria. Most posts were created by ophthalmologists (36.4%), followed by patients (29.0%), and optometrists (20.1%). Overall, ophthalmologists (0.077), optometrists (0.091) and patients (0.087) created posts with similar ER ($p>0.05$). While most content was educational (63%), self-promotional posts (0.182) were the most effective in terms of ER followed by personal experience (0.096) and education (0.081) ($p=0.08$). Photos were the most common media type (84.8%) followed by videos (7.9%) and graphics (7.3%). Curiously, video posts received the highest ER (0.234), followed by graphics (0.102), and photos (0.087) ($p<0.05$). When analyzing the top 100 posts ranked by ER, slit lamp photos were most engaging (0.204), followed by white coat photos (0.175) and photos of ophthalmologists (0.171) ($p<0.05$).

Conclusions: Most ophthalmic content on IG is created by non-ophthalmologists. The performance and reach of each post vary significantly based on factors related to post format and content type. Ophthalmologists have the opportunity to make a larger impact on social media by creating more engaging content, especially in areas related to eye education.

CONTROL ID: 3519523

SUBMITTER (NAME ONLY): Ying Liu

TITLE: A traceable and functional cone-rich donor for allogenic photoreceptor transplantation in mouse models of degenerative retinal diseases

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, D. Teng, G. Konar, D. Agakishiev, A. Biggs-Garcia, S. Harris-Bookman, M. McNally, C. Garzon, M. Singh, Retina, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|S. Sastry, Johns Hopkins University Zanvyl Krieger School of Arts and Sciences, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cone photoreceptor transplantation is a potential treatment for macular diseases. The optimal conditions for cone transplantation are poorly understood, partly because of the scarcity of cones in donor mice. To facilitate allogeneic cone photoreceptor transplantation studies in rodents, we aimed to create and characterize a donor mouse model containing a cone-rich retina with a cone-specific enhanced green fluorescent protein (EGFP) reporter.

Methods: We generated OPN1LW-EGFP/NRL^{-/-} mice by crossing NRL^{-/-} and OPN1LW-EGFP mice. We characterized the anatomical phenotype of OPN1LW-EGFP/NRL^{-/-} mice using multimodal confocal scanning laser ophthalmoscopy (cSLO) imaging, immunohistology, and transmission electron microscopy. We evaluated retinal function using electroretinogram (ERG), including 465 and 525 nm chromatic stimuli. Retinal sheets from OPN1LW-EGFP/NRL^{-/-} mice were transplanted subretinally into immunodeficient Rd1 mice.

Results: OPN1LW-EGFP/NRL^{-/-} retinas were enriched with S-opsin⁺ cone photoreceptors in a dorsal-ventral distribution gradient. EGFP reporter expression occurred in L/M- and S-opsin expressing cells. Rosettes formed preferentially in the ventral retina. The outer retina in P35 OPN1LW-EGFP/NRL^{-/-} was thinner than NRL^{-/-} controls. The OPN1LW-EGFP/NRL^{-/-} ERG response amplitudes to 465 nm stimulation were similar to, but to 535 nm stimulation were lower than, NRL^{-/-} controls. Three months after transplantation, there were more S-opsin⁺ than L/M-opsin⁺ outer segments detected in recipients.

Conclusions: OPN1LW-EGFP/NRL^{-/-} retinæ were enriched with S-opsin⁺ cells. Sustained expression of EGFP facilitated the longitudinally tracking of donor cells. Transplanted cone-rich retinal sheet from OPN1LW-EGFP/NRL^{-/-} mice survived and matured into subtype of cone photoreceptors. This novel cone-rich reporter mouse model is a useful tool for the study of cone photoreceptor transplantation as a treatment for macular diseases.

CONTROL ID: 3519542

SUBMITTER (NAME ONLY): Erin O'Neil

TITLE: Bardet-Biedl Syndrome-7 (BBS7) Shows Treatment Potential and a Cone-Rod Dystrophy Phenotype that Recapitulates the Non-Human Primate Model

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. O'Neil, T.S. Aleman, Y. Jiang, J.I. Morgan, J. Bennett, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|E. O'Neil, T.S. Aleman, K. O'Connor, Y. Jiang, I. Aleman, J.I. Morgan, J. Bennett, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|B. Toussaint, Christiana Health, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: To provide a detailed ophthalmic phenotype of two male patients with Bardet-Biedl Syndrome (BBS) due to mutations in the BBS7 gene

Methods: Two brothers ages 26 (Patient 1, P1) and 23 (P2) underwent comprehensive ophthalmic evaluations over a three years. Visual function was assessed with full-field electroretinograms (ffERGs), kinetic and chromatic perimetry, multimodal imaging with spectral domain optical coherence tomography (SD-OCT), fundus autofluorescence (FAF) with short- (SW) and near-infrared (NIR) excitation lights and adaptive optics scanning light ophthalmoscopy (AOSLO).

Results: Both siblings had a history of obesity and postaxial polydactyly; P2 had diagnoses of type 1 Diabetes Mellitus, Addison's disease, high-functioning autism-spectrum disorder and -12D myopia. Visual acuities were better than 20/30. Kinetic fields were moderately constricted. Cone-mediated ffERGs were undetectable, rod ERGs were 60-80% of normal mean. Static perimetry showed severe central cone and rod dysfunction. Foveal to parafoveal hypoautofluorescence, most obvious on NIR-FAF, co-localized with outer segment shortening/loss and outer nuclear layer thinning by SD-OCT, and with reduced photoreceptors densities by AOSLO. A structural-functional dissociation was confirmed for cone- and rod-mediated parameters. Worsening of the abnormalities was documented by SD-OCT and FAF in P2 at 3 years. Gene screening resulted in compound heterozygous mutations in BBS7 (p.Val266Glu:c.797T>A/c.1781_1783delCAT) in both patients.

Conclusions: BBS7-associated retinal degeneration may present as a progressive cone-rod dystrophy pattern, reminiscent of both the murine and non-human primate models of the disease. Predominantly central retinal abnormalities in both cone and rod photoreceptors showed a structural-functional dissociation, an ideal scenario for gene augmentation treatments.

CONTROL ID: 3519567

SUBMITTER (NAME ONLY): Landon Rohowetz

TITLE: Corneal abnormalities in the DBA/2J mouse model of glaucoma: DBA/2J-Gpnmb⁺/SjJ as a critical control

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.J. Rohowetz, S. Riordan, P. Koulen, Ophthalmology, University of Missouri Kansas City Vision Research Center, Kansas City, Missouri, UNITED STATES|P. Koulen, Biomedical Sciences, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Landon Rohowetz: Commercial Relationship: Code N (No Commercial Relationship) | Sean Riordan: Commercial Relationship: Code N (No Commercial Relationship) | Peter Koulen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The DBA/2J (D2) mouse strain is widely used as a model for glaucoma. We compared the D2 and DBA/2J-Gpnmb⁺/SjJ (D2G) mouse strains to determine the relative roles of age-related changes in IOP and corneal pathology on visual dysfunction in the D2 mouse model of glaucoma. D2G mice are genetically identical to D2 mice with the exception of a normally functioning Gpnmb gene resulting in a lack of iris pigment dispersion and the absence of IOP elevation and glaucomatous neuropathy.

Methods: IOP, visual acuity (VA) and corneal calcification were studied in D2 and D2G mice. IOP and VA were monitored over a 12-month period using tonometry and behavioral measures of the optomotor reflex. At 6, 9 and 12 months, corneas from each group were examined using confocal microscopy to measure the intensity, thickness and size of calcified regions.

Results: D2 mice developed elevated IOP between 9 (13.53 ± 0.88 mmHg) and 12 months of age (23.53 ± 1.72 mmHg), but D2G mice did not (12.34 ± 0.33 mmHg at 9 and 13.8 ± 0.47 mmHg at 12 months). Corneal calcification was found in 46.4% of D2 eyes and 56.7% of D2G eyes at 6 months ($P = 0.323$), 52.5% and 52.6% at 9 months ($P = 0.991$) and 83.3% and 60.0% at 12 months ($P = 0.1113$). When comparing 9 and 12 month-old mice with calcification, D2 mice demonstrated an increase in calcification thickness ($P = 0.005$) and D2G mice demonstrated increases in calcification intensity ($P = 0.006$) and thickness ($P = 0.036$). At 12 months of age, D2 mice with corneal calcification had greater mean IOP (25.38 ± 1.85 mmHg) than D2 mice without corneal calcification (17.5 ± 2.53 mmHg; $P = 0.048$). No difference in IOP was observed between D2G mice with and without calcification at any age. Calcification thickness correlated positively with IOP ($r = 0.415$, $P = 0.004$) and negatively with visual acuity ($r = -0.451$, $P = 0.014$) in D2 but not D2G mice.

Conclusions: Corneal calcification may affect noninvasive IOP measurements and visual function in D2 mice. While ocular hypertension secondary to iris pigment dispersion causes visual dysfunction, corneal abnormalities, such as corneal calcification, should be considered as potentially confounding factors for the assessment of vision loss in D2 mice.

CONTROL ID: 3519575

SUBMITTER (NAME ONLY): Ryan Zubricky

TITLE: Facedown Positioning Duration for Silicone Oil Tamponade and the Effect on Retinal Re-detachment

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zubricky, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|S. Platt, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ryan Zubricky: Commercial Relationship: Code N (No Commercial Relationship) | Sean Platt: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To analyze the incidence of retinal redetachments and other complications following pars plana vitrectomy for retinal detachment repair with silicone oil tamponade and the outcome of facedown positioning duration on these endpoints.

Methods: The retrospective study was performed on patients with retinal detachment repair via pars plana vitrectomy with silicone oil tamponade between 2015 and 2020. Surgery was performed by 10 physicians associated with a private retina practice in Cleveland, OH. The independent variable of interest was length of post-operative facedown positioning. Outcome variables were retinal re-detachment, epiretinal membrane (ERM) formation, cataract formation, and other complications.

Results: The study was composed of 227 eyes. The mean age of patients was 62.09 ± 13.65 years with 63% males and 37% female. Of the initial detachments, 27.88% were mac-on and 72.12% were mac-off. Overall, 42 patients had facedown positioning for 1 day, 50 for 3 days, 24 for 5 days, and $99 \geq 7$ days. Redetachment was seen in 45.2% of the 1-day group, 40% of the 3-day group, 41.6% of the 5-day group, and 29.3% of the 7-day group ($p=0.246$). Cataract formation was seen in 64.7% of the 1-day group, 47.8% of the 3-day group, and 74.5% of the 7-day group ($p=0.088$). ERM formation showed no clear trend nor statistical significance ($p=0.523$). Analysis was also performed grouping patients into a ≤ 6 day group and a ≥ 7 -day group. Redetachment was seen in 42.19% of the ≤ 6 -day group and 29.29% of the 7-day group ($p=0.045$). Relative risk for the 7-day group was 0.694. Cataract formation was seen in 51.9% of patients in the ≤ 6 -day group and 74.5% of the 7-day group ($p=0.021$). Relative risk was 1.434. No significant difference was found in ERM formation.

Conclusions: The data suggests a lower rate of retinal redetachment with increasing postoperative facedown positioning time, particularly with 7 days, although the result was not statistically significant. Additionally, there was a suggestive increase of cataract formation in the 7 day group although this also did not meet significance. When comparing patients that positioned ≥ 7 days to all others, significance was achieved. These relationships would be better studied with a larger sample size and a randomized control trial that could further define the associations found here and determine causality.

CONTROL ID: 3519599

SUBMITTER (NAME ONLY): Felicia Widyaputri

TITLE: Diabetic retinopathy prospective study in pregnant women with pre-existing diabetes in Metropolitan Melbourne

SESSION TITLE: DR: Epidemiology and service provision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) may be worsened by pregnancy. Findings from prior studies have been conflicting; many are outdated. Here, we report the prevalence, rate of DR progression and risk factors associated with progression in pregnant women with pre-existing diabetes.

Methods: Prospective longitudinal cohort study of pregnant women with type 1 (T1DM) or type 2 diabetes (T2DM) from two tertiary maternity hospitals in Melbourne, Australia (Nov 2017 - Sept 2019). Eye examinations were scheduled in each trimester and 3-months postpartum. DR severity was graded for each eye from 2-field retinal photographs. At least 2 exams (at early and late pregnancy) were required to evaluate DR change. Progression was defined as worsening by ≥ 1 -step of the Airlie House classification, development of diabetic macular edema (DME), or the need for laser treatment during pregnancy. Sight-threatening (ST) progression was defined as development of proliferative DR (PDR) or DME.

Results: A total of 147 from 191 eligible women (77%) were recruited, with at least one eye exam performed in 130 (88.4%). Mean age was 33.7 years (range 19-47). Sixty-two women (47.7%) had T1DM while 68 had T2DM (median duration 16.5 years and 4 years). DR and STDR prevalence during the study period were 20.8 (CI 16.3-26.1) and 6.6 (CI 4.1-10.4) per 100 eyes, respectively. Among the 144 eyes (72 women) with >1 eye exam, 10/76 (13.2%) and 4/68 (5.9%) from T1DM and T2DM women had DR progression, with an overall progression rate of 9.7%. Six eyes developed new DR. Elevated systolic blood pressure (SBP) (risk ratio 5.07, CI 1.90-13.49) and presence of any DR (RR 10.36, CI 3.14-34.12) in early pregnancy significantly increased the risk of progression. ST progression was observed in 6 eyes (1 developed PDR, 3 developed DME, 2 with treated-PDR required further laser during pregnancy).

Conclusions: The prevalence of DR in pregnant women was similar to the non-pregnant diabetic population in Australia. Nearly 1 in 10 eyes had DR progression between early to late pregnancy, with almost half of these developing STDR. Risk factors for progression included higher SBP in early pregnancy and pre-existing DR at

pregnancy onset. Worryingly, 1 in 5 participants failed to attend any eye exams during pregnancy, highlighting the need to address barriers to eye screening adherence given the significant risk of vision loss from DR in this population.

CONTROL ID: 3519624

SUBMITTER (NAME ONLY): Keiichiro Minami

TITLE: Power of diffractive intraocular lenses during an objective refraction examination using a near-infrared light source.

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Minami, Y. Ota, H. Bissen-Miyajima, Ophthalmology, Tokyo Dental Collage Suidobashi Hospital, Tokyo, JAPAN|K. Okamoto, M. Nakashima, Tomey Corporation, Nagoya, JAPAN|

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ABSTRACT BODY:

Purpose: Conventional subjective and objective refractions are examined under visible and near-infrared (NIR) lights, respectively. Diffractive extended depth of focus (EDOF) intraocular lenses (IOLs) utilizing an echelette optics form the far focus with the 1st-order diffraction, and differences between the subjective and objective refractions are clinically addressed. Hence, we evaluated experimentally the lens powers of diffractive bifocal and EDOF IOLs under NIR lights.

Methods: Lens power (D) was measured using a lensmeter (TL-7000, Tomey) that utilized the Hartmann pinhole plate and was modified to accommodate a LED with a peak wavelength of 850 nm. Three pieces of refractive monofocal, refractive (for far) and diffractive (for near) bifocal, and diffractive EDOF IOLs (ZCB00V, ZMB00, and ZXR00V, respectively, Johnson & Johnson Surgical Vision) with labeled powers of 10, 15, and 20D were immersed in water, and the pinhole images were captured with a CMOS camera. Mean distances of 9 pinholes at the center were measured with Image J, and lens powers were calculated with regression results of monofocal IOLs. Power differences from the monofocal IOLs were also obtained for bifocal and EDOF IOLs.

Results: The distances of pinholes were well correlated with the labeled power of monofocal IOLs ($P < 0.001$, $R^2 > 0.999$), and the calibration equation was obtained for water-immersed IOLs. The mean powers for the label of 10, 15, and 20D were 9.89, 14.69, and 19.80D with bifocal IOLs and 10.79, 15.73, and 20.98D with EDOF IOLs, respectively. The mean difference between the bifocal and monofocal IOLs were -0.21D (SD: 0.19D), while the difference between the EDOF and monofocal IOLs was 0.83D (SD: 0.14D).

Conclusions: The powers measured under NIR light were higher than the labeled value of the EDOF IOLs, but such a difference was not found with the bifocal IOLs. The results demonstrated that the lens power of the EDOF IOL increased with longer wavelength light as the 1st-order diffraction of an echelette optics forms the far focus. The difference could reflect the myopic shift in objective refraction from subjective results, as clinically observed.

CONTROL ID: 3519650

SUBMITTER (NAME ONLY): Jian Lian

TITLE: Image Registration for sequential Ocular Multispectral Slices via Heterogeneous Mapping

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lian, Y. Zheng, Shandong Normal University, Jinan, Shandong, CHINA|J. Lian, School of Intelligent Engineering, Shandong Management University, Jinan, Shandong, CHINA|

Commercial Relationships Disclosure (Abstract): Jian Lian: Commercial Relationship: Code N (No Commercial Relationship) | Yuanjie Zheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The quality of ocular Multispectral Imaging (MSI) can be spoiled by the relative movement between a sequence of MSI slices due to the inevitable saccadic movements of eyeballs. In clinical practice, this type of misalignment usually leads to ophthalmologists' misinterpretation of the MSI images and renders the corresponding diagnosis error prone. To address the issues caused by the GroupWise misalignment that existed in MSI slices, this study focuses on developing a GroupWise registration instrument for eliminating the misalignment between a set of MSI slices without relying on mutual information or cross-correlation, which is validated to be capable of dealing with the image samples with low resolution.

Methods: 32 sequences of slices were collected with an Annidis RHATH instrument. In total, there are 11 spectral slices captured from 11 discrete monochromatic optical sources. The slices were of the oculus dexter and oculus sinister from 6 patients and 10 healthy subjects in dicom file format (with 16-bit depth and resolution of 2048*2048). First of all, we proposed a novel similarity measure technique by introducing the heterogeneous mapping algorithm, with which the similarity between a group of MSI slices can be represented as their Euclidean distances in one latent space. Furthermore, the scale-invariant feature transform algorithm, an inter-image transformation approach, and alternating minimization were exploited to implement the landmark detection, motion model, and optimization in the registration process, respectively.

Results: The proposed pipeline achieved superior performance over state-of-the-art techniques. The average mean (standard deviation) of the distance between manually delineated points and the transformed ones is 2.9 (1.8). An instance of the MSI slices and the registration results by using the proposed approach are shown in Figure 1.

Conclusions: Transferring the images from varied models into one vector space not only can facilitate the measurement of the difference between sequential images but also can improve the quality of MSI slices and the outcome of the registration algorithms. It is potentially invaluable for the diagnosis and treatment of eye diseases.

CONTROL ID: 3519685

SUBMITTER (NAME ONLY): Colleen Howell

TITLE: Validity of Actiwatch and Clouclip Measures of Light Exposure

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.M. Howell, S.J. McCullough, L.A. Doyle, K.J. Saunders, Optometry and Vision Science Research Group, Ulster University, Coleraine, Derry, UNITED KINGDOM|C.M. Howell, M. Murphy, Sport and Exercise Sciences Research Group, Ulster University, Coleraine, Derry, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To compare measures of light exposure obtained with Actiwatch2 (AW) and Clouclip (CC) to 'gold standard' photometer (PHO) measures and evaluate the wearable devices' ability to categorise light into different levels of illumination.

Methods: Illumination was assessed by AW, CC and PHO in a range of lighting conditions and categorised (by PHO) as described in Table 1. Regression plots and Bland/Altman analyses evaluated the relationship between PHO output and the wearable devices. The ability of AW and CC to successfully categorise light into the four categories was examined.

Results: A strong linear relationship was found between light exposure measured by PHO and both AW ($r=0.999$, $p<0.001$) and CC ($r=0.989$, $p<0.001$). However, compared to PHO, both wearable devices underestimated light exposure. The disparity increased with increasing illumination and was greater for AW than CC. Mean differences and limits of agreement in light exposure were; AW vs PHO 430.92 lux (-1397.82 to 2259.66) and CC vs PHO 79.35 lux (-327.98 to 486.68), respectively. Categorisation of illumination level (SCO/MES/IN/OUT) by CC was more accurate than by AW (Figure 1). Adjusted criteria for categorisation of illumination levels by wearables were derived from regression equations (Figure 2).

Conclusions: These data illustrate that both CC and AW devices underestimate light exposure in comparison to 'gold standard' PHO measures, with increasing disparity at higher light levels, especially for AW. For researchers interested in categorising exposure into different levels of illumination, CC more accurately classifies illumination levels than AW in illuminations above SCO levels. Adjusted criteria should be applied to AW and CC data to more closely align with PHO outputs.

CONTROL ID: 3519690

SUBMITTER (NAME ONLY): Yoko Ikeda

TITLE: Trend of continuous intraocular pressure decrease over a 20-year period in Japanese normal tension glaucoma patients

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ikeda, K. Mori, M. Ueno, Y. Maruyama, K. Imai, Y. Yamamoto, C. Sotozono, Ophthalmology, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|Y. Ikeda, Oike-Ikeda Eye Clinic, Kyoto, JAPAN|K. Yoshii, Mathematics and Statistics in Medical Sciences, Kyoto Prefectural University of Medicine, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JP, academic/medsch, JAPAN|T. Yamazaki, Baptist Eye Institute, JAPAN|M. Nakano, R. Sato, N. Omi, F. Sato, K. Tashiro, Genomic Medical Sciences, Kyoto Prefectural University of Medicine, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JP, academic/medsch, JAPAN|S. Kinoshita, Frontier Medical Science and Technology for Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JP, academic/medsch, JAPAN|

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ABSTRACT BODY:

Purpose: We first established our original Kyoto Prefectural University of Medicine Glaucoma Registry (KPUM-GR) in 1995, and have continued inputting data since then. The purpose of this study was to analyze the data in the KPUM-GR and investigate the annual trend and seasonal variation of intraocular pressure (IOP) over the past 20 years in Japanese normal tension glaucoma (NTG) patients.

Methods: IOP data was extracted from the KPUM-GR data obtained at the KPUM Hospital and affiliate clinics under the following conditions: 1) 1 data point per patient per month, 2) if bilateral data was available, the right-eye data was used, 3) if measured more than twice within 1 month, the mean IOP data was calculated and used, and 4) if the patient had undergone glaucoma surgery, the postoperative data was excluded, but not excluded if cataract surgery or laser treatment, such as trabeculoplasty, was performed. In order to investigate the trends of IOP throughout the 20-year period, we first calculated the mean IOP from all available data of each month from January 1997 through December 2016. The data was then further divided into 5 groups of 4 consecutive years each (1997-2000, 2000-2004, 2005-2008, 2009-2012, and 2013-2016), and the mean IOP of each month within each group was then calculated. Seasonal variations of IOP over the 20-year period and in the 5 consecutive 4-year groups was then investigated via nonlinear multiple regression analysis.

Results: We ultimately extracted 49,007 independent data points derived from 1,774 Japanese NTG patients (665 males and 1,109 females; mean age: 59.8 ± 14.4 years, mean observation period: 5.6 ± 4.4 years) treated

with/without anti-glaucoma medications over the 20-year period. A continuous decrease of IOP, with seasonal variations, was detected throughout the 20-year period ($p < 0.001$). Annual mean IOP was highest (13.9 ± 2.7 mmHg) in the oldest 4-year group (1997-2000), followed by a gradual decrease in each subsequent group, finally becoming lowest (12.3 ± 2.7 mmHg) in the most recent group (2013-2016) (trend test: $p < 0.001$). The seasonal variations of IOP were clearly detected ($p < 0.001$) in each of the 5 consecutive 4-year groups.

Conclusions: Based on real-world longitudinal data, our findings revealed a continuous decrease and seasonal variations of IOP throughout the 20-year period in Japanese NTG patients.

CONTROL ID: 3519693

SUBMITTER (NAME ONLY): Rishika Chaudhary

TITLE: Vitreous metabolomic predictors of proliferative vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Chaudhary, S. Young, R. Scott, R.J. Blanch, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|R. Chaudhary, K. Blachford, Birmingham and Midland Eye Centre, Birmingham, Birmingham, UNITED KINGDOM|R.J. Blanch, Queen Elizabeth Hospital Birmingham, Birmingham, Birmingham, UNITED KINGDOM|A. Logan, University of Warwick, Coventry, West Midlands, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: We performed a prospective observational clinical study to differentiate eyes that did and did not develop proliferative vitreoretinopathy (PVR) on the basis of the metabolites and cytokines in human vitreous samples taken at the time of rhegmatogenous retinal detachment (RRD) repair.

Methods: Metabolomic analysis was performed on 66 vitreous samples, obtained at the start of pars plana vitrectomy from patients undergoing surgery for macular hole (n=21) and RRD (n=44), including patients who subsequently developed PVR (n=14) and patients who did not (n=31). One-dimensional ¹H spectra were acquired at 298 °K with 128 scans using a standard Bruker NOESY 1D pulse sequence with pre-saturation water suppression Bruker DRX 600MHz NMR spectrometer equipped with a cryoprobe. Chemical shifts were calibrated with respect to the chemical shift position of the TMSP resonance.

Multiplexed immunoassays with fluorescent microspheres were used to perform cytokine analysis in MH (n= 45); RRD (n= 71) and PVR eyes (n=22). Different disease groups were analysed using both univariate and multivariable approaches.

Results: High levels of 2-hydroxyvalerate, 2-phosphoglycerate, alanine, alloisoleucine, glutamine, histidine, methanol, urea, valine and myo-inositol predicted the development of post-operative PVR. Levels were lower in those eye with RD that did not develop PVR. Creatine was found to be higher in the MH group as compared to RD.

The cytokines IL-1 β and IL-7 were found to be significantly higher in the PVR group compared to the RD group (P=0.02 and 0.03 respectively). IL1ra, IL7, IL8, IL9, IP10 and MIP1b was found to higher in the RD group compared to MH group.

Conclusions: We report, for the first time, vitreous metabolic changes predicting PVR development. Through pathway analysis, increased histidine, glutamine, valine, alanine and isoleucine points to aminoacyl tRNA biosynthesis. High levels are predictive of PVR development. Upregulation is associated with increased protein synthesis required for proliferation of fibrocellular membranes in PVR.

The metabolite results are suggestive of increased glycolysis activity and glutamate signalling, associated with the enhanced cellular migration and proliferation plus excitotoxicity seen in PVR development.

The cytokines detected have a more proliferative than apoptotic profile, supporting the suggestion that the detected metabolic changes relate to cell migration and proliferation.

CONTROL ID: 3519701

SUBMITTER (NAME ONLY): Clayton Wisely

TITLE: Correlation of aqueous humor and plasma concentrations of amyloid and tau in older adults without dementia

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wisely, C. Robbins, J. Ma, T. Kim, D. Grewal, S. Fekrat, Ophthalmology, Duke University Hospital, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Plasma and cerebrospinal fluid (CSF) levels of protein biomarkers have been associated with Alzheimer's disease (AD). Limited prior studies have suggested amyloid beta 40 (A β 40) and 42 (A β 42) are present in human aqueous, but detection of tau proteins has not been previously reported. We sought to characterize normal concentrations of A β 40, A β 42, and total tau in human aqueous and compare to plasma concentrations and Montreal Cognitive Assessment (MoCA) scores.

Methods: Twenty adults with no history of dementia underwent simultaneous aqueous and plasma sampling and MoCA (blind version) testing at the time of cataract surgery. Aqueous and plasma samples underwent analysis in duplicate using the single-molecule array (SiMoA) SR-X platform (Quanterix[®], Middlesex, MA) to measure A β 40, A β 42, and total tau.

Results: Mean (standard deviation) age was 70.7 (6.6) years. Mean MoCA score was 19.3 (2.5). Two subjects were unable to give plasma. Three of 18 (17%) plasma samples could not be analyzed via SiMoA. Mean measured aqueous concentrations (pg/ml) of A β 40, A β 42, and total tau were 131.0 (67.1), 3.6 (3.6), and 39.2 (41.2) respectively, and corresponding plasma concentrations were 128.5 (57.2), 10.2 (5.7), and 5.6 (3.2). All aqueous samples contained A β 40 and total tau, but only 3/20 (15%) of samples contained detectable A β 42. All analyzed plasma samples (n=15) had detectable A β 40, A β 42, and total tau. Comparisons between first and second runs of aqueous samples demonstrated mean difference of 18% (24%) for A β 40 and 14% (15%) for total tau. There were minimal correlations between A β 40 ($r^2 < 0.01$) and total tau ($r^2 = 0.11$) in aqueous and plasma. Aqueous concentrations of A β 40 and total tau also demonstrated minimal correlation with MoCA scores, $r^2 = 0.07$ and 0.02 respectively or age, $r^2 = 0.01$ and 0.20 respectively.

Conclusions: SiMoA can measure A β 40 and total tau in human aqueous. A β 42 was not detectable in 85% of aqueous samples but was detectable in all plasma samples. In adults without dementia, there is minimal correlation between aqueous and plasma concentrations of A β 40 and total tau. Aqueous concentrations of A β 40 and total tau do not appear to correlate with MoCA scores. Further study in subjects with AD is indicated to determine whether aqueous A β 40 and total tau may differ between AD and controls or correlate with cognitive test scores or CSF protein concentrations.

CONTROL ID: 3519719

SUBMITTER (NAME ONLY): Dennis Akrobetu

TITLE: Assessment of retinal microvascular alterations in individuals with amnestic and non-amnestic mild cognitive impairment using optical coherence tomography angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Akrobetu, C. Robbins, S.S. Stinnett, S. Soundararajan, A. Liu, K. Johnson, D.S. Grewal, S. Fekrat, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Individuals with mild cognitive impairment (MCI) can be categorized into amnestic and non-amnestic subgroups based on the absence or presence of intact working memory. Patients with amnestic MCI have increased likelihood of progressing to Alzheimer's disease (AD); however, identification of predictive biomarkers distinguishing amnestic and non-amnestic MCI remains ambiguous. This prospective, cross-sectional study utilizes optical coherence tomography angiography (OCT-A) to assess how retinal microvascular density and structure might differ among amnestic and non-amnestic MCI patients.

Methods: One hundred and twelve eyes of 59 amnestic MCI participants, 32 eyes of 17 non-amnestic MCI participants, and 111 eyes of 56 cognitively healthy controls were included in our study. All participants were imaged using the Zeiss Cirrus HD-5000 AngioPlex. OCT-A vessel density (VD) and perfusion density (PD) in Early Treatment Diabetic Retinopathy Study (ETDRS) 3mm and 6mm circles and rings were assessed. Retinal thickness parameters on OCT including retinal nerve fiber layer thickness (RNFL), ganglion cell-inner plexiform layer (GC-IPL), and central subfield thickness (CST) were also analyzed. Generalized estimating equations accounting for correlation between two eyes of the same subject were utilized for statistical analysis.

Results: Assessment of PD in the 3x3mm inner ETDRS ring revealed a significant decrease in amnestic MCI when compared to non-amnestic MCI (0.29 ± 0.03 vs 0.34 ± 0.09 , $p = 0.025$), and was significantly lower in amnestic MCI when compared to healthy controls (0.29 ± 0.03 vs 0.39 ± 0.02 , $p < 0.001$), after adjustment for age and sex. Vessel density, subfoveal choroidal thickness, and other retinal thickness parameters (GC-IPL, RNFL, CST) showed no statistically significant difference among or between diagnostic groups.

Conclusions: After adjusting for age and sex, OCT-A perfusion density significantly differed among controls, non-amnestic MCI, and amnestic MCI. Other retinal parameters did not differ between groups after adjusting for covariates. Non-invasive retinal imaging deserves further study as a potential biomarker for diagnosing and classifying subtypes of MCI.

CONTROL ID: 3519720

SUBMITTER (NAME ONLY): Minh Trinh

TITLE: Dexamethasone intravitreal implant as monotherapy for birdshot chorioretinopathy

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Trinh, Ophthalmology, Northwell Health, Great Neck, New York, UNITED STATES|J. Jonisch, Vitreoretinal Consultants, Great Neck, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Minh Trinh: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Jonisch: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Birdshot chorioretinopathy (BCR) is an ophthalmic disease not commonly associated with other systemic findings. However, systemic steroids or immunomodulatory therapy (IMT) is often needed to treat acute or chronic BCR, and those have significant morbidity associated with treatment. We present six eyes with BCR undergoing monotherapy with intravitreal dexamethasone implantation 0.7mg (Ozurdex; Allergan, Inc.) to review the efficacy and limitations of this treatment modality.

Methods: A retrospective chart review was performed on patients at our practice with BCR. Eyes receiving Ozurdex monotherapy for the treatment of BCR with a minimum follow-up period of 6 months were included. Eyes which were concurrently receiving systemic steroids or IMT were excluded. Six eyes (3 patients) were included. The main outcome measure was quiescence of disease activity as measured by fluorescein angiogram, optical coherence tomography, ophthalmic exam, and patient symptoms. Secondary outcomes were improvement of best corrected visual acuity. We collected: visual acuity, central macular thickness (CMT), presence of vitritis, presence of retinal vasculitis on fluorescein angiography, intraocular pressure (IOP), and presence of cataract at baseline, 1 month, 3 months, and 6 months after beginning treatment.

Results: All eyes were injected at intervals of 3-6 months if there was clinical evidence of worsening vision, macular edema, vitritis, or retinal vasculitis. All eyes achieved quiescence of disease activity with Ozurdex. The mean LogMar visual acuity was 0.18 ± 0.15 at baseline, 0.16 ± 0.10 at 1 month, 0.16 ± 0.12 at 3 months, and 0.13 ± 0.11 at 6 months (all $p > 0.05$). There was a trend towards improved visual acuity but was not statistically significant. One eye presented with macular edema with a CMT of 409 microns at baseline which improved to 248 microns at 6 months. Two eyes had vitritis and four eyes had retinal vasculitis, all eyes improved with treatment. Four eyes developed elevated IOP after the first injection of Ozurdex, but was successfully managed with topical therapy alone. None of our patients developed cataracts as a consequence of therapy.

Conclusions: Our findings suggest that repeated injections of Ozurdex as monotherapy may be a valuable option in the treatment of BCR and could be used to delay the initiation of IMT. Further studies are warranted to evaluate the utility of local monotherapy with Ozurdex.

CONTROL ID: 3519753

SUBMITTER (NAME ONLY): Shavini Athukorala

TITLE: Comparison of Pre-operative Measured to Post-operative Refractive Astigmatism in Pseudophakes

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Athukorala, N. Kansara, T. O'Rourke, I.U. Scott, S. Pantanelli, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the relationship between various measures of pre-operative keratometric astigmatism and post-operative refractive astigmatism (RA).

Methods: Consecutive eyes evaluated between 11/2018 and 07/2020 underwent pre-operative biometry (IOLMaster 700), tomography/topography (Galilei G4), cataract surgery with implantation of a monofocal intraocular lens, and manifest refraction between 21 and 90 days after surgery. Eyes excluded from the analysis included those with biometry or topography of poor quality (as defined by the device's respective image quality metrics), history of ocular surgery other than laser, corneal disease of any kind, cataract surgery combined with another procedure, intraoperative complications, implantation of a toric or multifocal IOL, missing post-operative manifest refraction, or a best-corrected distance visual acuity worse than 20/40. Post-operative RA was compared to pre-operative astigmatism measured using the following methods: Keratometry (K; IOLMaster), Simulated Keratometry (SimK; Galilei G4), Total Keratometry (TK; IOLMaster), and Total Corneal Power (TCP2; Galilei G4). Difference vectors (DV) were calculated between RA and each of the four pre-operative measures.

Results: One-hundred eighteen eyes met criteria for inclusion in the analysis. The centroid of the DVs for the four measurement methods were 0.26 ± 0.75 D @ 173, 0.52 ± 0.75 D @ 177, 0.08 ± 0.77 @ 151, and 0.30 ± 0.81 D @ 174, respectively. K and TCP2 DVs were not significantly different from one another ($p = 0.58$); all other differences were significant ($p < 0.0001$). The proportion of eyes with DV magnitudes < 0.5 were 36.4%, 23.7%, 41.5%, and 28.8% ($p < 0.0001$), respectively. The proportion of eyes with DV magnitudes < 1.0 D were 85.6%, 67.8%, 83.9%, and 75.4%, respectively ($p < 0.0001$ for all comparisons except K vs. TK [$p = 0.48$]).

Conclusions: Of the pre-operative measurement methods evaluated, TK most closely approximated post-operative RA. The effect of surgically induced astigmatism (SIA) was not evaluated due to the retrospective nature of the study.

CONTROL ID: 3519764

SUBMITTER (NAME ONLY): Angelica Scanzera

TITLE: Adherence to Urgent Eye Visits During the COVID-19 Pandemic: A Population Characteristics Study

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Scanzera, A.Y. Chang, S. Thermoziar, R. Chan, Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|S.J. Kim, School of Public Health- Health Policy and Administration, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The rapid spread of coronavirus (COVID-19) has changed the way eye care practitioners provide care. As an early response to the pandemic, the Department of Ophthalmology at the University of Illinois at Chicago created a tele-triage system to screen patients requesting an urgent visit. The aim of this study was to explore demographic and community factors associated with adherence of patients scheduled for recommended urgent eye visits.

Methods: Surveys of all individuals requesting an acute same day in-person visit between April 6, 2020 and June 6, 2020 were reviewed, and medical chart review was completed for patients recommended an urgent visit.

Demographic data and adherence to visit were examined. Using ArcGIS, address was geocoded and census tract level variables were appended from the U.S. Census American Community Survey between 2014 and 2018. COVID-19 related death data during the study period were also included from the Cook County Medical Examiner's Office. Descriptive statistics, t-tests and binary logistic regression were used to compare variables. A p-value of ≤ 0.05 was considered statistically significant. Data was analyzed using SAS Institute Inc. 2018 (SAS 9.4M6, Cary, NC, USA).

Results: A total of 229 patients were recommended an urgent visit. Of 216 patients with matching criteria on chart review, mean age was 46.6 ± 18.6 years. The majority of patients were female (55.6%) and Black or African American (40.3%), and most common insurance was Medicaid (36.6%). 192 patients (88.9%) reported for their scheduled visit. When comparing personal characteristics by adherence to visit, there was no difference based on gender ($p=0.94$), race ($p=0.56$), insurance status ($p=0.28$), nor new versus established status ($p=0.20$). Community level data showed that individuals who did not adhere to their visit more commonly came from neighborhoods with a greater proportion of Blacks or African Americans (59.4% vs. 33.4%; $p=0.03$), greater unemployment rates (17.5% vs. 10.7%; $p<0.01$), and greater cumulative deaths from COVID-19 (56 vs. 31; $p=0.01$).

Conclusions: The findings from this study suggest that, in our patient population, COVID-19 itself disproportionately affects black communities in terms of mortality, but also affects adherence to appointments which, in return, increases gaps in health equity.

CONTROL ID: 3519790

SUBMITTER (NAME ONLY): Sean McCafferty

TITLE: Corneal Crosslinking Intracorneal Stress Measured by a Novel and Easily Implemented Differential Tonometry Method

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.J. McCafferty, Ophthalmology, Banner University Medical Center Tuscon, Tucson, Arizona, UNITED STATES|M. Wang, Ophthalmology, Banner University Medical Center South, Tucson, Arizona, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sean McCafferty: Commercial Relationship(s);Intuor Technologies:Code I (Personal Financial Interest);Reichert:Code C (Consultant) | Mingwu Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Evaluate corneal changes following corneal crosslinking (CXL) by paired differential tonometry intraocular pressure (IOP) measurements with a Goldmann tonometer (GAT) prism and corneal compensating, correcting applanation tonometry surface (CATS) prism.

Methods: Design: Prospective, controlled, open-label reference device comparison

Methods: IOP was measured on 23 unique eyes undergoing CXL for keratoconus with a GAT using a standard flat GAT prism and a curved corneal error correcting CATS prism before treatment and at 2 weeks, 2 months and 6 months after treatment. Concurrent measurements of central corneal thickness (CCT) and corneal hysteresis (CH) were completed.

Results: Randomized paired IOP measurements with standard GAT and corneal correcting CATS prisms indicated a significant sustained relative increase in the differential IOP between the two prisms after CXL ($p=0.005, 0.015, 0.001$). CH initially decreased at two weeks post-CXL then returned to sustained pre-op levels ($p=0.033, 0.20, 0.20$). CCT progressively decreased following CXL ($p=0.005$).

Conclusions: Differential tonometry between standard GAT and corneal biomechanical compensating CATS prisms demonstrates a simple and sensitive method for measurement of changes in corneal rigidity and corneal stress redistribution. Results suggest that CXL likely re-establishes a more “normal” biomechanical behavior to the keratoconic cornea.

CONTROL ID: 3519791

SUBMITTER (NAME ONLY): Gustavo Gameiro

TITLE: Orbicularis Oculi Muscle morphometry alterations in Hemifacial Spasm

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Gameiro, M.H. Osaki, T. Osaki, P. Schor, T.H. Osaki, Ophthalmology and Visual Science, Universidade Federal de Sao Paulo Escola Paulista de Medicina, Sao Paulo, SP, BRAZIL|S.K. Marie, Laboratory of Molecular and Cellular Biology, Department of Neurology, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Despite being phenotypically normal, the nonaffected side of hemifacial spasm patients (HFS) may have characteristic histopathological findings. This study focuses on objectively evaluating orbicularis oculi muscle (OOM) samples from patients with HFS and control subjects who underwent cosmetic blepharoplasty.

Methods: 21 OOM samples were included in this study. 7 samples from 4 normal control subjects and 7 paired eyelids (7 from the affected and 7 from the nonaffected side) from patients with HFS, virgin of treatment, were evaluated. OOM samples were prepared using Hematoxylin and Eosin (H&E) and Gomori staining. High-resolution slide photos (x400) were obtained. Image parameters were quantitatively analyzed using ImageJ by a blind expert operator. Outcomes were area of each fiber (calculated in H&E staining) and percentage of connective tissue (assessed in Gomori staining). T-student tests and paired-t test were used to compare measurements between groups.

Results: Both the nonaffected side ($13.46 \pm 1.59 \text{ mm}^2$) and the affected side ($12.64 \pm 3.10 \text{ mm}^2$) of HFS patients presented greater fiber size than the control group ($9.03 \pm 1.76 \text{ mm}^2$), $p < 0.01$ and $p = 0.02$, respectively. No statistically significant difference was observed between the paired sides of the patients. The affected HFS-OOM revealed increased connective tissue ($28.76 \pm 8.11\%$) than both the nonaffected ($20.07 \pm 9.04\%$) and control-OOMs ($14.12 \pm 5.38\%$), $p = 0.02$ and $p < 0.01$, respectively. No difference was detected between the control and the nonaffected group. Results presented as mean \pm SD.

Conclusions: There are interesting and significant morphometric differences in the OOM of both nonaffected and clinically affected sides of patients with HFS that may reflect homeostasis disturbances due to the facial movement disorder.

CONTROL ID: 3519819

SUBMITTER (NAME ONLY): Pooyan Tirandazi

TITLE: Interim Mixed Model Analysis of an Adjustable Magnetic Levator Prosthesis for Severe Ptosis

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tirandazi, R.L. Woods, M. Nadeau, E.I. Paschalis, K. Houston, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|P. Tirandazi, R.L. Woods, M. Nadeau, E.I. Paschalis, K. Houston, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Magnetic Levator Prosthesis (MLP) is a promising non-surgical intervention for severe ptosis that employs magnets placed on the spectacles and on the upper lid. We hypothesized that magnet orientation (Figure 1) would affect Interpalpebral Fissure (IPF) between and within blinks and subject-reported comfort.

Methods: IPF was measured manually using ImageJ from 15s video recording for 5 polarity angles: 0° (poles aligned), 30°, 60°, 90°, and 180° (reverse polarity). Participants reported comfort on a 10-point scale at each rotation position while wearing the MLP. Linear mixed models included rotation position as a fixed effect and also rotation position within subject-eye as random effects (allows subjects to differ from one another).

Results: Eye opening improved for 4 of 5 rotations by 0.9 to 2.5mm ($p<0.001$). Considerable unexplained variance suggested the presence of other factors not included in the model. Comfort rating varied between some rotation positions ($p<0.001$), and higher comfort was strongly associated with more eye opening between blinks ($p<0.001$), but only weakly with closure on the blink ($p=0.05$). Comfort with impeded blink would be expected to worsen with longer wear times.

Conclusions: Our primary hypothesis was confirmed, however, there are remaining factors that affect IPF pattern across rotation angles between subjects that need to be determined. Potential factors for future study include age, physiological differences (brow height and eyelid shape), and the baseline ptosis severity. The MLP's ability to adjust the force on the eyelids is promising for severe ptosis and potentially opens the possibility for complete blink re-animation in total paralysis.

CONTROL ID: 3519831

SUBMITTER (NAME ONLY): Henri Leinonen

TITLE: A disease-modifying therapy for retinal degenerations by drug repurposing

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To test the hypothesis that dampening intracellular second-messenger signaling by a combination of approved G protein-coupled receptor-targeting drugs provides an effective therapeutic approach against retinal degenerative diseases.

Methods: We investigated a drug combination (TMB) consisting of tamsulosin and metoprolol (alpha- and beta-adrenergic antagonists, G_q - and G_s -coupled, respectively); and bromocriptine (a D2-like dopamine-receptor agonist, G_i -coupled). Longitudinal drug efficacy was tested in four distinct translationally relevant disease models: Pde6 β^{Rd10} , Rho^{P23H}, and Rpe65^{-/-} mice; and Pde6a^{-/-} dogs. The duration of the drug trials ranged from 1-week to 7-months. Drug serum levels were measured by liquid chromatography-mass spectrometry (LC-MS). We primarily used photopic and scotopic electroretinography (ERG) and optical coherence tomography (OCT) to assess drug efficacy during the chronic trials. Immunohistochemistry, Western blotting, bulk and single-cell RNA-sequencing, and proteomics were used to document therapeutic mechanisms, as well as to confirm therapeutic effects at trial termination.

Results: Dietary TMB improved rod and cone function and slowed cone degeneration in Rho^{P23H} and Pde6 β^{Rd10} mouse models of Retinitis Pigmentosa (RP). Drug efficacy was associated with decreased lipid peroxidation preceding the onset of cone degeneration in dark-reared Pde6 β^{Rd10} mice. Dietary TMB improved retinal function and optomotor tracking behavior in Rpe65^{-/-} mouse model of Leber Congenital Amaurosis type 2, but did not halt rod or cone degeneration. Seven-month-long subcutaneous sustained infusion of TMB in Pde6a^{-/-} dog model of RP led to higher cone counts at the end of the trial, and was associated with improved ERG response kinetics during the trial. LC-MS analysis showed that efficacious drug serum levels in the context of blinding diseases were generally at or below the clinically relevant concentration ranges for the drugs' original clinical indications, extrapolated from published literature. Remarkably, monotherapies with the same drugs and dosages did not alleviate disease phenotypes in Pde6 β^{Rd10} or Rpe65^{-/-} mice.

Conclusions: Our results suggest that simultaneous inhibition of G_s - and G_q -coupled receptors and activation of G_i -coupled receptors by a combination of existing drugs is a versatile option to mitigate progressive retinal degeneration caused by distinct etiologies.

CONTROL ID: 3519837

SUBMITTER (NAME ONLY): Junsang Cho

TITLE: The association between the magnitude of surgical lateral rectus weakening and subsequent inferior oblique overaction in children

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cho, University of Missouri, Columbia, Missouri, UNITED STATES|A. Lee, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|S. Culican, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|B. Wilson, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|S. Khanna, Saint Louis University School of Medicine, Saint Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inferior Oblique Over Action (IOOA) is commonly associated with congenital esotropia. However, the association of new-onset IOOA with acquired esotropia has not been studied. To explore this further, we analyzed the correlation between lateral rectus recession (LRrc) surgery and the incidence of IOOA.

Methods: A retrospective chart review from January 2010 to December 2011 studied children over two and below 18 years who had lateral rectus recession for exotropia with subsequent post-operative esotropia. Exclusion criteria included patients who had an initial history of esotropia overcorrected by surgery resulting in a consecutive exotropia, patients for whom operative notes were unavailable and magnitude of lateral rectus recession was unknown. Sixty-five patients (116 eyes) met inclusion criteria. Baseline measurements of age, sex, presence of central nervous system pathology, number of surgeries, laterality, and magnitude of recession were tested for association with IOOA. Primary outcome was the relationship between baseline measures and incidence of IOOA.

Results: Included were 116 eyes and 65 patients total. IOOA was observed in 9 eyes of 6 patients (7.8 and 9.2% respectively) and demographics were similar for those with and without IOOA ($p > 0.05$). No statistically significant relationship was found between the incidence of IOOA and laterality ($p = 0.13$), number of surgeries ($p = 0.20$), age at most recent surgical lateral rectus recession ($p = 0.49$), presence of central nervous system pathology ($p = 0.99$), or sex ($p = 0.54$). A statistically significant association was found between magnitude of LRrc and the incidence of post-operative IOOA ($p = 0.005$). The mean distance of recession was 7.3 ± 0.1 mm (mean \pm SEM) for eyes that did not develop IOOA and 8.4 ± 0.4 mm for eyes that did develop IOOA. The odds ratio for the development of IOOA given a one millimeter increase in recession was 1.76 (CI 1.19 - 2.60, $p = 0.005$). This indicates that the odds of IOOA increase 76% for each additional millimeter of recession.

Conclusions: Magnitude of surgical LRrc is positively associated with the incidence of post-operative IOOA in a dose-dependent fashion in children with consecutive esotropia. This finding may help elucidate the etiology of IOOA.

CONTROL ID: 3519847

SUBMITTER (NAME ONLY): Subam Basuthkar

TITLE: Impact of monocular contact lens wear on tear film characteristics

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Basuthkar, N. Keir, Coopervision Inc, Pleasanton, California, UNITED STATES|U. Stahl, L.W. Jones, School of Optometry, Centre for Ocular Research & Education, University of Waterloo, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: It is well known that presence of a contact lens (CL) on the ocular surface partitions the tear film (TF), disrupting its integrity. However, there is little evidence regarding the impact of one eye on the other, with respect to TF parameters during CL wear. Hence this study was conducted to evaluate the impact of monocular lens wear on TF stability, volume and lipid layer characteristics.

Methods: This was a prospective, randomized, 2-day cross-over study on 15 symptomatic (SYM) and 15 asymptomatic (ASYM) soft CL wearers. On Day 1, no CL was worn on either eye (i.e. no CL wear) and on Day 2, a -0.25DS soft CL (comfilcon A) was worn on one eye only (i.e. monocular CL wear). Assessments of non-invasive tear break up time (NIBUT, seconds), lipid layer thickness (LLT, 0-5 grading; 0=absent, 5=colored fringes) and tear meniscus height (TMH, mm) were conducted in the AM (prior to CL insertion for Day 2) and in the PM, after 8 hours.

Results: The mean age in the SYM and ASYM groups was 31 ± 11.3 yrs (12 females and 3 males), and 37 ± 14.7 yrs (8 females and 7 males), respectively. In the AM: there was no significant difference in TF parameters between eyes or between study days for either group (all $p > 0.05$).

In the PM, after 8 hours: there was no significant difference in TF parameters between eyes on Day 1 (all $p > 0.05$). Day 2 showed significantly lower NIBUT, LLT and TMH in the CL-wearing eye compared to the fellow non-CL wearing eye in both SYM and ASYM groups (all $p < 0.05$).

In the SYM group, the non-CL wearing eye on Day 2 showed longer NIBUT (mean: 7.8 ± 5.9) and better LLT (mean: 3.7 ± 0.2) compared to the same eye on Day 1 (mean NIBUT: 5.0 ± 1.5 ; mean LLT: 3.3 ± 0.7). The difference, however, did not reach statistical significance ($p = 0.07$ for NIBUT and $p = 0.16$ for LLT). TMH was similar between study days ($p = 0.98$).

In the ASYM group, NIBUT, LLT and TMH were similar for the non-CL wearing eye on Day 2 (mean NIBUT: 10.3 ± 6.9 ; LLT: 3.3 ± 1.0 ; TMH: 0.21 ± 0.1) compared to the same eye on Day 1 (mean NIBUT: 10.6 ± 6.6 ; LLT: 3.5 ± 0.9 ; TMH: 0.22 ± 0.1); all $p > 0.05$.

Conclusions: Monocular lens wear resulted in differences between eyes for NIBUT, LLT and TMH, suggesting that these TF parameters are influenced by the interaction of the TF with the CL, but not through an inter-eye interaction. In SYM CL wearers, there was a trend for the non-CL wearing eye to exhibit longer NIBUT and better LLT, potentially to counteract the effects of CL wear in the fellow eye.

CONTROL ID: 3519870

SUBMITTER (NAME ONLY): Yuko Shinohara

TITLE: In Vitro Macrophage Response to a Degradable Poly(ethylene glycol)-based hydrogel as an Artificial Vitreous Body

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Shinohara, T. Fujii, M. Nakatani, T. Ueno, Bioengineering Institute, R&D Div., Nidek Co., Ltd., JAPAN|S. Hoshi, F. Okamoto, T. Oshika, Department of Ophthalmology, Faculty of Medicine, University of Tsukuba, JAPAN|T. Sakai, Department of Bioengineering, Graduate School of Engineering, University of Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Non-swelling, biodegradable poly(ethylene glycol)-based oligo-tetra-hydrogels have shown potential as a vitreous substitute with regard to their physical properties. However, for clinical application of this technology, the host response when the material is implanted must be well understood. This study was conducted to investigate in vitro macrophage reactions to oligo-tetra-hydrogels.

Methods: A degradable oligo-tetra-hydrogel, in which the polymers contain hydrolysable bonds, and a non-degradable oligo-tetra-hydrogel were evaluated. Each type of oligo-tetra-hydrogel was incubated in phosphate-buffered saline (PBS) at 45°C for 0, 18, or 25 days. Then, mouse macrophage-like RAW264.7 cells were cultured indirectly with each prepared hydrogel, which was inserted into the culture medium on a porous membrane insert, for 48 h at 37°C. The cells were also cultured in the presence of PBS or lipopolysaccharide as a negative and positive control, respectively. Viability of the RAW264.7 cells was determined by a Cell Counting Kit-8 assay, and their TNF- α production level was quantified by enzyme-linked immunosorbent assay. Student's t-test was used for statistical analysis of the results, and statistical significance was defined as P less than 0.05.

Results: The degradable oligo-tetra-hydrogel became completely degraded in 25 days at 45°C. Thus, RAW264.7 cells were exposed to the degradation products released from the hydrogel. Neither the degradable nor the non-degradable oligo-tetra-hydrogels had any effect on viability of the RAW264.7 cells during the 48-h incubation; relative cell viability of the hydrogel groups did not differ significantly from the control (degradable, P = 0.12; n = 3; non-degradable, P = 0.20; n = 3; Student's t-test). In addition, the level of TNF- α production was not significantly increased by either degradable or non-degradable hydrogels (control = 0.9 ± 0.13 pg/ μ g protein; degradable = 1.2 ± 0.41 pg/ μ g protein, P = 0.32; n = 3; non-degradable = 1.1 ± 0.85 pg/ μ g protein, P = 0.15; n = 3; Student's t-test).

Conclusions: These results show that macrophages were not activated by oligo-tetra-hydrogel degradation products, and they suggest that oligo-tetra-hydrogels are promising candidates for use as a biocompatible artificial vitreous body.

CONTROL ID: 3519872

SUBMITTER (NAME ONLY): Nicole Eter

TITLE: Design and rationale of the YOSEMITE and RHINE trials: two phase 3 studies of faricimab in patients with diabetic macular edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Eter, University of Münster Medical Center, Münster, GERMANY|J.R. Willis, C. Quezada Ruiz, F. Abreu, H. Lin, Z. Haskova, K. Asik, Genentech Inc, South San Francisco, California, UNITED STATES|D. Silverman, J. Ives, Roche Products Ltd, Welwyn Garden City, Hertfordshire, UNITED KINGDOM|K. Basu, Roche Products Ireland Limited, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is a multifactorial disease, and best-achievable visual responses to anti-VEGF monotherapy are difficult to achieve and maintain in clinical practice. Dual inhibition of angiopoietin-2 and VEGF-A with faricimab, the first bispecific antibody designed for intraocular use, may synergistically promote vascular stability and improve outcomes in DME. Herein we describe the design and rationale of the phase 3 YOSEMITE and RHINE trials, which assessed the safety, efficacy, and durability of faricimab in patients with DME.

Methods: YOSEMITE (NCT03622580) and RHINE (NCT03622593) are identical, randomized, double-masked, active comparator-controlled, 100-week, phase 3 trials of faricimab in DME. Treatment-naïve or previously anti-VEGF-treated patients with center-involving DME were randomized 1:1:1 to faricimab 6.0 mg every 8 weeks (Q8W) after 6 initial Q4W doses; faricimab 6.0 mg per personalized treatment interval (PTI) after 4 initial Q4W doses; or aflibercept 2.0 mg Q8W after 5 initial Q4W doses. Dosing intervals in the PTI arm were determined by an automated algorithm, and could be reduced or extended by 4-week increments (from Q4W up to Q16W) according to prespecified BCVA and CST criteria at active dosing visits. The PTI algorithm is based on the treat-and-extend concept, and was designed to enable personalized therapy for DME, reduce injection frequency, and potentially optimize real-world outcomes.

Results: Safety and efficacy were assessed Q4W through week 100. To account for differences in time from last treatment and BCVA variability, the primary efficacy endpoint was mean change in BCVA from baseline averaged over weeks 48, 52, and 56. Secondary endpoints included the proportion of patients with ≥ 2 -step ETDRS-DRSS improvement at week 52, change in CST from baseline, and the proportion of patients in the PTI arm receiving Q4W, Q8W, Q12W, or Q16W dosing at 1 year. Safety outcomes included the incidence and severity of ocular and nonocular adverse events.

Conclusions: YOSEMITE and RHINE were designed to evaluate whether dual inhibition of angiopoietin-2 and VEGF-A with faricimab may improve outcomes beyond anti-VEGF monotherapy in patients with DME. The PTI arm will examine the potential for individualized faricimab therapy, tailored according to patient needs, to reduce treatment burden while maintaining efficacy.

CONTROL ID: 3519915

SUBMITTER (NAME ONLY): Shotaro Shimokawa

TITLE: Recurrence Rate of Cystoid Macular Edema with Topical Dorzolamide Treatment and its Risk Factors in Retinitis Pigmentosa

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shimokawa, Y. Murakami, K. Fujiwara, J. Funatsu, S. Nakatake, Y. Koyanagi, M. Akiyama, N. Yoshida, A. Takeda, K. Sonoda, Ophthalmology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Fukuoka, JAPAN|S. Nakatake, Ophthalmology, Faculty of Medicine, University of Oita, Yufu, Oita, JAPAN|M. Akiyama, Ocular Pathology and Imaging Science,, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Fukuoka, JAPAN|N. Yoshida, Ophthalmology, Fukuoka Dental College, Fukuoka, Fukuoka, JAPAN|Y. Ikeda, Ophthalmology, Faculty of Medicine, University of Miyazaki, Miyazaki, Miyazaki, JAPAN|

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ABSTRACT BODY:

Purpose: We previously reported that topical treatment with 1.0% topical dorzolamide was effective in 59.1% patients with cystoid macular edema secondary to retinitis pigmentosa (RP-CME). However, the rate of RP-CME recurrence during follow-up have not been fully characterized. The purpose of this study is to investigate the recurrence rate of RP-CME after an initiation of topical dorzolamide and its risk factors.

Methods: We retrospectively reviewed the data of RP patients who was diagnosed as having RP-CME and treated with topical 1.0% dorzolamide 3 times a day from the electronic medical records. Patients who showed a treatment response to topical 1.0% dorzolamide, defined as the resolution of foveal cysts or >20% reduction of central subfield thickness (CST) from baseline in optical coherence tomography (OCT), were included in this study. The day of treatment initiation was set as the baseline and topical dorzolamide treatment was continued during follow-up. At each follow-up visit, the recurrence of RP-CME (defined as a reappearance of foveal cyst; >20% increase in CST compared to previous visit; or CST exceeding baseline) was evaluated. Risk factors for the recurrence were analyzed by Cox proportional hazards modeling. Kaplan-Meier survival analysis was used to evaluate the time to recurrent RP-CME.

Results: 40 RP-CME patients showed a treatment response to topical 1.0% dorzolamide.

During the mean 3.9-yr follow-up, 21 patients showed recurrent RP-CME. The recurrence rate of RP-CME was 20.2% at 1 year increasing to 46.3% and 57.8% at 3 and 5 years, respectively. High baseline central subfield thickness was significantly associated with recurrent RP-CME (hazard ratio [HR], 1.09 per 10 μ m increase; 95%CI, 1.03–1.14; $p=0.001$).

Conclusions: The recurrence rate of RP-CME increases during the follow-up periods. High baseline CST was a risk factor of recurrent RP-CME.

CONTROL ID: 3519926

SUBMITTER (NAME ONLY): Kenichiro Mori

TITLE: Downregulation of TNFRSF10A promotes RPE cell death via PKC deactivation

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mori, K. Ishikawa, I. Wada, Y. Kubo, T. Nakama, M. Akiyama, M. Arima, S. Notomi, Y. Murakami, S. Nakao, K. Sonoda, Ophthalmology, Kyushu University, Graduate School of Medical Sciences, Fukuoka, JAPAN|M. Akiyama, Ocular Pathology and Imaging Science, Kyushu University Graduate School of Medical Sciences, Fukuoka, JAPAN|T. Hisatomi, Ophthalmology, Fukuoka University Chikushi Hospital, Chikushi, JAPAN|S. Yoshida, Ophthalmology, Kurume University School of Medicine, Kurume, JAPAN|

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ABSTRACT BODY:

Purpose: We previously reported that downregulation of TNFRSF10A, a susceptibility gene for age-related macular degeneration (AMD) and central serous chorioretinopathy (CSC), can cause retinal pigment epithelium (RPE) cell death in vitro and Tnfrsf10knockout mice. In this study, we investigated the molecular mechanism of RPE cell death associated with TNFRSF10A downregulation.

Methods: All in vitro experiments were performed using primary fetal human RPE (hRPE) cells. After transfection with siRNA targeting TNFRSF10A, we treated the cells with or without different cell death inhibitors or phorbol 12-myristate 13-acetate (PMA), a PKC activator, and cell viability change were evaluated by Cell Counting Kit-8 and staining with FITC-conjugated annexin V/PI followed by flow cytometric analysis. Realtime RT-PCR was performed to examine the transcriptional levels of cell cycle regulatory proteins in the cells.

Results: Knockdown of TNFRSF10A by siRNA significantly reduced RPE cell viability and increased the percentages of annexin V+/PI- early apoptotic cells ($P<0.0001$). PMA inhibit the cell death induced by TNFRSF10A knockdown, while apoptosis inhibitors, a necroptosis inhibitor, a ferroptosis inhibitor and a pyroptosis inhibitor did not. TNFRSF10A knockdown changed mRNA levels of cell cycle regulatory proteins, downregulation of cyclinA1 ($P<0.05$) and upregulation of p27 ($P<0.005$), which were reversed by PMA treatment.

Conclusions: TNFRSF10A downregulation may contribute to the pathogenesis of AMD and CSC by promoting RPE cell death via PKC pathway.

CONTROL ID: 3519930

SUBMITTER (NAME ONLY): Alexander Rusakevich

TITLE: Research funding, income, and career satisfaction among clinician-scientists in ophthalmology in the United States

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Characterization of clinician-scientists and identification of success predictors may help to develop grant policies that maintain the viability of this career pathway in ophthalmology. The current survey study analyzed responses from a cohort of clinician-scientists in ophthalmology and identified factors associated with successful research funding, income, and career satisfaction.

Methods: A cross-sectional survey study of clinician-scientists in ophthalmology at U.S. academic institutions conducted between April 17 and May 19, 2019. Collected information include 1) demographic data, 2) amount, type, and source of startup funding, first extramural grant, and first R01-equivalent independent grant, 3) starting and current salaries, and 4) Likert-scale measures of career satisfaction. Multivariate regression analyses were used to evaluate factors associated with time to receiving R01-equivalent independent funding, salary, and career satisfaction measures.

Results: 98 clinician-scientists in ophthalmology were surveyed across different ages (mean 48±11 years), research categories, institutional types, geographic regions, and academic ranks. Median startup funding was \$50-99k, and median starting salary was \$150-199k. Most investigators (67%) received their first extramural award from the National Eye Institute mostly through K-award mechanisms (82%). The median time to receiving their first independent grant was 8 years, mostly through an R01 award (70%). Greater institutional startup support ($P = 0.048$) and earlier extramural grant success ($P = 0.035$) were associated with earlier independent funding. Male gender ($P = 0.038$) and MD degree ($P = 0.039$) were associated with higher current salaries, but not starting salaries. Overall career satisfaction increased with career duration ($P = 0.003$), but not with earlier independent funding ($P = 0.533$) or higher income ($P = 0.403$).

Conclusions: Success in research funding by clinician-scientists in ophthalmology may be linked to institutional support and earlier acquisition of extramural grants, but does not impact academic salaries. Nevertheless, career satisfaction among clinician-scientists improves with time, with little impact from research or financial success.

CONTROL ID: 3519937

SUBMITTER (NAME ONLY): Siggi Trier

TITLE: Corneal cystine crystal deposition: Online medical education can significantly improve knowledge, competence and confidence diagnosing and treating ocular manifestations of nephrotic cystinosis

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Trier, P. Aboulsaoud, J. Maeglin, Education, Medscape LLC, New York, New York, UNITED STATES|R.J. Bishop, (contractor), National Eye Institute, Bethesda, Maryland, UNITED STATES|P.C. Grimm, Department of Pediatric Nephrology, Lucile Packard Children's Hospital, Stanford University School of Medicine, Stanford, California, UNITED STATES|S. Cherqui, Division of Genetics, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if online medical education for ophthalmologists (Opht) could improve their knowledge, competence and confidence to diagnose and treat children with ocular manifestations of nephrotic cystinosis

Methods: Participants completed a 3-item questionnaire plus a confidence assessment before and after watching a 30-minute multispeciality expert roundtable discussion with accompanying slides. A matched pair design was used pre-/post-assessment, with scores compared to assess changes in the proportion of correct responses. A chi-squared test assessed statistical significance at the $P < .05$ level. Launch Jun 18, 2020; data through Aug 8, 2020. Assessment completers: 239

Results: An average of 44% of Opht responses on pre-assessment were correct, increasing to 66% on post-assessment ($p < .001$). The activity significantly increased knowledge of ocular manifestations of nephrotic cystinosis in children, including molecular genetics aspects (pre: 28%, post: 47%, $p < .001$). Diagnostic competence improved, measured in choosing the best diagnostic approach to examine cystine crystal deposition in an applied patient case (pre: 70%, post: 84% $p < .001$). Treatment competence increased for therapy and application choice for the same case, choosing topical cysteamine eye drops over a systemic dose increase, anti-inflammatory or antibiotic topical treatment (pre: 32%, post: 68%, $p < .001$). 54% of Opht had a measurable increase in confidence in their ability to treat ocular manifestations of cystinosis.

Conclusions: Nephrotic cystinosis is a rare inherited disease, diagnosis and specific treatment are frequently delayed with a significant impact on overall prognosis. Corneal cystine deposition is visible by slit lamp biomicroscopy and can lead to photophobia, blepharospasm, superficial punctate keratopathy and recurrent corneal erosions. To deplete deposition additional topical cysteamine treatment is required to reach the avascular cornea. Online medical education in the form of an multispeciality expert roundtable discussion with accompanying slides can significantly improve rare disease knowledge and diagnostic, and therapeutic competence and confidence. Additional education is warranted to shorten time to diagnosis for ocular manifestations of nephrotic cystinosis and share data for emerging therapies.

CONTROL ID: 3519968

SUBMITTER (NAME ONLY): Sebastian Wolf

TITLE: Neovascular age-related macular degeneration (nAMD) treated with intravitreal aflibercept (IVT-AFL) treat-and-extend (T&E): post-hoc analysis of injection intensive (I-I) requirement for patients in the ARIES study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Wolf, Reading Centre and Department for Ophthalmology, Inselspital, University of Bern, SWITZERLAND|F.G. Holz, Department of Ophthalmology, University of Bonn, GERMANY|P. Hykin, Ophthalmology, Moorfields Eye Hospital, UNITED KINGDOM|E. Midena, Department of Ophthalmology, University of Padova, ITALY|E.H. Souied, Department d'Ophthalmologie, Hopital Intercommunal de Creteil, FRANCE|G. Lambrou, Bayer Consumer Care AG, Basel, SWITZERLAND|T. Machewitz, Bayer AG, Berlin, GERMANY|H. Allmeier, Bayer Consumer Care AG, Basel, SWITZERLAND|P. Mitchell, University of Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To assess vision and anatomic outcomes in patients with nAMD and the requirement for IVT-AFL treatment more frequently than every 8 weeks (w).

Methods: ARIES (NCT02581891) was a multicenter, randomized, Phase 3b/4 study that compared the efficacy of 2 IVT-AFL T&E regimens over 2 years (Y) in treatment-naïve nAMD patients. Patients were determined as I-I if the study investigator identified need for treatment more frequently than every 8w and if patients had ≥ 1 treatment interval of 4 or 6w after 3 initial monthly doses. This was a post-hoc analysis of patients enrolled in ARIES and statistical analysis is descriptive.

Results: The full analysis set comprised 269 patients (treatment arms combined). Overall, 23.0% (n=62) of patients were determined as I-I; 13.8% (n=37) in Y1 and 9.3% (n=25) in Y2. There were no relevant differences in baseline characteristics between I-I and non-I-I patients. Time from IVT-AFL initiation to the visit where patients were determined I-I varied considerably (range: 16–100w; median: 43.2w). Mean treatment interval was 8.4w before patients were determined as I-I and 6.1w following I-I determination. Mean (SD) best-corrected visual acuity (BCVA) was lower and central retinal thickness (CRT) was higher in I-I patients at the visit when they were determined I-I compared with w16 (BCVA: 61.9 [16.7] vs 65.7 [12.6] letters; CRT: 410.7 [112.3] vs 379.0 [112.6] μm). With treatment more frequent than every 8w, these patients showed BCVA (62.6 [18.7] letters) and CRT (336.8 [101.0] μm) improvements at w104. Improvements in vision from baseline (BL) to w104 were smaller for I-I patients than non-I-I

patients (+2.3 [15.6] vs +5.9 [12.3] letters). Anatomic outcomes at w104 were similar between I-I and non-I-I patients (CRT change from BL: -160.4 [154.0] μm and -167.0 [136.1] μm). Overall, 59.7% of patients achieved treatment intervals of $\geq 8\text{w}$ following I-I determination.

Conclusions: The need for IVT-AFL treatment more frequently than every 8w may arise at various points over the course of nAMD treatment. Up to 1 in 4 patients may require more intensive treatment than every 8w. These patients showed improvements in vision and anatomic outcomes. For most, treatment intervals could be extended to $\geq 8\text{w}$ following I-I determination.

CONTROL ID: 3519976

SUBMITTER (NAME ONLY): Kristie Hing Chi Leung

TITLE: Retinal Vascular Changes are associated with PET-based Biomarkers of Alzheimer's Disease

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Leung, UCL Medical School, University College London, London, London, UNITED KINGDOM|V. Chan, C. Cheung, Department of Ophthalmology and Visual Sciences (DOVS), The Chinese University of Hong Kong, Hong Kong, HONG KONG|V. Mok, Department of Medicine and Therapeutics, Division of Neurology, The Chinese University of Hong Kong, Hong Kong, HONG KONG|

Commercial Relationships Disclosure (Abstract): Kristie Hing Chi Leung: Commercial Relationship: Code N (No Commercial Relationship) | Victor T. T. Chan: Commercial Relationship: Code N (No Commercial Relationship) | Vincent Mok: Commercial Relationship: Code N (No Commercial Relationship) | Carol Y. Cheung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The retina is a non-invasive channel for assessing changes in brain microvasculature, which has been implicated in the pathophysiology of Alzheimer's disease (AD). Previous studies revealed significant relationship between clinically diagnosed AD and retinal vasculature. However, clinical diagnosis has limited sensitivity and specificity, and those analyses were conducted from a limited view of the fundus. This cross-sectional study aims to determine changes in vasculature from a larger area of the retina between subjects with Positron Emission Tomography (PET) biomarker-confirmed AD compared to controls.

Methods: Participants were recruited from the community and Cognitive Disorder Clinic of Prince of Wales Hospital, Hong Kong. All subjects received ^{11}C -Pittsburgh compound B (PIB) and ^{18}F -T807 intravenously 35- and 85-minutes before PET scan, respectively. Uptake was quantified by global cortical to cerebellum Standard Uptake Value Ratio (SUVR). Significant amyloid beta ($\text{A}\beta$) burden was defined as increased PIB uptake in regions historically known to have $\text{A}\beta$ deposits in AD patients or $\text{SUVR} \geq 1.42$. Significant tau level was defined as increased ^{18}F -T807 uptake in regions previously known to have tau deposits in AD patients or $\text{SUVR} \geq 1.14$. Retinal imaging was performed with ultra-wide field scanning laser ophthalmoscopy (UWF-SLO). The retinal vasculature was analysed and quantified using semi-automated Singapore I Vessel Assessment (SIVA) software. Independent t-test and multivariable logistic regression analyses were performed to determine cross-sectional relationship of retinal vessel parameters with presence of cerebral $\text{A}\beta$ and Tau, adjusted for age, gender and systolic blood pressure.

Results: Out of the 39 patients, 20 were found to have significant cerebral level of either $\text{A}\beta$ or Tau on PET. Individuals with radiologically confirmed AD (i.e. A+ T+) showed significantly smaller arteriolar fractal dimension (1.32 v 1.38, $p=0.006$), compared with controls (i.e. A- T-). Presence of significant $\text{A}\beta$ and Tau burden was correlated with lower arteriolar fractal dimensions (odds ratio [OR] per SD decrease 0.26 [95% CI 0.09-0.78] $p=0.02$), which was not seen in controls.

Conclusions: Reduction of fractal dimension in retinal arterioles observed in UWF imaging are associated with cerebral PET $\text{A}\beta$ and Tau burden. Our results support that retinal imaging can indicate microvascular alterations related to AD.

CONTROL ID: 3520030

SUBMITTER (NAME ONLY): Andrea Unser

TITLE: Examining the Effects of Glaucoma Medications on the Trabecular Outflow Pathway Using Glauconix Bioscience's 3D-HTM™ Tissue Constructs

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Unser, F. Ahmed, H. Afzaal, H. Williams, K.Y. Torrejon, Glauconix Biosciences, Albany, New York, UNITED STATES|H. Afzaal, SUNY Polytechnic Institute, Albany, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Commonly prescribed glaucoma medications decrease the production of aqueous humor (β -blockers such as timolol) or increase the outflow of aqueous humor (Prostaglandin analogs such as latanoprost and bimatoprost) or both (alpha agonists such as brimonidine). With the exception of bimatoprost, each class of medication focuses mainly on facilitating uveoscleral outflow. This study further explores the effects of these medications on 3D- HTM tissue constructs that mimic the human trabecular outflow pathway, which is responsible for most of the aqueous humor drainage and shown to be affected in glaucoma patients.

Methods: Bioengineered human trabecular meshwork (3D-HTM™) tissue constructs were cultured to confluence, treated with TGFb-2 (5 ng/mL) for 6 days to induce a glaucomatous-like state. These diseased constructs were then exposed to 10mM brimonidine, bimatoprost, timolol, and latanoprost for 3 days. The responsiveness of these molecules under flow was investigated by perfusion studies using a 24-multichannel microfluidic system that constantly monitors pressure across the tissue constructs (N>4 per donor). The “outflow facility” was determined by the ratio of $\Delta(\text{flow rate})/\Delta(\text{pressure})$. An increase in outflow facility is correlated to a decrease in IOP.

Results: Of the four compounds studied, three of them significantly increased outflow facility in the following order: bimatoprost (*P<0.05) < latanoprost (**P<0.01) < timolol (****P<0.0001). Brimonidine did not significantly affect outflow facility in this model.

Conclusions: We report here that commonly prescribed eye drops including bimatoprost, latanoprost and timolol significantly increased outflow facility of glaucomatous 3D-HTM™; thereby indicating an alternative mechanism of action for these compounds through the trabecular meshwork. Further studies are currently ongoing to better understand how these treatments are affecting the trabecular meshwork.

CONTROL ID: 3520066

SUBMITTER (NAME ONLY): Yongsu Kwon

TITLE: Ceria-coated melanin as a novel antioxidant for age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kwon, M. Zheng, Z. Han, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yongsu Kwon: Commercial Relationship: Code N (No Commercial Relationship) | Min Zheng: Commercial Relationship: Code N (No Commercial Relationship) | Zongchao Han: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Excessive oxidative stress leads to nonspecific inflammation and is a major cause of pathogenesis of both wet and dry forms of age-related macular degeneration (AMD). Melanin is naturally present in pigmented tissues, such as the retinal pigment epithelium (RPE) in eyes, and has a strong ability to scavenge a broad range of free radicals. By combining melanin with nanoceria to take advantage of nanoceria's auto-regenerative antioxidant property, we have developed a novel nanoceria-coated melanin antioxidant (CCM) which can potentially achieve long-term effects through a single-dose administration and relieve pathological damages for AMD.

Methods: We introduced ceria nanoparticle on the melanin matrix for its auto-regenerative activity and demonstrated the size, shape, charge, and elemental composition through analytic methods, including TEM, DLS, and EDS. We investigated antioxidant and free radical scavenging by using DPPH, Evans blue bleaching, and Amplex red assays. Furthermore, we evaluated the cell cytotoxicity and antioxidative properties of melanin and CCM in vitro using a H_2O_2 -induced oxidative stress in mouse primary RPE cells (mRPE) through various biological experimental techniques.

Results: Melanin and CCM were characterized by different physicochemical techniques. The TEM of melanin was shown uniform nanospheres with an average diameter of ~100 nm. Cerium ions were effectively chelated with catechol groups in melanin matrices and grown to cerium oxide (~5 nm scale), which was clearly shown on the surface of melanin matrix through elemental mapping images. Notably, CCM was explored as highly water stable over 9 months (last time checked) at room temperature. Compared with melanin, CCM showed enhanced antioxidant activities with auto-regenerative properties against the deleterious effects of a broad range of reactive oxygen and nitrogen species (RONS). Furthermore, the cell viability toward the mRPE cells was above 80 % after 48 hours exposure of melanin or CCM, indicating that they are safe and well tolerated.

Conclusions: CCM can protect mRPE cells not only from chemically induced oxidative stress by scavenging a broad range of RONS molecules, but also has the ability to continually scavenge free radicals, owing to the added auto-regenerative property. The newly developed CCM is biocompatible and can be used as a robust antioxidant to attenuate pathological damages in AMD.

CONTROL ID: 3520071

SUBMITTER (NAME ONLY): Pablo Argueso

TITLE: CD147 contributes to maintain a nonkeratinized squamous epithelium in cornea

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Argueso, A.M. Woodward, M.N. Feeley, J. Rinaldi, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The presence of a non-keratinized stratified squamous epithelium protects organs that are in close contact with the external environment and regularly exposed to physical abrasion. Here we investigated the contribution of CD147 to promoting the differentiation and establishment of barrier function in human corneal epithelial cells.

Methods: CRISPR/Cas9-mediated gene editing was used to produce a human corneal epithelial cell line lacking CD147 expression. Transmission and scanning electron microscopy were used to investigate the ultrastructure of differentiated cell cultures. Protein biosynthesis and localization were determined by immunoblotting and immunofluorescence, respectively. The analysis of genes encoding for tight junction proteins was carried out using a human tight junction PCR array. Epithelial cell permeability was evaluated by transepithelial electrical resistance and rose bengal penetrance.

Results: Cell cultures lacking CD147 change shape and fail to produce a flattened squamous layer on the apical surface. This process is associated with the decreased biosynthesis of MUC16 and involucrin. Expression analysis of genes encoding tight junction proteins indicates that CD147 promotes the physiological expression of occludin and members of the claudin family. Functionally, disruption of CD147 expression leads to increased epithelial cell permeability as evidenced by the decrease in transepithelial electrical resistance and increase in rose bengal flux.

Conclusions: CD147 plays a distinctive role in maintaining the normal differentiation of stratified squamous corneal epithelium under homeostatic conditions.

CONTROL ID: 3520078

SUBMITTER (NAME ONLY): Terence Tyson

TITLE: Saccade-Pursuit coordination during ocular tracking across different impairment sources

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.L. Tyson, E.E. Flynn-Evans, L.S. Stone, Human Systems Integration Division, NASA Ames Research Center, Moffett Field, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Terence Tyson: Commercial Relationship: Code N (No Commercial Relationship) | Erin Flynn-Evans: Commercial Relationship: Code N (No Commercial Relationship) | Leland Stone: Commercial Relationship(s);NASA-held US patents Nos 9,730,582/10,420,465/10,463,249 awarded 8/2017, 9/2019, and 10/2019, respectively, but author has no direct role in any commercialization.:Code P (Patent)

ABSTRACT BODY:

Purpose: Sleep loss (Stone et al., 2019, doi: 10.1113/JP277779) and alcohol (Tyson et al., 2020, doi: 10.1113/JP280395) have been shown to impair smooth pursuit and its underlying visual motion processing in humans. This study examines the saccadic compensation for this poor pursuit.

Methods: Using an established behavioral ocular-tracking paradigm (Liston & Stone, 2014, doi: 10.1167/14.14.12), we examined the dose-response of ground lost (pursuit deficit integrated across our 300-ms steady-state tracking interval) and ground gained (increased saccadic response harnessed to compensate) across three separate studies – acute low-dose alcohol administration (LDA; n = 16 subjects), acute sleep loss (ASL; n = 12), and chronic sleep restriction (CSR; n = 12). We computed dose-responses as the linear regression slopes of ground lost and gained across treatment dose (% blood alcohol concentration [BAC] or hours awake). For the CSR study, we computed the mean effect for a single dose (5-hours nightly sleep for 1 week).

Results: For LDA, there was significantly increased ground lost ($P < 0.001$) and gained ($P < 0.001$) with increased %BAC. In addition, the dose-responses were not significantly different ($P = 0.35$), indicating effectively complete saccadic compensation due to significant increases in both saccadic rate ($P < 0.05$) and amplitude ($P < 0.001$). For ASL, there was significantly increased ground lost with time awake ($P < 0.01$), however ground gained was significantly lower ($P < 0.001$), indicating, at best, incomplete compensation due to a significant increase in saccadic rate ($P < 0.001$) but not amplitude ($P = 0.10$). With CSR, pursuit was again significantly impaired ($P < 0.05$), with saccadic rate significantly increased ($P < 0.05$) but, surprisingly, amplitude was significantly decreased ($P < 0.05$), effectively eliminating ground gained ($P = 0.90$).

Conclusions: Our analyses show that LDA, ASL, and CSR affect tracking differently, suggesting the involvement of different brain pathways. With LDA, the effect appears largely due to the cortical impairment of visual motion processing with largely healthy brainstem and mid-brain responses (driving effective saccadic compensation). ASL and CSR however appear to affect both cortical and sub-cortical pathways, with at best partial saccadic compensation. Lastly, CSR is associated with an additional compromise due to a maladaptive decrease in saccade amplitude.

CONTROL ID: 3520124

SUBMITTER (NAME ONLY): Zhengyang Liu

TITLE: Symmetry Between Left and Right Eyes in Bietti Crystalline Dystrophy

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Liu, L.N. Ayton, F. O'Hare, J. Arslan, M. Hu, J. Wang, D.G. Hickey, M. McGuinness, T.L. Edwards, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|L.N. Ayton, F. O'Hare, Departments of Optometry and Vision Sciences, and Surgery (Ophthalmology), The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|Z. Liu, J. Arslan, M. Hu, J. Wang, T.L. Edwards, Department of Surgery (Ophthalmology), The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|D.G. Hickey, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|M. McGuinness, The University of Melbourne School of Population and Global Health, Melbourne, Victoria, AUSTRALIA|A.L. Vincent, Eye Department, Greenlane Clinical Centre, Auckland, NEW ZEALAND|A.L. Vincent, Department of Ophthalmology, The University of Auckland New Zealand National Eye Centre, Auckland, Auckland, NEW ZEALAND|F.K. Chen, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|F.K. Chen, Department of Ophthalmology, Royal Perth Hospital, Perth, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Due to scarcity of eligible participants, treatment trials for rare inherited retinal diseases often employ the contralateral eye as an internal control. However, for people with Bietti Crystalline Dystrophy (BCD), there is uncertainty as to whether disease extent and course in one eye reflects that in the other. Therefore, we performed an observational clinical study with prospective and retrospective data aimed at evaluating the inter-eye symmetry of anatomical features and functional vision in individuals with BCD, with a focus on the number, area, and distribution of the characteristic retinal crystalline deposits.

Methods: Thirteen Australian and New Zealand participants with confirmed biallelic CYP4V2 mutations and a characteristic BCD fundus appearance underwent comprehensive multimodal clinical examination. Crystals visible on color fundus photography were manually counted and superimposed onto aligned fundus autofluorescence imaging. The distribution of fundus crystals and their phenotypic associations with areas of absent autofluorescence (absent-AF) were then analyzed. Spearman's correlation coefficients (ρ), intraclass correlation coefficients (ICCs), and Bland-Altman plots were used to quantify symmetry of functional and imaging parameters between eyes.

Results: Median participant age was 48 years, interquartile range 40–60 years. Nine (69%) were female, and five (38%) were of East Asian descent. Distance visual acuity ranged from 20/16 to light perception. Crystal density was higher in the foveal region, and decreased in the periphery. The peripapillary region and areas of well-demarcated absent-AF contained few crystals. Inter-eye correlation was high for fundus crystal area ($\rho=1.00$, 95% CI 1.00–1.00; ICC=0.97, 95% CI 0.88–0.99), fundus crystal count ($\rho=0.98$, 95% CI 0.92–1.00; ICC=0.97, 95% CI 0.89–0.99), and absent-AF area ($\rho=0.88$, 95% CI 0.53–0.98; ICC=0.98, 95% CI 0.90–0.99). Average foveal volume was moderately correlated between eyes ($\rho=0.73$, 95% CI 0.18–0.93; ICC=0.85, 95% CI 0.53–0.96). No significant correlation was found for foveal crystal count and area, average or central foveal thickness, best corrected visual acuity, and average macular or central foveal sensitivity.

Conclusions: This study demonstrated strong inter-eye symmetry measured by fundus crystal area, fundus crystal number, and absent-AF area. This data may influence the choice of outcome measures of future therapeutic trials for BCD.

CONTROL ID: 3520134

SUBMITTER (NAME ONLY): Hisataka Fujimoto

TITLE: Novel tear film dynamics underlying silicone hydrogel soft contact lens use

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Fujimoto, A. Masuda, M. Yumi, J. Kiryu, Kawasaki Ika Daigaku, Kurashiki, Okayama, JAPAN|S. Ochi, Y. Inoue, Inoue Eye Clinic, Tamano, Okayama, JAPAN|T. Yamashita, Kawasaki Ika Daigaku Fuzoku Byoin, Kurashiki, Okayama, JAPAN|

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ABSTRACT BODY:

Purpose: Tear film dynamics with soft contact lens (SCL) use remains poorly understood. Herein, we report a novel phenomenon wherein a portion of the silicone hydrogel (SH) SCL causes tears to move from the peripheral area to the center of the posterior SCL surface after an eye blink.

Methods: 100 eyes of 50 regular SH SCL users [Dailies Total 1 (DT1), Alcon and One-Day Acuvue-True-Eye (TE), Johnson & Johnson; 10 men, 40 women; average age, 33.41 years old] were analyzed with Video Placido topography Keratograph 5M (Oculus) and DR-1 α tear interferometer (Kowa, Japan). At visit 1 (v1), measurements were performed for the bare eye and for the eye with SCL in place after 15 min. At visit 2 (v2), which was scheduled 30 \pm 5 days after v1, measurements were performed after the SCL had been in place for a minimum of 5 h.

Results: In TE, thin aqueous layer break (TALB) which is unusual tear film break-up pattern in normal eyes was seen in 87% in v1 and 67% in v2 with DR-1 α . In eyes with TALB, Keratograph 5M detected no tear change in front of the SCL. Furthermore, in 72% of eyes with TALB, the brightness of the Placido ring on Keratograph 5M gradually increased from the periphery toward the center in the absence of tears on the SCL at least 6 seconds after eye blink. This finding captures the phenomenon of tear movement from the edge of SCL toward the center of the posterior SCL surface. In DT1, TALB was seen in 18% in v1 and 12% in v2. In bare eyes, TALB was not observed (0%).

Conclusions: This is the first study on tear film dynamics on the posterior surface of SCLs. Water gradient structure used in DT1 was useful for reducing TALB.

CONTROL ID: 3520139

SUBMITTER (NAME ONLY): Ayako Okita

TITLE: The role of oxidative DNA damage and response in NMDA-induced retinal ganglion cell death

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ikeda, Miyazaki Daigaku, Miyazaki, Miyazaki, JAPAN|A. Okita, Y. Murakami, S. Shimokawa, Y. Nakabeppu, K. Sonoda, Kyushu Daigaku, Fukuoka, Fukuoka, JAPAN|

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ABSTRACT BODY:

Purpose: Oxidative stress has been implicated in the pathophysiology of glaucoma; however, the biological mechanisms by which oxidative damage causes retinal ganglion cell (RGC) death remain to be elucidated. We previously reported that oxidative DNA damage triggers microglial activation and retinal degeneration via the activation of MutY Homolog (MUTYH), a DNA damage-associated glycosylase, in experimental retinitis pigmentosa. In the present study, we investigate the role of MUTYH in RGC cell death induced by N-methyl-D-aspartate (NMDA).

Methods: Mutyh^{-/-} mice and age-matched wild-type (WT) mice was employed in a model of NMDA-induced retinal excitotoxicity. Eight nM NMDA was intravitreally injected in the mouse eyes. Immunohistochemical analysis was performed using anti-8-hydroxy-deoxyguanosine (8-oxoG) monoclonal antibody (a marker of oxidative DNA damage), anti-Brn3a antibody (a marker of RGC), anti-Iba-1 antibody (a marker of microglia), and anti-ssDNA antibody [a marker of single strand breaks (SSBs)] at 24 hours and 7 days after injection.

Results: Substantial microgliosis and RGC loss were observed in the eyes of NMDA-injected WT mice. In contrast, Mutyh deficiency significantly reduced the density of microglia (P = 0.0152) and attenuated the RGC loss (P = 0.0021). Moreover, 8-oxoG was accumulated within the nucleus of microglia after 24 hours to 7 days and SSBs were developed in WT mice. In contrast, Mutyh deficiency prevented SSBs formation following NMDA-induced oxidative DNA damage.

Conclusions: MUTYH activation associated with oxidative DNA damage accelerates microgliosis and RGC cell death in NMDA-induced retinal excitotoxicity.

CONTROL ID: 3520142

SUBMITTER (NAME ONLY): Xiaoyin Zhou

TITLE: Risk factors associated with recurrence of CSC: a multicenter retrospective study

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhou, Y. Komuku, T. Araki, F. Gomi, Ophthalmology, Hyogo Ika Daigaku, Nishinomiya, Hyogo, JAPAN|K. Hozumi, Sumitomo Hospital, JAPAN|H. Terasaki, Kagoshima Daigaku, Kagoshima, Kagoshima, JAPAN|A. Miki, Kobe Daigaku, Kobe, Hyogo, JAPAN|S. Kuwayama, Nagoya Shiritsu Daigaku Daigakuin Igaku Kenkyuka Igakubu Gankagaku, Nagoya, Aichi, JAPAN|M. Niki, Tokushima Daigaku, Tokushima, Tokushima, JAPAN|H. Matsubara, Mie Daigaku, Tsu, Mie, JAPAN|T. Kinoshita, Shiritsu Sapporo Byoin, Sapporo, Hokkaido, JAPAN|T. Nishi, Nara Kenritsu Ika Daigaku, Kashihara, Nara, JAPAN|

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ABSTRACT BODY:

Purpose: We conducted a multicenter retrospective study to investigate potential risk factors for recurrence in patients with central serous chorioretinopathy (CSC).

Methods: The study was performed at 8 medical institutions from 2008 to 2020 in Japan on patients who had experienced an active episode of CSC. Exclusion criteria included indications of choroidal neovascularization (CNV), polypoidal choroidal vasculopathy (PCV), and any other ophthalmology related disease. Demographic data and medical history, including age, gender, best corrected visual acuity (BCVA), spherical equivalent, fellow-eye status, history of corticosteroid use or smoking, frequency of recurrence, and treatment choices were noted. In addition, significant differences in central retinal thickness, subfoveal choroidal thickness, chronic manifestation, numbers of leakage points, leakage intensity (intense/subtle), leakage sites in the inner or outer foveal avascular zone (FAZ), and choroidal hyperpermeability were analyzed as between recurrence and non-recurrence groups.

Results: Six hundred forty (640) of 699 patients with CSC (700 eyes; 478 males, 162 females; mean age 52.7 ± 12.1 years) were enrolled by application of the exclusion and inclusion criteria. Among these 640 patients, 323 (50.5%) presented ≥ 1 recurrence. The average time to the first recurrence was 35.8 ± 45.8 months (range 1-360 months), and the mean frequency of recurrence was 1.16 ± 0.50 .

There were no statistically significant differences in age or gender distribution, smoking history, BCVA at baseline and final visit, spherical equivalent, central retinal thickness, leakage site, or subfoveal choroidal thickness between the recurrence and non-recurrence groups. Nevertheless, history of corticosteroid use ($P = 0.0003$), bilateral CSC ($P < 0.0001$), non-therapy ($P < 0.0001$), chronic performance on FAF ($P < 0.0001$), ≥ 2 leakage points ($P = 0.0014$), and subtle fluorescein leakage ($P = 0.0309$) were significantly related to an increased risk of recurrence.

Conclusions: Knowledge of these data and multiple risk factors serving as predictors might aid in early detection or intensive treatment for patients with CSC at high risk of recurrence.

CONTROL ID: 3520149

SUBMITTER (NAME ONLY): Yuki Komuku

TITLE: Difference in characteristics of central serous chorioretinopathy with and without choroidal neovascularization on OCT angiography

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Komuku, X. Zhou, T. Araki, F. Gomi, Ophthalmology, Hyogo Ika Daigaku, Nishinomiya, Hyogo, JAPAN|Y. Komuku, X. Zhou, T. Araki, H. Terasaki, A. Miki, S. Kuwayama, T. Nishi, T. Kinoshita, F. Gomi, JCREST (Japan Clinical Retina Study) group, Kagoshima, Kagoshima, JAPAN|A. Miki, Kobe Daigaku, Kobe, Hyogo, JAPAN|H. Terasaki, Ophthalmology, Kagoshima Daigaku, Kagoshima, Kagoshima, JAPAN|S. Kuwayama, Ophthalmology, Nagoya Shiritsu Daigaku Daigakuin Igaku Kenkyuka Igakubu, Nagoya, Aichi, JAPAN|T. Nishi, Ophthalmology, Nara Kenritsu Ika Daigaku, Kashihara, Nara, JAPAN|T. Kinoshita, Ophthalmology, Shiritsu Sapporo Byoin, Sapporo, Hokkaido, JAPAN|

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ABSTRACT BODY:

Purpose: To compare the characteristics of central serous chorioretinopathy (CSC) with and without choroidal neovascularization (CNV) at final visit on optical coherence tomography angiography (OCTA) at multiple centers.

Methods: The subjects were 292 eyes of 264 patients (188males, 76 females, 52.0 ± 11.8 years) who were diagnosed with CSC at 6 JCREST participating institutions from 2016 through 2019 and underwent OCTA at the first and final visits. We excluded patients with CNV at first visits. On the basis of clinical assessment by OCTA detection of the presence of CNV at final visit, patients with CSC were divided into two groups (CNV group and non-CNV group).

We examined gender, age, spherical equivalent, best corrected visual acuity (BCVA), subfoveal retinal thickness, choroidal thickness, the presence or absence of recurrence during the course, and whether patients were acute or chronic CSC. Recurrence was defined as the emergence of new subretinal fluid following complete regression of the previous CSC episode. Acute CSC was characterized as the presence of visual symptoms for less than 6 months.

Results: During the three-year follow-up, secondary CNV at final visit was presented in 21 eyes (7.2%) based on the OCTA, whereas 271 eyes (92.8%) in non-CNV group. CNV group appeared worse visual acuity at final visit and older age, which were significantly different from the non-CNV group ($P = 0.002$, $P = 0.033$, respectively). In addition, 13 eyes (61.9%) was regarded as chronic CSC in CNV group, and 104 eyes (38.4%) in non-CNV group with statistical significance ($p = 0.034$). On the other hand, the recurrence rate and recurrence frequency in CNV group were 76.2% and 1.63 ± 0.81 , separately ($P = 0.035$, $P = 0.0018$) which were significantly higher than those in non-CNV group.

Conclusions: CNV appears in 7.2% of CSC patients in long-term follow-up. Patients with CNV secondary to CSC had older mean age, poor visual acuity, higher rates of chronic CSC and recurrence than patients without CNV.

CONTROL ID: 3520154

SUBMITTER (NAME ONLY): HIROYUKI YAZU

TITLE: Clinical Observation of Allergic Conjunctival Diseases with Portable and Recordable Slit-Lump Device

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. YAZU, H. Fujishima, Ophthalmology, Tsurumi Daigaku Tsurumi Daigaku Tanki Daigakubu, Yokohama, Kanagawa, JAPAN|H. YAZU, E. Shimizu, S. Sato, N. Aketa, T. Katayama, K. Fukagawa, Y. Ogawa, K. Tsubota, Ophthalmology, Keio Gijuku Daigaku, Shinjuku-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Not only ophthalmologists but also non-ophthalmologists often prescribe eye drops for allergic conjunctival diseases (ACDs); however, there are many cases that are treated without sufficient examination and diagnosis of the eyes. We have invented a portable, recordable, and smartphone-attachable slit-lamp device, called the Smart Eye Camera (SEC). The purpose of this study was to compare the diagnostic abilities of ACDs between the SEC and the conventional, non-portable slit-lamp microscope.

Methods: This prospective observational study included thirty-two eyes of 17 Japanese patients (mean age: 21.5±14.8 years; range: 11-51 years; female: 5). The severity of ten objective signs in the palpebral conjunctiva, bulbar conjunctiva, limbus and cornea were scored on a grading scale of 0 to 4 (0 = normal; 1+ = mild; 2+ = moderate; 3+ = severe), respectively. First, two ophthalmologists used the conventional slit-lamp microscope to examine the grade of the ACDs. Second, another ophthalmologist filmed the eyes in video mode by the SEC and two other ophthalmologists evaluated the grades on another day. The correlation and inter-rater reproducibility in total scores of ten objective signs among two devices were determined.

Results: Total scores of clinical signs evaluated by the two approaches showed a strong correlation with statistical significance (both eyes: $r = 0.918$ [95%CI: 0.839 to 0.959; $p < 0.001$]). Inter-rater agreement was substantial (weighted κ value = 0.631 [95%CI: 0.601 to 0.661; $p < 0.001$]).

Conclusions: This study suggests that the SEC is as reliable as the conventional non-portable slit-lamp microscope for evaluating ACDs.

CONTROL ID: 3520157

SUBMITTER (NAME ONLY): Lydie Tubene

TITLE: Comparison of Virtual Field Device to Humphrey Visual Field SITA-Fast in Normal Subjects

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Tubene, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|M.

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ABSTRACT BODY:

Purpose: Humphrey Visual Field (HVF) testing presents challenges for patients with limited mobility. Virtual reality-based visual field testing could provide a practical and portable alternative for visual field testing. This study examines the agreement between Virtual Field (VF), a virtual reality-based visual field test, and HVF.

Methods: HVF SITA-Fast and VF BOLT Threshold were performed on both eyes of 40 normal subjects (age 23-66), right eye tested first. The test strategies were randomized. Subjects wore surgical masks in accordance with COVID-19 protocol. Outcome measures included mean deviation (MD), test time and visual field index (VFI). Each patient completed a survey about their experience. Eight eyes were excluded due to unreliable results (FL >20%, FP > 15%).

Results: There was not a statistical difference between the right and left eye data on a paired t-test. P-values for HVF were 0.0824, 0.7206, and 0.5663 for MD, VFI and time respectively. P-values for VF were 0.3743, 0.9821, and 0.9872 for MD, VFI and time respectively. The right and left eyes were pooled for analysis.

Average MD values were -0.19 dB for HVF and -2.38 dB for VF. Average VFI values were 99.4% for HVF and 96.2% for VF. Average test times were 176.5 sec for HVF and 194.0 sec for VF. When comparing VF to HVF, VF had mean differences (SD) of -2.18 dB (3.36), -3.2% (7.1) and 17.6 sec (39.7) in MD, VFI and time respectively. 95% CIs [-2.98, -1.40], [-4.89, -1.53], and [8.25, 26.89] respectively. All parameters were level dependent on Bland-Altman analysis with greater bias as the results deviated from normal.

The bias in MD (mean difference \pm SD) was lower for the 29 eyes that did not require trial lenses (-1.0 \pm 2.5 dB) than for the 43 eyes that required trial lenses (-3.1 \pm 4.1 dB). 95% CI [-1.90, -0.04], [-4.33, -1.80] respectively. The difference in bias between the two groups was statistically significant (p=0.0163).

There was a statistically significant difference (p = 0.0011) between subjects who reported some level of fogging on VF (61.6%) compared to the subjects who reported some level of fogging on HVF (19.4%).

Conclusions: VF results did not agree with HVF results. There was more bias between the two tests when a trial lens was required. More subjects experienced fogging of the trial lens on VF than HVF.

CONTROL ID: 3520185

SUBMITTER (NAME ONLY): Alexander Shpak

TITLE: Glial cell line-derived neurotrophic factor in patients with age-related cataract

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Shpak, A.A. Troshina, The S. Fedorov Eye Microsurgery Federal State Institution, Moscow, RUSSIAN FEDERATION|A.B. Guekht, T.A. Druzhkova, Moscow Research and Clinical Center for Neuropsychiatry, Department of Health, Moscow, RUSSIAN FEDERATION|N. Gulyaeva, Institute of Higher Nervous Activity and Neurophysiology Russian Academy of Sciences, Moscow, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: A neuroprotective effect of glial cell line-derived neurotrophic factor (GDNF) was demonstrated in animal models of glaucoma. It is important to study GDNF content in the human eye and lacrimal fluid for clarification of GDNF role in glaucoma pathogenesis. However, in practice this analysis is impossible except of during surgical interventions. An age-related cataract has relatively weak influence on concentrations of neurotrophic factors. The aim of the study was to measure GDNF levels in the aqueous humor, lacrimal fluid, and blood serum in patients with age-related cataract.

Methods: Forty-seven patients (47 eyes) operated for age-related cataract were examined. Exclusion criteria were any serious ophthalmic or somatic pathology, high refractive errors. Mean age of patients was 74.0 ± 7.4 years (range 57-88 years); there were 17 men and 30 women. Collection of stimulated lacrimal fluid was performed by a pipette on the day preceding surgery; the aqueous humor of the anterior chamber and the blood were sampled during the phacoemulsification of a cataract. The concentration of GDNF was measured in the studied biological media by an enzyme immunoassay using RayBio® Human GDNF ELISA Kit (RayBiotech, USA) on a ChemWell 2910 automatic analyzer (Awareness Technology Inc., USA).

Results: Median (interquartile range) of GDNF concentration was 83 (59–119) pg/mL in aqueous humor, 196 (174–239) pg/mL in serum, and 314 (244–422) pg/mL in lacrimal fluid. In 3 cases, GDNF content in aqueous humor was less than minimum detectable value (4 pg/mL). The concentrations of GDNF in the studied biological media did not show significant correlation with each other. Only correlation of GDNF levels in lacrimal fluid and serum showed Pearson's correlation coefficient r over 0.2 ($r=0.27$, $P=0.07$).

Conclusions: In patients with age-related cataract, the median GDNF concentration in aqueous humor is more than 2 times lower than in blood serum and more than 3.5 times lower than in lacrimal fluid. The concentrations of GDNF in the studied biological media are not correlated with each other. These data could be used for comparison with those of patients with combined glaucoma and age-related cataract.

CONTROL ID: 3520214

SUBMITTER (NAME ONLY): Weder Bruce

TITLE: Innovative drug candidates for the treatment of glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Bruce, J. Behr, C. Grimm, Department of Ophthalmology, UniversitätsSpital Zurich, Schlieren, SWITZERLAND|E. Lone, R. Naef, Topadur Pharma AG, Schlieren, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Glaucoma is a heterogeneous group of eye diseases, which result in damage to the optic nerve causing irreversible vision loss. Current treatments for glaucoma focus on lowering intraocular pressure (IOP). However, only one-third to half of glaucoma patients have elevated IOP at the initial stages and disease progression can still occur despite adequate IOP control. Therefore, there is an urgent need to investigate novel therapeutic concepts that complement IOP regulation. We investigated novel compounds that increase cyclic GMP (cGMP) levels in retina by releasing NO and inhibiting PDE5 simultaneously. This dual mode of action may have neuroprotective potential by decreasing IOP and increasing ocular blood flow.

Methods: Candidate compounds were tested in various neuronal and epithelial cell types of the retina. cGMP response profiles were generated for each retinal cell type following compound treatment. In addition, cell viability and phagocytosis of human RPE cells were investigated upon treatment. cGMP levels in retina were determined upon treatment of ex vivo isolated mouse retina with the compounds. For in vivo studies, TOP-V122 (1%) was applied topically using a newly developed formulation in 129S6 mice. To investigate potential physiological effects of the treatment, fundus photography, optical coherence tomography and electroretinography were applied.

Results: Following compound treatment, cGMP levels increased in rMC-1, ARPE-19 and HRPEpiC cells in both time and dose dependent manner. Treatment did not affect the cell viability and phagocytosis of human RPE cells. 3-fold increased cGMP levels were measured in ex vivo isolated mouse retina upon TOP-V122 (1 μ M) treatment. The effect was not dependent on endogenous NO levels in retina, but on the presence of a functional soluble guanylate cyclase. In vivo, multiple topical applications of TOP-V122 (1%) increased cGMP levels in retina compared to the control treatment of the contralateral eye by 65% (27.87 ± 5.30 pmol/mg vs. 16.92 ± 1.67 pmol/mg, n=4, P=0.0076) without affecting retinal function.

Conclusions: Novel compounds targeting PDE5 effectively increase cGMP levels in various retinal cell types and the retina. Repeated dosing did not affect retinal function and structure. The results obtained substantially contribute to understanding the potential use of PDE5 inhibitors specifically designed for retinal neuroprotection and pave the way for future research in this area.

CONTROL ID: 3520257

SUBMITTER (NAME ONLY): Sen Yang

TITLE: Choroidal Thickness in Birdshot Chorioretinitis as Measured by Spectral Domain Optical Coherence Tomography

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yang, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|K. Bhavsar, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sen Yang: Commercial Relationship: Code N (No Commercial Relationship) | Kavita Bhavsar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Alterations in choroidal structure may occur in various inflammatory diseases. Spectral-domain OCT (SD-OCT) with enhanced depth imaging (EDI) can better characterize the choroidal structure. This study aims to quantify choroidal thickness from acute to convalescent stage of Birdshot Chorioretinitis (BSCR) utilizing enhanced depth imaging optical coherence tomography (EDI-OCT).

Methods: A retrospective review of 38 eyes in 17 patients with BSCR was conducted and the development of 20 acute and resolution of inflammatory episodes was evaluated. Choroidal thickness was measured from the posterior edge of the retinal pigment epithelium to the choroid/sclera junction at 500- μ m intervals up to 2500- μ m temporal and nasal to the fovea.

Results: The mean age was 59 ± 9 years (range 43-74). All patients self-identified as non-Hispanic Caucasians. 14 out of 17 patients were female (82.4%). The mean flare duration time was 34 weeks (range 7-102). Eighteen (90%) active flare episodes were bilateral. Common clinical exam findings include the presence of vitreous cells in 33 (87%) of 38 eyes and choroidal lesions in all 38 (100%) eyes. The average initial subfoveal choroidal thickness during acute stage BSCR was 280 ± 103 μ m and the average subfoveal choroidal thickness at follow-up examination during convalescent stage was 230 ± 84 μ m, ($p < 0.05$).

Conclusions: We report the novel finding of statistically significant changes in subfoveal choroidal thickness from acute to convalescent stage BSCR as measured by EDI-OCT in a group of 38 eyes. Our results indicate alterations in choroidal thickness occur during active stages of inflammation and may play an important role in the pathophysiology of BSCR.

CONTROL ID: 3520276

SUBMITTER (NAME ONLY): Gauri Shrestha

TITLE: Tear metabolite expression in bacterial keratitis: Outcomes of an untargeted approach

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.S. Shrestha, A. Vijay, F. Stapleton, N.A. Carnt, School of Optometry and Vision Science, The University of New South Wales, Sydney, New South Wales, AUSTRALIA|G.S. Shrestha, Ophthalmology, Institute of Medicine, Maharajgunj Medical Campus, Kathmandu, Bagmati, NEPAL|R. Pickford, Bioanalytical Mass Spectrometry Facility, UNSW Sydney, University of New South Wales, Sydney, New South Wales, AUSTRALIA|A.J. White, N.A. Carnt, Westmead Institute for Medical Research, University of Sydney, Sydney, New South Wales, AUSTRALIA|A.J. White, Department of Ophthalmology, Westmead Hospital, University of Sydney, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To identify and characterise tear metabolites expression in participants with bacterial keratitis and compare these to expression in healthy controls.

Methods: Twelve tear samples were received from participants with bacterial keratitis (n = 6) at initial presentation and age (case: median age = 59; control: median age = 52; P = 0.44) and sex (case: male:female = 2:4; control: male:female = 3:3; P = 0.70) matched healthy controls (n = 6). Metabolites underwent methanol extraction from the tear samples, chromatographic separation using the Ultimate 3000 System, along with C18 Column, and Mass Spectrometry using QExactive HF. Compound discoverer software v3.1 was used for data analysis. Differential analysis was used to explore fold-change and ratio between cases and controls. The difference in m/z features was adjusted using the Benjamini-Hochberg (B-H) correction for false discovery rate (FDR) with q = 0.05.

Results: Of six cases with bacterial keratitis, two were culture negative and four were culture positive for *S. lugdunensis*, *S. pneumonia*, Multidrug-resistant *S. aureus* or *M. lacunata*. Of 47 metabolites differentially expressed, 25 were upregulated, and 22 were downregulated in the cases compared to controls. Phenylalanyl-lysine (Log_2 fold-change = 11, $P_{\text{adj.}} < 0.0001$) and adenine (Log_2 fold-change = -6.4, $P_{\text{adj.}} < 0.0001$) were the most upregulated or downregulated metabolites in the study, respectively. Purine, tryptophan and amino acid metabolism pathways were primarily observed in tears of participants with bacterial keratitis.

Conclusions: A wide range of tear metabolites was detected in tears of participants with bacterial keratitis. Biologically plausible differences between several metabolite classes such as amino acids, indoles, carbohydrates and nucleosides were observed in tears of participants with bacterial keratitis compared to healthy controls.

CONTROL ID: 3520332

SUBMITTER (NAME ONLY): Maria Larsen

TITLE: Diabetic retinopathy as a potential marker of prevalent and incident Parkinson's disease: results from a nationwide register-based cohort study

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Larsen, A.S. Thykjær, F. Pedersen, J. Grauslund, Department of Ophthalmology, Odense Universitetshospital, Odense, DENMARK|A.S. Thykjær, F. Pedersen, M. Blaabjerg, K. Rubin, L. Stokholm, J. Grauslund, Department of Clinical Research, Syddansk Universitet, Odense, DENMARK|M.E. Larsen, Syddansk Universitet, Odense, DENMARK|K. Rubin, L. Stokholm, OPEN, Odense Universitetshospital, Odense, DENMARK|M. Blaabjerg, Department of Neurology, Odense Universitetshospital, Odense, DENMARK|

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ABSTRACT BODY:

Purpose: Evidence suggests that neurodegeneration is an early event in the pathogenesis of diabetic retinopathy (DR) and, hence, an association between DR and Parkinson's disease (PD) has been proposed. In this nationwide register-based cohort study, we investigated the prevalence and incidence of PD among patients screened for DR in a Danish population-based cohort.

Methods: Cases (n=173.568) above 50 years of age with diabetes included in the Danish Registry of Diabetic Retinopathy (DiaBase) between 2013 and 2018 were matched 1:5 by gender and birth year with a control population without diabetes (n=843.599). The prevalence of PD among cases and controls was compared at index date with an odds ratio (OR). To assess the association between DR and PD, we used a cox proportional hazard model adjusted for age, gender, systemic comorbidity, marital status and medication including insulin, glucose lowering drugs, antihypertensive drugs and cholesterol lowering drugs, to calculate the hazard ratios (HR) with 95% confidence intervals (CI). The study population was followed until earliest registration of PD-event, death, migration or end of follow-up (December 31, 2018), whichever occurred first.

Results: At index date, the prevalence of PD was 0.28% and 0.44% among cases and controls, respectively. Cases with no or any level of DR (level 0-4) were thus less likely to have PD compared to controls (adjusted OR 0.79, 95% CI 0.72-0.88). The multivariate adjusted HR for the association between DR (level 0-4) and PD were 0.88 (0.78-1.00). When looking solely at DR level 0 and 1-4, the adjusted HR were 0.91 (0.79-1.03) and 0.77 (0.56-1.05), respectively.

Conclusions: In a national cohort of more than one million persons, patients with diabetes were 21% less likely to have PD at index compared to a control population without diabetes, and, likewise, there was a general trend towards lower incident PD among cases. This is surprisingly in disagreement with recent published data and accordingly, this nationwide cohort study does not support the suggestion of DR as an independent risk factor for PD.

CONTROL ID: 3520355

SUBMITTER (NAME ONLY): Nimesh Patel

TITLE: 24-2 visual fields and circumpapillary RNFL thickness accurately predict retrobulbar axons in experimental glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.B. Patel, R.S. Harwerth, Vision Sciences, University of Houston, Houston, Texas, UNITED STATES|K. Antwi-Boasiako, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual thresholds and circumpapillary retinal nerve fiber layer (RNFL) thickness both are dependent on the underlying retinal ganglion cell (RGC) content, and are clinically used for the diagnosis and evaluation of progression of optic neuropathies. The purpose of this study was to determine the relationship between endpoint in vivo measures and retrobulbar RGC axonal counts in the non-human primate model of experimental glaucoma.

Methods: Intraocular pressure was elevated by laser scarring the trabecular meshwork in 8 non-human primates. Both experimental and control eyes were monitored with standard automated perimetry (SAP 24-2, full thresholds), and optical coherence tomography (OCT). At varying endpoints, SAP thresholds were converted to RGC counts using the eccentricity dependent non-linear model, accounting for individual differences in retinal scaling. Global RNFL thickness was determined from an elliptical scan path 550 μ m from the Bruch's membrane opening. Post-mortem complete axon counts were determined from thin optic nerve sections imaged with light microscopy using 100X magnification.

Results: The optic nerves of control eyes had an average of 1,309,496 \pm 160,025 axons. RGC estimates from SAP were on average 73,316 less than that established from total retrobulbar axon counts (95% limits of agreement = -365,187, 218,553). The slope of the regression comparing the two RGC counts ($R^2 = 0.89$, slope = 0.96) was not significantly different from 1 ($p = 0.44$). RNFL thickness was linearly related to retrobulbar axon counts ($R^2 = 0.85$, slope = 15322.9 axons/ μ m), and RGC estimates from SAP ($R^2 = 0.92$, slope = 15740 RGCs/ μ m).

Conclusions: Estimates of global retinal ganglion cell counts from visual thresholds are an accurate representation of the retrobulbar axonal count. This relationship is also reflected in objective measures of RNFL thickness, a measure often used as a surrogate of axonal counts.

CONTROL ID: 3520362

SUBMITTER (NAME ONLY): Neal Kansara

TITLE: Astigmatism Correction Accuracy with the Barrett and Nittany Toric Calculators

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Kansara, T. O'Rourke, I.U. Scott, S. Pantanelli, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|E. Lehman, Biostatistics, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the accuracy of residual refractive astigmatism (RA) predictions from the novel Nittany Toric Calculator v0.212 (NTC) to those of the Barrett Toric Calculator (BTC) in eyes implanted with a toric intraocular lens (IOL).

Methods: A nomogram was developed that used pre-operative biometry to predict post-operative RA in eyes implanted with a monofocal IOL. This nomogram was combined with the known effective toricities for Alcon Acrysof toric IOLs to create the NTC, which has as inputs pre-operative biometry and outputs residual RA for a given toric IOL implanted at a suggested axis. A separate testing database was assembled, which consisted of consecutive eyes that had toric IOLs implanted between 02/2016 and 02/2019, as recommended by the BTC. The residual RA predictions from the BTC were compared to those from the NTC for the implanted lens. A "remove and replace" method was used to account for differences between the recommended implantation axes of the toric IOL for the BTC and NTC. Outcome measures included the difference vector (DV) magnitude (defined as the vector difference between actual and predicted RA) and proportion of eyes with a DV magnitude <0.5 or <1.0 diopter (D).

Results: The testing database included 82 eyes. The centroid of the DV for all eyes was 0.06 ± 0.50 D x 177 for the BTC and 0.12 ± 0.65 D x 016 for the NTC ($p = 0.49$). Sub-group analysis revealed centroids of 0.02 ± 0.55 D x 008 and 0.23 ± 0.70 D x 011 in eyes with against-the-rule astigmatism ($p = 0.04$), 0.15 ± 0.42 D x 177 and 0.06 ± 0.55 D x 066 in eyes with with-the-rule astigmatism ($p = 0.06$), and 0.07 ± 0.43 D x 104 and 0.04 ± 0.64 D x 062 in eyes with oblique astigmatism ($p = 0.95$) for the BTC and NTC calculators, respectively. The proportion of eyes that had a DV magnitude <0.5 D were 73.2% and 69.5% ($p = 0.513$), while 93.9% and 92.7% had a DV magnitude <1.0 D, respectively ($p = 1.000$).

Conclusions: The current iteration of the NTC performs similar to BTC with respect to most outcome measures. Further refinements of the NTC to incorporate the impact of effective lens position may lead to improvements in prediction accuracy.

CONTROL ID: 3520376

SUBMITTER (NAME ONLY): Menglu Yang

TITLE: RvD2 Counter-regulates Histamine-induced $[Ca^{2+}]_i$ Increase and Mucin Secretion by Receptor Specific Protein Kinases in Rat Conjunctival Goblet Cells

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Yang, R. Hodges, D.A. Dartt, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T.P. Utheim, Faculty of Medicine, University of Oslo, Oslo, NORWAY|N. Botten, T.P. Utheim, Department of Medical Biochemistry, Oslo Universitetssykehus, Oslo, NORWAY|C.N. Serhan, Anesthesia, Brigham and Women's Hospital Center for Experimental Therapeutics and Reperfusion Injury, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: RvD2 is biosynthesized from docosahexaenoic acid (DHA) and was identified in murine self-resolving exudates during the resolution phase of self-limited acute inflammation in vivo. The resolution promoting action of RvD2 was observed in multiple organs and tissues. Histamine is an autacoid produced in the conjunctiva by mast cells in response to an allergen. All four histamine receptor subtypes, H1-4, are present on conjunctival goblet cells and with stimulation increase intracellular $[Ca^{2+}]_i$ ($[Ca^{2+}]_i$) and mucin secretion as a component of allergic conjunctivitis. To determine the molecular mechanism used by RvD2 to terminate the histamine-stimulated allergic response, we investigated the interaction of RvD2 with histamine and its receptors in conjunctival goblet cells.

Methods: Goblet cells were cultured from male rat conjunctiva. Signaling pathways were studied by measuring the $[Ca^{2+}]_i$ responses using fura 2/AM. Mucin secretion was determined using an ELLA.

Results: Thirty-minute treatment with RvD2 (10^{-8} M) significantly blocked the histamine (10^{-5} M) -induced increase in $[Ca^{2+}]_i$ and mucin secretion. Stimulation with an agonist selective for each of the four histamine receptors showed that RvD2 inhibited the $[Ca^{2+}]_i$ increase induced by the activation of H1, H3, or H4 receptors. Blockage of the H1 receptor agonist by RvD2 was reversed by inhibiting β adrenergic receptor kinase (β ARK) and protein kinase A (PKA), but not by inhibiting protein kinase C (PKC). Blockage of the H3 receptor agonist by RvD2 was only reversed by inhibiting PKA. Blockage of the H4 receptor agonist was reversed by inhibiting β ARK and PKC, but not by inhibiting PKA.

Conclusions: RvD2 counter-regulates histamine-induced $[Ca^{2+}]_i$ increase and mucin secretion by phosphorylating and down-regulating H1, H3, and H4 receptors by activating receptor-specific protein kinases.

CONTROL ID: 3520383

SUBMITTER (NAME ONLY): Hayley Favre

TITLE: Comparison of iStent Inject, Hydrus Microstent, and Kahook Dual Blade in a Predominately Hispanic Population with Primary Open Angle Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Favre, E. Sherry, A. Foster, C. Waldman, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Hayley Favre: Commercial Relationship: Code N (No Commercial Relationship) | Emily Sherry: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Foster: Commercial Relationship: Code N (No Commercial Relationship) | Corey Waldman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The goal of this study is to compare the outcomes of selected microinvasive glaucoma surgery (MIGS) devices in combination with cataract surgery.

Methods: This is a retrospective chart review of 93 eyes of 79 patients with mild to moderate primary open angle glaucoma (POAG) who underwent a combination of cataract surgery with either iStent inject (n=38), Hydrus microstent (n=24), or Kahook dual blade goniotomy (KDB) (n=31) by one surgeon. Inclusion criteria were no prior surgical intervention for POAG, no laser procedures within 2 years, mild to moderate POAG, and at least 6 months post-op (POM6) follow-up. Statistical analysis was performed using the Kruskal Wallis test.

Results: The percent of intraocular pressure (IOP) reduction at POM6 for iStent inject, Hydrus, and KDB were 10.55%, 4.24%, and 7.74% respectively, but there was no significant difference between the groups ($p=0.75$). There was a significant difference in the number of medications at both pre-op ($p=0.046$) and POM6 ($p=0.03$). The average pre-op number for iStent inject, Hydrus, and KDB were 1.27, 1.67, and 1.81 respectively. At POM6, Hydrus remained at the same average at 1.67 drops, while iStent inject decreased to 0.5 and KDB to 1.29. LogMAR visual acuity improved for all groups by POM6, but there was no significant difference between the groups. 71% of patients identified as Hispanic (Table 1). There were 2 cases of rebound iritis in the iStent inject group, a case of 1 mm hyphema and steroid response in the Hydrus group, and one patient with an IOP spike in the KDB group, all of which were self-limiting.

Conclusions: The MIGS procedures of iStent inject, Hydrus, and Kahook dual blade combined with cataract surgery are safe and effective at lowering IOP, improving visual acuity, and decreasing dependence on drops. However, there was little significant difference found between the groups. Only iStent inject had a significantly lower number of glaucoma medications at both pre-op and POM6. The high percentage of Hispanic patients in this study should be considered when reviewing this data and may be an area of further investigation.

CONTROL ID: 3520409

SUBMITTER (NAME ONLY): Jennifer Tingley

TITLE: Impact of the COVID-19 Pandemic on Quantity and Characteristics of Ophthalmology Consults

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tingley, J. Tauber, A. Barmettler, Ophthalmology, Montefiore Medical Center, Bronx, New York, UNITED STATES|T. Thuma, Touro College of Osteopathic Medicine, Middletown, New York, UNITED STATES|J. Moon, Epidemiology and Population Health, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine how the quantity and characteristics of ophthalmology consults at a New York City hospital system changed during the COVID-19 pandemic peak.

Methods: In an IRB approved, HIPAA compliant retrospective, comparative chart review study, ophthalmology (initial, follow-up, and electronic) consult notes from February to May 2019 were compared to those in February to May 2020. Statistical comparisons between 2019 and 2020 were made using T-tests and Fisher's exact tests.

Results: Of 2,215 notes analyzed, 1,374 (62%) were from 2019 and 841 (38%) were from 2020 ($p=0.0002$). Baseline characteristics between groups, including chronic medical conditions, did not differ significantly. In 2019, 41% of patients had a primary hospital diagnosis related to ophthalmology, whereas in 2020 this decreased to 32% ($p=0.002$). In 2019, 7.5% of patients were on ventilators; this increased in 2020 to 10.8% ($p=0.035$). Top reasons for consult requests were stable between years: eye pain/pressure (16.4%, 14.1%, $p=0.79$), trauma (13.1%, 13.7%, $p=1$), and blurry vision (12.9%, 11.2%, $p=0.85$) (Figure 1). After evaluation, the most common diagnoses in 2019 were trauma (14.0%) and glaucoma (10.9%). In 2020, they were trauma (15.2%) and retinopathy of prematurity (11.2%). In 2020, 1.8% of consults were in a newly available format, the e-consult (telephone visit). Within 2020, the number of consults decreased at the end of February (-47.5 %) and in mid-March (-44.1%) (Figure 2). In 2020, 22.5% of all consults were COVID tested and 2.4% of all consults were positive within 2 weeks of in-person evaluation.

Conclusions: These results reflect changes in the activity of the ophthalmology consult service during the peak of the COVID-19 crisis. Consult quantities decreased dramatically in late February and mid-March, which correlate with the timing of the first COVID-19 case in New York State (reported February 29) and the New York State on Pause Program that required all non-essential workers to stay home (ordered March 22). The lower number of ophthalmology consult requests in 2020 may reflect that patients with non-acute eye problems did not seek medical attention and/or primary teams deferred requests.

CONTROL ID: 3520422

SUBMITTER (NAME ONLY): Lingling Huang

TITLE: A novel pathogenic mutation of the TIMP3 gene in Sorsby Fundus Dystrophy

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Huang, K. Huffman, S. Borooah, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|B. Bakall, The University of Arizona College of Medicine Phoenix, Phoenix, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sorsby fundus dystrophy (SFD) is a rare, autosomal dominant macular dystrophy caused by variants in the Tissue Inhibitor of Metalloproteinase 3 (TIMP3) gene. We identified a novel pathogenic variant in the C-terminal domain of TIMP3 in two unrelated families.

Methods: Clinical imaging included spectral domain optical coherence tomography (SD-OCT), ultra-widefield pseudocolor, autofluorescence and fundus fluorescein angiogram (FFA) imaging, electroretinography (ERGs) and genetic testing.

Results: The 44-year-old proband from pedigree 1, developed nyctalopia and initially presented at the age of 41 with choroidal neovascularization in the left eye, treated with anti-VEGF injections. Her most recent vision was 20/25 OD and 20/60 OS. Ultra-widefield imaging demonstrated multiple discrete areas of nummular peripheral pigmentation and subretinal fibrosis near the fovea in the left eye (Figure 1). FFA showed masking in the areas of pigmentation, staining of deposits in the periphery bilaterally and leakage near the fovea in the left eye. SD-OCT confirmed choroidal neovascularization with development of a juxta foveal sub-retinal pigment epithelium deposit in the left eye. Scotopic ERGs demonstrated a marked reduction in response with standard dark adaptation.

The 64-year-old proband from pedigree 2 developed a sudden drop in central vision with choroidal neovascularization at the age of 39 treated with macular laser, and continued to develop central and peripheral vision loss. His most recent vision was hand motion at 4 feet OD and 20/100 OS. Imaging revealed a foveal scar OD, subretinal deposits and widespread discrete areas of chorioretinal atrophy bilaterally associated with severely reduced photopic and scotopic ERGs (Figure 2). The findings in both patients are consistent with SFD.

Genetic testing in both patients identified a heterozygous missense variant for TIMP3 c.446C>G, p.(Ser149Cys). This variant affects a moderately conserved amino acid at the C-terminal domain of TIMP3, and most of the in silico tools predict the variant as deleterious. To our knowledge, the variant has not been published or reported in the disease related variation databases such as ClinVar or HGMD.

Conclusions: A novel pathogenic variant of TIMP3 was identified in two unrelated families with SFD. To date The HGMD database reports 17 variants in TIMP3 in association with SFD. This expands the spectrum of disease-causing mutations in the TIMP3.

CONTROL ID: 3520434

SUBMITTER (NAME ONLY): Rain Wen

TITLE: Examination of retrotransposon expression in optic neuropathies

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Wen, B. Tanasa, X. Xia, M. Nahmou, K. Heng, A. Singh, J.L. Goldberg, Spencer Center for Vision Research, Byers Eye Institute, Palo Alto, California, UNITED STATES|R. Wen, B. Tanasa, X. Xia, M. Nahmou, K. Heng, A. Singh, J.L. Goldberg, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retrotransposons are repetitive DNA sequences constituting more than half of the human or mouse genome that can translocate from one location to another. Retrotransposons were considered as “junk DNA;” however, recent studies suggest that they are involved in many cellular activities, including in neurodegeneration. Optic neuropathies are a group of neurodegenerative diseases caused by damage to retinal ganglion cell (RGC) axons in the optic nerve. Our preliminary data showed that retrotransposons were induced by optic nerve injury in RGCs; here we determine whether retrotransposons play a role in optic neuropathy.

Methods: We performed optic nerve crush (ONC) on the left eyes of 6-8 week old adult mice on day 0, and then isolated RGCs from these animals or from healthy control eyes on day one or day five after ONC. Total RNA was extracted from RGCs and converted to cDNA for qPCR using primers amplifying different classes of retrotransposons, including LINE, SINE, and ERVs.

To inhibit retrotransposon expression in RGCs, we use antiviral drugs stavudine or lamivudine to inhibit their reverse transcription. We performed ONC and intravitreal injection of either drug on day 0 followed by daily intraperitoneal injection of the drug for two weeks. Two days before sacrifice, mice received an intravitreal injection of CTB-555 to anterogradely label RGC axons. Mice were transcardially perfused under deep anesthesia with 4% PFA on day 14. Retinas and optic nerves were further dissected, processed, and examined by fluorescent confocal microscopy.

Results: We found that retrotransposon expression levels were elevated in RGCs after optic nerve injury, especially the LINE family, which increased two- to four-fold after ONC. Inhibition of reverse transcription by antiviral drugs did not promote RGC axon regeneration after optic nerve injury in mice.

Conclusions: Our findings suggest that retrotransposon expression is induced by optic nerve injury in RGCs. Inhibition of retrotransposon reverse transcription by antiviral drugs didn't promote RGC axon regeneration, but may promote neuroprotection. Our future studies will focus on this question, as well as manipulation of retrotransposon expression itself by shRNA knockdown in RGCs.

CONTROL ID: 3520471

SUBMITTER (NAME ONLY): Raju Timsina

TITLE: Cholesterol and Cholesterol Bilayer Domains Inhibit the Binding of Alpha-Crystallin with Phospholipid Membranes

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Timsina, N.K. Khadka, L. Mainali, Physics, Boise State University, Boise, Idaho, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Raju Timsina: Commercial Relationship: Code N (No Commercial Relationship) | Nawal Khadka: Commercial Relationship: Code N (No Commercial Relationship) | Laxman Mainali: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The level of α -crystallin decreases in the eye lens cytoplasm, with the corresponding increase in the membrane-bound α -crystallin during cataract progression. Eye lens membrane consists of extremely high cholesterol (Chol) content that favors the formation of cholesterol bilayer domains (CBDs) within the membrane. The function of the high Chol level in the lens membrane is unclear. The purpose of this research is to understand the interaction of α -crystallin with Chol and CBDs in the phospholipid membrane.

Methods: Continuous-wave electron paramagnetic resonance (EPR) spin-labeling method was used to estimate the binding affinity (K_a) of α -crystallin with the Chol/POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine) membranes with varying Chol/POPC mixing ratio from 0 to 1.5. Also, the maximum membrane surface occupied (MSO) by the α -crystallin and the change in the membrane physical property (mobility parameter) after the α -crystallin binding was estimated using the EPR method. The small unilamellar vesicles of Chol/POPC membrane with 1 mol% CSL spin-label were prepared using the rapid solvent exchange method followed by probe-tip sonication. The CSL spin-labels incorporated into the membrane monitor the α -crystallin binding.

Results: The K_a and MSO followed the trends: $K_a(0) > K_a(0.3) > K_a(0.5) > K_a(1) = K_a(1.5)$ and $MSO(0) > MSO(0.3) > MSO(0.5) > MSO(1) = MSO(1.5)$, where numbers in the parenthesis represent the Chol/POPC mixing ratio. For Chol/POPC mixing ratio greater than 1, CBDs form within the membrane. These results indicate that Chol and CBDs inhibit the binding of α -crystallin to the POPC membrane. The profiles of the mobility parameter decrease with an increase in the α -crystallin binding; however, the decrease is pronounced for the lower Chol concentration compared to the high Chol concentration in the membrane. These results represent that membrane becomes more immobilized near the headgroup regions with the increase in α -crystallin binding.

Conclusions: Our results show that the Chol and CBDs inhibit the binding of α -crystallin to the phospholipid membrane, and the membrane physical property alters with α -crystallin binding. These results provide a molecular basis for understanding the functions of Chol and CBDs' in the eye lens membrane in maintaining lens transparency and possibly protecting against cataract formation.

CONTROL ID: 3520476

SUBMITTER (NAME ONLY): Abinaya Thenappan

TITLE: An Early Nasal Step Defect is Often a Sign of Macular Damage.

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Thenappan, E. Tsamis, G. De Moraes, D.C. Hood, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test the hypothesis that early glaucomatous eyes with nasal step defects on 24-2 visual fields (VFs) often have macular damage seen with optical coherence tomography (OCT).[1]

Methods: 216 individuals, including 162 patients with or suspected glaucoma and 54 healthy controls, underwent two baseline 24-2 SITA-Standard VF tests and 9x12mm widefield swept-source OCT scans within 4 weeks. Each hemifield of the 216 eyes was graded for a nasal step based on two definitions: one from the Ocular Hypertension Treatment Study (OHTS) and one we developed that was stricter and more clinically relevant. Figure 1 is a depiction of the minimum (a,c) and maximum (b,d) nasal steps that would satisfy the OHTS (a,b) criteria and our stricter criteria (c,d). Eyes with a nasal step were evaluated for topographical confirmation of the nasal step on OCT retinal nerve fiber layer (RNFL) probability maps. These nasal steps were then evaluated for evidence of macular damage by 2 experts (qualitative approach). For the quantitative approach, a custom R program assessed topographical abnormal structure/function agreement between 24-2 and 10-2 VFs and RNFL and retinal ganglion cell (RGC) probability maps.[2,3]

Results: For the 216 eyes, there were 11 nasal steps with OCT confirmation (10 eyes). 8 of these 11 replicated on the second baseline VF. Notably, 9 of 11 (82%) had macular damage based on the qualitative OCT method, and 1 of the 2 remaining eyes developed macular damage 14 months later (see black arrows in Fig. 2). Based upon the quantitative approach, 7 of the 11 eyes demonstrated abnormal macular structure-function agreement. In general, 8 of the 11 nasal steps were in the superior VF (inferior retina).

Conclusions: Early glaucomatous eyes with nasal step defects on 24-2 VF often have macular damage seen with OCT, as predicted given the prevalence of macular damage in eyes with early glaucoma and the proximity of the disc regions associated with the macular and nasal step regions of the VF.[1] Because of the clinical significance of untreated progressive macular damage, eyes with nasal steps on 24-2 VF should be examined for macular damage on OCT RGC probability maps and/or 10-2 VFs.

1. Hood, Tsamis, Bommakanti et al. IOVS, 2019. 2. Tsamis, Bommakanti, Sun et al. TVST, 2020. 3. Hood. PRER, 2017.

CONTROL ID: 3520491

SUBMITTER (NAME ONLY): Akira Obana

TITLE: Macular Pigment Changes in eyes implanted with yellow-tinted intraocular lens

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Obana, Y. Gohto, R. Asaoka, Ophthalmology, Seirei Hamamatsu Byoin, Hamamatsu, Shizuoka, JAPAN|A. Obana, Photochemical Medicine Department, Hamamatsu Ika Daigaku, Hamamatsu City, Shizuoka, JAPAN|

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ABSTRACT BODY:

Purpose: We previously reported that macular pigment optical density (MPOD) levels decreased during a long follow-up period after clear intraocular lens (IOL) implants surgery presumably due to excessive light exposure (Obana et al. Ophthalmol 2011;118). In the present study, we examined changes in MPOD levels after cataract surgery with yellow-tinted IOL implantation using a different technique to measure MPOD from the previous study.

Methods: This is a prospective, observational study under approval by institutional review board. Subjects were 55 eyes of 35 patients. MPOD levels were measured by a SPECTRALIS OCT (Heidelberg Engineering Inc.) equipped with a dual-wavelength autofluorescence technique on day 4, months 1, 3, and 6, and years 1 and 2 postoperatively. The average optical densities at 0°, 0.5°, 0.9°, and 2° eccentricities (local MPODs) and total MPOD volumes in the area within 9° eccentricity (MPOV) were analyzed.

Results: The mean local MPOD at baseline (on day 4) was 0.79 at 0°, 0.71 at 0.5°, 0.68 at 0.9°, and 0.32 at 2°. The mean MPOV within 1.5° and 9° at baseline was 2950 and 18897, respectively. Local MPOD at 0.9° and 2° and MPOV slightly decreased on month 1 and increased after that. The increase reached statistical significance in local MPOD at 0.5° and 2° and MPOV within 1.5° and 9° on year 2 (Tukey-Kramer test). The change rates of MPOV within 9° on year 2, ((MPOV on year 2 – MPOV on day 4) / MPOV on day 4), were from -0.21 to 1.18 (mean and standard deviation: 1.14±0.28). The MPOV of fifteen eyes increased more than 10% from the initial value, was maintained within 10% in 21 eyes and deteriorated more than 10% in only 3 eyes.

Conclusions: Local MPOD and MPOV tended to slightly decrease at month 1 postoperatively and gradually increase after that, but the increase rates of MPOD levels were small compared to the previous report (Nolan et al. IOVS2009;50). Yellow-tinted IOL that has lower transmittance of blue light might be preferable in the respect of preserving MPOD levels after surgery.

CONTROL ID: 3520511

SUBMITTER (NAME ONLY): Shunya Tatara

TITLE: Fluctuation of Intraocular Pressure with Noncontact Tonometer and Rebound Tonometer in the Normal Volunteers

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tatara, F. Maeda, Department of Orthoptics and Visual sciences, Faculty of Medical Technology, Niigata University of Health and Welfare, JAPAN|S. Tatara, Department of Vision Science, Faculty of Sensory and Motor Control, Kitasato University Graduate School of Medical Science, JAPAN|F. Maeda, Y. Tsukahara, Field of Orthoptics and Visual Sciences, Major in Medical and Rehabilitation Sciences, Graduate School of Health and Welfare, Niigata University of Health and Welfare, JAPAN|K. Yaoeda, Department of Ophthalmology, Yaoeda Eye Clinic, JAPAN|K. Yaoeda, Division of Ophthalmology and Visual Sciences, Niigata University Graduate School of Medical and Dental Sciences, JAPAN|

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ABSTRACT BODY:

Purpose: It is known that the intraocular pressure (IOP) measurement by the Goldmann applanation tonometer (GAT) tend to fluctuate because of several artifactual factors. This is thought to be mainly influenced by several factors on the observer sides of GAT measurements. In this study, we investigated the fluctuation of IOP by a noncontact tonometer (NCT) and a rebound tonometer (RT) which are considered that the influence of the observer's skill is small.

Methods: The subjects were 37 normal volunteers recruited from the university students. IOP was measured on the subjects by NCT and RT for 5 consecutive days (11:00 to 13:00). Six successive IOP measurements were carried out using CT-1 (Topcon) and Icare PRO (Icare Finland Oy) on the same day. IOP was measured in the first eye (right or left) and then in the fellow eye and IOP was again measured in the first eye and then in the fellow eye. Repeated-measures analysis of variance was used to test differences in IOP between the consecutive measurements (day 1 to 5) or the successive measurements (first to sixth). A P-value < 0.05 was considered statistically significant.

Results: IOP measured by a NCT was significantly higher in both the left and right eye on day1 than on other measurement days (P= 0.000-0.041). IOP measured by RT was significantly higher in both the left and right eye on day1 than that on the other days (P= 0.000-0.030). IOP measured by a NCT were no significant differences in the successive measurements. On the other hand, there were several differences in the successive measurements (e.g. the first IOP measurement was significantly higher than the second to sixth IOP measurements on day 1) with RT measurements.

Conclusions: IOP as measured by a NCT and a RT on day 1 were higher than that on the other day. IOP as measured by a NCT is more stable than that by a RT in the intrasession measurements.

CONTROL ID: 3520536

SUBMITTER (NAME ONLY): Clemens Strohmaier

TITLE: Episcleral venous pressure response to brain stem stimulation: effect of topical Lidocaine.

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Strohmaier, Ophthalmology, Kepler Universitätsklinikum GmbH, Linz, Oberösterreich, AUSTRIA|H.A. Reitsamer, Ophthalmology, Paracelsus Medizinische Privatuniversität, Salzburg, Salzburg, AUSTRIA|J.W. Kiel, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Episcleral venous pressure (EVP) is important for steady state intraocular pressure (IOP), as it has to be overcome by aqueous humor in order to leave the eye. It was long assumed to be constant, but recent evidence suggests neuronal control, with a vascular tone through the innervation present. The superior salivatory nucleus in the brainstem could be identified to elicit increases in EVP during electrical stimulation. In the present study the effect of topical anesthesia on the stimulation effect was investigated.

Methods: 8 Sprague Dawley rats were anesthetized, artificially ventilated with CO₂ monitoring and continuous blood pressure monitoring. Intraocular pressure was measured continuously through a cannula in the vitreous body. Episcleral venous pressure was measured by direct cannulation of an episcleral vein via a custom made glass pipette connected to a servonull micropressure system.

Results: Electrical stimulation of the superior salivatory nucleus (10µA, 200 pulses of 1ms duration) increased EVP from 8,51 ± 1,82 mmHg to 10,97 ± 1,93 mmHg (p<0,05). After topical application of topical lidocaine EVP increased from 7,42 ± 1,59 mmHg to 9,77 ± 1,65 mmHg (p<0,05). The EVP response to stimulation before and after lidocaine application was not statistically significantly different (2,45 ± 0,5 vs 2,35 ± 0,49 mmHg, p = 0,69), while the decrease in baseline EVP was (8,51 vs. 7,42 mmHg, p <0,05)

Conclusions: The present data suggest that distinct neuronal mechanisms controlling the episcleral circulation of rats exist. This is in keeping with previous reports of two distinct arterio-venous anastomoses, one in the limbal circulation and one in the conjunctival/episcleral circulation.

CONTROL ID: 3520562

SUBMITTER (NAME ONLY): Elena Solli

TITLE: Archetypal Analysis of Visual Fields in Optic Neuritis Reveals Functional Biomarkers Associated with Outcome and Treatment Response

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Solli, M.J. Kupersmith, Neurology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|H. Doshi, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L. Pasquale, M.J. Kupersmith, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|M. Wall, Ophthalmology, The University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Currently, there is no presentation biomarker that is significantly correlated with treatment outcome in optic neuritis (ON). Visual fields (VF) reveal global and regional deficits, reflecting visual pathway dysfunction. Archetypal analysis (AA), a form of unsupervised machine learning, has been used in glaucoma to monitor focal VF defects quantitatively. We theorized that AA could detect quantifiable, disease-specific patterns of VF loss that correlate with treatment effect and visual outcome, as well as reveal residual deficits in ON.

Methods: Using the R statistical environment, we performed AA on 3,892 VFs prospectively collected from 456 eyes in the ON Treatment Trial. We decomposed each study eye VF into a weighted sum of its component ATs (total weight=1.0). We defined a minimum AT weight change (7%) distinguishable from normal fluctuations by decomposing VFs of 61 control eyes into ON-specific ATs. To compare outcomes and recovery rates between treatment groups, we created a mathematical model to describe change in AT weight and MD over time.

Results: We used a 10-fold cross-validation model to create 16 ON-specific ATs (Figure 1), which were distinct from control VFs. At presentation, AT2, a severe global dysfunction pattern, had the highest weight (0.33 ± 0.40). Over 6 months, we observed an exponential increase in AT1, a normal AT (Figure 2), and an exponential decrease in AT2 weight. AT1 demonstrated the greatest relative weight increase due to intravenous methylprednisolone (IVMP: 0.57 ± 0.24 ; placebo: 0.51 ± 0.26 ; oral prednisone: 0.49 ± 0.27 , $p=0.01$). Eyes with AT1 weight ≥ 0.19 at baseline (≥ 1 SD above mean) had better visual outcomes for both MD (-1.13 vs. -3.86 dB, $p<0.001$) and AT1 weight (0.68 vs 0.50 $p<0.0001$); however, a treatment benefit for IVMP occurred only for eyes with AT1 weight <0.19 at baseline ($p=0.0115$). Patients receiving IVMP recovered fastest ($p<0.001$). At 6 months, 182/227 eyes with MD >-2.00 dB had at least one abnormal AT.

Conclusions: For the first time, AA reveals specific features of vision loss associated with outcome and treatment effect in ON. AT1 is a quantifiable biomarker of VF function, identifying patients who may benefit most from treatment. AA shows residual deficits in eyes labeled as normal by MD at outcome.

CONTROL ID: 3520587

SUBMITTER (NAME ONLY): Catherine Seeger

TITLE: Nittany-AK Calculator: A Novel Femtosecond Laser-assisted Keratotomy Nomogram for the Management of Corneal Astigmatism During Cataract Surgery

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Seeger, N. Kansara, A. Sun, A. Longenecker, I.U. Scott, S. Pantanelli, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|B. Ernst, G. Mishra, Schein Ernst Mishra Eye, Harrisburg, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: This prospective study determined the efficacy of a femtosecond laser-assisted keratotomy (FLAK) nomogram (Nittany-AK calculator) for the correction of astigmatism at the time of cataract surgery.

Methods: This study employed a novel nomogram which considered the posterior and non-keratometric contributions to total ocular astigmatism. The study included consecutive patients who underwent cataract extraction with planned FLAK and insertion of a monofocal intraocular lens by one of two surgeons. Eyes with greater than 0.5D of against the rule (ATR) or oblique astigmatism, or 1.0D of with the rule (WTR) astigmatism were treated in accordance with the nomogram. Biometry and manifest refraction were measured one month post-operatively. Target induced astigmatism (TIA) was compared to corneal and refractive surgically induced astigmatism (SIA). Outcome measures included the correction index (CI), index of success (IOS), and proportion of eyes in which the axis of astigmatism was flipped. A CI of 1.0 indicates that SIA is equal to TIA. An IOS of 0.0 indicates that there is no difference between SIA and TIA. CI and IOS were reported as geometric means for all groups.

Results: A total of 48 eyes from 36 patients have been treated thus far, of which 21 had ATR, 19 had WTR, and 8 had oblique astigmatism. The corneal CI indicated a slight under-correction of both ATR and WTR astigmatism (ATR = 0.93, WTR = 0.86), but the refractive CI revealed an over-correction of WTR (ATR = 1.01, WTR = 1.95). Refractive IOS (ATR = 0.58, WTR = 1.01) indicated greater efficacy of the surgical intervention than the corneal IOS for all groups (ATR = 0.77, WTR = 1.11). More ATR eyes had their axis flipped based upon corneal measurements (ATR = 14.29%, WTR = 21.05%), while more WTR eyes had their axis flipped based upon refractive measurements (ATR = 9.52%, WTR = 47.37%).

Conclusions: The Nittany-AK calculator appeared to be effective at correcting corneal astigmatism at the time of cataract surgery. Ongoing enrollment should translate to further refinements of the calculator and improvements in outcomes.

CONTROL ID: 3520606

SUBMITTER (NAME ONLY): Randolph Glickman

TITLE: Comparison of retinal characteristics in two rabbit strains

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.D. Glickman, Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|I. Nasonkin, Aivita Biomedical, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rabbits have long been used as a large eye model in ophthalmic research because of their relative moderate cost, ease of handling, and relevance to human ocular biology. Moreover, rabbit strains have been developed with different characteristics, such as albinism, variable pigmentation, and body size, to meet specific research needs. In the present study, we compared baseline ocular electrophysiology and biometric parameters between the Dutch Belted (DB) and New Zealand Pigmented (Red) (NZIP) rabbit strains.

Methods: Ocular characteristics were evaluated using fundus photography (Topcon TRC-50X), optical coherence tomography (OCT, Leica/Bioptigen Envisu R2200), and photopic flash and flicker electroretinography (Ocuscience HMsERG handheld tester) to characterize retinal gross morphology, thickness, and visual response, respectively. Three females of each strain were studied, and all animal procedures were carried out with the rabbits anesthetized with isoflurane.

Results: Fundus photography revealed no consistent differences in the gross morphology of the DB and NZP retinas. Photopic flash ERGS did not show significant differences in mean a-wave amplitude (DB: $21.3 \pm 4.7 \mu\text{V}$, NZP: $20.8 \pm 7.5 \mu\text{V}$), b-wave amplitude (DB: $113.9 \pm 20.0 \mu\text{V}$, NZP: $100.5 \pm 25.6 \mu\text{V}$), nor in implicit time (DB: $33.7 \pm 2.7 \text{ mS}$, NZP: $31.8 \pm 2.5 \text{ mS}$); $P > 0.05$ in all comparisons using one-way ANOVA with repeated measures. Photopic flicker mean amplitude did not differ significantly (DB: $49.6 \pm 27.8 \mu\text{V}$, NZP: $44.7 \pm 31.5 \mu\text{V}$, $P = 0.496$, Wilcoxon Rank Sum test). The retinal thickness, measured by OCT, differed significantly between the two strains (DB: $233.6 \pm 14.0 \mu\text{m}$, NZP: $295.7 \pm 15.6 \mu\text{m}$; $P < 0.001$, unpaired t-test).

Conclusions: It is well known that NZP rabbits are larger and heavier compared to DB animals (averaging 3.6 kg vs 1.9 kg, respectively, in our cohorts), and NZP eyes are also larger than DB eyes; however, to our knowledge, the difference in retinal thickness between the two strains has not been reported previously. Because retinal thickness may indicate ocular inflammation and reflect homeostasis, it is an important variable impacting the interpretation of ocular studies. Despite the difference in retinal volume, we did not find strain differences in the photopic ERG responses as reported by others. Although the DB and NZP rabbit strains are both suitable for eye research applications, the potential impact of retinal thickness difference must be considered.

CONTROL ID: 3520742

SUBMITTER (NAME ONLY): Mathilde Franklin

TITLE: Psychological Stress during COVID-19 and Central Serous Chorioretinopathy (CSCR)

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Franklin, A. Wagner, K. Kapoor, Ophthalmology, Wagner and Kapoor Research Institute, Virginia Beach, Virginia, UNITED STATES|M. Franklin, A. Wagner, K. Kapoor, Ophthalmology, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mathilde Franklin: Commercial Relationship: Code N (No Commercial Relationship) | Alan Wagner: Commercial Relationship: Code N (No Commercial Relationship) | Kapil Kapoor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Psychological stress is a well-documented risk factor for developing CSCR. Given the unprecedented nature of COVID-19, we wanted to analyze the relationship between the pandemic and CSCR cases in a retrospective, cross-sectional study.

Methods: All newly diagnosed CSCR cases were identified from nine clinics across Hampton Roads, VA (2015—2020). The medical billing system was used to query all CSCR cases, and other causes for retinal exudation were excluded, including inflammation, infiltration, hemorrhage, and choroidal neovascularization. Demographic data and previously reported risk factors were recorded, including recent stressors. CSCR cases and risk factors were compared between the pre-pandemic timeframe (Jan 2015—Feb 2020) and the COVID period (Mar 2020—Sept 2020). Cases were also compared using three-month rolling sums. Categorical variables were analyzed using Chi-square analysis and Fisher's exact test. Continuous variables were analyzed using the Student's t-test.

Results: A total of 247 patients with CSCR were identified with 205 patients in the pre-COVID-19 period and 42 during COVID-19. The total number of CSCR cases per month was analyzed over 69 months (Fig 1). There was an average of 3.61 CSCR cases per month (SD, 2.21; range, 0—10 cases; median, 3 cases). The highest number of cases occurred in May 2020 (10 cases, 99.3 percentile). When comparing the CSCR cases longitudinally (Fig 2), the highest number of cases occurred in 2020 with an average of 6.7 monthly cases. The year 2020 was significantly different from 2015, 2016, 2017, and 2018 ($P < 0.001$). When analyzing the cases using three-month rolling sums, May—July 2020 had the largest number of cases (22 cases, 99.25 percentile), and January—March 2020 had the second-highest total (21 cases, 97.8 percentile). Recent psychological stress was present in 19% of the COVID-era and only 9% of the pre-COVID patients, but was not significantly significant ($P = 0.065$).

Conclusions: The relationship between a worldwide pandemic in the development of CSCR has not been previously reported. While the largest number of monthly cases occurred during the pandemic, there was a relative increase shortly before the designated pandemic start-date. Larger, retrospective studies are warranted to evaluate the significance of these findings.

CONTROL ID: 3520801

SUBMITTER (NAME ONLY): Modupe Adetunji

TITLE: Effect of teprotumumab on intraocular pressure in thyroid-associated ophthalmopathy

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.O. Adetunji, E. Meer, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|B.J. Nguyen, B. Kwong, B. McGeehan, M.G. Maguire, M. Tamhankar, C.A. Briceño, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thyroid eye disease (TED) is a progressive, debilitating and potentially blinding autoimmune disease. Teprotumumab, a novel human monoclonal antibody, reduces orbital soft tissue volume and improves the clinical manifestations of TED, however, the effects on intraocular pressure (IOP) remain uncharacterized. We conducted a retrospective chart review to investigate changes in IOP in patients with TED following teprotumumab treatment.

Methods: A single-center retrospective review of TED patients treated with teprotumumab at the Scheie Eye Institute was conducted. Exclusion criteria included prior surgical treatment for TED and follow-up duration less than 3 weeks. Data was collected on baseline IOP, IOP post-treatment, clinical activity score, proptosis, and treatment duration. IOP was measured using a rebound tonometer in primary gaze. The main outcome measure was change in IOP at week 12 of treatment. Mean differences in IOP following treatment were estimated by modeling the effect of time on IOP using generalized estimating equations. Associations between IOP measurements, proptosis and clinical activity score were established using linear regression that accounted for inter-eye correlation by generalized estimating equations.

Results: 12 TED patients treated with teprotumumab were included. Mean age was 50.8 years (range 34-74); 92% of patients were female (Table 1). Average treatment duration was 13 weeks (range 6-24), average baseline IOP was 19.8 mm Hg (range 13-28) and average baseline clinical activity score was 3.6 (range 0-6). 24 eyes were examined at baseline, 10 at 6 weeks and 20 at 12 weeks. Mean IOP was decreased at 12 weeks of treatment (mean change = -2.8 mm Hg, 95% CI [-4.5 to -1.1], $p = 0.002$; Table 2) compared to baseline. There was no significant correlation between change in IOP and change in clinical activity score or between change in IOP and change in proptosis at 12 weeks ($p = 0.546$ and 0.911 , respectively).

Conclusions: Among patients with TED, teprotumumab treatment was associated with a significant reduction in IOP, likely due to reduced orbital congestion.

CONTROL ID: 3520813

SUBMITTER (NAME ONLY): Yuka Kihara

TITLE: Detecting Double Layer Signs with OCT volumes using a 3D Convolutional Neural Network (CNN)

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The presence of a double layer sign (DLS) on structural OCT B-scans is a critical predictor for subclinical choroidal neovascularization (CNV), a stage of non-exudative type 1 macular neovascularization (MNV) before onset of exudation. We sought to develop a 3D CNN to detect DLS of any size using only structural OCT B-scans.

Methods: Eyes with a DLS and eyes with drusen (Dr), to serve as a control, were imaged using 6x6mm swept source OCT angiography (SS-OCTA, PLEX Elite 9000, Carl Zeiss Meditec, Dublin, CA). Each scan pattern consisted of 500 A-scans per B-scan with each B-scan repeated twice at each of 500 B-scan positions along the 6mm y-axis. The OCTA data was used for manual labeling of DLS and Dr; only the structural OCT was used for deep learning.

Results: A total of 232 eyes (196 patients; 173 with DLS and 53 with Dr) were imaged using the SS-OCTA scan pattern. The deep learning model for multi-region segmentation (Figure 1) labels DLS and Dr on a single B-scan image (3D-2D model). We generated dense annotations by integrating manual annotations and predicted segmentation (Figure 2). After refining the labels, we trained a final 3D convolutional model that segments volumetrically (3D-3D model). Finally, eyes with MNV were identified based on en-face projection maps of the predicted masks. Accuracy of final classification was 92.85% (3D-2D model) and 94.28% (3D-3D model). Mean intersection over union (IoU) was DLS: 31.39%, Dr: 12.23% for the 3D-2D model, and DLS: 57.36%, Dr: 25.20% for the 3D-3D model.

Conclusions: Our network can detect DLS from structural B-scans alone by applying an annotation refinement technique for 3D CNN to a dataset with coarse annotations.

CONTROL ID: 3520876

SUBMITTER (NAME ONLY): John Cheng

TITLE: Effect of Resident Involvement in Ophthalmic Surgery on Patient Outcomes: A Meta-Analysis

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study seeks to determine the effect of resident- versus attending-performed surgeries on patient outcomes in ophthalmic surgery.

Methods: This paper followed Preferred Reporting Items of Systematic Reviews and Meta-Analyses guidelines. Two independent authors searched PubMed, EMBASE, and Cochrane Library from inception to July 2020 to find studies assessing the impact of resident involvement on patient outcomes in ophthalmic cases. All included studies utilized non-overlapping patient populations. 10 patient characteristics were compared between resident and attending arms to investigate participant similarity. 24 outcome variables potentially impacted by resident involvement were compared in this analysis. Study quality was assessed using Newcastle-Ottawa Scale for cohort analysis and given a quality label per Agency for Healthcare Research and Quality standards.

Results: 17 studies were included in this meta-analysis. The highest quality studies were those that employed propensity scoring in their patient analysis. Pooled estimate of only high-quality evidence demonstrated few negative effects of resident involvement. When considering these high-quality studies, the only statistically significant effects observed in the resident-performed arm were longer operative times (mean difference, 12.04 minutes; [95% confidence interval (CI)], [3.91, 20.17]), and increased odds of unplanned return to the OR (odds ratio, 2.58; [95% CI], [1.31, 5.06]), primarily related to nonspecific early postoperative complications in different surgery types with steep learning curves. Analysis of operative time, using propensity scored papers, included 3 studies with 260 patients. Analysis of odds of requiring reoperation, using propensity scored papers, included 4 studies with 342 patients. There was no significant difference between resident- and attending-performed surgeries in 15 other measured postoperative complications in these studies. Significant heterogeneity ($I^2 > 50\%$) was present in 1 of 15 outcomes.

Conclusions: When high-quality studies are considered, resident involvement in ophthalmic surgery has few negative effects on patient success rates and appears safe in carefully selected patients. We recommend future studies on this comparison, given limited sample size of this analysis.

CONTROL ID: 3520903

SUBMITTER (NAME ONLY): Kam Chun Ho

TITLE: Prevalence, Associated Factors and Health-related Quality of Life of Dual Sensory Impairment in Residential Care Facilities in Singapore

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate the prevalence of dual sensory impairment (DSI), its associated factors and relationship with health-related quality of life (HR-QoL) in residential care facilities (RCF) in Singapore.

Methods: This was a cross-sectional study of 123 residents aged ≥ 40 years from six RCFs, conducted between 2016 and 2018. DSI was defined as concomitant presenting visual acuity (better-eye) > 0.3 logarithm of the minimum angle of resolution and a pure-tone air conduction threshold (better-ear) > 40 dBHL in any of the four tested frequencies (500, 1000, 2000 and 4000 Hz). HR-QoL was quantified using the EuroQol five-dimension questionnaire. Multivariable Poisson regression was used to determine the associated factors of DSI. Multivariable linear regression was used to determine the association between DSI and HR-QoL adjusted for traditional confounders.

Results: Of the 123 residents (age [mean \pm standard deviation] 75.3 \pm 10.8 years; 56.9% male), 97 (78.9%[95% confidence interval(CI):71.6%, 86.1%]) had DSI, with 89.4% not on follow-up care for their sensory disabilities. In multivariable models, male gender (prevalence ratio(PR) [95%CI]=1.3[1.1, 1.6]), older age (per 10-year increase (1.2[1.1, 1.3]), education ≤ 6 years (1.3[1.1, 1.7]) and the presence of cataract (1.3[1.0, 1.7]) were independently associated with DSI. DSI was in-turn independently associated with a substantial worsening in HR-QoL (β =-0.61; 95%CI: -0.76, -0.45; $p < 0.001$).

Conclusions: DSI affects four in five residential care residents and is substantially associated with reductions in HR-QoL in these residents. Our finding highlights an urgent need for the implementation of routine vision and hearing screening and follow-up care for residents living in these facilities.

CONTROL ID: 3520904

SUBMITTER (NAME ONLY): Chhavi Saini

TITLE: Incidence and Prognostic Factors for Glaucoma Progression after Corneal Transplantation in Patients with Pre-existing Glaucoma

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Saini, E.C. Davies, L. Ung, J. Chodosh, J.B. Ciolino, U.V. Jurkunas, E.I. Paschalis, R. Pineda, H.N. Saeed, J. Yin, L.Q. Shen, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|E.I. Paschalis, J. Yin, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the incidence and prognostic factors for glaucoma progression within 1-2 years following corneal transplant surgery.

Methods: Retrospective longitudinal analysis of consecutive patients with glaucoma undergoing penetrating keratoplasty (PK), Descemet stripping endothelial keratoplasty (DSEK), DSEK under previous PK, Descemet membrane endothelial keratoplasty (DMEK), or Boston keratoprosthesis I (KPro) implantation from April 2016 to December 2017 at one institution with at least 1 year of follow up. Eyes with retinal and neuro-ophthalmic pathologies were excluded. One eye per patient was included. Glaucoma was defined by a cup to disc ratio (CDR) ≥ 0.6 , CDR asymmetry of >0.2 , history of glaucoma surgery or documented diagnosis of glaucoma and was not based on intraocular pressure (IOP) or use of glaucoma medication alone. Primary outcome measure was to assess for cumulative incidence of glaucoma progression post-transplant, which was defined as CDR progression by ≥ 0.2 or need for glaucoma surgery; and was not based on visual field due to lack of reliable tests for all subjects. Prognostic factors for glaucoma progression were also assessed.

Results: 74 eyes of 74 patients undergoing PK (21), DSEK (26), DSEK under previous PK (10), DMEK (8), KPro (9) with a mean follow-up of 23.9 months (12.3-33.2 months) were analyzed. The incidence of glaucoma progression over first year post surgery was 20.3% overall; by procedure, 14.3% (PK), 27% (DSEK), 0% (DSEK under previous PK), 12.5% (DMEK), and 44.4% (KPro) Figure 1. At 2 years of follow-up, 10.8% of all patients progressed by CDR and 20.3% needed additional glaucoma surgery. Multiple logistic regression showed that KPro surgery, age at surgery, average IOP and average glaucoma medications over follow-up were independently associated with glaucoma progression ($p < 0.03$ for all, Table 1), while gender, ethnicity and additional intra operative anterior or posterior vitrectomy were not ($p > 0.5$ for all).

Conclusions: A significant proportion of glaucoma patients undergoing corneal transplantation show glaucoma progression within 1 year of having surgery. Older patients and patients undergoing KPro implantation are at the highest risk. Average follow-up IOP and glaucoma medications had a marked influence on glaucoma progression and should be carefully managed.

CONTROL ID: 3520911

SUBMITTER (NAME ONLY): Abdelrahman Fouda

TITLE: Pegylated Arginase 1 as a Treatment for Acute Central Nervous System (CNS) Injury

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Arginase 1 (A1) is the enzyme that hydrolyzes the semi-essential amino acid, arginine, to ornithine and urea. We have previously shown that A1 deletion worsens retinal ischemic injury while intravitreal treatment with a pegylated form of the enzyme (PEG-A1: recombinant human arginase covalently attached to methoxy polyethylene glycol) is protective. In this translational study, we aimed to study the utility of systemic PEG-A1 treatment in mouse models of acute retinal and brain injury.

Methods: Cohorts of WT mice were subjected to retinal ischemia-reperfusion (IR) injury, traumatic optic neuropathy (TON), or brain stroke via middle cerebral artery occlusion (MCAO) and treated with intraperitoneal injections of PEG-A1 or vehicle (PEG only). Drug penetration into the CNS tissues was measured by western blotting for PEG. Neuroprotection was measured in a blinded fashion using NeuN (neuronal marker) immuno-labeling of retina flat-mounts and quantification of brain infarct area using triphenyl tetrazolium chloride (TTC) staining. Furthermore, ex vivo retina explants and in vitro retina neuron cultures were subjected to oxygen-glucose deprivation (OGD) followed by reoxygenation (R) and treatment with PEG-A1.

Results: PEG-A1 given systemically did not cross the intact blood-retina or blood-brain barriers in sham controls but reached the retina and brain tissues after the breakdown of the permeability barriers in all tested models of acute CNS injury. Systemic delivery of PEG-A1 provided statistically significant ($p < 0.05$) neuroprotection after retinal IR injury (increasing neuronal survival to 62% vs 40% in the vehicle group), TON (increasing neuronal survival to 78% vs 62% in the vehicle group), and stroke (reducing infarct size to 34% vs 41% in the vehicle group). PEG-A1 treatment was also neuroprotective in retina explants subjected to OGD/R (73% neuronal survival as compared to 55% in untreated or 48% in PEG only treated explants). PEG-A1 treatment was not effective in promoting survival in retinal neuronal cultures exposed to OGD/R.

Conclusions: Systemic PEG-A1 administration is neuroprotective and provides an excellent route to deliver the drug to the retina and the brain after acute CNS injury.

CONTROL ID: 3521017

SUBMITTER (NAME ONLY): Simon Stock

TITLE: Evaluation of Innovative SSVEP Stimulation Patterns for Neuro-Ophthalmology

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Steady-State Visually Evoked Potentials (SSVEPs) are the brain's response to periodical optical stimuli. They are great for analyzing and investigating the function of the whole visual system. No conscious patient feedback is required.

We looked at variations of conventional checkerboard patterns to determine how onset/reversal, superimposed noise, or pictures of faces can improve the elicited signals' magnitude. The resulting comparisons may be used to improve existing SSVEP-based procedures using novel types of stimuli.

Methods: Using our custom system, we designed two stimuli sets. Set 1 using checker and faces (7s) and set 2 using dartboard, checker, and faces (6s), both at 7.5Hz. The sets were shown to two groups of 5 participants each (age: 20-30). The resulting reactions to the SSVEP were recorded using an 8-channel EEG (500 Hz) with electrodes positioned on the occiput [P07,O1,Oz,O2,P08,P03,P04,Fz]. The data was analyzed using the Canonical Correlation Analysis (CCA) calculated over the stimulation window using the stimulation frequency and harmonics. Plots represent the mean value of all subjects in the set for the CCA.

Results: Set 1 shows a significant increase in evocation when using pattern onset instead of reversal. Showing faces instead of checkers lead to a slightly increased response. Set 2 indicates that cartoon characters elicit a stronger response than a checker pattern. Through the addition of noise, the response increased at low levels but decreased at higher levels.

Conclusions: SSVEP-based assessment of neuro-visual functions has immense potential in ophthalmology. However, checkerboard stimulations do not necessarily provide the best responses. The addition of low-level noise to the stimuli might improve the generation of SSVEPs in participants. Higher-level stimulation patterns like faces could improve the responses even further.

We suggest that Researchers in Neuro-Ophthalmology consider those or similar stimulation paradigms to improve SSVEP-based objective assessment methods. Especially stimulation with more complex structures like faces could lead to promising results.

CONTROL ID: 3521030

SUBMITTER (NAME ONLY): Eva Kiessling

TITLE: Retinal deficiency of MMACHC does not lead to an ocular phenotype in mice

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Methylmalonic aciduria with homocystinuria (cobalamin deficiency cblC type) is a severe but rare disease, caused by mutations in the MMACHC gene. cblC deficiency is multi-symptomatic and often includes ophthalmic manifestations such as macular degeneration, optic nerve pallor and vascular changes that may progress to complete blindness. Cobalamin supplementation can improve some symptoms, but the ocular phenotype remains progressive, suggesting that it might result from a local dysfunction of MMACHC in the retina. Here, we tested the potential ocular consequences of a pan-retinal Mmachc knockout in mice.

Methods: Expression of human MMACHC was tested in the central and peripheral retina and retinal pigment epithelium (RPE) of donor eyes and of mice by real-time PCR. A retina-specific knockout of Mmachc (retina^{ΔMmachc}) was generated using Pax6-Cre mice to delete E3 and E4 of Mmachc in a novel Mmachc^{flox/flox} mouse line. Knockout of Mmachc was confirmed on the genomic level by PCR and on the RNA level by in situ hybridization and real-time PCR. Retinal function was tested by electroretinography, Tissue integrity was investigated by light microscopy and immunofluorescence of tissue sections as well as by fundus imaging, optical coherence tomography and angiography. Metabolites were measured by LC-MS/MS and reversed-phase HPLC.

Results: MMACHC was stably expressed in human retina and RPE up to 91 years of age and in mice from day 1 to 365. In retina^{ΔMmachc} mice, expression of Mmachc was absent in the peripheral retina but was not affected in the central retina or the RPE. The overall reduction of Mmachc expression in the retina of retina^{ΔMmachc} mice was 76±4%. Retinas of knockout mice showed an elevation of cblC-related metabolites including methylmalonic acid (5.6-fold) and homocysteine (1.6-fold) that are known to accumulate also in the serum of patients. However, retinal morphology and function in knockouts was normal up to 1 year of age.

Conclusions: Our data indicate that Mmachc deficiency in the neuronal retina does not lead to ocular impairments in mice. It may be possible, that other supporting cells that do not carry the knockout allele, such as endothelial cells or the RPE, may help to nourish the cells of the retina to compensate them for their lack of Mmachc.

CONTROL ID: 3521031

SUBMITTER (NAME ONLY): Jakob Grauslund

TITLE: Diabetic retinopathy as a marker of prevalent and incident obstructive sleep apnea in type 2 diabetes: results from a national screening program.

SESSION TITLE: DR: Epidemiology and service provision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: In previous smaller studies, associations have been demonstrated between diabetic retinopathy (DR) and obstructive sleep apnea (OSA), but this has not been tested in national cohorts, and it is not known, if the level of DR acts as an independent predictive marker for OSA. This study aimed to assess the association between DR and OSA, and to evaluate if DR may serve as an independent risk factor of incident OSA.

Methods: As part of the Ocular And Systemic complications In diabetic retinopathy Study (OASIS), we performed a cross-sectional and 5-year longitudinal registry-based cohort study. Data of exposure and outcome as well as systemic morbidity and use of medications were identified in national registers including the Danish Registry of Diabetic Retinopathy (DiaBase), the Danish National Patient Register, the Danish National Prescription Registry, and the Danish Civil Registration System. The index date was defined as the date of the first DR screening registered in DiaBase.

For cases, we included 153,238 patients with type 2 diabetes, who had attended diabetic eye screening and were registered in DiaBase. Each of these were matched by five control persons without diabetes of the same age and gender (n=746,148).

Present and level-specific DR were used as exposures, and main outcomes were crude, age- and sex-adjusted, and multivariable adjusted odds ratio (OR) for prevalent OSA as well as hazard ratio (HR) for 5-year incident OSA.

Results: OSA was present in 5.8% and 2.0% of cases and controls. As compared to persons without diabetes, patients with type 2 diabetes were independently more likely to have prevalent OSA (OR 2.01, 95% CI 1.95-2.08) and to develop OSA within five years (HR 1.55, 95% CI 1.46-1.64). In comparison with cases without DR at the index date, those with DR were less likely to have prevalent (OR 0.57, 95% CI 0.52-0.62) and to develop incident OSA (HR 0.86, 95% CI 0.74-0.99).

Conclusions: In a registry-based national cohort study of 153,238 patients with type 2 diabetes and 746,148 non-diabetes controls, cases had a higher risk of OSA, but the risk of prevalent and 5-year incident OSA were 43% and 14% lower in those with DR, which identifies DR as a marker of reduced risk of OSA.

CONTROL ID: 3521048

SUBMITTER (NAME ONLY): Sabine Kling

TITLE: Biomechanical characterization of a Col5a1^{+/-} mouse model of classic type Ehlers-Danlos syndrome with tensile extensometry and OCT elastography

SESSION TITLE: Keratoconus and Corneal Biomechanics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To quantify biomechanical properties in a Col5a1^{+/-} mouse model for classic type Ehlers-Danlos syndrome (EDS) and to compare two different measurement approaches suited for murine corneal mechanical characterization.

Methods: A total of 14 adult eyes, 90 days old, of a Col5a1-haploinsufficient mouse model (Col5a1 het) and 14 eyes of the same age of wild-type littermates (wt) were analyzed by optical coherence elastography (OCE) and 2D stress-strain extensometry. Quasi-static OCE was conducted non-invasively during ambient pressure modulation by -3 mmHg. Corneal displacements were analyzed by phase-difference processing. 2D extensometry measurements consisted of a pre-conditioning cycle, followed by a stress-relaxation test and finally a rupture test.

Results: Compared to wt corneas, Col5a1 het corneas had a thinner corneal thickness (125±11 vs 148±10 mm, p<0.001). Short-term elastic modulus in Col5a1 het corneas was significantly increased in OCT measurements (506±88 vs 430±103 kPa, p=0.023), and the same trend was observed in stress-strain extensometry (30.7±12.1 vs 21.5±5.7 kPa, p=0.057). In contrast, in stress relaxation tests, Col5a1 het corneas experienced a stronger relaxation (55% vs 50%, p=0.010). The two distinct behaviors indicate increased short-term stiffness and reduced long-term stiffness in het corneas.

Conclusions: A reduced expression of collagen V in cornea seems to predominantly affect the viscoelastic properties of the tissue. The results presented here support and rationalize the counterintuitive clinical reported findings, in which even thinner corneas with potential alterations in the structure of collagen manage to maintain a normal topographic pattern.

CONTROL ID: 3521061

SUBMITTER (NAME ONLY): Guillermo Lehmann

TITLE: Identification and spatial distribution of novel molecular features of adult human corneal cell subtypes

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The human cornea has been defined as our “external window” to the visual world that serves as a barrier against the outside environment and as the main refractive lens to focus light into the retina. The histological structure is defined by three layers of cellular elements (epithelium, stroma, endothelium) and two layers of extracellular membranes. Here, we used a combination of single-cell RNA sequencing and in-situ hybridization to characterize the transcriptomic features of different cells and their localization in the human cornea

Methods: Six adult human corneas from healthy donors were processed by sequential tissue digestion and cell sorting. Single-cell suspensions were profiled using 10x Genomics Chromium Single Cell 3' (v2) Gene Expression workflow. Spatial distribution of cell markers was localized by RNA in situ hybridization (RNAscope) in human cornea cross-sections.

Results: Unsupervised clustering of individual cell transcriptomes based on overall gene expression similarity identified 16 transcriptionally distinct clusters within corneal cells, including stromal keratocytes, endothelium, several subtypes of corneal epithelium, and supportive cells in the limbal stem cell niche. Epithelial cells represent the most diverse cell type with eleven sub-clusters. By combining pseudotime bioinformatic analysis and RNAscope we mapped the epithelial cell fate trajectory and location including their initial generation in the limbal region, differentiation, and migration to superficial epithelial layers.

Conclusions: Our study reveals the single-cell map of the adult human cornea and expands the knowledge of the molecularly define cellular subsets of the cornea on a whole genome transcriptional level. This information can be applied to better understand normal corneal biology, serve as a reference to study corneal diseases, and provide potential insights into disease pathology and therapeutics.

CONTROL ID: 3521085

SUBMITTER (NAME ONLY): Mireille Jabroun

TITLE: Differential Corneal Thickness in Pediatric Eyes Implanted with Glaucoma Drainage Devices

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Children implanted with glaucoma drainage devices are at life-long risk of corneal decompensation. We evaluated the corneal thickness in different quadrants of pediatric eyes implanted with Ahmed glaucoma valve (AGV), as a surrogate indicator of early possible corneal endothelial compromise.

Methods: Corneal thickness in 28 eyes of 23 children (age: 0.8 to 12.8 years; mean: 4.8) successfully implanted with superotemporal AGV was compared to thickness in 63 eyes of 40 glaucomatous children of similar age (0.25 to 13.8 years; mean:3.5) without AGV implantation. Thickness was measured in both groups centrally and in the superotemporal, superonasal, inferotemporal and inferonasal quadrants using ultrasound pachymetry. Measurements were taken at 13.5 ± 8 months post valve implantation and without clinical evidence of tube-cornea touch. The study was conducted at Cairo University Hospitals

Results: The mean corneal thickness was greater in all quadrants in the AGV group, with the central (645 ± 112 vs 590 ± 93 μm ; $P = 0.02$) and superotemporal quadrant (695 ± 90 vs 634 ± 88 μm ; $P < 0.01$) being statistically significant. The superotemporal quadrant was the thickest of all quadrants ($P = < 0.01$) in the AGV but not in the control group. The difference in thickness between the superotemporal and the inferonasal (the furthest away from the tube end) quadrants was significantly higher in the AGV group (38.9 ± 53.3 vs 0.3 ± 35.3 μm ; $P = < 0.01$) indicating a localized subclinical corneal edema likely secondary to the tube implant.

Conclusions: The superotemporal corneal quadrant is significantly the thickest of all quadrants in eyes with a superotemporally implanted Ahmed valve, even in the absence of clinical evidence of tube-cornea touch. Ultrasound pachymetry is a useful tool to monitor for corneal decompensation in children where spectral microscopy is not feasible.

CONTROL ID: 3521101

SUBMITTER (NAME ONLY): Sharon Sabapathypillai

TITLE: Rate of falls, fear of falling, and avoidance of activities at-risk for falls in older adults with glaucoma

SESSION TITLE: Visual Impairment - Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Sabapathypillai, M. Goel, B. Wilson, M. Gordon, A. Bhorade, Ophthalmology, Washington University in St Louis, St Louis, Missouri, UNITED STATES|S. Sabapathypillai, SOM, University of Missouri Kansas City, Kansas City, Missouri, UNITED STATES|M. Perlmutter, Occupational Therapy, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the relationship between glaucoma severity and rate of falls, fear of falling, and avoidance of activities at-risk for falls.

Methods: Cross-sectional study. Glaucoma patients (n=138), ages 55-90 years, with mild (n=61), moderate (n=54), and advanced (n=23) glaucoma in the better eye based on Hoddap-Anderson-Parish glaucoma staging system, and age-matched controls (n=50) were recruited from the Eye Clinics at Washington University, St. Louis, MO. Participants completed questionnaires regarding rate of falls, fear of falling, and avoidance of activities at-risk for falls.

Results: Of the glaucoma participants, 36% reported at least one fall in the prior 12 months compared to 20% of controls (adjusted odds ratio [OR], 2.7; 95% CI, 1.18-6.17; p=0.018). Compared to controls, the mild glaucoma group trended towards a higher fall risk (adjusted OR, 2.43; 95% CI, 0.97-6.08; p=0.059) and the advanced group had the highest fall risk (adjusted OR, 7.97; 95% CI, 2.44-26.07; p=0.001). A high fear of falling and high avoidance of activities at-risk for falls relative to controls began at the moderate stage of glaucoma (adjusted OR, 4.66; 95% CI, 1.24-17.49; p=0.023 and adjusted OR, 4.49; 95% CI, 1.34-15.05; p=0.015, respectively).

Conclusions: Patient education, interventions, and appropriate referrals to minimize fall risk should be considered in patients with early glaucoma and continue with advancing disease. Decreasing a patient's rate of falls may decrease their fear of falling and avoidance of at-risk activities. Early reduction of rates of falls, fear of falling, and avoidance of activities at-risk for falls will not only decrease patient morbidity and mortality but also improve patients' emotional and social well-being.

CONTROL ID: 3521230

SUBMITTER (NAME ONLY): Aaron Coyner

TITLE: A risk model for early detection of treatment-requiring retinopathy of prematurity using a deep learning-derived vascular severity score

SESSION TITLE: Retinopathy of prematurity/vein occlusion

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Kalpathy-Cramer, P. Singh, Radiology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Kalpathy-Cramer, P. Singh, Center for Clinical Data Science, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|J.S. Chen, A. Hanif, J. Campbell, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|A.S. Coyner, K. Sonmez, Medical Informatic and Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D. Erdogmus, Electrical and Computer Engineering, Northeastern University, Boston, Massachusetts, UNITED STATES|R.V. Chan, Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a leading cause of blindness in children, although it is often preventable with accurate and timely diagnosis and treatment. ROP screening guidelines are designed to be highly sensitive to avoid missing cases of treatment-requiring (TR-) ROP; consequently, approximately 80% of exams in a screening population have no or mild disease. Current ROP risk models require multiple predictors and/or exams, and performance often decreases significantly when applied to more diverse populations. We aimed to develop a risk model that could reduce the screening burden without missing cases of TR-ROP by using demographic risk factors and a deep learning-derived vascular severity score (VSS, all of which can be evaluated during a single exam) using a large cohort of North American infants.

Methods: A multi-institutional ROP dataset consisting of retinal fundus images and clinical factors for 852 subjects was collected as part of the Imaging and Informatics in ROP (i-ROP) study. A reference standard ROP diagnosis was provided for each exam. Posterior pole images were assigned a vascular severity score ranging from 1.0 to 9.0. Considering that infants who develop TR-ROP often have increasing VSS prior to the diagnosis of TR-ROP, we developed a risk model based on demographic risk factors and the VSS at 32-33 weeks post-menstrual age. Using all combinations of birth weight, gestational age (GA), and VSS, 7 ElasticNet logistic regression models were tuned via 5-fold cross-validation. The best-performing model was evaluated using the held-out i-ROP test dataset consisting of 121 infants, and an independent dataset of 30 infants screened as part of a telemedicine program in Salem, OR.

Results: The best performing model used GA and VSS, based on the area under the precision-recall curve (Table 1). On each independent test set, the model achieved sensitivity of 100% with a positive predictive value ranging from 12% to 18%, and specificity ranging from 55% to 68% with a negative predictive value of 100% (NPV, Table 2).

Conclusions: This model, with just two predictors which can be collected during a single exam, can identify all subjects who will eventually develop TR-ROP, while correctly ruling out, with 100% NPV, more than half of those who will not.

CONTROL ID: 3521285

SUBMITTER (NAME ONLY): Michael James Gilhooley

TITLE: Compressed L7 promoter directed delivery of optogenetic tools for vision restoration

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Gilhooley, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Gilhooley, Neuro-ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|M. Lindner, S. Hughes, M. Hankins, University of Oxford Nuffield Laboratory of Ophthalmology, Oxford, Oxfordshire, UNITED KINGDOM|M. Lindner, Institut für Physiologie und Pathophysiologie, Philipps-Universität Marburg, Marburg, Hessen, GERMANY|

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ABSTRACT BODY:

Purpose: Basic levels of visual restoration have been achieved following delivery of light sensitive proteins to the surviving cells of the degenerate retina (optogenetics). Restricting delivery to specific cell populations demonstrates functional advantage over 'non-specific,' high efficiency promotor-based systems but cell specific promoters can often be too large for adeno-associated viral vector (AAV) envelopes. Here we repurposed a compressed promoter complex termed 'L7-6' derived from the L7 (pcp2) promoter to test the hypothesis that it can be used to restrict delivery of a functional optogenetic tool to retinal ON-bipolar cells using AAV in a mouse model.

Methods: At P45, retina-degenerate mice lacking native melanopsin ($Pde^{rd1/rd1} Opn4^{-/-}$) received intravitreal injections of saline or AAV2.2 containing the human melanopsin gene (hOpn4) driven by the L7-6 promotor construct (n=8 per group, 4 male, 4 female). Flat mount immunohistochemistry (IHC) (n=4 per group) and multiple electrode array (MEA) recordings of retinal ganglion cell (RGC) light responses (n=4 per group) were performed on intact retina explants 8 weeks post injection with a range of intensities of light. Comparisons of means were performed by unpaired t-test.

Results: L7-6.hOPN4 treated retinæ demonstrated IHC staining for hOPN4 restricted to $17.75 \pm 3.54\%$ of L7+ bipolar cells in the inner nuclear layer & $1.44 \pm 0.14\%$ of all cells in the GCL (N=4, n=16) compared to $0.00 \pm 0.00\%$ cells in either layer in the saline group ($p < 0.0001$). On MEA, 38 electrodes responded to a 480nm light at 10^{15} photons $cm^{-2} s^{-1}$ in the L7-6.hOPN4 treated (n=0 saline, $p < 0.0001$). A sigmoidal irradiance-response relationship was seen in the treatment group with an EC_{50} of 13.30 ± 0.08 photons $cm^{-2} s^{-1}$.

Conclusions: The L7-6 promotor can be used to deliver a functional melanopsin to retinal ON-bipolar cells using intravitreally delivered AAV vector. This provides a further method to replicate the power of cell-specific melanopsin optogenetics previously demonstrated in transgenic L7.Cre.lox mouse models.

CONTROL ID: 3521380

SUBMITTER (NAME ONLY): Penny Asbell

TITLE: Analysis of Longitudinal Antibiotic Susceptibility Trends in Staphylococci: Results from 12 Years of the ARMOR Study

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.A. Asbell, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|C.M. Sanfilippo, H.H. DeCory, Medical Affairs, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Staphylococci are among the most common causative bacteria in ocular infections, and antibiotic resistance in these pathogens may lead to treatment failure. The Antibiotic Resistance Monitoring in Ocular microorganisms (ARMOR) surveillance study informs on evolving antimicrobial susceptibility patterns in ocular bacterial pathogens. Here, we analyzed in vitro antibiotic resistance among staphylococcal isolates collected from 2009 through 2020 to date in ARMOR for trends over time.

Methods: Each year in ARMOR, *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS) isolated from ocular infections are collected and sent to a central laboratory for species confirmation and susceptibility testing. Minimum inhibitory concentrations (MICs) are determined and interpreted as susceptible/resistant to 16 different antibiotics based on Clinical and Laboratory Standards Institute methods and breakpoints. Data for resistance to various drugs among 2599 *S. aureus* and 2143 CoNS were evaluated here using the Cochran-Armitage test for linear trends in a proportion.

Results: Trend analysis showed a decrease in methicillin resistance (MR) among *S. aureus* (39 to 36%; $P < 0.001$) but no change in MR among CoNS (~50% each year $P = 0.176$). Additional decreasing trends in resistance were noted to azithromycin (62% to 57%), ciprofloxacin (39% to 33%), and tobramycin (24% to 16%) among *S. aureus* ($P < 0.001$ for all), and to ciprofloxacin among CoNS (46% to 26%; $P < 0.001$). In contrast, resistance increased to tetracycline among *S. aureus* (4% to 7%; $P = 0.034$) and to trimethoprim among CoNS (26% to 28%; $P = 0.026$). Multidrug resistance (≥ 3 antibiotic classes) among methicillin-resistant strains remained prevalent in 2020, although no isolates were vancomycin resistant. Besifloxacin retained consistently low MICs, with 2020 MIC₉₀s (1 $\mu\text{g/mL}$ for *S. aureus* and 2 $\mu\text{g/mL}$ for CoNS) up to 128-fold lower than other fluoroquinolones.

Conclusions: Over a 12-year span, staphylococci generally exhibited minimal or no change in in vitro antibiotic resistance. Although a small decrease in MR was observed among *S. aureus* (but not CoNS), the high level of MR in staphylococci warrants attention when selecting empiric antibiotic therapy, particularly with respect to multidrug resistance in these organisms.

CONTROL ID: 3521450

SUBMITTER (NAME ONLY): Cintia De Paiva

TITLE: Effects of age, TNF- α and calorie restriction on cathepsin S and other inflammatory markers in the lacrimal gland

SESSION TITLE: Lacrimal gland and Meibomian gland

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.S. De Paiva, A. Lee, K.E. Mauk, Z. Yu, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|E.N. DeJong, D.M. Bowdish, McMaster University, Hamilton, Ontario, CANADA|A.I. Sindikubwabo, R. Korstanje, Jackson Laboratory, Bar Harbor, Maine, UNITED STATES|H.P. Makarenkova, The Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Calorie restriction reduces the expression of inflammation and increases life span in many organisms. Aged C57BL/6 (B6) lacrimal glands (LGs) have increased inflammation and Th1 infiltration. In this study, we investigate the effects of calorie restriction (CR) or loss of Tnf- α . on the expression of Cathepsin S and markers of inflammation in the LGs of mice during aging.

Methods: B6 mice were used at 2-4, 12, and 24M of age. A separate group of 6M B6 mice received 40% CR or had food ad libitum (AL) for 4M. Young (2-4M) and aged (19-24M) TNF- $\alpha^{-/-}$ were compared to WT mice. LGs were excised and used for histology or gene expression analysis using qPCR. The number of inflammatory foci (>50 cells) was counted under a 10X microscope lens. H&E-stained LGs were scanned, photographed, and image analysis was used to calculate focus score/4mm² and foci area of foci (μm^2). Expression of TNF- α , IL-1 β , IFN- γ , MHC II, IL12, and Ctss was investigated by real-time PCR.

Results: A progressive increase in TNF- α (1.7 and 1.9-fold) and IFN- γ (2.8 and 6.2-fold) was observed in 12 and 24M B6 LGs (P<0.001). Expression of Ctss, MHC II, and IL-12 peaked at 12M (7, 5.8, and 122-fold, respectively, P<0.001) and remained significantly elevated at 24M (3.6, 3.6, and 56-fold, respectively, P<0.001). IL-1 β levels were increased at 24M (2.3-fold, P<0.001). 40% CR significantly decreased TNF- α (46%), IFN- γ (60%), MHC II (64%), Ctss (46%), and IL12 (81%) (all P<0.05) but not IL-1 β mRNAs. Aged TNF- $\alpha^{-/-}$ LGs had a 50% decrease in lymphocytic infiltration compared with aged WT (1 \pm 0.7 vs. 2 \pm 0.8 focus score/4mm², P<0.01) and smaller foci area (47046 \pm 34745 vs. 95730 \pm 49794 μm^2 , P=0.008). A significant increase in TNF- α (3-fold), IFN- γ (9.7-fold), MHC II (10-fold), IL-12 (260-fold), Ctss (7.2-fold), and IL-1 β (3.4-fold) mRNA was observed in aged WT compared with young WT LG (P<0.01). However, IFN- γ (1.3-fold), MHC II (4.4-fold), IL-12 (53-fold), and Ctss (2-fold) mRNA levels were decreased in aged TNF- $\alpha^{-/-}$ compared to WT LGs (P<0.01), but not IL-1 β (1.7 fold).

Conclusions: Taken together, our results indicate that anti-inflammatory therapies (such as CR) or inhibition of TNF- α can ameliorate the age-related increase in cytokine production, and in particular, Ctss, and can decrease LG inflammation. Further studies are needed to evaluate the role of Ctss during aging-related inflammation.

CONTROL ID: 3521466

SUBMITTER (NAME ONLY): DaNae Woodard

TITLE: Clinically-Identified C-terminal Mutations in Fibulin-3 are Prone to Misfolding and Destabilization

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Woodard, E. Nakahara, J. Hulleman, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): DaNae Woodard: Commercial Relationship: Code N (No Commercial Relationship) | Emi Nakahara: Commercial Relationship: Code N (No Commercial Relationship) | John Hulleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Distinct mutations in fibulin-3 (F3), a secreted extracellular matrix glycoprotein, have been associated with various ocular diseases including Malattia Leventinese (ML, p.R345W), primary open angle glaucoma (POAG, p.R140W), and age-related macular degeneration (AMD, p.D49A). Previous research has demonstrated that the R345W mutation, which causes ML, appears to lead to protein misfolding and inefficient secretion. However, it is unclear whether other potentially pathogenic or clinically-identified F3 variants reported in the human population also share these features, which we have tested herein.

Methods: Fifteen synonymous and missense mutations located throughout the F3 gene (EFEMP1) were identified using clinical databases. Site-directed mutagenesis was performed to generate the variants. F3 constructs were expressed in HEK293A and ARPE-19 cells and secretion/intracellular F3 levels were monitored by western blotting. Equal expression was confirmed by quantitative PCR.

Results: Of the fifteen new variants, only a single leucine (Leu) to phenylalanine (Phe) mutation at 451 (L451F) in the C-terminal fibulin type domain caused a significant ($p < 0.01$) secretion defect relative to WT F3 ($n \geq 6$). This mutation was found in two unrelated individuals, one with retinal dystrophy and the other with nystagmus. Surprisingly, charged (Arg, Asp), aromatic (Phe, Trp, Tyr), and restrictive (Pro) residues appear to be disfavored at this 451 position, also causing secretion defects ($p < 0.05$). Furthermore, the L451F variant relies heavily on N-linked glycosylation at Asn249 for secretion, consistent with observations made with R345W F3, suggesting that this new variant is also intrinsically unstable.

Conclusions: Secretion defects are not a shared feature of all pathogenic or clinically-identified F3 variants. The previously identified disease-associated D49A (cuticular AMD) and R140W (POAG) F3 variants displayed no signs of misfolding. The novel L451F variant has molecular properties very similar to that of R345W, suggesting that it is likely misfolded, intrinsically unstable, and potentially contributes to ocular disease.

CONTROL ID: 3521501

SUBMITTER (NAME ONLY): Oleksandra Kovalova

TITLE: Serial treatment of uveitis with intravitreal injections of Methotrexate during the COVID-19 pandemic

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Kovalova, K. Kapoor, Wagner and Kapoor Research Institute, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Oleksandra Kovalova: Commercial Relationship: Code N (No Commercial Relationship) | Kapil Kapoor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveitis is potentially sight-threatening and typically managed with steroids. However, chronic steroid therapy has known systemic and ocular adverse effects. Intravitreal methotrexate (MTX) is a unique option for local treatment that is steroid-sparing, but also immunosuppressive and anti-inflammatory. The purpose of our research is to assess the efficacy of serial intravitreal injections of MTX for uveitis.

Methods: This was a retrospective case series, reviewing three patients with non-infectious uveitis who received a series of intravitreal MTX from February to November 2020. Complete eye exams were performed at baseline and during each follow-up after the initial treatment, with recordings of key outcome measures including cystoid macular edema as measured by foveal thickness, intraocular pressure (IOP), visual acuity (VA), and anterior chamber activity.

Results: Three patients (2 female and 1 male) were diagnosed with panuveitis (33.3%) and posterior uveitis (66.7%) with mean age of 62.3 (59-68). Two patients received a series of three MTX injections (0.04ml of 25mg/ml) at one month intervals followed by one injection every three months thereafter; another patient received intravitreal MTX monthly without interval extension. Patient A formerly took 60 mg oral Prednisone daily, and reduced to 30 mg daily after bridging to local MTX without relapse; patient B received Ozurdex treatment that did not have interval extension but did have reduction in CME. Patient C had reduction in topical steroid therapy. The mean foveal thickness at baseline was 345 (range 248-469) and improved to 316 (range 361-397). Anterior chamber activity improved on average from a baseline of 1+ Cell/Flare to Trace Cell/Flare. The average IOP was in target range between 8-16 mmHg throughout treatment. The average VA improved by one line in the affected eye by the end of the studied treatment courses.

Conclusions: After initiation of intravitreal MTX treatments, all patients achieved measurably decreased clinical signs of inflammation and/or achieved significant reduction in steroid treatment. More research with randomized trials is needed to further elucidate the role of intravitreal MTX as a local steroid-sparing agent for uveitis. It may play an expanded role during the pandemic when systemic immunosuppression is relatively contraindicated and rheumatology support is less achievable.

CONTROL ID: 3521517

SUBMITTER (NAME ONLY): Marian Blazes

TITLE: Associations between retinal artery/vein occlusions (RAVO) and risk of vascular dementia

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Blazes, R.T. Yanagihara, A.Y. Lee, C.S. Lee, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|M.L. Lee, L.E. Gibbons, P.K. Crane, Department of Medicine, University of Washington, Seattle, Washington, UNITED STATES|J.P. Kam, Kaiser Permanente Washington, Seattle, Washington, UNITED STATES|E.B. Larson, Kaiser Permanente Washington Health Research Institute, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether RAVO is associated with risk of developing vascular dementia, Alzheimer's disease (AD), or all-cause dementia. Although retinal artery/vein occlusions are ophthalmic complications of systemic vascular pathology and vascular disease is a risk factor for AD and related dementia in older adults, associations between RAVO and dementia risk are unknown.

Methods: Data from Adult Changes in Thought (ACT) study participants were analyzed. This prospective, population-based cohort study recruited older adults (age ≥ 65) who were dementia-free at enrollment and followed them biennially for development of AD, vascular dementia, and all-cause dementia based on research criteria. The diagnosis of dementia and types were made based on consensus conference consideration of all relevant data. RAVO diagnoses were extracted from electronic medical records. Cox-regression survival analyses were stratified by APOE $\epsilon 4$ status (any $\epsilon 4$ versus none) and adjusted for sex, race, education, and smoking history. Secondary analyses controlled for potential confounders including diabetes, hypertension, congestive heart failure, coronary artery disease, transient ischemic attack, carotid endarterectomy, and ophthalmic comorbidities.

Results: On review of 41,216 person-years (4,743 participants), 266 had RAVO. Those with at least one APOE $\epsilon 4$ allele who developed RAVO had > four-fold higher risk for vascular dementia (HR 4.54, 95% CI 1.86, 11.10, $p = 0.001$) than those without RAVO.(Figure) When including other cerebrovascular disease in the model, the risk was three-fold higher (HR 3.06, 95% CI 1.23, 76.2). None of the other conditions evaluated in secondary analyses were found to confound this relationship. This association was not found in people who lacked APOE $\epsilon 4$ alleles (HR 1.03, 95% CI 0.37, 2.80). No significant associations were found between RAVO and AD or all-cause dementia in either APOE group.

Conclusions: Older dementia-free individuals who present with RAVO and carry at least one APOE $\epsilon 4$ allele are at higher risk for developing vascular dementia.

CONTROL ID: 3521585

SUBMITTER (NAME ONLY): Kyoko Murase

TITLE: Evaluation of unfolding speed and rotational stability of toric intraocular lenses under compression

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Murase, Y. Nakahata, S. Nagasaka, Y. Soda, IOL Development Dept., Eye Care Div.,, Kabushiki Kaisha Nidek, Gamagori, Aichi, JAPAN|I. Ota, Ganka Miyake Byoin, Nagoya, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: Causes of postoperative misalignment of toric IOLs include intraoperative axial misalignment and lens rotation due to capsular contraction. Hence, toric IOLs that unfold at an appropriate speed are beneficial because they allow intraoperative correction of misalignment and may be rotationally stable postoperatively. This study evaluates the unfolding speed of toric IOLs from various manufacturers and compares the rotation of toric IOLs under compression. Additionally, the fixation stability was clinically assessed in the early postoperative period.

Methods: The following toric IOLs were evaluated: XY1AT5 (HOYA), ZCV300 (Johnson and Johnson Vision), SN6AT5 (Alcon), and NS60YT5 (NIDEK) [20.0 D, three samples each]. The IOLs were held with forceps for 20 seconds at room temperature, and then the time for complete optic unfolding was measured in 20 to 29°C water bath (3°C increments). The position of the haptics were fixed to measure the magnitude of rotation of the optic when the IOLs were compressed from 10.0 mm to 9.0 mm. Additionally, the magnitude of rotation was calculated for a IOL with respect to the planned axis at 1 day, 1 week and 1 month postoperatively.

Results: All lenses unfolded faster at higher temperatures. The smallest difference in unfolding speeds at 20°C and 29°C was 30 seconds with the NS60YT5 IOL and the largest was 76 seconds with the ZCV300 IOL. On compression, the optics of all the lenses rotated. ZCV300 had the greatest magnitude of rotation at 6.5° and the SN6AT5 rotated the least at 5.0°. The planned-versus-actual rotation for NS60YT5 was, 3.0±1.7° at 1 day, 3.2±2.2° at 1 week and 2.4±1.3° at 1 month postoperatively.

Conclusions: Unfolding speed and rotation under compression were evaluated with toric IOLs in vitro. NS60YT5 had the smallest difference in unfolding speed due to temperature. ZCV300 had the largest rotation under compression. The amount of rotation for NS60YT5 from 1 day to 1 month postoperatively was no larger than 5 °.

CONTROL ID: 3521645

SUBMITTER (NAME ONLY): Masakazu Hirota

TITLE: Automatic Measurements of Eye Movements using Video Oculography and Single Shot MultiBox Detector

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hirota, T. Hayashi, Orthoptics, Teikyo Daigaku, Itabashi-ku, Tokyo, JAPAN|M. Hirota, T. Hayashi, E. Watanabe, Y. Inoue, A. Mizota, Ophthalmology, Teikyo Daigaku, Itabashi-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: The purpose of this study was to develop a technique that would combine video oculography (VOG) with single shot multibox detector (SSD) to accurately and quantitatively examine eye movements.

Methods: Eleven healthy volunteers (21.3 ± 0.9 years) participated in this study. Eye movements were recorded during the tracking of the target using a custom-made eye tracker based on EMR-9 (NAC Image Technology Inc.). The subjects were asked to fixate on the nose of the rabbit-like target (visual angle was 0.1°) that was manually moved to a distance of 1 meter by the examiner during the eye movement test. The test produced 500 images from the VOG external camera and these images were divided into 3 groups (300, 100, and 100) for training, verification, and testing. The performance of the SSD was evaluated with 75% average precision (AP_{75}), and the relationship between the location of the fixation target (calculated by the SSD) and the positions of both eyes (recorded by the VOG) was analyzed.

Results: The AP_{75} of the SSD on one class of targets was 97.7%. The horizontal and vertical target locations significantly and positively correlated with the horizontal dominant (horizontal, adjusted $R^2 = 0.984$, $P < 0.001$; vertical, adjusted $R^2 = 0.955$, $P < 0.001$) and nondominant (horizontal, adjusted $R^2 = 0.983$, $P < 0.001$; vertical, adjusted $R^2 = 0.964$, $P < 0.001$) eye positions.

Conclusions: Our findings suggest that using VOG with SSD is suitable to evaluate eye version movements in the standard clinical assessment.

CONTROL ID: 3521656

SUBMITTER (NAME ONLY): Myungjo J. Kim

TITLE: Cyclosporine A Dispersion without Surfactants Reveals its True Efficacy in Dry Eye Syndrome

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Kim, E. Kyoung, K. Kim, R&D Center, SCAI Therapeutics, Daejeon, KOREA (THE REPUBLIC OF)|C. Kim, J. Yang, Department of Ophthalmology, Busan Paik Hospital, Inje University College of Medicine, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Due to a poor solubility of cyclosporine A in water, conventional eyedrops for dry eye syndrome (DES) include surfactants that may cause burning sensation, stinging pain, blurred vision, and eye redness. To develop a patient-friendly eyedrop for DES, we prepared a surfactant-free dispersion of cyclosporine A (D-CsA) and evaluated its efficacies in a murine model.

Methods: D-CsA was prepared as a surfactant-free dispersion in water based on our proprietary technology. DES of 12- to 16-week-old NOD.B10.H2^b mice was induced by daily injections of scopolamine hydrobromide in a low humidity (30~40%) environment for 10 days. Efficacies were evaluated with three eyedrops (Vehicle, 0.05% Restasis, and 0.001% D-CsA) that were bilaterally given 5 µL/eye each twice a day, over 10 treatment days. (n=4 for each group)

Results: When treated with D-CsA, tear production increased more than 4-fold on day 5 already (cf. 10 days required for Restasis) and reached 6.3-fold on day 10. While scores of Restasis in corneal smoothness, fluorescein staining, and epithelial cell detachment, did not or barely changed over 10 days, those of D-CsA were drastically improved by 42.6%, 50.5% and 52.4%, respectively. Their conjunctival efficacies were confirmed to be comparable in goblet cell density and mucin-stained cell density, which increased around 2.2-fold and 2.5-fold, respectively.

Conclusions: We have demonstrated enhanced overall efficacies of D-CsA eyedrop for DES, particularly in tear production, goblet cell density, and corneal recovery. Given the fact that there is no surfactant used in the eyedrop, this demonstration exhibits the true intrinsic efficacies of CsA for DES which have been inevitably veiled in oils and surfactants. We expect that this formulation would provide a pain-free solution to chronic DES patients worldwide.

CONTROL ID: 3521758

SUBMITTER (NAME ONLY): George Berrett

TITLE: Adult gonococcal conjunctivitis: case series in the United Kingdom (UK)

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.B. Berrett, Ophthalmology, NHS Grampian, Aberdeen, Aberdeen, UNITED KINGDOM|Z.K. Johnson, M. Schmid, M. Narayanan, F.C. Figueiredo, Ophthalmology, NHS Newcastle Gateshead Clinical Commissioning Group, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|F.C. Figueiredo, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Gonococcal infections are rising in the Western world, as reflected in both the UK where case rates have increased by 90.3% from 2016 to 2019, and the United States, where rates have risen by 63.2% from 2014 to 2018. We suspect a corresponding increase in the incidence of adult gonococcal conjunctivitis (GC), and thus aim to investigate the incidence of the condition in a tertiary hospital in the UK, and further describe its clinical characteristics.

Methods: We report a retrospective, non-comparative, consecutive case series of all adult patients with either confirmed gonococcal growth on culture or positive gonococcal PCR, presenting to the Eye Emergency Department (EED) at the Royal Victoria Infirmary, Newcastle upon Tyne, UK between January 2014 and November 2019. Incidence, demographics and clinical course of these patients are presented, including clinical features, complications and organism sensitivities. Three cases are described further to illustrate the complications of pseudo-pterygia and secondary orbital inflammation.

Results: Of 122,694 EED attendances, 15 patients were included. Incidence increased in the latter years of the period, with 11 cases (73.3%) occurring in 2018-2019. The average patient was 21.3 years old (SD 6.2; range 18-28) and male (73.3%). Of twelve patients with adequate documentation, all presented with unilateral conjunctival injection and purulent discharge. Eight (66.6%) had reduced best corrected visual acuity, of which three (25%) were marked (20/60 or worse). Significant periorbital swelling occurred in eight patients (66.6%), and photophobia, malaise and painful eye movements were seen infrequently. Four patients (26.7%) required admission, including two with features of orbital inflammation. One patient remains under review for severe corneal scarring secondary to a large pseudo-pterygium, but the others recovered fully. Each organism identified was susceptible to ceftriaxone and ciprofloxacin.

Conclusions: Adult gonococcal conjunctivitis is a rare but sight threatening disease most common in young, sexually active males, and its incidence is expected to rise in concert with increasing rates of gonorrhoea internationally, as seen in our series. As such, GC remains an important consideration in adults with unilateral purulent conjunctivitis, who may have reduced visual acuity and periorbital swelling, and thus warrants a low threshold for exploring a sexual history.

CONTROL ID: 3521772

SUBMITTER (NAME ONLY): Meng Tian

TITLE: Standardization of optical coherence tomography angiography nomenclature in retinal vascular diseases

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tian, S. Wolf, M.R. Munk, department of ophthalmology, Inselspital Universitätsspital Bern, Bern, BE, SWITZERLAND|A.H. Kashani, Wilmer Eye Institute, Johns Hopkins Hospital, Maryland, UNITED STATES|R. Tadayoni, department of ophthalmology, Hôpital Lariboisière, FRANCE|J. Korobelnik, Service d'ophtalmologie, CHU Bordeaux, FRANCE|F. Pichi, Eye Institute, Cleveland Clinic Abu Dhabi, UNITED ARAB EMIRATES|

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ABSTRACT BODY:

Purpose: To develop a consensus nomenclature for reporting optical coherence tomography angiography (OCT-A) findings in the field of retinal vascular diseases.

Methods: Members of the Retina Society, the EURETINA and the Japanese Retina and Vitreous Society choose to participate in responding to an online questionnaire on their preferred terminology for reporting OCT-A findings in retinal vascular diseases. The respondents were divided into two groups based on the number of their publications in OCTA and retinal vascular diseases, including OCTA "experts" group who have five or more publications and the "users" who have less than five publications. Then an expert team of 25 OCTA experts in the field of retinal vascular diseases was formed and Delphi rounds based on the initial results of the survey are being carried out.

Results: The complete responses of 85 retina specialists were included in the analysis. Thirty-one were categorized as "experts". There was a consensus in both groups that OCTA parameters such as foveal avascular zone (FAZ) parameters, areas of nonperfusion and presence of neovascularization (NV) should be implemented in the identification and staging of DR and that OCTA can be applied to differentiate between ischemic vs. non ischemic retinal vein occlusion. Diabetic macular ischemia (DMI) can be also assessed via OCTA. Further, there was consensus that the terminology should differ based on the underlying causes of decreased vascular flow signal. There was disagreement in other areas, such as which terms should be applied to describe decreased OCTA signal from different causes, the definition of widefield OCTA and how to quantify DMI and area of decreased flow signal. These discrepancies form the basis for the upcoming expert Delphi rounds that aim to develop a standardized OCTA nomenclature. First results of the following Delphi rounds will be presented as well.

Conclusions: While there was agreement in some areas, significant differences were found in many areas of OCTA terminology among all respondents, but also between the "expert" and "user" groups. This indicates the need for standardization of the nomenclature among all specialists in the field of retinal vascular diseases.

CONTROL ID: 3521775

SUBMITTER (NAME ONLY): Zhaohua Yu

TITLE: Comparison of intraocular pressure measured with Goldmann applanation tonometry and with Icare tonometry

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Yu, P.G. Soderberg, Neuroscience/Ophthalmology, Uppsala Universitet Medicinska fakulteten, Uppsala, SWEDEN|

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ABSTRACT BODY:

Purpose: The purpose of the study was to compare the variation of intraocular pressure (IOP) measured with Goldmann applanation tonometry (GAT) and Icare tonometry, and if the methods were calibrated to each other.

Methods: Totally 20 persons with normal intraocular pressure were included and evenly divided into two groups. The IOPs were measured with GAT in one group and with Icare in another group. With each method, the IOPs were measured at two occasions and at each occasion 3 measurements were performed.

Results: The estimated variance among occasions for IOP with GAT was 7 times lower than the estimated variation with Icare. The estimated variance among measurements was 3 times lower with GAT than with Icare. The 95 % confidence intervals for each method's mean IOPs were 11.9 ± 1.0 mmHg for GAT and 14.2 ± 1.4 mmHg for Icare.

Conclusions: The variation among both measurements and occasions is smaller with GAT than with Icare, and therefore the reliability is different between the two methods. The methods are not calibrated to each other.

CONTROL ID: 3521805

SUBMITTER (NAME ONLY): JUNZHENG YANG

TITLE: Identification of a spontaneous mutation in Adiponectin receptor 1 in a complement factor H knockout mouse

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. YANG, A. Banks, N.M. Buchanan, S. Liao, E. Lima, N. Rangaswamy, I. Arellano, S. Hanks, J. Vrouvlianis, Y. Qiu, D.S. Rice, Novartis Institutes for BioMedical Research Inc, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: A subset of mice in our Cfh knockout (Cfh^{-/-}) colony exhibited rapid retinal degeneration, suggesting a spontaneous mutation occurred on mouse chromosome 1 (Chr 1). The retinal phenotype was similar to that in AdipoR1 knockout (AdipoR1^{-/-}) mice, whose gene is located near the Cfh locus on Chr 1. We attempted to determine if a mutation in AdipoR1 occurred on the Cfh^{-/-} background.

Methods: We performed an allele complementation test with a cross between a Cfh^{-/-} mouse with retinal degeneration and an AdipoR1^{-/-} mouse with retinal degeneration. RNA-seq, in situ hybridization, immunohistochemistry and protein analysis were used to profile Cfh^{-/-} and AdipoR1^{-/-} mice.

Results: About 50% of Cfh^{-/-} mice exhibited retinal degeneration. Cfh^{-/-} mice, regardless of retinal phenotype, demonstrated elevated complement activation in the eye compared to littermate controls. All offspring from the complementation test exhibited retinal degeneration, implying that AdipoR1 mutant alleles were responsible for the retinal degeneration. AdipoR1 protein, normally present in the RPE apical microvilli, was notably absent in Cfh^{-/-} mice with retinal degeneration. Cfh^{-/-} mice with normal retinal anatomy expressed AdipoR1 protein and were comparable to littermates[QY1]. AdipoR1 mRNA expression levels were comparable across the colony as measured by RNAscope and RNA-seq. Analysis of AdipoR1 mRNA sequence revealed a transversion at position c.841 C>T in the AdipoR1 gene concordant with mice exhibiting retinal degeneration. Further breeding identified mutant AdipoR1 mRNA in two Cfh^{+/-} mice and one Cfh^{+/+} mice with early onset retinal degeneration, implying a recent cross over on Chr 1. This missense mutation results in a proline to serine conversion (P281S) in the fifth transmembrane domain of AdipoR1 and is predicted to be detrimental to the AdipoR1 protein.

Conclusions: The spontaneous mutation in the AdipoR1 gene results in early onset retinal degeneration in a subset of our Cfh^{-/-} mouse colony. Elevated complement activity in the eye does not appear to affect the course of retinal degeneration, as gene signatures are comparable across all mice with retinal degeneration, regardless of Cfh genotype.

CONTROL ID: 3521870

SUBMITTER (NAME ONLY): Koenraad Vermeer

TITLE: Variance and bias of artificial intelligence based denoising and conventional averaging in optical coherence tomography angiography

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.A. Vermeer, L. Smid, Rotterdam Ophthalmic Institute, Rotterdam Eye Hospital, Rotterdam, NETHERLANDS|M.E. Van Velthoven, Rotterdam Eye Hospital, Rotterdam, NETHERLANDS|

Commercial Relationships Disclosure (Abstract): Koenraad Vermeer: Commercial Relationship(s);Canon:Code F (Financial Support) | Lisette Smid: Commercial Relationship(s);Canon:Code F (Financial Support) | Mirjam Van Velthoven: Commercial Relationship(s);Canon:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To examine the effect of artificial intelligence (AI) based denoising and conventional averaging on the reproducibility and bias of quantitative measurements, i.e., vessel density (VD) and foveal avascular zone (FAZ), derived from optical coherence tomography angiography (OCT-A) en face images.

Methods: In this retrospective cohort study, the non-pathological fellow eyes of patients with unilateral non-systemic disorders were included. OCT-A scans of two visits were analyzed on a Canon OCT-HS100 workstation. The VD and FAZ were measured on the first single scan (SS), best single scan (BSS), averaged scan (AS), and those scans after AI-denoising (SS-AI, BSS-AI, AS-AI). The reproducibility was calculated as the mean absolute difference (MAD) between the two visits, and the bias as the mean value (MV). A two-factor repeated-measures ANOVA for both the MAD and MV of the FAZ and VD was performed introduced by the factors AI-denoising and averaging.

Results: We analyzed 16 non-pathological eyes of 16 patients (61.9 ± 17.5 years). For VD, the reproducibility of AI-denoised scans (SS-AI, AS-AI) was significantly worse than scans without AI-denoising (SS, AS), but significantly better in BSS-AI than in BSS (Figure 1). AI-denoising also negatively affected the reproducibility of the FAZ measurement (Figure 2). AI-denoising and averaging both introduced a significant bias for the VD; for the FAZ, a significant bias was only introduced by AI-denoising. The marginal effects and results of the pairwise comparisons are presented in Table 1.

Conclusions: AI-denoising negatively affect the reproducibility and introduces a bias for quantitative OCT-A measurements, while the reproducibility of averaged scans was not significantly different from single scans. Only the VD measurement was biased after averaging. When the original single image is of high quality, the AI-denoising technology has a good reproducibility for VD. Otherwise, we recommend using conventional averaging for quantitative comparisons.

CONTROL ID: 3521895

SUBMITTER (NAME ONLY): Michael Dong

TITLE: Intracameral triamcinolone to reduce postoperative inflammation in uveitic cataract surgery

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.J. Hall, Ophthalmology, Alfred Health, Melbourne, Victoria, AUSTRALIA|M. Dong, A.J. Hall, Central Clinical School, Monash University Faculty of Medicine Nursing and Health Sciences, Clayton, Victoria, AUSTRALIA|L.L. Lim, Clinical Trials Research Unit, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|R. O'Day, L.L. Lim, Ophthalmology, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Intracameral triamcinolone (TA) is used at the time of uveitic cataract surgery to reduce postoperative inflammatory complications. However, there are currently no studies specifically investigating its use in this setting. We performed a retrospective study to evaluate the safety and efficacy of intracameral TA in reducing postoperative inflammation in uveitic cataract surgery.

Methods: A retrospective cohort study from 2005 to 2020 was conducted by reviewing medical records with a postoperative follow-up period of at least one month, through to 12 months. Consecutive adult patients with uveitis requiring cataract surgery with significant iris manipulation (use of iris hooks or a Malyugin Ring), were included in the study. Cases prior to 2009 where intracameral TA was not used (control group) were compared with cases after 2009 where intracameral TA was administered (study group).

Results: 54 eyes from 46 patients were included in the study group and 19 eyes from 16 patients were included in the control group with a mean follow up of 8.2 months and 9.2 months respectively. Significantly fewer eyes in the study group developed cystic macular edema (CME) during follow-up (22% vs 53%, RR 0.42 (95% CI 0.22 to 0.83), $p=0.020$). At one month, eyes that received intracameral TA had only $\frac{1}{4}$ the risk of having CME compared to the control group (9% vs 35%, RR 0.26, (95% CI 0.10 to 0.75), $p=0.019$). Visual acuity (VA) was not significantly different between the two groups at baseline ($p=0.06$), with the study group achieving a better median VA than the control group at one ($p=0.013$) and three months ($p=0.009$) postoperatively (Figure 1). Mean intraocular pressure (IOP) was lower in the study group at one week ($p=0.004$) and three months postoperatively ($p=0.015$). In the study group there were more cases of IOP-rise ≥ 10 mmHg (50% vs 37%, $p=0.425$) and ≥ 20 mmHg (36% vs 11%, $p=0.210$). There were low rates of other adverse events. Patterns of inflammation control were not significantly different at any time point.

Conclusions: Our findings support the use of intracameral TA as a safe and effective method of reducing postoperative inflammation for uveitic cataract surgery. It appears to be particularly effective for prevention of early CME which may confer a visual acuity benefit.

CONTROL ID: 3521921

SUBMITTER (NAME ONLY): Didar Abdulla

TITLE: OZURDEX® (dexamethasone intravitreal implant) vs ILUVIEN® (fluocinolone acetonide intravitreal implant) 0.19 mg in non-infectious posterior uveitis (NIPU)

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Abdulla, S. Taylor, Ophthalmology, Royal Surrey NHS Foundation Trust, Guildford, Surrey, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Didar Abdulla: Commercial Relationship: Code N (No Commercial Relationship) | Simon Taylor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine the effect of switching from Ozurdex to Iluvien in patients with NIPU

Methods: Data were collected retrospectively from medical records and ocular coherence tomography images. We looked at visual acuity (VA), central macular thickness (CMT), intraocular pressure (IOP) and complications three months pre and post treatments with Ozurdex and Iluvien. Patients with NIPU who received both Ozurdex and Iluvien were included. Primary outcomes were control of inflammation as measured by VA and CMT 3 months pre and post treatment, and need for rescue treatment. Secondary outcomes were IOP and complications. Statistical significance was assessed using the student t-test, with a significance level of $p < 0.05$

Results: Fourteen eyes of 8 patients were analysed. Both treatments were equally efficacious in control of inflammation, no significant changes in VA before or after switching from Ozurdex to Iluvien (VA 0.3 to 0.2 logMAR post treatment with Ozurdex vs. 0.1 to 0.2 LogMAR post treatment with Iluvien). Average CMT improved in both groups, 374µm pre Ozurdex, to 317µm 3 months post treatment, and 348µm to 332µm 3 months post Iluvien. A significant rise in IOP was seen in both groups, from 12 ± 3 mmHg to 17 ± 6 mmHg with Ozurdex and 14 ± 4 mmHg to 24 ± 9 mmHg pre and post Iluvien ($p < 0.010$). On average patients reported slower restoration of vision following Iluvien than with previous Ozurdex implants

Conclusions: Our case study shows no significant difference in control of inflammation in NIPU between Ozurdex and Iluvien implants, but a difference in steroid-induced ocular hypertension. Both groups had an increase in median IOP 3 months post treatment, Iluvien causing a more marked pressure rise. Three patients (6 eyes) required treatment in the form of selective laser trabeculoplasty, trabeculectomy and glaucoma drops to reduce IOP 1-3 months post Iluvien implants. Patients also noticed VA didn't improve as quickly with the Iluvien implants. Doctors found the Iluvien injector to be less efficient than the Ozurdex, it was more difficult to use and required more preparation.

Price comparison between the 2 implants is also a factor that needs considering, Iluvien costing £5,500 [ii] and Ozurdex costing £870[iii] per implant. Median requirement for Ozurdex implants for the 3 years prior to switching was 3, equating to a cost of £2,610.

CONTROL ID: 3521925

SUBMITTER (NAME ONLY): Mary Marte

TITLE: Imaging of Presumed Displaced Retinal Ganglion Cells in the Living Human Retina

SESSION TITLE: Advanced imaging technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Marte, K. Kurokawa, H. Jung, Y. Liu, M. Bernucci, B. King, D.T. Miller, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Large somas hypothesized to be displaced retinal ganglion cells (dRGCs) have previously been reported by our group at the inner edge of the inner nuclear layer (INL) of human subjects with adaptive optics optical coherence tomography (AO-OCT). dRGCs have been studied in numerous mammals but have not yet been classified in the human retina. To characterize this cell population, a prospective pilot study was performed obtaining AO-OCT images of the INL in human subjects.

Methods: The right eye from five healthy subjects aged 26.6 ± 1.3 years was imaged. Subjects with retinal pathology or high refractive error were excluded. The Indiana AO-OCT system was utilized to obtain $1.5^\circ \times 1.2^\circ$ volume images at 8 locations: 2° , 3° , 6° , 8° , and 13° temporal and 2° , 3° , and 6° nasal to the fovea, along the horizontal meridian of the retina. ImageJ™ software was used to manually view, count, and measure the en-face area of all large somas at the INL edge. Morphometric biomarkers of soma density, diameter and spatial distribution were measured. Also, AO-OCT images of subjects with glaucomatous arcuate defects were reviewed to assess dRGC presence in the defect.

Results: dRGC soma density was greatest near the fovea and decreased monotonically with increasing retinal eccentricity in all subjects (maximum average of 543.4 cells/mm^2 at 2° nasal; minimum average of 38.0 at 13° temporal). See Fig. 1. This trend is consistent with that of retinal ganglion cells (RGC), except near the fovea where RGC density peaks parafoveally^{1,2} and dRGC density continues to increase as close as 2° from the fovea. Soma size and its standard deviation increased monotonically with increasing retinal eccentricity, from $13.0 \pm 1.4 \text{ mm}$ at 2° temporal to $16.0 \pm 1.5 \text{ mm}$ at 13° temporal. Size and size variation are consistent with that of ganglion cell layer somas at the same retinal eccentricities as reported in the literature ($11.4 \pm 1.8 \text{ mm}$ at $1.5\text{-}3^\circ$ and $13.9 \pm 3.1 \text{ mm}$ at $12\text{-}13.5^\circ$).¹ All glaucoma images showed reduced numbers of dRGCs in the area of the arcuate defect compared to healthy individuals.

Conclusions: We obtained the first morphometric measurements of presumed displaced RGCs in the INL of the living human retina.

1. Liu, et al. PNAS. 2017;114(48):12803-8

2. Curcio, Allen. J. Comp. Neurol. 1990;300:5-25

CONTROL ID: 3521964

SUBMITTER (NAME ONLY): Svenja Deuchler

TITLE: Efficiency of simulation in combination with independent online learning within the framework of "EyesiNet" in ophthalmology education

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Schmack, T. Kohnen, Eye Clinic, Goethe-Universität Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|S. Deuchler, C. Sebode, P. Singh, F.H. Koch, Retina and Vitreous Unit, Eye Clinic, Goethe-Universität Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|H. Ackermann, Institute of Biostatistics and Mathematical Modelling, University Hospital, Goethe-Universität Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|

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ABSTRACT BODY:

Purpose: Ophthalmoscopy is part of the medical curriculum, but the teaching of medical contents is often unsatisfactory because there is no systematic learning of pathologies and their treatment options; instead of that healthy students examine each other. For this reason, we have developed a project to improve teaching at the Medical Faculty of the JWG University of Frankfurt/Main, which offers the opportunity to train ophthalmoscopically using a newly developed online platform (EyesiNet) in addition to simulator training. Defined learning contents are reproducible and made available to everyone equally.

The aim was to test the efficiency of the online platform EyesiNet in combination with the simulation of direct (Eyesi Direct) and indirect (Eyesi Indirect) ophthalmoscopy.

Methods:

At the beginning of the internship and on the last day of the internship, the students worked on cases in Eyesi Direct and Indirect. In the meantime, they were able to deal with the topic in the web-based EyesiNet on a voluntary basis. Results were scored on first and last day and compared to each other

Results:

Eyesi Direct: With $p=0.29$, both groups had the same starting conditions and did not have significantly different results in case processing on the first day of the internship. In the group of non-trainees ($n=54$), a significant improvement in simulator training was observed on the last day of the practical training with $p=0.02$, but with a small effect size of 0.1. Among the trainees ($n=32$), a highly significant improvement with an effect size of 0.3 was observed in the Wilcoxon Matched Pair Test with $p=0.0004$.

Eyesi Indirect: Both groups had no significant difference in the results in the Eyesi Indirect test at the beginning of the training period ($p=0.10$). 32 trainees performed unequivocally (but not significantly) better than 54 non-trainees.

Conclusions: The online platform EyesiNet impressively supports the learning of the most important disease patterns; the skills of direct ophthalmoscopy can be learned much faster than those of indirect ophthalmoscopy; a 3 days period is obviously way too short for the learning process. The online platform EyesiNet substantially accelerates the learning curve in ophthalmology - why not in other subspecialties, too? Home office conditions for sure take extra profit from such a modern tool.

CONTROL ID: 3521965

SUBMITTER (NAME ONLY): Michael Byrne

TITLE: Allele-selective reduction of P23H-mutant rhodopsin with stereopure oligonucleotides rescues phenotype associated with retinitis pigmentosa in preclinical models

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Byrne, V. Vathipadickal, L. Guo, Y. Yin, H. Yang, R. Looby, L. Norwood, C. Vargeese, Biology, Wave Life Sciences, Cambridge, Massachusetts, UNITED STATES|J.W. Fransen, A. jalligampala, J. Noel, M.A. McCall, University of Louisville, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: We tested whether a stereopure antisense oligonucleotide that selectively targets the P23H mutation in Rhodopsin (RHO) but that spares expression of healthy RHO transcripts can address phenotypes associated with the autosomal dominant form of retinitis pigmentosa (adRP) that is caused by this mutation.

Methods: We applied PRISMTM, Wave's proprietary discovery and drug development platform, to generate stereopure antisense oligonucleotides that selectively target the RHO P23H mutation. We evaluated allele-selective activity of the oligonucleotides against RHO alleles with a luciferase reporter assay in Cos7 cells and in human retinal pigment epithelial (ARPE-19) cells that overexpress RHO. To assess target engagement and efficacy of the oligonucleotides in vivo, we evaluated their activity in mouse and pig models for RHO P23H-induced adRP. Animals received intravitreal (IVT) injections, and eyes were evaluated for RHO P23H expression and expression of rod and cone cell markers by immunohistochemistry.

Results: We demonstrate that stereopure oligonucleotides selectively deplete expression of RHO P23H transcripts in vitro. After a single IVT eye injection of a stereopure oligonucleotide, expression of RHO P23H transcripts are decreased by at least 50% in mouse and pig models for RHO P23H-induced adRP. In the pig model, a single IVT injection led to the retention of rod outer segments and cone pedicles compared with untreated eyes 16-weeks post-injection.

Conclusions: These results confirm that stereopure oligonucleotides can selectively deplete expression of RHO P23H transcripts. These oligonucleotides deplete RHO P23H transcripts in vivo in multiple models and rescue phenotypes associated with adRP. Together, these data suggest stereopure oligonucleotides may provide a viable therapeutic opportunity for addressing RHO P23H-dependent adRP.

CONTROL ID: 3522024

SUBMITTER (NAME ONLY): Tutul Chakravarti

TITLE: Influence of perimetric parameters at abnormal points within the central 10 degrees in 24-2 visual field (VF) on the severity of 10-2 VF in early glaucoma.

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chakravarti, Glaucoma, Eye And Glaucoma Care, Kolkata, West Bengal, INDIA|

Commercial Relationships Disclosure (Abstract): Tutul Chakravarti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Evaluating the influence of perimetric parameters at abnormal points within the central 10 degree in 24-2 VF on the severity of 10-2 VF in early glaucoma (MD < -7dB).

Methods: This cross-sectional study included 54 eyes of 49 early glaucoma patients with central visual field defect (CVFD) on 24-2 VF and related parafoveal scotomas on 10-2 VF. CVFD, a glaucomatous defect with at least 1 abnormal 24-2 VF point, depressed P < 1% in the central 10 degrees (12 points: central-most 4 points and paracentral 8 points) on 3 consecutive tests either on total deviation (TD) or pattern deviation (PD) plot. Based on pattern defects, 10-2 VFs were categorized into 3: arcuate, partial arcuate and minimal defect groups, the arcuate defect being the most severe form. We compared the perimetric parameters differences between 24-2 VFs with central-most VF defects (CMVFD) or paracentral defects and related 10-2 VFs. We assessed the relationship between various perimetric factors at abnormal 24-2 VF points (central 4 and paracentral 8 points) and the severity of 10-2 VF using Pearson's correlation coefficients.

Results: The mean age of the population was 67.6 years and mean 24-2 mean deviation (MD) -3.76dB. On 24-2 VF, 4 (7.4%) eyes had only CMVFDs, 31 (57.4%) had both CMVFDs and paracentral defects and 19 (35.1%) had paracentral defects. On 10-2 VF, 25 (46%) eyes displayed arcuate defect, 11 (20%) partial arcuate and 18 (33%) minimal defect. Arcuate group had worse MD, PSD (pattern standard deviation) than partial arcuate and minimal defect groups (P < .001). High defect depth (> -25dB) and low threshold sensitivity (< 0 to 10dB) at abnormal 24-2 VF points were significantly associated with the presence of arcuate defect on the 10-2 test (P = 0.033; P = 0.002). PSD in arcuate group on the 10-2 test displayed negative correlation with threshold sensitivity (-0.638, P = 0.003) and defect depth [(TD: -0.765, P < .001); (PD: -0.542, P = 0.037)] of abnormal central-most 4 points in 24-2 VF.

Conclusions: High defect depth and low threshold sensitivity at abnormal points within the central-most 4 and/or paracentral 8 points in 24-2 VF are significantly associated with the presence of arcuate defect on 10-2 VF. Clinicians might consider measuring perimetric parameters at abnormal 24-2 VF points within the central 10 degrees to predict the severity and functional impacts of central glaucomatous visual field loss.

CONTROL ID: 3522065

SUBMITTER (NAME ONLY): Yue Wu

TITLE: Algorithmic optimization of residency matching for a win-win outcome

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wu, C.S. Lee, A.Y. Lee, R.N. Van Gelder, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The current system for pairing medical students to residency programs has been relatively unchanged for half a century. The residency matching algorithms, including SF Match for ophthalmology, are based on Gale-Shapley, a 'stable-marriage' method that favors applicant outcomes. We sought to develop a new matching algorithm (ResOpt) and compared it to Gale-Shapley.

Methods: We obtained anonymized rank lists and match data for applicants and programs in ophthalmology from SF Match between 2011 to 2019. The matches of SF Match and ResOpt were compared in terms of the average rank of matches for both applicants and programs, the percentage of applicants matching to their top choices, and the change in match composition.

Results: For 2011 to 2019, ResOpt always fully matches and avoids the Supplemental Offer and Acceptance Program. In addition, ResOpt consistently matches more applicants to their most preferred programs (Figure 1a). Under ResOpt, 78.7% (3308/4205) of applicants matched their top 3 choices compared to 71.5% (2991/4181) under SF Match. Furthermore, ResOpt achieves better average ranks for both applicants and programs (Figure 1b and 1c), without drastically changing the match composition (Figure 2a). Rank composition analysis (Figure 2b) shows the applicants whose outcomes improve often improve by multiple ranks, while applicants who worsen mostly drop 1 rank.

Conclusions: ResOpt is a credible alternative as a matching algorithm, as it consistently improves matches for most applicants and programs.

CONTROL ID: 3522070

SUBMITTER (NAME ONLY): Christina Le

TITLE: Prevalence Of Myopia Among Hispanic Children Examined By The UCLA Preschool Vision Program In Los Angeles

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Le, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|C. Le, W. Liu, F. Yu, S. Fung, A.L. Coleman, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Understanding the prevalence of myopia in young pediatric patients is crucial to prevent pathological complications such as, retinal detachment, myopic maculopathy, open-angle glaucoma, and cataracts. This study aims to determine the prevalence of myopia in Hispanic children aged 3 to 5-years-old over a 5 year period, 2012 to 2017, with the University of California, Los Angeles (UCLA) Preschool Vision Program (UPVP).

Methods: The UPVP performed visual acuity and undilated refractive screening on 3 to 5-year-old children between 2012 to 2017, and found the majority of the students to be Hispanic. Of these students, 10,903 underwent full cycloplegic examination after failing initial screening criteria. Myopia was defined as a spherical equivalent ≤ -0.5 D in one or both eyes. Prevalence of myopia was compared using Pearson's Chi-squared test and mean spherical equivalent were analyzed using Analysis of Variance (ANOVA).

Results: Across all examined participants, there was significant change in mean spherical equivalent over calendar years, 2012 to 2017 ($p = 0.002$). Of those who were myopic, the severity of myopia, measured by spherical equivalent, also changed significantly from 2012 to 2017 ($p = 0.04$). Additionally, when all participants were stratified by age group, 3 and 4-year-old participants demonstrated a significant increase in prevalence of myopia over time (from 2012 to 2017) ($p < 0.05$). 5-year-old participants demonstrated a positive trend towards increased myopia prevalence ($p = 0.09$). To exclude participants who might have been examined multiple times in the analysis of myopia prevalence over time, first and last calendar years (2012-13 vs 2016-17) were compared. Prevalence of myopia was observed to increase significantly amongst all ages, 3, 4, and 5-years-old, over calendar year ($p < 0.05$).

Conclusions: The severity of myopia is changing, and the prevalence of myopia has increased over time, from 2012 to 2017, in Hispanic pre-school aged children. This information will help in further myopia screening of preschool children to prevent serious pathological complications.

CONTROL ID: 3522104

SUBMITTER (NAME ONLY): Winnie Liu

TITLE: Investigation of Visual Acuity and Amblyopia Changes in Preschoolers from UCLA's Preschool Vision Program

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Liu, C. Le, J. Margines, L. Syniuta, B. Mondino, S. Fung, Department of Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|W. Liu, C. Le, J. Margines, F. Yu, L. Syniuta, B. Mondino, A.L. Coleman, S. Fung, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|F. Yu, A.L. Coleman, University of California Los Angeles Jonathan and Karin Fielding School of Public Health, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The UCLA Preschool Vision Program (UPVP) is a community outreach program that provided free on-site vision screenings and eyeglasses to Los Angeles preschoolers between 2012 – 2017. Here, we investigate the longitudinal visual outcome among those prescribed eyeglasses by UPVP.

Methods: This is a retrospective longitudinal case series. Preschoolers seen twice by UPVP were included. Study eye was designated as the eye with lower BCVA at initial visit. Data including best-corrected distance visual acuity (BCVA), refractive error, and severity of amblyopia were analyzed. Paired statistical analysis was performed using Wilcoxon signed rank and McNemar tests.

Results: 8,866 preschoolers were assessed twice by UPVP. 321 of them had a complete follow-up examination after being prescribed glasses. Mean(\pm standard deviation) BCVA at Visit 1 was 0.24 ± 0.15 (95% CI: 0.23 to 0.26) logMAR, and 10.6% had unilateral amblyopia with mean BCVA of 0.43 ± 0.13 (95% CI: 0.37 to 0.49) logMAR. At 11.5 \pm 2.5 months, 52% of preschoolers wore glasses as prescribed at Visit 1. Follow-up mean BCVA was 0.16 ± 0.12 logMAR (95% CI: 0.15 to 0.18) ($p = 2.2 \times 10^{-16}$). 88% of amblyopic preschoolers improved in BCVA, with mean change of 0.19 ± 0.13 (95% CI: -0.24 to -0.15) logMAR ($p = 2.51 \times 10^{-6}$). BCVA change for glasses compliant amblyopia preschoolers was -0.23 ± 0.12 (95% CI: -0.29 to -0.18) logMAR, while non-compliant group was -0.13 ± 0.11 (95% CI: -0.20 to -0.05) logMAR ($p = 0.025$).

Conclusions: UPVP identified otherwise undetected vision deficiencies, such as amblyopia, and provided timely interventions to improve visual outcome. Compliance to prescribed glasses remains an obstacle to vision care.

CONTROL ID: 3522130

SUBMITTER (NAME ONLY): Zixuan Shao

TITLE: Suppression of Murine Choroidal and Retinal Neovascularization by Risuteganib and the Accompanying Transcriptome Changes in the OIR Retina

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Shao, J.Y. Park, H.L. Karageozian, V.H. Karageozian, Allegro Ophthalmics, LLC, California, UNITED STATES|S.F. Hackett, R. Formica, Y. Kanan, P.A. Campochiaro, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|D. Zhou, J.A. Kornfield, California Institute of Technology Division of Chemistry and Chemical Engineering, Pasadena, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Wet age-related macular degeneration and diabetic retinopathy are leading causes of blindness with characteristic neovascularization (NV) of the choroid (CNV) or retina (RNV), respectively. This preclinical study explores effects of the investigational drug, risuteganib (RSG), in cell culture and three murine disease models using histology and transcriptomics.

Methods: In photocoagulation-induced CNV model, 1-50 μ g RSG or control peptides were intraocularly injected, followed by measurement of NV area on day 14 (n=4). The rho/VEGF model of subretinal NV was used to examine: i) injection of vehicle, 25 μ g RSG, 10 μ g ranibizumab, or combination of two drugs, followed by NV area measurement on day 7 (n=5), and ii) vascular leakage 1 day after PBS or 25 μ g RSG injection (n=8). In oxygen-induced retinopathy (OIR) RNV model, 0.1-50 μ g of RSG or PBS were injected and NV area was measured on day 5 (n=8). Student's t-test was used except with ANOVA in the rho/VEGF study of NV. Transcriptome changes associated with RNV and 10 μ g RSG injection was measured by RNA-seq. Changes in gene levels were determined by edgeR and enrichment of biological processes/pathways by goseq. RT-CES-based HREC cell adhesion and migration assays were used to test effect of 43-1393 μ M RSG on surfaces coated with vitronectin (VN) or fibronectin (FN) (n=2), statistical test by ANOVA.

Results: In the photocoagulation model, 10 and 25 μ g RSG reduced the area of CNV (p=0.0453, 0.0498). In the rho/VEGF model, RSG (p<0.001) and ranibizumab (p<0.001) both reduced NV area, while combination showed further reduction (p<0.05); RSG reduced vascular leakage by 24% (p=0.017). In OIR, 12.5, 25, and 50 μ g RSG (p=0.0271, 0.0414, 0.0403) reduced NV area. Transcriptome data showed biological processes and pathways related to angiogenesis, inflammation, integrin, cell adhesion and migration were enriched in genes elevated in OIR retina and reduced with RSG. Cell migration on FN was inhibited at low RSG dose (p<0.01), while migration on VN (p<0.01), adhesion on VN (p<0.05) and FN (p<0.01) were inhibited at high RSG dose.

Conclusions: RSG demonstrated anti-NV property, reduced retinal vascular leakage, and inhibited cell adhesion and migration. Transcriptome data suggest important pathological cellular responses are modulated by RSG, with possible therapeutic implication for treatment of human retinal diseases.

CONTROL ID: 3522151

SUBMITTER (NAME ONLY): Catherine Opere

TITLE: Regulation of Cataractogenesis by Hydrogen Sulfide-NSAID Hybrid Compounds in Cultured Bovine Lenses

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Opere, L. Maffoffou Nkenyi, N. Singh, Pharmacy Sciences, Creighton University School of Pharmacy and Health Professions, Omaha, Nebraska, UNITED STATES|S. Heruye, Pharmacology and Neuroscience, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|Y. Njie-Mbye, S.E. Ohia, Texas Southern University, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hydrogen sulfide (H_2S) releasing compounds and NSAIDs can mitigate cataractogenesis in vitro and in vivo (Zhang et al., Mol Vis, 14:862, 2008; Harding JJ et al., Acta Ophthalmol, 67:518, 1989). However, the role of NSAID- H_2S -releasing hybrid compounds on cataractogenesis has not been elucidated. In the present study, we compared the pharmacological effects of ATB343 (indomethacin & H_2S donor) and ATB337 (diclofenac & H_2S donor) on cataractogenesis in cultured bovine lenses and on lenticular antioxidants concentrations.

Methods: Freshly isolated bovine lenses were cultured in a DMEM buffer solution as follows: Group I: Control (DMEM); Group II: H_2O_2 (10 mM); Groups III-V: ATB343 (10^{-7} M); ATB337 (10^{-7} M); ascorbic acid (AA; 10^{-3} M) in presence and absence of H_2O_2 (10 mM). Lenses were incubated and were qualitatively and quantitatively assessed at 3, 6, 24, 48 and 72 h-time points by photographic captures and measurement of transmittance using a plate reader (Synergy H1 hybrid). Lenticular glutathione (GSH) and superoxide dismutase (SOD) were measured using Cayman Assay Kits.

Results: DMEM-cultured lenses exhibited a time-dependent decrease in transmittance (420nm) and a corresponding loss of lens optical clarity up to 72 h. Unlike ATB343 (10^{-7} M) and the endogenous antioxidant, AA (10 mM) which attenuated time-dependent lens degradation up to 24 h, ATB337 (10^{-7} M) decreased time-dependent transmittance, achieving an inhibition of $34.7 \pm 1.12\%$ ($n=12$; $p<0.01$) after 72 h. H_2O_2 (10 mM) reduced transmittance in a time-dependent manner, attaining an inhibition of $42.0 \pm 1.0\%$ ($n=12$; $p<0.01$) after 72 h. After 48 h, ATB343 (10^{-7} M) and ATB337 (10^{-7} M) enhanced time-dependent GSH depletion by $3.6\% \pm 0.05\%$ ($n=3$; $p<0.05$) and $2.7 \pm 0.5\%$ ($n=3$; $p<0.05$) and H_2O_2 -induced GSH depletion by $12.3 \pm 0.1\%$ ($n=3$; $p<0.01$) and $8.7 \pm 0.4\%$ ($n=3$; $p<0.05$), respectively. However, ATB343 enhanced SOD depletion by $35.3 \pm 2.7\%$ ($n=3$; $p<0.001$) but attenuated H_2O_2 -induced SOD depletion by $56.6 \pm 3.1\%$ ($n=3$; $p<0.001$) ($t=48$ h). Similarly, ATB337 enhanced time-dependent loss in SOD by $48.9 \pm 4.4\%$ ($n=3$; $p<0.001$) but reversed H_2O_2 -induced SOD loss by $31.8 \pm 4.9\%$ ($n=3$; $p<0.001$) ($t=48$ h).

Conclusions: The NSAID- H_2S hybrid compounds, ATB343 and ATB337 can partially protect cultured bovine lenses from cataract formation, presumably via an effect on lenticular SOD concentrations.

CONTROL ID: 3522161

SUBMITTER (NAME ONLY): Janet Tang

TITLE: Adaptive optics fluorescence lifetime imaging ophthalmoscopy of the human RPE mosaic

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tang, C.E. Granger, The Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|J. Tang, C.E. Granger, K. Parkins, K. Kunala, K. Huynh, K. Bowles-Johnson, Q. Yang, J.J. Hunter, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|K. Huynh, Department of Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|K. Bowles-Johnson, J.J. Hunter, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the retinal pigment epithelium (RPE), the fluorescence lifetime (FL) of lipofuscin granules, related to their composition, may be a useful biomarker of retinal health. Widefield fluorescence lifetime imaging ophthalmoscopy (FLIO) has been used to investigate RPE changes with age, eccentricity and disease but is limited by low sampling density and artifacts such as lens and macular pigment fluorescence. We improve the resolution and confocality by applying adaptive optics FLIO (AOFLIO), for the first time, to image the RPE mosaic in healthy people.

Methods: To specifically target lipofuscin, a custom-built adaptive optics scanning light ophthalmoscope was used for reflectance and FL imaging in 3 subjects (up to 12 locations across the macula; 30-38 yrs). RPE autofluorescence was excited with 532±10 nm (50 ps pulse width, 80 MHz repetition rate, 15 µW average power) and collected 575-725 nm (1.4-1.7° square field of view, 25 Hz frame rate, ≤60 s exposure). FL data was analyzed using custom and commercial software (Becker & Hickl GmbH). A two-component exponential function $\alpha_1 e^{-t/\tau_1} + \alpha_2 e^{-t/\tau_2}$ was fit to the decay curve at each binned pixel. Mean FL was calculated by $\tau_m = \alpha_1 \tau_1 + \alpha_2 \tau_2$ where τ_n is the FL and α_n is the relative contribution. τ_n and α_n were averaged across each AOFLIO image and compared using Student's t-test.

Results: Across all images, τ_m is 247.3±27.8 ps (ranging from ~200–270 ps, with an outlier at 330 ps); within an image, the average standard deviation of τ_m is 2.8±0.3 ps. α_1 was also consistent with mean 88.7±0.4% (ranging 88.1–89.4%). τ_1 and τ_2 ranged 120–230 and 830–1170 ps, respectively. The measured τ_m is within the range expected for lipofuscin (widefield FLIO long spectral channel attributed to lipofuscin: Dysli et al., 2017; ex vivo: Docchio et al., 1991; Schweitzer et al., 2007; Feldman et al., 2018). AOFLIO measurements taken 8 days apart in one subject showed no significant differences in τ_n and α_n ($p \geq 0.12$). Between two subjects, no significant differences were found in the FLs ($p \geq 0.058$), but α_1 showed a small but significant difference ($s1: 88.6 \pm 1.7\%$, $s2: 88.5 \pm 0.3\%$, $p < 0.001$).

Conclusions: These are the first measurements using AOFLIO to image the human RPE mosaic. Our results suggest AOFLIO will be repeatable within and between young healthy subjects. We expect larger variations with age and disease related to composition and function of the RPE mosaic.

CONTROL ID: 3522243

SUBMITTER (NAME ONLY): Anat Galor

TITLE: Efficacy and Safety of OCS-02 a novel, potent, topical TNF α antibody in acute anterior uveitis (AAU): a phase 2 study

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

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Commercial Relationships Disclosure (Abstract): Anat Galor: Commercial Relationship(s);Novaliq:Code C (Consultant);Dompe:Code C (Consultant);Oculis:Code C (Consultant);Novartis:Code C (Consultant);Oyster Point:Code C (Consultant)

ABSTRACT BODY:

Purpose: Due to the side effects of steroids, there is a medical need for new anti-inflammatory drugs to treat uveitis. Marketed TNF α antagonists are considered effective but are administered systemically. OCS-02 is a potent topical ocular anti-TNF α antibody fragment. This randomized, active-controlled study (ClinicalTrials.gov NCT02482129, registered 6/26/2015, study start 7/17/2015) assessed OCS-02 efficacy and safety in acute anterior uveitis (AAU) patients.

Methods: This was a Phase 2, multicenter, randomized, parallel-group, double-masked, active-controlled study. Dexamethasone was added for masking purposes with no inferential comparison to OCS-02. Patients aged ≥ 18 years with non-infectious AAU and Standardization of Uveitis Nomenclature anterior chamber (AC) cell score of 2+ or 3+ were recruited. Patients were randomized (3:1 ratio) to OCS-02 (60 mg/mL; 8 drops/day for 15 days, then 4 drops/day for 7 days, followed by matching vehicle for last 7 days to maintain masking with active control) or dexamethasone eye drops (8 drops/day for 15 days tapering to 1 drop/day over 14 days). The primary efficacy endpoint was Responder Status at Day 15- at least a two-step decrease in AC Cell Grade relative to baseline. Efficacy was determined if the Bayesian lower limit of the 95% posterior interval of the responder rate was $>30\%$. Safety assessments included adverse events and ophthalmic examination.

Results: Twenty nine patients were treated with OCS-02 and 10 patients with dexamethasone. The Day 15 response rate in the OCS-02 arm was 56%; the lower bound of the 95% credible interval was 40%, i.e. $>30\%$, thus demonstrating efficacy according to prespecified criteria. The proportion of patients with an AC Cell Grade of 0 increased from baseline to Day 29, despite the tapering and discontinuation of OCS-02 at Day 22: 76% had an AC Cell Grade of 0 on at least 1 post-treatment visit. Mean intra-ocular pressure was unchanged in the OCS-02 arm. There were no notable differences in ophthalmic examination results.

Conclusions: Administration of OCS-02, a novel TNF α antibody eye drop, demonstrated efficacy in resolving ocular inflammation in this phase 2 study of patients with AAU. The drug was well tolerated without steroid-type side effects or eye irritation suggesting its potential as a non-steroidal therapy for AAU. Confirmatory clinical studies are planned.

CONTROL ID: 3522312

SUBMITTER (NAME ONLY): Michael Doyle

TITLE: Comparison of 24-2C SITA Standard intervisit repeatability to legacy SITA tests

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Doyle, G.C. Lee, S. Yu, M.K. Durbin, N. Graves, C. Wu, T. Callan, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|I. Falkenstein, Glaucoma Specialists of San Francisco, Oakland, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Michael Doyle: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Gary Lee: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Sophia Yu: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Mary Durbin: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Noelleisha Graves: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code C (Consultant) | Charles Wu: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code C (Consultant) | Todd Severin: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code C (Consultant) | Iryna Falkenstein: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code C (Consultant) | Thomas Callan: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: The 24-2C test pattern increases sensitivity to central field defects by adding 10 test locations from the 10-2 pattern that are tested at the end of a 24-2 threshold test¹. The purpose of this ongoing, preliminary clinical study was to compare the repeatability of the 10 added test locations in a prototype 24-2C SITA Standard test to legacy SITA tests in normal and glaucomatous eyes.

Methods: Experimental 24-2C SITA Standard (SS-C), as well as 24-2C SITA Faster (SFR-C), 10-2 SITA Standard (SS-10), and 10-2 SITA Fast (SF-10) visual fields (VFs) were acquired on an HFA3 Model 860 perimeter (ZEISS, Dublin, CA) at each of two visits on one eye each for healthy and glaucomatous subjects. 24-2 SITA Standard VFs were extracted from SS-C as a reference for disease severity.

Repeatability was calculated by computing the test-retest standard deviation (TRT-SD) using both visit data for mean deviation (MD) and pattern standard deviation (PSD), as well as individual threshold values at the 10 added test locations.

Results: Mean age was 55.8 (standard deviation, SD: 6.4; range: 44.3 to 69.9) years for 17 healthy eyes and 73.6 (SD: 9.2; range 60.9 to 97.9) years for 16 glaucomatous eyes ($p < 0.001$). Mean 24-2 SITA Standard MD was 0.63 (SD: 1.15; range: -1.14 to 3.04) dB and -6.81 (SD: 6.86; range: -22.61 to 1.85) dB in healthy and glaucomatous eyes ($p < 0.001$), respectively.

TRT-SDs for MD were 0.61, 1.29, 0.52, and 0.49 dB for tests SS-C, SFR-C, SS-10, and SF-10, respectively. TRT-SDs for the 10 added locations were 1.57, 2.28, 1.85, 2.21 dB for tests SS-C, SFR-C, SS-10, and SF-10, respectively (see Table 1). Overall, the repeatability for SS-C MD and thresholds were comparable to their counterparts.

Conclusions: The findings in this preliminary cohort suggest the repeatability of the additional test locations added to 24-2C SITA Standard test is comparable to the repeatability of the same locations in the 24-2C SITA Faster and the 10-2 SITA tests. As a result, a 24-2C SITA Standard test may maintain comparable ability to detect progressive changes in the ten new test locations in the central visual field as compared to the current SITA tests.

References

[1] Callan et al. IOVS 2020; 61(7): Abstract 3876

CONTROL ID: 3522313

SUBMITTER (NAME ONLY): Alyssa Grant

TITLE: Visual impairment and 3-year change in cognitive function in the Canadian Longitudinal Study on Aging

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Grant, R. Buhrmann, E.E. Freeman, University of Ottawa, Ottawa, Ontario, CANADA|M. Aubin, M. Kergoat, Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Our goal was to explore the longitudinal associations between vision-related variables and cognitive test change scores in a community-dwelling sample of older adults and to examine whether sex, education, or hearing loss act as effect modifiers.

Methods: A 3-year prospective cohort study was performed using data from the Canadian Longitudinal Study on Aging consisting of 30,097 individuals aged 45-85 years. Visual impairment (VI) was defined as binocular presenting visual acuity worse than 20/40. Participants were asked if they had ever had a physician diagnosis of age-related macular degeneration (AMD), glaucoma, or cataract. Cognitive change was examined by calculating the difference between baseline and follow-up scores of the Rey Auditory Verbal Learning Test (RAVLT: a test of verbal memory), the Controlled Oral Word Association Test (COWAT: a test of verbal letter fluency), the Animal Naming Test (ANT: a test of verbal category fluency) and the Mental Alternation Test (MAT: a test of processing speed). Multiple linear regression was used and sampling weights were included in all models.

Results: Visual impairment was associated with the 3-year decrease in RAVLT ($\beta=-0.18$, 95% confidence interval (CI)= -0.28, -0.07), RAVLT-Delayed ($\beta=-0.13$, 95% CI= -0.25, -0.02), and ANT ($\beta=-0.95$, 95% CI= -1.44, -0.45) scores after adjusting for age, sex, ethnicity, income, smoking, diabetes, stroke, heart disease, baseline cognitive score, and province. A report of glaucoma was associated with a decrease in 3-year MAT change scores ($\beta=-0.40$, 95% CI -0.77, -0.04). The self-report of AMD or cataract were not associated with 3-year changes in cognitive test scores. No effect modification was detected.

Conclusions: These data indicate that VI and glaucoma are associated with 3-year declines in cognitive test scores. Further research is needed to elucidate the pathways to explain these associations.

CONTROL ID: 3522315

SUBMITTER (NAME ONLY): Joseph Martel

TITLE: Optogenetic GS030 Therapy in Subjects with Retinitis Pigmentosa: Safety and Tolerability Up to Two Years After Treatment Administration in the Phase 1/2a PIONEER Study

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.N. Martel, E. Boulanger-Scemama, J.A. Sahel, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|S. Degli Esposti, Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|F. Galluppi, L. Blouin, M. Tiel, GenSight Biologics SA, Paris, Île-de-France, FRANCE|J.A. Sahel, Institut de la vision, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The PIONEER study evaluates the safety and tolerability of GS030, an investigational optogenetic treatment combining a gene therapy and a light-stimulation medical device in subjects with late-stage non-syndromic retinitis pigmentosa (RP).

Methods: PIONEER is a Phase 1/2a open-label study including three dose-escalation cohorts (5E10, 1.5E11, 5E11 vg/eye) of 3 subjects each, and an extension cohort treated at the highest tolerated dose. Treatment is gene agnostic, and the optogenetic gene therapy encoding channelrhodopsin ChrimsonR-tdTomato (ChRtdT) is administered by intravitreal injection to target preserved retinal ganglion cells (RGCs). While RGCs are normally not light sensitive cells, expression of ChRtdT renders RGCs sensitive to light. After GS030 optogenetic therapy, controlled stimulation of the genetically reengineered retina using a visual interface stimulating goggles encode images of the visual world in real time and project them onto the retina by modulating a tailored light source at a specific wavelength, and mimicking natural visual processing.

Results: As of July 2020, six patients in the first two cohorts and one patient of the third cohort were treated with a single intravitreal injection of optogenetic gene therapy in their worse-seeing eye. Use of the visual interface medical device to stimulate RGCs expressing ChR-tdT was initiated two months after gene therapy injection and showed no safety concerns, before or after injection. Up to 2 years after gene therapy administration, no adverse event led to study discontinuation. The most common adverse events were mild or moderate anterior chamber or vitreous inflammation (4/7 patients) responsive to corticosteroid treatment, and transitory mild sensitivity to light (2/7 patients) that started before the use of light stimulation by the visual interface goggles.

Conclusions: The PIONEER study is the first clinical trial combining a gene therapy and a medical device using an optogenetic approach. The treatment was well tolerated up to two years after gene therapy administration.

CONTROL ID: 3522435

SUBMITTER (NAME ONLY): Gregory Anderson

TITLE: Aligning patients for fundus image capture – effects of a gameified interface on speed and ease of capture

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Anderson, A. Bender, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Gregory Anderson: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Andre Bender: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Correct alignment of patients' eyes is essential for capturing fundus images, but can be a challenge for inexperienced imaging technicians. Most devices overlay guides on a live view of the eye to show target positions along the x-, y-, and z-axes. These guides rely on mental computations on the part of users to convert colors and arrows to manual adjustments of the device.

This study investigated a new alignment feedback mechanism that uses gamified graphics without live images of the eye to provide feedback that requires fewer mental computations, to assess the impact on alignment times and ease-of-use ratings for imaging technicians.

Methods: Ten participants who are not imaging technicians, and have little to no experience with fundus cameras were asked to capture images on the CLARUS™ 500 (ZEISS, Dublin, CA) using both the commercial user interface (UI) and a modified alignment interface. In each case, participants were asked to capture two widefield (WF) color images of "acceptable" quality (as determined by a study cohort technician with more than 1 year of experience). The average alignment/acquisition times between the two UI conditions were compared using a t-Test. Participants were given 5 minutes of practice before acquiring images with each system, and the order of conditions was reversed for half the participants. Ease-of-Use ratings (5=Very Easy; 1=Very Difficult) were used to quantify perceived ease of use.

Results: Average alignment time to capture two images of acceptable quality was 74.5 seconds (SD=33.8) using the commercial UI, and 49.8 seconds (SD=20.6) using the gameified UI. These show that the gameified UI resulted in significantly faster acquisition times ($T=2.83$, $p<0.05$).

Average Ease-of-Use ratings were 3.1 (SD=1.1) using the commercial UI, and 3.9 (SD=1.0) using the gameified UI. Ease-of-Use ratings between the two UI's were not significantly different. ($T = -1.86$, $p = 0.096$).

Conclusions: An alignment UI design that applies video game elements and neuroergonomic principles to reduce cognitive load during acquisition is shown to speed up acquisition time for new and less-experienced imaging technicians. The practical impact is improved efficiency of fundus imaging workflows.

CONTROL ID: 3522454

SUBMITTER (NAME ONLY): Christopher Zhu

TITLE: Prevalence of Conjunctival Intraepithelial Neoplasia in Pterygium Specimens

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Zhu, M. Weiss, F. Scribbick III, D.A. Johnson, A. Kheirkhah, Department of Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the prevalence of conjunctival intraepithelial neoplasia (CIN) in pterygium specimens and to determine the possible risk factors for such occurrence.

Methods: This retrospective study included 557 pterygium specimens from patients with a clinical diagnosis of pterygium. None of the patients had clinical signs of CIN. Presence of CIN was evaluated using histopathologic evaluation with hematoxylin and eosin (H&E) and Ki67 staining. In addition, the following clinical data were collected from medical records: age, sex, self-reported race (White, African American, or Asian) and ethnicity (Hispanic versus non-Hispanic), and the involved eye. Logistic regression was performed to determine the possible risk factors for presence of CIN in pterygium specimens.

Results: There were 557 specimens from 557 eyes of 525 patients, which included 333 men and 224 women with a mean age at excision of 53.4 ± 13.1 years. Of all specimens, 95.9% were from patients identified as White, 2.2% from African Americans, and 2% from Asians. Self-identified ethnicity included Hispanic (69.7%) and non-Hispanic (30.3%). Among all specimens, 40 (7.2%) were positive for CIN. Patients with CIN were significantly older (59.2 ± 13.6 years) compared with those without CIN (53.0 ± 13.0 years, $P=0.008$). Furthermore, patients with CIN had a significantly higher percentage of male population (80% vs 58%, $P=0.007$). However, there were no significant differences between those with and without CIN in race and ethnicity. Regression analysis showed that older age ($P=0.01$) and male sex ($P=0.02$) had significant associations with presence of CIN in pterygium specimens.

Conclusions: Pterygium specimens from older male patients are more likely to have CIN. As the treatment and prognosis of these two conditions differ significantly, careful histopathologic evaluation of all pterygium specimens, especially in those with the risk factors, is warranted.

CONTROL ID: 3522514

SUBMITTER (NAME ONLY): Jordan Wilson

TITLE: Sensitivity of a combined OCT index in glaucomatous eyes

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wilson, T. Callan, S. Yu, M.K. Durbin, G.C. Lee, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|R. Chang, Ophthalmology, Byers Eye Institute, Palo Alto, California, UNITED STATES|I. Conner, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|T. Aung, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Glaucoma is often assessed with optical coherence tomography (OCT) and perimetry to provide clinicians a large number of quantitative parameters that aid in diagnosis. The OCT Early Glaucoma Diagnostic Structural Index (EGDSI), was previously proposed and validated providing a combined structural index for the detection of early glaucoma^{1,2}. In this retrospective clinical study, we compared the sensitivity of EGDSI to individual OCT summary parameters in a cohort with a range of glaucoma severity.

Methods: Retrospective OCT and visual field (VF) data were analyzed from a previous study including 74 eyes of 74 glaucoma subjects, using CIRRUS™ HD-OCT (ZEISS, Dublin, CA) and HFA™ II-i (ZEISS, Dublin, CA)³. At each visit, Optic Disc 200x200 and Macula 200x200 cube scans and SITA Standard 24-2 VFs were acquired. Sixteen OCT summary parameters (Rim Area, Cup-to-Disc area Ratio (CDR), vertical diameter CDR (vCDR), Average and four Quadrant RNFL thicknesses, Average, Minimum, and six Sectoral GCIPL thicknesses) were extracted for comparison and to calculate EGDSI from the last qualified visit data as previously described^{1,2}. A VF mean deviation (MD) cutoff of -4 dB was used to separate early and non-early glaucoma as done previously². Sensitivity at specificities of 95% and 99% were determined for EGDSI and component OCT parameters based on cut-off values from the CIRRUS reference database. McNemar's test was used to compare individual results to the EGDSI.

Results: Mean ± standard deviation (SD) age was 63.6±10.1 (range: 35.7 to 79.6) years. Mean ± SD VF MD was -3.9±4.1 (range: -18.2 to 1.2) dB. Sensitivities for EGDSI were 81.1% and 67.6% for 95% and 99% specificity, respectively (see Table 1). The best individual parameters were: a) GCIPL Minimum (70.3% and 54.1%); b) RNFL Inferior (64.9% 54.1%); and c) Rim Area (56.8% and 36.5%). Comparable sensitivities were seen in the split cohorts, though values for EGDSI and GCIPL Minimum became more comparable in non-early glaucoma (See Table 2).

Conclusions: The combined EGDSI shows improved sensitivity in early glaucoma and comparable sensitivity in non-early glaucoma eyes in this study. As such, EGDSI may be a useful aid for the detection in a clinical range of glaucoma.

References

[1] Mwanza et al. IOVS 2013; 54(13).

[2] Mwanza et al. TVST 2018; 7(2).

[3] Durbin et al. IOVS 2020; 61(9): Abstract PB00106.

CONTROL ID: 3522674

SUBMITTER (NAME ONLY): Yukari Nakano

TITLE: Suppressing electrode position fluctuation of scleral implants using spike-shaped array

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The visual reconstruction by means of retinal prostheses requires evoking pseudolight sensations (phosphene) by electrical stimulation. However, change in electrode position over time [P. J. Allen, et al. IOVS 2019;60:4983, Y. Terasawa, et al. IOVS 2017;58:4195] makes it difficult to evoke phosphene. In this study, we evaluated whether an electrode array including dorsal protrusions (spike-shaped array; Fig. 1) can reduce the movement of the electrode.

Methods: A control array without dorsal protrusions or a spike-shaped array were implanted in the scleral pocket of rabbits (n = 6). Both arrays had platinum electrodes (diameter; 0.5 mm, height; 0.3 mm). The electrode positions were observed by scanning laser ophthalmoscopy (SLO) images immediately after surgery, and 1 week and 1 month postoperatively. The movement of the electrodes was compared by superimposing the SLO images using the coagulation plaques or black dots around the optic nerve papilla as reference points. All procedures were in accordance with the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Ophthalmic and Vision Research. This study was approved by the Institutional Animal Care Committee of Nidek Co., Ltd.

Results: SLO imaging showed movement of the device, the control array shifted a mean of 0.20 ± 0.05 mm (n = 4) and the spike-shaped array shifted a mean of 0.12 ± 0.07 mm (n = 6) between the immediate postoperative period and the first postoperative week (p = 0.07, independent t-test). The control array shifted a mean of 0.37 ± 0.06 mm (n = 4) and the spike-shaped array shifted a mean of 0.23 ± 0.10 mm (n = 6) between the first postoperative week and the first postoperative month (p < 0.05, independent t-test).

Conclusions: The spike-shaped array had a smaller movement distance of the electrodes than the control array. It is speculated that the connection between the tissue and the protrusions become stronger with elapsed time after the surgery. These results suggested that using the spike-shaped array was effective as a countermeasure against the shifts in electrode position.

CONTROL ID: 3522693

SUBMITTER (NAME ONLY): Valerie Dawson

TITLE: The Risk of Posterior Capsule Rupture in Patients with Type 2 Diabetes Mellitus and Diabetic Retinopathy During Phacoemulsification Cataract Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.J. Dawson, J. Patnaik, M. Wildes, L. Bonnell, D. Miller, M. Taravella, A. Lynch, K. Christopher, Ophthalmology, University of Colorado Health, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether type 2 diabetes mellitus (T2DM) with and without diabetic retinopathy (DR) are independent risk factors for PCR during cataract surgery while accounting for previous intravitreal injections (IVI).

Methods: A retrospective study was conducted at the Sue Anschutz-Rodgers UCHHealth Eye Center from January 2014 to March 2019. The primary outcome was incidence of PCR during phacoemulsification surgery in patients with T2DM with and without DR, accounting for previous IVI. Univariate and multivariable analysis were utilized to calculate odds ratios (OR) and adjusted odds ratios (AOR).

Results: A total of 10,893 eyes were included. A PCR occurred in 59 (0.5%) of eyes overall: 35 (0.4%) eyes in patients without diabetes, comparatively to 13 (0.7%) eyes with T2DM without DR ($p=0.142$), and 11 (1.8%) eyes with DR ($p<0.0001$).

All groups with previous IVI demonstrated a significant increase in PCR compared to eyes without IVI or T2DM. In the absence of IVI, T2DM without DR was not significant ($p=0.520$), but T2DM with DR had a significantly increased risk of PCR in univariate analysis (OR 3.55, 95% CI: 1.49, 8.50, $p=0.004$) and an increased risk of borderline significance in multivariate analysis (AOR 2.33, 95% CI: 0.98, 5.56, $p=0.056$).

Conclusions: In the absence of IVI, T2DM without DR is not an independent risk factor for PCR. T2DM with DR is likely a risk factor but was of borderline significance due to small sample size. Previous IVI is an independent risk factor for PCR. Consideration of PCR risk should be given during surgical planning for patients with DR and/or previous IVI.

CONTROL ID: 3522732

SUBMITTER (NAME ONLY): Facundo Sanchez

TITLE: Biometric parameters can predict IOP change and IOP spikes after cataract surgery in glaucoma patients

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.G. Sanchez, J. Rees, S.L. Mansberger, Glaucoma research, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|F.G. Sanchez, S.K. Gardiner, S.L. Mansberger, Glaucoma research, Discoveries In Sight Research Laboratories, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: We sought to determine whether preoperative anterior segment parameters could predict postoperative day 1 intraocular pressure (IOP) after cataract surgery (CS) in glaucoma patients.

Methods: We used the Lenstar LS 900 Optical Biometer (Haag-Streit, Koeniz, Switzerland) to preoperatively measure axial length (AL), anterior chamber depth [(ACD), i.e. the distance between the posterior surface of the cornea and the anterior surface of the lens], crystalline lens thickness [(LT), i.e. the distance along the optical axis between the two surfaces of the lens], and white-to-white distance [(WTW), i.e. horizontal iris width] in glaucoma eyes scheduled for CS.

We used generalized estimating equations regression to determine the association of these parameters with IOP change from baseline on day 1 after CS, and to derive the odd ratios (OR) for the occurrence of an acute intraocular pressure elevation (IOP spike). We defined a "5 mmHg IOP spike" as a postoperative day 1 IOP \geq 21 mmHg that was also \geq 5 mmHg greater than preoperative IOP, and a "10 mmHg IOP spike" when the elevation was \geq 10 mmHg. All calculations were adjusted for the number of preoperative ocular hypotensive agents.

Results: Table 1 shows baseline characteristics of the eyes included.

The IOP on day 1 (22.2 mmHg, SD 8.4, range 11-54) was significantly higher than preoperatively (16.9 mmHg, 4.69, 7-31; $p=.004$). We found that 38.1% (16/42) of the eyes had a 5 mmHg IOP spike, and 14.3% (6/42) had a 10 mmHg IOP spike.

Patients with shallower ACD had a significantly higher increase in IOP on day 1 (0.64 mmHg per 0.1mm decrease in ACD, $p=.023$) (Fig. 1, top), and a higher risk of 10 mmHg IOP spike (OR 1.22, $p=.013$). Similarly, patients with thicker lens had a higher increase in IOP on day 1 (0.91 mmHg higher per 0.1mm increase in LT, $p=.005$) (Fig. 1, bottom), and were more likely to have a 5 mmHg IOP spike (OR 1.04, $p<.001$) or a 10 mmHg IOP spike (OR 1.19, $p=.053$). Patients with shorter AL were slightly more likely to suffer a 10 mmHg IOP spike (OR 1.04, $p=.046$). Bivariable models showed that AL and LT were significant predictors of a 5 mmHg IOP spike ($p<.001$ and $p=.009$, respectively).

Conclusions: Shallower ACD, shorter AL, and thicker LT were associated with increased risk of IOP spikes on postoperative day 1 in glaucoma patients. This is in contrast to these same parameters being associated with a long-term decrease in postoperative IOP.

CONTROL ID: 3522797

SUBMITTER (NAME ONLY): Eric Jiang

TITLE: Field testing of All Aboard, an AI app for helping blind individuals to find bus stops

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Jiang, Z. Ma, A. Singh, A. Bobba, S. Park, S. Pundlik, G. Luo, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many blind people take public transportation, especially in metropolitan cities. Due to the lack of pin-point accuracy of conventional geo-location information provided by mobile devices, when navigating to the bus stops, they sometimes may experience the 'last-10-meter' problem, which refers to a gap between the bus stop and the destination announced by the mobile devices. The gap may sometimes be large enough for bus drivers to misunderstand the blind people's intention and not stop the buses for them. This pilot study evaluates an AI solution to address the localization problem.

Methods: We developed a mobile AI app, All Aboard, which detects bus stop signs in the users' vicinity in the images captured by the smartphone camera in real-time. The deep neural network for bus stop sign detection was custom-trained using 5000 to 10000 images collected for a given city. The app guides the users to approach bus stop signs through auditory cues, with pitch coding the distance to the target. In a pilot test, we evaluated the accuracy of localizing bus stops using the All Aboard app versus the Google Map navigation for 20 bus stop locations in the Los Angeles area. 10 bus stops were in the downtown area near high-rises, and the other 10 stops were in suburban areas. The experimenter walked under the guidance of auditory cues given by All Aboard app and Google Maps, respectively, starting from about 25 meters away from each bus stop. The localization error was measured as the distance from the actual bus stop signs to the location where the apps indicated the user arrived at the destinations.

Results: The successful navigation rate with Google Maps was 60% (failed to localize 7 stops in downtown and 1 in suburban), and with All Aboard app was 95% (failed to detect 1 downtown stop). The All Aboard app was able to detect bus stop signs starting from an average distance of 9.7 ± 6.3 (SD) meters. Excluding navigation failures, the localization error with All Aboard app (average \pm SD: 1.1 ± 0.6 meters, max. = 2.2 meters) was significantly lower than Google Maps (7.4 ± 3.8 meters, max. = 13 meters) (paired t-test, $p < 0.001$).

Conclusions: The promising results suggest that the bus stop sign detection app can potentially address the "last-10-meter" problem for blind individuals taking bus transportation.

CONTROL ID: 3522847

SUBMITTER (NAME ONLY): Agne Markeviciute

TITLE: Differences of structural parameters in patients with open angle glaucoma, high myopia and both diseases concurrently

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Markeviciute, I. Januleviciene, Eye Clinic, Lithuanian University of Health Sciences, Kaunas, LITHUANIA|B.A. Siesky, A. Verticchio Vercellin, A. Harris, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai Hospital, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate differences of structural parameters in patients with open angle glaucoma (OAG), high myopia (M) and both diseases (OAG-M) concurrently.

Methods: 30 patients (22 women, 8 men) were included in the prospective pilot study: 10 patients with OAG (age in years) 54.2 (3.11), 10 patients with OAG-M (51.8 (8.0)) and 10 patients with M (48.2 (5.12)). The study groups did not vary significantly in age ($p=0.07$) or gender ($p=0.84$). Study eyes were chosen randomly. Peripapillary retinal nerve fiber layer (RNFL) thickness, macular ganglion cell complex (GCC), macular and peripapillary vessel density (VD%) were measured using optical coherence tomography (OCT) (swept source, TOPCON DRI Triton). Peripapillary VD was evaluated using ImageJ software (National Institute of Health, Bethesda, Maryland). Kruskal-Wallis test was used to determine the differences in median values between groups with $p<0.05$ considered statistically significant.

Results: The mean spherical equivalent (SE) in OAG was 0.62D (SD 0.53), M -7.2D (1.0), OAG-M -7.75D (3.07). The mean RNFL thickness was 91.7 (17) μm in OAG; 95.1 (6.6) μm in M and 82.7 (17.8) μm in OAG-M groups ($p>0.05$). The RNFL thickness was significantly different between groups in the temporal quadrant ($p=0.023$) with the lowest value found in the OAG group. OAG-M patients had significantly lower GCC thickness 87.6 (10.8) μm , compared to OAG 95.4 (11.34) μm and M 103.1 (3.1) μm patients ($p=0.01$). Significant positive correlations were found between mean RNFL thickness and mean peripapillary VD of the optic nerve head (ONH) ($r=0.532$, $p=0.004$). Higher myopia correlated with decreased RNFL thickness ($r=-0.571$, $p=0.001$). Lower macular GCC thickness positively correlated with thinner optic nerve head (OND) RNFL ($r=0.75$, $p<0.001$).

Conclusions: Peripapillary RNFL and macular GCC thickness were lowest in patients with concurrent OAG and high myopia. Additionally, higher myopia alone was related to a lower RNFL thickness. Specifically designed longitudinal studies are needed to better define and differentiate changes of structural parameters that occur in glaucomatous and myopic disease.

CONTROL ID: 3523295

SUBMITTER (NAME ONLY): Saray Tabak

TITLE: The effect of intraocular pressure-lowering drugs on non-pigmented ciliary epithelium-derived exosomes interactions and their impact on trabecular meshwork internalization

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tabak, E. Beit Yannai, S. Schreiber Avissar, Clinical Biochemistry and Pharmacology, Ben Gurion Heritage Institute, Midreshet Ben Gurion, Southern, ISRAEL]

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ABSTRACT BODY:

Purpose: Our purpose was to investigate the effect of physicochemical properties on exosomes interactions with glaucoma eye drops in the context of the pathway by which exosomes enter the target cells.

Methods: Exosomes were isolated by precipitation method and concentrations were determined by Tunable Resistive Pulse Sensing technology. To evaluate the ionic strength (IS) effects on exosomes size and ZP, different PBS buffer strengths, eye drops solutions used for POAG treatment; Alphagan-P®, V-OPTIC®, AZOPT®, Lumigan®, and Travatan®, their active ingredients; Timolol maleate, Brinzolamide or their preservative benzalkonium chloride were analyzed. The size, ZP, and IS of exosomes were measured using NTA and Zeta sizer devices, respectively. The contribution of exosomes interactions to the internalization ratio, regulated by TM cells, was examined at different time points.

Results: Exosomes size and ZP were affected by the IS of the buffer rather than exosomes type. Commercial glaucoma eye drops including β -blocker, α -2-agonist, and prostaglandin analogs, reduced NPCE exosomes ZP. Whereas, exposure of exosomes to carbonic anhydrase inhibitor caused an increase in the ZP. A correlation was found between increased ZP values and increased NPCE exosomes uptake by TM cells. We were able to show that Benzalkonium chloride stands behind this ZP effect and not Timolol or Brinzolamide.

Conclusions: Our findings suggest that exosomes size, surface membrane charge, and IS of the surrounding, have an impact on exosomes:exosomes interactions which affect the uptake of NPCE exosomes by TM cells.

CONTROL ID: 3523647

SUBMITTER (NAME ONLY): Eric Seemiller

TITLE: Dimension reduction reveals underlying factors of performance within a vision screening battery

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Seemiller, E. Palmer, E. O'Keefe, E. Shoda, KBR, Inc., Ohio, UNITED STATES|J. Gaska, M. Winterbottom, Air Force Research Laboratory 711th Human Performance Wing, Wright-Patterson AFB, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision tests within a screening battery should be quick, easy and independent. Because the early visual system has limited functional architecture, many vision screening tests ultimately provide redundant information. For example, while seeking information about parallel processes such as stereopsis and motion perception, certain test battery results may be muddled by colinear relationships and shared computations. These redundancies potentially make visual screening batteries inefficient and less informative. For career fields requiring extensive medical screening (e.g. commercial pilots/drivers, military aviation, etc.), the duration of the screening may be an important factor. However, by identifying independent factors underlying visual performance, a test battery can be streamlined. The goal of this dimension reduction analysis is to identify such underlying factors in a visual screening paradigm from a large and diverse subject population.

Methods: 192 subjects underwent the Operational Based Vision Assessment Laboratory Automated Vision Testing (AVT) procedure, which included computer-based tests for visual acuity, luminance and cone contrast sensitivity, motion coherence, stereopsis, and binocular oculomotor function. Psychometric thresholds and fusional vergence ranges were collected from each subject. Factor analysis was performed on a total of 14 normalized variables with a promax rotation.

Results: This rotation identified 5 factors that explained 74% of the variance in the dataset. These factors were related to the following: 1) medium and high spatial frequency vision, 2) stereoacuity and horizontal fusional range, 3) color vision, 4) motion perception, and 5) low spatial frequency vision. Variability within individual factor loadings revealed informative trends. For example, while horizontal fusion range was associated with factor 2, vertical fusion range was not well correlated with any factor.

Conclusions: These results suggest that the number of tests within the AVT battery may be reduced to as few as five with a limited loss in information. Furthermore, identifying these underlying factors may have additional utility in predicting performance in naturalistic or operational visual tasks.

CONTROL ID: 3523648

SUBMITTER (NAME ONLY): William Freeman

TITLE: Ophthalmic Properties of Targeted Fusogenic Nanoparticles as Therapeutic Carriers

SESSION TITLE: AMD: clinical research - new therapies and technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.R. Freeman, M. Cavichini, A. Warter, K. Huffman, Jacobs Retina Center at Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|J.F. Grondek, M.J. Sailor, Department of Chemistry and Biochemistry, University of California San Diego, La Jolla, California, UNITED STATES|R. Fan, Department of Materials Science and Engineering, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intraocular drug delivery faces many challenges including delivery of drugs for extended periods to targeted tissues without adverse systemic effects. Currently, free drug is injected into the vitreous cavity every four to eight weeks with initial overdosing of tissues. In addition, most current therapeutics simply bind pathogenic molecules but do not stop their production. The ability to deliver RNA interference therapeutics intracellularly via a cell receptor specific targeting approach would solve many of the problems of intravitreal therapy.

Methods: We synthesized siRNA carriers consisting of porous silicon nanoparticles that are incorporated into fusogenic liposomes by film hydration to deliver the nanoparticles intracellularly (Fig. 1). The iRGD targeting peptide (CRGDKGPDC), developed to deliver anticancer therapeutics to malignant tumors, was conjugated to the liposome surface and is specific for neovascular epithelium. DL- α -aminoadipic acid (DL-AAA) was used to induce retinal neovascularization (RNV) in rabbits to evaluate the ability of the targeted fusogenic nanoparticles (TFNP) loaded with VEGF siRNA to reduce vascular growth. Normal rabbit eyes were dosed intravitreally with TFNP loaded with 10 μ g VEGF siRNA in a 50 μ L volume. Toxicologic and optical evaluations included slit lamp, fundus, optical coherence tomography, and fluorescein angiography at 2 and 8 weeks.

Results: The vitreous cavity remained clear and all evaluations including histology and electroretinography showed no evidence of toxicity. Fluorescein leakage in the RNV model was absent in eyes treated with VEGF siRNA loaded TFNPs compared to control eyes at 8 weeks (Fig. 2).

Conclusions: TFNPs are a novel and safe vehicle to deliver RNA therapeutics intracellularly. The porous silicon nanoparticles load high quantities of the nucleic acid payload, and the fusogenic lipid coatings enable cell entry while avoiding endocytosis. Targeting of cell-surface receptors expressed more extensively during specific disease allows more accurate targeting of diseased tissues and permits longer acting effects from a single intravitreal injection.

CONTROL ID: 3523669

SUBMITTER (NAME ONLY): Sophie Gu

TITLE: Correlation between Change in Central Subfield Thickness and Change in Visual Acuity in Eyes with Macular Edema due to Branch Retinal Vein Occlusion Receiving Fixed-Dosing Intravitreal Aflibercept Regimens: A Post Hoc Analysis of the VIBRANT Clinical Trial

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Nanegrungsunk, Ophthalmology, Chiang Mai University Faculty of Medicine, Chiang Mai, THAILAND|S.Z. Gu, S.B. Bressler, N.M. Bressler, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|W. Du, H. Moini, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess correlation between change in central subfield thickness (CST) and change in best-corrected visual acuity (BCVA) in eyes with macular edema due to branch retinal vein occlusion (BRVO) receiving fixed-dosing intravitreal aflibercept injections (IAI) over 52 weeks.

Methods: Post hoc analysis of the VIBRANT clinical trial, in which eyes were randomized to IAI (6 doses every 4 weeks of 2 mg IAI, followed by IAI every 8 weeks) or macular laser photocoagulation at baseline. The relationship between functional (BCVA) and anatomical (CST) outcomes at weeks 12, 24, and 52 was determined using Pearson correlation coefficient.

Results: Of 181 eyes, 91 received IAI and represent the analysis cohort. The percentage of eyes with both BCVA and CST measurements available for analysis at weeks 12, 24, and 52 was 97%, 91%, and 80% of enrolled IAI-assigned eyes. At baseline, the correlation (r) between CST and BCVA was -0.41 (95% CI: -0.56 to -0.22). Correlations (r) between change in CST and change in BCVA from baseline at weeks 12, 24, and 52 were -0.34 (95% CI: -0.51 to -0.14), -0.32 (95% CI: -0.50 to -0.11), and -0.36 (95% CI: -0.54 to -0.14), respectively. In a linear regression analysis of correlation between changes in CST and changes in BCVA at week 52 adjusted for baseline factors (age, perfusion status, time since diagnosis, and baseline BCVA), CST changes accounted for only 23% of the variance in BCVA changes. At 52 weeks, every 100 μ m decrease in CST was associated with a 2.2 letter increase in BCVA (95% CI: -0.2 to 4.5, P = .07).

Conclusions: In eyes treated with fixed-dosing IAI for macular edema from BRVO, the magnitude of the correlation between change in CST and change in BCVA was weak to moderate. For any given change in CST from baseline, there was a broad range of change in BCVA at weeks 12, 24, and 52. While changes in CST may be important in determining the need for repeat anti-VEGF to manage macular edema due to BRVO, these findings do not support using changes in CST to predict visual acuity outcomes.

CONTROL ID: 3523694

SUBMITTER (NAME ONLY): Annika Balraj

TITLE: Refinement of optic nerve function and myelination during postnatal wildtype development

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Balraj, R.H. Miller, Anatomy, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cells generate a pattern of action potentials to communicate visual information. Myelin, an insulating sheath, facilitates signal propagation by wrapping around axons and, when deficient (as observed in patients with optic neuritis), can cause significant visual deficits. However, the relationship between optic nerve function and the extent of myelination is currently unknown.

Methods: We tested if myelination patterns are correlated with changes in optic nerve function during postnatal development using extracellular nerve recordings, immunohistochemistry, western blot, and scanning electron microscopy.

Results: Comparing compound action potentials from C57Bl6 mice across ages 4-12 wks revealed an increase in the number of functional axons and shifts toward more fast-conducting axon populations at 5 and 8 wks ($p < 0.05$, $n=8$). At these ages, nerve assessments suggest increases in myelin and neurofilament protein concentrations ($n=2$) and lower g-ratios ($n > 2$). Increased expression of a mature sodium ion channel (Nav 1.6) at nodes of Ranvier was observed at 6 wks ($p < 0.05$, $n=3$), while axon diameter, axon density, and nodal density remained unchanged across ages.

Conclusions: Changes in the normal optic nerve to favor faster axonal conduction correlate with additional myelin proteins, thicker myelin around axons, and node maturity, suggesting that these properties are critical in the refinement of optic nerve signaling during postnatal maturation.

CONTROL ID: 3523700

SUBMITTER (NAME ONLY): Onkar Dhande

TITLE: CCR3 inhibition reduces recruitment of peripheral immune cells to the eye in the sodium iodate model of age-related macular degeneration

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Dhande, S. Caryotakis, Y. Lopez, S. Minami, Alkahest Inc, San Carlos, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent Phase 2a clinical studies were completed with AKST4290, a potent CCR3 inhibitor, in treatment-naïve nAMD and refractory nAMD patients. The majority (83%) of nAMD subjects demonstrated stable or improved best-corrected visual acuity after 6 weeks of AKST4290 treatment. Preclinical studies were subsequently conducted to examine whether the efficacy observed in nAMD patients was in part due to blocking CCR3-mediated retinal homing of damage-promoting immune cells from the periphery which in turn dampens local inflammation and may subsequently modify disease progression.

Methods: The sodium iodate (NaIO₃) model (single iv injection, 20 mg/kg) was used to induce retinal inflammation and degeneration in C57Bl6 mouse eyes. Mice were treated with twice daily oral dose (60 mg/kg) of AKST4290. Flow cytometry was used to examine the immune cell composition in the retinal pigment epithelium (RPE) at 3 days post NaIO₃ injection. The effect of AKST4290 treatment on inflammatory cytokines in the eye was probed using Luminex immunoassays. Nested generalized linear model with pair wise comparison was used for statistical analysis.

Results: NaIO₃ induced a significant increase in number of immune cells in the degenerating RPE (Control vs NaIO₃; monocytes [cell counts, mean±sem]: 74±16 vs 1679±222; neutrophil: 14±3 vs 146±17; CD4 T cells: 33±5 vs 170±26; p<<0.01). AKST4290 treatment significantly reduced immune cell infiltration in NaIO₃ damaged RPE (NaIO₃+4290; monocytes: 1051±153; neutrophil: 82±15; CD4 T cells: 131±29; NaIO₃ vs NaIO₃+4290 p<0.01). Treatment with AKST4290 also significantly reduced NaIO₃ induced increase in chemokines CCL5 (Control vs NaIO₃ vs NaIO₃+4290 (mean±sem (pg/ml): 1.41±0.11 vs 2.05±0.13 vs 1.76±0.13, p<0.05) and CXCL9 (1.8±0.26 vs 5.56±0.67 vs 3.67±0.43, p<0.05).

Conclusions: These data demonstrate that systemic inhibition of CCR3 by AKST4290 reduces the accumulation of peripheral immune cells in the RPE, which is the primary injury site in the NaIO₃ model and in nAMD. This reduction in recruitment of immune cells was associated with a decrease in chemokines in the degenerating RPE. These findings help illustrate the mechanism of action for AKST4290, supporting its observed efficacy as a drug candidate in clinical trials of nAMD patients.

CONTROL ID: 3523797

SUBMITTER (NAME ONLY): Yesenia Lopez

TITLE: Determining the pharmacokinetics and ocular distribution of AKST4290, a clinical stage oral therapeutic for age-related macular degeneration

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lopez, R. Harish, S. Rege, J. Masumi, A. Teichert, O. Dhande, S. Minami, Alkahest Inc, San Carlos, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: AKST4290, a non-brain penetrant inhibitor of CCR3, has undergone Phase 2a clinical studies in treatment-naïve and refractory neovascular age-related macular degeneration (nAMD) patients. The majority of nAMD patients displayed stable or improved best corrected visual acuity (BCVA) after 6 weeks of treatment. The goal of these preclinical studies was to identify potential sites of action by determining the pharmacokinetics and biodistribution of AKST4290 in various ocular compartments.

Methods: Quantitative whole-body autoradiography (QWBA; [^{14}C]-AKST4290) and LC-MS/MS bioanalysis was performed to assess drug levels in the eye. Male and female C57BL/6 mice were used for the QWBA study, and both C57BL/6 and Balb/c male mice were used for LC-MS/MS. For QWBA, [^{14}C]-AKST4290 was administered orally (single dose, 10 mg/kg) and autoradiography was performed at various post-dose time points (15 mins to 12 weeks). AKST4290 levels were quantified by LC-MS/MS in the retinal pigment epithelium (RPE)/choroid and retina at 0.5h, 2h, and 24h post-dose (single oral dose, 30 mg/kg).

Results: QWBA showed maximal levels of AKST4290 derived radioactivity at 24h post-dose in both the whole eye (0.56 $\mu\text{g eq/g}$) and uveal tract (2.61 $\mu\text{g eq/g}$) of male C57BL/6 mice. In comparison, AKST4290 in the uveal tract of female C57BL/6 mice peaked at 48 h (1.37 $\mu\text{g eq/g}$), and both male and female samples showed sustained levels up to 12 weeks (0.18 and 0.0643 $\mu\text{g eq/g}$ respectively) post-dose. Bioanalysis detected high levels of AKST4290 in the RPE/choroid of C57BL/6 mice at 0.5h (mean \pm sem[ng/ml]: 447.8 \pm 143.89), 2h (1087.2 \pm 106.64), and 24h (941.5 \pm 273.09) post-dose. In comparison, levels of AKST4290 in the RPE/choroid of Balb/c were significantly less at 2h (235.6 \pm 27.05, $p=0.0079$, Mann-Whitney). Relatively low levels of AKST4290 were detected in the retina of both strains at the 2h time point (C57BL/6: 460.06 \pm 41.79; Balb/c: 12.98 \pm 1.61).

Conclusions: These data show a preferential accumulation of AKST4290 in the RPE/choroid, the primary site of nAMD pathologies. Moreover, these data show a strong effect of retinal pigmentation on the levels of drug accumulation in the eye. These data support the RPE/choroid as a potential site of AKST4290 action in nAMD and contextualize treatment efficacy observed in clinical trials.

CONTROL ID: 3523928

SUBMITTER (NAME ONLY): David Boyer

TITLE: Oral Administration of the Complement Factor D Inhibitor Danicopan (ALXN2040) in Preclinical Studies Demonstrates High and Sustained Drug Concentrations in Posterior Ocular Tissues for the Potential Treatment of Geographic Atrophy

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Boyer, J. Rivera, Y. Ko, S.D. Podos, M. Cartwright, X. Gao, J. Wiles, M. Huang, Alexion Pharmaceuticals Inc, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Danicopan is an investigational first-in-class small-molecule inhibitor of factor D, an essential enzyme of the complement alternative pathway, which, when dysregulated, is implicated in the pathogenesis of age-related macular degeneration (AMD). We explored, in animal models, delivery of PO danicopan to the posterior segment of the eye for the potential treatment of geographic atrophy (GA), an advanced form of AMD.

Methods: Tissue distribution of drug-related radioactivity was studied following PO administration of [^{14}C]danicopan 20 mg/kg to pigmented Long-Evans (LE) and albino Wistar Han (WH) rats. Danicopan binding to natural and synthetic melanin was determined in vitro. Ocular tissue distribution was studied in pigmented Dutch-Belted (DB) and albino New Zealand White (NZW) rabbits following PO danicopan at 15 and 50 mg/kg BID for up to 15 days.

Results: After PO administration to rats, [^{14}C]danicopan-derived radioactivity was absorbed rapidly and distributed widely to tissues. Radioactivity was present 1–8h and became nonquantifiable 24h post-dose in most tissues. In LE, but not WH rats, radioactivity remained quantifiable in the uvea 672h post-dose ($t_{1/2}=576\text{h}$), suggesting danicopan binding to melanin, which was confirmed in vitro (mean $K_D=8.6\mu\text{M}$). Distribution to ocular tissues was also observed following PO administration of danicopan to rabbits: C_{max} retina:plasma ratios were 0.5–1 in DB and NZW, demonstrating that danicopan crosses the blood–retinal barrier (BRB); AUC choroid/RPE:plasma ratios were 24 and 0.7, respectively, in DB and NZW after single dosing (15 mg/kg), further supporting danicopan binding to melanin; and AUCs increased 7- and 13-fold in choroid/RPE and retina, respectively, after 15-day dosing (15 mg/kg BID) versus single dosing (15 mg/kg) in DB, suggesting that melanin-bound danicopan in choroid/RPE may serve as a drug depot maintaining high concentrations of danicopan in retina. Danicopan was well tolerated and resulted in no toxicity or ophthalmic abnormalities.

Conclusions: PO danicopan crosses the BRB and binds to melanin, leading to high and sustained drug exposure in posterior ocular tissue. These results support clinical investigation of danicopan for the oral treatment of GA.

CONTROL ID: 3524055

SUBMITTER (NAME ONLY): Acner Camino

TITLE: Compensation of OCTA flow index dependence on OCT signal strength

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Camino, Y. Jia, Y. Guo, D. Huang, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Acner Camino: Commercial Relationship(s);Genentech:Code E (Employment) | Yali Jia: Commercial Relationship(s);Optovue:Code F (Financial Support);Optovue:Code P (Patent) | Yukun Guo: Commercial Relationship: Code N (No Commercial Relationship) | David Huang: Commercial Relationship(s);Optovue:Code F (Financial Support);Optovue:Code I (Personal Financial Interest);Optovue:Code P (Patent);Optovue:Code R (Recipient)

ABSTRACT BODY:

Purpose: Optical coherence tomographic angiography (OCTA) images have been used to measure retinal vessel density and quantify the effect of eye diseases on retinal perfusion. Another OCTA parameter, the flow index, has also been investigated. The flow index is the average value of the flow signal in an en face OCTA image. It may be a more sensitive indicator to detect changes in velocity or volumetric flow than vessel density. But, due to its strong dependence on the strength OCT reflectance signal, it is less reliable for disease diagnosis. In this work, we present a compensation method to remove this dependence.

Methods: $3 \times 3 \text{ mm}^2$ macular OCTA scans were acquired by a spectral-domain OCT system (AngioVue). The flow index of the superficial vascular complex (SVC) was defined as the averaged OCTA decorrelation outside the foveal avascular zone (FAZ) - defined as a circle of 0.3-mm radius centered in the fovea - excluding large vessels. Sixty images were acquired from 10 healthy eyes by attenuating the signal strength with neutral density filters (NDF). The decorrelation values of background voxels were set to zero by a thresholding algorithm that accounted for voxel reflectance, which yields a vessel density that is independent of signal strength. Then, capillary flow signal was normalized to the averaged large vessel decorrelation signal of the scan, by compensating the linear dependences of the average large vessel and capillary decorrelation on average OCT reflectance (Fig. 1).

Results: The flow signal compensation was tested on a separate set of nine healthy eyes scanned repeatedly between two and six times under optimal imaging conditions. The dependence of flow index on OCT signal strength (Fig. 2) was reduced after applying the compensation scheme (Pearson's $R = 0.86$, $p < 0.01$ before compensation vs. $R = 0.49$, $p < 0.01$ afterwards). The coefficient of variation on the flow index in the test set was reduced by the compensation scheme from 14.8% to 10.8 %. The repeatability of the flow index, measured as the pooled coefficient of variation per eye was improved from 5.8% before compensation to 4.9% afterwards.

Conclusions: The algorithm successfully reduced the flow index dependence on OCT signal strength and yielded a more repeatable flow index measurement. This metric has potential to describe capillary flow changes in diabetic retinopathy, retinal vein occlusion and glaucoma.

CONTROL ID: 3524078

SUBMITTER (NAME ONLY): Yu-Chi Liu

TITLE: Tear Neuromediator and Corneal Denervation following Small Incision Lenticule Extraction (SMILE)

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, M. Lin, Singapore Eye Research Institute, Singapore, SINGAPORE|J.S. Mehta, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate the changes in tear neuromediators and corneal subbasal nerve plexus following small incision lenticule extraction (SMILE).

Methods: Thirty patients were included for tear neuromediator analysis (40 eyes) and corneal nerve analysis using in-vivo confocal microscopy scans (20 eyes). Tear analysis included substance P (SP), calcitonin gene-related peptide (CGRP) and nerve growth factor (NGF) concentrations.

Results: Corneal nerve fiber density (CNFD), corneal nerve fiber length (CNFL), and corneal nerve branch density (CNBD) decreased significantly postoperatively, then gradually increased from 3 months onward, but did not recover to the baseline levels at 12 months. Tear SP and CGRP levels remained stable over 12 months. Tear NGF levels demonstrated a small peak at 1 week, before decreasing significantly compared to preoperative levels at 6 months ($P=0.03$) and 12 months ($P<0.01$). The 1-month reduction in CNFL, tear SP and CGRP concentrations were significantly correlated with the spherical equivalent (SE) corrected ($r=0.71$ for CNFL; $r=-0.33 \sim -0.52$ at different time points for SP and CGRP, respectively, all $P<0.05$). The high myopia group (corrected SE greater than -6.0 diopters), compared to the low-moderate myopia group, had significantly greater decrease in CNFD, and significantly higher tear SP concentrations at 1 week, 1 month and 6 months, as well as significantly higher tear CGRP concentrations at 1 and 6 months.

Conclusions: Our results provide new insight into the neuro-biological responses and their potential implications in corneal nerve damage and recovery after SMILE. High myopic treatment was associated with greater corneal denervation and neuroinflammation.

CONTROL ID: 3524256

SUBMITTER (NAME ONLY): Lewis Karapanos

TITLE: Functional vision in the real-world environment with a 44-channel suprachoroidal retinal prosthesis

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Bionic Vision Technologies Australia suprachoroidal retinal prosthesis ("bionic eye") has been shown to improve functional vision in patients with late stage retinitis pigmentosa (RP) in a first-generation trial in a laboratory setting. In a subsequent trial of a second-generation device (NCT03406416), we assessed whether patients with late stage RP could increase their performance in real-world functional visual tasks conducted with the prosthesis switched ON compared to OFF.

Methods: The Functional Low-Vision Observer Rated Assessment (FLORA) instrument was administered to three males (aged 39, 47 and 63) and one female (aged 66) before implantation and at 17, 20, 32, 44, 56 and 68 weeks after device fitting. The FLORA contains 13 self-reported and 35 observer-reported items. The ease of which participants completed each functional vision task was assessed with a four-point scale: impossible, difficult, moderate, and easy. The tasks were evaluated in four discrete domains: 'Visual Orientation', 'Visual Mobility', 'Daily Life' and 'Interaction with Others'. The distribution of person-level domain scores has been summarised via mode.

Results: Three participants completed the FLORA up to 68 weeks, with one participant being lost to follow up at 20 weeks for reasons unrelated to the device. For all participants after 17 weeks, the mode ease of task score with the device switched ON was higher or equal to when it was switched OFF (Figure 1). In general, ease of task score increased over time with the device switched ON. Tasks from the 'Visual Orientation' and 'Daily Life' domains were the main contributors to this effect. Qualitative analyses revealed participant-reported improvements in mobility, functional vision, and quality of life with device switched ON.

Conclusions: Participants with late-stage RP implanted with the second-generation suprachoroidal retinal prosthesis demonstrated improved ease of task scores over time with device ON relative to OFF. Improvement of ease of task scores over time with the device ON suggests a learning effect. The device shows potential utility in everyday life, and further research into its real-world use is warranted.

CONTROL ID: 3524322

SUBMITTER (NAME ONLY): Maja Magazin

TITLE: Utilizing a Mobile Platform to Obtain Quantitative Measurements of Exophthalmos

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Magazin, Ophthalmology, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|A.A. Tooley, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|A.Q. Tran, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hertel exophthalmometry has demonstrated limited reproducibility between observers and high variability between instruments of the same design. We conducted a prospective, comparative study to introduce a novel exophthalmometry method utilizing a mobile platform and compare its reliability to Hertel exophthalmometry. We hypothesize that a mobile platform can serve as a simple, socially distanced alternative for obtaining reliable and accurate measurements of globe position.

Methods: Fifty patients (99 eyes) were included for a total of 594 measurements. Healthy individuals from the community and individuals from a routine oculoplastics clinic were included to represent variety within the population. Exophthalmometric measurements were first obtained using a Hertel exophthalmometer by two masked observers. A widely accessible mobile ruler application was then used to obtain measurements through sagittal facial photos by using a credit card as a reference standard in the picture in order to scale measurements. The main outcome was the inter-modality correlation and agreement between Hertel and mobile exophthalmometry, and the intra-observer and inter-observer reliability with repeated mobile measurements.

Results: There was no significant difference between mobile measurements of each eye and those obtained by Hertel exophthalmometry (P-value for right and left eyes 0.726, 0.088). There was a strong linear correlation between Hertel and mobile exophthalmometry with a Pearson Correlation Coefficient of 0.910 and 0.888 for the right and left eyes, respectively ($p < 0.001$, 2-tailed). Bland-Altman plot analysis showed excellent agreement between the two modalities. The mobile platform demonstrated high intra-observer reliability with a Cronbach's alpha of 0.992 and 0.985 for the right and left eyes. An intraclass correlation coefficient of 0.992 (95% CI: 0.987-0.995) for the right eye and 0.986 (95% CI: 0.978-0.991) for the left eye demonstrated excellent reliability between observers.

Conclusions: The strong correlation and agreement between Hertel and mobile measurements suggest that a mobile platform can be a promising new alternative for obtaining reliable and accurate measurements of globe position. This alternative technique may be especially useful in situations where Hertel exophthalmometry may not be available or feasible such as in-patient settings and virtual office visits.

CONTROL ID: 3524399

SUBMITTER (NAME ONLY): Amar Pujari

TITLE: Accommodation study 1: Novel physiological changes in anterior segment structures during real-time long-range accommodation

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pujari, S. Modaboyina, S. Yadav, R. Sihota, P. Sharma, N. Sharma, T. Dada, J. Titiyal, Ophthalmology, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: To systematically study anterior segment changes during dynamic, long-range accommodation.

Methods: Design: Prospective, observational study.

Participants: A total of 26 young, healthy, third-decade subjects with less than $\pm 0.5D$ refractive error.

Methods: On swept-source anterior segment optical coherence tomography (CASIA-2, Tomey Corp, Japan), anterior segment structural changes were recorded on accommodation, from baseline (0 diopter) to 8 diopters.

Main outcome measures: Software generated automated changes in corneal thickness and volume, anterior chamber depth and area, iris area and curvature, lens curvature, lens thickness, lens tilt and decentration at each diopter, and qualitative changes in the ciliary body were noted.

Results: Results: 52 eyes of 26 subjects were evaluated, with mean age of 25.92 ± 1.64 years. Each successive dioptric accommodative stimulus from baseline, lead to progressive decremental responses in anterior lens curvature ($p < 0.001$), posterior lens curvature ($p < 0.001$), anterior chamber depth ($p < 0.001$) and anterior chamber area ($p = < 0.05$) with corresponding, incremental responses in lens thickness ($p < 0.001$) noted till 8D. However, the overall and inter-dioptric responses were more significant during the initial phases of stimulation, up to 4D, as compared to later. Likewise, iris (nasal and temporal) curvature ($p < 0.001$) and area ($p < 0.001$) also showed dynamic changes in a coordinated manner. Cornea and anterior chamber width changes were statistically insignificant, even though fluctuations were noted at higher dioptries.

Conclusions: Conclusions: On progressively increasing accommodation, initial significant changes were seen as primarily lenticular, complementary anterior chamber and associated iris changes. Whereas, accommodation at higher diopters showed significantly altered lens position and other complex anterior segment structural changes.

CONTROL ID: 3524802

SUBMITTER (NAME ONLY): Serpil Yazgan Akpolat

TITLE: Can bacterial cellulose membrane prevent bleb fibrosis in trabeculectomy surgery? An in vivo trabeculectomy study in a rabbit model

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the effectiveness of bacterial cellulose membrane (BCM) in preventing fibrosis in a rabbit model trabeculectomy surgery and to investigate the biocompatibility of BCM with eye tissues.

Methods: Twenty-one eyes of 21 adult male rabbits underwent fornix-based trabeculectomy. Standard surgery was applied to the control group (CG, n=7). In addition to the standard process; mitomycin-C (MMC, 0.3 mg/ml) was applied to the sclerotomy area for 3 minutes to MMC group (MMCG, n=7), and in the BCM group (BCMg, n=7), the sclerotomy area was covered with BCM (10x10 mm, ~ 100 µm thick) as a single layer before closing the conjunctiva. BCM was sutured to the sclera from the proximal edges, and the distal edge was extended to the fornix freely. Intraocular pressures (IOP) were measured before surgery (baseline) and on the postoperative 7th, 14th, 28th and 45th days (IOP-POD7, POD14, POD28 and POD45). The rate of decrease in IOP over time were calculated according to the baseline values and expressed as decrease in IOP% (DIOP%)-POD7, DIOP%-POD14, DIOP%-POD28 and DIOP%-POD45. The rabbits were sacrificed on the 45th day. The surgery area was examined histopathologically and immunohistochemically for conjunctival vascularity, fibrosis, inflammation, foreign body reaction and expression of α -smooth muscle actin (α -SMA).

Results: There was no difference between the three groups in terms of baseline IOP and DIOP%-POD7 ($p=0.126$, $p=0.620$, respectively). While DIOP%-POD14, 28 and 45 values were similar between BCM and MMC groups, they were significantly lower in the CG compared to the others ($p < 0.05$). The groups were similar with regard to conjunctival vascularity ($p = 0.122$). Only in the BCMg group, 2 cases had moderate and 5 cases had mild foreign body reaction. There was no difference between CG and MMCG regarding inflammation, but moderate reaction was detected in all cases in the BCMg ($p=0.01$). While fibrosis and α -SMA levels were found to be significantly higher in the CG ($p<0.001$), there was no difference between the MMCG and BCMg.

Conclusions: Bacterial cellulose membrane provided better control of IOP with minimal fibrosis compared to the control. It was also found to have a good biocompatibility with eye tissues. With these features, BCM may be a candidate for use as an adjuvant tissue not only in trabeculectomy but also in other ocular surgeries.

CONTROL ID: 3524949

SUBMITTER (NAME ONLY): Masato Matsuo

TITLE: 360-degree gonio-camera-based estimation of peripheral anterior synechiae formed after microhook ab-interno trabeculotomy

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Matsuo, Y. Inomata, N. Kozuki, M. Tanito, Ophthalmology, Shimane University Faculty of Medicine, Izumo, JAPAN|

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ABSTRACT BODY:

Purpose: Postoperative peripheral anterior synechiae (PAS) formation after microhook ab-interno trabeculotomy (μ LOT), a minimally invasive glaucoma surgery (MIGS) procedures is not well studied; however, it could potentially reduce the surgical effectiveness. Additionally, the investigation would contribute to a better understanding of outcomes of trabeculotomy-related surgeries. Therefore, the purpose of the current study was to investigate the characteristics of PAS formation after μ LOT with a 360-degree gonio-camera, gonioscope GS-1 (NIDEK Co., Gamagori, Japan).

Methods: Consecutive one hundred five eyes of 75 subjects with open-angle glaucoma were analyzed; the eyes had undergone μ LOT or combined μ LOT and cataract surgery as an initial glaucoma surgery. Postsurgical PAS formations were evaluated in 16 iridocorneal angle images with the best focus covering 360 degrees in each eye.

Results: Compared to baseline, at 225 ± 226 days postoperatively, the intraocular pressure and number of antiglaucoma medications decreased significantly ($P < 0.01$, respectively). PAS formed in 86% of the eyes. The mean number of iridocorneal angle images in all eyes that exhibited PAS was 4.1 (26%) in the total circumference, 3.1 (39%) within the μ LOT incision, and 1.0 (13%) outside of the μ LOT incision; the rate was significantly higher within the incision than outside of the incision ($P < 0.01$). Moreover, the higher PAS rate in total and that within the incision had the possible association with later postoperative days ($P < 0.01$, respectively); that outside of the incision had the possible associations with μ LOT alone rather than combined surgery, and with shallower preoperative central anterior chamber depth ($P < 0.05$, respectively), which were calculated by the mixed-effect model.

Conclusions: We could have performed the detailed observation of PAS formation after μ LOT with 360-degree gonio-images, and the formation rate was significantly higher within the μ LOT incision. The PAS within and outside of the incision would have different causes.

CONTROL ID: 3524973

SUBMITTER (NAME ONLY): Robin Hirt

TITLE: Evaluation of Federated Learning for OCT B-scan classification

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Building robust deep learning-based models requires large quantities of diverse training data. Due to medical data privacy regulations, it is often infeasible to collect sensitive patient data in a centralized data lake. Federated Learning (FL) sidesteps this difficulty by only sharing intermediate model training updates among them. In this study, we will show the effectiveness of FL in comparison to models trained on isolated and centralized data.

Methods: 76,544 OCT B-scans from 598 macular cubes acquired from 598 subjects using CIRRUSTM HD-OCT 5000 (ZEISS, Dublin, CA) were used as the training and test sets (478/120 split at cube level). 40% of B-scans were graded as “abnormal” by at least 1 of 2 retinal specialists.

A real-world scenario was simulated by splitting the training set into 3 originating regions for US (Region A), Europe (Region B), and Asia (Region C). For validation, the global test set consisted of 15,338 B-scans (38% “abnormal”) from the 120 cubes.

A ResNet50 was used to perform binary classification at the B-scan level. To evaluate the FL approach with meaningful baselines, we additionally trained isolated models on the regional data sets and one global model on the complete data set which share the same ANN settings and 50 epochs. All models have been tested on a global test set.

For applying FL, the decentralized ML framework mlx (prenodelabs, Germany, Karlsruhe) was used (see Fig. 1). Each model was trained for one epoch per region locally before centralizing their updated model weights (Δw) for aggregation. This cycled for 100 iterations.

Results: In Table 1, we show the performance (ACC, AUC, and 95% CI in %) of locally best models (selected by best validation score on the global test set) using local training data alone as well as after federated learning.

For Region B and C, a 7.1% relative improvement in accuracy can be observed when the federated model is applied.

Conclusions: Given our experimental results, we can see that FL in a simulated real-world scenario can both ensure a higher level of security and trust between data owners as well as increase the generalizability of the model across regions.

In addition, we observe no difference in the performance of a federated model in comparison to a model that has directly been trained on centralized data. Thus, we show the potential of FL replacing a conventional centralization of data to preserve confidentiality whilst developing robust models.

CONTROL ID: 3525192

SUBMITTER (NAME ONLY): Frank Koch

TITLE: Intraocular illumination – opportunities and risks of novel approaches

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.H. Koch, S. Deuchler, P. Singh, Eye Clinic, Retina and Vitreous unit, Goethe-Universität Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|C. Lingenfelder, Office Dornstadt, Dornstadt, GERMANY|P. koelbl, N. Siebert, R. Haag, M. hessling, Institute of applied sciences, Universität Ulm, Ulm, Baden-Württemberg, GERMANY|D. Sinning, Epigap Berlin, Berlin, Berlin, GERMANY|T. Kohnen, Eye Clinic, Goethe-Universität Frankfurt am Main, Frankfurt am Main, Hessen, GERMANY|

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ABSTRACT BODY:

Purpose: In 2015 the authors were presented with EURETINA European Society of Retina Specialists Innovation Award for their idea to directly place LEDs within the eye during intraocular surgery. Thus better and safer illumination should be reached. The results of their research over the last 4 years is presented. Due to availability of novel LED illumination systems ophthalmologists must consider their impact on patients. Various aspects of LED light when either used as an intraocular light source during surgery or a transscleral illumination system are discussed. Possible hazard of light to the retina and critical parameters will be identified.

Methods: Novel LED illumination concepts have been developed by integration of micro-SMD LED and SM-LED into trocars and diaphanosopes. The physical effects of the LED illumination have been studied by exposing both porcine and human eyes to various light sources.

Results: An anterior to posterior examination revealed a location and pressure dependent transmission of human and porcine sclera. Furthermore pressure dependent direct trans-tissue transmission of eyewall, sclera and vitreous body in the range of 350–1050 nm was confirmed. It was shown that there exists a higher risk of light-induced retinal damage due to increase of intraocular irradiance by endoillumination.

Conclusions: Novel LED based light sources offer a great potential for innovation in the ophthalmic environment. The results of our studies showed that the existing regulations should be reconsidered to further enhance patient safety. Because all our studies have been done in ex vivo settings the next step should be a human in vivo study to determine for surgical purposes relevant data.

CONTROL ID: 3525252

SUBMITTER (NAME ONLY): Jason Core

TITLE: Persistent Subretinal Fluid in the Comparison of Age-Related Macular Degeneration Treatments Trials (CATT)

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.Q. Core, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|M. Pistilli, E. Daniel, M.G. Maguire, G. Ying, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effect of persistent subretinal fluid (SRF) relative to resolved SRF on long-term visual acuity in eyes treated with ranibizumab or bevacizumab for neovascular age-related macular degeneration (nAMD) in the CATT.

Methods: Secondary analysis of CATT data from eyes with SRF at baseline and were treated pro re nata (PRN) for 2 yrs. OCT imaging was every 4 wks. Treatment was based on signs of active nAMD. Certified readers at the CATT reading center assessed OCT scans for macular presence and foveal thickness of SRF. Persistent SRF at wk 12 was defined as SRF present at wks 4, 8, and 12, while persistent SRF at 1 or 2 yrs was defined as SRF present at $\geq 80\%$ of visits over the 1- or 2-yr period. Mean visual acuity (VA) score and mean VA gain from baseline at 1 or 2 yrs were compared between eyes with vs. without persistent SRF using regression models that adjusted for persistent intraretinal fluid (IRF) and previously reported baseline VA predictors in CATT.

Results: Among 406 eyes with baseline SRF, 26.6% had persistent SRF at wk 12, 23.2% at yr 1, and 19.0% at yr 2. Eyes with vs. without persistent SRF at wk 12 showed similar mean VA score (letters) at yr 1 (68.3 vs. 69.9; $p=0.29$) and yr 2 (69.0 vs. 68.8; $p=0.93$), and similar VA gain at yr 1 (6.1 vs. 7.3; $p=0.30$) and year 2 (6.6 vs. 6.4; $p=0.94$) (Table 1). Yr 1 persistent SRF compared with no persistent SRF was not associated with significantly different mean VA scores at yr 1 (67.6 vs. 70.1; $p=0.12$) and yr 2 (68.5 vs. 69.0; $p=0.77$), or VA gain at yr 1 (5.2 vs. 7.8; $p=0.10$) and yr 2 (6.0 vs. 6.6; $p=0.74$). Yr 2 persistent SRF compared to no persistent SRF was not associated with significantly different mean VA scores at yr 1 (71.4 vs. 70.8; $p=0.71$) and yr 2 (70.0 vs. 69.5; $p=0.80$) or VA gain at yr 1 (7.9 vs. 7.8; $p=0.92$) and yr 2 (6.5 vs. 6.5; $p=0.97$). At yr 1 and earlier timepoints, SRF was absent at the foveal center in nearly half of eyes with yr 1 persistent SRF, and $<200\text{ }\mu\text{m}$ thick among most others (Table 2).

Conclusions: Among eyes with baseline SRF, mean VA in eyes with persistent SRF through 12 wks, 1 yr, or 2 yrs of PRN treatment was similar to eyes in which SRF resolved. Persistent SRF $>200\text{ }\mu\text{m}$ thick at the foveal center was rare.

CONTROL ID: 3525361

SUBMITTER (NAME ONLY): Jesper Erichsen

TITLE: Prednisolone and ketorolac versus ketorolac alone or dropless prophylaxis of macular thickening in cataract surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Choice of anti-inflammatory prophylaxis parallel to cataract surgery is contested. We performed a randomized controlled trial to determine if combination of prednisolone- and non-steroidal anti-inflammatory drug (NSAID) eye drops was superior in preventing increased central macular thickness (CMT) following uncomplicated cataract surgery compared with NSAID monotherapy and dropless surgery, and to test if preoperative initiation of eye drop treatment was superior to initiation on the day of surgery.

Methods: Low-risk participants scheduled for cataract removal were randomized to 1 of 5 anti-inflammatory prophylactic regimens; combination of prednisolone- (Pred Forte 1%) and ketorolac (Acular 0.5%) eye drops with or without preoperative initiation (Pred+NSAID-Pre (control) and Pred+NSAID-Post), ketorolac monotherapy with or without preoperative initiation (NSAID-Pre and NSAID-Post) or subtenon depot of dexamethasone (Dropless). Eye drops were administered 3 times per day until 3 weeks after surgery. Primary outcome was CMT 3 months after surgery. Secondary outcomes were intraocular pressure (IOP), visual acuity (VA) and subjective tolerance of treatment. Outcomes were measured at baseline, 3 weeks and 3 months postoperatively.

Results: We included 470 participants, mean age 72.2 (SD 7.0) years, 290 (62%) females – 94 participants in each group. Three months after surgery, CMT was (mean [95%CI]) 250.7 [247.6 ; 253.7] with Pred+NSAID-Pre, 250.7 [247.8 ; 253.7] with Pred+NSAID-Post, 251.3 [248.2 ; 254.4] with NSAID-Pre, 249.2 [246.2 ; 252.3] with NSAID-Post and 255.2 [252.0 ; 258.3] with Dropless. There were no significant differences compared with control and no differences between Pre- and Post-groups, but 56.6% in Dropless group needed additional treatment. NSAID monotherapy- and Dropless groups had significantly lower IOP until 3 weeks after surgery compared with control. There were no significant differences in VA or subjective tolerance at any postoperative time.

Conclusions: Combination of prednisolone and NSAID eye drops was not superior to NSAID monotherapy in preventing central macular thickening, but subtenon depot of dexamethasone was inefficient as a dropless approach. Initiating prophylactic treatment 3 days before surgery was not superior to initiation on the day of surgery. Adding prednisolone to NSAID eye drops resulted in higher IOP during treatment.

CONTROL ID: 3525402

SUBMITTER (NAME ONLY): Loka Thangamathesvaran

TITLE: National Emergency Department Trends for Endogenous Endophthalmitis: An Increasing Public Health Challenge

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Thangamathesvaran, A. Scott, F. Woreta, M. Breazzano, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To use a national database for understanding endogenous endophthalmitis in America and identify risk factors for admission and mortality.

Methods: The National Emergency Department Sample (NEDS) was queried from 2006 to 2017 with details encompassing emergency department (ED) visits: diagnostic codes, procedures, patient demographics, payment sources, total monetary charge, and hospital characteristics. Patients with diagnoses of endophthalmitis and septicemia were required for inclusion using International Classification of Diseases codes for precisely identifying cases of endogenous endophthalmitis, and to characterize patient comorbidities. P value of 0.05 was defined as statistically significant for all analyses.

Results: A total of 6,400 patients with endogenous endophthalmitis were identified. Incidence increased from 0.10 (95% CI: 0.07-0.12) per 100,000 in the American civilian population in 2006 to 0.25 (95% CI: 0.21-0.30) in 2017 ($p<0.05$). Most were female (55.4%), had Medicare (53.5%), were in the first income quartile (29.3%) [top 25% of income bracket], lived in the southern region (40.5%), and presented to a metropolitan teaching hospital (66.6%) ($p<0.05$). There were no seasonal trends in admission. The median ED visit cost increased from \$1,229 (interquartile range [IQR]: \$690-\$1,563) in 2006 to \$2,529 (IQR: \$1,538-\$4,038) in 2017 ($p<0.05$). Mortality increased from 8.6% in 2006 to 13.8% in 2017 ($p=0.94$). On multivariate analysis, factors that predicted admission included older age, and the following comorbidities: pneumonia, endocarditis, renal/urinary tract infection (UTI), and intravenous drug use (IVDU). Factors associated with increased mortality included: human immunodeficiency virus infection (HIV)/immune deficiencies, heart failure, pneumonia, renal/UTI, and hepatic infections/cirrhosis. Patients with diabetes had a decreased odds ratio for mortality.

Conclusions: Endogenous endophthalmitis has increased in incidence throughout America. Factors predicting increased hospitalization include older age, pneumonia, endocarditis, renal/UTI, and IVDU. Factors associated with mortality include HIV/immune deficiencies, heart failure, pneumonia, renal/UTI, and hepatic infections/cirrhosis. Additional exploration of the potential protective effect of diabetes from mortality in this context is needed.

CONTROL ID: 3525449

SUBMITTER (NAME ONLY): Elizabeth Lundeen

TITLE: Cardiovascular Disease Risk Factors in U.S. Adults with Vision Impairment

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.A. Lundeen, M. Kim, I. Mendez, J. Saaddine, Division of Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adults with vision impairment (VI) have a higher prevalence of cardiovascular disease (CVD) compared to those without VI. However, less is known about whether those with VI have a higher prevalence of CVD risk factors. We describe the relationship between VI and CVD risk factors in US adults.

Methods: We used cross-sectional, nationally representative data from the 2018 National Health Interview Survey of US noninstitutionalized civilians; data are self-reported. The analysis included 23,071 adults aged ≥ 18 years with data on CVD, CVD risk factors, and VI (defined as having trouble seeing, even when wearing glasses or contact lenses). By VI status, we describe the prevalence of CVD, defined as coronary heart disease, angina, myocardial infarction, stroke, or other heart disease. Generalized linear regression models with Poisson distribution and log link were used to generate adjusted prevalence ratios (aPR) for those with VI (reference: no VI) for CVD and seven CVD risk factors: current smoking, physical inactivity, excessive alcohol intake, obesity, hypertension, high cholesterol, and diabetes. Models for each outcome controlled for age, sex, race/ethnicity, education, marital status, employment, income, and health insurance.

Results: Participants' average age was 47.3 years (95% CI: 47.0, 47.7); 51.6% (CI: 50.8, 52.4) were female; 12.9% (CI: 12.3, 13.5) had VI. Crude prevalence of CVD was 26.5% (CI: 24.6, 28.5) in those with VI and 12.1% (CI: 11.6, 12.7) in those without VI (aPR=1.64 [CI: 1.48, 1.76]). Compared to adults without VI, those with VI had a greater number of CVD risk factors (Figure 1) and a higher prevalence for all seven CVD risk factors: current smoking (aPR=1.36 [CI: 1.24, 1.48]), physical inactivity (aPR=1.13 [CI: 1.05, 1.20]), excessive alcohol intake (aPR=1.29 [CI: 1.08, 1.54]), obesity (aPR=1.26 [CI: 1.19, 1.34]), hypertension (aPR=1.24 [CI: 1.18, 1.31]), high cholesterol (aPR=1.17 [CI: 1.11, 1.24]), and diabetes (aPR=1.46 [CI: 1.32, 1.63]).

Conclusions: Adults with VI had a higher prevalence of CVD and CVD risk factors compared to those without VI. Reducing CVD risk in adults with VI requires effective clinical and lifestyle interventions, adapted to accommodate VI-related disability, to aid in the prevention and management of CVD.

CONTROL ID: 3525801

SUBMITTER (NAME ONLY): Heidrun Deissler

TITLE: Brolucizumab's actions on unchallenged or VEGFA-exposed retinal endothelial cells

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: VEGFA-binding single-chain variable fragment brolucizumab is intravitreally injected to successfully treat retinal diseases associated with deregulated expression of VEGFA, but severe adverse effects, i.e. retinal vasculitis, have been reported. Using the well-established in vitro-model of immortalized bovine REC (iBREC) we studied brolucizumab's effects on unchallenged or VEGFA-exposed iBREC.

Methods: Confluent iBREC were exposed to PBSd or VEGFA₁₆₅ (final concentration: 50ng/ml) for 1d before brolucizumab (Beovu®, final concentration of 1mg/ml reached by intravitreal injection) was added for up to 5d. As a measure of barrier function, we continuously determined the cell index (CI) of iBREC cultivated on gold electrodes. Expression or subcellular localization of tight-junction proteins claudin-1 or claudin-5 or of adhesion proteins VEcadherin or CD9 were assessed. Secretion of VEGFA, IL-6, IL-8 or TNFα by iBREC was determined by ELISA.

Results: VEGFA treatment strongly reduced CI within 12h and persistent for up to 6d accompanied by the loss of claudin-1 and (subtle) changes of claudin-5's and CD9's subcellular localization; VEcadherin was not affected. Beovu reverted these disturbances within 1d, but 5d after its addition, the CI started to decline again although claudin-1 was still strongly expressed. VEGFA was not detected by competitive ELISA in the cell culture supernatant of unchallenged iBREC or those exposed to the growth factor and Beovu, and less VEGFA was then internalized by the cells. None of the inflammatory relevant cytokines studied was detected in the culture supernatant of iBREC at 2h or 30h after Beovu's addition to unchallenged or VEGFA-exposed iBREC. When added to a confluent monolayer formed by iBREC, Beovu induced a transient decline of the CI between 2h and 6h associated with subtle changes of CD9's subcellular localization.

Conclusions: As expected, Beovu strongly counteracts VEGFA-induced dysfunction of the barrier formed by iBREC. However, Beovu might interfere with the adhesion of unchallenged iBREC to the extracellular matrix.

CONTROL ID: 3525860

SUBMITTER (NAME ONLY): fangfang lu

TITLE: mTOR signaling in zebrafish retinal pigment epithelium regeneration

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. lu, J.M. Gross, L. Leach, Department of Ophthalmology, Louis J. Fox Center for Vision Restoration, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|F. lu, Department of Ophthalmology, The Second Xiangya Hospital, Central South University, Changsha, Hunan, CHINA|

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ABSTRACT BODY:

Purpose: Our previous work characterized zebrafish RPE (retina pigment epithelium) regeneration after genetic ablation and has begun to identify molecular and cellular regulators of the regenerative response. mTOR (mechanistic target of rapamycin) signaling has been shown to be activated after tissue injury and to regulate tissue regeneration in multiple contexts; however, whether mTOR signaling is involved in RPE regeneration is unknown. We hypothesized that mTOR signaling was involved in RPE regeneration and sought to identify mechanisms by which mTOR regulates RPE regeneration.

Methods: At 5 days post-fertilization (dpf), rpe65a:nfsB-eGFP larvae were exposed to 10mM metronidazole (MTZ) for 24 hours to ablate the RPE. Larvae were treated with mTOR antagonists (2 μ M rapamycin/0.9 μ M INK 128) or DMSO from 24 hours prior to RPE ablation until 4 days post-injury (dpi). BrdU incorporation and RPE pigment recovery were quantified to assess the effect of mTOR antagonists on RPE regeneration. Immunostaining of phosphorylated 40S ribosomal protein S6 (p-S6), a readout for mTORC1 activity, was performed at 3, 6 and 12 hours post-injury (hpi), and 1- 4dpi timepoints in RPE-ablated and age-matched unablated controls, as well as at 2dpi in larvae treated with mTOR antagonists or DMSO. p-S6 distribution in the RPE was quantified to evaluate mTOR activity during regeneration and to validate drug efficacy. To identify mechanisms by which mTOR modulates RPE regeneration, RNA-seq was performed on eGFP⁺ cells from rapamycin- or DMSO-treated larvae at 2 and 4dpi (n=3). Pathway enrichment analyses (STRING) were performed on groups of significantly differentially expressed genes (DEGs).

Results: Rapamycin and INK 128 treatment significantly decreased BrdU⁺ cells in the RPE (p \leq 0.0001) and impaired central pigment recovery at 4dpi, compared to controls (p \leq 0.0001). Quantification of p-S6 enrichment in the RPE showed significant increases from 6hpi-3dpi with peak expression at 12hpi (p \leq 0.01). p-S6 activity was abrogated in rapamycin/INK128 treated larvae at 2dpi. RNA-Seq results identified a variety of genes that were downregulated in the RPE at 4dpi.

Conclusions: mTOR signaling is required for RPE regeneration after genetic ablation. Putative mTOR targets have been identified and are being experimentally interrogated to determine the mechanisms by which mTOR regulates RPE regeneration.

CONTROL ID: 3525930

SUBMITTER (NAME ONLY): Jennifer Lim

TITLE: Long-term clinical impact of intravitreal anti-VEGF therapy for severe non-proliferative diabetic retinopathy (NPDR): Analyses through a discrete event simulation model

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To model the impact of treating severe NPDR with anti-VEGF therapy on PDR progression and blindness compared with delayed treatment.

Methods: A discrete event simulation (DES) model was used to assess the impact of treating patients with severe NPDR (DRSS 47-53) instead of delaying treatment until PDR development. A retrospective cohort of patients with untreated NPDR was identified in the IBM Explorys™ EMR database. Cox multivariable regression was used to model risk of PDR progression. Treatment impact (afibercept and ranibizumab) was estimated based on data from clinical trials (PANORAMA, RISE/RIDE) and averaged by weighted US market share. The DES examined PDR progression rates for a sampled set of 2 million patients scaled to US NPDR disease prevalence over 5 years using age- and gender-adjusted sampling weights, aggregating yearly progression events. Simulated PDR event rates were compared for two simulated cohorts with severe NPDR: untreated (no anti-VEGF treatment until they developed PDR), or treated (clones of the untreated patients modeled to receive early anti-VEGF treatment). Blindness (visual acuity <20/200) rates following PDR progression were obtained from literature. The probability of blindness was applied to all patients who progressed to PDR, and simulated events were compared over 10 years for treated vs untreated cohorts.

Results: A total of 1,174 patients with severe NPDR were identified in the database. The final Cox model included age, gender, baseline DR severity, diabetes control regimen, HbA1c, DME status, and other factors. The simulated cohort included 86,671 severe NPDR patients. Patients with severe NPDR had a 5-year risk of PDR of 37.5% (untreated) and 18.1% (treated); anti-VEGF therapy avoided 16,784 (51.7%) of PDR events for a 19.4% absolute risk reduction. The 10-year risk of blindness was 4.4% (untreated) and 1.9% (treated); treatment was associated with a 57.7% reduction blindness cases for a 2.6% absolute risk reduction.

Conclusions: The DES model suggests that severe NPDR treatment with intravitreal anti-VEGF therapy would significantly decrease PDR progression rates over 5 years and reduce incidence of blindness over 10 years.

CONTROL ID: 3526013

SUBMITTER (NAME ONLY): Elizabeth Ciociola

TITLE: Heritability of Primary Angle Closure Anatomic Traits and Predictors of Angle Closure in South Indian Siblings

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Data on heritability of anatomic traits in primary angle closure glaucoma (PACG) is sparse. The purpose of this study was to estimate the heritability of ocular biometric and anterior chamber morphologic parameters and to determine predictors of angle closure concordance in South Indian probands with primary angle closure suspect (PACS) or primary angle closure (PAC)/PACG and their siblings.

Methods: We prospectively collected data on a cohort of probands with PACS or PAC/PACG and their full siblings aged ≥ 30 years in South India. All subjects received a standardized ophthalmic examination, A-scan ultrasonography, pachymetry, and anterior segment optical coherence tomography imaging (ASOCT). Heritability was calculated using residual correlation coefficients adjusted for age, sex, and home setting. Concordant sibling pairs were defined as both proband and sibling with PACS or PAC/PACG. Predictors of angle closure concordance among sibling pairs were calculated using multivariable logistic regression models, corrected for collinearity.

Results: 345 sibling pairs participated, including 121 sibling pairs concordant for angle closure and 224 discordant sibling pairs. All anterior chamber parameters were highly heritable ($p < 0.001$ for all), Table 1. Similarly, all iris parameters, axial length, lens thickness (LT), central corneal thickness, anterior lens curvature, lens vault (LV), spherical equivalent, and intraocular pressure were moderately to highly heritable ($p < 0.004$ for all). LV and LT were significantly more heritable among concordant sibling pairs ($p < 0.05$ for both). In contrast, ASOCT angle parameters had statistically insignificant heritability estimates. In multivariable analyses, siblings older than their probands were more likely to be concordant for angle closure (OR=1.05 (95% CI 1.01, 1.09)) and siblings with a deeper anterior chamber depth (ACD) compared to their probands were less likely to be concordant for angle closure (OR=0.74 (95% CI 0.64, 0.86)), Table 2.

Conclusions: Iris, anterior chamber, and lens parameters were significantly heritable while angle parameters were not. LT and LV were significantly more heritable among concordant siblings and may play important roles in the pathogenesis of angle closure disease. Siblings who are older or have a shallower ACD have a greater likelihood of angle closure and may need more careful disease monitoring.

CONTROL ID: 3526021

SUBMITTER (NAME ONLY): Alejandra Torres Diaz

TITLE: Diabetic Retinopathy Screening in Primary Care: Implementation for Sustained Impact in Teleophthalmology (I-SITE)

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Torres Diaz, L. Lock, Y. Liu, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|T. Molfenter, Department of Industrial and Systems Engineering, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|J.E. Mahoney, Department of Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|T.D. Bjelland, Mile Bluff Medical Center, Mauston, Wisconsin, UNITED STATES|D. Boss, Department of Family Medicine and Community Health, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teleophthalmology provides evidence-based diabetic retinopathy screening that is underused even when readily available in primary care clinics. There is an urgent need to increase teleophthalmology use in U.S. primary care clinics. In this study, we describe the development of a tailored implementation program to increase teleophthalmology use (I-SITE) and report outcomes related to primary care provider (PCP) adoption.

Methods: We applied the NIATx Model for healthcare process improvement to develop and test I-SITE in a rural, U.S. multi-payer health system. We hypothesized that teleophthalmology use would be higher among PCPs who did versus those who did not participate in various components of I-SITE. We also surveyed PCPs and clinical staff to identify implementation strategies they perceived to have the greatest impact on increasing teleophthalmology use.

Results: Teleophthalmology use was nearly 5-fold greater among PCPs participating in the I-SITE implementation team (n=3) than other PCPs (n=22, $p < 0.001$). The proportion of all PCPs who elected diabetic eye screening for their performance-based financial incentive increased from 0% (n = 0) at baseline to 56% (n = 14) following I-SITE implementation ($p < 0.001$). PCPs who elected diabetic eye screening as a performance-based financial incentive referred nearly 5 times more patients for teleophthalmology each quarter than those who did not (7.4 vs. 1.5 referrals, respectively, $p = 0.06$). There was a trend towards increased teleophthalmology referrals following audit and feedback presentations at regularly-scheduled staff meetings ($p = 0.16$). PCPs and clinical staff reported the following implementation strategies to have the highest impact on teleophthalmology use: reminders to ask patients about diabetic eye screening during clinic visits, streamlining electronic health record (EHR) documentation, and patient outreach.

Conclusions: I-SITE provides a practical roadmap for tailored integration of teleophthalmology into primary care clinics and increasing teleophthalmology use (<https://hipxchange.org/I-SITE>). Implementation strategies effective for increasing provider adoption of teleophthalmology included enhancing perceived ease of use, participation in implementation, audit and feedback, and performance-based financial incentives.

CONTROL ID: 3526085

SUBMITTER (NAME ONLY): Nathan Hall

TITLE: Impact of Refresher Training on Outcomes of Trichomatous Trichiasis Surgery

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Trichomatous trichiasis (TT) is a severe, blinding consequence of chronic inflammation and scarring in the conjunctiva resulting from trachoma, which is the leading infectious cause of blindness worldwide. Our study evaluated the effectiveness of refresher training (RT), including the “Head Start” approach and live surgery following the WHO recommended procedure for the certification of TT surgeons on the outcomes of upper lid (UL) TT surgery in rural Ethiopia.

Methods: A total of N=283 eyes contributed by 173 patients were included in analysis. Patients were included in the study if they were undergoing UL TT surgery in at least one eye by one of the participating surgeons. Patients were split into two cohorts: Cohort 1 (C1) was comprised of patients enrolled prior to the RT, and Cohort 2 (C2) included those enrolled after the RT. Data were collected at 3 time points: baseline, 6-month, and 12-month follow-up. Surgical outcomes were recorded throughout follow-up using multiple response forms. The main outcome of interest was development of post-operation TT (POTT), which was defined as: presence of at least one UL lash touching the eye; and/or epilation; and/or repeat surgery. A series of multivariate generalized estimating equations (GEEs) were fit to model POTT against all potential covariates of interest, including demographic factors and clinical measurements. Odds ratios (ORs) and 95% CIs were calculated.

Results: Within C1, 37/128 eyes (28.91%) developed POTT while within C2, 22/133 eyes (16.54%) developed POTT ($p=0.03$). In the fully saturated GEE model, only the cohort covariate was significant at the $\alpha=0.05$ significance level ($p=0.03$) after adjusting for all other covariates. After performing stepwise model selection using the quasiliikelihood under the independence model criterion (QIC), our final model included cohort as the singular chosen covariate. The corresponding OR for an eye being in C2 relative to C1 was 0.41 (95% CI: 0.19, 0.86).

Conclusions: Our results indicate a substantial reduction in the odds of developing POTT for eyes receiving treatment after initiating RT including the “Head Start” approach followed by live surgery training as compared to eyes receiving treatment prior to the RT. This observation implies a significant potential benefit of the program’s effectiveness, even with experienced surgeons, and suggests comprehensive RT may be a valuable strategy to improve surgical outcomes.

CONTROL ID: 3526295

SUBMITTER (NAME ONLY): K V Chalam

TITLE: Evaluation of role of cathepsin and filensin in development of posterior vitreous detachment in humans with differential proteomic analysis

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chalam, R. Murthy, Ophthalmology, Loma Linda University, Loma Linda, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the protein profile of vitreous fluid from human subjects undergoing vitreoretinal surgery with or without pre-existing posterior vitreous detachment (PVD) with quantitative proteomics

Methods: In this study, protein profile of 2 cohorts of patients (pre-existing PVD vs. without PVD) undergoing vitreoretinal surgery was analyzed with quantitative proteomics to identify novel markers that may be involved in vivo induction of a PVD. Vitreous humor specimens were collected before initiation of vitrectomy. Presence of PVD was confirmed with ultrasonography prior to surgery. Five biological replicates (500 ul) were included for both control and disease groups. The protein was centrifuged at 15,000rpm, 4°C for 30 min assays were performed using a BCA® Protein Assay. iTRAQ labeling was performed with iTRAQ Reagents 8-plex kit.

After strong cation exchange, tryptic peptides were separated with a LC Packing C18 Pep Map HPLC column. Hybrid quadrupole-TOF QSTAR Elite MS/MS system was used for data acquisition. The MS/MS data were processed by a thorough search against the Uniprot human database (2,464,346 entries) with ProteinPilot v.4.2 software. The cutoff score was set to 1.3 (a confidence level of 95%), and the false discovery rate (FDR) was estimated with search against concatenated databases containing both forward and reverse sequences. Functional analysis of proteins was done with GO annotation (q-value ≤ 0.05). Protein with at least three spectra and fold change >1.2 or <0.8 ($p < 0.05$) was considered for significant differential expression.

Results: A total of 446 proteins were identified. 72 proteins overlapped with at least three peptides. Nine proteins were differentially expressed between two groups (8 up regulated and 1 down regulated in PVD). Filensin (15.75x), serotransferrin (11.9x) and cathepsin D (10.95) were overwhelmingly expressed ($p < 0.001$) in PVD

Conclusions: Our study provides comprehensive protein listing in vitreous humor samples in PVD. Filensin and Cathepsin D were identified as candidate proteins involved in induction of PVD. Further studies using microplex arrays to quantify protein levels in vitreous samples are required

CONTROL ID: 3526377

SUBMITTER (NAME ONLY): Molly Orban

TITLE: C-Reactive Protein (CRP) in Pediatric Orbital Cellulitis

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.W. Orban, D. Freeman, H. Hahn, R. Trivedi, A. Eiseman, Ophthalmology, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: C-Reactive Protein (CRP) levels have been shown to have prognostic value in pediatric bacterial infections, including orbital cellulitis. However, it is unclear how frequently CRP levels are utilized for diagnostic evaluation and management. The purpose of this study is to determine how frequently CRP levels were obtained and to evaluate for any correlation of CRP levels with presenting signs and symptoms, radiographic findings, or prognosis.

Methods: We performed a retrospective chart review of all cases of orbital cellulitis in patients age 1 – 18 years old in a large, tertiary-care academic institution from January 2008 to January 2018 to measure the frequency CRP levels were obtained. We explored the relationship between CRP levels and signs and symptoms at presentation, clinical prognosis (length of stay), and demographic data. Lastly, we examined how the CRP level changed throughout admission. Information recorded included laterality, association with sinusitis, sex, race, age, time of year during presentation, treatment course, laboratory values throughout the hospital course, and major complications including abscess, operations, etc. Patients were excluded if the final diagnosis was not orbital cellulitis or if insufficient data was available in the patient chart. SPSS statistical analysis software was used to perform statistical testing. Categorical variables were compared with chi squared tests (Fisher's exact tests). Categorical data were compared with continuous data with independent samples t-tests.

Results: 54 patients were included in the study, 15 who had a CRP level measured during admission and 39 who did not. CRP was elevated in 9/15 (60%) of patients at the time of diagnosis. CRP elevation at the time of diagnosis was not found to correlate with sex ($p=0.136$), race ($p=0.732$), length of stay ($p=0.494$), whether steroids were administered during admission ($p=0.791$), whether sinus symptoms were present at admission ($p=0.815$), or whether an abscess was present on imaging ($p=0.906$). There was insufficient data to determine trends in CRP levels as treatment course progressed.

Conclusions: CRP level was not routinely ordered in our pediatric population presenting with orbital cellulitis and was not often used prognostically. Our study had significant data limitations, mostly driven by the small sample size. Further studies should evaluate the diagnostic and prognostic utility of CRP in pediatric orbital cellulitis.

CONTROL ID: 3526452

SUBMITTER (NAME ONLY): Darren Lee

TITLE: A2Ar-dependent anti-uveitic Treg cells home to the eye to suppress uveitis

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.J. Lee, T. McDonald, K. Peters, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|D.J. Lee, Microbiology and Immunology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Experimental autoimmune uveitis (EAU) is used to gain a better understanding of human autoimmune uveitis. EAU-resolution is in part due to emergence of ocular antigen specific regulatory T cells (Tregs) found in the spleen of EAU-resolved mice. Multiple FoxP3⁺CD25⁺CD4⁺ Treg subsets in EAU-resolved mice (post-EAU Tregs) are PD-1⁺ (PD-1 Treg) or TIGIT⁺ (TIGIT Treg). The adenosine 2A receptor (A2Ar) is required for ocular Tregs at EAU-onset, but A2Ar^{-/-} mice still recover from EAU. This suggests each Treg subset may function through different mechanisms. One such mechanism is where the Tregs home to suppress disease, CCR6 homes to tissue, CCR7 to lymph. We asked where post-EAU Tregs home, and the chemokine receptors (CCR) required for each Treg subset to suppress disease.

Methods: CCR expression was determined on post-EAU Tregs by NanoString. Then the influence of the identified CCRs on EAU and Treg suppression was determined by transferring specific CCR⁺ post-EAU T cells, and TIGIT or PD-1 Tregs from CCR6^{-/-} or CCR7^{-/-} mice to recipient EAU mice. Homing to the eye and secondary lymphoid tissue by post-EAU Tregs was also monitored in recipient mice. Peripheral blood mononuclear cells from uveitis patients and healthy volunteers were A2Ar-stimulated, and assayed for CCR6 and CCR7 expression in each Treg subset.

Results: Post-EAU Tregs had transcript and protein for CCR6 and CCR7, homed to the eye, and lymphoid tissue, and CCR6⁺ and CCR7⁺ post-EAU Tregs suppressed EAU. Elimination of CCR6-CCL20 signaling in CCR6^{-/-} and CCL20^{-/-} mice delayed resolution, but CCR7^{-/-} mice had similar disease as WT mice, and more Tregs were in post-EAU CCR7^{-/-} mice compared to CCR6^{-/-} mice. CCR7 was not necessary for EAU suppression by PD-1 or TIGIT Tregs. Whereas, CCR6 was necessary for PD-1, but not TIGIT Treg EAU suppression. A2Ar^{-/-} mice had fewer CCR6 and CCR7 post-EAU Tregs compared to WT mice. A2Ar-induction of PD-1⁺ CCR6⁺ Tregs was reduced in uveitis patients (n=20) compared to healthy volunteers (n=19), but was not significantly different for TIGIT⁺CCR6⁺, PD-1⁺CCR7⁺, or TIGIT⁺CCR7⁺ Treg subsets.

Conclusions: This work indicates that different Treg subsets that may function during different phases of disease, have different homing requirements to suppress disease. Importantly, induction of the tissue homing Tregs in uveitis patients may be impaired. Therefore, a defect in Treg homing capacity may contribute to autoimmune uveitis.

CONTROL ID: 3526480

SUBMITTER (NAME ONLY): Heather Anderson

TITLE: Visual Acuity Outcomes in a Randomized Trial of Clinically Derived Refractions and Objectively Derived Wavefront Metric Optimized Refractions in Adults with Down Syndrome

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.A. Anderson, The Ohio State University College of Optometry, Columbus, Ohio, UNITED STATES|J.S. Benoit, J.D. Marsack, R.E. Manny, K.D. Fern, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Determining refractive corrections for individuals with Down syndrome (DS) is challenging due to the presence of elevated refractive error, optical aberrations, and cognitive impairment. This randomized clinical trial evaluated performance of spectacle corrections determined using clinical techniques versus objective refractions derived from wavefront aberration measures.

Methods: Thirty adults with DS received a comprehensive eye examination during which clinical refraction was determined by a single expert examiner experienced in examination of individuals with special needs using techniques appropriate for this population. To determine objective refractions, dilated wavefront aberration measures were obtained and processed post-visit to identify refractions based on the optimization of each of two image quality metrics: pupil fraction tessellated (PFSt) and visual Strehl ratio in the spatial domain (VSX). The three refractions were dispensed in random order in an identical spectacle frame selected by the participant. The primary outcome measure, binocular visual acuity, was obtained after 2 months of wear for each prescription type by a masked examiner administering a distance logMAR acuity test. To compare treatment types, mean acuity was compared using a 2-sided Type 3 F-test of the treatment effect in a linear mixed-effect regression model, where the final model included fixed-effects for treatment, period (1, 2, or 3), and first order carryover effects.

Results: The two-month estimated least square means in binocular visual acuity (logMAR) was 0.34 (95% CI: 0.25, 0.39) for clinical refraction, 0.31 (0.25, 0.36) for PFSt, and 0.33 (0.27, 0.38) for VSX. No statistically significant treatment effect was observed ($F=1.10$, $p=0.34$).

Conclusions: Objective refractions derived from wavefront aberration measures resulted in acuity similar to expert clinician derived refractions, suggesting the objective method may be a suitable alternative for patients with DS. Further study with younger patients is warranted to determine if improvements in acuity may be obtained when objective refractions are dispensed to patients with greater neural plasticity and less likelihood of long-standing amblyopia.

CONTROL ID: 3526818

SUBMITTER (NAME ONLY): Jack Rees

TITLE: OCT segmentation errors of Minimum Rim Width (MRW) and Retinal Nerve Fiber Layer Thickness (RNFLT) in glaucoma subjects

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rees, F.G. Sanchez, S.L. Mansberger, Research, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|J. Rees, F.G. Sanchez, H. Yang, S.K. Gardiner, S.L. Mansberger, Devers Eye Institute, Legacy Research Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: We were interested in whether differences exist in manual segmentation (MS) vs automatic segmentation (AS) of optical coherence tomography (OCT) in the Bruch's Membrane Opening–Minimum Rim Width (BMO-MRW) and Retinal Nerve Fiber Layer Thickness (RNFLT) in glaucoma eyes, and whether differences occur more frequently in the same clock-hour sectors.

Methods: We used spectral-domain OCT (Heidelberg Engineering, Heidelberg, Germany) to obtain BMO-MRW measurements in 24 radial Optic Nerve Head (ONH) B-scans, and RNFLT measurements in peripapillary circle scans (12 degrees) from 2 different timepoints in glaucoma eyes.

We obtained AS with the Heidelberg Eye Explorer Software. The software marked the position of the internal limiting membrane (ILM) and the BMO to calculate the MRW, and the ILM and posterior boundary of the RNFL. We then used custom software to perform manual corrections of the same parameters.

'Machine error' was the MRW or RNFLT AS value subtracted from the MS value. We calculated the proportional error by dividing the mean absolute error (AE) by the median MS value. To test whether errors occurred more often in any sector, we fit the AE per clock hour using a mixed effects model(R).

Results: We included the MRW and RNFLT scans from 162 glaucoma eyes (162 subjects) at 2 timepoints 4.28 years (SD 0.48, range 2.5-5.1) apart. Average age was 70.24 (10.21, 42-91), and 94 (58.02%) were female.

Mean MRW (SD, range) with AS and MS was 253.0µm (89.2, 22.6-523.4) and 249.8µm (90.1, 11.5-534.5), respectively; and RNFLT was 85.37µm (32.8, 8.6-208.2) with AS and 86.88µm (34.1, 8.6-208.2) with MS.

The mean AE for MRW was 11.36µm (16.4, 0-166.6), and for RNFLT was 3.35µm (4.6, 0-83.2). MRW showed a larger proportional AE than RNFLT (4.49% versus 4.13%, respectively, p=.004).

The AE in the superior sector of the MRW tended to be larger, although not significant (p=.075). RNFLT did not show sectors with larger errors (p>.1 for all). We found no evidence for errors happening in the same sectors between techniques (p=.79).

Conclusions: The error with AS is small and proportionally larger in MRW than RNFLT. The error in MRW tends to be larger in the superior sector. There is no evidence of sectorial correlation between the errors of MRW and RNFLT, suggesting no common source of error. This higher variability may decrease the ability to detect progression with MRW as compared to RNFLT.

CONTROL ID: 3526857

SUBMITTER (NAME ONLY): Yasuo Terasawa

TITLE: Visualizing Electric Field patterns generated by Temporal Interference Stimulation of Retina: Measurements using a phantom eye

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Terasawa, Artificial Vision Institute, Kabushiki Kaisha Nidek, Gamagori, Aichi, JAPAN| Y. Terasawa, H. Tashiro, J. Ohta, Materials Science, Nara Sentan Kagaku Gijutsu Daigakuin Daigaku, Ikoma, Nara, JAPAN|H. Tashiro, Health Sciences, Kyushu Daigaku Igakubu Daigakuin Igakukei Gakufu Daigakuin Igaku Kenkyuin, Fukuoka, JAPAN|

Commercial Relationships Disclosure (Abstract): Yasuo Terasawa: Commercial Relationship(s);Nidek Co., Ltd.:Code E (Employment) | Hiroyuki Tashiro: Commercial Relationship(s);Nidek Co., Ltd.:Code F (Financial Support) | Jun Ohta: Commercial Relationship(s);Nidek Co., Ltd.:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Stimulation via temporally interfering (TI) electric fields is attracting attention as a means of activating neural tissues distant from the stimulation electrodes. This stimulation strategy can be advantageous to suprachroidal retinal prosthesis in which stimulation electrodes are relatively distant from the target neurons of retina. The purpose of this study is to establish methods of direct measurements and visualization of the electric field generated when retina is stimulated using TI.

Methods: A phantom eye was constructed from a custom-made dish (dia.=24 mm). We placed 25 silver electrodes (dia.=0.5 mm) along the inside wall of the annular chamber at 6 mm from the bottom (Fig. 1). Sinusoidal waves of 1.4 mA amplitude were applied to the two selected electrodes. The frequencies of sinusoidal waves were 2 kHz for the first electrode and 2.05 kHz for the second, respectively. The electric field was recorded using two pairs of PTFE insulated platinum-iridium wires (dia.= 0.05mm), each pair making a 0.35 mm- spaced dipole electrode and aligned orthogonally to each other at the tip. These recording electrodes were connected to an oscilloscope via differential probe.

Results: The interference of two sinusoidal electric fields was successfully observed as shown in Fig.2. Phases of envelopes were 180 degrees different between X component and Y component, which was consistent with the theoretical prediction.

Conclusions: We successfully visualized the envelope waveform generated by TI. Our future work will include a qualitative and quantitative comparison of results from measurements and numerical calculation.

CONTROL ID: 3527031

SUBMITTER (NAME ONLY): Stephen Lau

TITLE: Augmented Reality Mobile Application for Glaucoma Education in the South Bronx

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A novel augmented reality mobile application for glaucoma education named EyeCU previously validated in an Asian population was adapted for our South Bronx population. We performed a prospective study to evaluate the impact of EyeCU on patient knowledge and to assess patient perceptions of this technology.

Methods: Thirty-one participants > 18 years old with a diagnosis of glaucoma on medical therapy for at least 4 months used EyeCU on a hospital-owned tablet during their clinic visit. Exclusion criteria included those with a non-glaucomatous optic neuropathy, visual acuity of 20/100 or worse in both eyes, visual field defects impairing fixation in both eyes, inability to use a tablet and inability to understand English or Spanish. Participant characteristic data was collected, and pre- and post-intervention National Eye Health Education Program Eye-Q tests were administered. Self-reported understanding was evaluated and a 5-point Likert scale (1 being “not at all” and 5 being “extremely likely”) assessed application acceptance. Fisher’s exact test, Mann-Whitney test and two-tailed Student’s t-test were used.

Results: The median test score was 70% for pre- and post-intervention groups ($p=0.84$). The three worst pre-intervention questions were “eye pain is often a symptom of glaucoma” (52% correct), “glaucoma is caused by increased eye pressure” (3% correct) and “a complete glaucoma exam consists only of measuring eye pressure” (42% correct). The pre-intervention median test score was 70% and 60% in those preferring English and Spanish respectively ($p=0.002$). The post-intervention mean test score was 72% and 61% in those preferring English and Spanish respectively ($p=0.02$). Those preferring English had higher educational attainment than their Spanish counterparts ($p=0.002$). 97% of participants reported improved understanding of glaucoma and the purpose of eye drops. The mean score for willingness to use this technology for health education and to recommend this technology to others was 4.2 and 4.4 respectively.

Conclusions: The current version of EyeCU did not demonstrate a statistically significant improvement in objective glaucoma knowledge. However, there was a high level of acceptance of the technology and subjective reporting of improved knowledge. Efficacy may be improved through targeted modifications of the application based on knowledge gaps and discrepancies between English and Spanish speakers.

CONTROL ID: 3527050

SUBMITTER (NAME ONLY): Masaki Tanito

TITLE: Estimation of aqueous outflow facility before and after the microhook ab interno trabeculotomy

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tanito, A. Tsutsui, K. Manabe, M. Mochiji, Shimane University Faculty of Medicine, JAPAN|

Commercial Relationships Disclosure (Abstract): Masaki Tanito: Commercial Relationship(s);Inami Co. Ltd.:Code R (Recipient);Inami Co. Ltd.:Code C (Consultant);Inami Co. Ltd.:Code P (Patent) | Aika Tsutsui: Commercial Relationship: Code N (No Commercial Relationship) | Kaoru Manabe: Commercial Relationship: Code N (No Commercial Relationship) | Mihoko Mochiji: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aqueous humor outflow facility was compared preoperatively and postoperatively to elucidate the mechanism of intraocular pressure (IOP) reduction by microhook ab interno trabeculotomy (μ LOT), a minimally invasive glaucoma surgery.

Methods: Fifty-one eyes of 37 subjects (mean age, 67.2 ± 11.8 years) were included in the study. The outflow facility coefficient (C) was estimated by pneumatonography ((Model 30 Classic, Reichert Technologies, Depew, NY, USA). Using the paired t-test, the IOP, number of medications, and C value were compared between pre- and post-operatively of μ LOT. Possible correlations between the C value and IOP or number of medications were assessed by using linear regression analysis. To adjust for biases derived from the inclusion of both eyes of a patient and differences in background, the pre- and post-operative C values were compared using a mixed-effects regression model.

Results: Compared to the preoperative IOP of 18.2 mmHg and number of medications of 2.8, the postoperative IOP of 13.5 mmHg and medications of 2.3 decreased significantly by 26% ($p < 0.0001$) and 18% ($p < 0.0001$), respectively. Compared to the preoperative C value of 0.27 μ l/min/mmHg, the postoperative C value of 0.51 μ l/min/mmHg increased significantly by 47% ($p < 0.0001$). By linear regression analysis, higher IOP was associated with lower C values (estimate, -0.01/mmHg, $p = 0.0107$), while number of medications was not associated with the C value (estimate, -0.04/medication, $p = 0.1739$). By mixed-effects regression analysis, the postoperative measurement (estimate, 0.11/preoperative measurement, $p < 0.0001$) was associated with higher C value, while age, sex, μ LOT procedure, IOP, and number of medications were not.

Conclusions: After μ LOT, significant increase of outflow facility was observed. The results provide the evidence that increased conventional outflow by elimination of the outflow resistance at the trabecular meshwork is the main mechanism of IOP reduction after μ LOT.

CONTROL ID: 3527063

SUBMITTER (NAME ONLY): Gary Lee

TITLE: Evaluation of an OCT B-scan of interest tool in glaucomatous eyes

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.C. Lee, K. Makedonsky, L. Tracewell, S. Yu, M.K. Durbin, N. Graves, C. Wu, T. Callan, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|I. Falkenstein, Glaucoma Specialists of San Francisco, Oakland, California, UNITED STATES|T. Severin, East Bay Eye Center, San Ramon, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: B-scans from optical coherence tomography (OCT) cube scans are commonly reviewed during clinical evaluation of the macula. A deep learning algorithm was previously trained to predict if a given B-scan might be flagged “of interest” based on ground truth labels from retinal specialists in healthy and eyes with retinal pathology or disease¹. In this preliminary study, the performance of a B-scan of interest tool was compared to a clinical assessment of OCT cube data in healthy and glaucomatous eyes.

Methods: A B-scan of interest algorithm was previously trained and tested on 76,544 B-scans (598 subjects) and 25,600 B-scans (200 subjects), respectively². Retrospective OCT data were analyzed from an ongoing visual field (VF) study including 19 eyes of 19 patients in both healthy and glaucoma groups, using CIRRUS™ 5000 HD-OCT (ZEISS, Dublin, CA) and HFA3 (ZEISS, Dublin, CA). At each visit, a qualified Macula 512x128 cube scan was used for inference. Mean Deviation (MD) of a SITA Standard 24-2 VF was used to indicate disease severity. A trained grader reviewed each cube and assessed if either a) <10% or b) ≥10% of total B-scans of interest should be flagged.

Results: Mean age was 56.4 (standard deviation, SD: 7.7; range: 44.3 to 73.1) years and 73.4 (SD: 9.5; range 60.6 to 97.9) years for healthy and glaucomatous eyes (p<0.001). Mean VF MD was 0.66 (SD: 0.91; range: -0.62 to 2.62) dB and -6.39 (SD: 6.67; range: -23.16 to 1.63) dB in healthy and glaucomatous eyes (p<0.001). Observed grader and algorithm agreement (95% confidence interval) was 100.0 (82.4,100.0)% and 79.0 (54.4, 94.0)% in healthy and glaucomatous eyes (see Fig 1). B-scans from the four disagreement cases included the presence of unusual retinal curvature (two cases), unusual contrast in the vitreous, and general false positives with inference scores near the algorithm cut-off (see Fig 2).

Conclusions: The findings in this study suggest excellent agreement in healthy eyes and reasonable agreement in glaucomatous eyes for detecting the presence of pathologies typically associated with retinal disease. As a result, a B-scan of interest tool may be a useful workflow aid to identify retinal disease co-morbidities in glaucomatous eyes.

References

[1] Yu et al. IOVS 2020; 61(9): Abstract PB0085.

[2] Ren et al. IOVS 2020; 61(7): Abstract 1635.

CONTROL ID: 3527308

SUBMITTER (NAME ONLY): Yi Gao

TITLE: Impact of myopia control spectacle lenses with aspherical lenslets on peripheral vision

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Gao, E. Lim, A. Yang, B. Drobe, R&D AMERA, Essilor International, Singapore, SINGAPORE|

Commercial Relationships Disclosure (Abstract): Yi Gao: Commercial Relationship(s);Essilor:Code E (Employment) | Ee Woon Lim: Commercial Relationship(s);Essilor:Code E (Employment) | Adeline Yang: Commercial Relationship(s);Essilor:Code E (Employment) | Bjorn Drobe: Commercial Relationship(s);Essilor:Code E (Employment)

ABSTRACT BODY:

Purpose: New spectacle lenses with concentric rings of contiguous aspherical lenslets have shown promising effects for myopia control. The purpose of the study was to evaluate peripheral visual performance through these lenses using psychophysical tasks.

Methods: Two types of experimental lenses were used - spectacle lenses with highly aspherical lenslets (HAL) and spectacle lenses with slightly aspherical lenslets (SAL) arranged in concentric rings in both lenses. A standard plano single vision lens was used as a control. We tested three visual functions consisting of motion detection (phase-shifting gabor), coherent motion direction discrimination (random dot kinematogram), and useful field of view (UFOV™, Posit Science®, United States). Each function was tested on a sample of 10 adults (mean age: 30.5, 26.3, 33.7 years, age range 20-37, 19-49, 26-49 years, for the three functions respectively). All subjects had normal or corrected-to-normal vision and all tests were done monocularly using their dominant eyes.

Results: No significant difference between the test lenses and control was found in any test. Specifically, the motion detection threshold was not affected by the lens in any quadrant of the visual field (one-way ANOVA, $p > 0.7$). For global motion direction discrimination, a two-way ANOVA found no significant effect of the lens ($p = 0.87$) on the coherence threshold in any direction. In the useful field of view test, one-way ANOVAs showed no significant effect of the lens on visual detection in the whole visual field ($p > 0.5$).

Conclusions: Myopia control lenses with concentric rings of contiguous aspherical lenslets (HAL and SAL) did not significantly impact peripheral visual functions including motion detection, coherent motion direction discrimination, and useful field of view, compared to single vision lenses.

CONTROL ID: 3527310

SUBMITTER (NAME ONLY): Qinqin Liu

TITLE: Cost-effectiveness of polygenic risk profiling for primary open-angle glaucoma in the United Kingdom and Australia

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Liu, J. Davis, A.W. Hewitt, School of Medicine, University of Tasmania, Hobart, Tasmania, AUSTRALIA|Q. Liu, J. Davis, A.W. Hewitt, Centre for Eye Research Australia, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|X. Han, S. MacGregor, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, AUSTRALIA|D.A. Mackey, Centre for Ophthalmology and Visual Science, Lions Eye Institute, Western Australia, AUSTRALIA|J.E. Craig, Department of Ophthalmology, Flinders University, Adelaide, South Australia, AUSTRALIA|L. Si, The George Institute for Global Health, Sydney, New South Wales, AUSTRALIA|L. Si, School of Health Policy & Management, Nanjing Medical University, Nanjing, Jiangsu, CHINA|

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) is the most common subtype of glaucoma worldwide. We evaluate the cost-effectiveness of polygenic risk score (PRS) profiling as a screening tool for POAG.

Methods: We used a Markov cohort model to evaluate the cost-effectiveness of implementing polygenic risk profiling as a new POAG-screening approach in the UK and Australia. Six health states were included in this model: death, early, mild, moderate, severe, and healthy individuals. The evaluation was conducted from the healthcare payer's perspective. We used the best available published data to calculate prevalence, transition probabilities, utility and other parameters for each health state and age group. The study followed the Consolidated Health Economic Evaluation Reporting Standards checklist. Our main outcome measure was the incremental cost-effectiveness ratio (ICER) and secondary outcomes were years of blindness avoided per person and a 'Blindness ICER'. We did one-way and two-way deterministic and probabilistic sensitivity analyses to reflect the uncertainty around predicting ICERs.

Results: Our proposed genetic screening programme for POAG in Australia is predicted to result in ICER of AU\$34,252 (95% CI AU\$21,324-95,497) and would avoid 1 year of blindness at ICER of AU\$13,359 (95% CI: AU\$8,143-37,448). In the UK, this screening is predicted to result in ICER of £24,783 (13,373-66,960) and would avoid 1 year of blindness at ICER of £10,095 (95%CI: £5,513-27,656). Using the willingness to pay thresholds of \$54,808 and £30,000, the proposed screening model is 79.2% likely to be cost-effective in Australia and is 60.2% likely to be cost-effective in the UK, respectively.

Conclusions: Although the level of willingness to pay for Australian Government is uncertain, and the ICER range for the UK is broad, we showed a clear target strategy for early detection and prevention of advanced POAG in these developed countries.

CONTROL ID: 3527315

SUBMITTER (NAME ONLY): Peter Wagner

TITLE: Novel device development to objectively assess “near-work”

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Wagner, A. Ho, R&D, BHVI, Sydney, New South Wales, AUSTRALIA|P. Wagner, A. Ho, J. Kim, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Research suggests that time spend on near-work is potentially an environmental risk factor for myopia. Although current technologies attempt to quantify near-work objectively (e.g. Clouclip, Glasson Technology Co. Ltd., Hangzhou, China), they simply estimate a general gaze direction (without measuring eye-movements) and just record an object distance within a limited field of view.

We aim to develop a device that can accurately quantify durations and distances to objects that the eyes are focusing on.

Methods: Head-mounted eye-trackers combining high-speed eye-observing cameras with a worldview camera (Figure 1 A) to map eye-versions onto worldview images to determine gaze coordinates in 2D. Using a time-of-flight camera (3D camera) as the worldview camera allows measurement of spatial information from the subject's field of view including the distance to the object the subject is looking at. To combine 2D gaze coordinates with the 3D point cloud data we developed a PicoFlexx depth plugin for Pupil Labs' eye-tracking software (Figure 1 B).

Results: Scene data was recorded as point cloud with 5 Hz (Figure 1 B). For precise time-matching of gaze directions and point cloud data, gaze was calculated from both eye-videos with 240 Hz. This method provides more than 90% high quality data with angular precision of +/- 3 degrees over extended periods.

Conclusions: The novel device is capable of quantifying direction and distances to objects that the subject is looking at during natural viewing conditions. Therefore, we can measure the time spend on and the distance to the accommodative and vergence stimuli the eyes are exposed to. This provides an additional objective facilitative function in myopia research for assessing factors such as near-work.

CONTROL ID: 3527318

SUBMITTER (NAME ONLY): Janine Reurink

TITLE: Molecular inversion probe sequencing to identify USH2A variants underlying Usher syndrome and non-syndromic retinitis pigmentosa

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Reurink, M. Aben, F.P. Cremers, S. Roosing, H. Kremer, Department of Human Genetics, Radboud university medical center, Nijmegen, NETHERLANDS|J. Reurink, E. van Wijk, F.P. Cremers, S. Roosing, Donders Institute for Brain Cognition and Behaviour, Radboud university medical center, Nijmegen, NETHERLANDS|A. Dockery, G. Farrar, The School of Genetics & Microbiology, Trinity College Dublin, Dublin, IRELAND|M. Oldak, Department of Histology and Embryology, Medical University of Warsaw, Warsaw, POLAND|J.B. ten Brink, A.A. Bergen, Department of Clinical Genetics, Amsterdam UMC, Amsterdam, NETHERLANDS|R.J. Pennings, J. Oostrik, E. van Wijk, H. Kremer, Department of Otorhinolaryngology, Radboud university medical center, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: A significant proportion of subjects with autosomal recessively inherited retinitis pigmentosa (arRP) and Usher syndrome type 2 (USH2) lacks a genetic diagnosis, subsequent prognosis and possibilities for future therapy. The USH2A gene is the most frequently mutated gene in USH2 and also prevalent in individuals with arRP. As such, USH2A is an important target for genetic screening. The aim of this study is 1) to screen genetically unexplained USH2 and arRP cases in which already one pathogenic USH2A variant was identified using targeted analyses and 2) to include genetically unexplained cases in our future whole genome sequencing effort.

Methods: Eleven unscreened or partially prescreened arRP cases with one previously detected USH2A variant and 29 USH2 cases were included for Molecular Inversion Probe (MIP)-based sequencing of USH2A coding regions, surrounding regions and published deep-intronic variants. After identification of pathogenic coding variants, data was prioritized based on four splice site prediction tools and the deep learning-based tool SpliceAI (Jaganathan et al. 2019). Wild-type and mutant minigene constructs were generated and transfected in Human Embryonic Kidney cells. Transcriptional analysis was performed to determine the splicing effects.

Results: Forty cases were assessed through MIPs. Four unique copy number variants and 107 rare (<1% in gnomAD) unique single nucleotide variants were identified. In 30 cases two (likely) pathogenic variants were identified and in three cases variants of unknown significance were found. One synonymous splice variant and one cryptic acceptor splice site variant that were absent or very rare (<0.001%) in gnomAD were identified. Subsequent minigene splice assays revealed partial exon skipping or no effect on splicing, respectively.

Conclusions: We identified five novel pathogenic variants and have shown the effect on splicing of one known synonymous USH2A variant. This analysis confirms that this MIPs approach is cost-effective. Through this study, genetic diagnoses were completed for at least 30 patients. Six of the unexplained cases will be included for WGS to explore the noncoding regions for pathogenic variants.

CONTROL ID: 3527322

SUBMITTER (NAME ONLY): Tomoyuki Yamazaki

TITLE: Oculo-facio-cardio-dental (OFCD) syndrome: four cases in two Japanese families

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yamazaki, K. Kurata, K. Hosono, Y. Hotta, Ophthalmology, Hamamatsu Ika Daigaku, Hamamatsu, Shizuoka, JAPAN|S. Naruse, I. Matsushita, H. Kondo, Ophthalmology, Sangyo Ika Daigaku, Kitakyushu, Fukuoka, JAPAN|A. Hiyoshi, Ophthalmology, Fukuoka Daigaku, Fukuoka, Fukuoka, JAPAN|M. Iwaizumi, Laboratory Medicine, Hamamatsu Ika Daigaku, Hamamatsu, Shizuoka, JAPAN|Y. Kiuchi, Ophthalmology and Visual Science, Hiroshima Daigaku, Higashihiroshima, Hiroshima, JAPAN|

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ABSTRACT BODY:

Purpose: Oculo-facio-cardio-dental (OFCD) syndrome is an extremely rare X-linked dominant disorder that is lethal in men. It is associated with congenital cataract, microphthalmia, and systemic complications including facial dysmorphic features, congenital heart disease, and tooth abnormalities. OFCD syndrome is caused by variants in BCOR. We performed a retrospective observational clinical study to assess the long-term clinical course of Japanese OFCD patients with BCOR variants.

Methods: We clinically examined and collected blood samples from four OFCD patients from two families who had been visiting our hospitals for a long time. To identify the causative variants, whole-exome sequencing (WES) was performed to identify the candidate variants, which were confirmed by Sanger sequencing.

Results: Case 1: A 12-year-old girl with a sporadic case, had congenital cataracts and microphthalmia immediately after birth. At 2 months of age, a lensectomy was performed on both eyes. Subsequently, she developed secondary glaucoma and was treated surgically several times; this included a tube shunt surgery in her right eye. She also had a broad nasal bridge, an atrial septal defect (which was surgically treated), and teeth dysplasia (radiculomegalies with prolonged dental roots). She had a de novo nonsense variant [c.4438C>T:p.(Arg1480*)] in BCOR.

Cases 2–4: A 16-year-old girl, a 46-year-old mother, and a 73-year-old grandmother, had congenital cataracts and microphthalmias. The girl underwent lensectomy in the right eye, and the grandmother had pseudophakia in her left eye. Nystagmus was observed in each patient. All patients had broad nasal bridges and elongated faces. The youngest had a heart murmur when she was a toddler. The girl had a cleft palate and the mother had teeth dysplasia. The girl and the mother had a toe malformation. They had a novel frameshift variant [c.717_729del:p.(Asn240Phefs*22)].

Conclusions: We reported the clinical features of four Japanese OFCD syndrome patients with BCOR variants. WES was useful for a precise diagnosis. Congenital cataracts and microphthalmia were common in all cases. Facial, cardiac, and dental abnormalities varied in severity. In some cases, skeletal abnormalities were observed. It is vital to obtain additional information on Japanese OFCD syndrome patients. The data from this study provides further insight into OFCD syndrome and may be useful for formulating an accurate diagnosis.

CONTROL ID: 3527329

SUBMITTER (NAME ONLY): Ahmad Elsahn

TITLE: Distribution and growth pattern of *Pseudomonas aeruginosa* bacteria in the corneal stroma during corneal infection

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Elsahn, I. Lewis, M. Stephens, H. Dua, I. Mohammed, University of Nottingham, Nottingham, Nottinghamshire, UNITED KINGDOM|A. Elsahn, Ophthalmology, Alexandria University, Alexandria, EGYPT|

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ABSTRACT BODY:

Purpose: To study the behaviour of *Pseudomonas aeruginosa* bacteria inside the corneal stroma after corneal infection in human microbial keratitis

Methods: Human whole donor corneas obtained from the eye bank were used in this project. Bacterial suspensions of GFP expressing PAO-1L or mCherry expressing *P. aeruginosa* PAO-1L with a fluorescence-based biosensors of c-di-GMP were prepared to a concentration of 10^7 cfu/ml. Two methods of infection were used. In the intrastromal injection method, 50 microlitres of bacterial suspension was injected into the middle of the corneal stroma from the endothelial using a 30G hypodermic needle. In the transepithelial method, the superficial epithelial layers were removed by a Kimwipe, 3 epithelial scores were made. An 8.75 mm corneal trephine was placed on the cornea creating a well. Fifty microlitres of bacterial suspension were placed inside the well. The corneas were incubated in medium for 24 to 72h and examined under a Laser Confocal Fluorescence Microscope (CFLM)

Results: In the intrastromal model, mCherry-expressing PAO-1L bacteria were observed to grow locally at the site of injection. The levels of c-di-GMP initially increased steadily, indicating the increase of bacterial association. Towards the end of the 72h period, bacterial growth rate and the levels of c-di-GMP increased rapidly, and bacterial spread was observed in the corneal stroma. In the transepithelial model, GFP expressing POA-1L bacteria formed large colonies on the corneal surface that penetrated deeper into the cornea with time

Conclusions: We have established an ex-vivo models of bacterial keratitis and demonstrated that *P. aeruginosa* can grow over the corneal surface and within the corneal stroma after an initial phase of slow growth

CONTROL ID: 3527334

SUBMITTER (NAME ONLY): Cynthia Jiang

TITLE: Accuracy of Kane and Hill-RBF V 2.0 Formulas Compared to Other Formulas for IOL Power Calculation

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.C. Jiang, N.M. Hodson, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|D.A. Johnson, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: As cataract surgery is nowadays considered a refractive surgery, new formulas are continually being developed in order to achieve optimal refractive outcomes after the surgery. This study compares newer IOL power formulas, Kane and Hill-RBF V 2.0, to other formulas for different axial lengths.

Methods: This retrospective study included 406 eyes of 406 patients who underwent cataract surgery. Eyes with previous refractive surgery, associated corneal or anterior segment abnormalities, or intraoperative complications were excluded. Biometry was performed using IOL-Master 700. Predicted refraction from 7 formulas (Hill-RBF V 2.0, Kane, Barrett Universal II, Haigis, Hoffer-Q, Holladay 2, and SRK/T) was compared to postoperative refraction at 1-3 months for different axial lengths: <22.5 mm (short), 22.5-25.5 mm (medium), and >25.5 mm (long). Post-hoc analyses and Bonferroni correction were applied for multiple comparisons.

Results: Overall and within short and medium eyes, all formulas had similar percentages of eyes within ± 0.5 D of the target refraction (Table 1). In long eyes, however, the percentages within ± 0.5 D were significantly higher for Barrett Universal II and Kane formulas (both 72%) compared to those for Hoffer-Q and Holladay 2 formulas (both 52%) ($P=0.004$). Mean numerical error (MNE) and mean absolute error (MAE) were similar for all formulas overall as well as within medium and long eyes. However, within short eyes, MNE was significantly lower for Barrett Universal II (0.27 ± 0.38 D) and Haigis (0.28 ± 0.42 D) compared to Holladay 2 (-0.06 ± 0.41 D) ($P=0.021$ and $P=0.014$, respectively).

Conclusions: The accuracy of newer IOL formulas may depend on the axial length. For long eyes, Kane and Barrett Universal II performed better than Hill-RBF V 2.0 and other formulas studied. For short and medium eyes, Kane and Hill-RBF V 2.0 had an accuracy similar to other formulas.

CONTROL ID: 3527338

SUBMITTER (NAME ONLY): Markus Linder

TITLE: Simultaneous Ang-2/VEGF-A inhibition prevents subretinal fibrosis progression in preclinical mouse models of choroidal neovascularization (CNV)

SESSION TITLE: AMD: clinical research - new therapies and technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Linder, R. Foxton, S. Uhles, F. Revelant, M. Lazendic, J. Canonica, M. Garcia Garrido, P. Westenskow, Roche Pharma Research and Early Development, Roche Innovation Center, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Faricimab, a bispecific antibody (ab) currently in phase (Ph) 3 trials, targets both angiopoietin-2 (Ang-2) and VEGF-A, key drivers of vascular instability, and demonstrated improvement in BCVA and sustained efficacy vs anti-VEGF monotherapy in Ph2 clinical trials of diabetic macular edema (DME) and neovascular AMD (nAMD). We present new preclinical data from 2 CNV mouse models showing that dual Ang-2/VEGF-A blockade significantly reduces fibrosis vs anti-VEGF monotherapy.

Methods: 7-week (W)-old JR5558 mice developing bilateral spontaneous neovascular fibrotic lesions were treated intraperitoneally (ip) with mouse cross-reactive tool abs against Ang-2, VEGF-A, or both (bispecific anti-VEGF-A/Ang-2 ab), and IgG (control). Fibronectin (FN) immunostaining was performed on retinal pigment epithelium (RPE)/choroid flat mounts to assess fibrosis at 1 (PT1), 3 (PT2), and 5 (PT3) W post treatment. Fluorophore-labeled collagen hybridizing peptides (CHPs) were used to detect collagen remodeling in active fibrotic lesions. Effect of Ang-2/VEGF-A blockade on subretinal fibrosis was analyzed in a laser-induced CNV mouse model by treating 10–12W-old wild-type mice ip with tool abs directly after and at 1W post laser injury. FN- and CHP-positive (+) areas were analyzed 3W post laser injury.

Results: There was significant reduction in FN+ area in the RPE/choroid of JR5558 mice with the bispecific ab (38%, $P<0.01$) and anti-Ang-2 (41%, $P<0.001$) vs IgG at PT1; effect of anti-VEGF-A alone was not significant. Only dual Ang-2/VEGF-A inhibition maintained significant reduction at PT2 (47%, $P<0.01$) and PT3 (54%, $P<0.05$). Dual inhibition significantly prevented collagen remodeling, as shown by reduced CHP in RPE/choroid lesions at PT2 (66%, $P<0.01$). Anti-VEGF-A or anti-Ang-2 alone showed no significant effect. In the laser-induced CNV mouse model, dual inhibition significantly reduced both FN+ (47%, $P<0.05$) and CHP+ (39%, $P<0.01$) areas at 3W; blocking VEGF-A or Ang-2 alone had no significant effect.

Conclusions: We present preclinical data from 2 independent CNV mouse models suggesting sustained prevention of scarring with dual Ang-2/VEGF-A pathway inhibition. Our findings support the hypotheses that Ang-2 and VEGF-A drive subretinal fibrosis. Future studies are underway to determine how dual Ang-2/VEGF-A inhibition limits subretinal scarring.

CONTROL ID: 3527340

SUBMITTER (NAME ONLY): Noah Hodson

TITLE: Effects of Panretinal Photocoagulation on the Ocular Surface and Tear Film

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.M. Hodson, C.C. Jiang, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|J. Sohn, H.S. Khalaf, J.R. Gallagher, D.A. Johnson, A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although research indicates proliferative diabetic retinopathy (PDR) itself is associated with changes in ocular surface parameters, it is still not clear whether panretinal photocoagulation (PRP) further affects these parameters. This study evaluated the effects of PRP, a commonly used treatment for PDR, on the ocular surface and tear film parameters.

Methods: In this prospective study, PRP was performed on 44 eyes of 37 patients with PDR. Patients with previous PRP, vitreoretinal surgery, recent use of contact lens, or cataract surgery within 3 months were excluded. The following were measured before and at 1 and 3 months after PRP: Ocular Surface Disease Index (OSDI) questionnaire, tear breakup time (TBUT), corneal fluorescein staining, conjunctival lissamine green staining, and Schirmer test with anesthesia. Wilcoxon signed-rank test was performed to determine changes in tear film and ocular parameters after PRP.

Results: This study included 19 men and 18 women, with a mean age of 53.6 ± 10.3 years. TBUT decreased from a pre-PRP value of 6.9 ± 2.4 s to 5.5 ± 2.7 s after 1 month ($P=0.02$) which subsequently increased to 7.0 ± 2.7 s at 3-month visit ($P=0.03$) and which was not different from the pre-PRP value ($P=0.93$) (Figure 1). There were no significant changes in other ocular surface or tear film parameters after PRP.

Conclusions: In patients with PDR, PRP causes transient instability of the tear film with values returning to the baseline at 3 months. Such tear film changes can transiently worsen the preexisting dry eye disease in patients with PDR.

CONTROL ID: 3527342

SUBMITTER (NAME ONLY): Minghan Chen

TITLE: Use of a Shack-Hartmann wavefront sensor to characterize the scattering properties of soft contact lenses

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chen, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Minghan Chen: Commercial Relationship(s); Johnson and Johnson Vision: Code E (Employment)

ABSTRACT BODY:

Purpose: Soft contact lenses (CL), with manufactured cosmetic patterns, not only correct patient's refractive error but also offer different forms of ocular cosmetic enhancement by changing the eye appearance. Various decorative designs with different colors are typically integrated around the peripheral region of the CL optical zone (OZ). When light passes through these regions, diffraction and scattering can be generated and degrade the retinal image contrast. Thus, it is essential to develop an instrument and associated methodology to quantitatively characterize the CL optical scattering properties and understand the on-eye performance of cosmetic patterns.

Methods: A benchtop Shack-Hartmann wavefront sensor (Lumetrics, Inc., NY) was installed with additional imaging optics. The collimated laser light (635nm) was made to pass through the CL and focused by a lenslet array into foci captured by a CCD camera. The ratio of the optical intensity within Airy disc versus the total intensity of the individual lenslet element was computed, and the averaged ratio of the lenslet within the measured pupil was defined as forward-scattering-ratio (FSR). The background signal (system without any sample) and nine lens samples (3 lenses for each brand), including Johnson & Johnson 1-DAY ACUVUE DEFINE with LACREON Fresh Green color (Fresh), 1-DAY ACUVUE® MOIST (Moist) lenses, and a lab-made hazy lens, were measured three times for each lens and the FSR were analyzed respectively. The ratio, defined as normalized forward scattering (NFS), between individual sample FSR versus the background FSR value, was utilized as the metric to characterize the magnitude of sample scattering. The higher the NFS value, the less CL scattering.

Results: Within the measured 6-mm pupil, on average, the NFS value for Fresh, Moist, and the hazy lens was 0.9918 ± 0.0028 , 0.9907 ± 0.0026 , and 0.9475 ± 0.0071 , respectively. Thus, both Fresh and Moist showed much less scattering than the hazy lens. There was no statistically significant difference between Fresh and Moist lenses. However, a significant difference was observed between the hazy lens versus Fresh ($p=0.0012$) and Moist ($p=0.0013$), respectively.

Conclusions: Within a 6-mm pupil, the Fresh lens does not generate stronger scattering comparing with the Moist lens, and thus its optical performance does not degrade by scattering.

CONTROL ID: 3527351

SUBMITTER (NAME ONLY): Mary Ann Croft

TITLE: Accommodative movements of vitreous structures were quantified and correlated with accommodative amplitude in live monkeys

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Croft, T. Nork, J.P. McDonald, A. Katz, P.L. Kaufman, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|G. Heatley, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Quantify accommodative movements of intravitreal structures/fluid in the monkey eye to determine if they are related to accommodative amplitude and presbyopia.

Methods: In eyes of 11 rhesus monkeys (aged 8-22 yrs), maximum accommodative responses were induced by central electrical stimulation of the Edinger-Westphal (E-W) nucleus. Ultrasound biomicroscopy (UBM; 50, 20 MHz) images were collected in the region of the lens, ciliary body and over the entire extent of the globe.

Results: During accommodation, the anterior hyaloid bowed backward by 0.26 ± 0.02 mm [mean \pm s.e.m.] ($p = 0.001$; $n=8$), the central vitreous moved posteriorly by 0.27 ± 0.05 mm ($p = 0.001$; $n=7$), while the peripheral lacunae (cistern) tips move forward by 0.42 ± 0.09 mm ($p = 0.002$; $n=8$), and inward (centripetally) by 0.14 ± 0.02 mm ($p = 0.001$; $n=8$). Accommodative central vitreous posterior movement was significantly related to accommodative amplitude; the more the central vitreous moved posteriorly during accommodation, the higher the accommodative amplitude (32.9 ± 9.64 diopters/mm; $p = 0.019$; $n=7$), and these movements declined significantly with increasing age (-0.0185 ± 0.0062 mm/yr; $p = 0.031$; $n=7$). In addition, the accommodative forward movement of the peripheral lacunae (cistern) tips increased with increasing accommodative amplitude; the greater the forward movement of the cistern tip the higher the accommodative amplitude (16.95 ± 6.52 D/mm; $p = 0.047$; $n=8$) and these movements tended to decline with age (-0.024 ± 0.011 mm/yr; $p = 0.08$; $n=8$). Accommodative backward bowing of the anterior hyaloid and centripetal movement of the cistern tip were not significantly related to accommodative amplitude and did not decline significantly with age.

Conclusions: There are statistically significant accommodative movements of various intravitreal structures. The posterior central vitreous movement and the forward movement of the cistern tip are related to accommodative amplitude and decline with age, and may be related to the mechanism of accommodation, presbyopia and perhaps glaucoma. These findings may also inform on the mechanism of accommodation and presbyopia, and the function of accommodating IOLs.

CONTROL ID: 3527353

SUBMITTER (NAME ONLY): Hong Fu

TITLE: Flap cut design for a new femtosecond laser for tissue-bridge-free corneal refractive surgery

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Fu, N. Khatibzadeh, J. Hill, D. Mehta-Hurt, A. Voorhees, L. Bing, L. Chen, M. Rahaman, C. Villanueva, H. liu, P. Gray, A. Facemire, Surgical Vision R&D, Johnson and Johnson Medical Devices, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: A new femtosecond laser aiming for tissue-bridge-free corneal refractive surgery has been developed. The scanning system creates a fast scanline as the cutting “blade”, then moves it to draw any 3D incision shape. The LASIK flap creation consists of three basic cutting shapes: a pocket cut for minimizing the undesired opaque-bubble-layer (OBL), a bed cut consisting of a ring annulus cut and a series of rectangular cuts, and a side cut. To design a robust flap cut, we hypothesize that the laser beam must not be blocked by the laser-tissue-interaction induced gas bubbles in any section of the cutting process.

Methods: Both ex vivo porcine eyes (N = 89) and invivo rabbit eyes (N = 110) were used in the flap experiments. To exacerbate bubble generation, we used higher-than-necessary laser pulse energy or dextran-immersed porcine eyes or both in some of the experiments. Since the flap pocket is a proven mitigation for OBL, which occurs frequently in flap creation for human but rarely in the animal tissue, we simply adopt it in the flap cut design. The R&D laser software allowed us to select and specify the different cut elements and apply them at different time orders. The flap lift dynamics was assessed on a scale of 1-4 (1 = no lift, 2 = moderate adhesion, 3 = minimal adhesion, 4 = no adhesion) by the subject matter expert (SME).

Results: First, the bed cut must be done before the side cut. If the side cut is done prior to the bed cut, the gas bubble generated during the bed cut can migrate through the side cut to the interface between the patient interface glass window and the cornea surface, causing uncut tissue island in the bed cut. Second, to minimize the gas bubble induced tissue adhesion, the side cut must be done in multiple layers. Third, the bed cut must double pass any location in the flap bed to minimize the tissue adhesion.

Conclusions: The results are consistent with our hypothesis. We arrived the final flap cut design with pocket cut → double-pass bed cut → multilayered side cut. The pocket is to minimize the OBL. The double-pass bed cut is to minimize tissue adhesion in the bed, and it is performed before the side cut to avoid uncut tissue island. The multilayered side cut minimizes the tissue adhesion induced by gas bubble interference with the laser focus during the side cut. All flaps created with the final flap cut design have achieved SME score 3-4 robustly.

CONTROL ID: 3527370

SUBMITTER (NAME ONLY): Scott Massa

TITLE: Designing a quality monitoring system for low-resource ophthalmology clinics using Bayesian analysis

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Massa, P. Misra, Z. Elkin, Department of Ophthalmology, New York University School of Medicine, New York, New York, UNITED STATES|Y. Lu, R. Anthopolos, Department of Population Health, New York University School of Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmology clinics with minimal statistical analytics capabilities may struggle to implement a quality monitoring system to evaluate patient outcomes. We performed a quality improvement study by designing a quality monitoring system for a low-resource ophthalmology clinic that would use small samples to estimate outcomes for larger patient populations.

Methods: We evaluated the proportion of primary open-angle glaucoma (POAG) patients who were treated “successfully” according to American Academy of Ophthalmology Preferred Practice Patterns (PPPs). We analyzed 100 patients seen in the clinic over 3 months in 2019 as the input for our Bayesian analysis. We also created a standardized note template for use by clinicians in the electronic medical record (EMR) for POAG patient visits to facilitate monitoring of treatment successes without requiring clinical expertise. We evaluated adherence to clinician template use in POAG patient notes on the weekly day of glaucoma patient visits over 9 weeks in 2020.

Results: Using Bayesian analysis based on our initial data, we created tables that allow for quality monitoring of future 3 month intervals using parameters from smaller samples. Using a small sample of 30 patients, we were able to determine that there was a 100% probability that the clinic as a whole was not achieving the pre-defined target percentage of 80% of POAG patients successfully treated, as defined by the PPPs. Regarding adherence to use of the note template for POAG patients, the median proportion of patients for which the template was used on a single clinic day was 27%, with a maximum of 53% and a minimum of 11%.

Conclusions: Based on the input parameters of the number of patients in the sample, the number of treatment successes in that sample, and the target proportion of successfully treated patients, a small sample Bayesian analysis can be used for quality monitoring of patient outcomes for larger patient populations in low-resource clinical settings. Future work includes creation of an open-access database of tables derived from Bayesian analysis for use as a reference by other low-resource clinics in quality monitoring efforts.

CONTROL ID: 3527384

SUBMITTER (NAME ONLY): Ping Situ

TITLE: Recovery of corneal threshold and symptoms in symptomatic contact lens wearers

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Situ, C. Begley, School Of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|T. Simpson, School Of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: To investigate the changes in symptoms and corneal thresholds to cooling stimuli in a group of symptomatic contact lens (CL) wearers when habitual CL wear is first ceased (washout phase) and then restarted (re-challenge phase) for 3-month periods, in an attempt to understand the neural mechanisms underlying CL discomfort.

Methods: Twenty-four symptomatic soft CL wearers (based on Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) scores and comfortable wearing time) completed the study. Corneal detection thresholds to cooling stimuli (approximately 22°C) were estimated by a modified Belmonte esthesiometer at study entry while still using habitual CLs (BL) and repeated at each month over the 3-month of washout (M1, M2, M3) and 3-month re-challenge phase (M4, M5, M6). The CLDEQ-8 was administered at BL, M4, M5 and M6. Repeated measures ANOVA and post-hoc tests with Bonferroni adjustment were used for data analysis.

Results: There was a significant difference in detection threshold between study visits ($p < 0.001$), with the threshold increasing gradually (become less sensitive) during no-CL lens wearing washout and then decreasing during the re-challenge phase (Figure 1). The cooling threshold at BL was significantly different than M2, M3, M4 and M6 (all $p \leq 0.035$), but not M1 ($p = 0.082$) and M5 ($p = 0.188$). The CLDEQ-8 was significantly different between visits ($p < 0.001$), with CLDEQ-8 scores for M4, M5 and M6 all significantly lower compared to baseline (all $p < 0.001$) but similar to score during the re-challenge phase (all $p \geq 0.941$) as shown in Figure 2.

Conclusions: The study demonstrated that corneal sensitivity to cooling stimuli decreased while symptoms improved following a no-CL washout in a group of symptomatic CL wearers. Sensitivity tended to increase again after restarting CL wear. These results suggest that sensory function contributes to CL discomfort and point to the complex role that corneal sensory processing plays in the group of symptomatic CL wearers.

CONTROL ID: 3527386

SUBMITTER (NAME ONLY): Linda Hazlett

TITLE: Matriptase Deletion: A Model of Dry Eye.

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.D. Hazlett, D. Bessert, S.A. McClellan, M. Somayajulu, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|K. List, Pharmacology, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Matriptase, a cell surface serine protease, is critical for function of several epithelia. Matriptase null mice die 1-2 days after birth due to decreased epidermal barrier function. Hypomorphic mice (low matriptase) have a mild transient epidermal barrier defect in pups but have a normal lifespan allowing studies of functionality in adults. Our purpose is to determine the effects of matriptase gene deletion on the eye and lacrimal gland in adult mice.

Methods: C57BL/6J-Matriptase hypomorphic and littermate control mice at 4-6, 11-12 and 13.5 months of age were sacrificed and eyes and lacrimal glands removed, fixed, embedded in epon-araldite and sectioned. Corneal epithelial thickness (cross sections through the pupil) was measured at 15 points across the central cornea. Corneal epithelial sheets were processed from both groups and Langerhans cells (dendritic cells) stained with a Langerin specific PE conjugated primary antibody. Eyes also were examined by slit lamp, and scanning EM. Mice also were infected with *Pseudomonas aeruginosa* and their response to infection scored for disease, and photographed using a slit lamp.

Results: Measuring corneal thickness revealed that matriptase hypomorphic mice of 6 months of age had a significantly thicker corneal epithelium when compared with control mice. Similar measurements of older mice showed no differences between the two groups. Photographs taken with a slit lamp did not reveal any noticeable differences in corneal or ocular surface morphology between mice at any age. However, scanning EM showed differences in corneal surface morphology and irregularities in structure in the 4-6 month vs older aged hypomorphic vs control mice. Hypomorphic vs control mice of younger age also had a two-fold increase in Langerin positive cells in the peripheral cornea; and, lacrimal glands differed from controls in that glands exhibited patches of abnormal vacuolated acinar cells and the presence of an inflammatory infiltrate. Infected mice responded similarly to eye infection, but only hypomorphic mice exhibited swollen facial features and ruffled fur.

Conclusions: In young vs older mice with low levels of matriptase we observed: a significant increase in corneal thickness, irregular surface cells, increased Langerhans cells, lacrimal gland abnormalities, and a worsened response to *P. aeruginosa* infection.

CONTROL ID: 3527388

SUBMITTER (NAME ONLY): Alejandra Sanchez

TITLE: Refractive outcomes using "Barrett True K Formula" for intraocular lens calculation in patients with radiated keratotomy

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sanchez, K. Zuniga, A.K. Escalona Brito, E. Chavez-Mondragon, Anterior Segment, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To assess reliability of intraocular lens (IOL) calculation using "Barrett True K" in patients with radiated keratotomy (RK).

Methods: Prospective, observational. Conducted in the Anterior Segment department of the Ophtalmology Institute "Fundacion Conde de Valenciana". Patients with RK and cataract diagnosis were included between September 2017 to October 2019. IOL calculation was carried out using "Barrett True K" with a -0.50 target of spheric equivalent (SE). The dioptric power of the implanted IOL was the closest suggested by Barrett True K. Refraction was obtained 1 month posterior to surgery. IOL Prediction Error (IOL PE) was calculated subtracting the power indicated by Barret True K to the implanted lens power and then the refractive predictive error (RPE) was calculated assuming that 1 diopter (D) of IOL PE corresponded to 0.7 D in aerial lenses.

Results: 24 eyes were included . 77.8% were women, the rest men with a 14.3%. Median age was 60.4 years. 57.1% were right eyes and 42.9% left. Average axial length was 24.19 ± 1.61 . The median of radiated cuts was 8.5. The median flattest keratometry was 34.9 ± 3.9 , and the steepest was 36.4 ± 3.33 . The median D of the lens implanted was 20.575. The month after the surgery a median residual ametropy of 0.7 D and ± 1.02 D of SE were found. Best corrected visual acuity was 0.21 LogMAR. The median IOL PE was calculated of $0.30 \pm .17$ and the median RPE was of $0.21 \pm .12$. 42% of the eyes had a RPE of ± 0.50 D and 58% a RPE de ± 1.00 D. 64.3% had a residual SE ≤ 0.50 D.

Conclusions: Barret True K was precise in predicting a refractive error of ± 1.00 D in approximately 65% of the eyes, it proved to be effective in 9 out of 14 cases.

CONTROL ID: 3527390

SUBMITTER (NAME ONLY): Nimra Ghani

TITLE: Postoperative linear movement and angular rotation of the implant in patients with the Argus II Retinal Prosthesis and its effects on visual function

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ghani, J. Bansal, A. Naidu, Ophthalmology, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|K. Chaudhary, Stony Brook University Hospital, Stony Brook, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study analyzes postoperative changes in the position of the Argus II Retinal Prosthesis's electrode array over a two-year period. It specifically assesses the presence or absence of linear implant movement and/or angular rotation around the axis of the implant tack over time, and evaluates any correlation that such movement had with postoperative visual function tests.

Methods: This is a single center, single surgeon cohort study that enrolled five patients with implantation of Argus II Retinal Prosthesis at Stony Brook University Hospital. Fundoscopy was performed at each postoperative follow up visit at month 1 (M1), month 3 (M3), month 6 (M6), month 12 (M12), and month 24 (M24). Visual function data (Direction of Motion (DOM) and Square Localization (SL)) from each visit was extracted from the Argus II Retinal Prosthesis Post Approval Study. Fundoscopy images were extracted and analyzed via NIH ImageJ. Data analysis was completed using IBM SPSS.

Results: The angle of the implant with respect to the horizontal (Δ) showed a statistically significant increase from both M1 to M6 and M1 to M24 (paired t-test, $p < 0.05$). The optic disc-tack-surgical handle angle (β) showed a significant increase from both M1 to M12 and M1 to M24 (paired t-test, $p < 0.05$). The linear distance from the optic disc to the surgical handle on the implant (AB) significantly increased between M1 and M12 (paired t-test, $p < 0.05$). There were significant negative correlations between length AB and SL ($r = -0.582$, $p < 0.01$) and DOM ($r = -0.0753$, $p < 0.01$), between angle β and SL ($r = -0.725$, $p < 0.01$) and DOM ($r = -0.459$, $p < 0.05$), and between angle Δ and SL ($r = -0.615$, $p < 0.01$). Based on multivariate regression analysis, angle β , angle Δ , and length AB were significant predictors of SL outcome ($p < 0.000$) and angle β , angle Δ , length AB, and length AC were significant predictors of DOM outcome ($p < 0.01$).

Conclusions: This study demonstrates that there is both statistically significant linear implant movement and angular rotation around the axis of the implant tack over time and that this movement had negative effects on visual function outcomes. It is important, moving forward, to take this into consideration when designing retinal implants, so that the implant's efficacy is not affected by such anatomic changes.

CONTROL ID: 3527398

SUBMITTER (NAME ONLY): Yi-Zhong Wang

TITLE: Evaluation of a UNet Convolutional Neural Network (CNN) for Automatic Measurements of Ellipsoid Zone (EZ) Area and Photoreceptor Outer Segment (POS) Volume in X-Linked Retinitis Pigmentosa (xLRP)

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, A. Cao, D.G. Birch, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|Y. Wang, D.G. Birch, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Manual segmentation of OCT volume scans is time-consuming and costly. CNN models may provide new tools to facilitate this task. Previously we reported that a UNet was effective and efficient for segmenting retinal layers of SD-OCT B-scan images of patients with RP (Wang et al., ARVO 2020). Here we evaluated this model for automatic measurements of EZ area and POS volume from volume scans in xLRP.

Methods: UNet was implemented in MATLAB and trained with 480 midline B-scan images obtained from 220 patients with RP and 20 control subjects. The test included 38 high-speed 9mm 31-line macular volume scans from a separate group of 38 patients with xLRP. All volume scans showed a POS transition zone within the scan window. The Spectralis segmentation of volume scans was corrected manually for EZ and apex RPE to serve as a reference. UNet was used for segmentation of B-scan images in a volume scan to obtain EZ and RPE boundary lines that defined POS. The 3-D POS map was reconstructed by interpolating the discrete 2-D POS layers from 31 B-scans over the grid of scan area. EZ area was measured by multiplying the area of a single grid pixel by the number of pixels having measurable POS. The POS volume was the sum of the products of the grid pixel area and the POS length at the pixel. Bland-Altman and correlation analyses were conducted to compare EZ area and POS volume measured by UNet to the reference.

Results: For EZ area (range: 0.17 to 27.8 mm²), Bland-Altman analysis revealed a mean±SE difference of -1.55±0.25 mm² and CoR of 2.98 mm² between UNet and the reference. EZ area estimated by UNet was highly correlated with the reference (r=0.98; slope=0.85). For POS volume (range: 0.002 to 0.65 mm³), Bland-Altman analysis showed a close agreement between UNet and the reference (mean±SE difference of 0.0004±0.004 mm³ and CoR of 0.05 mm³). POS volume measured by UNet was also highly correlated with the reference (r=0.99; slope = 1.05).

Conclusions: While both EZ area and POS volume determined by UNet had a similar correlation with the reference, UNet tended to underestimate EZ area but had a closer agreement with the reference in measuring POS volume. The deep machine learning method may provide an effective tool for studying the relationship between disease progression and POS volume and EZ area changes in RP.

CONTROL ID: 3527404

SUBMITTER (NAME ONLY): Li Chen

TITLE: Evaluating Iris Registration on a Femtosecond Laser for Refractive Corneal Lenticule Extraction Treatment

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chen, A. Voorhees, L. Bing, H. Fu, Johnson & Johnson Vision, Milpitas, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A new generation femtosecond laser is currently in development for corneal lenticule extraction for refractive surgery. Combined with iris registration and corneal mark registration, the new femtosecond laser will be used to perform a wavefront-guided lenticule treatment on a surgical eye. The goal of this paper is to evaluate iris registration on the new femtosecond laser system.

Methods: 33 paired eye images from 33 subjects were collected in a clinical study of the new femtosecond laser. Each paired images included one eye image captured by a diagnostic device (iDesign Wavefront Studio system, Johnson & Johnson Vision, Inc) when the subject was in a seated position, and an image of the same eye captured on the laser system before applanation at 40mm from the patient interface when the subject was in the supine position. The diagnostic eye images were imaged under the infrared illumination of 780 nm and 940 nm wavelength, while the laser eye images were imaged under the infrared illumination of 835 nm wavelength. An image processing software was used to evaluate the image processing quality and iris registration with the 33 paired eye images. The identified matched blocks in the unwrapped iris images from each paired images should be 21 or better for a successful iris registration capture.

Results: On average, the detected pupil diameter from the 33 diagnostic eye images was 6.444 ± 0.968 mm, (range from 4.176 mm to 8.088 mm), and the iris diameter was 12.383 ± 0.3222 mm (range from 11.784 mm to 13.019 mm). The pupil boundary and outer iris boundary in all 33 laser eye images were detected correctly. On average, the detected pupil diameter from the 33 laser eye images was 5.043 ± 0.981 mm (range from 2.719 mm to 7.130 mm), and the iris diameter 12.144 ± 0.316 mm (range from 11.265 mm to 12.648 mm). The average cyclotorsion angle detected in the 33 paired eye images was $0.62 \pm 2.53^\circ$ (range from -3.52° to 6.13°), and the matching blocks identified in each paired diagnostic eye image and laser eye image were all above the 21. The capture rate of iris registration between the diagnostic device and the new femtosecond laser system achieved 100%.

Conclusions: Pupil boundary and outer iris boundary were detected correctly in the 33 eye images from the new femtosecond laser. The infrared eye images captured on the new femtosecond laser are adequate for iris registration with human eyes.

CONTROL ID: 3527413

SUBMITTER (NAME ONLY): Jérémie Canonica

TITLE: VEGF-A/Ang-2 neutralization causes sustained prevention of subretinal macrophage infiltration in a mouse model of spontaneous choroidal neovascularization

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Canonica, S. Uhles, R. Foxton, N. Cole, M. Lazendic, M. Garcia Garrido, P. Westenskow, Roche Pharma Research and Early Development, Roche Innovation Center, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Faricimab, currently in phase 3 trials, is the first bispecific antibody for intraocular use. It independently binds and neutralizes both angiopoietin-2 (Ang-2) and VEGF-A, key drivers of vascular instability (vascular leakage, neovascularization [NV], and inflammation). Faricimab demonstrated sustained efficacy compared with anti-VEGF monotherapy in the phase 2 clinical trial for neovascular AMD. This abstract presents new preclinical data on the anti-inflammatory effect of targeting Ang-2 and supporting the vessel stabilization potential of Ang-2 inhibition in a mouse model of spontaneous choroidal NV (sCNV) in the context of observed phase 2 clinical data.

Methods: 7-week-old JR5558 mice developing bilateral spontaneous neovascular lesions were treated intraperitoneally with mouse cross-reactive tool antibodies against VEGF-A, Ang-2, or both (bispecific anti-VEGF-A/Ang-2 antibody), and IgG as controls. Subretinal macrophage infiltration, detected by Iba1 immunostaining, was evaluated ex vivo by flat-mounted retinal pigment epithelium (RPE)/choroid histology at 1, 3, and 5 weeks post treatment to assess immediate and long-term effects on the number of inflammatory cells around lesions.

Results: Treatment with the bispecific anti-VEGF-A/Ang-2 antibody significantly reduced the number of Iba1-positive macrophages around lesions on flat-mounted RPE/choroid histology by 23% and 38% ($P < 0.05$) vs IgG control at 1 and 3 weeks post treatment, respectively. The effect of VEGF-A or Ang-2 inhibition alone was not significant. At 5 weeks post treatment, only anti-Ang-2- and anti-VEGF-A/Ang-2-treated mice showed significant reduction in the number of Iba1-positive macrophages by 53% and 49% ($P < 0.0001$), respectively, vs IgG control. Anti-VEGF-A treatment alone did not prevent subretinal infiltration of Iba1-positive immune cells.

Conclusions: Preclinical experiments further elucidated the potential role of Ang-2 inhibition alone and in combination with anti-VEGF in reducing inflammation in the retina, and demonstrated that the prolonged anti-inflammatory effect was driven by Ang-2 neutralization. In a mouse model of sCNV, dual Ang-2/VEGF-A inhibition was superior to VEGF-A monotherapy in causing sustained prevention of subretinal macrophage infiltration around lesions on RPE/choroid, supporting the results of the phase 2 clinical trial.

CONTROL ID: 3527417

SUBMITTER (NAME ONLY): Onnisa Nanegrungsunk

TITLE: Correlation between Change in Central Subfield Thickness and Change in Visual Acuity in Eyes with Diabetic Macular Edema Receiving Fixed-Dosing Intravitreal Aflibercept Regimens: A Post Hoc Analysis of VISTA and VIVID Trials

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Nanegrungsunk, Ophthalmology, Chiang Mai University, Suthep, Chiang Mai, THAILAND|S.Z. Gu, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|O. Nanegrungsunk, S.B. Bressler, N.M. Bressler, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|W. Du, H. Moini, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess correlation between change in best-corrected visual acuity (BCVA) and change in central subfield thickness (CST) for diabetic macular edema receiving fixed-dosing intravitreal aflibercept injection (IAI) over 100 weeks.

Methods: Post hoc analysis of VISTA and VIVID wherein eyes were randomized to IAI 2 mg q 4 weeks (2q4) or IAI 2 mg q8 weeks after 5 initial monthly doses (2q8). The relationship between change in functional (BCVA) and change in anatomical (CST) outcomes at early (week 12) and later (week 52, and 100) visits was determined using Pearson correlation.

Results: Of 872 eyes, 290 were treated with 2q4 and 286 with 2q8. Percentage of eyes with BCVA and CST measurements available for analysis at weeks 12, 52, and 100 was 95%, 86%, and 74% in the 2q4 arm; and 97%, 85%, and 71% in the 2q8 arm. At baseline, the correlation (r) between CST and BCVA was -0.45 (95% CI: -0.53, -0.35) and -0.47 (95% CI: -0.55, -0.37) in the 2q4 and 2q8 arms. Change in CST and change in BCVA at weeks 12, 52, and 100 had r values of -0.39 (95% CI: -0.49, -0.29), -0.27 (95% CI: -0.38, -0.15), and -0.30 (95% CI: -0.41, -0.17) in the 2q4 arm and -0.28 (95% CI: -0.39, -0.17), -0.29 (95% CI: -0.41, -0.17), and -0.33 (95% CI: -0.44, -0.20) in the 2q8 arm. Linear regression analysis of correlation between changes in CST and changes in BCVA at week 100, adjusted for relevant factors showed CST changes accounted for 17% of variance in BCVA changes; every 100 µm decrease in CST was associated with a 1.2 letter increase in BCVA (P = .001).

Conclusions: Correlations between change in CST and change in BCVA following 2q4 or 2q8 fixed-dosing regimens of IAI for DME were modest. For any given change in CST from baseline, there was a broad range of change in BCVA from baseline at follow-up. These findings are consistent with a PRN regimen in the DRCR Retina Network Protocol T and suggest change in CST may be important in determining the need to withhold, continue, or resume anti-VEGF therapy for DME, but is a poor surrogate for predicting visual acuity outcome, even with fixed-dosing treatment regimens.

CONTROL ID: 3527419

SUBMITTER (NAME ONLY): Linda Burk

TITLE: Unique MIGS Combining Goniotomy and Direct Viscodilation of the Collector Channels in Eyes with Peripheral Laser Iridotomies

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Burk, J.E. Gilmore, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|L.L. Gilmore, Dallas Eye and Ear, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Linda Burk: Commercial Relationship: Code N (No Commercial Relationship) | Jane Gilmore: Commercial Relationship: Code N (No Commercial Relationship) | Linda Gilmore: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose was to evaluate Dual Blade Goniotomy and Direct Viscodilation of the collector channels in eyes with previous peripheral iridotomies for narrow angle glaucoma. Could the "clean the gutter and power wash the downspout" procedure effectively open the once aggravated trabecular meshwork?

Methods: After standard cataract surgery, 32 eyes had 180 degrees of trabecular meshwork removed with the Kahook Dual Blade exposing the ostium of the collector channels allowing direct visco-dilation of the collector channels. Viscoelastic was injected into the collector channels as the cannula was snugly held perpendicularly against the outer wall and dragged through the opened Schlemm's canal. Viscoelastic was used to break any anterior synechiae.

Results: 53% were African American. 72% were women. The average age was 68 years. 41% had moderate or advanced glaucoma. 51% were diabetics. 28% were on anticoagulants. Before surgery, the IOP was 22.4 mmHG (SD+/- 7.7) on 1.4 drops. At 3 months, the IOP was 15 mmHG (SD+/- 4/1) on 0.3 eye drops. IOPs were 16.1 mmHG (SD+/- 4.7) on 0.4 eye drops (1yr), 14.3mm HG (SD+/- 3.5) on 0.7 eye drops, and 14.7 mmHG (SD+/- 4.7) on 0.5 eye drops. Eye drops were eliminated in 74% (1yr), 53% (2yr), and 64% (3yr). A blush of blood was seen over the trabecular meshwork was common in the angle but was gone in two weeks. Avascular fibrosis was seen in several eyes and removed with the Dual Blade when the trabecular meshwork had been identified.

Conclusions: Narrow angles previously treated with laser iridotomies can be successfully treated with the Goniotomy-Visco-dilation-Cataract Surgery technique. This "clean the gutter and powerwash the downspouts' approach demonstrates that the once aggravated trabecular meshwork can be rejuvenated, improving IOP control and reducing the amount of drops required.

CONTROL ID: 3527420

SUBMITTER (NAME ONLY): Zahra Nafar

TITLE: Clinical benefits of a new swept-source OCT angio HD6x6 mm scan compared to angio 3x3 mm scan

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Nafar, T. Callan, W. Lewis, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|T. Bacci, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The usefulness of optical coherence tomography angiography (OCTA) in clinical practice is heavily influenced by the scan resolution. Angio 3x3 mm scans provide best commercially available scan resolution, however, due to its limited field of view (FOV), it is commonly complemented with an Angio 6x6 mm scan with a lower resolution. In this study we compare the image quality of a traditional Angio 3x3 mm scan with a High Definition (HD) 6x6 mm Angio scan.

Methods: A modified PLEX® Elite 9000 (ZEISS, Dublin, CA) was used to image 10 subjects (5 healthy and 5 diseased eyes) with the following protocol:

Pattern 1: 3x3 mm FOV consisting of 300 A-lines/B-scan and 300 B-scans acquired at 100kHz with 4 repetitions for angiography processing.

Pattern 2: 6x6 mm FOV consisting of 600 A-lines/B-scan and 600 B-scans acquired at 200kHz with 3 repetitions for angiography processing. HD 6x6 mm OCTA volumes are generated by processing clusters of three B-scan repetitions each for a shorter acquisition time, and the processing algorithm has been modified to enhance sensitivity to lower blood flow velocity.

An experienced grader compared quality and details of two scan patterns by grading the en-face slabs on a scale of 1-5 in a blind study. 6x6 mm images for every subject were cropped to a 3x3 mm FOV before comparison.

Results: As expected from the fact that the same sampling resolution was used in both patterns, HD 6x6 mm en-face views of the retinal slabs reveal comparable details and similar quality as seen in 3x3 mm scans (Figure 1). However, HD 6x6 mm scans also provide a larger FOV (Figure 1c), which is often necessary to visualize the extent of vascular lesions, for example in patients with macular neovascularization (MNV). Figure 2 shows the outer retina to choriocapillaris (ORCC) slab. Although both patterns provide the same resolution, the extent of MNV is only fully captured in the HD 6x6 mm en face projection.

Conclusions: We demonstrated that HD 6x6 mm scans provide a larger FOV while maintaining the same quality and detail as Angio 3x3 mm scans, and thus might be a suitable replacement for the Angio 3x3 mm scan in clinical practice.

CONTROL ID: 3527433

SUBMITTER (NAME ONLY): Antonio Bergua

TITLE: Impaired visual field while wearing mouth-nose masks in normal eyes

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bergua, A. Weber, B. Hohberger, Ophthalmology, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: The major route of infection of SARS-CoV-2 is supposed to be the respiratory way. Thus, mouth-nose masks are requested to prevent the viral transmission. The aim of the present study was to investigate, if wearing a mouth-nose mask impaired visual field function in normal eyes.

Methods: 30 healthy eyes of 30 subjects were recruited. Visual field function was tested by white-on-white perimetry (OCTOPUS 900; 90°). Sensitivity thresholds were analysed in 14 defined test points (P1-P14, inferior visual field) under 3 different test conditions while wearing a nose-mouth mask: (I) position 1: 1.5cm under the lower eyelid, nose clip not used; (II) position 2: 1.5cm under the lower eyelid, nose clip correctly positioned; (III) position 3: 0.5 cm under the lower eyelid, nose clip correctly positioned. All data were compared to sensitivity thresholds without wearing a nose-mouth mask (reference). Mean D was calculated as difference between each test condition and reference, respectively. The study was approved by the local ethics committee and was done in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from each participant.

Results: Mean sensitivity was not significantly different between all three test conditions (26.6 ± 2.4 dB (I); 28.3 ± 2.4 dB (II); 27.8 ± 2.2 dB (III) and reference (28.5 ± 2.4 dB), respectively. Subgroup analysis for test points P1-P14 yielded significantly different sensitivity thresholds between test condition (I) and reference at test point P3 – P12 ($p \leq 0.005$). Sensitivity thresholds at test point P7 were significantly different between test condition (II) and (III) compared to reference ($p < 0.001$), respectively. Mean D increased while wearing a mask at P7 in test condition (II) < (III) < (I) (-8.3 ± 7.3 dB; -11.3 ± 9.5 dB; -20.1 ± 7.6 dB).

Conclusions: Visual field function was significantly impaired inferior-nasal while wearing a nose-mouth mask in normal eyes, especially if the nose clip was not used correctly.

CONTROL ID: 3527456

SUBMITTER (NAME ONLY): Steffen Schmitz-Valckenberg

TITLE: Optical Coherence Tomography Signs of Early Atrophy in Age-related Macular Degeneration: Inter-Reader Agreement

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To determine the inter-reader agreement for structural features related to incomplete and complete retinal pigment epithelium and outer retinal atrophy (iRORA and cRORA respectively) in age-related macular degeneration (AMD).

Methods: Following formal training (reviewing literature, performing a pre-test twice and undergoing a web-based tutorial), readers qualitatively assessed 60 optical coherence tomography (OCT) B-scans from 60 eyes with AMD for nine individual features associated with early atrophy and performed seven different annotations to quantify the spatial extent of OCT features within regions-of-interests. Cases were selected to depict the entire spectrum of findings that may be observed in dry AMD eyes with and without atrophy. Inter-reader agreement based on kappa coefficients (κ) and smallest real difference (SRD) was assessed.

Results: Slight to substantial inter-reader agreement was observed for assessment of individual features associated with atrophy ($\kappa=0.19-0.70$), with lowest and highest agreement being for outer nuclear layer thinning and inner nuclear layer (INL) subsidence, respectively. The lowest SRD for horizontal annotations was observed for the zone of choroidal hypertransmission ($\pm 190.8\mu\text{m}$). Using the qualitative and quantitative gradings to derive atrophic features, there was moderate agreement for a two-category classification of the presence or absence of at least iRORA ($\kappa=0.53$), and substantial agreement for the presence or absence of cRORA ($\kappa=0.62$). There was moderate agreement for a three-category classification of no atrophy, iRORA and cRORA ($\kappa=0.52$). Exploratory analyses suggested a significantly higher level of agreement for a three-category classification using (i) no atrophy, (ii) presence of INL and outer plexiform layer subsidence, or a hyporeflective wedge-shaped band as a less severe atrophic grade and (iii) the latter plus an additional requirement of choroidal hypertransmission $\geq 250\mu\text{m}$ for a more severe atrophic grade ($\kappa=0.68$; $P=0.004$).

Conclusions: While current definitions of iRORA and cRORA allow for a consistent and robust assessment of early atrophy, a refined combination of individual features improved inter-reader agreement. This evaluation represents an important step towards a more detailed classification system for atrophic AMD and helps to inform the design and analysis of future early interventional clinical trials in AMD.

CONTROL ID: 3527460

SUBMITTER (NAME ONLY): Yuanzhi Liu

TITLE: OCT registration using macular thickness map and curvature maps

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, H. Bagherinia, T. Shagam, C. Leahy, S. Bello, Carl Zeiss Meditec, Inc., California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Registration of longitudinal OCT data is important for measuring the changes of retinal thicknesses over time. The registration based on OCT en face images becomes difficult when the OCT data is generated by a low-cost OCT system due to low contrast in the data. Here we propose to use the macular thickness and principal curvatures as alternative maps to provide sufficient number of landmarks for registration.

Methods: To obtain well distributed landmarks across the OCT field of view of two maps for robust registration, the macular thickness and corresponding principal curvature maps were used, where landmark correspondences were extracted from all three maps of each scan. Then, a subset of landmark correspondences with high confidence were selected using an exhaustive search method to compute the rigid transformation. Figure 1 shows an example of the thickness map registration. The mean registration error along with the number of landmarks between the landmark matches after registration were calculated for each pair of OCT volumes.

Results: Figure 2 shows the statistics for the registration error and landmark distribution for 243 pairs of OCT volumes of disease eyes acquired using a low-cost OCT prototype system (ZEISS, Dublin, CA). The mean and standard deviation of registration error in x, y and radial direction $\sqrt{x^2+y^2}$ are smaller than 70 and 15 microns respectively, which is acceptable for macular thickness analysis. The average number of landmarks used for registration is relatively high for computing three parameters of rigid transformation.

Conclusions: A registration method based on macular thickness and curvature maps has been explored in this study. We showed that this algorithm performed well for data acquired from low-cost OCT devices.

CONTROL ID: 3527463

SUBMITTER (NAME ONLY): Shruti More

TITLE: Comparison of retinal pigment epithelium elevation between scans acquired at 200 kHz and 100 kHz rates

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) angiography scans can be acquired at different scan rates. With faster scan rates becoming more prevalent, clinicians are expecting the most common OCT metrics to be available regardless of the rate at which these scans are acquired. The purpose of this study is to compare measurements of retinal pigment epithelium (RPE) elevation obtained on a swept-source OCT instrument at two different scan rates: 100 kHz and 200 kHz.

Methods: In this study, 25 dry AMD eyes were imaged on the swept-source OCT, PLEX[®] Elite 9000 (ZEISS, Dublin, CA) using 6×6 mm angiography scans. The acquisition consisted of 3 repeated scans at 200 kHz and 1 single scan at 100 kHz. The RPE elevations were computed over 3 mm and 5 mm circular areas and volumes centered on the fovea. The RPE elevation values from the scans acquired at both scan rates were plotted against each other. Linear regression was applied to the data to determine the R-squared value. The Bland-Altman analysis was used to determine the mean offset in RPE elevation measurements between the two scan rates. Paired t-tests were also calculated.

Results: The correlation plots (figures 1 and 2) show very good correlations ($R^2 > 0.98$) in area and volume of RPE elevation between 100 kHz and 200 kHz scan rate. The p-values from a paired t-test were all well above 0.05 (p = 0.47 and p = 0.73 for the area of RPE elevation computed over 3 mm² and 5 mm² circles respectively; p = 0.17 and p = 0.36 for the volume of RPE elevation computed over 3 mm³ and 5 mm³ circles respectively) indicating no statistical difference in measurement difference between the 2 scan rates.

Conclusions: Based on these results, there is very good agreement in the RPE elevation measurements between 100 kHz and 200 kHz scan rate. Therefore, the current RPE elevation measurements obtained at 100 kHz are also applicable at 200 kHz.

CONTROL ID: 3527468

SUBMITTER (NAME ONLY): David Krizaj

TITLE: TRPV4-mediated oscillatory calcium signaling in TM cells requires internal stores

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Krizaj, S.N. Redmon, J.M. Baumann, O. Yarishkin, Ophthalmology & Visual Sciences, University of Utah, Salt Lake City, Utah, UNITED STATES|J.M. Sherwood, D.R. Overby, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Intraocular pressure (IOP) is a mechanical oscillation with unknown physiological significance. TRPV4 (transient receptor potential isoform 4) channels partially mediate the trabecular meshwork (TM) response strain, shear, swelling and pressure. Their response to sustained stimulation is associated with stochastic regenerative $[Ca^{2+}]_{TM}$ spikes. The goal was to elucidate the cellular mechanisms that underlie this process.

Methods: Primary human TM cells were stimulated with the selective TRPV4 agonist GSK1016790A (GSK101). $[Ca^{2+}]_i$, $[Na^+]_i$ and transmembrane currents measured with optical imaging and patch clamp in the presence/absence of pharmacological modulators. mRNA and protein levels were determined with qPCR, Western blot and spatial expression determined with antibody labeling. Cells were transfected with GFP probes, shRNAs and exposed to modulators of plasma membrane and intracellular Ca^{2+} signaling pathways.

Results: Sustained TRPV4 activation triggered Ca^{2+} oscillations with periodicity of ~0.2 – 1 Hz, sustained depolarization and increase in $[Na^+]_i$. The oscillations were insensitive to blockers of Orai channels, voltage-operated Ca^{2+} and Na^+ channels but could be mimicked with inhibition of Ca^{2+} sequestration into ER stores. Inhibition of mitochondrial Ca^{2+} signaling and suppression of TRPM4, a Ca^{2+} -activated Na^+ channel blocked the oscillations. However, pharmacological inhibition of TRPM4 had no effect on trabecular outflow and genetic ablation did not affect IOP.

Conclusions: These results show that activation of pressure transducing ion channels in TM cells triggers amplitude- and time-dependent Ca^{2+} fluctuations that are regulated by steady-state $[Ca^{2+}]_i$ and activation history. The fluctuations require continual interactions between multiple plasma membrane TRP channels, endoplasmic reticulum and mitochondrial calcium sequestration/release mechanisms. TM calcium homeostasis, therefore, is a sophisticated, multi-pathway process that time-dependently coordinates molecular activity of plasma membrane, cytosolic and store compartments.

CONTROL ID: 3527484

SUBMITTER (NAME ONLY): Sophie Kubach

TITLE: Identification of diabetic retinopathy lesions: a comparison between widefield OCTA obtained by montaging 2 volumetric 15x15 mm scans and a single 15x15 mm angio scan.

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kubach, L. De Sisternes, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|J. Korobelnik, Centre Hospitalier Universitaire de Bordeaux Groupe hospitalier Pellegrin, Bordeaux, Aquitaine, FRANCE|S. Bonnin, Hopitaux Universitaires Pitie Salpetriere-Charles Foix, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Widefield optical coherence tomography angiography (OCTA) has the potential to improve the detection of peripheral retinal lesions in diabetic retinopathy (DR) that might otherwise be missed using conventional OCTA scans. Widefield OCTA can be obtained by combining multiple cube scans taken at different locations. In this study we assessed a new volumetric montage protocol designed to cover an area of 24 mm (Horizontal) x 15 mm (Vertical) for the identification of peripheral vascular lesions.

Methods: Ten eyes with diabetic retinopathy were imaged on PLEX® Elite 9000 swept-source OCT (ZEISS, Dublin, CA) by acquiring a central 15x15 mm angio scan of 17 um resolution followed by two lateral 15x15 mm angio scans at nasal and temporal fixations of same resolution as the central scan. The two lateral 15x15 mm angio scans were registered together such as to produce a volumetric 24 mm (H) x 15 mm (V) x 6mm (D) angio scan. The retinal slab from the resulting volumetric montage was compared to the retinal slab from the central single 15x15 mm scan to identify the extent of vascular lesion in the periphery.

Results: Figure 1 and Figure 2 show the retinal slabs and central B-scans from the volumetric montage protocol and from central 15x15 mm angio scan respectively. Out of 10 eyes with diabetic retinopathy, 8 were found to have lesions beyond the central 15x15 mm FOV. In addition, the quality of the montage, especially over the overlapping area of the 2 scans was preserved with no noticeable artifact. The sampling resolution of the montage protocol of 17 um was found to be adequate to identify the type of lesions: ischemic area, microaneurysm, vessels tortuosity were commonly reported. Some of these lesions were also visible on the structural B-scan with flow signal overlaid.

Conclusions: With a FOV of 24 mm (H) x 15 mm (V) and a sampling resolution of 17 um, the proposed volumetric montage protocol expands the imaging capability of OCTA for the detection and classification of vascular peripheral lesions.

CONTROL ID: 3527496

SUBMITTER (NAME ONLY): Maria Vittoria Cicinelli

TITLE: Retinal Findings in Alport Syndrome using Widefield and Ultra-widefield Imaging

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Most reports on Alport syndrome (AS) have focused on the posterior pole, while the retinal periphery has remained largely unexplored. Newer diagnostic modalities utilizing optical coherence tomography angiography (OCTA) and fundus photography have allowed for widefield (WF) and ultra-widefield (UWF) imaging of the retina. We performed a cross-sectional clinical study correlating the retinal findings on WF and UWF imaging with the clinical characteristics of our cohort of AS patients.

Methods: Demographics, past medical and ophthalmic history were collected at the inclusion visit. All patients underwent UWF color fundus photography and fundus autofluorescence (FAF), WF OCTA, and spectral-domain OCT (SD-OCT). Clinical associations were quantitatively explored with Pearson's correlation tests and chi-squared tests for quantitative and qualitative variables, respectively.

Results: Forty-two eyes of 21 patients (11 males, 55%; mean age 36.6 ± 12.9 years) with AS were included. Female carriers were older at time of inclusion (mean age 46 ± 15 years). Dot maculopathy was more frequent in male patients with X-linked AS; macular dots corresponded to inner limiting membrane (ILM) granularity on SD-OCT. Thirteen eyes (34%) had a consistent pattern of peripheral hypoautofluorescent ring on UWF-FAF. En-face OCT revealed multiple areas of retinal nerve fiber layer (RNFL) dehiscence in the macula, overlapping with temporal vascular lacunae seen on OCTA. Twenty eyes (52%) had absent RNFL raphe temporally. Mid-peripheral SD-OCT scans revealed a splintered and/or multi-lamellated ILM in 8 eyes (19%), which was likely progressive.

Conclusions: WF and UWF imaging allowed for the detection of new findings in AS patients. Most of the features are presumably congenital but some may be progressive and may share similar features to the renal pathology identified in this rare disorder.

CONTROL ID: 3527501

SUBMITTER (NAME ONLY): Jennifer Adeghate

TITLE: A Novel Agent in Prevention of Acute Radiation Toxicity in the Mouse Retina

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although radiation retinopathy is a well-recognized entity, preventive measures have not been defined. We aimed to study how a novel agent, JP4-039, may prevent acute radiation toxicity in the mouse retina by stabilizing mitochondria and preventing apoptosis after irradiation.

Methods: Forty-five BALB/c mice were sorted into three groups of 15 mice each. Anesthesia was then performed on all mice with 2% isoflurane. Mice in Groups 1 and 2 received a 32-gauge/10 microliter intravitreal injection of either 40 nanogram JP4-039 (n=5 per group) or 30% cyclodextrin (control; n=5 per group). The remaining 5 mice in either group did not receive an intravitreal injection. Group 3 mice (n=15) all received an injection of BODIPY-labeled JP4-039. Thirty minutes after injection and further anesthesia with Nembutal, all mice in Groups 1 and 2 were irradiated with a dose of 18 Gy via 6 MV photon beam (Varian TrueBeamTM STx linear accelerator), while Group 3 mice remained without irradiation. All mice were then sacrificed and enucleated according to the following sequence: Group 1 and Group 2 underwent TUNEL assay 24 hours after irradiation to determine rate of apoptosis, or flow cytometry 120 hours after irradiation in order to detect retinal migration of inflammatory cells. Group 3 underwent fluorescent microscopy at 0, 15, 30, and 60 minutes after injection only, in order to determine retinal uptake of intravitreal JP4-039.

Results: Eyes treated with JP4-039 prior to irradiation had lower levels of retinal apoptosis ($35.8 \pm 2.5\%$) compared to controls ($49.0 \pm 2.7\%$; $p=0.0066$), as well as reduced migration of apoptotic N1 cells ($30.7 \pm 11.7\%$) compared to controls ($77.7 \pm 5.3\%$; $p=0.0105$). Retinal uptake of intravitreal JP4-039 was detected in the mouse retina 15, 30, and 60 minutes after injection.

Conclusions: Intravitreal injection of the novel antioxidant, JP4-039, reduces the effects of acute radiation toxicity in the mouse retina.

CONTROL ID: 3527511

SUBMITTER (NAME ONLY): Meenakshi Kurup

TITLE: Vision-Related Quality of Life and Mental Health in Patients with Leber Hereditary Optic Neuropathy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Leber Hereditary Optic Neuropathy (LHON) is a mitochondrial optic neuropathy characterised by bilateral subacute central visual loss. The visual prognosis is poor. The majority of patients achieve visual acuities worse than 20/200. Anxiety and depression can compound the loss of visual function in LHON patients, exerting further detrimental effects on quality of life (QoL).

The aims of this study were to:

1. Assess vision-related QoL using the validated Visual Function Index-14 (VF-14) and National Eye Institute Visual Function Questionnaire-25 (VFQ-25).
2. Screen for anxiety and depression using the Hospital Anxiety and Depression Scale (HADS).

Methods: A standardised telephone interview, which included the VF14, VFQ25 and HADS, was conducted on 50 affected LHON patients and 28 unaffected LHON carriers.

Results: The mean VF-14 and VFQ-25 scores (\pm standard deviation (SD)) were significantly lower in affected patients compared with unaffected carriers (VF-14: 29.4 ± 24.0 vs 98.6 ± 2.51 , $p < 0.001$; VFQ-25: 48.3 ± 19.8 vs 92.9 ± 4.23 , $p < 0.001$). 54% of LHON patients were found to be anxious based on the HADS-Anxiety (HADS-A) score and 28% of LHON patients were depressed based on the HADS-Depression (HADS-D) score. The mean HADS-A (7.48 ± 3.9) and HADS-D (5.72 ± 4.13) scores for LHON patients were greater than the general population scores of 6.14 ± 3.76 and 3.68 ± 3.07 , respectively. The mean HADS-D score for LHON patients was significantly greater compared with unaffected carriers (3.68 ± 3.06 , $p = 0.024$). In affected patients, the duration of disease correlated moderately with VF-14 and VFQ-25 scores (both $r = 0.49$, $p < 0.001$), as well as the HADS-D score ($r = -0.41$, $p = 0.003$).

Conclusions: Vision-related QoL is significantly reduced in LHON patients who also have higher levels of depressive symptoms compared to unaffected carriers. Vision-related QoL and depressive symptoms correlate with disease duration, suggesting that both may improve as patients adapt to chronic disability. HADS-A and HADS-D scores of LHON patients are higher compared to the general population, highlighting their increased risk of anxiety and depression. Addressing mental health concerns and promoting enabling skills and strategies that overcome role limitations may improve QoL and mood in LHON patients.

CONTROL ID: 3527512

SUBMITTER (NAME ONLY): Kanza Aziz

TITLE: Primary proliferative vitreoretinopathy and the burden of multiple surgical failures: Analysis of 27,137 retinal detachment cases from a nationwide database

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is the most common cause of retinal detachment (RD) repair failure. The impact of primary (preoperative) PVR on the occurrence of multiple surgical failures has not been studied in detail. We aimed to characterize the association between primary PVR and multiple failures of RD repair using a nationwide healthcare claims database.

Methods: We selected cases of initial RD repair from the IBM® MarketScan® Commercial Claims and Encounters Database (2010-2017). Cases were categorized by the absence (P0 group) or presence (P1 group) of primary PVR. We defined surgical failure as the occurrence of a subsequent RD repair procedure with concurrent PVR. The frequency of surgical failures and the inter-surgical intervals (ISI) were compared between the groups. Kaplan-Meier analysis was used to estimate the probability of surgical failures in each group over time. Hazard ratios (HR) were adjusted for age, sex, and procedure.

Results: A total of 27,137 cases of initial RD repair were included, with 24,500 (90.3%) in P0 and 2,637 (9.7%) in P1. The median age of patients was 56 years. The frequency (%) of one, two, three, or four surgical failures in P0 vs. P1 was 1.88 vs. 10.24 ($p<0.001$), 0.26 vs. 2.50 ($p<0.001$), 0.07 vs. 0.64 ($p<0.001$), and 0.03 vs. 0.08 ($p=0.272$), respectively. The median ISI between the initial repair and the first failure was 70 days in P0 and 59 days in P1 ($p=0.021$). The cumulative probability of the first failure at 60 months was 2.8% in P0 and 16.3% in P1 ($p<0.001$). Subsequently, the cumulative probability of a second failure at 60 months was 19.2% in P0 and 29.6% in P1 ($p=0.002$). The risk of the first failure was higher in P1 than in P0 (HR: 6.02, 95% confidence interval (CI): 5.24-6.92, $p<0.001$). The risk of the second failure was also higher in P1 than in P0 (HR: 1.67, CI: 1.23-2.28, $p=0.001$). There was no difference in the risk of the third failure between the groups (HR: 0.76, CI: 0.41-1.40, $p=0.372$).

Conclusions: RD cases with primary PVR were >6 times more likely to undergo repeat surgery than those without. Primary PVR may increase the risk of requiring multiple RD repair surgeries. Healthcare claims analysis may be a useful tool to study population-based estimates of the incidence and recurrence pattern of RD repair failure.

CONTROL ID: 3527518

SUBMITTER (NAME ONLY): Ahmed Zanabli

TITLE: Evaluation of machine learning algorithms for prediction of trabeculectomy outcomes

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To utilize pre-operative patient features obtained from electronic medical records to assess the accuracy of machine learning (ML) algorithms to predict trabeculectomy outcomes.

Methods: Demographic, ocular and systemic health data resulting in 40 features from 220 consecutive trabeculectomy operations on 175 patients were input into four machine learning algorithms. The primary outcome classification was surgical failure at 1 year, defined as IOP > 21 or <5 at two consecutive visits after 3 months, less than a 20% IOP reduction, or a need for reoperation for glaucoma. Eyes that had not failed by the above criteria and were not receiving supplemental medical therapy to lower IOP were considered a complete success and the remaining eyes considered failures. Up-sampling was carried out to equalize the frequency of the underrepresented class. Random forest (RF), artificial neural network (ANN), logistic regression (LR) and support vector machine (SVM) algorithms were evaluated using accuracy, sensitivity, specificity and area under the curve (AUC) metrics with 10-fold nested cross-validation. The model with the best performance was further optimized using recursive feature elimination and hyper-parameter tuning. The data set was divided using 60% training/validation and 40% testing for evaluation of the final optimized model. The features most influencing the accuracy of each algorithm were identified using mean decrease in accuracy (MDA).

Results: 123 (55.90%) of the operations were classified as surgical failures and 97 (44.10%) as complete successes. The accuracy and AUC were highest in the RF algorithm, followed by SVM, LR and ANN as seen in Table 1. The accuracy and AUC of the final optimized RF model were 0.65 and 0.70, respectively. The most influential features on the accuracy of the final RF model are shown in Fig 1.

Conclusions: To our knowledge, this is the first study to leverage the use of machine learning algorithms to predict trabeculectomy outcomes. The four ML algorithms performed similarly, with the RF algorithm providing moderately higher accuracy and AUC. Future work will focus on combining trabeculectomy outcomes from other institutions to increase sample size and provide more generalized predictive algorithms.

CONTROL ID: 3527522

SUBMITTER (NAME ONLY): Julia Stingl

TITLE: Refractive change over 5 years and associated factors in the Gutenberg Health Study

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.V. Stingl, S. Ban, N. Pfeiffer, A.K. Schuster, Department of Ophthalmology, Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|M. Nagler, P.S. Wild, Preventive Cardiology and preventive Medicine/Center for Cardiology, Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|I. Schmidtman, Division of Pediatric Epidemiology, Institute for Medical Biostatistics, Epidemiology and Informatics, Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|P.S. Wild, Center for Thrombosis and Hemostasis (CTH), Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|K.J. Lackner, Institute of Clinical Chemistry and Laboratory Medicine, Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|T. Münzel, Center for Cardiology – Cardiology I, Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|M.E. Beutel, Department of Psychosomatic Medicine and Psychotherapy, Johannes Gutenberg Universität Mainz, Mainz, Rheinland-Pfalz, GERMANY|

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ABSTRACT BODY:

Purpose: There is only little knowledge existing about the refractive change over the course of a lifetime, particularly in adulthood. Therefore, the aim of this study was to examine the 5-year change in refractive error in phakic eyes and its risk factors in the retrospective population-based Gutenberg Health Study, representing a German general population.

Methods: The Gutenberg Health Study is a German population-based cohort study including 15,010 participants aged 35-74 years at baseline examination (2007-2012). After 5 years, a follow-up examination was carried out (82% participation). At both examinations, objective refraction was measured. Phakic eyes at follow-up examination were included in this analysis. 5-year change of spherical equivalent was computed and age- and sex-stratified analysed. Linear regression analysis was conducted analysing potential risk factors, namely sex, age spherical equivalent, intraocular pressure, cardiovascular parameters (HbA1c, HDL-cholesterol, LDL-cholesterol, triglycerides, body-mass index, physical activity, smoking) as well as level of education and occupation.

Results: 10,156 subjects were included. An age-related shift of refractive error was identified, namely -0.07 D for age 35-44 years, 0.20 D for 45-54, 0.19 D for 55-64, and -0.03 D for age 65-74 years. Smokers had a hyperopic shift ($B=0.03$; $p=0.02$), while higher intraocular pressure ($B=-0.006$ per mmHg; $p<0.001$) and female sex ($B=-0.04$; $p<0.001$) were linked with a myopic shift. Education, occupation and other cardiovascular parameters were not associated with change in refractive error.

Conclusions: The Gutenberg Health Study demonstrates a U-like shift in refractive error with a myopic change at younger and older age and a hyperopic shift at age 43 to 70 years. Smoking is associated with a hyperopic shift whereas a higher IOP is associated with a myopic shift. Educational level and occupation were not linked to a change in refractive error at age 35 to 74 years.

CONTROL ID: 3527534

SUBMITTER (NAME ONLY): Tsai-Chu Yeh

TITLE: HDF-Net: A Novel Convolutional Neural Network Approach of Image and Non-image Data Integration for Treatment Outcome Prediction in Neovascular Age-Related Macular Degeneration

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Yeh, Y. Chou, Ophthalmology, Taipei Veterans General Hospital, Taipei, TAIWAN|T. Yeh, Y. Chou, National Yang-Ming University, Taipei, TAIWAN|A. Luo, Y. Deng, Y. Lee, P. Chang, C. Lin, M. Tai, Industrial Technology Research Institute, Hsinchu, TAIWAN|M. Tai, National Tsing Hua University, Hsinchu, TAIWAN|

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ABSTRACT BODY:

Purpose: While prognosis and risk of progression is crucial in developing precise therapeutic strategy in treatment-naive neovascular age-related macular degeneration (nAMD) patients, limited predictive tools are available. We proposed a novel deep convolutional neural network (CNN) that enables feature extraction through image and non-image data integration to seize imperative information and achieve highly accurate outcome prediction.

Methods: A total of 698 evaluable nAMD patients who received intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) were analyzed. The Heterogeneous Data Fusion Net (HDF-Net) was designed to predict VA outcome in 12th months after anti-VEGF treatment. A set of baseline optical coherence tomography (OCT) image and non-image demographic features were employed as input data and the 12th-month VA as target data to train, validate, and test the HDF-Net. Accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) were evaluated.

Results: Of all evaluable patients, 163 patients had at least 2-line VA improvement, and 535 failed to achieve VA improvement (≥ 2 line). This newly designed HDF-Net was trained to perform 12-month VA forecast and demonstrated an AUC of 0.989 (95% CI, 0.970-0.999), accuracy of 0.936 (95% confidence interval [CI], 0.889-0.964), sensitivity of 0.933 (95% CI, 0.841-0.974), and specificity of 0.938 (95% CI, 0.877-0.969). The HDF-Net demonstrated superior performance to the classic AlexNet (AUC of 0.936 (95% CI, 0.894-0.978), accuracy of 0.895 (95% CI, 0.841-0.933), sensitivity of 0.824 (95% CI, 0.716-0.896), and specificity of 0.942 (95% CI, 0.880-0.973)). In the attention heatmap, focused locations that contributed most to decision making by HDF-Net showed validity and corresponded well to clinically relevant features within OCT images.

Conclusions: By simulating the real-world clinical decision process with mixed baseline information from OCT images and non-image data, HDF-Net demonstrated promising performance in predicting individualized treatment outcome. The results highlight the potential of deep learning to simultaneously process a broad range of clinical data to weigh and leverage the complete information of the patient. This novel approach is an important step toward personalized therapeutic strategy for nAMD.

CONTROL ID: 3527536

SUBMITTER (NAME ONLY): Cecilia Lee

TITLE: Diabetic retinopathy and dementia link is more than microvascular disease and poor glycemic control mechanisms

SESSION TITLE: DR: Epidemiology and service provision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the relationship between eye diseases-diabetic retinopathy (DR), age-related macular degeneration (AMD), and glaucoma-and the development of Alzheimer's disease and related dementia (ADRD) and the extent to which these might be explained by poor glycemic control and retinal microvascular disease burden.

Methods: The Adult Changes in Thought (ACT) is a 25-year-old ongoing longitudinal study of dementia-free adults aged >65 followed for the development of ADRD. Among participants with diabetes, we used information from the electronic health record and ACT study visits to ascertain time-varying exposures of DR, AMD, and/or glaucoma at study entry or during follow-up and how established these conditions were (onset <5 vs ≥5 yrs ago). Using estimated glomerular filtration (eGFR) as a marker for retinal microvascular disease burden, we also computed time-varying estimates of mean level, trajectory, and variability of eGFR, as well as mean blood glucose (BG), using fasting/random glucose and HbA1C. We fit Cox models to estimate the relationship between each eye disease and risk of ADRD after adjusting for eGFR, BG, sex, education, >1APOE ε4, race, and smoking. The potential modifying effect of BG and eGFR were assessed by changes in the magnitude of each association from adjusted models.

Results: Over 3342.4 person-years of follow-up among 526 ACT participants with diabetes, 131(25%) developed dementia including 98 (19%) who developed AD. A total of 85,439 eGFR and 72,960 GB measures were available for analysis. DR was associated with the development of both AD and dementia (the association was similar in magnitude to APOE ε4). (Figure) The hazard ratios (HR) for established DR vs. no DR and established AMD vs. no AMD changed very little after adjustment for eGFR and BG (from 1.65 [p=0.04] to 1.67 [p=0.03] for DR), (from 1.66 [p=0.07] to 1.74 [p=0.045]). There was no association between glaucoma and either outcome.

Conclusions: An association between diabetic retinopathy and the development of Alzheimer's and dementia in people with diabetes did not appear to be explained by markers of glycemic control and microvascular disease.

CONTROL ID: 3527537

SUBMITTER (NAME ONLY): Nicholas Tan

TITLE: Combination of split fixation and hypertensive phase is associated with vision loss in Latino and Black patients following Ahmed Glaucoma Valve surgery

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Tan, S.X. Chen, SUNY Downstate Health Sciences University College of Medicine, New York, New York, UNITED STATES|N.M. Radcliffe, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|N.M. Radcliffe, The New York Eye Surgery Center, The Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Few studies have explored reasons for vision loss after Ahmed Glaucoma Valve (AGV) insertion, especially among minorities. We hypothesized that in a Latino and Black population, eyes with both preoperative split fixation and a postoperative hypertensive phase (SFHP) were more likely to lose visual acuity (VA) 1 year after AGV surgery.

Methods: We reviewed charts of eyes followed for 12 months from Latino or Black patients who received standalone or combined AGV surgery (with phacoemulsification and/or cyclodestructive lasers). We excluded eyes with previous tube shunts and eyes missing visual field data or Snellen VA. A single surgeon conducted all procedures in the Bronx, NY from 2014-2019. Split fixation (SF) described <10 dB sensitivity in any of the four paracentral quadrants of the Humphrey 24-2 visual field. Hypertensive phase (HP) was defined as an IOP reading > 21 mmHg within the first 3 postop months after reduction of IOP to less than 22 in the first week, without tube malfunction. We used logistic regression to test the effect of SFHP on VA loss of two lines or more by 12 months. We considered 8 covariates: SF alone, HP alone, preop IOP, age, sex, race, diabetes, and systemic hypertension. Sterling IRB deemed this study to be exempt.

Results: Of 241 eyes from 186 patients, VA loss of 2+ lines occurred in 52 (21.6%). Univariate regression revealed that SFHP eyes were 5.96 times more likely (95% CI=3.06-11.79; $p<0.0001$) to experience this outcome. Of the 8 covariates, only preop IOP and HP alone modified the odds ratio by $>10\%$ when added. HP increased the OR by 53.3%, while preop IOP decreased the OR by 10.6%. In the model including SFHP, SF alone, HP alone, and preop IOP, SFHP eyes were 7.99 times more likely to have lost 2+ lines by 1 year (95% CI=2.92-25.95; $p=0.0001$).

Conclusions: SFHP moderately to greatly increased the odds of vision loss after AGV surgery in Latino and Black patients. HP alone and preop IOP were true confounders. In theory, SF may signify a severe glaucoma with fragile retinal nerve fibers, enabling a postoperative IOP spike to extinguish central vision. The confounding effect suggests that a hypertensive phase may even harm eyes without SF. Our findings indicate that prospective studies on controlling HP in severe glaucoma to protect vision may be warranted.

CONTROL ID: 3527539

SUBMITTER (NAME ONLY): James Wu

TITLE:

Introduction of a new silicone hydrogel contact lens with surface modification of MPC polymer

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wu, C. Shi, V. Sharma, D. Cantu-Crouch, R&D, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): James Wu: Commercial Relationship(s);Alcon:Code E (Employment) | Charlie Shi: Commercial Relationship(s);Alcon:Code E (Employment) | Vinay Sharma: Commercial Relationship(s);Alcon:Code E (Employment) | David Cantu-Crouch: Commercial Relationship(s);Alcon:Code E (Employment)

ABSTRACT BODY:

Purpose: A new silicone hydrogel (SiHy) material with surface modification of a cross-linkable bioinspired 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer was developed for outstanding ocular performance. The purpose of this study was to characterize the lens in fully hydrated conditions for its unique surface structure and properties, which are expected to contribute to the enhanced on-eye comfort and tear film stability of this novel contact lens.

Methods:

The surface structure of MPC polymer gel layer was imaged using a combination of environmental scanning electron microscopy (ESEM) and atomic force microscopy (AFM). The surface softness and lubricity of this new SiHy vs. comfilcon A, senofilcon A, and senofilcon C contact lenses were characterized via AFM nanoindentation and tribometer, respectively. All analyses were conducted in either 100% relative humidity or aqueous solutions to maintain lenses at hydrated state, mimicking on-eye conditions.

Results: A distinctive layer of hydrated MPC polymer was clearly visible on the top of the base material of the new SiHy lens under ESEM. MPC surface gel was further confirmed by both AFM phase image and ESEM image of the new SiHy lens cross-section. AFM nanoindentation testing showed the new SiHy lens surface was approximately 5 times softer than the surface of comfilcon A, senofilcon A, and senofilcon C lenses (~400nm vs. ~80nm of indentation depth under the eyelid contact pressure). The coefficient of friction of the new SiHy lens was also at least 5 times lower than that of comfilcon A, senofilcon A, and senofilcon C lenses.

Conclusions: A novel biomimetic MPC surface-modified SiHy contact lens was characterized for its surface structure and surface properties. The results indicate that the new SiHy lens has the exceptional characteristics of super-hydrophilicity, ultra-softness, and superior lubricity, which may enhance tear film stability and provide mechanical properties similar to ocular tissue, and is expected to achieve outstanding on-eye performance.

CONTROL ID: 3527547

SUBMITTER (NAME ONLY): Palak Patel

TITLE:

Analysis of PVD and Development of Complications using a Large Database of Retina Specialists

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Patel, O. Dajani, J. Minkowski, M.W. MacCumber, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|J. Minkowski, Eye Consultants of Atlanta, Atlanta, Georgia, UNITED STATES|N. Boucher, Vestrum Health, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Significant variability exists in the monitoring of acute posterior vitreous detachments (PVD) across ophthalmologists. This retrospective analysis hypothesizes that certain factors are associated with greater incidence of complications. It also examined the rate of delayed complications up to 6 months after initial presentation.

Methods: A case-control study of 9,635 eyes with symptoms for no more than 4 weeks prior to diagnosis were followed. Those eyes with a history of diabetic retinopathy, vitrectomy, retinal detachment, or panretinal photocoagulation were excluded. Cases were reviewed from the Vestrum database and included data from 65 retina practices and 316 individual physicians. Average age was 63 years old. Outcome measures included rate of development of vitreous hemorrhage, retinal detachment, or retinal tear at initial presentation, 3 months, and 6 months following initial presentation. Statistical analysis was done using a two-tailed t-test.

Results: Of 9,635 eyes, 12.2% (1,172 eyes) had retinal tears and 3.1% (299 eyes) had detachments at initial presentation. By 6 month follow-up, 3.1% (295 eyes) developed retinal tears and 1.1% (104 eyes) developed detachments. Among those with a tear, 61% occurred within one month after presentation, 28.5% within 1-3 months, and 10.5% within 3-6 months. Among those with a detachment, 48% occurred in the first month, 35.6% within 1-3 months, and 16.3% within 3-6 months. Men were more likely to have a detachment at presentation (57% vs. 43%, $p=0.025$) and within 6 months of presentation (67% vs 33%, $p<0.0006$). Phakic eyes compared to pseudophakic eyes were more likely to develop retinal breaks at presentation (44% vs. 16%, $p<0.00001$) and within 6 months of presentation (39% vs. 18%, $p<0.00001$). They were also more likely to have a detachment at initial presentation (37% vs. 25%, $p=0.011$). Peripheral retinal degeneration also correlated with increased retinal detachments at initial presentation (62% vs. 38%, $p<0.00006$).

Conclusions: Male sex, phakic eyes, and peripheral retinal degeneration were associated with increased incidence of complications after acute PVD, specifically retinal detachments. Several complications were also noted up to 6 months following initial presentation warranting appropriate counseling and consideration for repeat examination even up to 6 months after initial presentation.

CONTROL ID: 3527572

SUBMITTER (NAME ONLY): Joana Andoh

TITLE: Assessment of Vision Impairment among Individuals with History of Criminal Justice Involvement

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Andoh, T.A. Mir, C. Teng, K.H. Nwanyanwu, Ophthalmology and Vision Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|E.A. Wang, Section of General Internal Medicine, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|E.A. Wang, SEICHE Center of Health and Justice, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the US, incarcerated persons are three times more likely to report vision impairment (VI) compared to the general population. However, there is a paucity of studies that examine VI and criminal justice involvement (CJI). The purpose of this study was to investigate the prevalence and predictors of VI among National Survey on Drug Use and Health (NSDUH) respondents with a CJI history.

Methods: This study was a retrospective cross-sectional analysis. Using 2015-2018 NSDUH data, we compared sociodemographic and health characteristics, stratified by CJI history. We labeled respondents as having a CJI history if they had ever been arrested or had a history of parole or probation in the past year. We used logistic regression to investigate the association between VI and CJI history. Among those with a CJI history, we identified variables associated with VI.

Results: The total study sample consisted of 226,632 respondents, representative of 270,745,251 people in the US. A weighted total of 2,431,106 (0.91%) people reported VI and CJI. VI was more prevalent in the CJI group (2,451,071 [5.8%]) compared to those with no CJI (9,532,920 [4.2%], $p < 0.001$). The VI and CJI cohort was 62.9% male, with racial distributions 57.8% white, 19.6% Black, 15.5% Hispanic, and 1.1% Asian (Table 1). Those with VI and CJI were more likely to be ages 50-64, have lower education, have less employment, earn $\leq \$20,000$, and have Medicaid. High blood pressure was the most common chronic condition. Physical impairment was the most common co-disability. Nearly half of the VI and CJI cohort reported to have a fair/poor health status. In multivariable analysis, controlling for sociodemographic and health factors, CJI history was associated with a 20% increased risk of VI (OR 1.2, CI 1.1-1.2, $p < 0.01$). Among those with CJI, significant predictors of VI were female gender, lower income, not having private insurance, recent arrest, diabetes, heart condition, hearing, cognitive, and physical impairment (all $p < 0.05$).

Conclusions: There is a higher prevalence of VI among individuals with CJI compared to those with no CJI. Predictors of VI among those with a CJI history include female gender, lower income, insurance type, recent arrest, select chronic conditions and disabilities. Further research exploring the etiologies of VI among formerly incarcerated persons would help to elucidate these findings and guide allocation of resources.

CONTROL ID: 3527585

SUBMITTER (NAME ONLY): Yi Zhou

TITLE: Association between depression and severity of dry eye symptoms and signs among patients in the Dry Eye Assessment and Management (DREAM) Study

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhou, G. Ying, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|M.G. Maguire, Y. Yu, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|J. Murrough, Icahn School of Medicine at Mount Sinai Department of Psychiatry, New York, New York, UNITED STATES|N. Roy, P.A. Asbell, Department of Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|R.R. Sayegh, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Depression is a common and serious medical condition more prevalent in dry eye disease (DED) patients than the general population. To further elucidate the relationship between depression and DED, we performed a secondary longitudinal analysis to assess the association of the severity of DED symptoms and signs with depression in participants of the multi-center Dry Eye Assessment and Management (DREAM) Study.

Methods: Ocular Surface Disease Index (OSDI) and the Brief Ocular Discomfort Index (BODI) were administered at baseline, 6 and 12 months. Clinical signs of DED were evaluated in each eye by corneal fluorescein staining, tear break-up time, Schirmer's test, conjunctival lissamine green staining, meibomian gland abnormality, and tear osmolality. Patients scoring ≤ 42 on the Mental Component Summary (MCS) of the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) were considered positive for depression based on the SF-36 user manual guidelines. We compared the score of DED symptoms, signs, and composite severity score of signs between patients with and without depression using generalized linear models adjusted for age, gender, race, time, and longitudinal observations per person. Effect sizes ($[\text{mean difference}]/[\text{SD}]$) were calculated to assess the magnitude of their associations.

Results: Among 535 patients with moderate to severe DED, 15.7% had depression at baseline, 17.3% at 6 months and 13.2% at 12 months. When baseline, 6 and 12 months data were combined, patients with depression had worse DED symptoms ($P < 0.001$), ocular discomfort ($P < 0.001$), composite severity score of DED signs ($P = 0.006$), and corneal staining scores ($P = 0.02$) compared to patients without depression (Table 1). The effect size for the OSDI (0.45) and BODI (0.46) were larger than for the composite severity score of signs (0.21) (Table 1). Lower MCS scores (i.e., higher likelihood of depression) were significantly correlated with higher OSDI score (i.e., worse DED symptoms) at baseline (Spearman $\rho = -0.09$, $P = 0.03$), 6 months ($\rho = -0.20$, $P < 0.001$) and 12 months ($\rho = -0.21$, $P < 0.001$).

Conclusions: DED symptoms and signs were worse in moderate to severe DED patients screening positive for depression. However, depression was more strongly associated with severity of the symptoms than clinical signs of DED, which may relate to the discordance between symptoms and signs of DED.

CONTROL ID: 3527587

SUBMITTER (NAME ONLY): Sammie Fung

TITLE: Impact of neurotrophic keratopathy on quality of life: A utility study

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Fung, K.S. Park, University of California San Diego School of Medicine, La Jolla, California, UNITED STATES|E. Groessl, University of California, San Diego Herbert Wertheim School of Public Health, California, UNITED STATES|E. Groessl, UC San Diego Health Services Research Center, California, UNITED STATES|B.M. Fung, The University of Arizona College of Medicine Phoenix, Phoenix, Arizona, UNITED STATES|D.O. Kikkawa, B.S. Korn, Division of Oculofacial Plastic and Reconstructive Surgery, Department of Ophthalmology, University of California San Diego Health System, La Jolla, California, UNITED STATES|D.O. Kikkawa, B.S. Korn, Division of Plastic Surgery, Department of Surgery, University of California San Diego Health System, La Jolla, California, UNITED STATES|D.J. Ozzello, N.A. Afshari, C.Y. Liu, Viterbi Family Department of Ophthalmology, University of California San Diego Health System, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neurotrophic keratopathy (NK) is a rare disease leading to impaired corneal sensation and function. This cross-sectional study measured the utility values of NK in an effort to better understand the impact of this disease on patients.

Methods: Patients with a clinical diagnosis of NK were recruited from an urban ophthalmology clinic. Utility was assessed with the time trade off (TTO) and standard reference gamble (SRG) methods; the anchor points were defined as 0 being death and 1 being perfect health (ph) or perfect eye function (pf). Visual acuity, comorbidities, and responses to the 25-question Vision Function Questionnaire (VFQ-25) were also collected.

Mean, standard deviation, and 95% confidence interval were calculated for each measure of utility and compared to an anchor of 1.0 using a one sample t-test. Simple linear regressions were used to predict the relationship between utility values of NK and variables investigated in this study.

Results: A total of 24 patients (mean age 66.5 ± 14.8 years; 12 males, 12 females) were recruited for this study. The utility values for NK ranged from 0.69 to 0.86 depending on the TTO/SRG method and pf/ph anchor points (Table 1). Patients were willing to trade approximately 3 years of an additional 10-year life expectancy in return for perfect eye function or health. Subcategories of VFQ related to activity limitation (role difficulty and dependence) were found to be significantly associated with NK utility (Table 2). Utility values for NK were not significantly associated with age, gender, comorbidities, visual acuity, or severity of NK disease.

Conclusions: Our study found that NK has a significant impact on quality of life measured as health utility. The TTO utility values for patients with NK are similar to those with a hand amputation (0.70). Utility values for NK appear to be directly related to the functional loss from the disease rather than the degree of vision loss. Participants who felt limited in what they could accomplish, required more help, or felt a loss of control due to their ocular condition reported lower utility. As treatment options for NK are expanding and increasing in efficacy, this study can provide a foundation for future cost-effectiveness analyses on the various treatments for NK.

CONTROL ID: 3527597

SUBMITTER (NAME ONLY): Ewa Niechwiej-Szwedo

TITLE: Maturation of hand-eye coordination in typically developing children and adolescents

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Niechwiej-Szwedo, S. Wu, Kinesiology, University of Waterloo, Waterloo, Ontario, CANADA|L. Christian, Optometry and Vision Science, University of Waterloo Faculty of Science, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Spatial and temporal coordination between eye and hand movements is essential for the performance of most daily activities. Studies with adults demonstrate a highly stereotypical coordination pattern during reaching and grasping tasks. Specifically, eye movements precede the hand by ~100 ms, and the eyes fixate on the object during a manipulation task. To date, the developmental profile of hand-eye coordination has not been examined in children. The purpose of this study was to characterize age-related changes in temporal hand-eye coordination in typically developing children.

Methods: Children (n=28, age=9.0±0.6yrs) and adolescents (n=29; age=12.3±1.3yrs) were assessed during the performance of a bead threading task, which requires precision grasping and placement. A group of adults (n=12, age=22±2.2yrs) were also tested. Eye and hand movements were recorded concurrently using the Eyelink 2 eye tracker and the Optotrak motion capture system. Temporal hand-eye coordination was assessed by calculating the latency of the motor responses for the primary movement of the eyes and hand towards the bead, and the secondary movements towards the needle, as well as the duration of eye fixation when grasping and placing the bead on the needle.

Results: Statistical analysis revealed significant differences between the groups of children, adolescents, and adults for all measures (p<0.05). When reaching for the bead, the eye-hand latency difference was longer in children (174±16ms) compared to adolescents (134±10ms) and adults (117±8ms). Similarly, the fixation duration during grasping was longer in children (243±21ms) compared to adolescents (146±16ms) and adults (165±17ms). There was also a longer delay between the eye and hand movements when reaching towards the needle in children (38±11ms) compared to adolescents (7±11ms) and adults (12±15ms). Fixation duration on the needle while placing the bead was longer in children (657±31ms) and adolescents (497±24ms) compared to adults (336±28ms).

Conclusions: Temporal hand-eye coordination pattern for a precision grasping and placement task becomes more efficient during adolescence in typically developing children with normal vision. Further investigation is required to determine the impact of decorrelated binocular vision on the development of hand-eye coordination profile.

CONTROL ID: 3527605

SUBMITTER (NAME ONLY): Brian Ballios

TITLE: Lineage specification and molecular characterization of cone photoreceptor progenitors in the developing mammalian retina

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.G. Ballios, V. Wallace, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|J. Belair-Hickey, S. Khalili, K. Grise, B.B. Coles, J. Liu, G. Bader, D. van der Kooy, Department of Molecular Genetics, University of Toronto, Toronto, Ontario, CANADA|G. Bernier, Centre de recherche, Hopital Maisonneuve-Rosemont, Montreal, Quebec, CANADA|M.S. Shoichet, Department of Chemical Engineering and Applied Chemistry, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Adult retinal stem cells (RSCs) give rise to all retinal cell types. Clonal RSC progeny treated with taurine/retinoic acid (T+RA) produce 95% rod progeny, while coco (BMP/Wnt/TGF β triple-inhibitor) induces 60% cones. We hypothesized that cone lineage-specific progenitors, specified using exogenous factors, display unique transcriptome signatures that can identify stage-specific molecular markers. No markers exist for these lineage-specific progenitors and literature is divided on their existence in vivo.

Methods: Adult RSCs were isolated from mouse and human donor eyes, while neural retinal progenitor cells (RPCs) were isolated from the embryonic mouse retina. We used single cell/well sorting to isolate individual progenitor clones.

Results: Embryonic RPCs (E14) show similar rod differentiation in T+RA (>95%) compared to adult RSCs and increased cone differentiation in coco (>90%). Coco permitted differentiation from single non-pigmented RSC progeny to >95% cone-only clones, while single pigmented RSC progeny were unable to produce any cones. Constant coco exposure causes E12, E14 and E19 RPCs to adopt a cone-restricted fate. We compared gene expression between RSC-derived and endogenous cones with RNAseq, and profiled the transcriptome throughout rod and cone differentiation from embryonic RPCs. Principal component analysis showed a distinct progression of rod and cone lineages. Pathway analysis showed clustering of stem cell-derived and endogenous cones, as well as candidate progenitor markers. SOX15 may be a unique marker of a cone restricted progenitor; its expression follows other factors that bias photoreceptor differentiation, including OTX2 and OLIG2. SOX15 is expressed in early proliferating RPCs in vivo, and persists in some early-born post-mitotic cells, but not photoreceptors. SOX15 knockdown reduced colony formation from E14 RPCs, but not E19 RPCs or adult RSCs. After 4-6 weeks of coco, 60% of human RSC progeny differentiated into cones; both the time-course and efficiency is similar to mouse RSC progeny.

Conclusions: Exogenous signals instruct early lineage decisions in fate-restricted retinal progenitors, and we identify potentially new markers. SOX15 may promote cone differentiation by prolonging or promoting proliferation of early RPCs, or by inhibiting factors that specify alternative, late-born, cell fates and promoting a default cone differentiation.

CONTROL ID: 3527606

SUBMITTER (NAME ONLY): Alexander Schuster

TITLE: Intraocular pressure and its relation to ocular geometry: results from the Gutenberg Health Study

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Schuster, F. Aghayeva, F.M. Wagner, A. Fieß, N. Pfeiffer, E.M. Hoffmann, Department of Ophthalmology, University Medical Center Mainz, GERMANY|M. Nagler, P.S. Wild, Preventive Cardiology and Preventive Medicine, Center for Cardiology, University Medical Center Mainz, GERMANY|T. Münzel, Center for Cardiology, University Medical Center Mainz, GERMANY|M.E. Beutel, Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Mainz, GERMANY|I. Schmidtman, Institute of Medical Biostatistics, Epidemiology and Informatics, University Medical Center Mainz, GERMANY|K.J. Lackner, Institute of Clinical Chemistry and Laboratory Medicine, University Medical Center Mainz, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the associations between intraocular pressure (IOP) and ocular geometry.

Methods: The Gutenberg Health Study is a population-based cohort study in Mainz, Germany including 15,010 subjects at age 35 to 74 years at baseline examination. Study participants underwent a comprehensive ophthalmologic examination including non-contact tonometry (NT 2000™, Nidek Co., Japan), objective refraction, optical biometry (LenStar, Haag-Streit, Bern, Switzerland) and Scheimpflug imaging (Pentacam, Oculus, Wetzlar, Germany) of the anterior segment at the first 5-year follow-up examination (in the year 2012-2017). Anterior chamber angle width was analyzed on Scheimpflug images using proprietary software. Multivariable linear regression analyses with generalized estimating equations were carried out to determine associations of IOP and geometric parameter, namely central corneal thickness (CCT), corneal curvature, anterior chamber depth, lens thickness and posterior segment length with adjustment for age and sex. In an additional model, anterior chamber angle width was also included.

Results: 13,280 phakic eyes of 6,640 participants (mean age 57.3 ± 10.2 years, 49.1% female) were included in this cross-sectional analysis. No included eye showed angle closure on Scheimpflug imaging. Mean IOP was 14.84 ± 2.92 mmHg in right eyes and 14.91 ± 2.93 mmHg in left eyes. IOP increased with higher CCT ($B=0.042$ per μm ; 95%CI: 0.040-0.044), longer posterior segment length ($B=0.20$ per mm; 95%CI: 0.14-0.25), higher age ($B=0.20$ per 10 years; 95%CI: 0.13-0.26) (all $p<0.001$), thicker crystalline lens ($B=0.25$ per mm; 95%CI: 0.08-0.42; $p=0.003$) and female sex ($B=0.12$; 95%CI: 0.00-0.24; $p=0.05$), while anterior chamber depth and corneal curvature was not associated. IOP increased with a narrower anterior chamber angle in univariate analysis ($B=-0.02$ per degree; 95%CI: -0.03 - -0.01; $p<0.001$), but not in multivariable analysis ($p=0.34$).

Conclusions: IOP measurement is related to the individual ocular geometry. Thus, those ocular parameters should be taken into consideration when clinically interpreting non-contact tonometric data. In eyes with an open anterior chamber angle, there is no correlation between anterior chamber angle width and IOP level in our multivariable model.

CONTROL ID: 3527608

SUBMITTER (NAME ONLY): Daniel Wisotsky

TITLE: Post-injection Anti-inflammatory Drops

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Wisotsky, Yeshiva University, New York, New York, UNITED STATES|D. Strauss, Omni Eye Services, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Daniel Wisotsky: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Strauss: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

Patients receive intraocular anti-VEG-F injections for multiple retinal vascular diseases. While vision threatening side effects are rare, many patients will note some level of discomfort after an injection. A common practice for many retina specialists is to recommend that the patient call the office if he or she has significant discomfort. It is our experience that patients will with some frequency come in for their next injection stating that they had significant discomfort after the injection but did not call the office. The purpose of our study is to determine whether patients will use post-injection eye drops if made available to them for mild to moderate discomfort.

Methods:

Prior to the intraocular injection patients were given a handout with five options: 1. No discomfort - no drops necessary. 2. Mild discomfort - artificial tear drops as needed. 3. Mild to moderate discomfort - topical nonsteroidal eye drops (acular) every 4 hours as needed for one day. 4. Moderate discomfort - topical steroid eye drops (pred forte 1%) every 4 hours as needed for one day. 5. Severe discomfort - call office immediately. Patients were then anesthetized with topical anesthetic drops and tetracaine gel. Betadine was applied to the conjunctiva and lid twice. The anti-VEG-F injection was performed 2-5 minutes later via the pars plana. Topical antibiotic drops and IOP lowering drops were applied. The patient was discharged home. A follow-up phone call was made the next day.

Results:

125 consecutive anti-VEG-F injection patients were included in the study. 94 patients responded to the follow-up questionnaire the day after the injection. 31 patients used an eye drop on the day of the injection (33.0%). Of the patients that used eye drops, 6 (19.4%) used artificial tears, 9 (29%) used acular, and 16 (51.6%) used pred forte. All patients stopped the eye drop after the follow-up phone call.

Conclusions: The study confirms that a significant number of patients undergoing anti-VEG-F injections in an office setting will develop mild to moderate discomfort the day of the injection. We recommend counseling the patient about possible discomfort and making topical drops including lubricating drops, nonsteroidal, and steroid drops available on a short term basis following injections. This will increase patient satisfaction and lessen the number of post-injection phone calls regarding mild to moderate discomfort.

CONTROL ID: 3527624

SUBMITTER (NAME ONLY): Kamran Rahmatnejad

TITLE: The Effect of Small Incision Phacoemulsification on Intraocular Pressure in Patients with Primary Open Angle Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Rahmatnejad, F.J. Gross, P.B. Wu, Ophthalmology, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|R. Chaganty, Mathematics and Statistics, Old Dominion University, Norfolk, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kamran Rahmatnejad: Commercial Relationship: Code N (No Commercial Relationship) | Fredric Gross: Commercial Relationship: Code N (No Commercial Relationship) | Patrick Wu: Commercial Relationship: Code N (No Commercial Relationship) | Rao Chaganty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the effect of small incision phacoemulsification on intraocular pressure (IOP) of patients with primary open angle glaucoma (POAG)

Methods: We retrospectively reviewed the charts of 353 patients who had small incision phacoemulsification cataract surgery between 2017 and 2018 and identified patients who had a diagnosis of POAG for further analysis. All procedures were performed by the same surgeon using the same technique. Patients with complicated cataract surgery or a history of incisional glaucoma surgery were excluded from the analysis. The study population is composed of 30 eyes from 26 patients who had stable glaucoma treated with medication, laser, or a combination of both prior to cataract surgery.

We defined preoperative IOP as the average of up to 3 IOP measurements in the 18 months period prior to cataract surgery and postoperative IOP as the average of up to 3 postoperative IOP measurements 2 to 18 months after surgery. Age, race, sex, eye laterality, number of pre-operative and post-operative glaucoma medications, and history of glaucoma laser were recorded for all patients.

Results: The age mean +/- standard deviation (SD) was 71.53 +/- 9.13 years. The patients were mostly male (63.33%) with a small predominance of Caucasians compared to African Americans (56.67% vs. 43.33%). Right and left eyes were equally distributed (50%) and 70% of the patients had a history of glaucoma laser treatment. After confirming the normality assumption, paired t-test was performed for the difference between preoperative and postoperative data. The IOP (mean +/- SD) was decreased from 15.17 +/- 2.77 mmHg preoperatively to 14.00 +/- 2.40 mmHg postoperatively ($p < 0.001$). Twenty-one patients had an IOP reduction (range 1-5 mmHg), one patient's IOP remained unchanged, and 8 patients had an increase in IOP (range 1-2 mmHg). The number of IOP-lowering eye drops decreased from 0.73 to 0.67 which was not statistically significant.

Conclusions: In this study, uncomplicated small-incision phacoemulsification resulted in a small but statistically significant reduction in IOP on average in patients with POAG. Interestingly, some patients experienced small increases in IOP after surgery. Further studies are needed to evaluate clinical parameters that could explain this observation.

CONTROL ID: 3527635

SUBMITTER (NAME ONLY): Rishi Singh

TITLE: Impact of Duration of Exposure to Residual Intraretinal Fluid on Visual Function Outcomes in Neovascular Age-Related Macular Degeneration

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.P. Singh, Center for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|R.P. Singh, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Rishi Singh: Commercial Relationship(s);Genentech:Code C (Consultant);Regeneron:Code C (Consultant);Novartis:Code C (Consultant);Zeiss:Code C (Consultant);Bausch and Lomb:Code C (Consultant);Apellis:Code F (Financial Support);Graybug:Code F (Financial Support);Aerie:Code F (Financial Support)

ABSTRACT BODY:

Purpose: This analysis assessed the impact of duration of exposure to residual intraretinal fluid (IRF) on visual function outcomes in eyes with neovascular age-related macular degeneration (nAMD) treated with anti-VEGFs in the VIEW 1 and 2 trials.

Methods: This post hoc analysis included patients that received either ranibizumab 0.5 mg q4 weeks (Rq4) or intravitreal aflibercept injection 2 mg q4 weeks (IAI 2q4) or q8 weeks after 3 monthly doses (IAI 2q8) in VIEW 1 and 2. Duration of IRF from baseline through week 52 was evaluated as quartiles in both pooled treatment groups (Q1: ≤ 2 weeks, n=581; Q2: 3– ≤ 8 weeks, n=411; Q3: 9– ≤ 18 weeks, n=389; Q4: > 18 weeks, n=423) and within each treatment group (Rq4, n=588; IAI 2q4, n=612; IAI 2q8, n=604). Visual function outcomes assessed included best corrected visual acuity (BCVA) and Visual Function Questionnaire 25 (VFQ-25) near activities and driving subscale scores.

Results: In the pooled analysis of treatment groups, mean BCVA gains from baseline at week 52 for Q1–Q4 were 10.9, 10.1, 9.4, and 6.6 ($P < 0.0001$, Q4 vs Q1) letters, respectively. The corresponding proportions of patients with a ≥ 5 letters gain at week 52 were 71.4%, 72.0%, 72.6%, and 59.9% ($P < 0.05$, Q4 vs Q1), and for those with a ≥ 5 letters loss at week 52 were 10.0%, 9.7%, 11.2%, and 16.5% ($P < 0.05$, Q4 vs Q1), respectively. The mean change from baseline in the VFQ-25 near activities subscale score in Q1–Q4, respectively, were 9.7, 8.3, 7.2, and 5.3 ($P < 0.001$, Q4 vs Q1) points, and for the driving subscale score were 3.0, 1.6, 2.4, and -2.4 ($P < 0.01$, Q4 vs Q1) points. In the quartile analysis within each treatment group, the mean BCVA gains for Q1–Q4 were 11.0, 11.1, 9.3, and 5.8 ($P < 0.05$, Q4 vs Q1) letters for Rq4; 10.7, 9.7, 9.2, and 7.7 letters for IAI 2q4; and 11.3, 11.2, 8.6, and 6.3 ($P < 0.05$, Q4 vs Q1) letters for IAI 2q8, respectively.

Conclusions: In this analysis of patients treated with intravitreal aflibercept and ranibizumab in VIEW 1 and 2, longer duration of exposure to residual IRF was associated with lower visual acuity gain and worse vision-related quality of life outcomes.

CONTROL ID: 3527648

SUBMITTER (NAME ONLY): Andrea Bordewyk

TITLE: Cataract Surgery Refractive Outcomes in Long Eyes: A Comparison of 7 Formulas

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Bordewyk, I.U. Scott, S. Pantanelli, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|S. Athukorala, C. Seeger, Penn State College of Medicine, Pennsylvania, UNITED STATES|I.U. Scott, Public Health Sciences, Penn State College of Medicine, Pennsylvania, UNITED STATES|B. Ernst, Schein Ernst Mishra Eye, Harrisburg, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to compare the performance of 7 IOL power prediction formulas in axial myopes.

Methods: Retrospective consecutive case series of eyes with axial length (AL) greater than 25.0 mm that underwent cataract extraction with implantation of a monofocal IOL (Akreos AO60, Bausch & Lomb) between January 2016 and October 2018 by a single surgeon. Eyes were excluded if they had history of surgery or trauma, inflammatory conditions, intraoperative complication, cataract surgery combined with another procedure, or a postoperative best-corrected visual acuity worse than 20/40. Residual refractive error for each eye was predicted for the implanted IOL using 7 formulas (Holladay1 [H1], Linear Wang-Koch adjusted Holladay1 [I-WKH1], SRK/T, Barrett II Universal [BU-II], Hill-RBF v3.0, EVO, and Kane). The same nominal A-constant (118.4) was used in all formulas. Prediction error was calculated as the difference between the actual and predicted spherical equivalent (SE). Mean prediction errors (MPEs) and absolute errors (MAEs) were compared using a Friedman with Dunn post-test. Comparison of proportions was done using a Cochran Q test with McNemar's post-test.

Results: Among the 200 study eyes, the MPE was 0.36 ± 0.51 , 0.00 ± 0.53 , 0.22 ± 0.52 , 0.11 ± 0.46 , 0.23 ± 0.48 , 0.09 ± 0.47 , and 0.13 ± 0.47 D for H1, I-WKH1, SRK/T, BU-II, Hill-RBF, EVO, and Kane, respectively ($p < 0.0001$). The MAEs were 0.48 ± 0.40 , 0.39 ± 0.36 , 0.41 ± 0.38 , 0.35 ± 0.33 , 0.40 ± 0.35 , 0.35 ± 0.32 , and 0.36 ± 0.32 D, respectively ($p < 0.0001$). The proportion of eyes within 0.5 D of predicted SE was 60.5%, 71%, 68%, 76%, 70.5%, 76.5%, and 74%, respectively, with BU-II and EVO each performing better than H1, I-WKH1, SRK/T, and Hill-RBF ($p < 0.0001$). EVO ($p < 0.0001$), but not BU-II ($p = 0.49$) performed better than Kane with regards to this metric. There was no significant difference between BU-II and EVO regarding proportion of eyes within 0.25, 0.5, 0.75, or 1.0 D of predicted SE. Hyperopic prediction errors occurred in 82%, 49%, 71.5%, 61.5%, 73%, 61%, and 66.5% of eyes, respectively ($p < 0.0001$), with SRK/T being similar to Hill-RBF ($p = 1.0$) and BU-II being similar to EVO ($p = 1.0$).

Conclusions: The I-WKH1 improves outcomes over H1. Modern formulas (BU-II, EVO, Hill-RBF, and Kane) outperform older ones (H1 and SRK/T). An AL adjustment or modern formula should be used when performing IOL power calculations in axial myopes.

CONTROL ID: 3527649

SUBMITTER (NAME ONLY): Joana Mesquita

TITLE: Comparison of Vascular Endothelial Growth Factors (VEGFs) A and B with diabetic retinopathy severity and diabetic macular edema. Correlation between growth factors and anatomical parameters

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.P. Castro-de-Sousa, Ophthalmology, Centro Hospitalar de Leiria, Leiria, PORTUGAL | J. Mesquita, J.P. Castro-de-Sousa, C. Tomaz, Health Sciences Research Centre, University of Beira Interior (CICS-UBI), Covilhã, PORTUGAL | P. Tavares-Ratado, Faculty of Health Sciences, University of Beira Interior (UBI), Covilhã, PORTUGAL | C. Tomaz, Faculty of Sciences, University of Beira Interior (UBI), Covilhã, PORTUGAL

Commercial Relationships Disclosure (Abstract): Joana Mesquita: Commercial Relationship(s); Allergan: Code E (Employment) | João Castro-de-Sousa: Commercial Relationship: Code N (No Commercial Relationship) | Paulo Tavares-Ratado: Commercial Relationship: Code N (No Commercial Relationship) | Cândida Tomaz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) affects a sizeable group of the population, leading to blindness, which can be reduced with proper monitoring and treatment. As the disease progresses from non-proliferative diabetic retinopathy (NPDR) to PDR, diabetic macular edema (DME) may occur at any stage. It was proven the increase of vascular endothelium growth factors (VEGFs) levels with disease stage, from NPDR to PDR, while DME appears to be independent of VEGF levels. This fact may lead ophthalmologists to opt for different initial treatments depending if patients are in an inflammatory or angiogenic stage. This study aimed to compare VEGF-A and VEGF-B levels with disease severity and the presence of DME and correlate VEGF levels with central retinal thickness (CRT) and macular volume (MV).

Methods: Vitreous samples were collected from 41 DR patients undergoing vitrectomy. VEGF-A and B were quantified by ELISA. Optical coherence tomography (OCT) was evaluated for CRT and MV.

Results: Forty-one patients with DR, 61% (n=25) male, with a mean age of 67.9 ± 10.0 (mean \pm standard deviation). Mean vitreous VEGF-B levels were 18.13 ± 22.10 pg/mL for NPDR and 115.70 ± 278.42 pg/mL for PDR, with a statistically significant difference ($p=0.004$) showing higher values for PDR patients. VEGF-B was increased in DME (120.47 ± 288.97 pg/mL) in comparison with non-DME (24.38 ± 20.44 pg/mL), however, the difference was not statistically significant ($p=0.204$). Vitreous VEGF-A was significantly increased in PDR in comparison with NPDR, (576.88 ± 681.15 vs 39.11 ± 71.13 pg/mL, $p=0.019$, respectively). DME patients showed higher values of VEGF-A than non-DME, despite not statistically significant (456.10 ± 651.84 vs 83.21 ± 80.30 pg/mL, $p=0.371$, respectively). The correlation of NPDR with VEGF-B, CRT, and MV was not statistically significant, ($r_{sp}=0.636$, $p>0.05$), while was statistically significant in PDR ($r_{sp}=0.590$, $p=0.008$). The correlation of NPDR with VEGF-A, CRT, and MV was $r_{sp}=-0.975$, $p=0.005$ and with PDR was $r_{sp}=0.590$, $p=0.008$.

Conclusions: VEGF-A and B are increased in vitreous of DR patients and values increase with disease stage, while the absence of relation of VEGF-A and B with DME suggests VEGF levels may not be increased in all patients with DME. The strong correlations showed a simultaneous increase of VEGF levels with anatomical parameters.

CONTROL ID: 3527667

SUBMITTER (NAME ONLY): Yao Liu

TITLE: Low macular pigment levels are associated with manifest primary open-angle glaucoma in the Carotenoids in Age-Related Eye Disease Study

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Liu, Z. Liu, M. Nalbandyan, J.A. Mares, Dept of Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|T. Lawler, Dept of Nutritional Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|C. Thuruthumaly, Eye Institute, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|T.S. Vajaranant, Dept of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|R.B. Wallace, Dept of Epidemiology, The University of Iowa Hospitals and Clinics Department of Pathology, Iowa City, Iowa, UNITED STATES|S. Bailey, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|B. Hammond, Dept of Psychology, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Emerging evidence suggests that low macular pigment levels—modifiable through dietary intake of the carotenoids (lutein and zeaxanthin)—may be a novel risk factor for glaucoma. We evaluated whether macular pigment levels are associated with manifest primary open-angle glaucoma (POAG) within a longitudinal cohort of older women from the Carotenoids in Age-Related Eye Disease Study (CAREDS).

Methods: The CAREDS2 follow-up study (2016-2019) included 685 participants. Macular pigment optical density (MPOD) was measured at both CAREDS baseline (2001-2004) and CAREDS2 using customized heterochromatic flicker photometry at 0.5° from foveal center. Manifest POAG status at CAREDS2 was adjudicated by 2 glaucoma specialists (YL, CT) masked to MPOD in 1258 eyes (630 participants) based on abstracted medical records, intraocular pressure, visual fields, stereo disc photos, and peripapillary retinal nerve fiber layer optical coherence tomography. Associations between MPOD and manifest POAG were investigated utilizing age-adjusted logistic models in the: (1) full sample and (2) 'worst' eyes based on severity of visual field loss. We conducted additional sensitivity analyses among the subset of eyes with stable MPOD over 15 years (± 0.20 optical density units).

Results: Manifest POAG was present in 79 eyes (51 participants). Women in the lowest quartile of baseline MPOD (quartile 1) were significantly more likely to have manifest POAG than those in quartiles 2-4. In the full sample ($n=1258$ eyes), odds ratios (OR(95%CI)) for manifest POAG were 0.49(0.25-0.93), 0.63(0.32-1.26), and 0.53(0.24-1.20) for MPOD quartiles 2-4 vs. quartile 1, respectively ($p=0.04$). The association was stronger in the subsample of eyes with stable MPOD over 15 years ($n=242$ eyes, $p=0.001$). Analyses of the 'worst' eye ($n=630$ eyes) resulted in ORs of 0.51(0.23-1.15), 0.72(0.34-1.52), and 0.43(0.18-0.99) for quartiles 2-4 vs. quartile 1, respectively ($p=0.06$); with a stronger association in the subset of 'worst' eyes with stable MPOD ($n=242$, $p=0.003$).

Conclusions: This is the first study to identify an inverse association between MPOD and manifest POAG in a longitudinal cohort of older women. Further studies are warranted to confirm whether low macular pigment levels may be a novel modifiable glaucoma risk factor and support the development of low-cost, dietary interventions for glaucoma prevention.

CONTROL ID: 3527672

SUBMITTER (NAME ONLY): Carl Danzig

TITLE: Clinical trial versus real-world outcomes with anti-VEGF therapy for branch and central retinal vein occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Danzig, Rand Eye Institute, Deerfield Beach, Florida, UNITED STATES|S. Blotner, V. Steffen, Z. Haskova, Genentech Inc, South San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Carl Danzig: Commercial Relationship(s);Genentech, Inc.:Code C (Consultant);Novartis:Code C (Consultant);Regeneron:Code C (Consultant) | Steven Blotner: Commercial Relationship(s);Genentech, Inc.:Code E (Employment) | Verena Steffen: Commercial Relationship(s);Genentech, Inc.:Code E (Employment) | Zdenka Haskova: Commercial Relationship(s);Genentech, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Landmark trials of anti-VEGF treatment for macular edema due to branch (BRVO) and central retinal vein occlusion (CRVO) show that clinically significant vision gains are achievable with frequent initial injections, monthly monitoring, and timely re-treatment; however, this is burdensome and not feasible in clinical practice. This study assessed the impact of anti-VEGF injections and monitoring frequency on BCVA outcomes in patients with BRVO and CRVO.

Methods: This was a cross-trial comparison between controlled clinical trials, long-term extension (LTE) trials, and real-world studies of anti-VEGF therapy in patients with macular edema due to BRVO or CRVO. Published data were used to compare average 12-month injection frequencies and BCVA outcomes achieved with fixed, as-needed, treat-and-extend, and real-world anti-VEGF treatment regimens; and with monthly or less-frequent monitoring visits.

Results: Analyses included 7 controlled clinical trials (2 BRVO, 5 CRVO; all with monthly monitoring), 4 LTE trials (2 BRVO/CRVO, 2 CRVO; most with less-than-monthly monitoring), and 2 real-world studies (both BRVO/CRVO; monitored per investigator discretion). Patients with BRVO in clinical trials received 8.5–9.0 injections over 12 months versus 1.6–4.9 injections in LTE trials and real-world studies. In clinical trials, mean BCVA change over 12 months was 17.1–18.3 letters versus –0.7 to –2.1 letters in LTE trials with less-frequent visits. Mean BCVA change over 12 months in real-world BRVO studies was only 7.7–13.1 letters. Patients with CRVO in clinical trials received 7.8–11.8 injections over 12 months versus 1.5–5.1 injections in LTE trials and real-world studies. Patients with CRVO in clinical trials gained 10.7–21.9 letters over 12 months. However, these gains were not maintained in LTE trials (–7.6 to 0.2 letters), nor achieved in real-world studies (4.1–7.1 letters).

Conclusions: In real-world studies, patients with BRVO or CRVO were monitored less frequently, received fewer anti-VEGF injections, and did not achieve the BCVA gains seen in clinical trials. Likewise, patients who achieved vision gains in clinical trials on average experienced BCVA loss with fewer follow-up visits in LTE trials. These data highlight the need for new strategies that extend the durability of treatment to reduce treatment burden and need for frequent monitoring, and to improve real-world vision outcomes.

CONTROL ID: 3527686

SUBMITTER (NAME ONLY): Pimpiron Ploysangam

TITLE: Role of iExaminer as a Teaching and Diagnostic Tool for Medical Students

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Ploysangam, V. Varikuti, C. Zhang, A. Reynolds, Department of Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The iExaminer allows the user to utilize the view from the PanOptic and an instructor to coach the user on relevant findings. This study assesses the role of the iExaminer as a teaching and diagnostic tool for medical students compare to the PanOptic alone.

Methods: Prospective cross-over study of medical students performing direct ophthalmoscopy on patients after a didactic session at a single academic center in 2018. Students used the PanOptic and the PanOptic with iExaminer and were blinded to the correct diagnoses. For control, students were shown images taken with the iExaminer. Students documented their findings and level of confidence in making diagnoses in each scenario. A paired t-test was used to compare end points between all three groups.

Results: This study enrolled 81 second-year medical students, and a total of 4 glaucoma patients were examined. Mean percentage of correct findings was 63% for the exams with the PanOptic, which was more than the 60% found with the PanOptic with iExaminer ($p=0.03$) and 53% with the control iExaminer image ($p<0.01$). More confidence was reported with the PanOptic with iExaminer than with the PanOptic, with mean confidence scoring at 2.43 and 2.04 on a five-point scale, respectively ($p=0.02$).

Conclusions: The iExaminer is a useful teaching tool and confidence booster for medical students with instructor help as opposed to a diagnostic device in the hands of an inexperienced user. Relatively low absolute scoring with the iExaminer image alone suggests baseline ophthalmic knowledge as the limiting performance factor. This study emphasizes the need for practice in correctly identifying findings in patients and using the equipment. Higher confidence with the PanOptic with iExaminer may increase the likelihood of students practicing direct ophthalmoscopy outside the confines of our session. Further studies looking into sequential workshops for students will hopefully show improvement in their exams.

CONTROL ID: 3527717

SUBMITTER (NAME ONLY): Homayoun Bagherinia

TITLE: Robust registration using multiple OCT/OCTA en face images in advanced disease cases

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Bagherinia, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Homayoun Bagherinia: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Mary Durbin: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Robust registration of longitudinal data is required to measure the changes of OCT/OCTA slabs and retinal thicknesses over time. The pathological changes in the retina from one visit to another makes the registration of two OCT/OCTA slabs a challenging task. This abstract proposes a robust registration method that utilizes multiple slabs.

Methods: The OCT registration consists of aligning the corresponding keypoints in a pair of images. The well distributed keypoints matches were ensured by extracting the keypoints from OCT/OCTA slabs at different depth. OCT images were generated from 1) superficial and deep retinal layer, 2) RPE and 3) choroidal slabs. OCTA images were generated from 1) superficial (SRL), 2) deep capillary plexus and 3) RPE and choriocapillaris slabs. An exhaustive search method was used to fit best rigid transformation to a subset of matched keypoints. 15, 25, and 5 pairs of OCT volumes over 6x6 mm using CIRRUSTM HD-OCT 5000 (ZEISS, Dublin, CA), PLEX[®] Elite 9000 SS-OCT (ZEISS, Dublin, CA), and CIRRUSTM HD-OCT 5000 with AngioPlex[®] OCT Angiography (ZEISS, Dublin, CA) were used with eye diseases such as diabetic retinopathy and age-related macular degeneration. The performance of 5 registration methods were measured using keypoints extracted from 1) RPE, 2) all 3 OCT, 3) SRL, 4) all 3 OCTA and 5) all OCT and OCTA images. The nonparametric statistics of the RMSE of the matched keypoints along with the number and keypoints image area coverage for each pair of OCT volumes were reported for all 5 methods.

Results: Fig 1 shows examples using multiple slabs for registration. Fig 2 shows the box plots for RMSE of the matched keypoints, the number and keypoints image area coverage for 5 registration methods. The number and the keypoints area coverage increase significantly when multiple OCT/OCTA slabs were used for keypoints extraction, which is important for robust image registration with small RMSE. The RMSE using multiple slabs shows tighter distribution with a median value around 10 μ m indicating robustness and higher success rate. This may meet the accuracy requirement of OCT registration with A-scan spacing of 12 to 20 μ m.

Conclusions: We introduced a novel registration approach based on matched keypoints extraction from multiple slabs. We showed that using multiple slabs outperforms using a single slab for registration which is essential for measuring changes in longitudinal data.

CONTROL ID: 3527720

SUBMITTER (NAME ONLY): Yee Ling Wong

TITLE: Percentile Charts for Normal Axial Length Changes in Chinese Schoolchildren with Stable Emmetropia

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wong, A. Yang, B. Drobe, Essilor International, SINGAPORE|Y. Yuan, Y. Ding, Y. Ye, H. Chen, J. Bao, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|Y. Wong, Y. Yuan, Y. Ding, Y. Ye, A. Yang, B. Drobe, H. Chen, J. Bao, Wenzhou Medical University-Essilor International Research Centre, Wenzhou Medical University, CHINA|

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ABSTRACT BODY:

Purpose: To describe the normal growth pattern of axial length (AL) with age in a cohort of schoolchildren with stable emmetropia.

Methods: Stable emmetropia was defined as spherical equivalent (measured by subjective refraction) > -0.5 D and $\leq +0.75$ D in the right eye for 2 consecutive annual visits. A total of 700 schoolchildren with stable emmetropia enrolled in the Wenzhou Medical University-Essilor Progression and Onset of Myopia (WEPrOM) prospective cohort study, aged between 7 to 9 years with at least 2 years of follow-up between 2014 to 2018, were analysed. Ocular biometry, including AL measurements, was performed.

Results: A logistic function model was used to describe the changes in axial length with age, and a chart for AL changes versus age was plotted in percentiles (2.5th, 5th, 25th, 50th, 75th, 95th, and 97.5th; Figure). For children with stable emmetropia, the predicted change in AL in the next year was 0.22 (interquartile range [IQR; 25th to 75th percentile], 0.2-0.32) for children aged 7-9 years, 0.21 (0.13-0.3) for aged 10 years, 0.18 (0.08-0.27) for aged 11 years, and 0.12 (0.03-0.2) for aged 12 years. The lines with the predicted change in AL in the next year decreased gradually with age, till they plateaued nearing the age of 15 years, indicating that eyes of children with stable emmetropes continue to have AL growth till late adolescence.

Conclusions: Normal AL growth of approximately 0.2 mm/year (50th percentile) occurs among stable emmetropic Chinese schoolchildren aged 7-11 years. Percentile growth curves of changes in AL among stable emmetropes may be useful for clinicians to assess the effectiveness of myopia control interventions in slowing down axial elongation of myopic patients to that of a normal emmetrope.

CONTROL ID: 3527732

SUBMITTER (NAME ONLY): XUE LI

TITLE: Short-term visual performance through myopia control spectacle lenses with lenslets

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the impact on central distance visual acuity (VA) and contrast sensitivity (CS) in children of three different spectacle lens designs with lenslets used for myopia control while looking through the peripheral zones containing the lenslets.

Methods: Distance VA and CS were measured using Freiburg Visual Acuity and Contrast Test (FrACT) and CSV-1000 (Vector Vision Corp, USA), respectively. For each test, four spectacle lens designs were evaluated in random order: standard single vision lens (SVL) as a control, spectacle lens with concentric rings of highly aspherical lenslets (HAL), spectacle lens with concentric rings of slightly aspherical lenslets (SAL) and spectacle lens with honeycomb configuration of spherical lenslets (HC). To ensure vision through the lenslets zones, zones without lenslets were patched. 50 myopic children (mean age 12.7 ± 1.7 years, range 10 to 15 years, mean spherical equivalent refraction (SER) 3.22 ± 1.57 D, range -6.50 to -0.38 D) participated in the VA test; 36 myopic children (mean age 13.2 ± 1.2 years, range 10 to 16 years, mean SER 3.20 ± 1.67 D, range -7.25 to -0.75 D) participated in the CS test. All tests were done monocularly on the right eye with corrected-to-normal vision.

Results: Compared to SVL, VA through the lenslet zones of HAL, SAL and HC decreased significantly by 0.07 ± 0.09 , 0.06 ± 0.09 , 0.09 ± 0.07 LogMAR, respectively (all $p < 0.01$). Decrease in VA was similar in HAL and SAL ($p > 0.9$) while significantly larger in HC compared to HAL ($p = 0.02$) and to SAL ($p = 0.03$). VA changes induced by lenslets showed no significant correlation with SER (all $p > 0.05$), but had a weak positive association with age for SAL ($r = 0.36$, $p = 0.01$) and HC ($r = 0.31$, $p = 0.03$), but not for HAL ($p = 0.3$). The lenslet structures did not affect CS at low spatial frequency (3 cycles per degree (cpd), $p = 0.8$). At mid to high spatial frequencies (6 to 18 cpd), CS was significantly reduced by HAL and HL (all $p < 0.05$), but not SAL ($p > 0.05$) compared to SVL. At high spatial frequencies (12 to 18 cpd) both SAL and HAL reduced CS significantly less than HC (all $p < 0.01$).

Conclusions: When looking through the lenslet structures, short-term visual performance was minimally reduced by spectacle lenses with lenslets compared to SVL. Concentric rings of aspherical lenslets had significantly lower impact on both VA and CS than honeycomb configuration of spherical lenslets.

CONTROL ID: 3527733

SUBMITTER (NAME ONLY): Yingying Huang

TITLE: Effect of Myopia Control Spectacle Lenses with Aspherical Lenslets on Choroidal Thickness in Myopic Children: 1-Year Results

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Choroidal thinning is usually associated with myopia progressing. This study aimed to assess changes in choroidal thickness (ChT) in Chinese children wearing two new types of myopia control spectacle lenses with concentric rings of contiguous aspherical lenslets over a period of one year.

Methods: Within a randomized, controlled, double-masked clinical trial, 160 children (age 8 to 13 years, myopia between -0.75 D and -4.75 D) wore either spectacle lenses with highly aspherical lenslets (HAL), slightly aspherical lenslets (SAL) or single-vision lenses (SVL). We acquired ChT from central 6 mm radial OCT scans (Topcon Triton) at the baseline, 6 months, and 12 months. The changes from the baseline were compared between groups at foveal locations according to the Early Treatment Diabetic Retinopathy Study (ETDRS) areas.

Results: After one year, the ChT decreased at all regions in the SVL group by up to $-10.29 \pm 20.11 \mu\text{m}$ in the central fovea. This trend was significantly less pronounced in all regions in the SAL group ($p < 0.05$) that showed a maximal thinning of $-2.94 \pm 21.78 \mu\text{m}$ also in the central fovea. Most remarkably, the HAL group exhibited an increase in choroidal thickness in all regions by up to $18.24 \pm 18.22 \mu\text{m}$ in the superior regions and this effect was significantly different from both SVL and SAL ($p < 0.05$).

Conclusions: We observed the expected choroidal thinning associated with myopia progression in the SVL group. Wearing SAL lenses reduced this effect and wearing HAL lenses reversed this effect. These results are in agreement with the superior myopia control effect of the HAL lenses.

CONTROL ID: 3527740

SUBMITTER (NAME ONLY): Sophia Joseph

TITLE: Effect of Preoperative Anterior Chamber Depth and Intraocular Lens Power on Postoperative Pseudophakic Accommodation Following Monofocal Phacoemulsification Cataract Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Joseph, J. Eikenberry, D.K. Wallace, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Following phacoemulsification cataract surgery with a monofocal intraocular lens, patients generally experience good visual acuity at distance but have varying degrees of accommodative ability. We performed a prospective clinical study to test the hypothesis that preoperative anterior chamber depth (ACD) and/or implanted intraocular lens (IOL) power influence postoperative accommodative ability.

Methods: We enrolled fifteen adult patients (one eye each) who had undergone uncomplicated phacoemulsification cataract surgery more than one month prior by a single surgeon. Eligibility criteria included in-the-bag intraocular lens placement, surgery not requiring mechanical pupil stretching, and postoperative best-corrected distance visual acuity of 20/25 or better. We measured each patient's near visual acuity with only distance correction in place at 40 centimeters. We then measured amplitude of accommodation by placing a 2.5D lens over the distance correction and asking the patient to read a 20/30 near chart line. The chart was moved forward until blurred and back until clear to establish the near point. This was repeated 10 times and the average near point was used to determine the accommodative amplitude. The preoperative anterior chamber depth as measured by the IOL Master 700 as well as the IOL power implanted was obtained from the patient's medical record. Multiple linear regression analysis was used to determine if ACD and/or IOL power were associated with pseudophakic patients' accommodative ability.

Results: Postoperative accommodative ability was associated with larger ACD ($p=0.004$) but was not associated with IOL power ($p = 0.918$). For every 1 mm increase in ACD, there was a 2.63 D increase in accommodation.

Conclusions: Larger preoperative ACD predicts better postoperative accommodative ability in our pseudophakic patients. Larger ACD has been shown to correlate with younger age, and it is possible that younger pseudophakic patients retain more accommodation. Additionally, larger ACD has been shown to correlate with larger corneal diameter, and perhaps the larger cornea has more multifocality. These data could potentially be used to inform preoperative decision making when choosing between monofocal and multifocal lenses.

CONTROL ID: 3527757

SUBMITTER (NAME ONLY): Yuta Saito

TITLE: Investigation on the Efficacy and Safety of Carteolol/Latanoprost Combination Ophthalmic Solution Compared to Timolol/Latanoprost Combination Ophthalmic Solution in Patients with Glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the impact of the instillation timing of carteolol hydrochloride/latanoprost combination ophthalmic solution (LCFC) , in the morning or at night, in patients with glaucoma on the diurnal variations of IOP and on the circulatory system, comparing with timolol/latanoprost combination ophthalmic solution (LTFC) as a control.

Methods: Twenty-two eyes of 22 patients with POAG or OH on monotherapy with a prostaglandin ophthalmic solution were included. They were randomly assigned to either a group of switching from LCFC to LTFC or a group of switching from LTFC to LCFC. Both drugs were administered at 8 p.m. every night for 2 months each.

At the start of evaluation, the diurnal variation in IOP, vital signs (pulse rate, blood pressure), fluorescein corneal staining test and ophthalmological subjective symptoms at 2 months after the start of administration of each ophthalmic solution were evaluated. The adverse events during the evaluation period were also surveyed.

Results: The diurnal variation in IOP at 2 months after the start of evaluation period showed a similar transition in the LCFC group and the LTFC group, with a maximum value of 16.21 mmHg and 16.55 mmHg at a.m. 4:00 and a minimum value of 13.06 mmHg and 12.42 mmHg at p.m. 4:00, respectively. There were no differences in the range of the diurnal variation and the changes from the start of evaluation.

For the diurnal variation in pulse rate at 2 months after the start of evaluation period, there were significant differences in the changes from the start of evaluation, i.e., -0.8 and -4.3 at 22:00, -2.6 and -7.0 at 2:00, -3.1 and -7.1 at 4:00, and -3.7 and -8.0 at 6:00 in the LCFC group and the LTFC group, respectively.

No adverse events with a causal relationship with the treatment occurred in the both groups.

Conclusions: The IOP-lowering effect was equivalent in the diurnal variation of IOP at 2 months after the start of the administration in the LCFC group and the LTFC group. The transitional changes were similar, showing the maximum IOP at a.m. 4:00. For the diurnal variation at 2 months after the start of the administration, the pulse rate is less affected in the LCFC group, and the safety of night instillation was shown.

CONTROL ID: 3527758

SUBMITTER (NAME ONLY): Hirofumi Yogo

TITLE: Whole eye imaging using swept-source optical coherence tomography with vertical cavity surface emitting laser

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Some ocular diseases can affect eye shape and size, hence, high-resolution imaging with whole eye optical coherence tomography (OCT) may be necessary to examine these pathological changes. Here we report a prototype OCT that allows measurement of the whole eye and axial length (AL) measurement.

Methods: We used a swept-source OCT with vertical cavity surface emitting laser (VCSEL) with 1060 nm center wavelength and a modifiable wavelength sweep frequency (WSF). In vivo imaging was performed on healthy patients. Low-speed and high-speed WSF allow low-resolution or high-resolution imaging. The anterior segment and fundus can be captured in one shot in low-speed mode (Fig. 1A). This image was registered as a reference image to construct the whole eye image. In high-speed mode, anterior segment and fundus OCT image capture were performed separately. The whole eye OCT image was constructed by registration of the image captured at high-speed mode with the reference image from the low-speed mode. AL was the distance between the corneal vertex and fovea based on the low-speed OCT image. AL measurements were compared to those from a commercially available optical biometer (AL-Scan; NIDEK).

Results: Figure 1B present a reference OCT image in low-speed mode and Figure 1C presents the whole eye OCT image. The optical design precluded imaging of the area around the equator and ora serrata. The axial length was 25.56 mm with the prototype OCT and 25.34 mm with the AL-Scan.

Conclusions: A prototype OCT was developed that allows whole eye OCT imaging and axial length measurement, to simultaneously assess the fundus to the equator and the anterior segment in a single device. We confirmed similar measurement capability of the prototype and the AL-Scan. Incorporation of this prototype into clinical practice may decrease diagnostic workup time and increase patient turnover and patient comfort.

CONTROL ID: 3527762

SUBMITTER (NAME ONLY): Jasmin Rezapour

TITLE: Macular thickness and vessel density in glaucoma eyes with and without high axial myopia

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the association between various macular layer thicknesses and superficial vessel density measurements and both axial length (AL) and glaucoma severity to improve glaucoma detection in highly myopic eyes.

Methods: 248 glaucoma patients (401 eyes) with AL measurements and macular optical coherence tomography (OCT) imaging were stratified into three axial myopia groups of no- (146 eyes), mild- (208 eyes) and high-axial myopia (AL > 26mm) (47 eyes). Ganglion cell inner plexiform layer (GCIPL) thickness, macular retinal nerve fiber layer (mRNFL) thickness, ganglion cell complex (GCC) thickness and the macular superficial vessel density (sVD) were measured with the built-in software and macular choroidal thickness (mCT) was assessed using deep learning strategies for each axial myopia group. Univariate and age- and VFMD-adjusted models were assessed to evaluate the association between structural measures and AL and VFMD.

Results: Thinner global GCIPL and GCC were not associated with AL ($p < 0.350$) but were significantly associated with visual field mean deviation (VFMD) ($R^2 = 35.1$; and $R^2 = 33.4$; respectively $p < 0.001$). Thicker mRNFL showed a weak association with larger AL ($R^2 = 3.4$; $p = 0.001$) and a positive association with VFMD (global $R^2 = 20.5$; $p < 0.001$). Lower sVD was moderately associated with worse VFMD ($R^2 = 31.8$; $p < 0.001$) and weakly associated with larger AL ($R^2 = 2.3$; $p = 0.016$). Thinner MCT was not associated with VFMD ($P = 0.262$) but was associated with larger AL ($R^2 = 17.3$; $p < 0.001$).

Conclusions: Thinner GCIPL and GCC were associated with more severe glaucoma and were not associated with AL suggesting that these measurements might be useful for glaucoma detection in myopic eyes.

CONTROL ID: 3527777

SUBMITTER (NAME ONLY): Melinda Toomey

TITLE: Glaucoma prescribing trends by Australian Optometrists and Medical Practitioners from 2009 - 2019

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Australian optometrists manage glaucoma in shared care agreements with ophthalmologists. Optometrists gained access to the Pharmaceutical Benefits Scheme (PBS) for glaucoma drugs in 2008. PBS data was explored to determine the extent of optometrists' role in glaucoma management and compare prescribing patterns of optometrists and medical practitioners over time.

Methods: PBS data were retrieved from 2009 to 2019 for topical glaucoma drugs. The number of scripts dispensed per year for each glaucoma drug and drug classes (α -agonists, β -blockers, carbonic anhydrase inhibitors (CAI), miotics, prostaglandins (PGA) and fixed combinations (FC)), and preservative free (PF) were determined. The proportion of optometrists' scripts was calculated as a proxy measure for shared care uptake. Percent change over time, relative proportions of drug classes and most prescribed drug within each class were calculated for each professional group.

Results: The number of glaucoma scripts dispensed per year (mean 3.70M, IQR 3.43 – 3.84M) has been stable since 2009 despite population ageing with the number of scripts prescribed per person (65y/>) ranging from 1.23 in 2009 to 0.86 in 2019. The proportion of optometrists' scripts to total scripts has increased (0.04% in 2009 to 2.61% in 2019) but appears to be plateauing. Optometrists' (OP) largest increases were for PGA (924 to 238,936) and FC (338 to 146,556). Medical practitioners' (MP) scripts for miotics (-51.1%), β -blockers (-45.8%), PGA (-27.3%) have decreased, FC (55.8%) and CAI (17.5%) have increased, while α -agonists remained stable. PF use has increased since first introduced in 2013 accounting for 7.5% of scripts. Relative proportions of drug classes in 2019 were similar for both professions: PGA (OP 47%, MP 41%), FC (OP 35% , MP 39%), and others (OP 18.3%, MP 20.0%) The most frequently prescribed drugs in each class were the same for both professions.

Conclusions: Optometrists prescribed a small but increasing proportion of glaucoma scripts indicating slow uptake of shared care agreements. Both professions exhibit similar prescribing patterns. The reduced number of scripts per person, decreased PGA and β -blockers, and increased FC prescribing by medical practitioners may reflect changes in glaucoma treatment paradigms. Opportunity exists for more optometrists to engage in glaucoma management via shared care agreements to assist with increased future demand.

CONTROL ID: 3527798

SUBMITTER (NAME ONLY): Yu-Chieh Yang

TITLE: The Prevalence Trend of Myopia after Promoting Outdoor Activity among Preschoolers, 2014-2019: A Serial Cross-sectional Study in Yilan, Taiwan

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: A better understanding of the association between policy intervention promoting outdoor activities and the changes in the prevalence of myopia among preschoolers is critical for improvement of preventive strategies against myopia during early childhood. This study aimed to report the prevalence of preschool myopia and its secular trend after implementing a policy intervention promoting outdoor activities in a Taiwan preschool population.

Methods: The repeated countywide population-based, cross-sectional surveys were based on the Yilan Myopia Prevention and Vision Improvement Program (YMVIP) which has been conducted since August 2014. Myopia prevention strategies, such as increasing outdoor exercises (2 hours/weekday), have been promoted in all kindergartens in Yilan County, and school-based eye examinations, including cycloplegic autorefraction, and caregiver-administered questionnaires have been performed annually for all preschoolers aged 5-6 years.

Results: Among 20,419 kindergarteners aged 5-6 years in 6 school-year cohorts from 2014 through 2019, a total of 18,621 (9,715 [52.2%] boys) were finally included for analysis. The prevalence of myopia (spherical equivalent $\leq -0.5D$ in either eye) among preschoolers aged 5-6 years declined continuously from 15.4% (95% confidence interval [CI], 14.1%-16.6%) in the 2014 cohort which was not yet exposed to the YMVIP before eye examinations to 8.4% (95% CI, 7.4%-9.4%) in the 2016 cohort which had been exposed to the YMVIP for up to 2 years and remained relatively stable in the subsequent cohorts with 2-year YMVIP exposure (8.5% [95% CI, 7.6%-9.5%] in 2017, 10.0% [95% CI, 9.0%-11.0%] in 2018, and 9.1% [95% CI, 8.1%-10.1%] in 2019). Multivariable logistic regression analysis showed a significant and dose-response association between the duration of exposure to preventive strategy and the prevalence of myopia (one-year YMVIP exposure: odds ratio [OR], 0.86; 95% CI, 0.75-0.999; two-year YMVIP exposure: OR, 0.55; 95% CI, 0.49-0.61) after controlling other myopiogenic factors.

Conclusions: This population-based evidence showed high prevalence of preschool myopia and an L-shaped decline after introducing strategies to promote outdoor activities in kindergartens.

CONTROL ID: 3527804

SUBMITTER (NAME ONLY): Stine Bolme

TITLE: Task shifting of intravitreal injections from physicians to nurses: a qualitative study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bolme, D. Austeng, Department of Neuromedicine and Movement Science, Norges teknisk-naturvitenskapelige universitet, Trondheim, NORWAY|S. Bolme, D. Austeng, Ophthalmology, Sankt Olavs Hospital Universitetssykehuset i Trondheim Avdeling Broset, Trondheim, NORWAY|K.H. Gjeilo, Department of Public Health and Nursing, Faculty of Medicine, NTNU, Trondheim, Norway, Norges teknisk-naturvitenskapelige universitet, Trondheim, NORWAY|

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ABSTRACT BODY:

Purpose: Intravitreal injections of anti-vascular endothelial growth factor is traditionally administered by physicians and represents a considerable workload on ophthalmology departments. To optimize the available resources, we developed a training program for nurses with the aim to inject equally as efficient and safe as physicians. In a randomized controlled trial (RCT) we showed nurses to be non-inferior to physicians.

In this qualitative study we aimed to evaluate if the nurses were confident and in control having participated in the training program, and if the nurses were satisfied with the training program and the new task.

Methods: During 2014-2018, twelve registered nurses were trained in a tertiary clinic covering about 300.000 inhabitants in Central Norway. Work experience ranged from two to thirty-one years. All nurses were interviewed with a semi structured interview guide, either individually (n=7) or in a focus group (n=5). We analyzed the interviews using Granheim and Lundemans qualitative content analysis.

Results: Twelve sub-themes clustered in four main themes 1) responsibility and safety, 2) motivation and respect, 3) collaboration and 4) organization. The nurses felt confident and in control when administering injections but experienced moments of insecurity. The new task gave the nurses a sense of achievement, mastering a task that is not part of their usual training. Improvement of patient's lives were mentioned as a positive effect. A greater level of responsibility gave the nurses pride in their profession. They were satisfied with the training program but had suggestions that could improve the efficiency of the training.

Conclusions: Our study showed that the nurses trained were satisfied with the training and learning a new task led to higher self-esteem and gained respect. They had several suggestions on how the training could be improved, which should be considered before recommending it to other departments.

CONTROL ID: 3527810

SUBMITTER (NAME ONLY): Danny Lam

TITLE: Telehealth in an acute ophthalmic setting during COVID-19

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Lam, C. Downie, E.E. Cornish, P.J. McCluskey, S. Zagora, Sydney Hospital and Sydney Eye Hospital, Sydney, New South Wales, AUSTRALIA|E.E. Cornish, P.J. McCluskey, S. Zagora, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Telehealth consultations will be increasingly used to assess eye patients during the COVID-19 pandemic. An audit was performed at a major quaternary referral centre for Ophthalmology in Sydney, Australia. This study assesses the outcomes of teleconsultation in an acute ophthalmic clinic setting.

Methods: 242 patients with an Acute Ophthalmic Service clinic appointment at the Sydney Hospital & Sydney Eye Hospital between 19th March 2020 and 9th April 2020 inclusive were included in this study. These patients were separated into two study groups - 162 patients attended their pre-arranged appointment, whereas 80 patients had their appointment changed to a telehealth consultation.

A final year Ophthalmology Registrar performed an online medical records review of all patients and selected 80 patients for teleconsultation, following which re-presentation rate and reason for re-presentation was collected each month for five months for the two patient populations.

The primary outcome measure was the rate of re-presentation and reason for re-presentation to the Eye Emergency Department.

Results: There were no significant differences in the number of re-presentations after each month during the five months ($P = 0.166, 0.113, 0.139, 0.266$ and 0.390 at each month). There were also no significant differences in the reason for re-presentation after each month during the five months ($P = 0.999, 0.999, 0.872, 0.663$ and 0.517 at each month).

Conclusions: There were similar short-term outcomes between the two study groups suggesting that telehealth is a viable alternative for the provision of acute care to appropriately selected patients.

CONTROL ID: 3527812

SUBMITTER (NAME ONLY): E Craven

TITLE: Corneal endothelial cell loss associated with selective laser trabeculoplasty

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.R. Craven, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|M.Y. Chen, X. Gu, M.R. Robinson, Allergan, an AbbVie company, California, UNITED STATES|D.L. Wirta, David Wirta, M.D. & Associates, California, UNITED STATES|W.C. Christie, Scott & Christie and Associates, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): E Craven: Commercial Relationship(s);Alcon Laboratories, Inc.:Code C (Consultant);Allergan (an AbbVie company):Code C (Consultant);Aqueous Biomedical:Code C (Consultant);Ivantis:Code C (Consultant);Santen, Inc.:Code C (Consultant);W. L. Gore & Associates:Code C (Consultant) | William Christie: Commercial Relationship(s);Allergan (an AbbVie company):Code C (Consultant);Johnson & Johnson:Code C (Consultant) | Michelle Chen: Commercial Relationship(s);AbbVie Inc.:Code E (Employment) | Xuemin Gu: Commercial Relationship(s);AbbVie Inc.:Code E (Employment) | Michael Robinson: Commercial Relationship(s);AbbVie Inc.:Code E (Employment) | David Wirta: Commercial Relationship(s);Aerpio:Code F (Financial Support);Allergan (an AbbVie company):Code C (Consultant);Allergan (an AbbVie company):Code F (Financial Support);Annexon:Code F (Financial Support);Dompe:Code F (Financial Support);Eyenovia:Code C (Consultant);Eyenovia:Code F (Financial Support);Mallinckrodt:Code F (Financial Support);Nicox:Code F (Financial Support);Novartis:Code F (Financial Support);Novaliq:Code F (Financial Support);Santen:Code F (Financial Support);SilkTech:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Selective laser trabeculoplasty (SLT) is a procedure increasingly used as first-line therapy to reduce intraocular pressure (IOP) in patients with ocular hypertension (OHT) or glaucoma. This subgroup analysis evaluated corneal endothelial cell loss (CECL) associated with SLT treatment in a randomized, phase 3 study.

Methods: A 52-week, randomized, phase 3, paired-eye comparison study (NCT02636946) evaluated bimatoprost implant compared with SLT in patients with open-angle glaucoma or OHT whose IOP was inadequately managed with topical medication for reasons other than medication efficacy. SLT was performed on Day 1 using single-burst mode and a standard fixed 400 µm spot size with ~100 contiguous, non-overlapping spots delivered 360° in the angle; power began at ~0.6 mJ and was titrated between ~0.4 and ~1.2 mJ as needed. Patients were randomized to treatment with implant or SLT in the worse eye; contralateral eyes received the alternate treatment. Corneal endothelial cell density (CECD) was assessed as a safety parameter at multiple time points throughout the study with a Konan CellChek noncontact specular microscope present at each site. The imaging technician was qualified by an experienced reading center (Cornea Image Analysis Reading Center [CIARC], Case Western Reserve University) commonly used for registration studies. CECD was quantified by the reading center. All available data from the primary database lock, when the last enrolled patient completed the Week 24 visit, were analyzed.

Results: Mean (SD) CECD in SLT-treated eyes (n=141) was 2487 (311) cells/mm² at baseline and decreased during the study; at Week 24 the mean (SD) CECD was 2422 (329) cells/mm². Among all SLT-treated eyes, 9.9% (14/141) had ≥10% corneal endothelial cell loss (CECL), 5.7% (8/141) had ≥15% CECL, and 3.5% (5/141) had ≥20% CECL during a mean (SD) follow-up of 317 (83) days.

Conclusions: Previous open-label studies with 1 month follow-up have generally reported transient corneal changes and reduction in CECD after SLT with limited follow up. Results of this phase 3 study suggest that persistent CECL may be a previously unrecognized side effect of SLT that becomes evident with longer follow-up.

CONTROL ID: 3527824

SUBMITTER (NAME ONLY): Paul Oyler

TITLE: Surface softness comparison of select contact lenses by nanoindentation

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Oyler, B. Tucker, Vision Care, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Paul Oyler: Commercial Relationship(s);Alcon Laboratories, LLC:Code E (Employment) | Bob Tucker: Commercial Relationship(s);Alcon Laboratories, LLC:Code E (Employment)

ABSTRACT BODY:

Purpose: The objective of the study was to determine surface softness differences between a new contact lens material with biologically inspired water gradient surface and five other contact lens types using nanoindentation and to assess any in-vitro to ex-vivo softness differences among the lenses.

Methods: In-vitro: Contact lenses made from a new contact lens material (NCLM) (5 lenses) and 5 other comparator lenses (samfilcon A, comfilcon A, senofilcon C, senofilcon A, and fanfilcon A; n=6 each) were removed from their packaging and placed in PBS/0.1% Pluronic F-127 testing solution for 30 minutes. All tested lenses were then mounted on a steel ball for nanoindentation using an Optics 11 Piuma nanoindentation system. In order to determine the surface softness the depth required for the probe to apply 5 kPa of pressure to the lenses was calculated.

Ex-vivo: NCLM lenses (n=6) were worn by patients daily and disinfected in OPTI-FREE® RepleniSH® nightly during the 30-day clinical trial. These lenses were tested using the same method as above and compared to the in-vitro NCLM from the same manufacturing lot as well as the 5 comparator lens types (Figure 1).

Results: In-Vitro: NCLM lenses were found to have a significantly greater ($p<.05$) depth to reach 5 kPa (490 ± 72 nm) than the other 5 lens types tested (68 ± 35 nm, 83 ± 39 nm, 79 ± 36 nm, 82 ± 58 and 64 ± 31 for samfilcon A, comfilcon A, senofilcon C, senofilcon A, and fanfilcon A, respectively).

Ex-vivo: Clinically worn NCLM lenses had comparable depth (518 ± 89 nm) to in-vitro controls.

Conclusions: The in-vitro surface softness characterized by nanoindentation of the NCLM lenses showed they were significantly softer than samfilcon A, comfilcon A, senofilcon C, senofilcon A, or fanfilcon A lenses. The surface softness of the ex-vivo NCLM did not decrease after being worn on-eye, which indicates the integrity of the water gradient surface was maintained throughout daily wear for 30 days. Surface softness may provide good correlation with lubricity, which could indicate greater comfort during lens wear.

CONTROL ID: 3527828

SUBMITTER (NAME ONLY): Sriganesh Ramachandra Rao

TITLE: Dhdds ablation in photoreceptor and bipolar progenitor cells causes early-onset retinal degeneration

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Ramachandra Rao, S.J. Fliesler, Ophthalmology and Biochemistry, SUNY The State University of New York, Buffalo, New York, UNITED STATES|S.J. Pittler, Optometry and Vision Science, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|S. Ramachandra Rao, S.J. Fliesler, Research Service, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sriganesh Ramachandra Rao: Commercial Relationship: Code N (No Commercial Relationship) | Steven Pittler: Commercial Relationship: Code N (No Commercial Relationship) | Steven Fliesler: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the requirement for dehydrolipoyl diphosphate synthase (Dhdds) gene expression in the early development of photoreceptor and bipolar cells.

Methods: Dhdds was ablated in rod and cone photoreceptor and bipolar cells by crossing Dhdds^{flx/flx} mice to CRX (cone-rod homeobox) promoter-driven Cre recombinase transgenic mice, to initiate Dhdds knockout (KO) at E12.5 days. Dhdds^{flx/flx} CRX-Cre⁺ (KO) and Dhdds^{flx/flx} CRX-Cre⁻ (control) mice were selected by PCR for the presence of the loxP-modified Dhdds allele and CRX-Cre transgene. Cre recombinase expression and activity were tested by crossing CRX-Cre mice with ZsGreen reporter mice. Western blot (WB) analysis was performed, ±PNGase-F treatment, on retinas from PN 4-wk old KO and control mice, probing with 1D4 Mab to assess opsin N-glycosylation status. Eyes from PN 3-4-wk old KO and control mice were subjected to TUNEL labeling and immunohistochemistry (IHC), using cell type-specific antibodies, or probed with fluor-conjugated lectins (Con-A, PNA) or Cholera toxin-B (CTx). Retina whole mounts were probed with PNA to assess cone density. ERG analysis was performed on control and KO mice at PN 4-5 wk (N=3/group). Statistical analysis: Student's t-test, P<0.05.

Results: ZsGreen reporter analysis demonstrated Cre recombinase activity in rods, cones, and bipolar cells, as well as patchy expression in Mueller glia. ERG analysis showed extinguished scotopic and photopic a- and b-waves in KO mice at PN 4-wk. Relative to controls, IHC of PN 4-wk KO retinas revealed significant (>90%) loss of cones and bipolar cells, shortened rod outer segments, and gliosis; TUNEL+ cells were observed only in the ONL, with a cone-rod degeneration pattern. CTx binding revealed aberrant ganglioside GM1 accumulation in KO retinas; however, no overt protein N-glycosylation defects were evident by WB or Con-A staining.

Conclusions: Despite initiation of Dhdds ablation at E12.5 days in progenitors of photoreceptor and bipolar cells, retinal degeneration (not dysplasia) was observed. These findings suggest the presence of a long-lived, progenitor-derived dolichol pool that persists even after differentiation of photoreceptors and bipolar cells has occurred and after de novo synthesis has ceased in those cells. This may explain the absence of obvious glycosylation defects in other Dhdds mutant mouse models of RP59.

CONTROL ID: 3527835

SUBMITTER (NAME ONLY): Pushkar Varde

TITLE: Water gradient wettability and durability of a new monthly replacement contact lens

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Varde, B. Tucker, Alcon Laboratories Inc, Johns Creek, Georgia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Pushkar Varde: Commercial Relationship(s);Alcon Inc:Code E (Employment) | Bob Tucker: Commercial Relationship(s);Alcon Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: A new contact lens material (NCLM) was designed with a unique phosphoryl choline water gradient surface. This work evaluates the durability and wettability of this water gradient surface after 30 days of on-eye daily wear use.

Methods: The NCLM (n=5) were worn on a daily wear regimen for 30 days that included nightly manual cleaning (rubbing) and disinfection in OPTI-FREE[®] RepleniSH[®]. The control group was out of pack (OOP) lenses (n=5). The lenses were pre-soaked in PBS for 16 hrs and then tested with the Interfacial Dewetting and Drainage Optical Platform (iDDrOP) wettability measurement (Bhamla, 2015), which provides quantitative in vitro surface material property analysis without interference from packaging solution, tears, or patient variation. A video of the lens dewetting in PBS allows objective water break-up time (WBUT) to be collected. The same lenses were then stained using Sudan Black to assess the loss of the gradient surface coating. Staining was analyzed using a custom software that generates a percent stain metric.

Results: The WBUT for ex vivo lenses (21 ± 5.62 sec) was comparable to the OOP control lenses (27 ± 3.28 sec) even after 30 days of on-eye daily wear, The ex vivo lenses demonstrate significantly higher WBUT compared to the OOP WBUT for other inherently wettable CL: comfilcon A: 6 ± 2 sec, senofilcon A: 9 ± 3 sec, samfilcon A: 15 ± 5 sec, and senofilcon C: 14 ± 4 sec (Fig 1). The staining metric on either group of lenses was less than 1% (ex vivo: $0.12 \pm 0.09\%$ vs OOP: $0.43 \pm 0.65\%$) indicating uniform coverage of the hydrophilic water gradient coating. However, for competitor lenses, the staining metric was higher than 10%.

Conclusions: The surface coating durability of ex vivo CL for a new 30-day wear lens product was comparable to OOP lenses, and the surface wettability was superior to the OOP properties of other inherently wettable CL even after 30 days of on-eye wear. Moreover, the biologically inspired water gradient coating maintains uniform coverage on the lens even after 30 days of daily wear.

CONTROL ID: 3527856

SUBMITTER (NAME ONLY): Tom Lawler

TITLE: Lutein and zeaxanthin supplement use is associated with increased macular pigment density over 15 years and greater contrast sensitivity in the Carotenoids in Age-Related Eye Disease Study of older-adult women

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lawler, Nutritional sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|Z. Liu, M. Nalbandyan, Y. Liu, J.A. Mares, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|B. Hammond, Psychology, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|R.B. Wallace, Epidemiology, The University of Iowa College of Public Health, Iowa City, Iowa, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Tom Lawler: Commercial Relationship: Code N (No Commercial Relationship) | Zhe Liu: Commercial Relationship: Code N (No Commercial Relationship) | Marine Nalbandyan: Commercial Relationship: Code N (No Commercial Relationship) | Yao Liu: Commercial Relationship: Code N (No Commercial Relationship) | Billy Hammond: Commercial Relationship: Code N (No Commercial Relationship) | Robert Wallace: Commercial Relationship: Code N (No Commercial Relationship) | Julie Mares: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Carotenoids lutein and zeaxanthin (L/Z) accumulate in the macula to form macular pigment, which may be neuroprotective and preserve vision. L/Z supplements increase macular pigment density (MPOD) and improve vision in trials of younger/middle-aged adults, but less is known of their long-term effects in older adults (age 70-100). Using data from the Carotenoids in Age-Related Eye Disease Study (CAREDS), a cohort study of postmenopausal women, we examined associations between L/Z supplement use and MPOD over 15 years, best-corrected visual acuity (BCVA) and contrast sensitivity (CS).

Methods: We used linear models and generalized estimating equations to evaluate relationships between L/Z use, MPOD, BCVA, and luminance CS. The main exposure was self-reported L/Z supplement use ≥ 1 mg/day (≥ 1 month) assessed via questionnaire prior to CAREDS2. The primary outcome was 15-year MPOD change. MPOD was measured at 0.5° from foveal center using heterochromatic flicker photometry at CAREDS and CAREDS2. Other outcomes included BCVA and luminance CS measured at CAREDS2 using Snellen and Pelli-Robson charts, respectively, in eyes without ocular pathology (assessed at CAREDS2 visits) or self-reported diabetes to mitigate confounding.

Results: Of 2,005 women enrolled in CAREDS baseline (2001-2004), 487 participated in CAREDS2 visits (2016-2019). For those with complete data (n=417), L/Z supplement use was reported by 76 (18.2%). L/Z use was more common in women with advanced AMD (68.3%). L/Z use was associated with larger increases in MPOD over 15 years (0.22 ± 0.03 optical density units (ODU) vs. 0.12 ± 0.01 (mean \pm SE), $p < .001$). However, a linear dose-response (up to 20+ mg/day) was not observed. MPOD change was maximal in those consuming 10-19.9 mg/day (0.29 ± 0.04 ODU). In eyes without pathology (n=414), L/Z use was not associated with BCVA (83.3 ± 1.1 letters vs. 82.8 ± 0.4 (20/25), $p = .65$), but was associated with greater CS (12.3 ± 0.2 triplets vs. 11.8 ± 0.1 , $p = .006$).

Conclusions: In this cohort of older women, L/Z use was associated with a greater increase in MPOD over 15 years and greater CS (in eyes without pathology), consistent with clinical trials in younger and middle-aged adults. Greater CS related to L/Z use may help maintain quality of life in older adults.

CONTROL ID: 3527860

SUBMITTER (NAME ONLY): Joanne Wen

TITLE:

Using Fixed-Force Goldmann Applanation Tonometry to measure the Ocular Pulse Amplitude

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.C. Wen, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|T. Spaide, Y. Wu, A.Y. Lee, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joanne Wen: Commercial Relationship: Code N (No Commercial Relationship) | Theodore Spaide: Commercial Relationship: Code N (No Commercial Relationship) | Yue Wu: Commercial Relationship: Code N (No Commercial Relationship) | Aaron Lee: Commercial Relationship(s);US Food and Drug Administration:Code E (Employment);Santen:Code F (Financial Support);Carl Zeiss Meditec:Code F (Financial Support);Novartis:Code F (Financial Support);Microsoft:Code F (Financial Support);NVIDIA:Code F (Financial Support);Genentech:Code C (Consultant);Verana Health:Code C (Consultant);Topcon:Code R (Recipient)

ABSTRACT BODY:

Purpose: The role of the ocular pulse amplitude (OPA), which is the difference in measured IOP during the diastolic and systolic cardiac cycle, in glaucoma pathogenesis is under-studied due to the limited methods for measuring OPA. We present a novel method for measuring OPA using standard ophthalmic equipment and fixed-force Goldmann Applanation Tonometry (GAT).

Methods: The methods for automated fixed-force GAT have been previously described.¹ Briefly, an iPod Touch clamped to the ocular of a standard slit lamp microscope (Fig A) recorded the applanation mires (Fig B) created with the GAT set at a fixed force. IOP values from each frame of the video were calculated from the mire diameters (Fig C) and plotted over time (Fig D). In this post hoc analysis, we analyzed previously collected videos used for validation of the automated GAT method. The right eyes of subjects diagnosed as POAG or glaucoma suspect (GS) were included. The OPA was calculated by measuring the difference in IOP between the upper and lower IOP measurements in each cycle and taking the mean of these differences. The OPA of POAG eyes were compared to GS eyes.

Results: 41 POAG eyes and 20 GS eyes were included. Mean age (67.5 ± 8.2 vs 66.5 ± 13.5 years), IOP (14.5 ± 4.8 vs 16.9 ± 4.6 mmHg) and CCT (535 ± 39 vs 550 ± 32 μ m) for POAG vs GS eyes did not differ significantly ($p=0.71$, 0.08 , 0.13 , respectively). OPA was found to be decreased in POAG eyes (1.18 ± 0.7 mmHg) compared with GS eyes (1.62 ± 0.94 mmHg) ($p=0.05$, t-test). A significant correlation between OPA and IOP was found ($r=0.62$, $p<0.0001$) while no significant correlation was found between OPA and CCT ($r=0.14$, $p=0.30$) and OPA and age ($r=-0.01$, $p=0.91$).

Conclusions:

Preliminary measurements of OPA using automated fixed force GAT are promising. This method is easily incorporated into standard ophthalmic equipment and may become a tool to improve our understanding of the role of OPA in ocular disease.

CONTROL ID: 3527866

SUBMITTER (NAME ONLY): Marilyn Chwa

TITLE: Cell Viability and Transcriptome Changes Associated with Hydrogen Peroxide and Risuteganib Exposure in Human Retinal Cells In Vitro

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chwa, S. Atilano, M. Kenney, University of California Irvine, Irvine, California, UNITED STATES|Z. Shao, J.Y. Park, H. Karageozian, V. Karageozian, Allegro Ophthalmics, San Juan Capistrano, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Marilyn Chwa: Commercial Relationship: Code N (No Commercial Relationship) | Zixuan Shao: Commercial Relationship(s);Allegro Ophthalmics:Code E (Employment) | Shari Atilano: Commercial Relationship: Code N (No Commercial Relationship) | John Park: Commercial Relationship(s);Allegro Ophthalmics:Code E (Employment) | Hampar Karageozian: Commercial Relationship(s);Allegro Ophthalmics:Code E (Employment) | Vicken Karageozian: Commercial Relationship(s);Allegro Ophthalmics:Code E (Employment) | M. Cristina Kenney: Commercial Relationship(s);Allegro Ophthalmics:Code C (Consultant)

ABSTRACT BODY:

Purpose: Emerging research identifies elevated oxidative stress as central to the pathogenesis of many degenerative retinal diseases, such as dry age-related macular degeneration and retinitis pigmentosa. Treatment options for these diseases are limited, resulting in visual loss affecting millions of patients worldwide. In the present study, we investigated the cytotoxicity of hydrogen peroxide (H_2O_2) and protection by an investigational drug, risuteganib (RSG), in cultured human RPE (ARPE-19) and Müller (MIO-M1) cells.

Methods: ARPE-19 (n=3) and MIO-M1 (n=8-9) cells were treated according to the following five regimes: (1) untreated control for 36 h, (2) RSG treatment for 36 h, (3) untreated for 24 h, then H_2O_2 for 12 h, (4) RSG pre-treatment for 24 h, then H_2O_2 for 12 h, and (5) RSG for 24 h, then RSG and H_2O_2 co-treatment for 12 h. 400 μ M RSG and 100 μ M H_2O_2 were used. After exposure, cells were incubated for 48 h in fresh media before cell viability was measured by Trypan Blue dye exclusion assay. Statistical analysis was by Student's t-test. Control, H_2O_2 , and [RSG pre-treatment + H_2O_2] samples (n=6) were analyzed by RNA-seq for whole transcriptome gene expression. Differentially expressed genes were determined using edgeR and over-represented biological processes/pathways using goseq.

Results: H_2O_2 treatment significantly reduced cell viability by 27.7% (p=0.023) and 20.5% (p<0.0001) in ARPE-19 and MIO-M1 cells, respectively. Cell viability was significantly rescued by RSG pre-treatment (30.3%, p=0.015; 7.7%, p=0.0454) and RSG co-treatment (26.3%, p=0.027; 10.4%, p=0.0046) in ARPE-19 and MIO-M1 cells, respectively. RNA-seq showed H_2O_2 exposure regulated genes in the angiogenesis, immune system, cell adhesion/migration, cell proliferation/death, and metabolic processes. Biological pathway analysis showed integrin cell surface interaction was significantly regulated by H_2O_2 . RSG effectively reversed the harmful effects of H_2O_2 treatment across many of the biological processes and pathways.

Conclusions: H_2O_2 induced significant cytotoxicity that was mitigated by RSG. Expression data showed H_2O_2 regulated genes across many disease-relevant processes and pathways, whereas RSG treatment lessened these effects. Our results suggest RSG may be effective in reducing oxidative stress-induced toxicity in retinal cells with relevance to human diseases.

CONTROL ID: 3527875

SUBMITTER (NAME ONLY): Sabrina Chen

TITLE: Evaluation of Three Minimally Invasive Glaucoma Surgeries (MIGS) Combined with Phacoemulsification for Treatment of Open-Angle Glaucoma and Visually Significant Cataract

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chen, H. Goyal, L. Raju, Ophthalmology, New York University School of Medicine, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sabrina Chen: Commercial Relationship: Code N (No Commercial Relationship) | Himani Goyal: Commercial Relationship: Code N (No Commercial Relationship) | Leela Raju: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the efficacy and safety of combined cataract extraction (CE) and either excisional goniotomy performed with Kahook Dual Blade (KDB), iStent or iStent inject trabecular bypass implantation in patients with mild to moderate open-angle glaucoma and visually significant cataract.

Methods: A retrospective analysis was performed on 55 eyes of 51 adults with mild to moderate open-angle glaucoma treated with one or more intraocular pressure (IOP)-lowering medications who underwent combined CE and iStent, iStent inject or KDB. Inclusion criteria included no previous glaucoma surgeries and one year of postoperative follow up. Data included best-corrected visual acuity (BCVA), IOP, IOP lowering medications, and adverse events (AE) collected through 12 months postop. The primary outcome variables were IOP reduction and reduction in number of IOP lowering medications.

Results: 35 iStent eyes, 7 iStent inject eyes and 13 KDB eyes were included in the study. Mean preoperative IOP was 19.15 ± 5.29 mmHg on a mean number of 1.67 medications. At 12 months postoperative, mean IOP decreased 3.70 ± 4.50 mmHg ($p < 0.001$) in iStent group, 6.64 ± 2.38 mmHg ($p < 0.001$) in the iStent inject group and 3.59 ± 3.84 mmHg ($p = 0.082$) in KDB group. Mean number of medications decreased 1.06 ± 0.32 ($p < 0.001$) in iStent group, 1.25 ± 0.96 ($p < 0.001$) in the iStent inject group and 0.57 ± 0.60 ($p = 0.061$) in KDB group. A favorable safety profile included no intraoperative AE, and BCVA of 20/40 or better in 96% of eyes at 12 months.

Conclusions: iStent and iStent inject with CE led to statistically significant and clinically meaningful reductions in IOP and glaucoma medication burden at 12 months, adding to existing literature that these implants are safe and effective add-on procedures for cataract surgeons to incorporate into practice. KDB did not show statistically significant reductions, which may be due to inherent technique variability. iStent and iStent inject allow anterior segment surgeons to offer, in a single low-risk procedure, increased visual potential by removing the cataract and improved quality of life by decreasing dependence of eye drops, maintaining long term IOP control and slowing the progression of glaucoma. Prospective large-scale studies would help further elucidate the role of these MIGS procedures with CE.

CONTROL ID: 3527883

SUBMITTER (NAME ONLY): Weihong Lang

TITLE: Surface characterization of a new contact lens water gradient using fluorescent staining

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Lang, B. Tucker, R&D, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Weihong Lang: Commercial Relationship: Code N (No Commercial Relationship) | Bob Tucker: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

A fluorescently labelled C-reactive protein (CRP) was used to characterize a new contact lens material (NCLM) with a water gradient surface containing embedded phosphoryl choline (PC) groups. The uniformity and functionality of these groups were verified before and after 30 days of daily wear.

Methods: PC polymers with unique biocompatibility may inhibit nonspecific protein deposition. With strong affinity binding to PC groups, CRP was used to identify these groups.

Each new contact lenses material (NCLM) with the PC containing water gradient surface was treated with Alexa 488 labelled CRP. The treated lenses were rinsed in DI water and set on glass slide for fluorescent microscope study. Full view of lenses were collected to evaluate surface coating integrity. The same treated lenses were also cross sectioned and imaged to verify coating layer uniformity. This process was repeated using NCLM after worn for 30 days of daily wear and use of OPTI-FREE® RepleniSH®.

NCLM lenses were treated with Pyrenebutyric acid (PBA) for staining the silicone bulk, followed by Alexa 488-CRP staining. Each lens was cryosectioned and microscope images collected on both CRP and PBA channels for dual fluorescent stains.

Results: Top view new contact lenses material showed uniform coverage of the PC-containing water gradient layer. After 30 days of daily wear, the contact lens material still shows good coating layer uniformity, shown in Figure 1. In cross-section, the CRP-stained layer was visibly distinct from the PBA stained hydrophobic silicone section of the lens shown in figure 2.

Conclusions: The in vitro and ex vivo fluorescent staining technique showed evidence of a stable PC containing water gradient layer on the NCLM. After 30 days of daily wear, excellent coating uniformity remained, indicating the integrity of the water gradient structure despite on eye wear, exposure to OPTI-FREE® RepleniSH® and daily insertion, handling, rubbing, and removal.

CONTROL ID: 3527885

SUBMITTER (NAME ONLY): Sally Baxter

TITLE: Predictive Analytics for Glaucoma using Data from the All of Us Research Program

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.L. Baxter, B. Radha Saseendrakumar, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|S.L. Baxter, B. Radha Saseendrakumar, P. Paul, J. Kim, L. Bonomi, T. Kuo, L. Ohno-Machado, Department of Biomedical Informatics, University of California San Diego Health Sciences, La Jolla, California, UNITED STATES|R. Loperena, F. Ratsimbazafy, Vanderbilt Institute for Clinical and Translational Research, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|A. Ramirez, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|L. Ohno-Machado, Division of Health Services Research and Development, Veterans Affairs San Diego Healthcare System, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sally Baxter: Commercial Relationship: Code N (No Commercial Relationship) | Bharanidharan Radha Saseendrakumar: Commercial Relationship: Code N (No Commercial Relationship) | Paulina Paul: Commercial Relationship: Code N (No Commercial Relationship) | Jihoon Kim: Commercial Relationship: Code N (No Commercial Relationship) | Luca Bonomi: Commercial Relationship: Code N (No Commercial Relationship) | Tsung-Ting Kuo: Commercial Relationship: Code N (No Commercial Relationship) | Roxana Loperena: Commercial Relationship: Code N (No Commercial Relationship) | Francis Ratsimbazafy: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Ramirez: Commercial Relationship: Code N (No Commercial Relationship) | Lucila Ohno-Machado: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The All of Us Research Program is a nationwide prospective cohort study. As the only alpha phase demonstration project related to ophthalmology, our aims were to (1) externally validate a previously published model predicting need for surgery among individuals with glaucoma, (2) develop new models using All of Us data, and (3) share insights regarding the use of this data for ophthalmic research.

Methods: Electronic health record data were extracted for 1231 adult participants in All of Us diagnosed with primary-open angle glaucoma. We compared a previously published single-center cohort and the All of Us cohort with respect to demographics and need for glaucoma surgery. The performance of the single-center model was evaluated on All of Us data, based on area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, and specificity. All of Us data were then used to train new models using multivariable logistic regression (LR), artificial neural networks (ANN), and random forests (RF). These were cross-validated on All of Us data. Performance was evaluated based on AUC, accuracy, precision, and recall.

Results: The mean (standard deviation) age of the All of Us cohort was 69.1 (10.5) years, with 57.3% women and 33.5% Black or African American, both significantly exceeding representation in the single-center cohort ($p=0.04$ and $p<0.001$, respectively). Of 1231 participants, 286 (23.2%) needed glaucoma surgery. When applying the single-center model to All of Us data, accuracy was 0.69, and AUC was 0.49, indicating that the model was not generalizable to All of Us data. Using All of Us data to train new models resulted in superior performance: AUCs ranged from 0.80 (LR) to 0.99 (RF). Blood pressure (BP) had the highest relative importance for driving predictions in RF models.

Conclusions: Models trained with national All of Us data achieved superior performance compared to using single-center data. The relationship between BP and glaucoma warrants ongoing investigation. Novel big-data sources such as All of Us offer numerous opportunities for ophthalmic research.

CONTROL ID: 3527897

SUBMITTER (NAME ONLY): Jacob Fondriest

TITLE: Assessing Visual Function and Quality of Life in Children with JIA and JIA-Uveitis Younger than 7 years Old

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fondriest, Ophthalmology, Summa Health System, Akron, Ohio, UNITED STATES|A. Cassidy, T. Hennard, J. Lipscomb, V. Utz, S.T. Angeles-Han, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|C. Drews-Botsch, C. McCracken, S. Prahalad, J. Shantha, S. Yeh, Emory University, Atlanta, Georgia, UNITED STATES|J. McDonald, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Children with juvenile idiopathic arthritis (JIA) aged 7 and younger are at a greatest risk for uveitis. The impact of JIA-associated uveitis (JIA-U) on quality of life (QOL) and visual function of young children is not well characterized. We administered questionnaires in a cross-sectional study to compare visual function and QOL of children ages 2 to 7 with JIA and JIA-U.

Methods: Three validated questionnaires were administered to parents of 51 children, ages 2-7, diagnosed with JIA alone or JIA-U during their regular clinic visits at Cincinnati Children's Hospital Medical Center and Emory University. The Children's Visual Function Questionnaire (CVFQ) measures visual function from 0-1 with general health, general vision, competence, personality, family impact, and treatment subscales. The Pediatric Quality of Life Inventory (PedsQL) measures overall QOL from 0-100 with total, physical (e.g. sports), and psychosocial subscales. The Childhood Health Assessment Questionnaire (CHAQ) measures physical function (e.g. activities of daily living) from 0-3. Higher scores indicate better function and QOL in the CVFQ and PedsQL, respectively, but worse function in the CHAQ. Group differences were tested using the Student's T-Test.

Results: Of 51 children, 38 had JIA alone and 13 had JIA-U (Table 1). They were predominantly white (92%), non-Hispanic (96%), and female (84.%). Oligoarticular was the most common JIA subtype (33%), ANA was positive in 65%, and mean age at JIA diagnosis was 2.4 years (SD 0.99). There were no significant differences in the demographic or clinical characteristics of the groups.

CVFQ general vision and family impact subscales were significantly worse among children with JIA-U compared to those with JIA alone (0.83 vs. 0.93, $p=0.013$; and 0.83 vs 0.93, $p=0.004$, respectively). The CHAQ score was worse for children with JIA alone compared to JIA-U (0.38 vs 0.00, $p=0.009$). There were no significant differences in PedsQL scores.

Conclusions: Young children with JIA-U have worse visual function and impose a larger family burden, but have comparatively less physical limitation with activities of daily living than children with JIA alone. Emotional and labor-intensive burdens on families may be related to social interactions, appointments, and uncertainty of prognosis. Further studies are needed to characterize the impact of uveitis in young children with JIA.

CONTROL ID: 3527898

SUBMITTER (NAME ONLY): Larissa Lachi Silva

TITLE: Oral APX3330 treatment reduces L-CNV lesions in preclinical mouse model and confirms Phase 2 DR/DME clinical dose with sufficient distribution to human retina using PBPK modeling

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Lachi Silva, R.E. Stratford, S.K. Quinney, T.W. Corson, M.R. Kelley, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|N. Lambert-Cheatham, Michigan State University, East Lansing, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: APX3330 is a small molecule inhibitor of Ref-1, a target involved in key vascular and inflammatory ocular disease processes including diabetic retinopathy (DR), diabetic macular edema (DME) and wetAMD. The purpose was to determine the efficacy of oral administration of APX3330 to reduce lesion size in a laser-induced choroidal neovascularization (L-CNV) mouse model and to develop a physiological-based pharmacokinetic (PBPK) model for retinal delivery of APX3330 to confirm dosing for a Phase 2 trial.

Methods: Following laser treatment, mice received twice daily gavages of 25 or 50 mg/kg APX3330 or vehicle for 14 days. Optical coherence tomography (OCT), fundoscopy, and 3-dimensional quantification of agglutinin stained CNV were performed. The Ocular Compartmental Absorption and Transit (OCAT™) model within GastroPlus 9.6 was used to build a mechanistic compartmental model accounting for APX3330 systemic absorption and retinal distribution in the human eye. ADMET Predictor™ 9.5 was used to model systemic distribution and clearance using physicochemical and biopharmaceutical properties. PBPK simulation results for single oral doses of APX3330 (60, 180, and 240 mg) were compared to plasma concentrations observed in multiple Phase 1 clinical trials. Simulations for retinal exposure using 480 and 600 mg total daily doses across different dosing regimens were also performed.

Results: At both 25 and 50 mg/kg doses, APX3330 reduced size of L-CNV lesions by >50%. No obvious signs of ocular toxicity were observed during treatment. PBPK model predictions matched reported human plasma concentrations of APX3330 after oral administration and demonstrated predictive capability of the developed model. Predicted retinal exposures were 13.5; 12.3; 15.4; 16.5 and 20.7 ug*h/mL after 200 mg TID, 240 mg BID, 300 mg BID, 480 mg QD and 600 mg QD, respectively.

Conclusions: Oral administration of APX3330 safely and effectively reduced neovascularization in an L-CNV preclinical model. The PBPK model resulted in important insights into delivery of orally administered APX3330 to the human retina with predicted human retina levels significantly higher than observed and required for efficacy in preclinical studies. These findings confirm the 600 mg dose BID for APX3330 in a planned DR/DME Phase 2 trial.

CONTROL ID: 3527904

SUBMITTER (NAME ONLY): Michael Woodfin

TITLE: The Impact of COVID-19 Pandemic on the University of Washington Ophthalmology Residency Training Experience

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Woodfin, J. Huang, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|A. Roldan, K.D. Bojikian, M.T. Nguyen, S. Feng, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has significantly impacted surgical resident education. We sought to assess the impact of COVID-19 on ophthalmology resident training and wellness at the University of Washington through observing changes in volume of overnight on-call consults, resident clinics, and resident surgical cases, in addition to studying changes in sleep, activity, and resident wellness survey results.

Methods: A retrospective cohort study of ophthalmology residents at the University of Washington comparing clinical volumes, sleep and activity data recorded by a wrist actigrapher, and wellness surveys during a “pre-COVID” period from February 1st, 2020 to March 15 to the period of initial COVID response (“COVID period”) from March 16 to May 1st, 2020.

Results: The initial response to the COVID-19 pandemic resulted in a 64% decrease in resident clinic volume, 64% decrease in resident-surgical cases, and 50% decrease in on-call consult volume, see figure 1. The fraction of consults involving an open globe injury increased more than four-fold. Resident depersonalization as measured by Maslach Burnout Inventory decreased during the pandemic ($p=0.038$), see figure 2. Most residents experienced decrease emotional exhaustion and increased anxiety during the pandemic. There was no statistically significant change in recorded sleep or activity among residents before and during the pandemic.

Conclusions: The initial response to the COVID-19 pandemic at the University of Washington resulted in a large decrease in clinical, surgical, and on call volumes with mixed effect on ophthalmology resident well-being.

CONTROL ID: 3527913

SUBMITTER (NAME ONLY): Janelle Tong

TITLE: Applying cluster analysis to macular OCTs for prediction of visual field defects in glaucoma

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Tong, M. Kalloniatis, B. Zangerl, Centre for Eye Health, University of New South Wales, Sydney, New South Wales, AUSTRALIA|J. Tong, M. Kalloniatis, B. Zangerl, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|D. Alonso-Caneiro, Contact Lens and Visual Optics Laboratory, Centre for Vision and Eye Research, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To develop a normative model of the macular ganglion cell-inner plexiform layer (GCIPL) and evaluate its accuracy in prediction of visual field (VF) defects in patients with glaucoma.

Methods: Macular OCTs were acquired for 493 healthy and 37 glaucoma participants using the Spectralis OCT. GCIPL measurements from the healthy cohort were used to develop a normative model incorporating hierarchical cluster analysis, to identify locations with similar structural properties under considerations of normal variations in optic disc tilt position and aging characteristics. Glaucoma participants underwent 10-2 and 30-2 VFs using the Humphrey Field Analyzer, and GCIPL locations were binarized to VF-normal and VF-defective based on a pattern deviation cut-off of <2% for the corresponding VF location. Receiver operator characteristic (ROC) analyses based on the normative model were conducted to generate GCIPL cut-off values per cluster using Youden's criterion. Global and cluster-specific accuracy of the model was assessed by applying derived GCIPL cut-offs to individual locations and comparing areas under the ROC curves (AUROCs) respectively.

Results: The normative model resulted in 10 quasi-concentric clusters (Figure 1A) that largely co-locate despite various fovea to optic disc tilts, reflecting robust classification. The model demonstrated moderate global sensitivity and specificity in predicting VF defects from GCIPL thicknesses, at 0.75 and 0.76 respectively. AUROCs were significantly different between clusters ($P < 0.0001$, Welch's ANOVA), with central clusters demonstrating higher accuracy than peripheral clusters ($P = 0.009-0.04$, Figure 1B).

Conclusions: Normative models applying cluster analysis principles can predict VF defects from macular GCIPL measurements with moderate accuracy. However, spatial variability in peripheral macular locations were associated with poorer accuracies, suggesting that OCT alone may be insufficient to holistically predict macular function.

CONTROL ID: 3527914

SUBMITTER (NAME ONLY): Zaina Kahiel

TITLE: The 3-Year Incidence of Visual Impairment and its Risk Factors in Canada: The Canadian Longitudinal Study on Aging

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Kahiel, E.E. Freeman, School of Epidemiology and Public Health, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|M. Aubin, Department of Ophthalmology, Université de Montréal, Montréal, Québec, CANADA|M. Aubin, Hôpital Maisonneuve-Rosemont, Montréal, Québec, CANADA|R. Buhrmann, Department of Ophthalmology, University of Ottawa, Ottawa, Ontario, CANADA|M. Kergoat, Institut Universitaire de Geriatrie de Montréal, Montréal, Québec, CANADA|E.E. Freeman, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Canada does not have published data on the incidence of visual impairment. Our goal was to determine the 3-year incidence of visual impairment (VI) in Canada and its risk factors.

Methods: Data from 23,973 adults taking part in the Canadian Longitudinal Study on Aging Comprehensive Cohort baseline and 3-year follow-up exams were included in this prospective 3-year cohort study. Inclusion criteria included being 45 to 85 years of age, community-dwelling, and living near one of the 11 data collection sites across 7 Canadian provinces. Presenting binocular visual acuity was measured using the Early Treatment of Diabetic Retinopathy Study chart. VI incidence was defined as the development at follow-up of visual acuity worse than 20/40 in those with acuity better than or equal to 20/40 at baseline. Logistic regression was used to account for the complex survey design.

Results: 3.99% (95% Confidence Interval (CI) 3.75, 4.25) of Canadian adults developed VI over a 3-year period. There was a high degree of variability in the incidence rates between Canadian provinces with a low of 1.42% in Manitoba and a high of 7.33% in Nova Scotia. Uncorrected refractive error was the leading cause. Risk factors for incident VI included older age (odds ratio (OR)=1.07, 95% CI 1.06, 1.07), Black race (OR=2.64, 95% CI 1.36, 5.14), lower household income (OR=1.73 for those making less than \$20,000 per year, 95% CI 1.24, 2.40), current smoking (OR=1.78, 95% CI 1.37, 2.32), and province.

Conclusions: Incidence of visual impairment is common in older Canadian adults, varies markedly between provinces, and is largely due to treatable causes. Risk factors for VI suggest sub-groups that may benefit from interventions to improve access to eye care.

CONTROL ID: 3527916

SUBMITTER (NAME ONLY): Ranjay Chakraborty

TITLE: Effects of mild- and moderate-intensity illumination on axial length and choroidal thickness in young adults

SESSION TITLE: Effects of Light Intensity and Blur on Refractive Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Chakraborty, N. Anstice, Optometry, Flinders University, Adelaide, South Australia, AUSTRALIA|K. Baranton, P. Lacan, M. Guillon, C. Barrau, T. Villette, Center Innovation & Technologies Europe, Essilor International SAS, Charenton-le-Pont, Île-de-France, FRANCE|D. Spiegel, Essilor Asia Pacific Pte Ltd, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Rearing under high-intensity illumination produces a hyperopic shift in chicks and inhibits the development of form-deprivation myopia in chicks and primates. Recent studies also show that time spent outdoors is protective against the development of myopia in children. In this study, we examined the effects of 120 minutes of exposure to 500 and 1000 lux of bright illumination on axial length and choroidal thickness (ChT) in young adult participants.

Methods: Fifteen participants (mean age, 21.60 ± 2.16 years) with a mean refraction of -0.30 ± 0.39 D were exposed to 500 ($142 \mu\text{W}/\text{cm}^2$) and 1000 ($284 \mu\text{W}/\text{cm}^2$) lux of illumination for 120 minutes in a dark room on two different days, using a pair of custom-made light-emitting glasses. On each day, a series of ocular measurements were performed in the left eye before the light exposure (0 minutes), at 30, 60 and 120 minutes of light exposure, and 30 minutes after light offset to measure recovery. All ocular measurements were repeated on a third measurement day without any light stimulus in darkness (~ 5 lux). Axial length was measured using the Lenstar optical biometer and the changes in the subfoveal ChT were measured using the Cirrus 5000 optical coherence tomographer. Measurements are reported as mean \pm standard error mean and statistical comparisons were made using two-way ANOVA.

Results: Axial length increased significantly across all time points in darkness. Exposure to 500 and 1000 lux of continuous illumination resulted in a gradual and significant reduction in axial length at 30, 60, and 120 compared to darkness (change in axial length at 60 minutes: darkness, $+0.014 \pm 0.003$ mm; 500 lux, -0.007 ± 0.002 mm; 1000 lux -0.010 ± 0.004 mm, $p < 0.001$). Exposure to 500 and 1000 lux of illumination caused a significant thickening of the choroid (change in ChT at 60 minutes: darkness, -0.011 ± 0.006 mm; 500 lux, $+0.006 \pm 0.003$ mm; 1000 lux $+0.008 \pm 0.004$ mm, $p = 0.025$). None of the ocular changes were significantly different between the 500 and 1000 lux illumination levels ($p > 0.05$). All ocular changes recovered to normal within 30 minutes of light offset.

Conclusions: Our results show that exposure to mild- or moderate-intensity illumination can induce a significant reduction in axial length and thickening of the choroid in young subjects. Similar to animal models, these changes were found to be sensitive to the duration of light exposure.

CONTROL ID: 3527926

SUBMITTER (NAME ONLY): Jack Phu

TITLE: Static automated perimetry using a new head-mounted virtual reality platform, Virtual Field, compared with the Humphrey Field Analyzer in glaucoma and optic nerve disease

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Phu, M. Kalloniatis, University of New South Wales, UNSW Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure (Abstract): Jack Phu: Commercial Relationship(s);Virtual Field:Code F (Financial Support) | Michael Kalloniatis: Commercial Relationship(s);Virtual Field:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To compare the visual field outputs obtained using Virtual Field against the Humphrey Field Analyzer (HFA) in subjects with glaucoma or optic nerve head disease, and to determine its potential deployment as a portable, low-cost alternative for perimetric testing.

Methods: One eye (the eye with more severe disease) from 43 subjects with open angle glaucoma or optic nerve disease underwent testing using both Virtual Field and the HFA. Both devices presented Goldmann size III stimuli in the 24-2 test grid arrangement. Virtual Field uses a screen with a background luminance of 0.218 cd.m^{-2} , whereas the HFA uses a projection system with a background luminance of 10 cd.m^{-2} . All patients undertook three tests on each device in random order. We compared conventional global indices (mean deviation [MD], pattern standard deviation [PSD], "cluster" criterion pass/fail, Glaucoma Hemifield Test [GHT]), pointwise sensitivity and probability scores, and the overall number of defects found using each device, after averaging all indices across all three tests.

Results: MD and PSD were correlated between both devices (Fig 1). There were differences in the individual decibel values reported by each device due to the differences in background luminance and hence retinal adaptation. Bland-Altman analysis revealed a bias of 6.1 dB, with 95% limits of agreement between -1.8 to 14.0 dB, with the HFA results returning higher readings. 10 (23%) subjects showed more defects on the HFA, 3 (7%) had more defects on Virtual Field, and the others had no differences between devices. On average, the HFA identified 3 more defects on the pattern deviation map compared to Virtual Field. Using a combinatory criterion of PSD ($>2\text{dB}$), GHT (outside normal limits) and "cluster" cut-offs, there were no significant differences between devices in identifying the presence of disease (6 cases identified by only Virtual Field, 1 only by the HFA, 31 by both, and 5 by neither).

Conclusions: Virtual Field is a head-mounted perimeter that produces functionally indistinguishable results to the HFA, offering a low-cost, portable alternative to specialised clinic-based perimetry devices.

CONTROL ID: 3527930

SUBMITTER (NAME ONLY): Siri Uppuluri

TITLE: Demographics of Ocular Injury in Infants: An Analysis of the NEISS Database

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Uppuluri, A. Uppuluri, M.A. Zarbin, N. Bhagat, Department of Ophthalmology & Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The objective of this project was to describe the demographics and characteristics of ocular injuries among infants ages 0 to 12 months using data documented by the National Electronic Injury Surveillance System (NEISS) database from 2009 to 2019.

Methods: The NEISS Database was used to identify cases of ocular injury among the infant population (0-12 months) between 2009 to 2019. The NEISS Database is a collection of data regarding consumer product-related injuries in the United States derived from a representative probability sample of hospital emergency departments (ED) in the U.S. and its territories. The patient population was divided into three age subgroups (1-4 months, 5-8 months, 9-12 months), and statistical analysis was performed using IBM SPSS 23.

Results: In total, 21,013 cases of ocular injury in the infant population (0-12 months) were identified. Among infant ocular injuries, males (55%), the 9-12 months age group (54.9%), and Whites (45.3%) accounted for the plurality of cases by gender, age group, and race, respectively. Temporally, the plurality of injuries occurred on Sunday (17.4%) and in July (11.0%) with regard to day of the week and month of the year for all cases of ocular injury. The most common diagnosis in cases of infant ocular injury over the study time period was contusion, accounting for 45.8% of cases, which was nearly three times more common than the second most common diagnosis of dermatitis/conjunctivitis (16.6%). The vast majority of infant ocular injuries occurred at home (71.0%), and the three most commonly involved consumer products among the cases of ocular injury were detergents and chemicals (26.1%), toys (12.9%), and home furniture (10.9%). When stratifying ocular injuries by age, toys (12.9%) were the most commonly involved consumer product in the 1-4 months age group, while detergents and chemicals were the most commonly involved product in the 5-8 months and 9-12 months age groups. By gender, detergents and chemicals were the most common consumer product involved in ocular injury in both boys (23.6%) and girls (29.2%).

Conclusions: In the infant population studied (ages 0-12 months) in the ED, between 2009-2019, ocular injuries occurred most commonly in males, in the oldest age subgroup of 9-12 months, in Whites, and in July. The most common diagnosis for ocular injury was contusion, and the most commonly associated consumer product was detergents and chemicals.

CONTROL ID: 3527931

SUBMITTER (NAME ONLY): Albert Liao

TITLE: Vitrectomy for vitreous hemorrhage in infants with retinopathy of prematurity: clinical characteristics and anatomic outcomes

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Liao, T. Xu, G.B. Hubbard, P. Rao, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Albert Liao: Commercial Relationship: Code N (No Commercial Relationship) | Tan Xu: Commercial Relationship: Code N (No Commercial Relationship) | G Hubbard: Commercial Relationship: Code N (No Commercial Relationship) | Prethy Rao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a sight-threatening illness due to abnormal development of retinal vasculature in premature infants. While non-clearing vitreous hemorrhage (NCVH) in ROP patients is associated with progression to late-stage disease, controversy exists regarding the management, surgical timing, and outcomes of these cases. We performed a retrospective, observational clinical study to evaluate patient characteristics, anatomical outcomes, and visual outcomes in infants with ROP who underwent pars plana vitrectomy (PPV) for NCVH.

Methods: This is a single institution, retrospective chart review of ROP infants who underwent PPV for NCVH from November 1st, 1998 to April 30th, 2019. Data collected included postmenstrual age (PMA) at time of NCVH diagnosis, ROP status at time of VH, previous treatments, time between diagnosis of NCVH and PPV, intraoperative findings, and anatomic outcomes.

Results: Seven eyes of 7 patients were included (table 1). Median (range) gestational age was 25.0 (23.0-27.0) weeks. Median birth weight was 652.0 grams (445.0-822.0). PMA at the time of NCVH diagnosis was 37.6 weeks (31.0-45.3). At the last preoperative visit, all eyes were noted to have attached retinas by clinical exam. The median time to PPV from diagnosis of NCVH was 37.0 days (5.0-45.0). Median post-menstrual age (PMA) at PPV was 40.8 (36.3-47.0) weeks. The overall median time from NCVH diagnosis to PPV was 37.0 days (5.0-45.0). Intraoperatively, 3 of 7 eyes (42.9%) were noted to be detached. Median time from NCVH diagnosis to PPV was 42.0 days (5.0-45.0) in eyes with retinal detachments (RD) versus 29.0 days (20.0-37.0) in eyes without RDs. Five of 7 (71.4%) eyes remained attached at the last follow up. Of the 4 eyes with documented visual acuity upon follow-up, 2 eyes exhibited fixation behavior and 2 eyes did not exhibit fixation behavior. The median follow up time was 27.0 months (1.0-152.0).

Conclusions: NCVH in ROP requiring PPV is rare. These eyes may be at higher risk for developing a RD, particularly if there is an extended duration of time between VH diagnosis and PPV. The visual prognosis for these patients remains poor despite surgical intervention.

CONTROL ID: 3527936

SUBMITTER (NAME ONLY): Edmund Tsui

TITLE: Objective measurement of anterior chamber cells in children with uveitis using anterior segment optical coherence tomography

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Tsui, J.L. Chen, O. Leyva, S. Fung, G.N. Holland, Ophthalmology, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|E. Tsui, H.A. Rasheed, S. Fung, S.R. Sadda, G.N. Holland, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|E. Baghdasaryan, S.R. Sadda, Doheny Eye Institute, Los Angeles, California, UNITED STATES|D.K. McCurdy, Pediatrics, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|N.J. Jackson, Division of General Internal Medicine and Health Services Research, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the feasibility of anterior segment optical coherence tomography (AS-OCT) for the measurement of anterior chamber (AC) cells in children with uveitis and to evaluate different AS-OCT acquisition modes for measuring AC cells.

Methods: We prospectively enrolled children younger than 18 years of age with histories of uveitis involving the anterior chamber and healthy children without histories of uveitis or intraocular surgery as controls. All children underwent a comprehensive eye examination and grading of AC cell using the Standardization of Uveitis Nomenclature (SUN) grading system. All were imaged using the Optovue Avanti RTVue XR AS-OCT. Each underwent AS-OCT scans using two acquisition modes: a single cross-sectional line scan and 8 cross-sectional line scans in an asterisk formation. Two independent, masked graders manually counted cells (represented by hyperreflective foci in AS-OCT images). Rater agreement was assessed using intraclass correlation (ICC).

Results: We evaluated 59 eyes of 30 children with histories of uveitis (mean age 12.1 years, range 3-17 years; 19 [63%] females) and 40 eyes of 20 control children (mean age 10.9 years, range 4-17 years; 9 [45%] females). Of 59 eyes with uveitis, 32 (54%) had Grade 0 cell; 12 (20.3%) had 0.5+ cell; 5 (8.5%) had 1+ cell; 8 (13.6%) had 2+ cell; and 2 (3.4%) had 3+ cell on clinical examination. For line scans, mean OCT cell counts for each grade were: Grade 0, 0.17 (range 0-5); 0.5+, 0.88 (0-3); 1+, 2.9 (0-7); 2+, 9.7 (0-25); and 3+, 25.8 (17-35). For asterisk formation scans, mean OCT cell counts for each grade were: Grade 0, 0.11 (range, 0-4); 0.5+, 0.49 (0-3); 1+, 1.4 (0-6); 2+, 5.5 (0-18); and 3+, 22.0 (12-31). ICC of graders for line and asterisk formation scans were 0.87 and 0.90, respectively, with no significant difference between acquisition modes (95% confidence interval -0.04 to 0.14). No eyes of control children had cells on AS-OCT images.

Conclusions: Quantification of AC cell in children with uveitis is feasible with AS-OCT and has excellent reliability between different graders. Given the similarity in cell counts between line and asterisk formation scans, AS-OCT line scans may be a more suitable option given the relative speed of image acquisition compared to asterisk formation scans, especially in children.

CONTROL ID: 3527939

SUBMITTER (NAME ONLY): Jinhua Bao

TITLE: Myopia control with spectacle lenses with aspherical lenslets: a 2-year randomized clinical trial

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Bao, Y. Huang, X. LI, H. Chen, Eye Hospital and School of Ophthalmology and Optometry of Wenzhou Medical University, CHINA|J. Bao, Y. Huang, X. LI, A. Yang, E. Lim, D. Spiegel, B. Drobe, H. Chen, Wenzhou Medical University–Essilor International Research Center (WEIRC), CHINA|A. Yang, E. Lim, D. Spiegel, B. Drobe, R&D AMERA, Essilor International, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate the myopia control efficacy of two new designs of spectacle lenses with concentric rings of contiguous aspherical lenslets in a 2-year clinical trial.

Methods: One hundred and seventy Chinese children (aged 8 to 13 years old, myopia between -0.75D and -4.75D) with myopia were randomly assigned to wear one of the three spectacle lenses: spectacle lenses with highly aspherical lenslets (HAL), spectacle lenses with slightly aspherical lenslets (SAL), or control single-vision lenses (SVL) for 2 years. Spherical equivalent of cycloplegic autorefraction (SER) and axial length (AL) were measured on a six-monthly basis. Wearing time was assessed using a questionnaire at each visit.

Results: A total of 157 children completed the 2-year study, of which, 54, 53, and 50 were in the HAL group, SAL group, and SVL group, respectively. After 2 years, the mean SER and AL (\pm SEM) of the SVL control group increased by -1.46 ± 0.60 D and 0.69 ± 0.26 mm, respectively. Compared with SVL, spectacle lenses with aspherical lenslets significantly slowed myopia progression (HAL, -0.66 ± 0.08 D, difference 0.80 D; SAL, -1.04 ± 0.06 D, difference 0.42 D) and axial elongation (HAL, 0.34 ± 0.03 mm, difference 0.35 mm; SAL, 0.51 ± 0.03 mm, difference 0.18 mm; all $p < 0.001$). In children who wore their lenses every day for at least 12 hours per day, the reduction in SER and AL, compared to SVL group, was greater at 0.99 D ($p < 0.001$) and 0.41 mm ($p = 0.03$) for HAL ($n = 32$) and at 0.57 D ($p = 0.04$) and 0.26 mm ($p = 0.02$) for SAL ($n = 28$), respectively.

Conclusions: Spectacle lenses with aspherical lenslets were effective in slowing myopia progression and axial elongation in children over a two-year period, compared with SVL. Myopia control efficacy was higher in children who wore their lenses full-time (≥ 12 hours/day) and spectacle lenses with highly aspherical lenslets.

CONTROL ID: 3527984

SUBMITTER (NAME ONLY): John Dodd

TITLE: Protective Effects of 2 Melanocortin Agonists Delivered by Intravitreal Injection in Mouse Models of Retinopathy

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Dodd, M. Makhlina, W.H. Yang, C. Spana, Palatin Technologies Inc, Cranbury, New Jersey, UNITED STATES|A.W. Taylor, T. Ng, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): John Dodd: Commercial Relationship(s);Palatin Technologies Inc:Code E (Employment) | Marie Makhlina: Commercial Relationship(s);Palatin Technologies Inc:Code E (Employment) | Wei Yang: Commercial Relationship(s);Palatin Technologies Inc:Code E (Employment) | Andrew Taylor: Commercial Relationship(s);Palatin Technologies Inc:Code F (Financial Support);Palatin Technologies Inc:Code C (Consultant) | Tat Fong Ng: Commercial Relationship(s);Palatin Technologies Inc:Code F (Financial Support) | Carl Spana: Commercial Relationship(s);Palatin Technologies Inc:Code E (Employment)

ABSTRACT BODY:

Purpose: Targeting the melanocortin system, which plays a key role in promoting resolution of the inflammatory process, may be protective against ocular disease. The studies presented here investigated the effects of 2 melanocortin receptor pan-agonists, PL8331 and PL9654, delivered by intravitreal (IVT) injection in mouse models of retinopathy.

Methods: In Study 1, mice received 40-mg/kg intraperitoneal streptozotocin once daily for 7 days to induce hyperglycemia. They were then left untreated or were given uniocular 1- μ l IVT injections of 3.3 μ M PL8331 at 1, 4, 8, 12, and 16 weeks following hyperglycemia induction. At 17 weeks, retinas were evaluated for retinal ganglion cell (RGC) density and vascular endothelial growth factor (VEGF) concentration.

In Study 2, mice received 5 uniocular laser burns to the retina to induce choroidal neovascularization. They then received 1 of 6 IVT treatments immediately after laser burn and again on Day 15: vehicle, anti-VEGF antibody, 10 or 100 μ M PL8331, or 10 or 100 μ M PL9654. Fundus fluorescein angiography and immunohistochemistry were used to quantify the extent of leakage, neovascularization, and fibrosis.

Results: In Study 1, RGC density was significantly reduced and VEGF concentrations were significantly increased in hyperglycemic mice versus normal glycemic controls ($P \leq 0.05$ and $P < 0.005$, respectively), but there were no statistically significant differences in RGC density or VEGF concentration between retinas of hyperglycemic mice treated with PL8331 and healthy control retinas. In Study 2, the extent of leakage, neovascularization, and fibrosis were significantly reduced ($P < 0.05$) in mice treated with anti-VEGF antibody or either dose of PL8331 or PL9654 compared with vehicle.

Conclusions: IVT delivery of the melanocortin agonists PL8331 and PL9654 significantly reduced several markers of retinal damage in mouse models of eye injury, supporting the continued development of PL8331 and PL9654 for the treatment of ocular disease.

CONTROL ID: 3527990

SUBMITTER (NAME ONLY): Harris Ahmed

TITLE: The Relationship of the Atopic Triad and Acute Ocular Outcomes in Patients with Stevens-Johnson Syndrome

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Ahmed, J.T. Kwan, T. Succar, J. Chodosh, H.N. Saeed, Cornea, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|H. Ahmed, Ophthalmology, Loma Linda University, Loma Linda, California, UNITED STATES|M. Kimura, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Controversy exists as to the exact autoimmune pathophysiology of Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN). Because atopy is a common immune disorder, we conducted a retrospective, observational chart review to determine the incidence of components of the atopic triad (AT; atopic dermatitis, asthma, or allergic rhinitis) in patients with history of SJS/TEN and then examined if a difference exists in acute ocular outcomes in SJS/TEN patients who have AT vs those who don't have AT.

Methods: Patients with history of any of the AT constituents were identified using the Research Patient Data Registry of Mass General Brigham (MGB). A combined search was then run to identify all SJS/TEN patients within this group. Diagnosis of SJS/TEN was confirmed by biopsy report or exam by dermatology or burn service as documented in the medical record. Chart review was done to confirm clinical diagnosis of the atopic conditions and that they were documented as occurring prior to the diagnosis of SJS. The primary outcome was the worst acute ocular severity (AOS) score reached during the acute SJS hospitalization. All statistics were performed in R version 4.0.2. Means with standard deviations are presented for ordinal variables.

Results: Twenty-three unique patients with atopic conditions and confirmed history of SJS/TEN were included. Four patients had a history of atopic dermatitis, 10 of allergic rhinitis, and 18 of asthma.* One hundred seventy seven SJS/TEN patients without history of any atopic conditions were included as controls. One hundred fifty-five of these patients had AOS scores available for analysis. Worse mean AOS score was seen in those with any component of the AT vs controls ($p=0.01542$). The prevalence of atopy in this SJS population exceeded that in the general MGB population ($P < .0001$).

*Total number of unique patients is fewer than the sum of the groups as several patients had more than one atopic condition.

Conclusions: In this study, there was worse acute SJS-induced ocular disease in those with a history of atopy compared to those without. A history of atopy may exist at a higher-than-expected rate in SJS/TEN. The underlying mechanisms to explain these associations are not known. Plausible contributory factors may include baseline immune dysregulation, increased inflammatory markers, and an IgE mediated component of disease onset or exacerbation in SJS/TEN.

CONTROL ID: 3528013

SUBMITTER (NAME ONLY): Hiten Doshi

TITLE: Unsupervised Machine Learning Identifies Relevant Patterns of Loss, and Quantifies Response to Treatment in Visual Fields from Eyes with Idiopathic Intracranial Hypertension

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Doshi, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|E. Solli, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|L.R. Pasquale, M.J. Kupersmith, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|M. Wall, The University of Iowa Hospitals and Clinics Department of Pathology, Iowa City, Iowa, UNITED STATES|M.J. Kupersmith, Neurology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Assessment of regional visual field (VF) changes typically requires qualitative, subjective analysis by a clinician. A type of unsupervised machine learning known as archetypal analysis (AA) identifies objective, quantitative patterns of VF loss in glaucoma. We investigated the use of AA to quantify and monitor disease-specific VF defects in idiopathic intracranial hypertension (IIH).

Methods: We performed AA within the R statistical environment on 2,862 VFs prospectively collected from 165 participants in the IIH Treatment Trial. We decomposed each study eye VF into a weighted mixture of the ATs (total weight =1.0). We decomposed VFs from 61 control eyes according to the IIH ATs to define a minimum AT weight change of 9% as clinically relevant. We developed an AT score based on the cumulative changes in weights for all ATs, which showed recovery, decline or no change in visual function from baseline.

Results: Using a 10-fold cross-validation model, we identified 14 IIH-specific archetypes that were distinguishable from controls (Figure 1). AT scores correlated strongly with change in MD ($R^2=0.80$, $p<0.001$). Mean AT scores distinguished treatment failures from non-treatment failures ($p<0.001$). The treatment benefit of acetazolamide was best reflected in the relative weight of AT2 (a near-normal AT) at trial outcome (0.27, 95% confidence interval (CI): 0.24-0.30 for acetazolamide, vs. 0.21, 95%CI: 0.18-0.24 for placebo, $p=0.007$). Study eyes with AT2 weight $\geq 44\%$ (≥ 1 SD above mean) at baseline had a better visual outcome based on AT2 weight at 6 months ($p<0.001$); however, a significant treatment effect for acetazolamide was only demonstrable among eyes with AT2 weight $<44\%$ at baseline ($p=0.034$; Figure 2). In addition, AA revealed residual VF defects in 70 eyes deemed normal ($MD \geq -2.00$) at 6 months, which frequently included enlarged blind spots, step, and arcuate defects.

Conclusions: AA quantifies changes in regional IIH-specific VF defects over time, thus increasing the utility of VF analysis. AT2 weight at baseline identifies patients who may respond best to treatment, suggesting that AA can provide prognostic value. Further, AA uncovers residual defects not otherwise revealed by global VF indices, such as MD.

CONTROL ID: 3528020

SUBMITTER (NAME ONLY): Christos Boutopoulos

TITLE: A smart vitrector equipped by a fiber-based OCT sensor mitigates simulated iatrogenic retinal injuries during vitrectomy in pigs

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Boutopoulos, A. Abid, F. Rezende, R. Duval, Universite de Montreal, Montreal, Quebec, CANADA|F. Rezende, R. Duval, Hopital Maisonneuve-Rosemont, Montreal, Quebec, CANADA|C. Boutopoulos, A. Abid, Hopital Maisonneuve-Rosemont Centre de Recherche, Montreal, Quebec, CANADA|

Commercial Relationships Disclosure (Abstract): Christos Boutopoulos: Commercial Relationship(s);United States Provisional Patent Application No. 63/109,040,:Code P (Patent) | Alexandre Abid: Commercial Relationship(s);United States Provisional Patent Application No. 63/109,040,:Code P (Patent) | Flavio Rezende: Commercial Relationship(s);United States Provisional Patent Application No. 63/109,040,:Code P (Patent) | Renaud Duval: Commercial Relationship(s);United States Provisional Patent Application No. 63/109,040,:Code P (Patent)

ABSTRACT BODY:

Purpose: The occurrence of iatrogenic retinal breaks (IRB) in pars plana vitrectomy (PPV) is a complication that compromises the overall efficacy of the surgery. A subset of IRB occurs when the retina (rather than the vitreous gel) is cut accidentally by the vitrector. We hypothesise the a smart vitrector, equipped by a fiber-based optical coherence tomography (OCT) sensor, can detect intraoperatively the onset of IRB and activate promptly a PPV machine response to prevent them. We developed such a system and performed PPV on pigs to validate it.

Methods: We fabricated the smart vitrectors by attaching a miniaturised fiber-based OCT sensor (125 µm in diameter) on commercial vitrectors (25G). The OCT sensor was appropriately positioned to detect undesirable retina displacement towards the vitrector orifice (i.e., IRB onset). The smart vitrector was connected to a commercial vitrectomy machine as in standard PPV. We used a customized OCT machine and a built-in algorithm to process the intraoperative signal. The system response time to an IRB onset was measured and compared to that of the average surgeon. Finally, two surgeons validated its ability to prevent simulated IRB (i.e., vitrector manipulations aiming to “bite” attached or detached retina) by performing PPV in 2 two pigs. Note that the system requires no signal interpretation by the surgeons.

Results: We found that the response time of the system (28.9 ± 6.5 ms) is 12-times faster compared to that reported for intraocular maneuvers performed by surgeons ($p < 0.0001$). We show that an additional 2-times improvement can be attained with minor technical modifications that require proprietary access to the vitrectomy machine that was used. Ex-vivo validation (porcine eyes) showed that the system prevents 78.95% (15/19) (95% CI: 54.43 – 93.95) of simulated IRB, while in-vivo validation showed that the system prevents or mitigates 70.37% (38/54) (95% CI: 56.39 – 82.02) of simulated IRB.

Conclusions: Our results are consisted with the hypothesis that an OCT – sensor attached to the vitrector can prevent IRB by providing intraoperative feedback to the PPV machine. Importantly, the use of the smart vitrector with its safety mechanism requires no modifications of the established PPV procedure. It can mitigate a significant proportion of IRB and thus improve the overall efficacy of the surgery.

CONTROL ID: 3528047

SUBMITTER (NAME ONLY): Lars Omlor

TITLE: High resolution retinal defocus measurement using digital structured illumination

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Omlor, Corporate Research and Technology, Carl Zeiss Inc., Pleasanton, California, UNITED STATES|K.G. Foote, C. Leahy, A. Carpenter, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lars Omlor: Commercial Relationship(s);Carl Zeiss Inc.:Code E (Employment) | Katharina Foote: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Conor Leahy: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Amanda Carpenter: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment)

ABSTRACT BODY:

Purpose: Retinal defocus maps can provide clinically relevant information for diagnosis and monitoring of disease. We investigated a novel construction of defocus maps of the retina using novel analyses of slit-scanning ophthalmoscopy data.

Methods: The CLARUSTM 700 (ZEISS, Dublin, CA) slit-scanning ophthalmoscope projects broad stripes onto the retina and records images of stripe illuminations. Using prototype software this stripe scanning was done with strongly overlapping stripes (1-pixel step) which can be converted into digital structured illumination using sinusoidal weighted sums. Sinusoidal illumination has the special property of staying a sine wave under defocus with changing amplitude. This amplitude change is a direct measure of optical defocus and can be analyzed to produce high-res. retinal defocus map, especially when different frequencies of illumination are used. We demonstrate the validity of the method on test-object and real eye data.

Results: Defocus maps generated from the sinusoidal illumination show both the optical defocus due to the optics, and the aberrations of the eye and retinal height of structures. The sine-amplitudes as a function of frequency represent the illumination modulation transfer function and a width-analysis generates a retinal defocus map. The defocus map of a ridged test-object (Fig.1) clearly shows the different height features (e.g. ridges and plateaus), and the defocus map of a human eye (Fig. 2) shows features with expected retinal elevations (e.g. vessels, fovea, optic nerve). Quantitative analysis of defocus as height is difficult as it is not clear at which depth the light is reflected.

Conclusions: Overlapping stripe illumination provides an information rich dataset which can be analyzed in many different ways. Here we showed that conversion into structured illumination allows the direct analysis of the illumination defocus, which is a direct measure of the optical properties of the eye and the retinal height profile. This analysis could enhance the detection of retinal elevations with clinical significance, including tumors, retinal detachments, or staphylomas.

CONTROL ID: 3528048

SUBMITTER (NAME ONLY): Irmak Karaca

TITLE: Association of oral montelukast with reduced odds of developing neovascular age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Karaca, W. Matsumiya, A. Akhavanrezayat, G. Uludag, C. Yasar, A. Mobasserian, J.J. Hwang, S. Lajevardi, B.C. Lam, R. Afridi, D.V. Do, Y.J. Sepah, Q.D. Nguyen, Ophthalmology, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Given the role of chronic inflammation in the pathogenesis of age-related macular degeneration (AMD), montelukast might have a potential protective impact on the development of neovascular AMD (nAMD) through an anti-inflammatory effect including its selective antagonism for cysteinyl leukotriene receptor 1 (CysLTR1). The proposed case-control study aimed to evaluate the association of oral montelukast with reduced odds of nAMD development.

Methods: The index study was conducted using Institutional Cohort Finder tool, and included 1913 patients who were diagnosed as nAMD (ICD: H35.32 and 362.52) and visited the Byers Eye Institute at Stanford from 1991 to 2020, and 1913 age- and gender- matched control subjects without nAMD. The subjects were assessed for the presence of nAMD risk factors (e.g. smoking history, Caucasian race, hypertension, hyperlipidemia) and for the use of specific medications (e.g. oral montelukast, nasal or oral cromolyn [mast cell stabilizer], oral steroids, oral NSAIDs, oral H1-antihistamines). Then, the odds ratio (OR) calculations using multivariable conditional logistic regression analyses were performed in order to assess the effect of oral montelukast use on reducing the odds of nAMD development, adjusting for possible risk factors.

Results: A total of 47 (2.5%) nAMD cases were identified to have a history of oral montelukast use prior to nAMD diagnosis, compared to 84 (4.4%) controls (crude OR: 0.54, P=0.0001). In the multivariable analysis, montelukast usage was significantly associated with reduced odds of nAMD (adjusted OR: 0.57, P=0.004). On the other hand, Caucasian race (adjusted OR 1.52, P<0.0001), history of smoking (adjusted OR: 1.91, P<0.0001), and NSAIDs use (adjusted OR: 0.75, P=0.005) were found to have significant relationship with increased odds of nAMD.

Conclusions: The study results suggested that oral montelukast consumption is linked to reduced odds of nAMD development. Future prospective cohort studies is needed to validate these findings.

CONTROL ID: 3528050

SUBMITTER (NAME ONLY): Cheng-Hui Lin

TITLE: Identification of cis-regulatory elements that allow for AAV-based Müller glial-specific labeling and manipulation in the retina

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lin, C. Chan, M. Wu, A. Davis, S. Wang, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Cheng-Hui Lin: Commercial Relationship: Code N (No Commercial Relationship) | Candace Chan: Commercial Relationship: Code N (No Commercial Relationship) | Man-Ru Wu: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Davis: Commercial Relationship: Code N (No Commercial Relationship) | Sui Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Müller glial cells (MG), the major type of glia in the retina, provide structural and functional support to retinal neurons, and play important roles in a variety of retinal diseases. Recent advances in cell reprogramming also suggest that regeneration of desired neurons from MG in mammalian retina may offer promising cues for retina diseases. To study the function of MG and stimulate their regeneration, developing the molecular tools that allow for easy access of MG in vivo in mammalian retina are of fundamental importance. Adeno-associated viruses (AAVs)-based tools that can specifically label MG have been developed. However, there are critical limitations. First, the commonly used GFAP promoter often responds to disease insults in MG, leading to uneven expression under control and diseases conditions. Second, AAVs that can direct gene manipulation via the Cre-LoxP system in MG are not available. The goal of this study is to overcome these limitations, and develop engineered AAVs that allow for MG-specific labeling and manipulation in mammalian retina.

Methods: We first searched for cis-regulatory elements (CREs) that could drive MG-specific expression and were unresponsive to disease insults. We then integrated these CRMs into AAV vectors to drive EGFP or Cre/CreER expression, and tested their specificity in vivo in mice. The neurotoxin NMDA was used to investigate whether these CRMs respond to injuries. We compared the specificity of the identified CRMs with the published GFAP promoter in this study.

Results: We identified multiple novel CRMs that can direct expression specifically in MG in vivo in mice. When integrated into AAVs, one of these CRMs, namely MG1, was able to drive MG-specific expression, and its activity was not affected in the presence of NMDA. In addition, the AAV-MG1-CreER virus can activate the tdTomato reporter gene specifically in MG in a tamoxifen and Cre-dependent manner in Ai9 mice. More importantly, the MG1 CRM was only 93bp, which does not impact the packaging capacity, allowing for additional genes in AAVs.

Conclusions: We identified novel MG-specific cis-regulatory elements, and developed novel AAV tools that can specifically label and manipulate MG in an injury-independent manner in vivo. These tools can significantly benefit the study of MG function and regeneration in mammalian retina.

CONTROL ID: 3528051

SUBMITTER (NAME ONLY): William Swanson

TITLE: Use of Oriented Sinusoidal Stimuli to Identify Shallow Scotomas

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.H. Swanson, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|H.J. Wyatt, SUNY College of Optometry, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): William Swanson: Commercial Relationship: Code N (No Commercial Relationship) | Harry Wyatt: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have found that glaucomatous perimetric defects can show good agreement with structural defects, and that an elongated sinusoidal stimulus can be oriented based on structural defects to identify scotomas. Here we extend this finding, by testing angioscotomas in healthy eyes.

Methods: Right eyes of healthy adults were tested with a DLO (Digital Light Ophthalmoscope, Aeon Imaging, Bloomington IN) which gathered fundus images during stimulus presentation to allow registration of eye movements. The first stimulus was the size III perimetric stimulus (circle at top in Figure 1). Thresholds were measured at 247 locations in a 13 x 19, 0.5°-interval grid from 11° to 17° horizontally, and -3° to +6° vertically. A ZEST algorithm used 6 trials to estimate contrast threshold at each location. The fundus images were used to infer retinal stimulus location on each trial. Three custom stimuli were developed, each being the first derivative of a Gaussian (D1) times an orthogonal Gaussian: "Small" had peak spatial frequency of 1.0 cycle/deg (cpd) and orthogonal standard deviation (SD) = 1°; "Medium", had peak 1.0 cpd and SD = 2°; "Large" had peak 0.25 cpd and SD = 4°. Each D1 stimulus was used to measure contrast threshold at 33 locations in an 11x3, 0.5°-interval grid from 11° to 16° horizontally and 4° to 5° vertically, chosen on the basis of size III results and anatomical information.

Results: Findings for one participant are shown; the same pattern was observed for the other participants. When the size III stimulus had Weber contrast > 200% it was seen unless it fell on the optic disc, a region between the disc and the vasculature, or on larger vessels (Fig. 1, bottom). When maximum likelihood estimation was used to estimate contrast sensitivity for local regions, an angioscotoma was seen with an orientation near -45° (Fig. 2, top). The D1 stimuli were therefore oriented at -45°, and results were plotted as "defect depth" (Fig. 2, bottom). Locations in color have contrast sensitivity below the mean contrast sensitivity for that retinal region. All three stimuli revealed a scotoma.

Conclusions: We confirmed our prior finding that oriented sinusoidal stimuli can be effective for identifying mild scotomas, and extended it to larger stimuli. The use of oriented stimuli holds promise for structure-guided perimetry, and results are consistent with our models of cortical pooling.

CONTROL ID: 3528053

SUBMITTER (NAME ONLY): Maureen Anne Naguit

TITLE: Two novel mutations in the KCNV2 gene exhibit a variation of Cone Dystrophy with Supernormal Rod Response (CDSRR) in an 8-year old Asia Pacific Islander: A Case Report

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Naguit, P. Villa, Eye and Vision Institute, The Medical City, Pasig City, Manila, PHILIPPINES|P. Villa, Eye Institute, St. Luke's Medical Center Global City, Taguig City, PHILIPPINES|E. Collantes, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Maureen Anne Naguit: Commercial Relationship: Code N (No Commercial Relationship) | Edward Ryan Collantes: Commercial Relationship: Code N (No Commercial Relationship) | Patricia Yukiji Villa: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Inherited retinal disorders (IRD) are challenging to diagnose because of genetic heterogeneity and overlapping phenotypes. Genetic testing helps determine the underlying molecular pathophysiology, confirms the clinical diagnosis, estimates the risk of recurrence, and determines possible eligibility for future gene-based therapies. We report a case of a patient with two previously unreported mutations in KCNV2, a gene strongly linked to CDSRR.

Methods: Ocular assessment was done, which included visual acuity assessment, slitlamp, and dilated fundus examination. Magnetic resonance imaging, full-field electroretinography (ffERG), and optical coherence tomography were done. Whole blood was obtained, DNA extracted, and genetic testing was performed through the My Retina Tracker Program of Blueprint Genetics, which screened 285 genes for disease-causing mutations implicated in IRDs.

Results: An 8-year old Chamorro female presented with congenital nystagmus, high myopia progression, and preferential right gaze since infancy. Medical and family histories were unremarkable. Ocular exam showed BCVA of 20/200, myopic fundus, and thin macula in both eyes. ffERG was consistent with cone dystrophy. Neurologic workup was unremarkable. The IRD gene panel test showed the patient was compound heterozygous for two nonsense mutations in KCNV2: c.153T>A, p.(Tyr51*) and c.625G>T, p.(Glu209*). Tyr51* is absent in the Genome Aggregation Database control population cohort while one individual is heterozygous for Glu209*.

Conclusions: To our knowledge, this study is the first to identify these two nonsense mutations in KCNV2 in a patient with CDSRR. Both mutations are predicted to lead to loss of normal protein function either through protein truncation or nonsense mediated decay. KCNV2 encodes the voltage-gated potassium channel subunit Kv8.2. Deficiency of Kv8.2 can influence the photoreceptor membrane potential and is thought to cause the visual symptoms of patients. Identifying these novel mutations highlights the value of genetic testing, especially in underrepresented minorities such as Asia Pacific Islanders, as these guided the clinical management and anticipation of disease progression.

CONTROL ID: 3528057

SUBMITTER (NAME ONLY): Gabrielle Zacks

TITLE: Joint ILM and RPE segmentation confidence map improves macular thickness analysis for low-cost OCT

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Zacks, H. Bagherinia, C. Leahy, T. Shagam, S. Bello, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Gabrielle Zacks: Commercial Relationship(s);Carl Zeiss Meditec Inc:Code E (Employment) | Homayoun Bagherinia: Commercial Relationship(s);Carl Zeiss Meditec Inc:Code E (Employment) | Conor Leahy: Commercial Relationship(s);Carl Zeiss Meditec Inc:Code E (Employment) | Taylor Shagam: Commercial Relationship(s);Carl Zeiss Meditec Inc:Code E (Employment) | Simon Bello: Commercial Relationship(s);Carl Zeiss Meditec Inc:Code E (Employment)

ABSTRACT BODY:

Purpose: The robustness of macular thickness analysis (MTA) depends on the performance of the inner limiting membrane (ILM) and retinal pigment epithelium (RPE) segmentation. With a low-cost OCT, multiple scans are acquired to increase the probability of a successful MTA. This abstract proposes a method to generate a joint ILM/RPE segmentation confidence map to automatically select the most reliable scans for analysis.

Methods: A low-cost OCT prototype system (ZEISS, Dublin, CA) and a CIRRUSTM HD-OCT 5000 (ZEISS, Dublin, CA) imaged 43 patients (70 eyes) with pathologies, including age-related macular degeneration. On the low-cost device, each eye was imaged 2-3 times using a 5.78x7 mm OCT volume capturing 512 A-scans/B-scan and 128 B-scans with 2.77 mm of depth. A 6x6 mm scan with the same density was also captured on CIRRUS.

The ILM and RPE layers were segmented in all images acquired with the low-cost device. A confidence map for each layer was generated from the processed image at each segmentation point. The algorithm was trained using maps data classified as high or low confidence, using a threshold to generate likelihood functions for Bayesian inference. The joint segmentation confidence maps (JSCM) of each set of OCT volumes were created by a posterior probability using the likelihood functions (Fig 1a). The ETDRS grid has 3 concentric circles of 0.5, 1.5, and 2.89 mm radius placed at the fovea center (Fig 1b). The confidence index for a scan was calculated by averaging the JSCM over the full grid.

From 215 scans on the low-cost device and JSCM, 70 high and 70 low-confidence scan MTAs of the same eyes (no scan overlap) were compared to 70 baseline CIRRUS MTAs of the same eyes.

Results: Table 1 shows the correlation and Bland-Altman agreement for each ETDRS subfield between the low-cost OCT and CIRRUS MTA. There was a dramatic improvement when high confidence scans were used vs. low confidence scans.

Conclusions: We demonstrated a joint ILM/RPE segmentation confidence method that shows the best scans for MTA. Multiple scans of the same eye can be acquired to increase the probability of acquiring a high confidence scan. Improved MTA in a low-cost device is important for detection and management of retinal diseases.

CONTROL ID: 3528078

SUBMITTER (NAME ONLY): Torcato Santos

TITLE: Characterization of macular edema in the initial stages of diabetic retinopathy: a 3-year longitudinal study

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Santos, CNTM, Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|I. Marques, A. Santos, CEC, Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|I. Marques, M.H. Madeira, C.F. Lobo, iCBR, University of Coimbra, Faculty of Medicine, Coimbra, PORTUGAL|M.H. Madeira, UTT, Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|A. Santos, Department of Orthoptics, School of Health, Polytechnic of Porto, Coimbra, PORTUGAL|C.F. Lobo, J.G. Cunha-Vaz, Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|J.G. Cunha-Vaz, University of Coimbra, Faculty of Medicine, Coimbra, PORTUGAL|

Commercial Relationships Disclosure (Abstract): Torcato Santos: Commercial Relationship(s);OCT-Leakage - EPO 3 289 565:Code P (Patent) | Inês Marques: Commercial Relationship: Code N (No Commercial Relationship) | Maria Madeira: Commercial Relationship: Code N (No Commercial Relationship) | Ana Rita Santos: Commercial Relationship: Code N (No Commercial Relationship) | Conceição Lobo: Commercial Relationship: Code N (No Commercial Relationship) | Jose Cunha-Vaz: Commercial Relationship(s);Carl Zeiss Meditec:Code C (Consultant);Alimera Sciences:Code C (Consultant);Allergan:Code C (Consultant);Bayer:Code C (Consultant);Gene Signal:Code C (Consultant);Novartis:Code C (Consultant);Pfizer:Code C (Consultant);Oxular:Code C (Consultant);Roche:Code C (Consultant);Sanofi:Code C (Consultant);Vifor Pharma:Code C (Consultant);Adverum Biotechnologies:Code C (Consultant);OCT-Leakage - EPO 3 289 565:Code P (Patent)

ABSTRACT BODY:

Purpose: To characterize the prevalence and progression of macular edema in minimal to moderate non-proliferative diabetic retinopathy (DR) using measurements of tissue optical reflectivity (OCT-Leakage).

Methods: Seventy-four eyes from 74 diabetic DR type 2 patients were imaged annually during a 3-year follow up with the CIRRUS™ HD-OCT 5000 with AngioPlex (Zeiss, Dublin, CA) using the “Angiography 6mmx6mm” protocol. Forty healthy eyes from 40 control volunteers were also imaged on a single visit.

OCT-A structural data was segmented using an in-house segmentation algorithm. OCT-Leakage, an algorithm to detect sites of low optical reflectivity (LOR) was applied to the full retina and to each retinal layer. Extracellular fluid was measured by the LOR area ratio, which stands for the fraction of the number of A-scans with LOR and the total number of A-scans, within the considered area. DRCR.net standards were used to identify eyes with subclinical (SCME) and clinical macular edema (central involved macular edema - CIME).

Results: The 74 eyes from 74 patients were classified using the ETDRS severity scale, Grade 10 to 20 (n=23), 35 (n=31) and 43 to 47 (n=20).

CIME was found in the first visit in 8.7% of eyes in ETDRS group 10-20, 9.7% of eyes in ETDRS group 35 and 15.0% of eyes in ETDRS group 43-47. In the eyes with increased central retinal thickness (CRT), the inner nuclear layer (INL) is the layer showing most frequent increase in thickness (52.9%). In the eyes with CIME at baseline, there is a strong correlation between the INL OCT-Leakage LOR (LOR-INL) and CRT value differences from V01 to V04 (Spearman rho=0.73, p-value=0.03). The changes in CRT and LOR-INL occur in parallel and are characterized by frequent fluctuations. The variations observed in the LOR-INL showed a much wider range well demonstrated by the standard deviation of the measurements of the average value (The Table).

Conclusions: Eyes from diabetic patients in the initial stages of DR with different ETDRS retinopathy grading shows similar prevalence of macular edema, showing that it increases only moderately with severity of the retinopathy. OCT-Leakage measurements of INL correlate with the presence of CIME and its evolution over a series of 4 visits during a 3-year period of follow up, showing that its course is characterized by frequent fluctuations.

CONTROL ID: 3528085

SUBMITTER (NAME ONLY): Maria Madeira

TITLE: Retinal neurodegeneration in type 2 diabetic individuals with mild retinopathy is independent of retinopathy severity progression: a 5-year longitudinal study

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Madeira, I. Marques, T. Santos, A. Santos, D.S. Tavares, J. Figueira, C.F. Lobo, J.G. Cunha-Vaz, AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|M.H. Madeira, I. Marques, J. Figueira, C.F. Lobo, J.G. Cunha-Vaz, Coimbra Institute for Clinical and Biomedical Research (iCBR), Universidade de Coimbra Faculdade de Medicina, Coimbra, Coimbra, PORTUGAL|A. Santos, Department of Orthoptics, School of Health, Polytechnic of Porto, Porto, PORTUGAL|

Commercial Relationships Disclosure (Abstract): Maria Madeira: Commercial Relationship: Code N (No Commercial Relationship) | Inês Marques: Commercial Relationship: Code N (No Commercial Relationship) | Torcato Santos: Commercial Relationship: Code N (No Commercial Relationship) | Ana Rita Santos: Commercial Relationship: Code N (No Commercial Relationship) | Diana Tavares: Commercial Relationship: Code N (No Commercial Relationship) | Joao Figueira: Commercial Relationship(s);Alimera:Code C (Consultant);Allergan:Code C (Consultant);Bayer:Code C (Consultant);Boheringer:Code C (Consultant);Novartis:Code C (Consultant) | Conceição Lobo: Commercial Relationship: Code N (No Commercial Relationship) | Jose Cunha-Vaz: Commercial Relationship(s);Carl Zeiss Meditec:Code C (Consultant);Alimera Sciences:Code C (Consultant);Allergan:Code C (Consultant);Bayer:Code C (Consultant);Gene Signal:Code C (Consultant);Novartis:Code C (Consultant);Pfizer:Code C (Consultant);Oxular:Code C (Consultant);Roche:Code C (Consultant);Sanofi:Code C (Consultant);Vifor Pharma:Code C (Consultant);Adverum Biotechnologies:Code C (Consultant)

ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) has always been considered a microvascular disease, but it has been suggested that neurodegeneration also plays a key role in this complex pathology. In the context of a 5-year prospective longitudinal study, we evaluated the progression of DR neurodegenerative events and its correlation with microvascular events and disease severity progression.

Methods: 142 patients with type 2 diabetes (T2D) and mild NPDR (ETDRS grades 20 or 35) were followed in a 5-year longitudinal study. Ophthalmological examinations were performed at baseline, 6-months and annually. Optical coherence tomography (OCT) was performed to evaluate average thickness of the ganglion cell layer (GCL). An aged-matched population of 58 healthy individuals was evaluated with OCT as a control for layer segmentation. ETDRS and severity progression was assessed in T2D individuals by grading of 7-fields CFP performed at the initial and last visits. Microaneurysm turnover (MAT) was evaluated using the RetMarkerDR.

Results: At baseline GCL thickness ($80.06 \pm 7.71 \mu\text{m}$) in T2D individuals was significantly reduced when compared to controls ($82.67 \pm 5.46 \mu\text{m}$, $p=0.0201$), indicating the presence of neurodegenerative changes since in the initial stages of retinopathy (ETDRS 20 and 35). Ganglion cell layer average thickness remained stable through the 5-year period in T2D individuals, showing no significant associations with baseline ETDRS, severity progression or MAT (Table 1).

Conclusions: Neurodegeneration, represented by GCL thinning, is present since the initial stages of non-proliferative DR, however it does not progress significantly over a 5-year period and is independent of the microvascular alterations (considering MAT), ETDRS grade and DR severity progression.

CONTROL ID: 3528097

SUBMITTER (NAME ONLY): Marlene Sassmannshausen

TITLE: Inter-reader repeatability of structural biomarkers in age-related macular degeneration in the multi-center MACUSTAR study

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Behning, M. Schmid, Institute of Biostatistics, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M. Sassmannshausen, M. Pfau, S. Thiele, F.G. Holz, Ophthalmology, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M. Sassmannshausen, M. Pfau, S. Thiele, F.G. Holz, S. Schmitz-Valckenberg, GRADE Reading Center, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Nordrhein-Westfalen, GERMANY|S. Schmitz-Valckenberg, Moran Eye Institute, University of Utah Health Hospitals and Clinics, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Analysis of inter-reader reliability of structural biomarkers for intermediate age-related macular degeneration (iAMD) based on the observational European multi-center study MACUSTAR (ClinicalTrials.gov: NCT03349801).

Methods: For the analysis of the inter-reader repeatability of discrete features (measured by Cohen's kappa), double gradings of maximum drusen size, presence of pigment epithelium detachment (PED), reticular pseudodrusen (RPD) and vitelliform lesions were performed by two independent readers. The overlap (Dice similarity coefficient [DSC]) of retinal multilayer segmentation was compared between readers as well as readers and a deep-learning (DL) based segmentation model. Mixed-effects models were fitted to data from each retinal layer with the DSC as dependent variable and patient as random intercept term to compare the different pairings (R1-vs.-R2; R1-vs.-DL; R2-vs.-DL), which were included as independent variable.

Results: For the discrete parameters (based on 168 study eyes) almost perfect agreement was obtained for the presence of PED (Cohen's kappa = 0.87 [0.69–1.00]), while agreement for presence of RPD (0.75 [0.63–0.87]) and vitelliform lesions (0.65 [0.39–0.91]) was substantial and moderate, respectively. For multilayer segmentation, the inter-reader-overlaps (R1-vs.-R2) were comparable between the retinal-nerve fiber layer (RNFL) (DSC estimate [95% CI] of 0.85 [0.80–0.90]), the outer nuclear layer (ONL) (0.82 [0.69–0.94]), the inner photoreceptor segments (IS) (0.78 [0.67–0.90]) and the retinal-pigment-epithelium-drusen complex upper segment (RPEDC-upper) (0.64 [0.52–0.77]) and lower segment (RPEDC-lower) (0.76 [0.66–0.85]). For nearly all retinal layers the reader-DL-segmentation-overlap was overall similar to the inter-reader-overlap ($p>0.05$). Only the R2-vs.-DL-overlap for the inner plexiform layer (IPL) (+0.03 [0.00–0.06], $p=0.04$), the RPEDC-upper (+0.07 [0.03–0.11], $p=0.002$) and the RPEDC-lower

segment appear to be minimally worse than the inter-reader-overlap.

Conclusions: Qualitative and quantitative imaging biomarkers exhibited moderate to perfect agreement among readers. Fully-automated DL-based image segmentation provides comparable results in terms of retinal multilayer segmentation. Analysis of inter-reader variability will be important to establish robust structural endpoints for future interventional clinical trials in iAMD eyes.

CONTROL ID: 3528108

SUBMITTER (NAME ONLY): Barbara Swiatczak

TITLE: Emmetropic, but not myopic human eyes distinguish positive defocus from calculated blur

SESSION TITLE: Effects of Light Intensity and Blur on Refractive Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Swiatczak, F. Schaeffel, Institute of Molecular and Clinical Ophthalmology Basel (IOB), Basel, SWITZERLAND | F. Schaeffel, Eberhard Karls Universitat Tübingen, Tübingen, Baden-Württemberg, GERMANY |

Commercial Relationships Disclosure (Abstract): Barbara Swiatczak: Commercial Relationship: Code N (No Commercial Relationship) | Frank Schaeffel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is well established that defocus blur imposed by positive lenses induces hyperopia development while blur imposed by diffusers induces deprivation myopia. While it is known that such ocular growth changes are controlled by the retina, it is unclear whether the retina can distinguish between both conditions when the magnitude of blur is matched. We have studied this question in young human subjects.

Methods: Ten emmetropic (average refractions 0.0 ± 0.3 D) and ten myopic (-2.7 ± 0.9 D) young subjects (average age: 24 ± 4 years) watched a movie on a large screen (65") at 2 m distance. The movie was presented either unfiltered ("control"), or with calculated low-pass filtering equivalent to a defocus of 2.5 D, or with real optical defocus of +2.5D that was imposed by +3D spectacle lenses in both eyes. Before and after 30 minutes of movie watching, axial length was measured using low coherence interferometry (Lenstar LS-900 with autopositioning system). Spatial filtering movies was done in real-time by software written in Visual C++. Defocus was simulated by convolving each pixel with a blur circle that was calculated for 2.5D of defocus, using the average pupil size of the subjects (6.5 ± 0.7 mm).

Results: Watching unfiltered movies ("control") caused no changes in axial length. In emmetropes, watching movies with calculated defocus caused axial eye elongation ($+9.8 \pm 7.6 \mu\text{m}$) while watching movies with real positive defocus caused shorter eyes ($-8.8 \pm 9.2 \mu\text{m}$; difference between both $p < 0.0001$). Also in myopes, calculated defocus caused longer eyes ($+8.4 \pm 9.0 \mu\text{m}$) compared to control ($-3.0 \pm 8.3 \mu\text{m}$, $p = 0.001$). Strikingly, myopic eyes responded differently to positive defocus since they became also longer ($+9.1 \pm 11.2 \mu\text{m}$, $p = 0.02$, compared to control). The difference in responses to positive defocus between emmetropic and myopic subjects was highly significant ($p = 0.001$).

Conclusions: Two conclusions emerge: (1) in emmetropic human subjects, the retina appears to be able to distinguish between real positive defocus and calculated defocus even when the modulation transfer function was matched, (2) in myopic eyes, the retina apparently no longer distinguishes between both conditions since the eyes became longer in both cases. These results suggest that the retina in a myopic eye has reduced ability to detect positive defocus and restrain axial growth.

CONTROL ID: 3528111

SUBMITTER (NAME ONLY): Charles Wykoff

TITLE: Impact of Baseline Retinal Non-Perfusion (NP) and Leakage on Center-Involved Diabetic Macular Edema (CI-DME) and/or Vision-Threatening Complications (VTC) in Non-Proliferative Diabetic Retinopathy (NPDR) in the PANORAMA Trial

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.C. Wykoff, Retina Consultants of Texas (Retina Consultants of America), Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Charles Wykoff: Commercial Relationship(s);Acucela, Adverum, Aerpio, Alcon, Alimera Sciences, Allergan, Alnylam, Apellis, Arctic Vision:Code C (Consultant);Bausch + Lomb, Bayer, Bionic Vision Technologies:Code C (Consultant);Chengdu Kanghong Biotechnologies (KHB), Clearside Biomedical, Corcept Therapeutics:Code C (Consultant);DORC, EyePoint (formerly pSivida):Code C (Consultant);Genentech, Gyroscope, IVERIC Bio:Code C (Consultant);Kodiak Sciences, Merck, NGM Biopharmaceuticals:Code C (Consultant);Notal Vision, Novartis, OccuRx, ONL Therapeutics:Code C (Consultant);Opthea, Oxurion, Palatin, Polyphotonix, Recens Medical:Code C (Consultant);Regeneron Pharmaceuticals, Inc, RegenXBio, Roche:Code C (Consultant);Santen, Takeda, Thea Open Innovation, Verana Health:Code C (Consultant);Adverum, Aerie Pharmaceuticals, Aldeyra, Allergan, Apellis:Code F (Financial Support);Boehringer Ingelheim, Chengdu Kanghong Biotechnologies (KHB):Code F (Financial Support);Clearside Biomedical, Gemini Therapeutics, Genentech:Code F (Financial Support);Graybug Vision, Gyroscope, IONIS Pharmaceutical:Code F (Financial Support);IVERIC Bio, Kodiak Sciences, LMRI, Mylan:Code F (Financial Support);Neurotech Pharmaceuticals, NGM Biopharmaceuticals, Novartis:Code F (Financial Support);Opthea, Outlook Therapeutics, Recens Medical:Code F (Financial Support);Regeneron Pharmaceuticals, Inc, RegenXBio, Roche:Code F (Financial Support);Samsung Bioepis, Santen, Senju:Code F (Financial Support);Taiwan Liposome Company, Xbrane BioPharma:Code F (Financial Support);Regeneron Pharmaceuticals, Inc.:Code S (Non-remunerative)

ABSTRACT BODY:

Purpose: Impact of baseline retinal NP and leakage on rates of CI-DME and/or VTC (PDR/anterior segment neovascularization) was assessed in patients receiving intravitreal aflibercept injections (IAI) or sham injections through 100 weeks in PANORAMA.

Methods: This post hoc analysis included patients with moderately severe to severe NPDR (Diabetic Retinopathy Severity Scale [DRSS] 47–53) without baseline DME who received IAI 2 mg q16 weeks (N=135) or q8 weeks (PRN dosing in year 2; N=134) (both after initial loading doses) or sham (N=133). IAI groups were combined. Baseline NP (mm^2) was analyzed in 4 groups: G1: ≤ 0 , n=201; G2: $>0\text{--}\leq 0.24$, n=52; G3: $>0.24\text{--}\leq 0.66$, n=53; G4: >0.66 , n=51. Baseline leakage area (mm^2) was analyzed by quartile: Q1: ≤ 10.20 , n=98; Q2: $>10.20\text{--}\leq 19.76$, n=97; Q3: $>19.76\text{--}\leq 30.41$, n=97; Q4: >30.41 , n=97.

Results: Proportions of patients who developed CI-DME/VTC across increasing baseline NP or leakage groups increased with sham but were similar with IAI (Figures 1, 2). Risk of developing CI-DME/VTC increased with baseline NP area (per 1 mm^2 increase) with sham, hazard ratio (HR): 1.32 (95% confidence interval [CI]: 1.06, 1.64; P=0.0125) but not with IAI, 1.06 (0.88, 1.27; P=0.5669). Results were similar for impact of baseline NP on risk of CI-DME alone, HR (95% CI): 1.32 (1.04, 1.67) with sham and 0.95 (0.68, 1.33) with IAI; and VTC alone, 1.44 (1.08, 1.92) with sham and 1.10 (0.89, 1.38) with IAI. Similarly, risk of CI-DME/VTC increased with baseline leakage area (per 1 mm^2 increase) with sham, HR 1.05 (95% CI: 1.02, 1.07; P<0.0001) but not IAI, 1.03 (1.00, 1.05; P=0.0550). The HR (95% CI) for impact of baseline leakage on risk of CI-DME alone was 1.02 (0.99, 1.05) with sham and 1.03 (1.00, 1.07) with IAI; and for VTC alone was 1.08 (1.04, 1.12) with sham and 1.00 (0.96, 1.04) with IAI. Sham but not IAI was associated with a lower proportion of patients with ≥ 2 -step DRSS improvement and higher proportion with ≥ 2 -step DRSS worsening with increasing baseline NP and leakage areas, although the trend was not significant for baseline NP.

Conclusions: Increasing baseline retinal NP and leakage areas were associated with increased rates of CI-DME/VTC in the sham group. This association was not observed in the IAI-treated group.

CONTROL ID: 3528117

SUBMITTER (NAME ONLY): Fahd Naufal

TITLE: A Hands-Free, Augmented-Reality, Smartphone Camera System to Document the Prevalence of Active Trachoma.

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As the prevalence of trachoma declines in districts worldwide, standardizing graders for surveys to document elimination becomes increasingly expensive. The use of photographs to train graders may play a role. The purpose of this observational study is to develop an Image Capture and Processing System (ICAPS) that will permit hands free image acquisition of the tarsal conjunctiva. This device will allow a single person to evert the eyelid and then take, store and upload photographs to a virtual Reading Center for grading. This can potentially eliminate the need for expensive grader standardization currently used in trachoma prevalence studies.

Methods: This study was conducted as part of the Chamwino, Tanzania district survey. The ICAPS was integrated with the WHO Tropical Data system to examine 1305 children ages 1-9 years for trachomatous inflammation – follicular (TF). Three trachoma graders were trained for the survey over one day with technical training and field training components. The ICAPS comprised of Samsung's Gear VR headset and Galaxy S8 smart phone.

Results: The ICAPS system has proved successful in being able to scan and assign bar codes to images, achieve focus on the everted eyelid, and capture images with sufficient magnification. It permits the use of augmented reality features to save and delete images and maintain a reasonable battery life. Grading of the ICAPS images compared to the field grades at the child level yielded a kappa agreement score of 0.53 but a similar proportion of children with TF (Field: 5.2%, ICAPS: 5%). The lower agreement was due to difficulties in grading follicles in the images taken in the field. This may be resolved with a newer system that can quickly take higher quality images. For 199 children, there were ungradable images for at least one eye (15%) and more ungradable images occurred in younger children ages 1-3 (18.5%) than older children ages 4-9 (4.3%). The percent of ungradable images remained consistent over the course of the study.

Conclusions: More training and ability to certify trainers is needed to reduce the percentage of ungradable images. Better understanding of the causes of disagreement in graded images and field grades is necessary before ICAPS can replace field graders. Newer phone-cameras can potentially improve image quality for more accurate follicle assessment.

CONTROL ID: 3528139

SUBMITTER (NAME ONLY): Shandiz Tehrani

TITLE: Rho kinase inhibition promotes stellation in primary cultured optic nerve head astrocytes

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Astrocytes are stellate-shaped glia that support optic nerve head (ONH) axons with numerous actin-rich processes. With intraocular pressure (IOP) elevation in animal models, ONH astrocytes retract their processes. Here, we determined if Rho kinase inhibition with fasudil promotes stellation in cultured primary ONH astrocytes.

Methods: Adult rat ONH astrocytes were collected and validated as previously described. Cultures of passages 10-15 were seeded at 25,000 cells/cm². After 24h, cells were treated with fasudil (0, 1, 5, 10, 25, 50, and 100µM) for an additional 24h. Cells were fixed in 4% paraformaldehyde solution, labeled for actin and nuclei, and imaged using confocal microscopy. MTT uptake and LDH release assays were performed to determine any cytotoxic effects from fasudil. Cell shape and Sholl-like analyses (5-170µm radii circles from the cell center) were used to determine cell area and perimeter, cell circularity (graded on a scale of 0-1, where 1 represents a circle), and mean/maximum process lengths, respectively, via Adobe Photoshop. Data were analyzed using ANOVA statistical analysis (n=53±14 cells/group) and presented as mean ± SEM.

Results: Control astrocytes were non-stellate in shape. Mean cell area and cell viability remained unchanged with 1-100µM fasudil treatment. With increasing fasudil concentration, cells became more stellate in shape. Mean cell perimeter increased with fasudil treatment (significant at fasudil concentrations ≥50µM: 377.9±14.3µm in experimental vs. 293.4±12.0 in controls; p=0.001). Mean cell circularity decreased with fasudil treatment (significant at fasudil concentrations ≥10µM: 0.24±0.01 in experimental vs. 0.31±0.01 in controls; p=0.001). In Sholl-like analyses, mean astrocyte process number of intersections at various radii increased with fasudil treatment (most intersections at 25µm from the cell center; significant at fasudil concentrations ≥50µM: 3.7±0.2 in experimental vs. 3.0±0.1 in controls; p=0.03). Mean maximum cell process length increased with increasing fasudil concentrations (by up to 1.4x in experimental vs. control cells; linear regression slope=3.5, r²=0.63, p<0.0001).

Conclusions: Rho kinase inhibition promotes stellation in cultured ONH astrocytes, mirroring astrocyte morphology described in ONH tissue. Rho kinase inhibition in vivo may maintain astrocyte stellate morphology in the setting of elevated IOP.

CONTROL ID: 3528146

SUBMITTER (NAME ONLY): Laurent Kodjikian

TITLE: Efficacy and safety of intravitreal aflibercept (IVT-AFL) treat-and-extend (T&E) compared with fixed dosing (q8) for neovascular age-related macular degeneration (nAMD): The AZURE study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare the efficacy and safety of 2 IVT-AFL dosing regimens, T&E and q8, for patients with nAMD beyond Year (Y) 1 of treatment.

Methods: AZURE (NCT02540954) was a randomized, multicenter study. All patients completed $\geq 1Y$ of IVT-AFL treatment prior to enrollment. Patients were randomized 1:1 to fixed q8 (2mg IVT-AFL every 8 weeks [w]) or T&E dosing (IVT-AFL $\geq 8w$ [no upper limit] per functional/anatomic criteria). Primary endpoint was mean change in best-corrected visual acuity (BCVA) from baseline (BL) to w52. Key secondary endpoint was proportion of patients losing < 15 letters.

Results: The full analysis set comprised 332 patients ($n=167$ [q8] and $n=165$ [T&E]). Mean (standard deviation) BCVA at IVT-AFL treatment initiation (1Y prior to study BL) was 60.9 (9.9; q8) and 59.4 (10.5; T&E) letters. At study BL, mean age was 74.7 (7.0; q8) and 76.2 (8.3; T&E) and mean BCVA was 70.1 (10.9; q8) and 69.0 (12.1; T&E) letters. At w52, mean BCVA change from BL was -0.5 (8.4; q8) and -0.3 (7.5; T&E) letters. Least-squares mean difference (95% CI) vs q8 dosing was 0.22 (-1.51 ; 1.96). Compared with q8 dosing, T&E achieved a non-inferior change in mean BCVA at w52 (pre-specified margin of 5 letters; $P<0.0001$). At w76, mean BCVA change from BL was -0.9 (10.4; q8)

and -1.5 (10.9; T&E) letters. From BL to w52, 94.0% (q8) and 95.2% (T&E) of patients maintained vision (<15-letter loss). Mean central retinal thickness change from BL was -33.4 μ m (47.1; q8) and -24.4 μ m (55.2; T&E) at w52, and -37.8 μ m (51.1; q8) and -21.7 μ m (57.0; T&E) at w76. Mean number of IVT-AFL injections was 6.8 (0.8; q8) and 6.0 (1.0; T&E) at w52, and 9.6 (1.4; q8) and 8.0 (1.8; T&E) at w76. Ocular treatment-emergent adverse events in the study eye were similar for q8 (48.8%) and T&E (45.5%) dosing regimens.

Conclusions: In patients who previously received ≥ 1 Y of IVT-AFL treatment for nAMD, T&E dosing achieved similar functional outcomes as q8 dosing. Functional and anatomic improvements achieved during Y1 were maintained in Y2 and Y3 of IVT-AFL treatment with both regimens. Of the 2 regimens, T&E required fewer injections. No new safety signals were identified, which is consistent with prior studies.

CONTROL ID: 3528204

SUBMITTER (NAME ONLY): Julie Lim

TITLE: Molecular identification of circadian clock proteins in the rat lens: evidence of circadian regulation of glutathione homeostasis?

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To determine whether the lens acts as a circadian clock that controls the rhythmic expression of genes involved in glutathione (GSH) redox regulation

Methods: Western blotting and immunohistochemistry were used to confirm the expression of circadian clock core proteins (BMAL1 & CLOCK) in rat lenses. Reverse transcription-quantitative PCR (RT- qPCR) was performed on RNA extracted from rat lenses collected every 4 hours over a 24-hour period to determine if there were cyclic differences in the expression of clock component genes (Bmal1, Clock, Per and Cry) and GSH related redox genes involved in GSH synthesis and regeneration.

Results: Western blotting for circadian clock proteins from lens homogenates revealed bands consistent with the predicted molecular weights for BMAL1 and CLOCK. Immunohistochemistry revealed labelling for BMAL1 and CLOCK in the epithelium and fibre cells in the outer cortex. RT-qPCR revealed fluctuations for both the clock component genes and redox genes over a 24-hour period suggestive that the lens may utilize circadian time keeping mechanisms to regulate GSH homeostasis

Conclusions: Collectively, these findings reveal that the lens contains the core molecular components of the circadian clock, and that fluctuations in the expression of clock component genes and GSH related genes occurs during the day/night cycle. This implies that the lens may act as a circadian clock that controls the rhythmic expression of genes involved in GSH homeostasis to provide protection against UV insults. Since circadian rhythms are altered with advancing age, this implies that disruption of the circadian regulation of redox balance may be an initiating factor in age related lens cataract.

CONTROL ID: 3528207

SUBMITTER (NAME ONLY): Abhishek Bhat

TITLE: Objective method for limbus detection of anterior segment topography

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bhat, K.D. Tran, K. Barbarossa, R. Lum, K.A. Tuan, Mojo Vision, California, UNITED STATES|C.W. Sindt, M. Bauer, Department of Ophthalmology, University of Iowa, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Successful contact lens designs are predicated on the accurate identification of the limbus. Custom scleral lens designs can now be fabricated using 3D ocular surface maps from scanning and impression-based methods. Utilizing 3D topography maps, an objective method of defining the limbus was developed.

Methods: Thirty impression-based 3D topography maps were selected based on ocular conditions that do not affect the limbal region.

Subjective Detection: An expert clinician identified at least 5 points on the topography map using the EyePrint Designer (EPD) software to represent the limbal margin. Visual selection of points was guided by known anatomical features such as expected curvature change and limbus size.

Objective Detection: A custom algorithm in MATLAB detects changes in 3D ocular surface profile at the limbal region. An initial estimate of candidate limbal points represent locations with large gradient magnitudes. An adaptive varying threshold is applied since the gradient magnitude of the limbus is not constant across all meridians. Candidate points away from the probable limbal region are rejected. Further testing for outliers using Random Sample Consensus (RANSAC) is done to remove points that do not fit an elliptical profile. The detected limbal points tend not to be planar, resulting in a best fit hyperbolic paraboloid shape.

Comparison: Limbal parameters from subjective and objective methods collected using the EPD software were compared. All objective limbus designs were reviewed by another expert clinician. Lens designs with >75% similarity of the limbal region between the two methods were clinically acceptable.

Results: Limbal parameters were reported as: major diameter, minor diameter, and axis of major diameter. The average difference between the two methods were 0.16mm, 0.07mm, and 1.92 degrees, respectively. The median difference between the two methods were 0.05mm, 0.03mm, and 2.95 degrees, respectively. Review of objectively determined limbal points found 80% of designs to be clinically acceptable.

Conclusions: This objective method of identifying the limbus may be an effective way of guiding novice contact lens designers to create custom scleral lenses. Further investigation of irregular ocular surfaces is necessary to address the broader ocular demographic who wear scleral lenses.

CONTROL ID: 3528213

SUBMITTER (NAME ONLY): Qi Yang

TITLE: Multi-modal Geographic Atrophy Lesion Growth Rate Prediction using Deep Learning

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Q. Yang, N. Anegondi, V. Steffen, C. Rabe, D. Ferrara, S.S. Gao, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To predict geographic atrophy (GA) lesion growth rate from fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (OCT) using a multi-modal multi-task deep learning approach.

Methods: This study was performed retrospectively on study eyes of patients with bilateral GA enrolled in the lampalizumab clinical trials. The macular Spectralis (Heidelberg Engineering, Inc. Heidelberg, Germany) OCT volumes of 496x1024x49 voxels and macular 30 degree FAF images of 768x768 pixels from baseline visits were used to predict baseline GA lesion area and annualized GA growth rate. For OCT volumes, each B-scan was flattened along Bruch's membrane (BM) and three en-face maps averaged over full, sub-BM and above-BM depths were combined as a three-channel input. The growth rate (mm^2/year) of GA lesion area (mm^2 , measured from FAF images by an independent reading center and graded by two readers and an adjudicator if necessary) was estimated as the slope from a linear regression model fitted for each individual patient using all available visits. The datasets from 1279 patients were divided into 80% training and 20% test datasets. Further, the training data were randomly divided into 5 cross-validation (CV) folds. Three multi-task convolutional neural network (CNN) models were trained to simultaneously predict GA lesion area and GA growth rate: OCT only, FAF only and multi-modal (OCT and FAF). The performance was evaluated by calculating the in-sample coefficient of determination (R^2) defined as the square of Pearson correlation coefficient (r) between true and predicted GA area and growth rate.

Results: Table 1 shows the CV and test set performance of the three multi-task CNN models: OCT only, FAF only and multi-modal input. The multi-modal model had the best CV performance with mean R^2 of 0.92 and 0.46 for GA lesion area and GA growth rate predictions, respectively. On the test set, the same model showed R^2 of 0.94 for GA lesion area prediction and 0.56 for GA growth rate prediction.

Conclusions:

These findings show the feasibility of using baseline FAF and/or OCT images to predict individual GA growth rate with a multi-task deep learning approach and that a multi-modal approach could improve performance. This work can potentially be useful for clinical trial adjustment, stratification and/or enrichment. Meanwhile, further validation in additional datasets is needed to confirm robust performance.

CONTROL ID: 3528216

SUBMITTER (NAME ONLY): Ajay Kolli

TITLE: Studying Visual Disability in a Nationally-Representative Panel Study of Older Adults

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kolli, L. De Lott, M. Hu, Y. Zhou, J.R. Ehrlich, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Self-reported visual disability (SRVD) is an important indicator of the perceived impact of vision on an individual's life. The National Health and Aging Trends Study (NHATS) is an ongoing, nationally-representative panel study of late-life disability. Using survey items with binary response options, we sought to develop an ordinal indicator of SRVD in NHATS in order to improve measurement precision and facilitate future studies of disability trajectories related to vision in older adults.

Methods: Sociodemographic factors, medical comorbidities, SRVD, functional activity scores (mobility, self-care, household activity), and a subjective well-being scale were assessed in NHATS. Participants were asked questions (yes/no) to assess vision: blindness; sight adequate to recognize someone across the street; sight adequate to read newspaper print; use of glasses or corrective lenses; and use of any low vision aid (LVA). We categorized participants into one of six ordinal groups: 1) Blind; 2) Near and distance SRVD without use of LVA; 3) Near and distance SRVD with LVA; 4) Near or distance SRVD without LVA; 5) Near or distance SRVD with LVA; or 6) No SRVD. Multivariable Poisson regression models were used to assess convergent validity of the SRVD scale with functional activity (household, self-care, mobility) and subjective wellbeing scores.

Results: 7061 Individuals, age 65 years or older were included in this analysis. Weighted percentages of individuals in each of the six ordinal SRVD categories, and weighted mean functional activity and wellbeing scores by vision category are shown in Table 1. In models adjusted for sociodemographic and medical comorbidities, worse SRVD was significantly associated with lower scores for mobility ($p<0.0001$), self-care ($p<0.0001$), household activity ($p<0.0001$), and subjective wellbeing ($p<0.0001$) (Figure 1).

Conclusions: More severe SRVD on this novel scale was associated with worse scores for mobility, self-care, household activities, and subjective wellbeing among aging adults. This scale provides a new tool to capture the range of impacts that poor vision may have on the lives of older adults in a nationally-representative cohort. Use of this scale may facilitate analyses of the impact of SRVD on late-life disability trajectories.

CONTROL ID: 3528217

SUBMITTER (NAME ONLY): Fawzia Bardag-Gorce

TITLE: Thrombospondin is Up Regulated by Proteasome Inhibition

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate the effect of proteasome inhibition in neovascularization induced by limbal stem cell deficiency (LSCD). By understanding the molecular mechanisms that control neovascularization, it may be possible to design therapeutic strategies to selectively prevent or halt pathologic vascular growth. The anti-angiogenic thrombospondin-1 (TSP-1) has been shown to be a natural inhibitor of neovascularization. An increase in TSP-1 expression might decrease corneal vascularization in case of LSCD

Methods: Rabbits with experimentally induced LSCD were used to quantify the expression of TSP-1. Cultured Autologous Oral Mucosal Epithelial Cell Sheets (CAOMECS) was grafted back to reconstruct corneal epithelium. Using immunofluorescent staining, the levels of TSP-1 were compared between control, diseased and CAOMECS treated corneas. In addition, oral mucosal epithelial cells were cultured and treated with proteasome inhibitor to analyze TSP-1 levels. Treated cells were analyzed for the expression levels of (TSP-1) and its downstream signaling involved in angiogenesis.

Results: The immunofluorescent staining of normal healthy ocular surface showed that TSP-1 was expressed in corneal epithelial cells, and had a much lower expression in conjunctival epithelial cells. The limbal cells did not express TSP-1. In the LSCD diseased ocular surface, TSP-1 expression was greatly decreased in cornea epithelial cells. Conjunctival and goblet cells were present on the corneal surface. CAOMECS-grafted corneas greatly expressed TSP-1, in comparison to LSCD-disease corneas, but to a much lower extent compared to the healthy corneas. In an attempt to stimulate TSP-1 expression, cultured oral mucosal epithelial cells were treated with proteasome inhibitor. Results showed that treatment with proteasome inhibitor lead to an increase in the expression levels of TSP-1.

Conclusions: TSP-1 expression may be activated in CAOMECS tissue prior to grafting back onto cornea to reconstruct the ocular surface, and maintaining corneal avascularity in case of LSCD.

CONTROL ID: 3528223

SUBMITTER (NAME ONLY): Brandon Lam

TITLE: Comparison of ocular biometric parameters between Hispanic and non-Hispanic ethnicities

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To compare ocular biometric parameters between Hispanic and non-Hispanic white populations among adult patients undergoing cataract surgery.

Methods: This retrospective study included 433 adult patients who underwent surgery for senile cataract. Only patients with self-reported ethnicities of Hispanic and non-Hispanic white were included. We excluded those with a history of anterior segment surgeries or abnormalities. The following parameters as measured by the IOLMaster 700 (Carl Zeiss Meditec, Jena, Germany) were compared between Hispanic and non-Hispanic patients: mean keratometry, corneal astigmatism, anterior chamber depth, lens thickness, vitreous length, axial length, white-to-white diameter, and emmetropic intraocular lens power. Average of both eyes of each patient was used for analysis.

Results: There were 219 Hispanic and 214 non-Hispanic patients with a mean age of 70.1 ± 7.7 years (range, 50 to 88 years), and 66.7% were females. Although sex distribution was similar between the two groups, Hispanic patients had a lower age compared to non-Hispanics (69.3 ± 8.3 vs 70.9 ± 6.9 years, $P=0.02$). In biometric values, anterior chamber depth was significantly lower in Hispanics (3.067 ± 0.403 mm) than in non-Hispanics (3.159 ± 0.367 mm, $P=0.013$). Such statistically significant difference persisted even after adjustment for age ($P=0.004$). No other significant differences were found in other ocular parameters measured. Hispanics had a higher percentage of corneal with-the-rule astigmatism (29.7% vs 26.2%) and a lower percentage of corneal against-the-rule astigmatism (23.7% vs 28.0%); however, the difference was not statistically significant.

Conclusions: Anterior chamber depth is significantly lower in Hispanics compared with non-Hispanics. Such ethnic difference should be considered when performing cataract and corneal surgeries as it may be associated with a higher risk of corneal endothelial injury.

CONTROL ID: 3528225

SUBMITTER (NAME ONLY): Yuan Lei

TITLE: Airborne particulate matter topical exposure triggers ocular hypertension

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lei, L. Li, X. Sun, Eye and ENT Hospital of Fudan University, CHINA|J. Zhou, Shanghai Key Laboratory of Meteorology and health, CHINA|

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ABSTRACT BODY:

Purpose: Over 90% of the global population is exposed to air pollution. Latest epidemiological studies have found that particulate matter (PM), especially PM_{2.5} (aerodynamic diameter $\leq 2.5 \mu\text{m}$), is associated with glaucoma. However, it is controversial as the association is linked to intraocular pressure elevation or retinal damage. This study aims to determine how PM_{2.5} affects IOP and the underlying molecular mechanism involved.

Methods: Atmospheric PM_{2.5} samples were obtained from May 2016 to Dec 2018 in Lanzhou, China. PM_{2.5} suspension was given as topical eyedrops (1 mg/mL) to the right mouse eyes (C57BL/6, male, 6 weeks old, n=10) 3 times a day for 104 days, the contralateral left eyes serving as the control. Human trabecular meshwork (HTM) cells (three cell lines) were subjected to various PM_{2.5} concentrations (25 - 400 mg/mL) for 48 hours. Cell viability, ROS production, NLRP3/caspase-1, IL-1 β , and GSDMD expression was measured by western blot or ELISA. HTM cells were pre-treated with N-acetyl-L-cysteine (NAC, 3 mM) for 2 hours before cultured with PM_{2.5} (100 ug/mL) for 48 hours.

Results: In mouse eyes exposed to PM_{2.5}, IOP elevation was steadily significant from day 30 compared with the controls (n = 10; P < 0.05). Western blot analysis showed that PM_{2.5} increased the expressions of NLRP3 inflammasome mediated pyroptosis pathway (NLRP3/caspase 1/IL-1 β /GSDMD) in the mouse cornea and outflow tissues (NLRP3, n = 3, caspase-1, n = 4, IL-1 β , n = 3, GSDMD n = 4, p < 0.05). Cell experiments showed that PM_{2.5} exposure elevated ROS levels (n = 3, p < 0.05), decreased cell viability (n = 5, p < 0.05) and encouraged cell contraction in HTM cells (n = 3, p < 0.05). Antioxidant NAC improved HTM cell viability (n = 5, p < 0.05), inhibited the activation of the NLRP3 inflammasome axis (n = 3, p < 0.05) and HTM cell contraction (n = 3, p < 0.05).

Conclusions: This study provides novel evidence that PM_{2.5} has a direct toxic effect on intraocular tissues and may contribute to the initiation and development of ocular hypertension. This occurs as a result of increased oxidative stress and the subsequent induction of the NLRP3 inflammasome mediated pyroptosis signaling pathway in trabecular meshwork cells.

CONTROL ID: 3528230

SUBMITTER (NAME ONLY): Yash Karandikar

TITLE: Predicting High Impact Ophthalmology Articles Using Machine Learning and Natural Language Processing

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Karandikar, Occidental College, Los Angeles, California, UNITED STATES|S.Y. Wang, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yash Karandikar: Commercial Relationship: Code N (No Commercial Relationship) | Sophia Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study was to understand characteristics of top-cited ophthalmology articles by building machine learning predictive models to predict top-cited ophthalmology articles based on bibliometric and natural language processing features. We also investigated which were the most important features for predicting a top-cited ophthalmology article. We also evaluated model performance on the subset of glaucoma-related articles.

Methods: Ophthalmology papers published between January 2000 to June 2020 and their metadata were downloaded from Scopus, including publication year, titles, abstracts, journal, number of authors, page-range, funding source, and author and index keywords. Text of titles and abstracts were lowercased and tokenized (split into constituent words) and individual key words were represented as one-hot vectors for inputs into models. Gradient boosted machine (GBM) predictive models were created to identify whether or not each paper would be in the top 25th percentile of citations. The model was evaluated on a held-out test set on F1 score and areas under the receiver operating curve (AUROC) and precision-recall curves (AUPRC). The model was also evaluated on a subset of glaucoma-related articles, which had glaucoma-related keywords. Relative importance of features in the GBM model was determined to find the most predictive features.

Results: The gradient boosting machine model had an AUROC of 0.846, an AUPRC of 0.531, and an F1 score of 0.206 for all ophthalmology papers, and a similar performance on the glaucoma subset (AUROC 0.885). The most influential predictive factors were standard bibliometric variables, namely publication year (133.209), paper length (74.064), and author count (31.152). Between the tokenized and scored keywords, the most influential were the index keyword study, with a relative influence of 29.882; ophthalmology, 22.177; and RNA, 19.345.

Conclusions: This study found that natural language processing, especially with algorithmic scoring of specific keywords, is a useful tool to predict citation count in addition to standard bibliometric variables. This study also found that the most effective variables for predicting citation count are bibliometric variables, followed by certain index keywords.

CONTROL ID: 3528234

SUBMITTER (NAME ONLY): Thomas Khuu

TITLE: Subciliary Rotating Sutures Combined with Modified Hotz Procedure for Correction of Congenital Lower Eyelid Entropion

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Khuu, Washington State University Elson S Floyd College of Medicine, Spokane, Washington, UNITED STATES|K. Michels, Northwest Eyelid and Orbital Specialists, Spokane, Washington, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Thomas Khuu: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Michels: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report and evaluate the use of combined subciliary rotating sutures with modified Hotz procedure for repair of lower eyelid congenital entropion.

Methods: A retrospective chart review was conducted of all patients who underwent lower eyelid congenital entropion repair by a single surgeon (K.M.) using subciliary rotating sutures combined with a modified Hotz procedure between 2016 and 2020. Study variables included patient demographics, follow-up period, postoperative complications, and need for further intervention. In brief, a skin incision was made at the lower lid crease and dissection was carried superiorly to separate the anterior lamella from the tarsus. Any overriding orbicularis oculi muscle was removed inferior to the incision. Horizontal mattress sutures were passed starting inferior to the lash line, through the anterior lamella and inferior border of the tarsus, then reversed in the same direction as entry to rotate the lid margin. The lid crease was then reformed in the manner of the Hotz procedure.

Results: Twelve patients (19 eyelids) met the study inclusion criteria. The mean patient age was 7.1 ± 6.1 (range 0.2–22) years. Nine of the patients were female (75%) and 3 were male (25%). The distribution of eyelids was 8 right (58%) and 11 left (42%). The mean follow-up time was 19.5 ± 15 (range 2.5–45) months. There were 2 cases (11%) of entropion recurrence in 2 patients (17%) following initial repair, one which recurred after a patient underwent craniosynostosis surgery and another which recurred in a patient with pediatric thyroid eye disease. Repeat entropion surgical repair using the same technique was performed in these two cases for which no recurrence was noted during the follow-up period. Overall, the described entropion repair technique was successful and without recurrence in 17 cases (89%) in 10 patients (83%). There were no cases of ectropion, lid retraction, or other complications.

Conclusions: Subciliary rotating sutures combined with modified Hotz procedure is effective for correction of congenital lower eyelid entropion. The technique does not manipulate the posterior layer of the lower eyelid retractors which may reduce the risk of lower eyelid retraction and overcorrection in particular cases. It is also useful for when retractor reinsertion may not yield adequate improvement.

CONTROL ID: 3528241

SUBMITTER (NAME ONLY): Rui Ji

TITLE: Effects of Liposome-encapsulated Ripasudil on Proliferative Vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ji, K. Ishikawa, K. Mori, I. Wada, T. Nakama, S. Nakao, K. Sonoda, Department of Ophthalmology , Graduate School of Medical Sciences, Kyushu University, Fukuoka, Fukuoka, JAPAN|N. Matsunaga, S. Ohdo, Department of Pharmaceutics, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka, Fukuoka, JAPAN|

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ABSTRACT BODY:

Purpose: We previously reported ROCK inhibitor, Ripasudil could inhibit epithelial to mesenchymal transition of retinal pigment epithelium (RPE). The purpose of this study was to investigate the inhibitory effects of liposome-encapsulated Ripasudil (Lipo-Ripa) on an animal model of proliferative vitreoretinopathy (PVR).

Methods: PVR was induced in the eyes of Dutch rabbits as previously reported. After PVR induction, we performed single vitreous injection of BSS (control), Ripasudil (Ripa) and Lipo-Ripa in each group. We collected the vitreous fluid at 6 h, 24 h and 48 h after injection and measured the concentration of Ripasudil. PVR progression was observed by fundus camera and the stage was graded.

Results: Vitreous concentration of Ripasudil was significantly higher (4-32 times) in Lipo-Ripa group compared to Ripa group over time. In Ripa group, PVR progression was significantly suppressed on day 7 and 14 compared to control group ($p<0.05$). In Lipo-Ripa group, PVR progression was significantly suppressed on day 7, 14, 21 and 28 ($p<0.05$).

Conclusions: Lipo-Ripa could efficiently suppress PVR progression by its prolonged residency in the vitreous.

CONTROL ID: 3528243

SUBMITTER (NAME ONLY): Ahmed Roshdy Alagorie

TITLE: Impact of Slab Selection on the Relationship between Choriocapillaris Flow Deficits and Enlargement Rate of Geographic Atrophy.

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Alagorie, G. Corradetti, I. Byon, L. Tiosano, Y. Ji, M. Nittala, S. Velaga, M. Nassisi, S.R. Sadda, Doheny Eye Institute Doheny Image Reading Center, Los Angeles, California, UNITED STATES|A. Alagorie, Tanta University, Tanta, EGYPT|

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ABSTRACT BODY:

Purpose: To assess the impact of slab selection on the correlation between choriocapillaris (CC) flow deficits percentage (FD%) in eyes with geographic atrophy (GA) and the yearly enlargement rate (yER) of GA.

Methods: In this retrospective study, spectral domain optical coherence tomography (SD-OCT) and SD-OCT angiography (OCTA) images acquired on the Cirrus HD-OCT device (Carl Zeiss Meditec, Dublin, CA) were collected from patients with GA. Each patient underwent a 6x6 mm OCTA scan at baseline and two 6x6 mm structural SD-OCT volume scans, one at baseline and one after a minimum of 12 months. The edge of the GA lesion was delineated on the en face OCT fundus image and the yER was calculated after square root transformation. OCTA images were generated from three 10 µm thick slabs 11, 21 and 31 µm posterior to the RPE-fit line. A grid composed of 100 µm wide concentric rings was created around the GA on the compensated OCTA CC image and the FD% was calculated. FD% from each ring was correlated with the yER of GA. This was repeated for OCTA images from the different slab positions.

Results: Twenty-nine eyes of 22 patients were included in the study. For the 11-21 µm slab, the FD% was not significantly correlated with the yER for any of the evaluated rings. For the 21-31 and 31-41 µm slab, the FD% in the first five rings (from 0 to 500 µm from the border of GA) was significantly correlated with the yER. In all slab locations, there was no statistically significant correlation between the yER and CC FD% beyond 500 µm from the GA lesion.

Conclusions: Slab selection for quantification of CC FD% may have a significant impact on quantitative results and the correlation with other parameters of interest in eyes with GA.

CONTROL ID: 3528253

SUBMITTER (NAME ONLY): Romina Lasagni Vitar

TITLE: Substance P/Neurokinin-1 receptor pathway blockade alleviates epithelial stem cell deficiency

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Lasagni Vitar, P. Fonteyne, P. Rama, G. Ferrari, Eye Repair Lab, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY]

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ABSTRACT BODY:

Purpose: To evaluate the role of substance P (SP)/neurokinin-1 receptor (NK1R) pathway in corneal epithelium wound healing in a pre-clinical model of stem cell deficiency (SCD).

Methods: Eight-week-old C57BL6/N (WT) and B6.Cg-Tac1tm1Bbm/J (TAC1-KO) male mice underwent complete corneal disepithelization, including the limbus. Animals were followed-up for 14 days, corneal epithelial wound closure and transparency were assessed by biomicroscopy. To test the effect of NK1R blockade, WT mice received 0.1 or 1 mg/mL NK1R antagonist Fosaprepitant solution topically for 16 days after disepithelization (FOSA 0.1 and FOSA 1). After animal sacrifice, the number of goblet and conjunctival cells infiltrating the cornea was quantified with Periodic Acid Schiff and cytokeratin-8 and 19 stainings, respectively. Cytokeratin-12 was employed as a marker of corneal epithelial cells. The number of stem cells was quantified with p63 and BrdU co-staining.

Results: TAC1-KO mice showed a significant increase in epithelial wound healing rate ($p<0.001$) and corneal transparency ($p<0.001$) up to 14 days after disepithelization, compared to WT. Similarly, FOSA 1 mice showed a significant improvement in wound closure rate and transparency starting from day five when compared to WT mice ($p<0.05$), while FOSA 0.1 group did not show any improvement. TAC1-KO and FOSA 1 mice showed reduced number of infiltrating goblet and conjunctival cells ($p<0.05$) and increased number of corneal epithelial stem cells ($p<0.01$).

Conclusions: These results suggest that excessive expression of SP is associated with SCD and results in conjunctival infiltration and exhaustion of residual stem cells, supporting the hypothesis that blockade of neurokinin-1 receptor could be used as an adjuvant treatment in SCD.

CONTROL ID: 3528259

SUBMITTER (NAME ONLY): Nathalia Spier

TITLE: Improving OCT B-Scan classification feature attribution maps with adversarial training

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Feature attribution methods provide insight into the decision-making process of convolutional neural networks by highlighting pixels that strongly influence the classification decision. Training a network using adversarial examples causes it to emphasize the most relevant image features, resulting in more focused feature maps in comparison to conventional training. In this study, we investigated if an adversarially trained network produces more robust feature maps for an OCT B-scan classifier.

Methods: 61,058 B-scans from 478 independent eyes were used for training an Xception network both conventionally and with adversarial attacks for a binary classification task (i.e. B-scan is either normal or abnormal). A B-scan is considered “abnormal” if it was graded by at least one (of two) retina specialist to contain one of the pathologies shown in Table 1. The performance of each network was evaluated on a hold-out test set containing 15,338 B-scans of 120 eyes. The percentage of samples where pathology is present/absent for training and test set was, respectively, 41%/59% and 38%/62%. All B-scans were acquired with CIRRUSTM HD-OCT 4000 or CIRRUSTM HD-OCT 5000 devices (ZEISS, Dublin, CA).

Five different feature attribution methods – Grad-CAM, SmoothGrad2, VarGrad2, Integrated Gradients, and Vanilla Gradients – were used to generate feature maps indicating how much each feature in the model contributed to the predictions. The maps were qualitatively compared for the two types of training regimes.

Results: In all feature attribution methods except Grad-CAM, the model trained with adversarial examples displays clearer and more focused feature maps, as shown in Figure 1. However, the gains in feature attribution map interpretability come at the cost of a small loss in model performance. The conventionally trained model obtained an accuracy of 96.14% and AUC of 0.992, while the adversarially trained model obtained an accuracy of 94.74% and AUC of 0.989.

Conclusions: The results consistently show that when using feature attribution maps for model interpretability, one can obtain enhanced feature attribution maps by adversarially training the models

CONTROL ID: 3528266

SUBMITTER (NAME ONLY): Konstancija Kisonaite

TITLE: AI estimation of the non-pathological loss rate for the waist of the nerve fiber layer in the optic nerve head

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kisonaite, Z. Yu, C. Sandberg Melin, P.G. Soderberg, Neuroscience, Ophthalmology, Gullstrand lab, Uppsala Universitet, Uppsala, Uppsala, SWEDEN|C. Sandberg Melin, Ophthalmology clinic, Gavle sjukhus, Gavle, SWEDEN|G. Carrizo, C. Wang, Biomedical engineering and health systems, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: There is agreement on pathological loss rate of nerve fiber layer (NFL) in the optic nerve head (ONH) in glaucomatous individuals, as well as non-pathological due to aging. Morphometric measures of the NFL allow for assessment of the loss rate. Previous studies of non-glaucomatous individuals have reported a normal loss rate ranging from -1 to -2 $\mu\text{m}/\text{year}$. So far, a fully automatic method has never been used in studies for morphometrical measurement of the NFL.

Our clinical experimental study was performed with the use of an in-house developed AI-algorithm for automatical annotation and measurement of the NFL waist along the ONH, to investigate whether there is an age-related NFL loss rate in non-glaucomatous subjects.

Methods: Altogether 16 non-glaucomatous individuals were enrolled and equally stratified according to sex and age in four age groups of [30 39], [40 49], [50 59], [60 69] years. Three left-eye volumes were obtained from each participant. In each volume 500 annotations of the central limit of pigmental epithelium and their shortest distances to the inner limit of the retina were detected by the AI algorithm. The average distance was calculated in each volume. Then, all three volumes were averaged for each subject.

ANOVA and simple linear regression analysis were performed to evaluate the obtained data.

Results: Automatic measurement of one volume took approximately 1 minute. The 95% CI for the mean in age groups of [30 39], [40 49], [50 59], [60 69] years were estimated as 376.0 ± 33.5 , 292.3 ± 51.4 , 364.6 ± 61.6 and $344.3 \pm 49.9 \mu\text{m}$.

Variation among volumes and subjects was $7.7 \mu\text{m}^2$ (d.f.= 32) and $2758 \mu\text{m}^2$ (d.f.= 12) respectively. In a linear regression graph a negative trend was found, equivalent to a NFL loss of $-2.43 \mu\text{m}/\text{year}$.

Conclusions: Our automatical algorithm successfully annotated and computed the NFL waist thickness and produced results in line with current research, although general conclusions about normal loss rate in the population are difficult to draw due to our small sample size.

A fully automated approach to track changes in NFL thickness over time for glaucoma follow-up is possible.

Comparison of loss rate in the glaucomatous and non-glaucomatous population enables new glaucoma follow-up method to detect pathological changes earlier than current clinical perimetry.

CONTROL ID: 3528285

SUBMITTER (NAME ONLY): Tomas Blanco

TITLE: CD103⁺ Dendritic Cells Suppress Th1 Alloimmunity by Modulating CD11b⁺ Antigen Presenting Cells via IL-10

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Blanco, H. Nakagawa, H. Alemi, R.B. Singh, S. zhu, Y. Taketani, S. Anchouche, Y. Chen, S. Chauhan, J. Yin, R. Dana, Ophthalmology, Mass Eye and Ear, Harvard Medical School, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conventional dendritic cells (cDC) are critical for initiating T helper-1(Th1) alloimmunity post-corneal transplantation; however, the differential roles and molecular mechanisms of migratory CD103⁺ cDC and CD11b⁺ Ag-presenting cells (APC) subsets in Th1 alloimmunity have not been completely investigated. Herein, we examined the function of CD103⁺ DC in regulating CD11b⁺ APC-mediated anti-allograft Th1 immunity

Methods: High risk (HR) and low risk (LR) allogeneic corneal transplantation were performed using C57BL/6 mice as donors and BALB/c as hosts. On days 1,3,4,7,and 14 post-transplantation, CD103⁺CD11c⁺ DC, B220⁻CD11b⁺MHC-II^{high} APC, CD4⁺CD25⁺FoxP3⁺ regulatory T cells (Treg), and CD4⁺IFN-g⁺ (Th1) cells, were assessed by flow cytometry in graft recipient mice. On day 14, CD103⁺ DC of LR graft recipients and CD11b⁺ APC of HR graft recipients were FACS-sorted, incubated, and assessed for production of IL-10 and IL-12 by ELISA. CD11b⁺ APC were co-cultured with syngeneic CD103⁺ DC, syngeneic and CD4⁺CD25⁻ T cells, and allogeneic corneal lysate. Anti-IL10R blocking antibody was added, and IL-12 and IFN-g were measured by ELISA in supernatants

Results: CD103⁺ DC frequencies were significantly higher in LR setting compared to HR (p<0.001). CD11b⁺MHC-II^{high} APC frequencies were found significantly augmented in the HR setting compared to LR (p<0.001). Functional Treg (measured by FoxP3 expression) were found significantly higher in LR vs. HR (p<0.01), but no significant change in Treg-frequencies was observed. Th1 cell frequencies were significantly increased in HR vs. LR (p<0.001). IL-10 production was significantly reduced (p<0.001) and IL-12 significantly increased (p<0.001) by CD11b⁺ APC compared to CD103⁺ DC. The presence of CD103⁺ DC with CD11b APC led to a significant reduction in IL-12 secretion by CD11b⁺ APC (p<0.001) and modulation of allosensitization measured by IFN-g production by Th1 cells compared to CD11b⁺ DC alone (p<0.001). Blocking IL-10R, abrogated the modulatory effect of CD103⁺ DC on CD11b⁺ APC

Conclusions: These results provide novel insights into the distinct roles of migratory DC subsets in the regulation of Th1 immunity. Additionally, they show that CD103⁺ DC are critical for regulating Th1 immunity following corneal transplantation

CONTROL ID: 3528286

SUBMITTER (NAME ONLY): Faisal Jarrar

TITLE: Optic Disc Photography vs. Optical Coherence Tomography (OCT) in Detection of Glaucoma Progression

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Jarrar, Medicine, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, CANADA|J. Gao, B.D. Eadie, L. Shuba, P. Rafuse, M. Nicolela, B.C. Chauhan, J.R. Vianna, Department of Ophthalmology and Visual Sciences, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, CANADA|

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ABSTRACT BODY:

Purpose: To compare glaucoma specialists' evaluation of progression of glaucoma using optic disc photos and OCT, according to the intra- and inter-rater reproducibility of each technique, agreement between techniques, and ability of each technique to detect visual field (VF) progression.

Methods: We collected monoscopic disc photos, OCT reports (minimum rim width and retinal nerve fiber layer scans) and 24-2 VF tests from glaucoma subjects and healthy controls followed in longitudinal observational cohorts. Subjects with a baseline disc photo and OCT (taken on the same day) and a follow-up disc photo and OCT with at least 3 years of follow-up were included. Five glaucoma specialists evaluated the disc photos and OCT reports, ranking the likelihood of glaucoma progression as follows: definitely no progression, likely no progression, likely progression, definitely progression, corresponding to scores 1-4, respectively (Fig 1). Eight subjects were duplicated to determine intra-rater reproducibility and another 8 subjects were duplicated and presented in reverse order to estimate false positive (FP) progression detection. The controls were used to provide another estimate of FP and excluded from other analyses. VF glaucoma progression was defined as a classification of 'possible' or 'likely' on Guided Progression Analysis software, using VFs between the baseline and follow-up examinations. Reproducibility analyses were conducted with intraclass correlation (ICC). Average scores given by examiners were compared with Wilcoxon test. Accuracy to detect VF progression was explored using area under receiver operating characteristics curve (AUC).

Results: We included 72 glaucoma and 7 control subjects. Intra-rater reproducibility was higher for OCT than disc photos (mean ICC= 0.82 vs. 0.55). Intra-rater agreement between disc photos and OCT was poor (mean ICC= 0.23). Inter-rater agreement between the 5 examiners was moderate for OCT and poor for disc photos (ICC= 0.62 vs. 0.37). The mean score for inverted order images was higher in photos than OCT (2.1 vs. 1.6, $p=0.07$), which could suggest greater FP in photos than OCT. However, the mean score in controls was the same (1.6) with both techniques. The techniques had a comparable AUC (Fig 2).

Conclusions: OCT evaluations had higher intra and inter-rater agreement than evaluations of optic disc photos. Both techniques had similarly low detection of VF progression.

CONTROL ID: 3528309

SUBMITTER (NAME ONLY): Yinxi Yu

TITLE: Association of oral statin use with dry eye symptoms and signs in the DRY Eye Assessment and Management (DREAM[®]) Study

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yu, M.G. Maguire, K. Yu, G. Ying, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|N. Roy, P.A. Asbell, Department of Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Several studies suggest that statins have anti-inflammatory effect besides their cholesterol-lowering effect, and therefore may be beneficial for dry eye disease (DED). Data on the association between oral statin use and severity of DED is limited. We examine the association between statin use and severity of DED symptoms and signs among participants in the DREAM[®] study, a randomized multi-center clinical trial to evaluate the effect of omega-3 fatty acid supplements for the treatment of dry eye.

Methods: Self-reported oral statin use and daily dosage were collected at baseline. Statin use was further classified as low-intensity, moderate-intensity, and high-intensity according to American College of Cardiology guidelines. At baseline, 6 and 12 months, DED symptoms were evaluated using the Ocular Surface Disease Index (OSDI), DED signs in each eye were tear break up time (TBUT), Schirmer's test, corneal fluorescein staining, conjunctival lissamine green staining, and Meibomian gland dysfunction (MGD). Generalized linear models adjusted for age, gender, race, time and inter-eye correlation were used to compare the score on OSDI, scores of DED signs and a composite score of DED signs between statin users and non-users, and among users of different statin intensities.

Results: Among 535 participants with moderate to severe DED, 129 (24.1%) were statin users, with 15 (2.8%) low-intensity, 77 (14.6%) moderate-intensity and 31 (5.9%) high-intensity statin use. Statin users were significantly older than non-users (mean [SD] age 64.7 [9.4] vs. 55.9 [13.5], $p<0.001$). When data from baseline, 6 and 12 months were combined, statin use at baseline was not associated with severity of dry eye symptoms or signs (Figure 1, all adjusted $p\geq 0.09$). Higher intensity statin use was associated with lower MGD (Figure 2, adjusted trend $p=0.049$); although the mean score for non-users was similar to the mean score for moderate intensity users.

Conclusions: Among participants with moderate to severe DED, statin use was not associated with severity of dry eye symptoms and signs. Use of higher intensity statin was associated with lower MGD. Further analysis is needed to identify whether there is a specific type of MGD associated with intensity of statin use.

CONTROL ID: 3528313

SUBMITTER (NAME ONLY): Ashley Li

TITLE: Mendelian Randomization Supports a Casual Effect of Low Vitamin D on Non-infectious Uveitis Risk

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Li, G. Susarla, W. Chan, S. Davoudi, T. Ahmadi, S. Sathe, L. Sobrin, Retina, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|J. Mercader, Broad Institute, Cambridge, Massachusetts, UNITED STATES|G. Papaliodis, Uveitis, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|L.M. Tom, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Leong, General Internal Medicine, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|A. Leong, 2.Diabetes Unit and Center for Genomic Medicine, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Infectious and non-infectious uveitis (NIU) are significant causes of vision loss. Several studies have reported an association between NIU and low Vitamin D levels. However, a causal relationship between low Vitamin D level and NIU has not been established. We employed Mendelian randomization (MR) to investigate a possible causal association between Vitamin D levels and NIU.

Methods: Cases and controls were identified from the Massachusetts General Brigham Biobank. NIU cases were found by diagnostic codes and verified with an electronic medical record review. Controls were identified by the absence of uveitis diagnostic codes. Systemic diseases associated with NIU and diseases associated with Vitamin D metabolism were recorded for cases and controls. Genome-wide genotyping was performed on all patients using the Illumina Multi-Ethnic Global Array followed by imputation based on the European Haplotype Reference Consortium Panel. Then, 25-hydroxy Vitamin D (25OHD) candidate instruments (genetic variants) were selected from the summary statistics of a large genome-wide association study for Vitamin D level. Two-sample MR was performed where the causal effect was evaluated by the random-effects inverse-variance weighted (IVW) method. Individual 25OHD loci were evaluated for association with NIU.

Results: 375 cases and 4,167 controls were identified. 75 genetic variants were used in the primary MR analysis. We found a suggestive association of genetically decreased 25OHD with increased NIU risk (OR=2.17, 95%CI=0.99-4.73, P=.05; Fig. 1). Other MR methods and the leave-one-out analysis yielded consistent results. Excluding variants in the vitamin D binding gene (GC) showed a significant association (OR=2.40, 95%CI =1.06-5.46, P=.04; Fig. 1). In analyzing individual loci, genetically decreased 25OHD was associated with increased NIU risk using 6 variants within the CYP2R1 locus ($r^2 < .01$ and > 1 kb apart) (OR=7.09, 95%CI =2.76-18.25, $P=4.8 \times 10^{-5}$; Fig. 2). We identified no heterogeneity of effects or outlying genetic variants in the primary MR or individual locus analyses.

Conclusions: Our findings support a causal association between low Vitamin D levels and higher risk of NIU. This provides further support for a clinical study of Vitamin D supplementation as an adjunct intervention for preventing NIU recurrences or inducing remission.

CONTROL ID: 3528316

SUBMITTER (NAME ONLY): Frank Schaeffel

TITLE: Effects of reading with different letter size and contrast polarity on short term changes of axial length

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Schaeffel, B. Swiatczak, Institute of molecular and clinical Ophthalmology Basel (IOB), Basel, SWITZERLAND|F. Schaeffel, Ophthalmic Research Institute, University of Tübingen, Tübingen, GERMANY|

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ABSTRACT BODY:

Purpose: Animal studies have shown that selective stimulation of ON and OFF pathways in the retina can induce bi-directional changes in the eye growth. Recently, it has also been found that choroidal thickness increases in young human subjects when they read text with inverted contrast but decreases when they read normal text. The effect was assumed to be associated with asymmetrical stimulation of ON vs OFF pathways but the receptive field sizes were not studied.

Methods: Ten young adult subjects (average age: 23 ± 1 year) with a mean refraction of -0.7 ± 1.9 D (range: $+1.7$ to -4.2 D) read text from a large screen (65") in the dark room at 2 m distance. Four kinds of texts were tested: (1) small standard text (black letters on bright background, 0.8 cm height), (2) like 1 but contrast inverted, (3) large standard text (2 cm height), (4) like 3, but contrast inverted. The visual angle for a large text was similar as for newspaper letters read at 40 cm distance. All displays were matched in brightness (40 cd/m^2) and were presented to the subjects for 30 min on two separate days (one day small text, other day large text). Changes in axial length were measured using low coherence interferometry with autopotitioning system (Lenstar LS-900) before and after reading.

Results: Averaged over all subjects, the small text did not cause any significant changes in axial length after 30 minutes of reading (standard text $+0.6 \pm 7.7 \mu\text{m}$ and inverted text $-3.9 \pm 10.6 \mu\text{m}$, n.s.). However, large text with inverted contrast induced significant axial shortening of the eye, compared to standard large text ($-11.7 \pm 8.5 \mu\text{m}$ vs. $-1.6 \pm 5.9 \mu\text{m}$, $p=0.015$). Also in myopes the large inverted text caused significant axial shortening despite the small sample size ($n=3$, $-16.3 \pm 9.6 \mu\text{m}$ vs. $0.8 \pm 5.8 \mu\text{m}$, $p=0.05$).

Conclusions: As previously described for choroidal thickness, we find that reading text with inverted contrast induces significant shortening of the eyeball. However, in this study this only worked when the visual angle of the text height was about 0.6 deg but not when it was only 0.2 degrees.

CONTROL ID: 3528318

SUBMITTER (NAME ONLY): Kamran Ahmed

TITLE: Comparing Refractive Accuracy of Cataract Surgery Using Multiple Keratometric Platforms

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Ahmed, Ophthalmology, Washington University in St Louis, St Louis, Missouri, UNITED STATES | S. Naing, P. Dickinson, Ophthalmology, Wake Forest University, Winston-Salem, North Carolina, UNITED STATES |

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ABSTRACT BODY:

Purpose: We compare accuracy of spherical equivalent prediction in patients undergoing cataract surgery using keratometric values from the manual keratometer, IOL Master 500 and 700, and Pentacam. Our null hypothesis is that there is no difference in predicted spherical equivalent accuracy when comparing different keratometry platforms.

Methods: This study was an ongoing retrospective case series of all eyes undergoing cataract surgery by a single surgeon from 2019 to 2020 at Wake Forest University. Preoperative, biometric, intraoperative, and post-operative data were collected including keratometry measurements from each platform, predicted spherical equivalent based on the Barrett Universal II formula, and post-operative manifest refraction. All manual keratometry measurements were performed by the surgeon.

Results: 133 eyes met inclusion criteria for the study. Average best-corrected visual acuity improved from 20/50 (0.40 logMAR) pre-operatively to 20/22 (0.04 logMAR) post-operatively. Average spherical equivalent was -0.83 D pre-operatively and -0.31 post-operatively. There was no significant difference in prediction error: -0.05 D for the IOL Master 700, -0.05 D for the IOL Master 500, -0.10 D for the manual keratometer, and -0.19 D for the Pentacam ($p = 0.17$). There was also no significant difference in percentage of cases within 0.5 D of predicted spherical equivalent: 72% IOL Master 700, 87% IOL Master 500, 73% manual keratometer, and 73% Pentacam ($p = 0.65$).

Conclusions: There was no significant difference in keratometry measurements and accurate prediction of spherical equivalent after cataract surgery across the four platforms. This can reduce time and expense in obtaining multiple keratometry measurements unless there is suspicion for unreliability. Refractive accuracy of this study is similar to what is reported in the literature. IOL Master prediction tends toward more myopia and accuracy which is likely due to the smaller keratometric ring diameter measuring the steeper central cornea. Reaching 100% refractive accuracy will involve improved prediction of effective lens position, incorporating direct measurements of posterior corneal power, and post-operative refraction modification.

CONTROL ID: 3528351

SUBMITTER (NAME ONLY): Jonathan Bumstead

TITLE: Imaging the zonules using OCT with folded obliquely-aligned optics

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bumstead, S. Kubach, A. Carpenter, T. Callan, K. Arianta, Y. Wang, S. Bello, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|S.T. Zhao, University of Alberta, Edmonton, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: The zonules are the suspensory ligaments that connect the ciliary body to the crystalline lens and are critical for transferring force to the lens during accommodation. Because the zonules are positioned behind the iris, they are difficult to image using slit lamps and optical coherence tomography (OCT) and are therefore usually visualized using a gonioscope that contacts the patient's eye. Here we present a folded optical system that redirects the OCT scanning beam for imaging the zonules without contacting the patient.

Methods: An add-on lens was designed to redirect the scanning beam from a PLEX[®] Elite 9000 (ZEISS, Dublin, CA) swept-source OCT system to image the zonules. The add-on system maintains the same working distance and avoids the center of the field-of-view, so the iris viewer and internal fixation target of the OCT system can be used as the patient maintains central fixation. The design consists of several lenses and mirrors folded to redirect obliquely-scanned light at an angle of 70° into the patient pupil (Figure 1). Due to the non-uniform optical path length over the scan, the B-scans were transformed to more closely reflect the anatomical structure of the zonules.

Results: B-scans of the zonules were imaged in one volunteer (Figure 1d). Our design was capable of imaging the zonules over an 8.5° field-of-view with approximately 27.5µm 1/e² beam diameter at the zonules. In comparison to previous studies, the subject does not need to tilt the head or rotate the eye, which simplifies alignment.

Conclusions: Our proposed imaging system has the potential to improve assessment of whether an intraocular lens is viable for a patient by simplifying imaging of the zonules using OCT. Future designs will aim to increase imaging coverage to include the full circumference of the crystalline lens.

CONTROL ID: 3528389

SUBMITTER (NAME ONLY): Aditya Nair

TITLE: Patient fixation analysis in a combined OCT and fundus imaging system.

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nair, H. Bagherinia, P. Sha, A. Fard, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The quality of fixation achieved can greatly improve the OCT image acquisition by reducing eye motion. The patient fixation analysis serves as a measure of feedback during and after acquisition. This assessment can then be used during or after the scan to remind the patient to fixate better. In this work we demonstrate that meticulous patient fixation analysis can improve the acquisition workflow.

Methods: The motion of the eye is determined by calculating movement of the retina in the infrared-reflectance (IR) fundus image that appears in a sequence. IR images are acquired by using an IR fundus imager which is a separate sub-system from the OCT. This motion can either be horizontal (x) or vertical (y) direction along with some minor rotation. IR tracking prototype software of the CLARUSTM 500 (Zeiss, Dublin, CA) computes the tracking parameters of x and y eye motion relative to a fixation position. We analyzed the overall eye motion during an OCT image acquisition using these tracking parameters. Each eye was scanned using 3 different motion levels: good fixation, systematic eye movement, and random eye movement. The mean and standard deviation of the eye motion were reported for each motion level and each scan.

Results: Around 500 CLARUS IR images per scan (768x624 pixels over 11.52x9.36 mm² at the frame rate of 50Hz) of 15 eyes were captured with induced eye motion. Figure 1 shows the x and y eye motion relative to the initial fixation for three subjects with different induced eye motion. Figure 2 shows the statistics of eye motion for each scan of the 15 subjects. The mean value indicates the overall fixation offset from the initial fixation position. The standard deviation indicates a measure of overall eye motion within an acquisition. Scans containing systematic or random eye movement show significantly greater mean and standard deviation compared to good fixation, which is used as an indicator for poor fixation.

Conclusions: We track the retina and perform fixation analysis to highlight its use as feedback for the operator or the patient by providing informative messages during or after acquisition for reduced motion in OCT images, which is important for subsequent data processing.

CONTROL ID: 3528415

SUBMITTER (NAME ONLY): Ying Wang

TITLE: Refraction vs. Keratometry Comparisons After Wavefront-Guided LASIK and Wavefront-Guided Photorefractive Keratectomy

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, C. McKinnon, S. Kasthurirangan, Johnson and Johnson Medical Devices, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the changes in refractive error and keratometry (K) in wavefront guided (WFG) LASIK and WFG photorefractive keratectomy (PRK) for correction of myopic refractive errors.

Methods: A retrospective analysis of 334 eyes (170 patients) with manifest refractive spherical equivalent (MRSE) of $-6.21 \text{ D} \pm 2.78 \text{ D}$ (range: -12.13 D to -1.25 D) who underwent WFG Lasik, and 334 eyes (167 patients) with MRSE of $-4.08 \text{ D} \pm 1.97 \text{ D}$ (range: -8.75 D to -0.63 D) who underwent WFG PRK was performed. Outcome measures were changes in keratometry measurements taken with a full gradient corneal topographer and corresponding refractive changes compared preoperatively and at 6 months postoperatively. A correlation analysis was performed to determine the relationship between changes in refractive error (ΔSE) and changes in keratometry (ΔK). Ratio ($\Delta\text{K}/\Delta\text{SE}$) of change in keratometry (ΔK) to change in refractive error (ΔSE) was calculated and compared.

Results: A strong negative correlation (LASIK: $r = -0.897$ (ΔSE vs ΔK), and PRK: $r = -0.903$ (ΔSE vs ΔK), $p < 0.0001$ for both) was seen between the change in refraction and change in average K for both. The mean ratio for ΔK and ΔSE was -0.78 ± 0.28 for LASIK and -1.03 ± 0.52 for PRK. A larger ratio ($\Delta\text{K}/\Delta\text{SE}$) for the WFG PRK compared to the WFG LASIK (ratio difference of 0.25 with 95% CI of (0.19, 0.31), $p < 0.0001$) was found. WFG PRK required more corneal flattening for a given change in refractive error when compared to WFG LASIK. The accuracy of intended versus achieved MRSE outcomes at 6 months indicate good accuracy of treatment per MRSE outcomes (LASIK, slope: 0.99, $r = 0.988$, $p < 0.001$ and PRK, slope: 1.04, $r = 0.975$, $p < 0.001$).

Conclusions: The refractive outcomes after both LASIK and PRK were comparable with good predictability at correcting myopia. However, WFG LASIK measurements showed a smaller amount of corneal flattening for a given degree of myopic refractive correction compared to WFG PRK.

CONTROL ID: 3528425

SUBMITTER (NAME ONLY): Xinyi Chen

TITLE: Trachoma and facial cleanliness are associated with environmental factors and hygiene behaviors in Tanzania

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Chen, B. Munoz, M. Wolle, H. Mkocha, S.K. West, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Facial cleanliness and environmental improvement are parts of the SAFE strategy to eliminate trachoma, but the impact of environmental factors on children's facial cleanliness and trachoma have not been extensively explored, especially when disease burden is low. We performed a cross-sectional clinical study to identify environmental factors affecting children's facial cleanliness and trachoma in Kongwa, Tanzania, where the overall prevalence of trachoma was 7% but varied between villages.

Methods: A standardized survey was carried out to observe characteristics of household environment and hygiene behaviors in a random selection of 1,798 households in 92 villages. Children aged 0-5 in these households were examined for facial cleanliness. In 50 randomly-selected villages, children aged 1-9 were randomly selected and examined for trachoma.

Results: Time spent on obtaining water was generally short and not correlated with clean faces. In a multivariate model adjusting for child age and household wealth, children were more likely to have clean faces if the yard was clean, if the household had an improved latrine, if the household had greater water storage capacity, and if there were clothes drying around the house. Based on our findings, we constructed a cleanliness index which was a summary score of the following markers: clean yard, washing clothes, improved latrine, ≥ 1 child in the household having clean faces. When the community prevalence of trachoma was $<5\%$, more than 50% of household in the community had a score of 2 or higher. If the trachoma prevalence was more than 10%, less than 50% of households had a score of 2 or higher. An ordinal logistic regression predicting category of trachoma prevalence (0-5%, 5-9.9%, $\geq 10\%$) found that a 0.5 unit increase in the community average clean index score was associated with a 2.3 increase in the odds of dropping trachoma prevalence by one category.

Conclusions: A household cleanliness index that increases with increasing number of cleanliness factors was significantly correlated with decreased community prevalence of trachoma, suggesting that a multi-pronged approach to improve household cleanliness is valuable for trachoma elimination.

CONTROL ID: 3528437

SUBMITTER (NAME ONLY): Kyoung Woo Kim

TITLE: Time-dependent serial changes of antigen-presenting cell subsets are distinct between the corneal sterile inflammation and allosensitization

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kim, H. Lee, H. Kim, M. Kim, Laboratory of Ocular Regenerative Medicine and Immunology, Seoul Artificial Eye Center, Seoul National University Hospital Biomedical Research Institute, Seoul, KOREA (THE REPUBLIC OF)|K. Kim, Ophthalmology, Chung-Ang University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|M. Kim, Ophthalmology, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: The kinetics of antigen-presenting cells (APCs) vary depending on their resident tissues and the manner of sensitization. We investigated the long-term kinetics of APCs in Balb/c mouse models of corneal quiescent or potent sterile inflammation and allosensitization using corneal partial trephination, syngeneic, and allogeneic corneal transplantation.

Methods: Balb/c mice were assigned into 4 groups: control, corneal partial trephination (PT), 2.5 mm-to-2.0 mm syngeneic (Syn) and C57BL/6 to Balb/c allogeneic corneal transplantation (Allo). The serial changes in CD11b⁺CD11c⁺MHCII^{hi}, CD11b⁺CD11c⁺MHCII^{hi}, and CD11b⁺CD11c⁻MHCII^{hi}, and CD69^{hi} or interferon gamma (IFN γ)^{hi} effector T cell subsets were evaluated in the ocular surface, draining lymph nodes (dLNs), and spleen for over 4 weeks.

Results: In PT, CD11b⁻CD11c⁺MHCII^{hi} and CD11b⁺CD11c⁺MHCII^{hi} subsets increased until 4 weeks with increases in ocular IFN γ ^{hi} T cells. In Syn, ocular CD11b⁺CD11c⁺MHCII^{hi} and CD11b⁺CD11c⁻MHCII^{hi} cells increased until 4 weeks with an increase in ocular CD69^{hi} T cells. However, in Allo, the ocular and lymph nodal CD11b⁺CD11c⁺MHCII^{hi} and CD11b⁺CD11c⁻MHCII^{hi} cells and ocular CD11b⁺CD11c⁻MHCII^{hi} cells significantly increased until 4 weeks and primed both the ocular and lymph nodal IFN γ ^{hi} and CD69^{hi} T cell subsets. Ocular CD11b⁺CD11c⁺MHCII^{hi} subset appears to be a major population that becomes mature MHCII^{hi} APCs, regardless of the inflammation type.

Conclusions: This indicates that allosensitization activates the corneal CD11b⁻CD11c⁺MHCII^{hi}, CD11b⁺CD11c⁺MHCII^{hi} and CD11b⁺CD11c⁻MHCII^{hi} cells leading nodal maturation of CD11b⁻CD11c⁺MHCII^{hi} and CD11b⁺CD11c⁺MHCII^{hi} subsets to interact with nodal T cells, whereas sterile inflammation seems to induce ocular T cell interaction independently of the nodal activation of APCs.

CONTROL ID: 3528442

SUBMITTER (NAME ONLY): Bhav Parikh

TITLE: A novel approach for the prevention of retinal scarring by a polymer

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.H. Parikh, Z. Liu, G. Lingam, X. Su, Ophthalmology, National University of Singapore, Singapore, SINGAPORE|B.H. Parikh, Z. Liu, X. Su, Institute of Molecular and Cell Biology, Singapore, SINGAPORE|Q. Lin, X. Loh, Institute of Materials Research and Engineering, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: One of the most common causes of vision loss after retinal surgery is the formation of scar tissue on, in or under the retina, which can result in proliferative vitreoretinopathy (PVR). The current standard practice involves surgical removal of scar tissue, which carries intrinsic risk. Even if PVR is successfully treated by surgery, vision impairment could still result, and hence there is an urgent need to find alternative non-surgical solutions for PVR prevention.

Methods: Thermogelling polymer, composed of poly(ethylene glycol) (PEG), poly(propylene glycol) (PPG) and poly(ϵ -caprolactone) (PCL), referred to as poly(CEP), was synthesized. A surgically induced rabbit model of PVR was used to validate poly(CEP)'s efficacy in preventing PVR, in comparison to Sulfur Hexafluoride (SF_6). The polymer-cell interactions and the effect on scarring were further investigated in an in vitro model of PVR using human embryonic stem cell-derived retinal pigment epithelial (ES-RPE) cells. Cellular assays to study poly(CEP)'s effects on hyper-proliferation and increased migratory capacity of RPE cells, were conducted. Poly(CEP) internalization was observed using flow cytometry. Key epithelial-mesenchymal transition (EMT) markers were analyzed at both mRNA and protein level.

Results: Poly(CEP) prevented fibrosis, scarring and tractional retinal detachment in the rabbit model of PVR, in addition to acting as an effective vitreous tamponade. Poly(CEP) at 1wt%, in its micellar form and in a concentration-dependent manner, completely inhibited the formation of contractile fibrocellular membranes in the in vitro model of PVR. Furthermore, at the same concentration of 1wt%, poly(CEP) showed the highest suppression of proliferation and migration of RPE cells. Poly(CEP) exerted this anti-scarring property after internalization and through the modulation of EMT-related transcription factor genes.

Conclusions: In this work, we show that a thermogelling polymer prevents retinal scarring in a pre-clinical rabbit model of PVR. This is mediated via a polymer-induced impairment of EMT, which results in suppression of RPE cell proliferation and migration. This is the first report wherein a synthetic polymeric material, without the use of any small molecule therapeutics, is shown to inhibit EMT and prevent retinal scarring. This study highlights the potential of the next generation of nanomedicine whereby small molecule drugs are no longer required.

CONTROL ID: 3528444

SUBMITTER (NAME ONLY): Tsz King Wong

TITLE: Efficacy of elastic Breath-O Correct orthokeratology on myopia control in a 1-year study period

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Wong, K. Choi, H.H. Chan, C.T. Lam, School of Optometry, The Hong Kong Polytechnic University, Kowloon, HONG KONG|H.H. Chan, C.T. Lam, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: This study is to evaluate the myopia reduction effect and myopia control efficacy of the novel elastic Breath-O Correct orthokeratology (OK) lenses.

Methods: A total of 85 subjects aged 9 to 12 years with spherical equivalent refraction (SER) between -1.00D and -4.00D were recruited, then randomly assigned into OK (n=49) or spectacle control (n=36) groups. Breath-O Correct lenses were prescribed in OK group with routinely scheduled aftercares. Corneal topography, SER, unaided and best-corrected visual acuity in LogMAR (BCVA), anterior chamber depth (ACD), and axial length (AL) were measured at baseline and 1-year visit. For the control group, update of spectacles was indicated if there was a 0.50D difference in spherical or cylindrical power by subjective refraction in a 6-month follow-up.

Results: Seventy-one subjects (OK: 42, Control: 29 Age 9.46 ± 1.32 years) completed the 1-year study. Seven OK subjects withdrew due to poor visual quality, inconvenient lens care, and COVID-19 pandemic. Seven control subjects withdrew due to fast myopia progression and COVID-19 pandemic. In OK group, the 1-year simulated flat and steep K decreased significantly (Flat K: -1.57 ± 0.95 D; Steep K: -1.59 ± 1.07 D; $p < 0.001$) with a mean unaided visual acuity of 0.09 ± 0.13 . The mean dry subjective SER in control and OK groups were -2.92 ± 1.32 D and -0.07 ± 0.66 D ($p < 0.001$) respectively without significant difference in BCVA (Control: 0.01 ± 0.04 , OK: 0.00 ± 0.05 ; $p > 0.05$). The mean AL elongation was significantly different between two groups (Control: 0.35 ± 0.2 mm, OK: 0.14 ± 0.17 mm, $p < 0.001$). A significant ACD elongation was also noted in control group but absent in OK group (Control: 0.073 ± 0.096 mm, $p < 0.001$; OK: -0.054 ± 0.326 mm $p > 0.05$). RM-ANOVA with post-hoc Bonferroni correction revealed significant interaction between OK treatment and the rate of myopia progression in 1 year ($p < 0.001$).

Conclusions: The novel elastic Breath-O Correct OK lens effectively retarded AL elongation, and hence, myopia progression in school-aged children without compromising BCVA and with maintenance of good unaided daytime vision.

CONTROL ID: 3528456

SUBMITTER (NAME ONLY): David Sousa

TITLE: Retinal vascular reactivity in type 1 diabetes patients without retinopathy using optical coherence tomography angiography

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We hypothesize that patients with type 1 diabetes (T1D) may have abnormal retinal vascular responses before diabetic retinopathy (DR) is clinically evident. Optical coherence tomography angiography (OCTA) was used to dynamically assess the retinal microvasculature of diabetic patients with no clinically visible retinopathy.

Methods: Controlled non-randomized interventional study. The studied population included 48 eyes of 24 T1D patients and 24 demographically similar healthy volunteers. A commercial OCTA device (AngioVue®) was used and two tests were applied: (i) the hypoxia challenge test (HCT) and (ii) the handgrip test, in order to induce a vasodilatory or vasoconstrictive response, respectively. The HCT is a standardized test that creates a mild hypoxic environment equivalent to a flight cabin. The handgrip test (i.e. isometric exercise) induces a sympathetic autonomic response. Changes in the parafoveal superficial and deep capillary plexuses in both tests were compared in each group. Systemic cardiovascular responses were also comparatively evaluated.

Results: In the control cohort, the median parafoveal superficial and deep plexuses' vessel density increased during hypoxia ($F_{1,23}=15.69$, $p<0.001$ and $F_{1,23}=16.26$, $p<0.001$, respectively). In the T1D group, this physiological response was not observed in neither the superficial, nor the deep retinal plexuses. Isometric exercise elicited a significant decrease in vessel density in both superficial and deep plexuses in the control group ($F_{1,23}=27.37$, $p<0.0001$ and $F_{1,23}=27.90$, $p<0.0001$, respectively). In the T1D group, this response was noted only in the deep plexus ($F_{1,23}=11.04$, $p<0.01$).

Conclusions: Our work suggests there is an early impairment of the physiologic retinal vascular response in patients with T1D without clinical diabetic retinopathy.

CONTROL ID: 3528460

SUBMITTER (NAME ONLY): Giulio Ferrari

TITLE: Modulating ocular surface pain through Neurokinin-1 receptor blockade

SESSION TITLE: Corneal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Ferrari, R.M. Lasagni Vitar, P. Fonteyne, P. Rama, Eye Repair Lab, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY]

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ABSTRACT BODY:

Purpose: The aim was to test the role of Substance P and its receptor Neurokinin 1 (NK1R) on ocular surface pain.

Methods: 8-week-old C57BL6/N (WT) and B6.Cg-Tac1tm1Bbm/J (TAC1-KO) male mice were used. 5 M NaCl was topically applied on the cornea, followed by topical application of NK1R antagonist Fosaprepitant 2, 10, 50 mg/mL; 4 mg/mL Oxybuprocaine chloride, or 0.1% Diclofenac. The eye-wiping test was used to quantify ocular surface pain. Substance P (SP) content was quantified in the tear fluid and trigeminal ganglia (TG), and TAC1 mRNA was assessed in the cornea. Corneas were immunostained for β 3-tubulin and NK1R to image peripheral nerves.

Results: TAC1-KO mice or a single dose of 10 or 50 mg/mL Fosaprepitant applied topically to WT displayed a significant reduction of nociception ($p < 0.001$) compared to vehicle, while 2 mg/mL Fosaprepitant induced corneal analgesia when it was administered for 10 days, ($p < 0.05$). Diclofenac or Oxybuprocaine reduced corneal nociception when compared to vehicle or Fosaprepitant ($p < 0.05$). Fosaprepitant or Oxybuprocaine treated groups showed lower SP content in tear secretions and TG ($p < 0.05$), and reduction in TAC1 mRNA ($p < 0.05$) in the cornea. Co-localization of NK1R and β 3-tubulin was detected in mouse corneas.

Conclusions: Topical administration of the NK1R antagonist Fosaprepitant effectively reduces ocular surface pain, SP release in the tear fluid and TG. Fosaprepitant repurposing shows promise for the treatment of ocular pain.

CONTROL ID: 3528463

SUBMITTER (NAME ONLY): Grace George

TITLE: The Heidelberg Flex™ imaging system as a non-invasive bedside test of intracranial pressure

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. George, Northumbria Healthcare NHS Foundation Trust, North Shields, Tyne and Wear, UNITED KINGDOM|J. Hogg, K. Hodson, J. Shelton, C. Cowie, W. Innes, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|M. Gough, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|S. Dlay, Newcastle University Faculty of Science Agriculture and Engineering, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diagnostic delay in identifying intracranial pressure (ICP) elevation may lead to permanent visual impairment or profound neurological disability. Invasive, poorly tolerated methods currently used have associated clinical risk. Optical Coherence Tomography (OCT) and retinal infrared (IR) video offer a non-invasive, non-contact imaging method. Absence of spontaneous venous pulsation (SVP) on IR video alongside OCT optic nerve head (ONH) swelling raises suspicion of elevated ICP.

However, OCT is typically table-top mounted, installed in primary eye care centres or hospital ophthalmology departments and is inaccessible in acute or high dependency care settings. We aim to establish the feasibility of OCT, OCT-Angiography (OCTa) and IR video as a bedside investigation for acutely unwell hospital inpatients including intensive care.

Methods: The Heidelberg Flex™ imaging system is a flexible and mobile ophthalmic imaging solution with a highly capable imaging head mounted on a flexible arm on a wheel-based structure. One individual using a foot pedal took images in healthy control and conscious hospital inpatients laying supine. Three individuals were needed to image unconscious patients. One individual held patients' heads still and lids open, one operated the computer interface and one operated the imaging head. Due to the flexibility of the mobile imaging head, it was possible to capture ONH imaging independent on patient fixation, a significant advantage in unconscious patients. Hypromellose 0.3% eye drops were used prior to imaging for unconscious patients. No mydriatic drops were used.

Results: OCT and OCTa box scans plus IR en-face video centred on the ONH were acquired from both eyes for all conscious study patients. OCT videos, positioned to intersect a main branch of the retinal vein, were also captured. OCTa was not possible on unconscious patients due to poor fixation and lack of patient blink. OCT video failed to identify SVP possibly due to the fact that several images are averaged to produce each frame. However, SVP was clearly detectable on IR en-face video.

Conclusions: The Heidelberg Flex™ imaging system presents a useful method to non-invasively confirm normal ICP in acutely unwell hospital inpatients, including intensive care patients. En-face IR video is more effective than OCT video in identifying SVP and thus normal ICP.

CONTROL ID: 3528467

SUBMITTER (NAME ONLY): Julian Rapp

TITLE: The diverse angiogenic effect of IL6-family cytokines on vascular endothelial cells and the modulatory influence of STAT3 signaling

SESSION TITLE: Cytokines, growth factors, anti-inflammatory

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Rapp, J. Wolf, C. Lange, H. Agostini, G.R. Schlunck, F. Bucher, Eye Center, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, GERMANY|R. Klar, R. Fritsch, Department of Medicine I, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, GERMANY|O. Gorka, O. Groß, Institute of Neuropathology, Medical Center - University of Freiburg, Faculty of Medicine, University of Freiburg, GERMANY|

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ABSTRACT BODY:

Purpose: The role of IL6-family cytokines, potent activators of the STAT3 pathway, on angiogenesis and in vascular retinal disease is controversial. Despite STAT3 as a shared signaling pathway, some IL-6 family members like oncostatin M (OSM) seem to be proangiogenic, others like ciliary neurotrophic factor (CNTF) appear to inhibit retinal angiogenesis.

This study tries to explain those differences and the role of STAT3 in retinal angiogenesis by comparing the effect of cytokine-induced activation and knock-down in vascular endothelial cells.

Methods: Angiogenic responses of human umbilical vein cells in response to VEGF, OSM or CNTF treatment were assessed by spheroid sprouting- and migration assays. Cytokine-dependent signaling was evaluated by western blot and metabolic alterations by extracellular flux. A STAT3 knock-down was established using siRNA. Transcriptomic shifts were assessed by RNA sequencing.

Results: OSM elicits proangiogenic responses on top of VEGF-induced cell sprouting ($\Delta = +31\%$, $p < 0.05$) and migration ($\Delta = +29.2\%$, $p < 0.05$) whereas CNTF has antiangiogenic effects on sprouting ($\Delta = -21.9\%$, $p < 0.05$) and a small influence on migration ($\Delta = +6.1\%$, $p < 0.05$). Both cytokines activate STAT3 while OSM also signals through ERK and AKT. Furthermore, OSM phosphorylates STAT3 at serine 727 and shifts cells to an active metabolic state by increasing mitochondrial performance. RNA-Seq revealed a transcriptomic shift favoring migration in response to OSM but not CNTF treatment. STAT3 knock-down reduced VEGF-induced cell sprouting ($\Delta = -39\%$, $p < 0.05$) by affecting the cytoskeleton assembly. Interestingly, STAT3 knock-down changed CNTF's antiangiogenic effect to a proangiogenic response ($\Delta = +77.8\%$, $p < 0.05$) while enhancing OSM's proangiogenic drive ($\Delta = +369.9\%$, $p < 0.05$). No other pathways showed compensatory upregulation on protein level. RNA-Seq analysis determined a clear shift to a state of proliferation and migration in OSM-stimulated knock-down cells.

Conclusions: The divergent angiogenic properties of OSM and CNTF can be explained by individual differences in signaling, influence on metabolism and transcriptomic shifts. The shared STAT3 pathway seems to be essential to keep proangiogenic responses in check. In conclusion, this study sheds light on IL6-family endothelial cell interaction and reveals a novel perspective on the role of STAT3 in angiogenesis.

CONTROL ID: 3528475

SUBMITTER (NAME ONLY): Peter Essig

TITLE: OKN-onset is influenced by the contrast level of a visual stimulus

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Essig, Y. Sauer, S. Wahl, Institute for Ophthalmic Research, Tübingen, GERMANY|S. Wahl, Carl Zeiss Vision International GmbH, Aalen, GERMANY|

Commercial Relationships Disclosure (Abstract): Peter Essig: Commercial Relationship: Code N (No Commercial Relationship) | Yannick Sauer: Commercial Relationship: Code N (No Commercial Relationship) | Siegfried Wahl: Commercial Relationship(s); Carl Zeiss Vision International GmbH: Code E (Employment); Carl Zeiss Vision International GmbH: Code F (Financial Support)

ABSTRACT BODY:

Purpose: Search for an objective approach to measure contrast sensitivity has already been commenced, while the use of eye movements showed a potential solution. The current study aimed to search for the onset time of the optokinetic nystagmus (OKN) quick-phase (QP) in respect to various contrast levels over a range of spatial frequencies (SF) of a moving grating. A trend in timing of the first-OKN-QP for different parameters of a visual stimulus may give a theoretical implementation in the stimulus-presentation-time optimization.

Methods: To stimulate the OKN response, a 3 seconds sequences of horizontally moving bars with a velocity of 2.5 °/sec, of selected spatial frequencies (SF=1,2,3,4 cpd) and a contrast range C=0.1-58 %, with 22 log-steps in between, were used, whereas the contrast levels were uniformly distributed over 184 trials. Furthermore, as the clinical approach for measuring contrast sensitivity was followed (monocular stimulation), an infra-red filter was installed in front of the left eye of all seven subjects with normal vision. Extracting the OKN events was performed first using a velocity-based algorithm for saccadic (OKN-QP) detection, in continuation with directional and velocity analysis of the slow-phase of OKN (OKN-SP) between two detected OKN-QPs. Next, the search for time of the first OKN-QP after stimulus onset was performed just in trials in which at least two OKN events were detected, requesting a robust response to given parameters of the visual stimulus. On top of that, the found times were clustered with respect to the stimulus parameters (SF, C) for all subjects and the mean time was calculated within a 7.5 % contrast windows.

Results: The application of Spearman's correlation, showed a robust propensity of decreasing the mean first-OKN-QP time with increasing contrast level for all four used SFs ($R_{all}^2 > 0.76$), while the effect of SF was shown as not significant ($p=0.1$; $\chi^2=6.27$). In all SFs combined, the first-OKN-QP time was found to be 361 ± 12 ms for the highest contrast level (C = 58%), whereas it changed towards 525 ± 32 ms for the lowest contrast level (C=0.1 %).

Conclusions: In conclusion, this study showed an influence of contrast level on the time of OKN onset, hence this study discloses a possible methodological approach of improving the time efficiency of contrast sensitivity testing using the OKN reflexes, by adjusting the presentation time of a visual stimulus of particular parameters.

CONTROL ID: 3528490

SUBMITTER (NAME ONLY): Alessandro Zandonà

TITLE: Deep learning based best focus image detection in automated gonioscopy

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zandonà, L. Cappellari, NIDEK Technologies Srl, Albignasego, Padova, ITALY|

Commercial Relationships Disclosure (Abstract): Alessandro Zandonà: Commercial Relationship(s);NIDEK Technologies Srl:Code E (Employment) | Lorenzo Cappellari: Commercial Relationship(s);NIDEK Technologies Srl:Code E (Employment)

ABSTRACT BODY:

Purpose: NIDEK GS-1 (NIDEK CO., LTD Japan) provides a 360° view of the iridocorneal angle by acquiring multiple images on different focus planes over the whole angle depth. The device also provides a feature-based algorithm (FB) to automatically detect the images with the best focused Target Region (TR), i.e. the trabecular meshwork or, in case of angle closure, the iridocorneal interface. In this work, we developed a deep learning based algorithm (DLB) to improve the detection accuracy of the images with the best focused TR (henceforth best focus shots).

Methods: The algorithm includes two steps: first, the extraction of a ROI centered at the TR (not part of this work), then the processing of image pairs by a Siamese Convolutional Neural Network (SCNN) that predicts the probability that one shot has a more focused TR than the other. The SCNN is coupled with a concatenation and a fully-connected layer with a softmax activation function, and optimizes a categorical cross entropy loss. The SCNN is trained inside a Cross-Validation (CV) on 288 stacks of 17 images each, and a Bayesian optimization is performed over the CV folds to tune the SCNN hyperparameters. To test the predictive performance of our solution, both DLB and FB algorithms are run on 96 image stacks that were not considered for training, and the results are compared with the manually identified best focus shots. In detail, the performance is assessed by computing the distance between predicted and actual best focus shots.

Results: DLB achieves better mean performance over the stacks with respect to FB, being both mean and median distance between predicted and actual best focus shots smaller (Tab. 1, Fig. 1). Moreover, DLB's smaller standard deviation suggests a more stable performance over the stacks than FB (Tab. 1).

Conclusions: Our algorithm has the potential to improve the detection of shots with the best focused TR; consequently, our solution increases the automation of the examination, making it more accessible to non-expert personnel, and providing an exam quality that is less operator dependent.

CONTROL ID: 3528503

SUBMITTER (NAME ONLY): Andrea De Giusti

TITLE: Deep Neural Network for the Automatic Evaluation of Gonioscopic Image Quality

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. De Giusti, Software Department, Nidek Technologies Srl, Albignasego (PD), ITALY|A. Zorgati, Student, Università degli Studi di Padova, Padova, Veneto, ITALY|

Commercial Relationships Disclosure (Abstract): Andrea De Giusti: Commercial Relationship(s);Nidek Technologies Srl:Code E (Employment) | Alessandro Zorgati: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: NIDEK GS-1 (NIDEK CO., LTD. Japan) captures 360° exams of the iridocorneal angle. The angle is split into 16 sectors each acquired on 17 focal planes. Incorrect alignment conditions, patients' movements during exam acquisition, difficulty in keeping the eye open may degrade the quality of acquired images possibly preventing a correct pathology assessment. The aim of this work is to use Deep Neural Networks (DNNs) for assigning a quality index to GS-1 images.

Methods: A total of 1835 images (RGB, 1280x960) taken from healthy and pathologic eyes were used. For each image a 224x224 ROI centered on the most relevant part of the angle (trabecular meshwork or irido-corneal interface for closed angles) was considered as input to the DNN. The dataset was manually split into two classes: "good" and "bad". The former enclosed all images whose ROI was not saturated and rich of details, whereas the latter contained the remaining images (see examples in Fig 1). Since good and bad classes were unbalanced (1-to-10 ratio), 5 partially overlapping ROIs for good images and 1 ROI for bad images were considered, respectively. Transfer Learning was chosen in place of training a DNN from scratch. Hence, a pretrained network was chosen and partially retrained for the new quality-index task, with the advantage of reducing training time and computational requirements. For this study, the VGG16 and Xception DNNs trained on ImageNet were considered. The input dataset was divided into training, validation, and test sets having 70%, 20%, and 10% of images, respectively.

Results: The Xception-based DNN gave the best results with ~95% accuracy and fast convergence (<15 epochs). The quality index has been assessed both on the test set and by visually comparing the best-quality image with the best-focus image in a focus sequence (see Fig 2).

Conclusions: Transfer learning based on off-the-shelf DNNs can be successfully used for giving a quality index to GS-1 images. The proposed algorithm could reduce the time spent by clinicians for selecting the best images on which to perform the clinical assessment and could be also used for automatically retaking the examination if an insufficient quality is detected improving the effectiveness of the device.

CONTROL ID: 3528513

SUBMITTER (NAME ONLY): Ramin Tadayoni

TITLE: HAWK and HARRIER 48-week data: potential for treatment interval extension in patients with nAMD disease activity at Week 16

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The Phase 3 HAWK (NCT02307682) and HARRIER (NCT02434328) studies evaluated the efficacy and safety of brotacizumab (Bro) versus aflibercept (Afl) in previously untreated patients with neovascular age-related macular degeneration. All patients received three monthly loading injections, then brotacizumab was injected q12w unless disease activity (DA) was identified resulting in permanent adjustment to q8w, while aflibercept was dosed q8w throughout the study, as per label at study initiation. Due to the study design, Bro patients adjusted to a q8w regimen at the end of the matched loading phase at Week 16 owing to DA could not subsequently extend to a q12w interval. The aim of this post-hoc analysis is to assess subsequent DA in patients with DA at Week 16 to determine the potential for interval extensions during the first year of treatment if the protocol had allowed it.

Methods: In Year 1 of HAWK and HARRIER, disease activity assessments (DAA) were conducted at Weeks 16, 20, 32, and 44 in both studies for all Bro and Afl patients regardless of whether DA was detected at earlier visits or not; presence of DA was determined at the discretion of the masked investigator. This post-hoc analysis evaluated the absence of DA, and thus potential for interval extension, in the matched cohort of Bro and Afl patients with DA at Week 16 using pooled data from the Bro 6 mg arms and Afl arms of both studies. Absence of DA at two consecutive DAA was considered a surrogate for stable disease control.

Results: At the first DAA at Week 16, more Bro vs Afl patients had no DA (77.0% [n=540/701] vs 67.5% [n=470/696]). Within the subgroup of patients with DA at Week 16, more Bro than Afl patients had absence of DA at each subsequent DAA in Year 1 (Fig 1). Furthermore, a higher proportion of Bro vs Afl patients had DA absence at two consecutive DAA (Week 20/32: Bro=56.8%, Afl=45.2%; Week 32/44: Bro=66.9%, Afl=51.2%).

Conclusions: Conclusions: In HAWK and HARRIER, more Bro- vs Afl-treated patients with DA at Week 16 had no DA at subsequent assessments from as early as Week 20, including at consecutive DAAs. These findings indicated a higher potential for treatment interval extension and robust and stable disease control with Bro within the first year of treatment.

CONTROL ID: 3528519

SUBMITTER (NAME ONLY): Maria Esther Santos Blanco

TITLE: RETIPROGRAM: A CLINICAL DECISION SUPORT SYSTEM FOR DIABETIC RETINOPATHY WITH PREDICTIVE VALUE

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Santos Blanco, P.R. Aroca, R.V. Pujol, R.N. Gil, M.B. Bernaldiz, A. Valls, D. Puig, A. Moreno, Hospital Sant Joan, SPAIN|

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ABSTRACT BODY:

Purpose: RETIPROGRAM is a registered clinical decision support system program for diabetic retinopathy (DR) screening. The algorithym calculates the risk of developing DR in the next years attending to medical variables. The initial results were already shown previously in ARVO 2020. Currently the aim is not only to show its accuracy as much as its prediction capability, detecting future DR in short term in patients without DR.

Methods: The program was developed since a statistical analysis was based on fuzzy random forest methodology, assessing different medical variables.

The sample included 98873 of diabetes mellitus type 2 population. The medical variables registered were age, gender, diabetes mellitus duration, arterial hypertension, HbA1, glomerular filtration rate, microalbuminuria and body mass index. Attending to these variables it is calculated an estimated risk and it is suggested a date for the next control.

Results: To validate the results consistency the risk percentage were compared with the presence of DR in the retinography.

The test sensibility was 60.36%, specificity 78,61% and 19644 were considered false positive. The false positive group images were reviewed after two years and it was shown that 11.949 had already DR. The progression rate in the false positive group was 60,82% in two years.

The initial sensitivity and specificity values were good enough, but if they are corrected according the results after two years, the sensitivity (84,20%) and specificity (90,37%) values would be even better.

False positive group, is commonly considered as a test error, but in this case, analyzing it carefully it would report some added test value, the capability of prediction in absence of DR in the retinography.

Conclusions: In general, and also in DR, screening models efficacy means its capability to detect pathologies in early stages and their risk of progression. Currently all patient without DR in the retinography are usually considered into low risk group, ignoring their medical risk and they would be misdiagnosed. On other hand, an isolated retinography offers an accurate information about the current patient status but it has to be completed with medical factors related with the progression risk (RETIPROGRAM).

In our opinion RETIPROGRAM offers a predictive value of DR progression in short term and completes the retinographies information, offering a more personalized and accurate acting plan.

CONTROL ID: 3528538

SUBMITTER (NAME ONLY): Shuhe Zhang

TITLE: A double-pass fundus reflection model for efficient single retinal image enhancement

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zhang, Universiteit Maastricht Faculty of Health Medicine and Life Sciences, Maastricht, Limburg, NETHERLANDS|W. Carroll, T. Berendschot, Maastricht Universitair Medisch Centrum+, Maastricht, Limburg, NETHERLANDS|

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ABSTRACT BODY:

Purpose: High contrast is a prerequisite for fundus images to be used for successful diagnosis in clinical practice. Current contrast enhancement models show promising results, but they have not been optimized for retinal images, due to the ignorance of specific double-pass fundus reflection feature. In this study, we propose the double-pass fundus reflection (DPFR) model and test the hypothesis that the DPFR model can be more efficient and simpler for retinal image enhancement than previous methods.

Methods: The DPFR model is derived according to the light propagation in a fundus camera. Based on the model, the dark-channel prior de-hazing is applied twice to a raw retinal image to correct the uneven illumination, and reduce the straylight effect of the image. Then we convert the de-hazed image into CIE-Lab color space to apply the Contrast Limited Adaptive Histogram Equalization to its L channel, resulting in the final enhanced image. We compared the performance of the DPFR model with two state-of-art methods including the Luminosity and Contrast Adjustment (LCA) and Pixel Color Amplification (PCA). All methods are applied to the data from four public databases, namely the DRIVE-, the STARE-, the DiaRet- and the Cataract database. Both visual and objective assessments are shown. For objective assessments, we use the multiscale image contrast, C_{RAMM} , and the color difference between raw images to evaluate enhancement performance.

Results: Figure 1 shows that the DPFR model effectively balances the uneven illumination, and improved the clarity of retinal images since structures like blood vessels that were hidden behind the cataract in the raw image could be observed after enhancement. Table 1 shows the mean value of C_{RAMM} and color differences of raw and enhanced images from the four separate databases for the LCA, PCA, and DPFR methods, respectively. We found significant differences between the three methods (all $P < 0.001$). Although the PCA resulted in higher C_{RAMM} than other methods, it has worse color preservation (larger color difference value), as can be seen in Fig. 1, which makes this method less suitable for clinical use.

Conclusions: The DPFR model enables efficient illumination correction, contrast improvement, and color preservation. It on average enhances image contrast by two-fold, while the color differences are less than 10%, and show better performance compared to existing methods.

CONTROL ID: 3528561

SUBMITTER (NAME ONLY): Emily Patterson

TITLE: Macular rod and cone photoreceptor structure in patients with X-linked cone dysfunction

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: X-linked cone dysfunction has been shown to cause variable structural and functional disruption of the long (L) and/or middle (M) wavelength-sensitive cone mosaic. Although the condition is considered to be isolated to L and M cones, the effect, or lack thereof, on rod density has not yet been confirmed. Adaptive optics scanning light ophthalmoscopy (AOSLO) enables in vivo visualization of the photoreceptor mosaic. Here we quantify the density of rods – derived from the density recovery profile (DRP) – and cones within the macula in patients who do not have normal L or M opsin, and thereby present with symptoms of blue cone monochromacy.

Methods: Eight patients (aged 16 to 51 years) with quantifiable parafoveal AOSLO images were selected for analysis. All patients had genetically confirmed mutations affecting both L/M opsin genes: four had the Cys203Arg missense mutation, three had abnormal exon-3 haplotypes (two with LVVVA; one with MIAVA + LIAVA), and one had a deletion of the locus control region (LCR). Where possible, rods and cones were counted (using confocal and split-detection AOSLO images respectively) in 1° increments from 3° to 10° along the temporal meridian.

Results: Although the overall mean (SD; n) cone density (cones/mm²) was reduced from normal, ranging from 6,446 (5,817; 4) at 3° to 1,750 (636; 2) at 10°, there were differences between the genotypes, with Cys203Arg trending towards lower cone density (Fig 1). Mean (SD; n) cone-corrected DRP-derived estimates of rod density (rods/mm²) ranged from 54,383 (28,276; 5) at 4° to 81,810 (1,4621; 3) at 9°, although, again, there were genotype differences, with Cys203Arg trending towards higher rod density (Fig 2).

Conclusions: Understanding the cone and rod topography within the macula is crucial for assessing the potential impact and monitoring efficacy of future therapeutic efforts in X-linked cone dysfunction. Our data suggest that, in patients who lack expression of normal L and M opsin genes, rod density and/or distribution across the retina may be affected by genotype.

CONTROL ID: 3528581

SUBMITTER (NAME ONLY): David Brown

TITLE: Brolucizumab for the treatment of visual impairment due to diabetic macular edema: 52-week results from the KITE and KESTREL studies

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Presentation of the 52-week results from KITE and KESTREL, two prospective pivotal Phase III studies evaluating the efficacy and safety of brolucizumab (BRO) versus aflibercept (AFL) for the treatment of patients with visual impairment due to diabetic macular edema (DME).

Methods: KITE (NCT03481660) and KESTREL (NCT03481634) are 2-year, ongoing, double-masked, randomized, active-controlled, multicenter studies. Adults (≥ 18 years of age) with type 1 or type 2 diabetes mellitus, visual impairment due to DME with a BCVA score between 78 to 23 ETDRS letters, and DME involving the center of the macula with a central subfield thickness (CSFT) $\geq 320\mu\text{m}$ on SD-OCT in the study eye at screening were included. In KITE, patients were randomized 1:1 to BRO 6mg or AFL 2mg; in KESTREL, the randomization was 1:1:1 to BRO 3mg, BRO 6mg and AFL 2mg. Patients in the BRO groups received 5 loading doses every 6 weeks (q6w) followed by q12w dosing in the first year, with an option to adjust to q8w at predefined disease activity assessment visits. The AFL group received 5 loading doses monthly followed by fixed q8w dosing. The primary endpoint was the change from baseline in BCVA at Week 52; secondary endpoints included the proportion of BRO patients maintained at q12w dosing up to Week 52 and the change from baseline in CST. Results from the KITE study only are included here, results from the KESTREL study (estimated primary completion, December 2020) will be available to present at congress.

Results: In KITE, the primary objective was met with BRO 6mg non-inferior to AFL 2mg in the change from baseline in BCVA at Week 52. More than 50% of BRO 6mg patients were maintained on a q12w dosing interval through Week 52, following the loading phase. BRO 6mg showed superior improvements versus AFL 2mg in the change from baseline in CST over the period of Week 40 through Week 52. BRO 6mg demonstrated an overall well-tolerated safety profile that was comparable to AFL 2mg; in addition, the rate of intraocular inflammation was equivalent between BRO 6mg and AFL 2mg.

Conclusions: Results from the KITE study show that brolucizumab offers the potential for robust vision gains and superior anatomical outcomes with q12w treatment intervals in more than 50% of patients with DME. The data from KESTREL are expected later this year.

CONTROL ID: 3528589

SUBMITTER (NAME ONLY): Karanveer Johal

TITLE: Myo/Nog Cells Migrate to Areas of Stress Within the Eye in a Mouse Model of Glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Johal, P. Lecker, J. Spikes, J. Bernstein, A. McGrath, V. MacPherson, R. Brahmabhatt, M. Martin, B. Bisco, S. Adams, M. Hossain, J. Johal, G. Gorski, A. Bravo Nuevo, J.V. Gerhart, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myo/Nog cells express MyoD, Bai1 and the bone morphogenic protein inhibitor Noggin. They are critical for normal embryonic development, including eye morphogenesis. In adults, they respond to stress and injury. Depletion of Myo/Nog cells in the mouse retina was associated with increased photoreceptor cell death, while their addition to the vitreous preserved function and reduced cell death following light damage in the rat. Here we examine the behavior of endogenous and exogenous Myo/Nog cells in response to increased intraocular pressure (IOP) in a mouse model of glaucoma.

Methods: Glaucoma was induced in the right eye of each animal by impeding the outflow of the aqueous humor with microbeads injected into the anterior cavity of C57BL/6J mice (D0). IOP was measured periodically from D0 to D32. Seven days after insertion of microbeads, three of four groups received bilateral AC injections of PBS, unsorted brain cells or Myo/Nog cells isolated from the brain with the G8 monoclonal antibody and prelabeled with a fluorescent dye. The fourth group received no follow up injections. Eyes were collected at D32, and immunofluorescence localization of exogenous and endogenous G8+ cells was performed.

Results: Myo/Nog cells injected into the anterior chamber were tracked to areas of stress, such as the trabecular meshwork, the ciliary body and the canal of Schlemm. The highest concentration of Myo/Nog cells were found in the cornea and retinal ganglion cell layer. H&E staining showed a statistical deficit in living retinal ganglion cells within the RGC layer of the glaucomous eye compared to the non-glaucomous eye among the PBS and mixed population treatment groups, and no statistical loss of cells within the glaucomous eye compared to the non-glaucomous in the exogenous Myo/Nog treatment group.

Conclusions: Myo/Nog cells increase in number in response to elevated IOP and are concentrated in areas of stress in the eye. Endogenous Myo/Nog cells were increased around the optic nerve and periphery of the retina compared to normal retinas. Myo/Nog cells injected into the anterior chamber showed evidence of integration into tissues that are affected by impaired aqueous humor outflow and migrate to areas of increased endogenous Myo/Nog concentration within the eye. Injection of exogenous Myo/Nog cells also showed preservation of retinal ganglion cells in glaucomous eyes.

CONTROL ID: 3528618

SUBMITTER (NAME ONLY): Yelena Bagdasarova

TITLE: Segmentation of reticular pseudodrusen (RPD) lesions in OCT B-scans using deep learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: RPD are currently considered a high-risk feature for progression in early age-related macular degeneration. We thus sought to train a deep learning model to reliably segment RPD on B-scans in order to automatically detect and quantify the extent of these lesions.

Methods: 478 B-scan images with visible RPD from 29 participants with bilateral large drusen were used. An expert assigned each pixel a binary classification of RPD or normal. Using Dice coefficient loss, a U-Net was trained on randomly sampled regions of 359 B-scans of 20 participants. The network was then validated on the 119 B-scans of the remaining 9 participants. Sensitivity to training patch size and the number of scans used for training was investigated.

Results: The model segmentation (Figure 1) achieved a Dice of 0.67 and 0.8 on the validation and training sets, respectively. Horizontal flipping and rotation imparted no appreciable gain on the Dice. Training patch widths were varied from 32 pixels to the full size 1024 pixels (Figure 2A), resulting in the decrease of the Dice for the 32 pixel case, which is attributed to a higher fraction of lesion segments being cut off for this patch width. A patch width of 256 pixels was selected for training thereafter. For the data subtraction study (Figure 2B), the number of scans in the training set were varied from 359 down to 1 scan. With a training set of 1 B-scan the Dice was 0.48.

Conclusions: A U-Net was successfully trained to segment RPD lesions achieving a Dice of 0.67. Our results suggest that patch width should be chosen to avoid cutting off most lesions. The data subtraction study suggests that the dataset is uniform enough for the network to learn a general set of features from a single B-scan. Our preliminary findings demonstrate promise for developing a reliable method for detecting and quantifying RPD.

CONTROL ID: 3528644

SUBMITTER (NAME ONLY): Shayan Shokoohi

TITLE: Effect of bevacizumab on the viability and metabolism of human corneal cells

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shokoohi, A. Iovieno, S. Yeung, Department of Ophthalmology and Visual Sciences, The University of British Columbia, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: The biocompatibility of intravitreal bevacizumab has been established over the past two decades for the safe and effective treatment of retinal neovascular diseases. The topical application of bevacizumab, however, for the treatment of corneal neovascularization raises concerns due to its potential corneal cytotoxicity. In this in vitro, experimental study, we evaluated the cytotoxic effects of bevacizumab on the viability and metabolism of human corneal epithelial cells (HCEpCs) and human corneal endothelial cells (HCEncs), as well as human retinal pigment epithelial cells (ARPE-19) for comparison.

Methods: Cell lines of HCEpCs, HCEncs and ARPE-19 were exposed to clinically relevant concentrations of bevacizumab (0.313-5.00 mg/ml). The ApoTox-Glo Triplex Assay was used to assess cell viability, cytotoxicity and apoptosis and the Mitochondrial ToxGlo Assay was used to assess cell membrane integrity and ATP levels of the three cell types after a 24-hr. treatment period.

Results: Across all three cell types, we observed similar results of a decrease in cell viability at 5.00 mg/ml ($p < 0.05$) and an increase in cytotoxicity at 5.00 mg/ml ($p < 0.05$), while apoptotic activity remained unchanged ($p > 0.05$), which is a profile consistent with cells undergoing primary necrosis at high concentrations. Additionally, cell membrane integrity was compromised at 5.00 mg/ml ($p < 0.05$), while no decrease in ATP levels were observed ($p > 0.05$). This indicates no interference with mitochondrial oxidative phosphorylation in ATP production and thus, the cells were able to maintain normal metabolic levels at high concentrations.

Conclusions: HCEpCs, HCEncs and ARPE-19 experience a decrease in viability and undergo primary necrosis when exposed to bevacizumab at concentration of 5.00 mg/ml, however they are able to maintain normal metabolism and mitochondrial function at high concentrations used for the treatment of corneal neovascularization.

CONTROL ID: 3528649

SUBMITTER (NAME ONLY): Reena Durai

TITLE: Binocular summation of cone- and rod-specific signals in flicker-threshold tasks

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.R. Durai, S.R. Bharadwaj, A. Rugvedi, Brien Holden Institute of Optometry and Vision Sciences, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|J. Barbur, M. Rodriguez, City University of London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Binocular summation of briefly-presented, central and peripheral, spatially-distributed stimuli has been investigated in numerous studies with emphasis on stimulus size, location in the visual field and state of background adaptation. This study examined the binocular threshold summation of cone- and rod-specific, flickering stimuli as a function of stimulus size and retinal location.

Methods: Flicker modulation thresholds (FMT's) were measured under monocular and binocular viewing conditions in 13 subjects with normal vision (mean age:23±3yrs, best-corrected visual acuity $\leq 0.0\log\text{MAR}$, stereoacuity $\leq 40\text{arc sec}$ and normal trichromatic colour vision). Rapid flicker thresholds were measured using the Flicker-Plus test (City Occupational Ltd., London) for 5 different target sizes (7, 15, 30, 45 and 60arc min) in central vision (0°) and at an eccentricity of 5° in each quadrant using a 5-alternative forced-choice psychophysical technique. The temporal frequency, duration, luminance and chromaticity of the flickering stimuli was optimized to favour either cone- or rod-photoreceptors. The ratio of the subject's monocular FMT (measured in the best eye) and the corresponding binocular threshold was used to quantify binocular summation.

Results: Monocular FMT's decreased monotonically with target size for both cone- and rod-optimized stimuli ($p<0.001$). Not surprising, the extreme percentage FMTs corresponded to the smallest (7') and the largest (60') stimuli with $m\pm s$ values of: 9.69 ± 1.06 and 2.35 ± 0.20 (for cones) and 20.92 ± 2.50 and 4.45 ± 0.50 (for rods). Binocular FMT's followed the same trend for all viewing conditions but were smaller than their monocular counterparts ($p<0.001$). The mean summation ratios was 1.28 ± 0.49 for cones and 1.41 ± 0.35 for rods. There was no indication of significant changes in binocular summation with either target size ($p<0.12$) or retinal location ($p=0.67$).

Conclusions: Detection thresholds for luminance-modulated flicker exhibit large binocular summation with both cone- and rod-enhanced stimuli. Although both monocular and binocular FMTs show large, systematic variation with target size and retinal location, the binocular summation ratio remains largely invariant of these parameters.

CONTROL ID: 3528651

SUBMITTER (NAME ONLY): Juliette Bitard

TITLE: YAP protects the eye from uveitic glaucoma by preserving retinal and anterior chamber homeostases

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The role of the transcription coactivator YAP has been studied during eye development but its implication in ocular homeostasis and diseases is much less documented. YAP is expressed by several ocular cell types including the non-pigmented cells of the ciliary body (CB) as well as Müller glial cells (MGs) of the neuroretina. Here, we assessed whether postnatal Yap deletion in these two cell types could affect eye homeostasis during aging.

Methods: Specific Yap deletion in CB and MGs was induced in a conditional mouse model (Yap cKO) at P10. The phenotype was investigated by western-blot, immunohistochemistry, and RNA-sequencing (RNA-seq). Blood defects were identified by fluorescein angiography. Optic nerve degeneration was assessed by optical coherence tomography. Intraocular pressure (IOP) was recorded by a rebound tonometer. Imaging of the CB in healthy and uveitic human patients was performed by ultrasound biomicroscopy.

Results: At two months, Yap cKO eyes exhibited distended ciliary processes and blood leakage from the iris. Anterior uveitis became chronic with age resulting in collapse of the CB as observed in human patients. At nine months, the CB was dysfunctional as inferred by pathway analysis of RNA-seq data showing deregulation of genes belonging to the GO group "symporter activity" that encode regulators of aqueous humor composition. In line with this, IOP was increased in aged female mice whereas males had a trend towards hypotony. Since such a phenotype is highly reminiscent of glaucoma, we assessed whether Yap cKO mice exhibited other hallmarks of the disease, focusing on the neuroretina. At two months, MGs-derived glutamine synthetase – the key enzyme in the regulation of glutamate metabolism – was downregulated. By six months of age, MGs gliosis and microglial cell activation were evident. Finally, nine-month-old Yap cKO retinas harbored signs of blood defects, disturbed glutamate metabolism, reduced number of retinal ganglion cells, and excavation of the optic nerve head.

Conclusions: Altogether, these results show that Yap deletion in both the CB and MGs causes chronic anterior uveitis followed by secondary glaucoma. This highlights a novel and unsuspected function of YAP in homeostasis maintenance of both the neuroretina and the anterior chamber which may open new avenues towards a better understanding of glaucoma etiology.

CONTROL ID: 3528659

SUBMITTER (NAME ONLY): Kang-Jung Lo

TITLE: Risk factors for neovascularization after central retinal artery occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Lo, M. Chen, Taipei Veterans General Hospital Department of Ophthalmology, Taipei, TAIWAN|M. Chen, National Yang-Ming University School of Medicine, Taipei, TAIWAN|

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ABSTRACT BODY:

Purpose: Central retinal artery occlusion (CRAO) is a rare disease with prevalence about 1/100,000, not to mention the ocular neovascularization (NV) after CRAO was only account for 10-20%. With such a low occurrence rate, most related articles were published in case reports or case series. In recent four decades, only few articles mentioned about the risk factors that associate with this scenario. As a prestigious tertiary referring center in Taiwan, we possessed much cases of ocular NV after CRAO. Hence, in this article, we try to find the risk factors in patients with ocular NV after CRAO in recent fifteen years in our hospital.

Methods: We reviewed medical records of all patients who visited Taipei Veterans General Hospital from January 2006 to May 2020 and enrolled patients with a diagnosis of acute CRAO. All charts were further reviewed for the occurrence of ocular NV and the period between CRAO and ocular NV. In addition, systemic conditions, first visit ocular conditions, age and gender were all recorded for analysis. The mean and standard deviation of continuous variable parameters were analyzed using the Student t test, and the hazard ratio (HR) and their 95% confidence intervals (95% CIs) of risk factors in two cohorts (with or without ocular NV after CRAO) were analyzed by using the Cox proportional hazards regression model.

Results: Eighty-seven eyes were eligible for this study. Among them, 13 patients were found ocular NV after CRAO while 74 patients were found no ocular NV after CRAO. The percentage of hypertension, diabetes mellitus, history of stroke, chronic kidney disease (CKD) and age at first visit were found higher in patients with ocular NV after CRAO than patients without ocular NV after CRAO. Moreover, most CKD patients in ocular NV group were found underwent dialysis. After multivariate Cox regression analysis, CKD (HR:9.27, 95% CI: 1.87-46.05) and patient has glaucoma (HR:7.52, 95% CI: 1.14-49.46) were considered as risk factors in patients with ocular NV after CRAO.

Conclusions: In this study, we found CKD and patient has glaucoma were two risk factors in patients who have ocular NV after CRAO, especially in patients who underwent dialysis. The unstable hemodynamic condition during dialysis was thought to be the main contributor. Therefore, it is important to strictly control of hemodynamic variation during dialysis and receive at least annual fundoscopic exam in patients underwent dialysis.

CONTROL ID: 3528672

SUBMITTER (NAME ONLY): Faisal Raeme

TITLE: Comparison of best corrected visual acuity estimated with a digital chart and the ETDRS chart

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Raeme, P.G. Soderberg, Z. Yu, neuroscience/ophthalmology, Uppsala Universitet, Uppsala, SWEDEN|

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ABSTRACT BODY:

Purpose: To compare the best corrected visual acuity (BCVA) estimated with a digital visual acuity chart, the AxAnlvls system, and with the ETDRS chart at different visual acuity classes.

Methods: Total 26 subjects ≥ 55 years were divided into 4 visual acuity classes of [1.0 0.8], [0.7 0.5], [0.4 0.2] and [0.1 -0.1] logMAR. The BCVA of each subject was measured with both the ETDRS chart and the AxAnlvls system on two separate occasions. The examination time, spherical error, cylindrical error and axis angle were recorded.

Results: The estimated 95% CI for the mean BCVA difference between two charts (AxAnlvls – ETDRS) was -0.03 \pm 0.03 logMAR. No systematic difference between the charts was found (Test statistic = 2.60, $F_{1,16,0.95} = 4.49$), and there was no statistically significant difference between the charts depending on visual acuity class (Test statistic = 0.67, $F_{3,8,0.95} = 3.24$). The examination time for the AxAnlvls system was 40s shorter than that for the ETDRS chart.

Conclusions: The findings that no significant difference between the two charts, and no significant difference between the charts depending on visual acuity class indicate the AxAnlvls system can be an alternative of the ETDRS chart. This digital system has shorter testing time compared to the ETDRS chart

CONTROL ID: 3528676

SUBMITTER (NAME ONLY): Rithambara Ramachandran

TITLE: Evaluation of Teleophthalmology During The COVID-19 Pandemic At A Single Outpatient Clinical Practice

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ramachandran, Z. Elkin, S.E. Brodie, E. Kim, I. Belinsky, D. Lazzaro, J.F. Panarelli, I. Haberman, L. Sperber, L.A. Al-Aswad, Ophthalmology, New York University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has necessitated a global paradigm shift regarding healthcare delivery, replacing the traditional in-office visit with a virtual platform, in order to limit viral exposure and spread. The purpose of this study is to evaluate agreement between the diagnosis and management of common eye diseases seen in virtual eye care visits versus traditional in-office visits.

Methods: This is a retrospective chart review of patients who presented to a single center for a video televisit between March and June 2020. Agreement was based on a qualitative comparison between the documented primary diagnosis and treatment plan at the first synchronous video visit and first subsequent in-office visit.

Results: During the NY State Lockdown, a single-center practice saw 779 distinct patients virtually. The most common diagnostic categories were Lids/Adnexa (29%), Cornea (18%), and Glaucoma (16%). Of these, 425 (55%) were subsequently seen at an in-office visit. When comparing the primary diagnosis at the two visits, a similar diagnostic code was maintained for 354 patients (83%). There were no known significant adverse outcomes for any patient seen virtually.

Medication changes were made at 268 (34%) video visits. These were guided by symptoms and external exams, although a minority were prophylactic or part of post-operative care. The new treatment plan was maintained for the same diagnosis at 50% of the subsequent in-office visits. Overall, there was an escalation of care for 131 patients (31%), a de-escalation of care for 32 patients (7.5%), and no change in management for 257 patients (60.1%) at the follow-up traditional office visit. Glaucoma patients were the most likely to require additional management (either drops or procedural intervention) when seen in the office.

Conclusions: Based on the results of this study, teleophthalmology provides a safe, feasible, and fairly accurate means of providing routine outpatient eye care.[1] There was an agreement in diagnoses between the virtual and traditional visit in 83% of patients and management plans remained unchanged for at least 60% of patients. Particularly given the importance of the ophthalmic exam, there are limitations to this model of care resulting in missed diagnoses or escalations of care. Addressing these limitations will require further investigation. 1. Tan et al., J Telemed Telecare, 2017.

CONTROL ID: 3528718

SUBMITTER (NAME ONLY): Susanne Hopf

TITLE: Five-Year cumulative Incidence and Progression of Myopic Maculopathy in the German population – results from the Gutenberg Health Study

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Hopf, F. Heidt, C.A. Korb, N. Pfeiffer, A.K. Schuster, Department of Ophthalmology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, GERMANY|A. Schulz, P.S. Wild, Preventive Cardiology and Preventive Medicine, University Medical Center of the Johannes Gutenberg-University Mainz, GERMANY|T. Münzel, Department of Cardiology, University Medical Center of the Johannes Gutenberg-University Mainz, GERMANY|F. Heidt, P.S. Wild, German Center for Cardiovascular Research (DZHK), Mainz, GERMANY|M.E. Beutel, Department of Psychosomatic Medicine and Psychotherapy, University Medical Center of the Johannes Gutenberg University Mainz, GERMANY|I. Schmidtman, Institute of Medical Biostatistics, Epidemiology and Informatics (IMBEI), University Medical Center of the Johannes Gutenberg-University Mainz, GERMANY|K.J. Lackner, Institute of Clinical Chemistry and Laboratory Medicine, University Medical Center of the Johannes Gutenberg-University Mainz, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the five-year cumulative incidence and progression of myopic maculopathy in the general population in Germany and to analyze potential risk factors.

Methods: The Gutenberg Health Study (GHS) is a population-based cohort study, including 15,010 participants aged 35 to 74 years at baseline. Myopic maculopathy incidence and progression was assessed by grading of fundus photographs according to a recent international photographic classification system (META-PM), in phakic eyes with spherical equivalent $\leq -6D$ (baseline). 509 eyes of 334 participants (mean age 50.4 ± 9.2 years; median: $-7.25D$ myopic refractive error) without myopic maculopathy at baseline and 34 eyes of 27 subjects (mean age 56.7 ± 9.1 years; median $-9D$ myopic refractive error) with myopic maculopathy met the conditions and had gradable fundus photographs at baseline and five-year follow-up. Multivariable logistic regression analysis was used to assess risk factors for progression of myopic maculopathy.

Results: 5-year cumulative incidence of myopic maculopathy was 0.3% (95%CI: 0.02-1.92%; n=1). Progression occurred in 17 of 34 eyes (50%) with prior myopic maculopathy over 5 years with 4 changes in category. The most common types of progression were enlargement of chorioretinal and patchy atrophy; a new pathology was present in 8 eyes. Higher IOP (OR=1.62, 95%CI: 1.03-2.53, p=0.035) was associated with progression of myopia, while female gender (OR=5.54, 95%CI: 0.93-32.92, p=0.060) and higher myopic refractive error (OR=1.62 per diopter, 95%CI: 0.99-1.49, p=0.063) showed a tendency towards progression.

Conclusions: Incidence of myopic maculopathy is rare in highly myopic eyes in the general population in Germany at age 35 to 74 years. Progression of eyes with myopic maculopathy in the German population occurred in 50% of prior diseased highly myopic eyes. These population-based five-year follow-up data on incidence and progression of myopic maculopathy are the first in Europe.

CONTROL ID: 3528739

SUBMITTER (NAME ONLY): Bradley Beatson

TITLE: Repair of Progressive Retinal Detachment Complicating Degenerative Retinoschisis: Surgical Management and Outcomes in Phakic Eyes

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Beatson, A. Pham, S. Ong, I. Ahmed, J. Arevalo, J.T. Handa, Wilmer Eye Institute, Johns Hopkins School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Since the surgical approach for progressive symptomatic retinal detachment complicating degenerative retinoschisis (PSRDCR) is controversial, the purpose of this study is to identify factors important for selecting the appropriate surgical intervention. We present the outcomes following surgical intervention for PSRDCR via pars plana vitrectomy (PPV), scleral buckle (SB), or combined PPV/SB in a retrospective case series of 18 phakic eyes.

Methods: Patient records from Jan 1, 2008-Dec 31, 2019 were reviewed. Charts with retinal detachment (RD) surgeries were identified using billing codes, and those with PSRDCR were included following manual screening. Charts with diagnoses other than degenerative retinoschisis or less than 6 months of follow-up following primary RD repair were excluded. Data regarding demographics, surgical approach, post-operative complications, and anatomic/functional outcomes were collected from patient records.

Results: Of the 4973 charts reviewed, 36 eyes (0.7%) had retinoschisis with RD. Eighteen eyes of 17 patients met inclusion criteria. The median age was 54 years (range 18 to 74). All eyes were phakic and 10/18 presented with cataracts. 10/18 eyes had outer layer breaks (OLBs), 17/18 had inner layer breaks (ILBs), and 9/18 had a concurrent ILB and OLB. The single surgery anatomic success (SSAS) rate and final anatomical success rate were 66% (12/18) and 100% (18/18) respectively. Eyes treated with PPV/SB had the highest SSAS rate at 75% (9/12), while PPV and SB had SSAS rates of 66% (2/3) and 33% (1/3), respectively.

Conclusions: The SSAS rate in this series is lower than for uncomplicated rhegmatogenous RD. The low SSAS rate may be caused by poor visualization of ILBs, especially with cataract, and the inability to remove peripheral vitreous leading to vitreous base contraction with resultant vitreoretinal traction. Due to low sample size, statistical conclusions regarding optimal surgical technique are not possible. However, a combination of PPV to enhance visualization of ILBs, and SB to mitigate vitreous base contraction should be considered for extensive PSRDCR. We further postulate that in eyes with concurrent cataract, combining phacoemulsification and IOL placement with RD repair may improve visualization of ILBs and allow the removal of peripheral vitreous.

CONTROL ID: 3528762

SUBMITTER (NAME ONLY): Hyun Soo Jang

TITLE: Confidence Intervals for Assessing Ectatic Changes Post-Crosslinking Using the ABCD Grading System

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The ABCD progression display (Pentacam, Oculus GmbH, Wetzlar, Germany) monitors progression in corneal ectasia and reports statistically significant changes by displaying one-sided 80% and 95% confidence intervals (CI) of each measured parameter. The parameters are anterior (A) and posterior (B) radii of curvature taken from a 3.0 mm optical zone centered on the thinnest point and thinnest pachymetry reading (C). The current system does not display CI after corneal cross-linking (CXL), as measurement noise of this population has not been established. Our prior study on noise post-CXL showed large CI in eyes with less than a year follow-up period. This study aimed to measure noise of post-CXL eyes after a year or longer and provide CI for this group.

Methods: Patients from ELZA Institute (Zurich, Switzerland) and Homburg Keratoconus Center (Homburg, Germany) with a minimum of 12 months post-CXL were enrolled. Three separate Pentacam measurements were taken for each eye, removing the patient from the Pentacam device between each measurement. A minimum 7.5 mm of coverage and an acceptable quality score were required. Pooled variance, standard deviations (SD), and one-sided CI were computed. Site specific and time specific comparisons were made using nonparametric statistics.

Results: 60 eyes (38 Zurich, 22 Homburg) of patients aged 29.5 ± 12.3 (range 11-62) were enrolled. Patients were 26.1 ± 19.3 months (range 12-28 Zurich, 16-115 Homburg) post-CXL. The values of A, B, and C parameters and their respective noise measured as SD were all comparable between sites. A subgroup analysis of eyes from Homburg comparing 16-35 months to 38-115 months post-CXL showed no difference in SD. Spearman's Rho demonstrated no correlation between time post-CXL and SD in all parameters. The 80% CI of A, B, and C parameters were 0.0283, 0.0492, and 3.682, respectively. The 95% CI were 0.0553, 0.0962, and 7.196, respectively.

Conclusions: Measurement noise of each parameter on the ABCD progression display was analyzed in eyes post-CXL with at least 12-month follow-up period. Noise, after 12 months post-operatively, was not correlated with time post-CXL in this group. CI of each measured parameter were computed as above and will be incorporated into the next iteration of the Belin ABCD progression display.

CONTROL ID: 3528767

SUBMITTER (NAME ONLY): Justin Muste

TITLE: Novel Image Grading Scale for Novel Flavoprotein Fluorescence Imaging

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Muste, R.P. Singh, Center for Ophthalmic Bioinformatics, Cole Eye Institute, Ohio, UNITED STATES|S. Daguridas, J.C. Liu, School of Medicine, Case Western Reserve University, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Flavoprotein fluorescence (FPF) imaging has emerged as a technology to better understand retinal metabolism. There is no disseminated, standardized method of grading these images. The purpose of this study was to apply a novel Likert-based grading scale to an existing image database to test its ability to select for high quality images, reduce variability in scores, and improve intergrader reliability.

Methods: 3664 images and their associated flavoprotein fluorescence (FPF) and heterogeneity score (CW) were automatically generated by Ocumet® Image Analysis software at the time of patient presentation. The images had been analyzed by a combination of graders on a three point Likert scale without a rubric. Three independent, blinded graders were trained on appropriate use of a novel, five point novel grading rubric. A database was populated with the images and graders completed the images. Intergrader reliability was assessed by Fleiss Kappa metric.

Results: Fleiss Kappa metric for the novel grading scale was 0.584, indicating moderate agreement. Of the mismatches occurring in the old grading scale roughly 33.3% were between adequate/inadequate images (highest/lowest category). Of all mismatches occurring in the new grading scale only 11.7% occurred between Grade A and B images and Grade C,D, F images (highest/lowest categories). With only 2.4% occurring in Grade A images. When applied to Diabetes Mellitus and Age-related Macular Degeneration the new model reduced the variability in FPF and CW images classified as grade A or B. The greatest variance in FPF and CW occurred in images classified as Grade D or F. The total number of usable images decreased from 62.3% to 11.7%.

Conclusions: The Likert-based grading scale enhanced selection of high-quality images, reduced score variability, and improved inter-grader reliability. It has promise for future applications in similar settings.

CONTROL ID: 3528778

SUBMITTER (NAME ONLY): Sarunas Daugirdas

TITLE: Retinal mitochondrial flavoprotein fluorescence in non-exudative or neovascular age-related macular degeneration

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Daugirdas, J.C. Liu, R.P. Singh, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|J. Muste, A. Iyer, R.P. Singh, Center for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland, Ohio, UNITED STATES|C. Rich, OcuSciences, Inc., Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress and subsequent damage to retinal mitochondria is thought to play a key role in the pathogenesis of several retinal diseases including age-related macular degeneration (AMD). When oxidized, retinal mitochondrial flavoproteins auto-fluoresce green light when excited by a particular wavelength of blue light. This emitted flavoprotein fluorescence (FPF) can be measured and used as a quantifiable marker for oxidative damage-induced mitochondrial dysfunction. This study aims to assess FPF in a sample of AMD patients grouped by stage of disease progression.

Methods: This study was a retrospective chart review of patients diagnosed with early, intermediate, or advanced non-exudative AMD or neovascular AMD between 2012-2019 based on AREDS criteria. The comparison group included retinal images from healthy age-matched controls. Patients with comorbid glaucoma, ocular hypertension, concomitant retinopathy or uveitis, history of retinal detachment, history of cataract surgery, retinal surgery within three months, fluorescein angiogram prior to imaging, or pseudophakic lens were excluded. For each patient image, FPF score (i.e., intensity) and curve width (i.e., heterogeneity) were recorded using the OcuMet Beacon (OcuSciences, Ann Arbor, MI).

Results: The final analysis included 369 images. The multivariable regression included early, intermediate, and advanced non-exudative AMD and neovascular AMD as well as age, smoking status, gender, ethnicity, and eye location. Intermediate and advanced non-exudative AMD and neovascular AMD were significant predictors of increased FPF score intensity (13.86, CI 8.46–19.25, $p < 0.001$; 30.85, CI 17.86–43.83, $p < 0.001$; 17.79, CI 11.91–23.67, $p < 0.001$ respectively), but early non-exudative AMD was not (-3.83, CI -12.82–5.16, $p = 0.40$). Early, intermediate, and advanced non-exudative AMD and neovascular AMD were significant predictors of increased FPF score heterogeneity (0.39, CI 0.17–0.60, $p < 0.001$; 0.43, CI 0.31–0.56, $p < 0.001$; 0.83, CI 0.52–1.13, $p < 0.001$; 0.69, CI 0.55–0.83, $p < 0.001$, respectively)

Conclusions: Non-exudative and neovascular age-related macular degeneration are associated with increased retinal mitochondrial oxidative stress as evidenced by increased intensity and heterogeneity of flavoprotein fluorescence in patients with this disease.

CONTROL ID: 3528785

SUBMITTER (NAME ONLY): Masahiko Ayaki

TITLE: Tear strip meniscometry and its clinical application-2000+ case series

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ayaki, H. otake, A. o'hira, M. Arai, T. sakai, Otake Clinic Moon View Eye Center, JAPAN|K. miyasaka, Echo Electricity Co., Ltd., JAPAN|

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ABSTRACT BODY:

Purpose: To evaluate the association of the strip meniscometry (SM) tear meniscus volume measurement with dry eye-related signs and symptoms in over 2000 sample case series.

Methods: This cross-sectional study enrolled 2234 consecutive outpatients and we used dry eye symptomatology and related ocular surface examinations including the Schirmer Test (ST), fluorescein tear film break-up time (BUT), corneal fluorescein vital staining (FLUO), and SM. The cut-off of SM was estimated using ROC analysis. The subjective symptoms consisted of binarized seven items: dryness, fatigue, photophobia, pain, irritation, blurring, and lacrimation. The clinical signs were also binarized by the cut-off in each test. The entire presence of signs and symptoms were then analyzed using Hayashi's quantification theory type III to depict their mutual similarities.

Results: The mean age of subjects was 59.3 ± 17.3 yrs. The mean values were 13.6 ± 9.6 mm for ST, 3.1 ± 2.1 s for BUT, 0.40 ± 0.66 for FLUO, and 2.4 ± 2.7 mm for SM. ST had a weak negative correlation with age ($r = -0.152$, $p < 0.01$), whereas BUT and SM did not. All pairs among ST, BUT and SM had significant correlations; the highest value was found in the BUT-SM pair ($r = 0.238$, $p < 0.01$). On the basis of the large-scale sample size ($n = 1162$), a cut-off length of SM was newly suggested as 2.5 mm (AUC = 0.618) in reference to former 4.5 mm. The quantification type III analysis elucidated the high similarity among the presence of signs by SM, BUT and FLUO, while that by ST appeared to be isolated from the other signs. Three symptoms (pain, irritation and dryness) had a distinct similarity.

Conclusions: SM results with the cut-off = 2.5 mm could be a useful clinical indicator for initial screening of dry eye.

CONTROL ID: 3528792

SUBMITTER (NAME ONLY): Taj Nasser

TITLE: Anti-VEGF Therapy and Elevated Intraocular Pressure: A Race-Based Analysis

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Nasser, A. Michael, V. Chen, Z. Zhang, Ophthalmology, Tulane University, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Taj Nasser: Commercial Relationship: Code N (No Commercial Relationship) | Abenet Michael: Commercial Relationship: Code N (No Commercial Relationship) | Victor Chen: Commercial Relationship: Code N (No Commercial Relationship) | Ze Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Since the advent of anti-VEGF therapy, many reports of associated elevated intraocular pressure (IOP) have come to light. It is known that race has an important role in patient care where African American (AA) patients are at higher risk of reaching adverse glaucomatous endpoints more frequently. However, the literature lacks race-based studies regarding anti-VEGF therapy and incidence of elevated IOP. The aim of this study is to compare the incidence of elevated IOP following anti-VEGF therapy between AA and Caucasian patients as well as evaluate for possible risk factors.

Methods: This is a retrospective study of adult patients treated with intravitreal Bevacizumab injections (IVI) at two tertiary referral centers and two Veteran Affairs clinics over the past decade. Subjects were included if they were >18 y.o. with a minimum of two years of follow up after the first IVI. Exclusion criteria were current or history of intravitreal steroid or topical steroid therapy and neovascular glaucoma. Subjects were categorized into three groups: group 1 were subjects receiving IVI with no previous diagnosis of ocular hypertension (OHTN) or glaucoma, group 2 were subjects receiving IVI with pre-existing diagnosis of OHTN/glaucoma, and the control group were subjects who did not receive IVI. Data collected included race, age, gender, indication of IVI, elevation of IOP above baseline ($\geq 20\%$, $\geq 21\text{mmHg}$, $\geq 25\text{mmHg}$), months until first IOP elevation, and phakic status.

Results: There was a statistically significant association between incidence of IOP elevation and IVI whereby our study showed that after about 5 IVI, patients were found to have a higher incidence of elevated IOP. There was no statistical significance between Caucasian and AA subjects receiving IVI. The elevated IOP occurred at an average of about 6-7 months following the first IVI in both groups. Furthermore, we found that there was no statistically significant difference based on indication for IVI, phakic status, gender or age.

Conclusions: This study confirmed that there is a statistically significant relationship between anti-VEGF therapy and incidence of elevated IOP. We found that this relationship was not significant based on history of glaucoma/OHTN, race, indication, gender, age, and phakic status. These results further reinforce the importance of monitoring the IOP of patients receiving anti-VEGF therapy and contribute to patient-centered care.

CONTROL ID: 3528794

SUBMITTER (NAME ONLY): Peter Alsaloum

TITLE: Incremental Economic Burden of Depression in Ophthalmic Patients

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Alsaloum, C. Rasendran, School of Medicine, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|R.P. Singh, K. Talcott, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|Y. Imran, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The total economic burden of ophthalmic pathologies is rising exponentially. In addition, there is a correlation between the development of depression in patients with vision problems; yet, little is known about the additional economic stress of depression placed on these co-morbid patients. A retrospective cross-sectional analysis was performed to analyze the incremental economic burden of depression on adults with ophthalmic conditions in the United States.

Methods: Adults with at least one outpatient ophthalmology visit were identified by ICD-9-CM codes within the Medical Expenditure Panel Survey (MEPS, 2007-2015). These patients were stratified based on the presence of concurrent depression. A multivariate two-part regression model was used to compare economic burden, healthcare utilization, and expenditures between ophthalmic patients with and without depression.

Results: Ophthalmic patients diagnosed with depression (n=2474) had a mean expenditure of \$15,385.48±731.38 while ophthalmic patients without depression (n=7944) had a mean expenditure of \$11,744.26±350.98. Patients with depression were more likely to be female, white, and lower-income (p<0.001). These patients faced \$2,564.25 (p<0.001) in incremental economic expenditures due to depression, resulting in an additional \$4.52 billion annually when extrapolating nationally. These patients also had higher expenditures for inpatient (p=0.002) and prescription medications (p<0.001) (Table 1).

Conclusions: The increase in inpatient and medication expenditures were the major drivers of high healthcare utilization seen in ophthalmic patients with depression. However, there was no difference in outpatient expenditures, suggesting possible inadequate outpatient management of depression in these patients with increased reliance on inpatient care. Alternatively, these patients may have confounding systemic diseases that require inpatient hospitalization and eye-related exams. The presence of a bidirectional relationship between ophthalmic and psychiatric conditions and the demonstrated financial burden for patients with both, displays the need for ophthalmologists to be more cognizant of the financial burdens of depression among their patients.

CONTROL ID: 3528838

SUBMITTER (NAME ONLY): Timothy-Paul Kung

TITLE: Uveitis incidence in the United States (US): a database study using the Intelligent Research in Sight (IRIS)® Registry

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kung, M.S. Hunt, M. McKay, R.T. Yanagihara, A.Y. Lee, R.N. Van Gelder, C.S. Lee, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|T. Kung, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|M.S. Hunt, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the incidence of uveitis in the US for new and established patients in the IRIS Registry.

Methods: IRIS® Registry patients receiving eye care prior to and during the 2017 period of interest (POI) were included. Cases of uveitis and their anatomic location were identified and subdivided using ICD-10 codes: anterior uveitis (AU), intermediate uveitis (IU), posterior uveitis (PU), panuveitis (PanU), scleritis, retinal vasculitis (RV), and “mixed” (scleritis + any intraocular inflammation). New patients were those not previously registered in IRIS who presented with a uveitis diagnosis during the POI. Established patients were defined as the cohort seen prior to 2016 with ≥1 year of follow-up who received a new diagnosis of uveitis in 2017. To exclude postoperative uveitis, patients who had an intraocular procedure in or 90 days before 2017 were excluded. Cumulative incidence rate and demographic factors were analyzed.

Results: Among established patients, the cumulative uveitis incidence rate during the POI was 112.84 per 100,000 person-years, with incident cases being most common in the 7th and 8th decades of life (DOL).(Table) Among new patients, the percentage of patients who presented with a uveitis diagnosis was highest in the working-age population, with a peak percentage of 0.63% in the 4th DOL. Black or African-American patients had the highest incidence among established patients and also the highest percentage of uveitis among new patients.(Table) The baseline age distribution of both established and new patients diagnosed with IU was wider than the rest of the uveitis categories and patients without a diagnosis of uveitis.(Figure)

Conclusions: The incidence of uveitis within the IRIS dataset is comparable to that reported in other population-based studies. Among established patients, uveitis incidence was highest in the 7th and 8th DOL. Among new patients, the working-age population was predominantly affected. Black or African-Americans were disproportionately affected by uveitis, compared to other races.

CONTROL ID: 3528841

SUBMITTER (NAME ONLY): Federico Corvi

TITLE: Topography of Choriocapillaris Flow Deficit predicts development of Neovascularization or Atrophy in Age-Related Macular Degeneration

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Corvi, G. Corradetti, L. Tiosano, S.R. Sadda, Doheny Eye Institute UCLA, California, UNITED STATES|L. Tiosano, Hadassah-Hebrew University Medical Center, ISRAEL|J. McLaughlin, T.K. Lee, Retina Centre of Ottawa, Ontario, CANADA|F. Corvi, Luigi Sacco Hospital, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the relationship between choriocapillaris (CC) flow deficits (FD) and structural optical coherence tomography (OCT) biomarkers, and the progression of intermediate age-related macular degeneration (iAMD) to complete retinal pigment epithelial and outer retinal atrophy (cRORA) or macular neovascularization (MNV).

Methods: Multicenter retrospective analysis of consecutive patients with iAMD. Odds ratios for IHRF, hDC, SDDs, and high drusen volume, fellow eye with late AMD, duration of follow-up, peripheral and central CC FD estimated from logistic regression.

Results: 30 iAMD eyes from 30 patients were enrolled into each group. Among eyes which progressed to cRORA, there was a significantly higher proportion of eyes with IHRF, hDC and high drusen volume. The CC FD was greater in the peripheral sectors of the macula of eyes which progressed to cRORA compared to the other two groups ($P < 0.0001$). The central CC FD was also significantly impaired in eyes that progressed to cRORA or MNV compared to those that did not progress ($P = 0.001$ and $P = 0.02$, respectively). CC FD in the peripheral macula was significantly and independently associated with the development of cRORA, while CC FD in the center was significantly and independently associated with the development of MNV.

Conclusions: While the CC is diffusely impaired throughout the macula in iAMD eyes that progress to cRORA, it is relatively spared in the more peripheral macula among eyes which progress to MNV. These differential findings may have implications for the pathophysiology of the different late stage manifestations of AMD.

CONTROL ID: 3528917

SUBMITTER (NAME ONLY): Abhinav Bheemidi

TITLE: Examining the Necessity of Day-1 Postoperative Review After Pars Plana Vitrectomy: A Meta-Analysis

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.R. Bheemidi, V.D. Roan, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|J. Muste, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The current standard of care following retina surgery, particularly pars plana vitrectomy (PPV), is an in-person evaluation conducted on postoperative day 1 (POD1). Given the inherent difficulty of patients with visual disability attending POD1 visits and the safety concerns raised during the COVID-19 pandemic, a critical examination of this standard of care is needed. This study is a meta-analysis that aims to evaluate the necessity of the POD1 review following PPV.

Methods: The analysis included available literature documenting medical and surgical interventions performed on POD1 review following PPV. 2262 patients across 14 eligible studies were included in the analysis. A meta-analysis of proportions was conducted using a binomial-normal model to analyze datasets consisting of all interventions, medical interventions, and surgical interventions. The primary outcome measured was the proportion of patients requiring an intervention on POD1. Heterogeneity and publication bias analyses were performed. Statistical analyses were performed using R (version 3.5.1).

Results: Of the 80 references identified as being of potential relevance, 14 studies met all eligibility criteria. POD1 reviews of 2262 patients were analyzed to yield an intervention rate estimate of 4.7% [95% CI 3.0-13.9]. The proportion of patients requiring medical interventions (4.1% [95% CI 1.4-11.6]) was significantly greater than that of surgical interventions (0.7% [95% CI 0.3-1.3]). Elevated intraocular pressure was the most frequent POD1 complication, accounting for 77.0% and 40.0% of medical and surgical interventions respectively. The heterogeneity analysis revealed significant inter-study variation, with I^2 values of 97.93%, 97.80%, and 20.99% for the all intervention, medical intervention and surgical intervention datasets respectively. Attempts to integrate the different indications for surgery into this analysis were unsuccessful due to variability in reporting of indications and interventions.

Conclusions: Given the wide confidence interval of the estimated intervention rate, variability in postoperative practices, and range of interventions performed, the POD1 review cannot be discarded. Future analyses could identify clinical characteristics associated with patients at a higher risk of requiring POD1 intervention.

CONTROL ID: 3528928

SUBMITTER (NAME ONLY): Yashar Seyed-Razavi

TITLE: JR5558 transgenic mice are a reliable model to investigate subretinal fibrosis

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Seyed-Razavi, S. Lee, J. Fan, W. Shen, M.C. Gillies, Ophthalmology, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA

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ABSTRACT BODY:

Purpose: The development of subretinal fibrosis is a major and untreatable cause of poor outcomes in eyes with neovascular (n)AMD. JR5558 transgenic mice develop subretinal neovascularization along with subretinal hyperreflective lesions similar to areas of subretinal fibrosis seen in eyes with nAMD. This project aims to characterise JR5558 mice as a model to study subretinal fibrosis.

Methods: Colour fundus photographs (CFP) and optical coherence tomography (OCT, Phoenix Micron IV) were utilised to non-invasively track hyperreflective lesions and subretinal fibrosis from 4 weeks in JR5558 transgenic mice. The number and area of lesions in CFP was quantified in ImageJ. Fluorescein angiography was performed to investigate vascular leak. Immunohistochemistry (IHC) of retinal sections was performed with antibodies against α SMA, GFAP and CD31. Protein expression in the neural retina was assessed by Western blot and compared to age-matched controls. Data presented as mean \pm sem with one-way ANOVA performed to compare the data.

Results: Analysis of CFP revealed subretinal lesions expand between 4 and 8 weeks (0.32 ± 0.20 vs $0.41\pm0.23\text{mm}^2$, $p=0.0005$), becoming established in size and location around 12 weeks ($0.38\pm0.49\text{mm}^2$, vs. 4wks $p=0.06$; vs. 8wks $p=0.55$). The number of lesions increased in 60% of animals between 4-8 weeks (15.2 ± 1.5 vs. 16.6 ± 1.1 , $p=0.68$) and remained static at 12 weeks (16.8 , $p=0.99$). Analysis of OCT images revealed alterations in the layers of the neural retina and underlying subretinal lesions. Retinal sections confirmed alterations in the neural retina layers and revealed Muller-glia (GFAP⁺) penetrate through the photoreceptor layer, becoming an integral part of the lesions at 8 weeks. Analysis of neural retina protein expression revealed a significant increase in fibronectin (4wk: $386\pm54\%$; 8wk: $357\pm24\%$, both $p<0.001$) at the early timepoints, while CTGF (20wks: $161\pm7\%$, $p<0.001$), MMP2 (12wks: $159\pm15\%$, $p<0.01$; 20wks: $150\pm15\%$, $p=0.014$) and α SMA (12wks: $188\pm33\%$, $p=0.02$; 20wks: $226\pm24\%$, $p=0.002$) significantly increased later. Increased GFAP expression (8wk: $247\pm30\%$, $p<0.001$; 12wk: $180\pm6\%$, $p=0.01$) confirmed the IHC results.

Conclusions: Our study provides evidence that naturally occurring subretinal lesions in JR5558 mice have a fibrotic component that grows reliably and predictably between 4-8 weeks, making these mice a good model to further study the mechanisms of subretinal fibrosis and how it may be prevented.

CONTROL ID: 3528929

SUBMITTER (NAME ONLY): Amy Lu

TITLE: Safety and Efficacy of Topical, Transzonular, and Intracanalicular Corticosteroids for the Prevention of Postoperative Inflammation after Cataract Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lu, T. O'Rourke, I.U. Scott, S. Pantanelli, Penn State Eye Center, Pennsylvania, UNITED STATES|M. Rizk, Penn State College of Medicine, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the safety and efficacy of topical prednisolone, transzonular triamcinolone-moxifloxacin, and intra-canalicular dexamethasone ophthalmic insert for the prevention of post-operative inflammation after cataract surgery.

Methods: Retrospective consecutive case series. Patients undergoing phacoemulsification cataract surgery received topical prednisolone acetate (Jan 2018-Dec 2019), transzonular triamcinolone-moxifloxacin (Tri-Moxi, ImprimisRx)(Nov 2016-Jan 2018), and intracanalicular dexamethasone (Dextenza, Ocular Therapeutix)(Dec 2019-Nov 2020). Patients with a history of glaucoma suspect, glaucoma, intraocular pressure (IOP) elevation, or uveitis were excluded. Primary endpoints were proportion of eyes with breakthrough inflammation requiring escalation of anti-inflammatory therapy and proportion of eyes with IOP increase ≥ 10 mmHg at 4-8 weeks follow-up. Secondary endpoints included post-operative visual acuity (VA) and intra-operative complications. The Kruskal-Wallis test was used to compare between groups of data. Data were reported as mean \pm standard error. Statistical significance was assumed at $p < 0.05$.

Results: Of 161 study eyes, 59 eyes from 35 patients received drops, 54 eyes from 33 patients received transzonular injection, and 48 eyes from 30 patients received the intracanalicular insert. Three (5.1%), 9 (16.7%), and 4 (8.3%) eyes from each group, respectively, developed symptomatic rebound inflammation ($p=0.11$). IOP increase ≥ 10 mmHg from baseline was measured in 0 (0.0%), 1 (1.9%) and 1 (2.1%) eye, respectively ($p=0.55$). Mean baseline VA in logMAR was 0.33 ± 0.04 , 0.33 ± 0.04 , and 0.27 ± 0.03 , respectively ($p=0.34$). Mean logMAR VA at the 4-8 week post-operative visit was 0.13 ± 0.03 , 0.18 ± 0.04 , and 0.10 ± 0.02 , respectively ($p=0.17$). Two eyes in the drops group did not receive drops as prescribed due to poor compliance. One eye in the injection group was not successfully injected with drug and was placed on topical drops. Three eyes in the dexamethasone insert group that developed rebound inflammation did so due to extrusion of the inserts.

Conclusions: "Dropless cataract surgery" may yield similar rates of breakthrough inflammation and IOP elevation as topical drops. Whereas drops are susceptible to non-compliance, transzonular and intracanalicular corticosteroids rely on delivery and sustained presence of the dispensed agent.

CONTROL ID: 3528933

SUBMITTER (NAME ONLY): Kai Yip Choi

TITLE: Association between initial mfERG responses and myopic progression in children with and without prescription of Breath-O Correct orthokeratology lenses.

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Choi, T. Wong, T. Lam, H.H. Chan, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, HONG KONG|T. Lam, H.H. Chan, Centre for Eye and Vision Research, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: To investigate the relationship between the initial retinal electrophysiological response and axial elongation (AE) in children with and without prescription of Breath-O Correct orthokeratology (OK) lenses.

Methods: Eighty-five subjects aged 9 to 12 years with spherical equivalent refraction (SER) between -1.00D and -4.00D were recruited and randomly assigned into OK (n=49) or spectacle control (n=36) groups. Breath-O Correct lenses were prescribed in OK group with routinely scheduled aftercare. Retinal electrophysiological responses were measured by global flash multifocal electroretinogram (mfERG) in 49% contrast at baseline before any intervention. Responses from the 61 hexagons were averaged into 5 concentric rings to investigate the localized responses at different retinal eccentricities. Axial length measurements were performed at baseline and one-year to monitor refractive changes. Spearman's correlation with Bonferroni correction was used to assess the relationship between mfERG and AE.

Results: Seventy-one subjects completed this one-year study (Control: 29, OK: 42). The baseline SER for control and OK group were -2.49D and -2.97D (t-test, $p>0.05$), respectively. The mean AE in OK group was significantly lower than the control group (Control: $0.35\pm0.2\text{mm}$, OK: $0.14\pm0.17\text{mm}$, $p<0.01$). In OK group, no significant correlation was noted between AE and the initial mfERG responses ($p>0.05$). In contrast, for the control group, the AE was negatively correlated with baseline Ring 1 induced component amplitude ($\rho=-0.484$, $p<0.01$, representing the central inner retinal response) and Ring 3 direct component amplitude ($\rho=-0.488$, $p<0.01$, representing the para-central outer retinal response), respectively.

Conclusions: Without OK intervention, weaker retinal response was associated with faster myopic progression. However, this risk factor did not predispose faster AE under the effect of Breath-O Correct OK intervention. It indicates that the OK intervention is suitable for children with different myopia progression rates.

CONTROL ID: 3528935

SUBMITTER (NAME ONLY): Barsha Lal

TITLE: Changes in Optical Coherence Tomography Angiography metrics over 24 hours in healthy adults

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lal, D. Alonso-Caneiro, S.A. Read, B. Tran, C. Van Bui, D. Tang, J.T. Fiedler, S. Ho, A. Carkeet, School of Optometry, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA

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ABSTRACT BODY:

Purpose: Diurnal variations have been observed in a range of posterior eye structures, yet the pattern of diurnal variation in retinal vasculature over 24 hours has not been established. We performed a prospective observational study to explore the magnitude and pattern of diurnal variation in retinal vasculature over 24 hours using optical coherence tomography angiography (OCT-A) among healthy myopes and non-myopes.

Methods: Healthy young adult participants (n=44, 23.2±4.1 years (range:18-35)) underwent measurements every 4h for 24h starting at 9 AM. AngioPlex OCT-A macula images were captured to determine a range of retinal vascular metrics including foveal avascular zone (FAZ) metrics (area, perimeter, and circularity) as well as the vessel, and perfusion density in the 3mm ETDRS central, and inner subfields. Blood pressure, intraocular pressure (IOP) and axial length were also assessed. Acrophase and amplitude of diurnal variation for each measurement were calculated and compared between 24 myopes and 20 non-myopes.

Results: Vessel and perfusion density showed significant variations over 24h (ANOVA, p<0.05) whereas none of the FAZ metrics changed significantly (ANOVA, p>0.05). Central vessel and perfusion density had their minima phase at 4:48 AM ± 4.44h and 5:45 AM ± 4.14h respectively, with a diurnal amplitude of 1.09±0.65 mm⁻¹ and 1.95±1.25 %. The inner vessel and perfusion density peaked around 5 PM. Myopes and non-Myopes showed different 24h variation patterns for inner vessel density (Figure 1) and perfusion density (with a significant time of day and refractive groups interaction; p=0.04 for both) but not in the central subfield. The myopes and non-myopes had minima at 4:35 AM and 6:06 AM, respectively however, the amplitude of daily variations was not significantly different (p>0.05) between them. The minimum pulse pressure was also in the morning (5:56 AM). Axial length and IOP both demonstrated an acrophase in the afternoon at 2:24 PM and 12:22 PM respectively.

Conclusions: This study, for the first time, demonstrates that significant diurnal variation exists in OCT-A metrics of macular retinal vasculature when evaluated over a full 24h duration while the FAZ does not exhibit any significant variations

CONTROL ID: 3528938

SUBMITTER (NAME ONLY): Michael Offutt

TITLE: Success of Micropulse Cyclophotocoagulation following Tube Shunt Surgery

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Offutt, B. Moody, A. Kheirkhah, C. Waldman, Ophthalmology, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the outcomes of micropulse cyclophotocoagulation (MP-CPC) in patients with and without a history of tube shunt surgery.

Methods: This is a retrospective chart review of patients who underwent MP-CPC from May 2017 to December 2020, comparing those with and without a history of tube shunt surgery. The treatment group is referred to as the tube-group and the control group is referred to as the non-tube group. All forms of glaucoma were included, and the patients were followed for at least 12 months. Success (S) was defined by an intraocular pressure (IOP) of 8-18mmHg, requiring fewer drops than before MP-CPC, vision greater than no light perception (NLP), and requiring no further intervention. If any alternative procedural (i.e. repeat MP-CPC) or surgical intervention was required to control IOP, this would qualify as a failure.

Results: The tube group (n=21) had an average age of 57.62 ± 10.53 , male preponderance (52.4%), and neovascular glaucoma the most common glaucoma diagnosis. 57.1% of the tube group was phakic. This contrasts to the non-tube group (n=41) with average age of 59.68 ± 15.7 , female preponderance (53.7%), and primary open angle glaucoma the most common diagnosis (46.3%). Pre-op IOP for the tube group was 28.29 ± 7.68 with the number of pre-op topical glaucoma medications 3.90 ± 0.525 ; pre-op IOP for the non-tube group was 30.46 ± 10.68 with the number of topical glaucoma medications 3.29 ± 0.74 ($P=0.37$). Principal data suggests greater success in the tube group than the non-tube group at six months of follow up (IOP of 14.6 versus 15.67; $P=0.024$). In addition, at 3-, 6-, and 12- month follow ups, there were statistically significant decreases in IOP and the number of medications used for the tube group – 13.5mmHg with 2.67 topical drops, 14.6mmHg with 2.67 topical drops, and 12.33mmHg with 2.50 topical drops. For the 3-, 6-, and 12- month follow ups, the success rate, as defined above, was 33% & 17%, 43% & 14%, and 33% & 7% for the tube group and the non-tube group, respectively. The most common complication was hypotony (as defined by ≤ 7 mmHg) occurring four times in each group.

Conclusions: This data suggests that MP-CPC is more effective in patients with previous tube shunt surgery compared to those without while maintaining a good safety profile.

CONTROL ID: 3528985

SUBMITTER (NAME ONLY): Penelope Allen

TITLE: A 44 Channel suprachoroidal retinal prosthesis : two year safety and stability results

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The success of our prototype clinical trial (NCT01603576) of a suprachoroidal retinal prosthesis led us to develop a 44 channel fully implantable device with a transcutaneous receiver stimulator system, with the aim of providing visual information to profoundly visually impaired patients, allowing them to utilise this device at home.

Methods: Four patients (P1, P2, P3 and P4) with end-stage rod - cone dystrophy and perception of light visual acuity were implanted with a 44 channel electrode array in the suprachoroidal space during 2018 (NCT03406416). After recovery they commenced stimulation of the device in the psychophysics laboratory.

Post operative follow-up included clinical examination, fundus photography and optical coherence tomography (OCT) to assess surgical recovery and impact on the eye.

OCT imaging was used to track the retinotopic location of the leading edge of the implant. The translation and rotation of the array relative to baseline (1 week post-implantation) was calculated at 108 weeks post-implantation.

Primary outcome measure was safety as assessed by device related serious adverse events (SAEs), secondary measure efficacy as assessed by tests of visual function and functional vision.

Results: The surgical procedures were uncomplicated. At the completion of surgery, impedance testing showed in all electrodes were functional in all patients. Post operative recovery was uneventful . Fundus imaging and OCT imaging confirmed the position of the devices under the macula and the absence of retinal trauma.

No device related serious adverse events occurred during the two years of the study.

OCT imaging showed some minor movement of the device for all four patients. P3 had the most significant movement with 15 degrees of rotation at 108 weeks compared to baseline, however no functional changes were noted.

Translational movement was minimal in all patients.

Conclusions: A 44 channel retinal prosthesis can be safely implanted in the suprachoroidal space, with no serious adverse events, device related or not, recorded for 4 patients. Over twenty four months of post operative follow-up

clinical findings, fundus photography and OCT imaging confirm safety and stability of the suprachoroidal approach with only slight movement on OCT imaging, which is usually rotational. The devices were functional for the 24 months of the study and continue to be used in the home environment.

CONTROL ID: 3528991

SUBMITTER (NAME ONLY): Zain Hussain

TITLE: Occurrence of Second Primary Malignancy (SPM) in Lacrimal Squamous Cell Neoplasms (LSCN): A Surveillance, Epidemiology, and End Results (SEER) Analysis

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Hussain, Texas Tech University Health Sciences Center El Paso Paul L Foster School of Medicine, El Paso, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zain Hussain: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: As diagnostic and therapeutic advances continue to enhance longevity in patients with lacrimal squamous cell neoplasms (LSCN), comparative second primary malignancies (SPM) are showcasing increasing relevance in long-term management. Current market analysis demonstrates lack of SPM characterization in LSCN. This retrospective cohort analysis evaluates SPMs and latency periods in patients with LSCN.

Methods: The Surveillance, Epidemiology, and End Results (SEER) Program acted as provision for cases of first primary LSCN from 2000 to 2015. Standardized incidence ratios (SIR), excess absolute risk (EAR), were extracted, computed, and analyzed via multiple outcome analysis within the SEER software. Strict utilization of index records was performed. 95% confidence intervals (CI) are provided with statistical significance achieved at $p < 0.05$.

Results: Extraction of 132 patients diagnosed with LSCN revealed mean(\pm SD) age of 62.20 (\pm 12.52) years with distribution of sex as 41.66% (55) female and 58.34% (77) male. Within the sub-cohort of patients afflicted with SPM, mean age upon diagnosis of SPM is 61.08 years. Relative to the US general population, patients diagnosed with LSCN demonstrated significantly increased risk for SPM on multiple fronts. Cumulative SPM (SIR 5.63, CI 3.22 – 9.15, EAR 256.52), ocular & orbital SPM (SIR 7205.07, CI 3294.62 – 13677.47, EAR 175.42), and non-epithelial skin SPM (SIR 193.34, CI 39.87 – 565.02, EAR 58.18) showcased statistically significant increases in overall SPM occurrence at 5- and 10-years post-LSCN diagnosis.

Conclusions: In contrast to the US general population, diagnosis of LSCN entails heightened propensity for development of second primary malignancy, including ocular, orbital, and non-epithelial skin cancers. Diagnostic and therapeutic advancements pertaining to LSCN prolong quality and longevity of patient life, thereby emphasizing the need for long-term risk management via real-time reconnaissance of malignancy-related signs and symptoms.

CONTROL ID: 3528992

SUBMITTER (NAME ONLY): Sophiana Lindenberg

TITLE: The Influence of Stimulus Size on Heterochromatic Modulation Electroretinograms in Onset Dry Age-Related Macular Degeneration

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Electroretinography (ERG) is an important clinical tool for evaluating retinal integrity and the physiology of retinal circuits involved in visual processing. Recent studies show that ERGs elicited by heterochromatic modulation stimuli (HF-ERG) can reflect the activity of cone opponent and luminance pathways at 12 and 36 Hz respectively. The aim of this study was to evaluate cone opponent and luminance reflecting ERGs in patients with onset dry age-related macular degeneration (AMD) stages using a 20° diameter stimulus in the center of the retina (target) and compare the results to those elicited by the full field (FF) stimuli.

Methods: Twenty seven patients with early stage AMD, recruited from the Prevent Senior Institute, and 18 age-matched healthy volunteers participated in this study. Flicker ERGs were recorded from one randomly chosen dilated eye. A heterochromatic flicker stimulus for ERG-HF was generated by a Ganzfeld apparatus using the RETIport system (Roland Consult, Germany). This controlled the modulation of red and green LEDs with average luminance of 100 cd.m⁻² each. The contrasts in red (R) and green (G) LEDs were varied while keeping the total contrast (R+G) constant. The fraction of red modulation (R/(R+G)) was varied between 0 (green modulation only) and 1 (red modulation only).

Results: ERGs measured in AMD patients displayed similar amplitudes and phases to FF and targeted stimuli at 12Hz and 36Hz frequencies compared to those measured in the control group. The amplitudes to R/(R+G)=0 stimuli at 12 Hz were higher for target than for FF stimuli in both the control and dry AMD groups. Conversely, the target stimuli resulted in smaller responses compared to FF stimuli at 36Hz.

Conclusions: The HF-ERGs suggest that there are no alterations in post-receptoral processes in early stages of dry AMD. The larger amplitudes to target stimuli R/(R+G)=0 stimuli at 12 Hz may be caused by rod stimulation through stray light. Because, targeted stimuli elicited large responses at 12 Hz, their use could be an alternative, non-invasive method to study the cone opponency in other types of macular diseases compared to FF ERGs.

CONTROL ID: 3529005

SUBMITTER (NAME ONLY): Takashi Ono

TITLE: Morphology and cell density of the corneal endothelium of healthy Japanese eyes

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ono, Y. Mori, R. Nejima, T. Iwasaki, K. Miyata, Ophthalmology, Miyata Eye Hospital, JAPAN|T. Ono, Ophthalmology, the University of Tokyo, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: The density and morphology of corneal endothelial cells are important factors for endothelial function and the maintenance of corneal clarity. Although they reportedly differ among populations, only a few previous studies have examined them in ophthalmologically healthy young patients. Therefore, we aimed to examine the density and morphology of corneal endothelial cells in healthy Japanese.

Methods: This observational study included eyes without ophthalmologic diseases other than refractive errors examined at the Miyata Eye Hospital between 1996 and 2015. The eyes with a previous history of ophthalmologic diseases or contact lens wear were excluded. Medical records of patient age, corneal endothelial cell density (ECD), coefficient of variation (CV), the appearance rate of hexagonal cells (6A), and cell area were retrospectively reviewed. The corneal endothelium data were obtained using non-contact specular microscopy.

Results: We included 16842 eyes of 8421 patients in the study (mean age, 19.6±8.7 years): 6668 eyes of 3334 male patients and 10174 eyes of 5087 female patients. The mean ECD of patients aged 1-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70 years was 3312.0±319.1, 3168.0 ± 284.0, 3032.8±285.9, 2891.1±284.9, 2815.8±294.6, 2741.2±278.3, and 2771.3±297.9 cells/mm², respectively. The relationship between ECD and age was expressed as $Y = -12.63 X + 3364.53$ ($R^2 = 0.359$, $p < 0.001$). The relationship between CV and age was expressed as $Y = 0.158 X + 24.50$ ($R^2 = 0.267$, $p < 0.001$). The relationship between 6A and age was expressed as $Y = -0.31 X + 72.08$ ($R^2 = 0.232$, $p < 0.001$). The relationship between endothelial cell area and age was expressed as $Y = 1.45 X + 295.97$ ($R^2 = 0.387$, $p < 0.001$). The reduction in ECD per year was significantly higher in patients younger than 21 years than in those aged 21 years or older (-19.4 cells/mm²/year and -10.1 cells/mm²/year, $p < 0.001$).

Conclusions: ECD, 6A, CV, and cell area are significantly related to age. Because the reduction in ECD per year is significantly higher in patients younger than 21 years than in those who are older, it is important to monitor corneal endothelial cells in young patients.

CONTROL ID: 3529011

SUBMITTER (NAME ONLY): Maximilian Pawloff

TITLE: Association between retinal thickness and retinal fluid volumes measured by deep learning in the HAWK & HARRIER trials

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pawloff, H. Bogunovic, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|Z. Mulyukov, D. Lorand, Novartis AG, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To investigate whether central subfield retinal thickness (CSFT) values correlate with exudative activity of patients undergoing treatment with anti-VEGF substances (Brolucizumab and Aflibercept). Fluid measurements i.e. intraretinal fluid (IRF) and subretinal fluid (SRF) were obtained by deep learning based on spectral-domain optical coherence tomography (SD-OCT) scans.

Methods: We utilized a previously validated, fully automated deep learning approach based on convolutional neural networks to detect and quantify macular fluid in SD-OCT volumes (Cirrus, Spectralis, Topcon) from patients gathered from multicenter studies HAWK (1078) & HARRIER (739) with neovascular age-related macular disease. Volumes (nl) for IRF and SRF were measured at baseline and monthly under anti-VEGF therapy in the central mm. The dataset was analyzed using descriptive statistics. We summarized the association between fluid volumes and CSFT measured from ILM to outer retinal pigment epithelium (RPE) boundaries, using the Pearson's r correlation coefficient.

Results: 41,906 SD-OCT volume scans underwent fluid volume analysis using deep learning. Detection level AUC values for IRF in the central millimeter were 0.849 in HAWK and 0.933 in HARRIER. For SRF, AUC values were 0.874 for HAWK and 0.871 for HARRIER. In HAWK, IRF volumes showed only a moderate association with CSFT at baseline ($r=0.54$) and an even weaker correlation between CSFT and IRF under therapy ($r=0.44$). Correlation of SRF and CSFT was very weak at baseline ($r=0.29$) and did not increase much under therapy ($r=0.38$). Consistently, in HARRIER, IRF volumes had a moderate correlation of $r=0.62$ with CSFT at baseline. Under therapy, association of CSFT and IRF was weak ($r=0.34$). Correlation between SRF and CSFT was very weak at baseline ($r=0.22$) and increased only marginally under therapy ($r=0.45$).

Conclusions: In patients with nAMD, CSFT does not adequately represent exudative activity and IRF and SRF volumes are more clinically relevant particularly during therapy. Due to the limited correlation of CSFT with retinal fluid, our findings do not support the use of CSFT as the main anatomical measure for treatment guidance and disease management. In contrast quantitative deep learning methods allow for a precise determination of fluid volumes and may be used as an optimal clinical decision support tool in anti-VEGF therapy in patients with nAMD.

CONTROL ID: 3529023

SUBMITTER (NAME ONLY): Andrea Peroni

TITLE: Semantic segmentation of gonioscopic images exploiting adaptive ROI localization and uncertainty estimation

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Peroni, E. Trucco, VAMPIRE Project, Computing, School of Science and Engineering, University of Dundee, Dundee, UNITED KINGDOM|M. Campigotto, A. Paviotti, NIDEK Technologies Srl., Albignasego, ITALY|

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ABSTRACT BODY:

Purpose: To develop a semantic segmentation algorithm highlighting anatomical structures of interest in digital gonioscopic images acquired by a semi-automatic ophthalmic device, and to overcome ground truth limitations (e.g. missing or incomplete target annotations) by adaptive identification of the most informative region of interest (ROI) in the data and estimation of spatial prediction uncertainty.

Methods: In gonioscopic acquisitions, only the central part of each image is well illuminated, and the focus varies according to the selected focal plane; therefore, only part of the image can be reliably annotated. A dataset of 274 irido-corneal sector images have been annotated by four experienced ophthalmologists and used to train (202), validate (41) and test (31) a custom Dense-Unet from scratch. The network is trained to achieve two simultaneous, complementary aims: exploiting the ground truths to maximise the segmentation accuracy within the annotated region of the images, and learning to evaluate the informative value of local regions based mainly on sharpness and lightness, locating a ROI. The ROI is then used to filter out uncertain segmentation outputs. Moreover, the use of drop-out during inference makes it possible to generate multiple predictions, enabling us to estimate uncertainty via the pixel-wise variance of the predicted probabilities.

Results: With a test set representative for relevant clinical cases and un-correlated with the training and validation ones we obtain an overall pixel-wise classification accuracy above 90% within the annotated area of the ground truth data. The automatic ROI identification can locate the most informative region in every test image and the uncertainty estimation proves to effectively highlight most of the un-correctly predicted image pixel sub-sets.

Conclusions: The proposed system can maximise the information learnt from ground truth annotations and combine it with an effective ROI localization to provide an accurate segmentation of irido-corneal angle layers. Uncertainty estimation can help for a better interpretation of model predictions and may act as an important support in clinical applications.

CONTROL ID: 3529042

SUBMITTER (NAME ONLY): Andrew Carkeet

TITLE: Refractive ametropia induced by contact lenses changes OCT-A macular indices

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Carkeet, B. Lal, S.A. Read, D. Alonso-Caneiro, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA

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ABSTRACT BODY:

Purpose: It is unclear how Optical Coherence Tomography Angiography (OCT-A) indices are influenced by refractive ametropia. This research used spherical contact lenses to vary refractive ametropia in healthy young participants and assessed whether OCTA indices changed in a way that could be predicted by changes in retinal image transverse magnification (TM).

Methods: 11 participants (mean age 26 ± 5 years, 5M:6F) took part in the study. For each participant, spherical soft contact lenses (-6D to +6D in 2D steps) were used to vary spherical refractive error. This varies anterior surface power, but leaves axial length unchanged. For each condition, OCT-A measurements of macular vasculature were made using a Zeiss HD-OCT 5000 OCT-A imaging system and the following indices generated: foveal avascular zone (FAZ) area, perimeter, circularity and vessel density and perfusion density, for the central 1mm zone. Optical modelling was also used to calculate TM based on biometry and autorefraction. TM of en face images was also empirically measured for each condition.

Results: Empirical TM measures matched theoretical calculations, (regression slopes: mean 1.02, 95% CI 0.74 to 1.30). Without magnification correction, contact lens power had a significant effect on all OCT-A indices assessed (F6,60 from 2.39 to 8.51, $p < 0.05$), and all OCT-A indices showed linear relationships with induced refractive ametropia that were significantly different from zero (magnitude $t(10) > 3.79-7.93$, $p < 0.05$). Corrected for TM, FAZ area (Fig 1) showed no relationship with induced refractive error ($t(10) = 1.13$, $p = 0.28$). FAZ perimeter and vessel density showed reduced but still significant relationships with refractive error even after correction for TM ($t(10) > 2.77$, $p < 0.02$).

Conclusions: This study is the first to demonstrate that refractive spherical ametropia affects OCT-A indices to an extent that may be clinically significant, with changes of up to 12%. Simple correction for transverse magnification can reduce but not fully compensate for the effect of refraction on most OCT-A indices tested. TM changes may also change perfusion density and vessel density measurements, by including different vessel beds in calculations as magnification changes.

CONTROL ID: 3529057

SUBMITTER (NAME ONLY): Katherine Talcott

TITLE: Baseline Factors Influencing Resolution of Diabetic Macular Edema (DME) Following Treatment with Intravitreal Aflibercept Injection (IAI) or Laser in VISTA and VIVID

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Talcott, C.C. Valentim, R.P. Singh, Center for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the relationship between baseline factors and DME resolution in patients randomized to IAI or laser control in VISTA/VIVID.

Methods: Of 862 patients in VISTA/VIVID full analysis set, this analysis included 558 patients treated with IAI 2 mg (given either q4 weeks or q8 weeks after 5 monthly doses) and 274 patients treated with laser control; 30 patients with baseline central subfield thickness (CST) <290 µm were excluded. Effect of baseline factors (age, gender, race, ethnicity, diabetes type and duration, HbA1c, hypertension, hyperlipidemia, smoking status, CST, best-corrected visual acuity [BCVA], and DRSS) on time to first DME resolution (CST <290 µm) was assessed in univariate and multivariate models and was further evaluated by Kaplan–Meier method based on tertiles of baseline factors.

Results: IAI patients had a 2.5-fold higher rate of DME resolution, with median (95% confidence interval [CI]) time of 33.0 (28.1, 40.0) weeks vs not achieved with laser. Based on multivariate analysis of baseline factors, lower DME resolution rate was associated with thicker CST (HR [95% CI] per 100 µm CST increase: 0.79 [0.72, 0.86]) and better BCVA (HR [95% CI] per 5 letters increase: 0.87 [0.83, 0.92]) in the IAI group. Based on Kaplan–Meier analysis, in the IAI group, tertiles of increasing CST (T1: ≤419, T2: 419–541, T3: >541 µm) were associated with significantly longer median time to DME resolution (20.1, 39.1, and 49.1 weeks for T1–T3, respectively; P≤0.0001 for T2 and T3 vs T1) and lower cumulative incidence of the event (HR of 0.6, and 0.6 for T2 and T3 vs T1, respectively, P<0.001 for T2 and T3 vs T1). In the IAI group, tertiles of increasing BCVA (T1: ≤57, T2: 57–66, T3: >66) were also associated with relatively longer median time to DME resolution (28.4, 31.7, and 44.1 weeks for T1–T3, respectively; P<0.05 for T3 vs T1) and lower cumulative incidence of events (HR of 0.9, 0.8 for T2 and T3 vs T1, respectively; P<0.05 for T3 vs T1).

Conclusions: Thicker CST and better BCVA in the IAI group were baseline factors associated with longer time to and lower rate of DME resolution in VISTA and VIVID. These findings may inform physicians and patients regarding expectations of DME therapy.

CONTROL ID: 3529061

SUBMITTER (NAME ONLY): Rishi Subrahmanyam

TITLE: MIOCT-generated topography maps for astigmatism magnitude and axis calculation in corneal phantoms

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Corneal surgeries such as penetrating keratoplasty (PKP) can result in significant postoperative refractive errors that are difficult to assess intraoperatively with the current standard of care. Microscope-Integrated OCT (MIOCT) has the potential to characterize corneal astigmatism intraoperatively to help improve post PKP refractive outcomes. Here, we report accurate detection of astigmatism magnitude and axis in software-generated and 3D-printed phantom corneas.

Methods: Software phantoms were designed using MATLAB to simulate the corneal surface with astigmatism from 0 – 6 diopters (D). Plastic, 3D-printed phantom corneas were designed with astigmatism from 0 – 6 D. Four phantoms in each group have astigmatism with steep axis at 180°, and two have astigmatism with steep axis at 0° to evaluate anisotropy in imaging direction. Printed phantoms were imaged with MIOCT. After manually segmenting the first frame as a pilot, each subsequent Bscan in the volume was automatically segmented to identify the epithelial surface. Segmentations were fit to a 6th order Zernike function and corrected for system-specific distortions. Astigmatism magnitudes and axes were calculated according to ANSI standards for all phantoms.

Results: Topography maps are shown for software (Figure 1) and 3D-printed (Figure 2) phantoms. For software phantoms, the mean absolute difference between calculated and reference astigmatism magnitude and axis was 0.012 D and 0 degrees, respectively, for phantoms with steep axis at 90° and was 0.016 D and 0 degrees, respectively, for phantoms with steep axis at 0°. For printed phantoms, the mean absolute difference between calculated and reference astigmatism magnitude and axis was 0.26 D and 2.7 degrees, respectively, for phantoms with steep axis at 90° and was 0.25 D and 8.1 degrees, respectively, for phantoms with steep axis at 0°.

Conclusions: We used the MIOCT-based corneal topography system on software and 3D-printed corneal phantoms to calculate astigmatism magnitude and axis. The system calculates astigmatism magnitude within approximately 0.25 D and detects axis within 10 degrees. This system has potential for intraoperative astigmatism assessment during procedures such as PKP.

CONTROL ID: 3529066

SUBMITTER (NAME ONLY): Shan Fan

TITLE: Effects of a proprietary de-novo IOP lowering compound (ID-65-CW69) on aqueous humor dynamics in monkeys

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this study was to identify the mechanism by which a novel selective soluble guanylate cyclase activator (ID-65-CW69) lowers intraocular pressure (IOP) and alters aqueous humor dynamics in monkeys with unilateral laser induced glaucoma.

Methods: Fifteen female cynomolgus monkeys with unilateral laser-induced glaucoma were dosed with one 30 μ l drop of ID-65-CW69 or its vehicle to the cornea of both eyes at 6:00 PM the day before the measurement day in a masked crossover fashion. Intraocular pressures (mmHg) were measured by pneumatonometry at 6:00 PM (IOP1), just before dosing; and again at 10:00 AM (IOP2) and noon (IOP3) the following day. Other measurements were aqueous flow (Fa, μ l/min) by fluorophotometry, outflow facility (C, μ l/min/mmHg) by fluorophotometry (C) and uveoscleral outflow (Fu, μ l/min) by mathematical calculation.

Results: The hypertensive eyes showed a significant decrease in IOP to the level of the normotensive eyes. Results in the hypertensive eyes are summarized in the Table. Values are Means \pm SD. Drug treatments and corresponding vehicle treatments were compared by two-tailed paired t-tests (p). No significant changes were found in the normotensive eyes.

Conclusions: ID-65-CW69 reduced IOP in hypertensive eyes by increasing uveoscleral outflow by over two-fold. Outflow facility increased but this did not reach significance. The drug did not significantly lower IOP in the normotensive eyes.

CONTROL ID: 3529105

SUBMITTER (NAME ONLY): Julia Owen

TITLE: Student becomes teacher: faster deep learning (DL) lightweight models (LWM) for automated detection of abnormal OCT B-scans using student-teacher framework

SESSION TITLE: Deep learning for classification and segmentation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose:

Significant barriers to OCT automated diagnosis include need for expert-labeled training data and long computing times required by state-of-the-art algorithms. We explore a student-teacher framework for training LWMs with fewer parameters leveraging unlabeled images to perform fast automated detection of abnormal B-scans.

Methods:

The dataset consisted of 76,396 expertly labeled B-scans from 598 patients (45,698 normal and 30,698 abnormal) and 478,588 unlabeled B-scans from 3,148 patients, acquired using a CIRRUS™ HD-OCT 5000 (ZEISS, Dublin, CA). B-scans were labeled abnormal if intraretinal/subretinal fluid; disruption of inner retinal layers, IS/OS, or vitreoretinal interface; or RPE atrophy/elevation were present. A ResNet50 “teacher” model and 27 “student” DL networks from 4 LWM families (SqueezeNet, SqueezeNext, MobileNet, and ShuffleNet) were trained to identify abnormal B-scans. The labeled dataset was split by patients into 80% training and 20% validation. Average inference time on a NVIDIA P100 and best validation accuracy over epochs were reported. The unlabeled B-scans were artificially labeled using the teacher network (Figure 2A) and then combined with the labeled B-scans to retrain the LWMs from random initialization.

Results: Figure 1 presents the accuracy versus inference-time tradeoff for all models. ResNet50 achieves 96.1% validation accuracy and the LWM range from 83.2% to 95.0%. The best performing LWM, a SqueezeNet model with residual connections (SRN.1), is 4.13 times faster than ResNet50 (0.109s vs. 0.452s). Figure 2 shows student-teacher training results, revealing that all models benefit from increasing training set by including unlabeled B-scans. SRN.1 again obtains the highest validation accuracy (96.3%), narrowly exceeding the teacher network.

Conclusions: We demonstrate the effectiveness of a student-teacher framework for training fast LWMs for automated abnormal B-scan detection leveraging unlabeled, routinely-available data.

CONTROL ID: 3529138

SUBMITTER (NAME ONLY): John Romanowski

TITLE: Identification of Coagulase Negative Staphylococci Isolated from Endophthalmitis Using Biolog GEN III Microplate, API Staph Ident, and DNA Sequencing

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Romanowski, S.V. Nayyar, E.G. Romanowski, R.M. Shanks, R.P. Kowalski, The Charles T. Campbell Ophthalmic Microbiology Laboratory, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although part of periocular normal flora, coagulase-negative staphylococci (CNS) are frequent opportunistic pathogens after ocular surgery that cause endophthalmitis. CNS is generally not identified to the species level from eye cultures, but some species may be more common than others. The goal of the current study was to evaluate three methods of species level identification (Biolog GEN III, API Staph Ident, DNA sequencing) of CNS isolated from cases of endophthalmitis and determine whether they are in agreement with their identification of staphylococcal species that cause endophthalmitis.

Methods: We compared the identifications of 47 isolates of CNS from endophthalmitis from the Charles T. Campbell Ophthalmic Microbiology Laboratory using Biolog GEN III Microplates, (phenotypic substrate system) (Hayward, CA), API Staph IDENT (biochemical system) (bioMerieux, USA), and DNA sequencing of the *sodA* gene. Sample preparation followed the standardized procedures for each test.

Results: The identification of CNS to the species level were identical for Biolog and DNA sequencing except for 1 isolate. Of the 47 isolates for Biolog, 42 were *Staphylococcus epidermidis*, 3 were *Staphylococcus lugdunensis*, 1 was *Staphylococcus hominis*, and 1 was *Staphylococcus haemolyticus*. For DNA sequencing, 43 isolates were *S. epidermidis*, 2 were *S. lugdunensis*, 1 was *S. hominis*, and 1 was *S. haemolyticus*. Species identification differed for API Staph IDENT by 6 isolates compared to DNA sequencing and by 5 isolates compared to Biolog. Of the 47 isolates, 40 were *S. epidermidis*, 2 were *S. lugdunensis*, 2 were *S. hominis*, 1 was *Staphylococcus capitis*, 1 was *S. haemolyticus*, and 1 was *Staphylococcus aureus* (a possible weak producer of protein B?).

Conclusions: CNS identification to the species level by all three methods indicated that *S. epidermidis* is the predominant species of CNS isolated from cases of endophthalmitis. Identification of CNS from keratitis, conjunctivitis, and blepharitis may indicate different distributions of CNS species.

CONTROL ID: 3529156

SUBMITTER (NAME ONLY): Daniel Palanker

TITLE: Simultaneous Perception of Prosthetic and Natural Vision in Patients with Geographic Atrophy

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the central prosthetic vision with the photovoltaic subretinal implant activated by augmented-reality glasses and simultaneous perception of the natural peripheral vision in patients with geographic atrophy.

Methods: Five patients with visual acuity $\leq 20/400$ due to geographic atrophy of at least 3 optic discs diameters and no foveal vision have been implanted with a wireless photovoltaic chip (PRIMA, Pixium Vision) of 2x2mm in size, 30 μ m in thickness, containing 378 pixels of 100 μ m in width. Each pixel in the implant converts pulsed near-infrared light (880nm) projected from video glasses into electric current to stimulate the nearby neurons in the inner nuclear layer of the retina. Prosthetic acuity was assessed using electronic magnification of 1, 2, 4 and 8. Simultaneous perception of central prosthetic and peripheral natural vision was evaluated under room lighting.

Results: In all patients, chip implanted under the macula remains stable and functional, with a follow-up extending now up to 3 years. No decrease in natural eccentric visual acuity was observed in any of the study eyes. All 5 patients perceive white-yellow patterns with adjustable brightness, in retinotopically correct locations within previous scotomata. All 4 patients with subretinal placement of the chip achieved acuity without zoom in the range of 20/438 – 20/564, corresponding to the average of 1.17 ± 0.13 implant pixels. With electronic magnification of up to a factor of 8, patients demonstrated acuity in the range of 20/63-20/98. Under room lighting, patients could simultaneously use prosthetic central vision and the remaining peripheral vision in the operated eye and in the fellow eye.

Conclusions: Wireless chip PRIMA implanted under the atrophic macula in patients with geographic atrophy remains stable and functional during the 2-3 years of follow-up. The implant provides central visual perception with acuity close to the single pixel size of the photovoltaic array. Augmented reality glasses enable simultaneous perception of the central prosthetic and natural peripheral vision under room lighting, while electronic zoom provides significantly higher resolution.

CONTROL ID: 3529163

SUBMITTER (NAME ONLY): David Richter

TITLE: Intervisit specificity of a combined retinal ganglion cell index in glaucoma

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Glaucoma results in retinal ganglion cells (RGC) loss and is commonly assessed from structural changes detected by optical coherence tomography (OCT) and functional changes detected by perimetry. Progression analyses are available for both types of data to indicate when change exceeds test-retest variability and have been shown to have acceptable specificity. A structure-function RGC index (RGCI) provides a combined model to monitor progression instead of isolated structure or functional metrics¹. In this short-term, multi-visit clinical study, we investigated the specificity of several progression methods based on RGCI.

Methods: Visual field (VF) and OCT data were acquired from 74 eyes of 74 glaucoma subjects at 5 repeat visits within 4 months, using HFA™ II-i (ZEISS, Dublin, CA) and CIRRUS™ HD-OCT (ZEISS, Dublin, CA). At each visit, SITA Standard 24-2 VFs and Optic Disc 200x200 and Macula 200x200 cube scans were acquired.

RGCI progression was flagged and specificities calculated for two sets of methods. One set used results of linear regression (trend), assuming a visit interval of 0.5 years: a) reg_nonzero – significant non-zero slope; b) reg_less_cross, reg_less_long – slopes significant and less than previously reported cross-sectional and longitudinal rates, respectively^{1,2}; and c) reg_less_zero_confirm – slope significant and negative at final two visits (confirmation). The second set was patterned on change from baseline (event) based OCT GPA analyses using RGCI variability previously reported³: a) cfb_possible – “Possible” or “Likely” progression at final visit and b) cfb_likely – “Likely” progression at final visit.

Results: Mean age was 63.6 (SD: 10.1; range: 35.7 to 79.6) years. Mean MD was -3.9 (SD: 4.1; range: -18.2 to 1.2) dB. Specificities were 93.2% for reg_nonzero, 98.6% for reg_less_cross, reg_less_long, reg_less_zero_confirm, cfb_possible, and 100% for cfb_likely (see Table 1).

Conclusions: The combined RGCI shows excellent specificity in a short-term, multi-visit study design in a glaucoma population where no progression, only random fluctuation, is expected. As such, the RGCI may be a reasonable parameter for monitoring glaucomatous progression for both event-based and trend-based progression analyses.

References

¹Medeiros et al. Arch Ophth 2012; 130(9). ²Medeiros et al. AJO 2012; 154(5). ³Yu et al. IOVS 2018; 59(9): Abstract 2124.

CONTROL ID: 3529173

SUBMITTER (NAME ONLY): Sarah Rahman

TITLE: Racial Differences in Rhegmatogenous Retinal Detachment Repair Outcomes

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rhegmatogenous Retinal Detachment (RRD) is a serious ocular condition that carries risk for vision loss. However, there remains a paucity of information on the impact of demographics on RRD repair outcomes. The purpose of this retrospective chart review is to characterize how RRD repair outcomes differ between racial groups.

Methods: Data was collected from electronic medical records of adult patients who underwent an RRD repair at Cole Eye Institute from 2012 to 2020. Patients were excluded if they had previous penetrating trauma to the presenting eye, previous posterior intraocular segment surgery to presenting eye, or less than 90 days of follow-up after surgery. Demographic differences were characterized. Univariate and multivariate logistic regression was used to compare retinal reattachment rate and macula-off status at diagnosis by race.

Results: Preliminary results are that 1012 patients underwent surgical RRD repair. Mean age of the patients was 63.8 years. 61.0% of the patients were male and 39.0% were female. 86.8% were white, 10.1% were black, 1.1% Asian and 2.1% other race. 95.1% of all patients, 95.6% of white patients, and 92.2% of black patients had successful retinal reattachment at 90 days following the procedure ($p=0.162$). Of patients who underwent one surgery, black patients had higher odds of repeat retinal detachment than white patients (OR 3.13, $p=0.020$, $n=805$), controlling for age, gender, and smoking status. Black patients also had higher odds of macula-off status at the time of diagnosis than white patients (OR 1.51, $p=0.079$, $n=952$). Current smokers have higher odds of macula-off status than non-smokers (OR 2.39, $p=0.001$, $n=952$).

Conclusions: Black patients have higher odds of their retina detaching after RRD repair when compared to white patients. There is also a trend for black patients to have relatively higher odds of macula-off detachment at presentation, however this is not statistically significant. This suggests that black patients may have both more severe presentation at diagnosis and worse outcomes of RRD surgical repair than white patients. Further studies are needed to determine factors that may mediate this association.

CONTROL ID: 3529174

SUBMITTER (NAME ONLY): Quan Nguyen

TITLE: The HORNBILL study: A Phase I/IIa trial examining the safety of BI-X in patients with diabetic macular ischemia and diabetic retinopathy treated with pan-retinal photocoagulation

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Diabetic macular ischemia (DMI) is a vision-threatening and common complication of diabetic retinopathy (DR) that can lead to irreversible vision loss. At present, there is no approved treatment to prevent either the onset or progression of DMI. We are conducting a non-randomized, open-label, single rising dose/multiple rising dose study (NCT04424290) to investigate the safety and tolerability of intravitreal BI-X, an ischemia modulator agent.

Methods: Patients with DR treated with pan-retinal photocoagulation and evidence of DMI are eligible for inclusion. DMI was defined as any degree of disruption in retinal vascularity within the superficial and/or deep retinal plexus, imaged with optical coherence tomography angiography. A total of 6 patients have been enrolled into two dosing cohorts (0.5 mg and 1.0 mg of BI-X, n=3 per cohort) to date, with a future cohort at 2.5 mg (n=6) planned. Patients received a single intravitreal dose of BI-X. The primary endpoint is the number of dose-limiting events, with secondary endpoints being the number of drug-related adverse events (AEs) and number of ocular AEs.

Results: The mean age of the 6 patients was 62.8 (standard deviation ± 10.7) years, 4 were female. No drug-related AEs or dose-limiting events were reported in either cohort, but 2 procedure related AEs were reported in the 0.5 mg cohort. One patient with glaucoma experienced a temporary increase in intraocular pressure (IOP), from 19 mmHg at baseline to 44 mmHg after injection. The patient was treated with topical anti-glaucoma therapies, after which IOP reduced to 35 mmHg; the patient reported no pain or discomfort. At follow up visits on days 4 and 8, IOP was 27 mmHg and 22 mmHg, respectively. A second patient had a subconjunctival hemorrhage that resolved without sequelae.

Conclusions: Single doses of BI-X were well-tolerated by patients with DMI, with no dose-limiting events, no SAEs and no drug related AEs reported to date. A single-masked, randomized, multiple rising dose study is planned to further examine the efficacy of BI-X in patients with DMI.

CONTROL ID: 3529230

SUBMITTER (NAME ONLY): Susannah Paine

TITLE: The Relationship of the Timing to Ophthalmology Consultation on Acute Ocular Severity in Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.T. Kwan, J. Chodosh, H.N. Saeed, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|S. Paine, Brown University, Providence, Rhode Island, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stevens-Johnson Syndrome (SJS) is a severe hypersensitivity reaction affecting skin and mucous membranes with potentially debilitating ocular sequelae. Acute ocular severity (AOS) may correlate with long-term ocular outcomes. AOS can progress rapidly and early ophthalmology consultation (OC) is of paramount importance. We performed a retrospective, observational chart review to clarify the relationship of AOS and initiation of ophthalmologic care.

Methods: All patients with history of SJS in our hospital system were considered. Included patients had documented confirmed SJS diagnosis by biopsy or clinical exam by dermatology or burn service. 127 patients were included. The outcome measures included frequency of OC in the acute phase, AOS score at initial OC, and length of time in days to first OC. AOS score was compared between those seen within 1 day of admission and those seen after 1 day. Statistics were performed in R version 4.0.2. Means with standard deviations are presented for ordinal variables.

Results: 85 (66.9%) patients were seen by ophthalmology within 1 day, 26 (20.5%) were seen after 1 day, and 16 (12.6%) were not seen. Those seen occurred at a mean of 1.47 days after admission. Greater AOS scores were present in those seen within 1 day of admission compared to those seen after 1 day ($p = 0.003$). Worse systemic disease was seen in those patients seen within 1 day versus after 1 day. 23% of eyes in patients seen after 1 day of admission went on to develop chronic disease complications.

Conclusions: Most patients with SJS were seen by ophthalmology during the early acute phase. More severe eye disease was noted in those seen within 1 day of admission. As the workup of SJS is complex, often requires biopsy, and therefore increases time to diagnosis, this finding suggests more significant acute ocular and/or systemic disease may prompt more expedient ophthalmologic care when SJS is suspected. However, those not seen within 1 day of admission still have significant chronic complications. While large improvements have been made in the practice of OC for SJS, we suggest that all patients suspected of having SJS/TEN be examined by ophthalmology as early as possible as ocular disease can rapidly progress and even initially mild cases can have chronic complications.

CONTROL ID: 3529262

SUBMITTER (NAME ONLY): Fernanda Maria Silveira Souto

TITLE: Vogt-Koyanagi-Harada disease (VKHD) after systemic treatment discontinuation

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Silveira Souto, R.F. Missaka, M.M. Lavezzo, P.F. Nóbrega, M.K. Oyamada, C.E. Hirata, J.H. Yamamoto, Ophthalmology, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|V.M. Sakata, Ophthalmology, Universidade Federal do Parana, Curitiba, PR, BRAZIL|

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ABSTRACT BODY:

Purpose: To describe the clinical course of VKHD after systemic treatment discontinuation

Methods: Retrospective study with 11 patients (22 eyes) with VKHD after systemic treatment discontinuation for at least 12mo. All patients were followed from acute disease onset with systematic clinical and imaging evaluation (indocyanine green and fluorescein angiographies and enhanced depth imaging optical coherence tomography (Spectralis HRA+OCT)). All patients were treated with methylprednisolone pulse therapy followed by oral prednisone (1mg/kg/day) with slow tapering; 5 patients also received non-steroidal immunosuppressive therapy. Presence/fluctuation of clinical sign of inflammation (anterior chamber cells (ACC)); optic disc (OD) or perivascular leakage, dark dots (DD), subfoveal choroidal thickness (CT) increase $\geq 30\%$ (subclinical inflammation); and complications were analyzed during treatment period (TP) and post-treatment period (PTP). Criteria for treatment discontinuation were no anterior uveitis relapse, stable subclinical inflammatory signs and stable full-field electroretinogram (ffERG) parameters for at least 12mo. Binary ocular data were analyzed by descriptive statistics and generalized estimated equations. This study was approved by the Institutional Ethics Committee and followed the Helsinki declaration

Results: Mean disease duration at TP and PTP was 37.6 ± 15.8 mo (range 12-59mo) and 33.6 ± 21.3 mo (range 12-87mo), respectively. At the last TP visit, visual acuity (VA) was 0.1 ± 0.2 logMAR; no eyes had ACC; DD were present in all eyes (mean score 5.3 ± 0.9), while OD leakage was observed in 2 eyes (1 patient). During PTP, 1 patient (2 eyes) had transitional ACC, but none had systemic treatment restarted. All evaluated parameters (events/year and at last visit) improved in PTP, with statistical significance only for DD score fluctuation ($p=0.004$). ffERG parameters remained stable on PTP despite some subclinical inflammatory signs were still present. Table 1 describes TP and PTP data.

Conclusions: This is a pioneer description of VKHD course after systemic treatment discontinuation. After a systematic follow-up, criteria used for treatment discontinuation seems adequate. Subclinical inflammation tends to ameliorate during PTP. Further studies with longer follow-up are needed to better understand subclinical inflammation signs in VKHD after treatment discontinuation and to detect risk factors for late recurrence.

CONTROL ID: 3529346

SUBMITTER (NAME ONLY): Abhinav Golla

TITLE: Association Between E-Cigarette Use and Visual Impairment

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Golla, A. Chen, V.L. Tseng, S.Y. Lee, D. Pan, F. Yu, A.L. Coleman, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Smoking tobacco is a known risk factor for many eye diseases. However, the association between electronic cigarettes (e-cigarettes), which contain nicotine (a by-product of tobacco), and eye diseases is not fully known. The purpose of this study was to use the Behavioral Risk Factor Surveillance System (BRFSS) to study the association between e-cigarette smoking and visual impairment.

Methods: A population-based, cross-sectional study was performed using data from 2016-2018 BRFSS surveys. BRFSS is a nationwide telephone survey that interviews U.S. adults ages 18+ about health behaviors. E-cigarette use for tobacco was assessed by the questions: "Have you ever used an e-cigarette or other electronic vaping product, even just one time, in your entire life?" and "Do you now use e-cigarettes or other electronic vaping products every day, some days, or not at all?". Visual impairment was defined as: "Are you blind or do you have serious difficulty seeing, even when wearing glasses?". Logistic regression was performed to assess the association between e-cigarette use and visual impairment, while controlling for the covariates of age, sex, race/ethnicity, marital status, education, employment status, family income, heavy alcohol use, BMI, physical activity, and mental health. Cigarette smoking was not included because it was highly correlated with e-cigarette use. All analyses were performed by incorporating sampling design and weights according to the BRFSS analytic guidelines.

Results: The study included 1,173,646 total individuals. 6.2% of current e-cigarette smokers and 5.8% of former e-cigarette smokers stated they were visually impaired, as opposed to only 4.7% of never e-cigarette smokers. These are weighted percentages which BRFSS uses to more accurately represent the total population from the survey. The odds ratio of visual impairment in current e-Cigarette smokers compared to never smokers was 1.37 (95% CI, 1.14-1.64) adjusted, and 1.36 (95% CI, 1.15-1.61) unadjusted. The odds ratio of visual impairment in former e-Cigarette smokers compared to never smokers was 1.21 (95% CI, 1.09-1.35) adjusted, and 1.20 (95% CI, 1.09-1.31) unadjusted.

Conclusions: E-cigarette smoking was associated with visual impairment in the BRFSS survey. Given the strong association between tobacco smoking and other behaviors like alcohol use, a future study is needed to determine the independent risk of e-cigarette smoking on visual impairment.

CONTROL ID: 3529377

SUBMITTER (NAME ONLY): Daniella Lent-Schochet

TITLE: Natural History and Predictors of Vision Loss in Eyes with Diabetic Macular Edema and Good Initial Visual Acuity

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To identify clinical and anatomic factors associated with vision loss in the eyes with treatment-naïve diabetic macular edema (DME) and good initial visual acuity (VA).

Methods: Retrospective cohort study following the long-term natural history of eyes with untreated center-involving DME and baseline VA $\geq 20/25$ seen at the University of California, Davis Eye Center between March 2007 to March 2018. We collected clinical characteristics including diabetes type, hemoglobin A1c, presence of visual symptoms, VA, and diabetic retinopathy (DR) severity; and spectral domain-optical coherence tomography (SD-OCT) biomarkers including central subfield thickness, intraretinal cyst size, intraretinal hyperreflective foci, disorganization of the retinal inner layers (DRIL), and outer retinal layer disruptions, to determine factors associated with vision loss as defined by the DRCR Protocol V study as the threshold for initiating aflibercept therapy.

Results: 76 eyes (67 patients) with untreated DME and mean baseline VA of logMAR 0.05 ± 0.05 (Snellen 20/22) was followed for an average of 4.3 ± 3.2 years, with a median time to vision loss of 335.5 days (11 months). Older age (hazard ratio (HR) 1.027/year, $P = 0.04$) and eyes with severe non-proliferative DR (HR 2.42, $P = 0.01$) or proliferative DR (HR 3.79, $P < 0.001$) showed a higher risk of vision loss, while no SD-OCT biomarker showed a significant association.

Conclusions: In eyes with DME and good initial vision, older patients or those with worse DR severity should be monitored more closely for prompt treatment initiation when vision loss occurs.

CONTROL ID: 3529406

SUBMITTER (NAME ONLY): Jie Shen

TITLE: A Minipump Continuous Drug Infusion Dog Model System to Identify Candidate Drugs and Drug Delivery Rates for Intracameral IOP-lowering Implants

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Shen, M.R. Robinson, M. Attar, Allergan, an AbbVie company, California, UNITED STATES|J. Burke, Burke Science LLC, California, UNITED STATES|T.T. Lam, Consultant, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intracameral implants providing sustained release of drug to lower intraocular pressure (IOP) have the potential to bypass the ocular surface and manage IOP in glaucoma without use of daily eye drops. To facilitate the development of intracameral drug implants for lowering IOP, we developed a dog model to determine optimal drug release rates in the intracameral space.

Methods: Female normotensive Beagle dogs were used (n=5-8 per treatment). Under general anesthesia, an Alzet osmotic microinfusion pump was surgically placed subcutaneously in the back of the neck of each dog, with a cannula opening into the intracameral space of the right eye; the main body of the cannula was sutured to the sclera. Patency of the cannula was confirmed with fluorescein (Figure). After recovery from surgery, a solution of prostaglandin/prostamide analog at varying concentrations was delivered continuously into the intracameral space at 2.5 μ L/hr for 10 to 15 days. Aqueous humor samples were collected to determine drug concentration. IOP was measured in awake animals with a TonoVet rebound tonometer.

Results: Infusion of bimatoprost, bimatoprost acid, or latanoprost acid lowered IOP; infusion of latanoprost did not affect IOP. The IOP lowering during bimatoprost infusion was relatively steady and sustained. When the infused bimatoprost dose was increased to two higher doses, the magnitude of IOP lowering was similar, ranging from -32.9% to -34.3% at steady state with no clear dose-dependency. The aqueous humor bimatoprost concentration increased with increasing bimatoprost dose; bimatoprost acid was detected only at the highest dose. These results suggest that the lowest dose would represent a good target release rate when developing an intracameral bimatoprost drug implant. Ophthalmic observations were as expected with the surgical procedure, and no adverse findings were attributed to the tested drugs.

Conclusions: This dog model can be used to effectively screen IOP-lowering drugs as candidates for intracameral sustained-release platforms. Use of this model system to determine an optimal release rate and initial target dose to be used for in vivo testing of a sustained-release drug delivery device can accelerate intracameral implant drug development.

CONTROL ID: 3529417

SUBMITTER (NAME ONLY): Min Zhao

TITLE: Effect of intravitreal spironolactone released from PLGA microspheres in diabetic retina of Goto-Kakizaki rat

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhao, E. Gelize, M. Berdugo, K. Delaunay, F.F. Behar-Cohen, Team 17, INSERM UMRS 1138, Centre de Recherche des Cordeliers, Paris, FRANCE|A. Moulin, Department of Ophthalmology, University of Lausanne, Jules Gonin Eye Hospital, Fondation Asile des Aveugles, SWITZERLAND|F. Azan, Ophthalmopole, Hôpital Cochin Assistance Publique Hôpitaux de Paris, FRANCE|J. Guegan, Institut du Cerveau, ICM, iCONICS, Hôpital de la Pitié-Salpêtrière, FRANCE|E. Pussard, Inserm U1185, Fac Med Paris-Sud, FRANCE|I. Bravo-Osuna, R. Herrero-Vanrell, Department of Pharmacy and Pharmaceutical Technology, Instituto Universitario de Farmacia Industrial, Faculty of Pharmacy, Universidad Complutense de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy remains a major cause of vision loss worldwide. Mineralocorticoid receptor (MR) is expressed in the retina and its antagonism has anti-inflammatory and anti-angiogenic effects. While MR pathway overactivation is recognized in the pathogenesis of diabetic nephropathy, its role in diabetic retinopathy is unknown. We aimed to evaluate the effect of intravitreal MR antagonist spironolactone in the retina of type2 diabetic Goto-Kakizaki (GK) rat and to establish the link between MR overactivation and diabetic retinopathy.

Methods: Young (3-4 months) and old (≥ 1 year) GK rats were injected intravitreally with PLGA microspheres controlled releasing spironolactone or non-loaded microspheres. Age and gender matched Wistar rats were used as control. One month later, retinal morphology, immunofluorescence of ion (Kir4.1) and water channels (AQP4) and microglia/macrophages (IBA-1), gene expression of inflammatory factors were analyzed. In old rats, we also assessed the effect of spironolactone on retinal vascular permeability and a transcriptomic analysis was performed to identify spironolactone-regulated genes and pathways in the diabetic retina. Human ocular media and retina have been used to confirm the relevance.

Results: The sustained local delivery of spironolactone decreased the early and late features of diabetic retinopathy such as retinal inflammation, vascular leakage and retinal edema in diabetic GK rats. The transcriptomic signature of the retina of old diabetic rats treated with spironolactone highlighted the regulation of genes encoding proteins known to intervene in vascular permeability and retinal edema such as Vldlr, Sesn2, Adcyap1, Dusp8, Pten, Slc7a1, Tjp1, Dlg1 and Sema7a. In human diabetic retina, MR expression was enhanced and cortisol was the preferential ligand binding to MR. Lipocalin 2 and galectin 3, two known MR target molecules increased in GK rat retina, were also enhanced in human diabetic retina.

Conclusions: Sustained intravitreal delivery of spironolactone reduces early inflammation and late retinal edema and vascular permeability in the retina of diabetic GK rats, suggesting involvement of MR pathway overactivation in the pathogenesis of diabetic retinopathy. Increase in MR expression, and in its ligand and target molecules in human diabetic retina further confirms the hypothesis.

CONTROL ID: 3529472

SUBMITTER (NAME ONLY): Allen Hu

TITLE: Safety of intravitreal pegcetacoplan in patients with neovascular age-related macular degeneration receiving anti-VEGF therapy

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hu, Meritus Medical Center, Hagerstown, Maryland, UNITED STATES|D.M. Brown, Retina Consultants of Texas, Texas, UNITED STATES|R. Ribiero, C. Bliss, D. Jones, Apellis Pharmaceuticals Inc, Waltham, Massachusetts, UNITED STATES|D. Esmaili, Retina-Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pegcetacoplan (APL-2) is a C3 therapy targeting complement overactivation driving geographic atrophy (GA) progression. Neovascular age-related macular degeneration (nAMD) can coexist with GA. APL-203 was designed as an 18-month, Phase 1b/2, multicenter, open-label study evaluating the safety of monthly intravitreal (IVT) APL-2 for 12 months in patients with nAMD receiving anti-VEGF, with an additional 6 months of follow up.

Methods: Patients age ≥ 60 years with nAMD and BCVA of ≥ 24 ETDRS letters (20/320 Snellen equivalent) in the study eye were enrolled. Eyes had received ≥ 6 months of IVT anti-VEGF therapy (at ≤ 8 -week intervals for the most recent 2 injections). At screening, response to anti-VEGF was confirmed by reduction in macular fluid or thickness on optical coherence tomography (OCT). The primary endpoint was the incidence and severity of ocular and systemic treatment-emergent adverse events (TEAEs). APL-2 was administered ≥ 30 minutes apart from anti-VEGF.

Results: 17 patients (mean 77.2 years; 58.8% men; 94.1% white) received ≥ 1 dose of APL-2. Mean baseline VA in study eyes was 69.5 EDTRS letters. The majority of TEAEs were either mild or moderate. Common ocular TEAEs included increased intraocular pressure (IOP), uveitis, and conjunctival hemorrhage. Mean IOP was generally unchanged, and no deaths occurred. Two TEAEs of mild ocular hypertension were controlled with IOP-lowering drugs. Decline in BCVA (≥ 15 letters) in the study eye was observed in 8 patients; 6 fully recovered. In the other 2 patients, BCVA loss at the last study visit was deemed related to an ocular AE (unrelated to APL-2) or nAMD progression. During the study, patients remained on monthly anti-VEGF therapy. All patients had received a lyophilized APL-2 formulation for up to 7 months with no events of intraocular inflammation (IOI). A liquid formulation was introduced mid-study in 4 patients who then developed events of mild to severe IOI. All these events were transient, without long-term sequelae, and likely caused by a low-level impurity in the active pharmaceutical ingredient of the liquid formulation. The study was subsequently terminated early because sufficient data were collected for the sponsor's objectives.

Conclusions: Administration of APL-2 in combination with anti-VEGF therapy in patients with nAMD appears to be safe and well tolerated.

CONTROL ID: 3529477

SUBMITTER (NAME ONLY): Mary Durbin

TITLE: Detecting progression in the center of the visual field

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The 24-2 visual field test has limited ability to detect change in the center of the visual field (VF). One approach to detecting change is to apply the change limits estimated from the central points in repeated 24-2 scans to 10-2 scans. In this study we use short-term reproducibility data to determine the specificity of using the 24-2 inner zone change limits from the HFA guided progression analysis (GPA) to detect change in the 10-2 VF.

Methods: VFs were acquired from 74 eyes of 74 glaucoma subjects at 5 repeat visits within 4 months, using HFA™ II-i (ZEISS, Dublin, CA). At each visit, SITA Standard 10-2 and 24-2 VFs were acquired. Because the repeated visits occurred over a short period of time, any change observed in this data would by definition be a false positive. In HFA, GPA change limits in the 24-2 field depend on location as well as baseline mean deviation (MD), and baseline pattern deviation (PD). For this study, we substituted 10-2 MD for the 24-2 MD. We plotted the correlation between the MDs to confirm that this was reasonable.

As in HFA GPA the first two scans in the series were averaged to create a baseline. The first and second follow-ups were compared to the baseline for each test point and the differences compared to the change limits used for the central portion of the 24-2 in the commercial version of GPA. False positive rates (FPR) with 95% confidence intervals (CI) were pooled for all 74 patients and all 68 test points in the 10-2 for both follow-ups. Specificity was defined as $1 - \text{FPR}$. GPA was not performed on test locations where the MD or PD are too poor(censoring), which would be denoted as "out of range" or "X" on the report and in the analyses. FPR was calculated two ways: pooling all points, and pooling only points not marked "X".

Results: Mean age was 63.6 (35.7 to 79.6) years. Mean MD was -3.9 (-18.2 to 1.2) dB. Correlation of 24-2 MD with 10-2 MD showed an R^2 of 0.67, a slope of 0.89 and an offset of 0.19, so it is reasonable to substitute the MD from 10-2 to determine change limits. FPR was 0.47 (CI: 0.43 to 0.52) considering all 10064 pooled points and 0.51 (CI: 0.46 to 0.55) considering 9380 pooled valid points, consistent with specificity of ~95%.

Conclusions: Specificity was ~95% for detecting progression in 10-2 fields using limits established in the central portion of the 24-2, indicating that a simple GPA for 10-2 can be created using existing data.

CONTROL ID: 3529498

SUBMITTER (NAME ONLY): Tobias Strunz

TITLE: Gene expression in liver is influenced by coordinated activities at genetic loci associated with age-related macular degeneration

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The currently most comprehensive genome-wide association study (GWAS) for age-related macular degeneration (AMD) identified disease associations for 52 independent genetic variants at 34 genomic loci. Collectively, the AMD-associated loci are enriched for genes contributing to a number of shared cellular processes. Of note, most current approaches focus on single loci and their influence on AMD pathogenesis without considering epistatic interactions. Here, we present a novel approach to investigate combined effects of apparently independent GWAS variants associated with AMD.

Methods: The influence of genetic variants on genome-wide gene expression was analyzed in harmonized post-mortem liver tissue (n = 588; Strunz et al. Sci Rep. 8:5865, 2018). Multiple combinations of AMD-associated genetic variants were used to generate genetic risk scores (GRS) and gene expression in liver was compared between the respective low and high-risk groups.

Results: We determined 26 genes (eGenes) with a significantly altered expression in high-risk vs. low-risk combinations. Seven of these, namely LIPC, CFHR1, CFHR4, CFHR3, PILRA, PILRB, and TSPAN10 were previously reported to be regulated by single AMD-associated variants in expression quantitative trait locus (eQTL) studies. Nineteen eGenes represent exciting new candidates for AMD etiology. Among the novel candidates, BRCA1 and ASNS show the highest effect sizes (ESs), whereby a high genetic risk for AMD is correlated with a downregulation of BRCA1 (ES = -1.18, SE = 0.21, Q-Value = 1.55×10^{-7}), and an upregulation of ASNS (ES = 1.17, SE = 0.20, Q-Value = 9.36×10^{-8}).

Conclusions: Here we present a novel method combining GRS and eQTL mapping to investigate joint effects of seemingly independent genetic variants on gene expression. We replicated earlier eQTL findings, and report 19 novel genes to correlate with the genetic risk to develop AMD. All genes were exclusively identified by jointly analyzing several AMD-associated variants, which is in-line with the theory that the signals underlying GWAS associations contribute to shared biological mechanisms.

CONTROL ID: 3529522

SUBMITTER (NAME ONLY): Ravid Ben-Avi

TITLE: The Prevalence of Cystoid Macular Edema in Children with Retinitis Pigmentosa and Leber Congenital Amaurosis

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ben-Avi, A. Rivera, K. Hendler, D. Sharon, E. Banin, C. Yahalom, Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: Cystoid macular edema (CME) is a common complication in retinitis pigmentosa (RP) and Leber congenital amaurosis (LCA) patients, with a reported prevalence of 11-50% in adults. However, CME prevalence in the pediatric RP population has not been addressed. The aim of our study was to assess the prevalence of CME in pediatric RP/LCA patients detected by optical coherence tomography (OCT).

Methods: Medical records of children up to age 18 with a diagnosis of RP/LCA were reviewed retrospectively; only those who performed an OCT scan were included in the study. Diagnosis was based on history of poor vision since birth, nyctalopia, visual field constriction, characteristic fundus findings on clinical examination or electroretinogram (ERG), and/or genetic testing. OCT images were reviewed and assessed for macular cystic changes. Patients with more than one hyporeflective cystic macular space with well-defined boundaries were included.

Results: Of the 51 children (age 4-18 years, mean 10.8±4.0) diagnosed with RP, 16 had CME (31.3%) diagnosed by OCT, 14/16 (87.5%) had bilateral CME and 2 patients (12.5%) had unilateral CME. Among children with CME, 8 had an identified causative gene; among them 7/8 (87.5%) were inherited in an autosomal recessive fashion and 3/8 (37.5%) children had biallelic CRB1 mutations. CME was treated in 11/16 children and 4/11 had some improvement; 1/4 had improved vision (one line gain in vision for distance and near) and 3/4 had reduced central foveal thickness with stable vision.

Conclusions: Our results show that as many as one-third of children with RP/LCA will manifest cystic changes on OCT, comparable to the reported prevalence of CME in adults. Since clinical suspicion of cystic retinal lesions is challenging in children, it is necessary to screen these children by OCT to exclude the presence of CME. Early treatment of CME may potentially lead to better visual outcome. Additional long-term research is needed to assess recommended treatment and its efficacy on CME in pediatric RP/LCA patients.

CONTROL ID: 3529550

SUBMITTER (NAME ONLY): Marisa OBrien

TITLE: Correcting Aphakia in Children with Marfan Syndrome: Analysis of Four Strategies

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Correcting aphakia in pediatric eyes that lack capsular support can be a challenge. Reports addressing this issue in children with Marfan Syndrome or the FBN1 mutation have been few. Here we compare safety and efficacy outcomes for 4 different approaches: 1. An iris-enclaved anterior chamber IOL (Artisan-Ophtec, AO IOL); 2. An angle-supported anterior chamber intraocular lens (AC IOL); 3. A trans-scleral sutured IOL (TSS-IOL); and 4. Aphakic (Aph) managed only with spectacles/contact lenses.

Methods: Outcomes were collated for correction of aphakia in 38 patients (68 eyes) with a history of lensectomy-vitreectomy and complete capsulectomy for ectopia lentis. 17 children (30 eyes) were implanted with an AO IOL; 10 (16 eyes) with an ACIOL; 9 (17 eyes) with a TSS-IOL; and 8 (15 eyes) remained Aph. Average follow up was: 3.8 yrs (range 0.5-10 yrs) for the AO IOL group; 5.5 yrs (0.25-15) for AC IOL; 9.6 years (5-15) for TSS-IOL; and 4.9 years (0.5-13) for Aph.

Results: At last follow-up visit, CDVA was better than pre-implantation VA in 90% of AO IOL eyes, 87% of AC IOL eyes and 47% of TSS-IOL eyes. 73% of Aph eyes had a CDVA of ≤ 0.18 logMAR (20/30). Major complications encountered in follow-up were least with the AO IOL and most with the TSS-IOL approach. Complications for each approach were: AO IOL eyes, ocular hypertension (OHT) (10%, 3/30 eyes) and haptic dislocation (3.3%, 1/30); Aph eyes, OHT (13.3%, 3/15) and retinal detachment (6.7%, 1/15); and AC IOL eyes, angle closure (20%, 3/15), OHT (6.7%, 1/15), vitreous hemorrhage (6.7%, 1/15), and retinal detachment (6.7%, 1/15). TSS-IOL complications were more prevalent: haptic suture breakage necessitating re-suturing or explantation (65%, 11/17), iris capture, (24%, 4/17), and retinal detachment (41%, 7/17). Endothelial cell density tended to be lower in TSS-IOL and higher in Aph eyes. Likewise, corneal thickness tended to be lower in Aph and higher in TSS-IOL eyes.

Conclusions: The pediatric eyes with the best longer-term outcomes appear to be those implanted with the AO IOL or those that remain aphakic. TSS-IOL implantation was associated with more complications. On-going follow-up will help clarify CDVA outcomes and the state of corneal health.

CONTROL ID: 3529566

SUBMITTER (NAME ONLY): Robert Linsenmeier

TITLE: Extracellular K^+ as an indicator of retinal energy metabolism

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Linsenmeier, A. Dmitriev, A.V. Dmitriev, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|R.A. Linsenmeier, Neurobiology, Northwestern University, Evanston, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Robert Linsenmeier: Commercial Relationship: Code N (No Commercial Relationship) | Alexander Dmitriev: Commercial Relationship: Code N (No Commercial Relationship) | Andrey Dmitriev: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal neurons spend most of their energy to support the transmembrane movement of ions. Light-induced electrical activity is associated with a redistribution of ions, which affects the energy demand and results in a change in metabolism. Light-induced metabolic changes are expected to be different in distal and proximal retina due to differences in the light responses of different retinal cells. Extracellular K^+ concentration ($[K^+]_o$) is a reliable indicator of local electrophysiological activity, and the purpose of this work was to compare $[K^+]_o$ changes evoked by steady and flickering light in distal and proximal retina.

Methods: Intraretinal recordings were made from isolated mouse (C57Bl/6J) retinæ. Diffuse steady and flickering (1 and 10 Hz) light of scotopic and photopic intensities was applied in both dark- and light-adapted conditions. Double-barreled K^+ -selective microelectrodes were used to record $[K^+]_o$. Simultaneously recorded local ERGs assisted in verification of the electrode position.

Results: In the distal retina, photoreceptor hyperpolarization led to suppression of ion transfer, a decrease in $[K^+]_o$ by 0.3-0.5 mM, reduced energy demand, and, as previously shown in vivo, decreased metabolism. Flickering light had the same effect on $[K^+]_o$ in the distal retina as steady light of equivalent intensity. The conductance and voltage changes in photoreceptor neurons are cell-specific, but the overall effect of steady light in the proximal retina is excitation, which was reflected in a $[K^+]_o$ increase there (maximally 0.2 mM). In steady light the $[K^+]_o$ increase lasts only 1-2 seconds, but a sustained $[K^+]_o$ increase was evoked by flickering light. A squarewave low frequency (1 Hz) flicker of photopic intensity produced the largest increases in $[K^+]_o$.

Conclusions: Judging by measurements of $[K^+]_o$, steady illumination decreased energy metabolism in the distal retina, but not in the proximal retina (except for the first few seconds). Flickering light evoked the same decrease in the distal retina, but also evokes a sustained $[K^+]_o$ increase in the proximal retina, suggesting an increase of metabolic demand there, especially at 1 Hz, when neurons of both on- and off-pathways appear to contribute maximally. This proximal retinal metabolic response to flicker underlies the increase in blood flow during flicker that constitutes neurovascular coupling.

CONTROL ID: 3529582

SUBMITTER (NAME ONLY): Tiffany Huang

TITLE: Comparison of Pressure-Volume Ratios in Diabetic vs. Normal Eyes

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.L. Huang, M.P. Ohr, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|A. Mahmoud, C.J. Roberts, Ophthalmology and Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Tiffany Huang: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Ohr: Commercial Relationship(s);Alimera:Code C (Consultant);Alimera:Code I (Personal Financial Interest) | Ashraf Mahmoud: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Roberts: Commercial Relationship(s);Oculus Optikgeräte GmbH:Code C (Consultant);Ziemer Ophthalmic Systems AG:Code C (Consultant);Optimo Medical:Code C (Consultant)

ABSTRACT BODY:

Purpose: To date, little is known regarding the biomechanical response of the eye to diabetes or the relationship of such changes to clinical retinopathy. In this study, we use static pressure-volume (PV) ratios as a surrogate for ocular rigidity and compare it among subjects with diabetic retinopathy (DR), diabetes without retinopathy (DIA), and controls (NL).

Methods: A total of 240 subjects (475 eyes) were analyzed; 150 NL (n=297 eyes), 45 DIA (n=90 eyes), and 45 DR (n=88 eyes). Intraocular pressure (IOP) was obtained using corneal compensated IOP from Ocular Response Analyzer, Goldmann applanation tonometry, PASCAL dynamic contour tonometer, and Corvis ST. Anterior chamber volume (ACV) was measured using the Pentacam. Four PV ratios were calculated using the IOP obtained from the different methodologies over ACV. PV was correlated to two stiffness parameters (SP) calculated as load over displacement, from undeformed state to first applanation for cornea (SP-A1), and from applanation to highest concavity for sclera (SP-HC) using regression analysis. ANCOVA was performed to compare PV between groups with pachymetry and age as covariates. Significance threshold was $p < 0.05$.

Results: PV ratios were significantly greater in DR compared to DIA and NL using all 4 methods of measuring IOP, with no difference between DIA and NL. For SP-HC, DR was significantly stiffer compared to DIA (< 0.0001) and NL (< 0.0001), with no difference between DIA and NL ($p = 0.19$). No relationship was observed for SP-A1 among the 3 groups. PV ratio had stronger correlation to SP-HC ($R^2 = 0.39$, $p < 0.0001$) than SP-A1 ($R^2 = 0.15$, $p = 0.0002$), with the strongest relationship noted in DR group.

Conclusions: In this report, we used PV ratios as a surrogate for ocular rigidity. Our results showed greater PV ratios in DR than both DIA and NL. Furthermore, there is high correlation between PV ratio and the scleral stiffness parameter. Clinically, the scleral stiffness parameter can be thought of as the entire posterior ocular shell, encompassing structures beyond the sclera including the retina, choroid, and supporting vasculature and connective tissue. Our results suggest eyes with DR have stiffer posterior ocular shell and we are currently investigating potential mechanisms.

CONTROL ID: 3529588

SUBMITTER (NAME ONLY): Zora Marlowe

TITLE: Dose uniformity of loteprednol etabonate (submicron) ophthalmic gel 0.38% compared with prednisolone acetate ophthalmic suspension 1.0%

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z.T. Marlowe, M.J. Coffey, Pharmaceutical Product Development, Bausch + Lomb, Rochester, New York, UNITED STATES|M.E. Cavet, Medical Affairs, Bausch + Lomb, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zora Marlowe: Commercial Relationship(s);Bausch Health US, LLC:Code E (Employment) | Megan Cavet: Commercial Relationship(s);Bausch Health US, LLC:Code E (Employment) | Martin Coffey: Commercial Relationship(s);Bausch Health US, LLC:Code E (Employment)

ABSTRACT BODY:

Purpose: Dose uniformity can be challenging with ophthalmic suspensions since drug particles may settle over time and patients often fail to adequately shake the bottle prior to instillation. Loteprednol etabonate (submicron) ophthalmic gel 0.38% (LE gel 0.38%) is a polycarbophil-based formulation that is a semi-solid at rest to prevent drug particle settling. This study compared dose uniformity of LE gel 0.38% and prednisolone acetate (PA) 1% suspensions under shaken and unshaken simulated in-use conditions.

Methods: One set of 5 mL bottles of LE gel 0.38% and branded and generic PA suspensions was shaken for 5 seconds immediately prior to drop expression at simulated dosing time points over two weeks, whilst a second set of bottles was not shaken prior to drop expression. The dispensing time points followed product label recommendations: LE gel 0.38% was dispensed three times daily (7 AM, 12 PM, and 10 PM, \pm 1 h), while PA suspensions were dispensed four times daily (7 AM, 12 PM, 5 PM and 10 PM, \pm 1 h). The first and last daily dispensed drops were collected and drug concentrations analyzed by high pressure liquid chromatography. Data were expressed as mean \pm SD percent of the declared (labeled) concentration for each drug.

Results: Dispensed drops of LE gel 0.38% showed consistent on-target mean drug concentrations over 2 weeks of dosing whether expressed from shaken ($103.2 \pm 1.3\%$) or unshaken ($103.3 \pm 1.5\%$) bottles. In contrast, while mean drug concentrations for both branded and generic PA suspensions were on-target over 2 weeks of dosing following expression from shaken bottles ($102.2 \pm 1.39\%$ and $98.3 \pm 2.87\%$, respectively), they were highly variable over the two weeks when dispensed from unshaken bottles ($89.2 \pm 18.59\%$ and $78.3 \pm 13.47\%$, respectively). Drug concentrations of dispensed PA drops from unshaken bottles were lowest at the start of the study and were outside of 90-110% of the declared concentration for the majority of dispensed drops over the 2 weeks.

Conclusions: Drops of LE gel 0.38% delivered the declared concentration of LE under both shaken and unshaken simulated in-use conditions whereas drops of PA 1% suspensions were on-target when shaken, but highly variable when the bottles were not shaken. LE gel 0.38% is expected to provide consistent dosing and therefore consistent efficacy over the entire 2 week dosing regimen regardless of shaking.

CONTROL ID: 3529589

SUBMITTER (NAME ONLY): Xuehan Qian

TITLE: The critical period of myopia, insight from the myopic shift in school age children after COVID-19 home confinement

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Qian, Tianjin Medical University Eye Hospital, Tianjin, Tianjin, CHINA|Y. Li, J. Wang, Emory University, Atlanta, Georgia, UNITED STATES|D.C. Musch, Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Time spent in outdoor activities is decreased due to home confinement for the Covid-19 epidemic. Concerns have been raised about whether it may have worsened the burden of myopia due to substantially decreased time spent outdoors and increased screen time at home. The purpose of this study is to investigate the refractive change and prevalence of myopia for school-aged children during the Covid-19 home confinement.

Methods: In this school-based cross-sectional study in 10 elementary schools in Feicheng, China, and a total of 123,535 children aged 6 to 13 years were screened during 6 consecutive years (2015-2020). The Non-cycloplegic photorefractive was examined by Spot photoscreener. The Spherical Equivalent Refraction (SER) was recorded for each child and the prevalence of myopia for each age group in each year was calculated. The mean SER and prevalence of myopia were compared between the year of 2020 (after home confinement) and the previous 5 years for each age group.

Results: A total of 194,904 test results (389,808 eyes) from 123,535 children were included in the analysis. A substantial myopic shift (around -0.3D) was found in the 2020 school-based photoscreenings when compared with previous years (2015-2019) for younger school-aged children aged 6 (-0.32D), 7 (-0.28D), and 8 years (-0.29D). The prevalence of myopia in the 2020 photoscreenings was much higher than the highest prevalence of myopia within years of 2015-2019 for children at age of 6 (21.5% vs 5.7%), 7 (26.2% vs 16.2%), and 8 (37.2% vs 27.7%). The differences in SER and prevalence of myopia between 2020 and previous years were minimal in children aged 9-13 years.

Conclusions: Covid-19 home confinement was associated with a significant myopic shift for younger children (aged 6-8 years) according to the 2020 school-based photoscreenings. Younger children's refractive status may be more sensitive to environmental changes than older ages, given they are in a critical period for the development of myopia.

CONTROL ID: 3529593

SUBMITTER (NAME ONLY): Weilin Song

TITLE: A two-step model of PVL and ROP

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Song, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|W. Song, G. Hoppe, D. Hanna, J.E. Sears, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although both the retina and the brain are central nervous system tissues, pathology of each created by preterm birth is ascribed different etiologies. Retinopathy of prematurity (ROP) is created by a two-step mechanism of oxygen induced retinovascular growth attenuation and vasoobliteration (phase 1) followed by ischemic hypoxia and pathological angiogenesis (phase 2). However, the current hypothesis of the etiology of periventricular leukomalacia (PVL) relies on hypoxic ischemia alone that drives inflammation and hypomyelination. We have noted a similar metabolic response of brain cortical astrocytes and retinal Müller cells during hyperoxia, which stimulated the idea that the pathogenesis of PVL may resemble the two-step origin of ROP. In this study, we have developed a murine PVL model to correlate retinal and brain pathology using phase 1 hyperoxia and phase 2 relative hypoxia.

Methods: C57BL/6J pups and their nursing dam were placed into 80% oxygen from P4-P8, control pups from the same litter were placed with a second nursing dam. Dams were switched every 24 hours. Brains and retinas were dissected at P8 and P11. Brain tissue was processed for immunofluorescence staining (MBP, lectin, GFAP, Caspase 3) and western blots (CD31, HIF-1a). Retinal vasculature was revealed by lectin staining. Immunofluorescent images of brain and retina were analyzed with ImageJ and AngioTool. Statistical analysis was performed by comparing means using Student's t-test.

Results: Mice in the hyperoxia group demonstrated hypomyelination and increased apoptosis in periventricular zones at P8 and P11. Astrocytes demonstrated decreased GFAP expression at P8 compared to normoxic controls but increased expression at P11, consistent with PVL. Hyperoxic mice also had decreased cerebral capillary density on the roof of the lateral ventricles with decreased CD31 and HIF-1a expression. Retinal vasculature contemporaneously revealed vaso-obliteration at P8.

Conclusions: A two-step model of PVL using hyperoxia followed by relative hypoxia results in hypomyelination, decreased cerebral capillary density, and downregulation of HIF-1a. These findings support the hypothesis that hyperoxia results in dysregulation of periventricular vasculature development and hypomyelination and provides an experimental correlate of PVL.

CONTROL ID: 3529601

SUBMITTER (NAME ONLY): Megan Cavet

TITLE: Occurrence of steroid-associated adverse events with loteprednol etabonate formulations

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Cavet, H.H. DeCory, Medical Affairs, Bausch + Lomb, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Megan Cavet: Commercial Relationship(s);Bausch Health US, LLC:Code E (Employment) | Heleen DeCory: Commercial Relationship(s);Bausch Health US, LLC:Code E (Employment)

ABSTRACT BODY:

Purpose: Use of topical corticosteroids (CSs) to treat ocular inflammation may be limited by CS class-associated adverse events (AEs) including intraocular pressure (IOP) increase, glaucoma, cataracts, delayed healing, and infections. Loteprednol etabonate (LE) is a topical ophthalmic CS which undergoes rapid metabolism following exertion of its anti-inflammatory effect and therefore has a low propensity for eliciting AEs. A next generation LE formulation (LE SM gel 0.38%) with reduced (submicron-sized) drug particles and improved ocular penetration was introduced in early 2019. We report on occurrence of ocular CS class-associated AEs for this and other LE ophthalmic formulations.

Methods: The Bausch + Lomb pharmacovigilance (PV) AE database system (ARISGlobal[®]) was queried for all CS class-associated AEs (spontaneous, study, literature) reported in the US for LE ophthalmic formulations since development and launch of the first LE suspensions in the late 1990s through September 2020. The following formulations were included in the analysis: LE 0.5% and 0.2% suspensions, LE 0.5% and tobramycin 0.3% suspension, LE 0.5% ointment, LE 0.5% gel, and LE SM 0.38% gel. Throughout the reporting period, AEs were entered into the PV database using preferred MedDRA terms.

Results: Corticosteroid-associated AEs for LE SM 0.38% gel were infrequent, with 8 reports of IOP increase, 2 reports of cataract, and 1 reported eye infection. Across all LE formulations, there were a total of 19 reports of cataract, 131 reports of IOP increase, 19 reports of glaucoma or ocular hypertension, 8 reports of impaired healing, and 56 reports of ocular infections. Most AEs were categorized as non-serious, with the exception of several reports of glaucoma and cataract. During this reporting period, nearly 67 million units were shipped for these products in the US.

Conclusions: Corticosteroid class-associated AEs were reported infrequently in the PV AE database for all LE formulations, including for the recently introduced LE SM 0.38% gel formulation, suggestive of a very low incidence rate for these AEs with LE treatment. Data limitations include possible underreporting of AEs due to the voluntary nature of the reporting and uncertainty as to whether the AE was causally related to LE treatment.

CONTROL ID: 3529603

SUBMITTER (NAME ONLY): Nathaniel Hafford-Tear

TITLE: Investigation of transcriptional dysregulation events driving Posterior Polymorphous Corneal Dystrophy type 1

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Dudakova, P. Liskova, Research Unit for Rare Diseases, Department of Pediatrics and Inherited Metabolic Diseases, First Faculty of Medicine, Charles University and General University Hospital, Prague, CZECHIA|N. Hafford-Tear, S.J. Tuft, A.N. Sadan, N. Bhattacharyya, C. Zarouchlioti, A.J. Hardcastle, A.E. Davidson, University College London Institute of Ophthalmology, London, UNITED KINGDOM|S.J. Tuft, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|P. Liskova, Department of Ophthalmology, First Faculty of Medicine, Charles University and General University Hospital in Prague, Prague, CZECHIA|

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ABSTRACT BODY:

Purpose: Posterior Polymorphous Corneal Dystrophy (PPCD) is associated with a dysregulated cell state, induced by mutations that alter the levels of epithelial mesenchymal transition (EMT)-regulating transcription factors ZEB1, GRHL2 or OVOL2. Here we investigate the transcriptomic signature of dysregulation in PPCD type 1 (PPCD1) corneal endothelial cells (CECs) to identify biomarkers of the disease mechanism as potential therapeutic targets.

Methods: We cultured primary CECs from five individuals affected with PPCD1 and seven controls. All PPCD1 individuals were confirmed to harbour the same regulatory mutation in the OVOL2 promoter (NM_021220:c.-370T>C), previously hypothesised to lead to ectopic expression of OVOL2 within the corneal endothelium. Total RNA was extracted from each primary culture using NucleoSpin RNA XS isolation kit (Macherey Nagel). We enriched mRNA using oligo(dT) beads and paired-end Illumina RNA sequencing was performed using a stranded library preparation. Transcriptomic analysis was performed using DESeq2, rMATS and IsoformSwitchAnalyzeR programs to investigate differential gene expression and splicing events in PPCD1 CECs compared to control CECs.

Results: Utilizing the EMT Gene Database, 279 EMT-associated genes were found to be highly dysregulated (false discovery rate (FDR) corrected p-value <.05; Log-2 fold change > 1) in PPCD1 including CDH1, OVOL2, GRHL2, GATA6, members of the mir200 family, numerous keratins, and the epithelial splice regulator ESRP1. Alternative splicing was further identified for ESRP1 targets, CD44 and FGFR2.

Conclusions: Our study confirms the aberrant upregulation of OVOL2 in PPCD1 and suggests that EMT-associated genes and pathways are significantly disrupted in PPCD1 CECs. Our data suggests that overexpression of the epithelial cell type-specific splicing regulator, ESRP1, induces aberrant splicing of CD44 and FGFR2. We hypothesise that this mechanism contributes to the 'epithelialisation' of the corneal endothelium observed in PPCD1 and may act as a target for future therapeutic interventions.

CONTROL ID: 3529635

SUBMITTER (NAME ONLY): Nicholas Russell

TITLE: Optic disc drusen prevalence in the retinitis pigmentosa population

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Russell, C. Fraser, J.R. Grigg, Sydney Hospital and Sydney Eye Hospital, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure (Abstract): Nicholas Russell: Commercial Relationship: Code N (No Commercial Relationship) | Clare Fraser: Commercial Relationship: Code N (No Commercial Relationship) | John Grigg: Commercial Relationship(s);Novartis:Code C (Consultant)

ABSTRACT BODY:

Purpose: Optic disc drusen (ODD) are acellular benign deposits originally reported to occur in 0.3-0.5% of the normal population. More modern studies of the normal population involving histopathology and improved imaging put the prevalence of ODD at 1.8-2.4%. ODD are understood to be associated with retinitis pigmentosa (RP) and the prevalence of ODD in individuals with RP is reported to range from 3-80%. The higher rates within this range however, of 80% (4/5 individuals) and 38% (9/24 individuals), were identified in small populations with the less common RP subtype of preserved para-arteriole RPE and more recent population studies have shown rates of 2.95-3.6%. Usher's syndrome is also associated with elevated rates of ODD ranging from 7.6-35% depending on the subtype of Usher's syndrome. Visible ODD may be identified on fundoscopic examination, whereas ultrasonography, OCT or autofluorescence may assist in identifying buried ODD. This retrospective study was undertaken to further investigate the prevalence of ODD using imaging techniques in an RP population.

Methods: A database of electrophysiologically confirmed RP patients (N=195) was retrospectively examined and fundus photography, autofluorescence and OCT images were assessed in each patient for signs of ODD. Two clinicians examined fundus photographs for changes consistent with ODD. Genetic testing results were not available for all patients but were included when possible.

Results: The prevalence of ODD was 3.1% (N=6) with 2 patients having bilateral ODD. Three of these cases were X-linked with an identified RPGR gene and three cases did not have genetic testing completed. A total of 11 patients with confirmed Usher's syndrome and 4 patients with suspected Usher's syndrome were examined with no patients demonstrating ODD. No individuals in this population had preserved para-arteriole RPE RP.

Conclusions: Our results are consistent with the lower range of reported ODD prevalence. These results are more in keeping with the normal population prevalence of ODD within an RP population. The variation in results may be explained by particular subtypes of RP having stronger genetic associations with ODD. The link with RPGR is worth further investigation.

CONTROL ID: 3529648

SUBMITTER (NAME ONLY): Austin Igelman

TITLE: Effect of pupil dilation on dark adapted perimetry using an Octopus 900 perimeter

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Igelman, C.A. Ku, M.M. da Palma, P. Yang, M.E. Pennesi, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.M. da Palma, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Pupil dilation is often performed before patients undergo dark adapted perimetry testing. We tested the hypothesis that the mean of the average sensitivity differs based on dilation status in individuals without retinal pathology.

Methods: 15 healthy adults (9 female) ages 23-63 without retinal pathology underwent a 45-minute dark adaptation period followed by sequential undilated and dilated two color perimetry testing of the left eye. 14 (8 female) ages 23-63 of these adults also underwent repeat undilated testing using the same protocol on a separate day to evaluate intervisit variability. A modified Octopus 900 perimeter utilizing size III Goldman targets with a 500nm (blue) or 650nm (red) filter were used. The mean differences in average sensitivity were compared using two-sided paired t-tests.

Results: The average sensitivity to the red stimulus was 26.68dB (SD: 2.43dB) under undilated conditions and 27.31dB (SD: 1.79dB) under dilated conditions. The mean difference in the average sensitivity between the undilated and dilated conditions using the red stimulus was -0.63dB (SD: 1.40dB; 95% CI: [-1.40dB, 0.14dB]; $p = 0.102$). The average sensitivity to the blue stimulus was 41.84dB (0.87dB) for the undilated condition and 41.75dB (SD: 1.00) for the dilated condition. The mean difference in the average sensitivity between the undilated and dilated conditions using the blue stimulus was 0.09dB (SD: 0.57dB; 95% CI: [-0.23dB, 0.40dB]; $p = 0.557$). The mean difference in the average sensitivity between the initial and subsequent undilated test using the red stimulus and blue stimulus was -0.63dB (SD: 1.01dB; 95%CI: [-1.22db, -0.05dB]; $p = 0.036$) and -0.14dB (SD: 0.66dB; 95%CI: [-0.52dB, 0.24dB]; $p = 0.451$) respectively.

Conclusions: These findings show no statistically significant difference in the mean of the average sensitivity to red or blue stimuli under scotopic conditions based on dilation status. The intervisit variability was similar to that observed between the same day undilated and dilated conditions. Finally, the absolute value of the 95%CI's for all mean differences was <1.5dB were suggesting that dilation may not have a clinically meaningful effect on the average sensitivity to red or blue stimuli under scotopic conditions in patients without retinal pathology.

CONTROL ID: 3529656

SUBMITTER (NAME ONLY): Zi Zhen (Ginny) Liu

TITLE: MMP9 differentially regulates proteins involved in actin polymerization and cell migration during EMT of lens epithelial cells

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Liu, A. Taiyab, J.A. West-Mays, Pathology and Molecular Medicine, McMaster University Faculty of Health Sciences, Hamilton, Ontario, CANADA|

Commercial Relationships Disclosure (Abstract): Zi Zhen (Ginny) Liu: Commercial Relationship: Code N (No Commercial Relationship) | Aftab Taiyab: Commercial Relationship: Code N (No Commercial Relationship) | Judith West-Mays: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Posterior capsular opacification and anterior subcapsular cataract are attributed to transforming growth factor- β (TGF β) induced epithelial-to-mesenchymal transition (EMT) of lens epithelial cells (LECs). Previous studies from our lab have identified matrix metalloproteinase-9 (MMP9) as a potential regulator of cytoskeletal reorganization during EMT of LECs. Here, we studied the effect of MMP9 inhibition on TGF β activation of proteins involved in actin reorganization and cell migration.

Methods: A NanoString gene expression analysis was performed on LEC explants from 1.5-2 month-old wild-type (WT) mice, transgenic mice overexpressing TGF β in the lens (TG^{tg}) or TG^{tg} mice on a MMP9 knockout background (TG^{tg}:MMP9KO). A cytoskeletal protein array was conducted using similar samples as above. For validation, rat LEC explants were obtained from 17-19 days old Wistar rat pups, and a novel MMP9-specific inhibitor, JNJ0966, was used. These explants were either treated with <5% dimethyl sulfoxide (Rat^D), 6ng TGF β (Rat^{TG}), 20 μ M JNJ0966 (Rat^{JNJ}) for 48 hrs or pretreated with 20 μ M JNJ0966 for 2 hours followed by 6ng TGF β for 48 hours (Rat^{TG:JNJ}). Immunofluorescence and Western Blot analyses were performed using antibodies specific to proteins identified from the protein array and imaged for analysis.

Results: Gene expression analyses revealed significant decreases in alpha-smooth muscle actin (α SMA)(p<0.01) and F-actin formation (p<0.01) in TG^{tg}:MMP9KO LECs when compared to TG^{tg} LECs. Furthermore, the protein array identified fold changes of 0.41 for cortactin, 0.93 for phosphorylated lim-kinase 1 (LIMK1) and 0.64 for phosphorylated focal adhesion kinase (FAK) in TG^{tg}:MMP9KO LECs when compared to TG^{tg} LECs. Rat^{TG:JNJ} explants showed cortical staining of E-cadherin and minimal staining of α SMA polymerization when compared to Rat^{TG} explants. Immunofluorescence and Western Blot analyses further revealed a marked decrease in phosphorylated FAK (Y397) and LIMK1 (T508) in Rat^{TG:JNJ} explants when compared to Rat^{TG} explants.

Conclusions: The protein array and its validation indicate that MMP9 deficiency results in lowered levels of activated LIMK1 and FAK, proteins known to be involved in TGF β -induced actin polymerization and cell migration. Further analyses should be performed to understand the mechanism by which MMP9 regulates the activity of these proteins during TGF β -induced EMT.

CONTROL ID: 3529660

SUBMITTER (NAME ONLY): Nick Di Girolamo

TITLE: Inducing dry eye disease using a custom engineered desiccation system: impact on the ocular surface including keratin-14-positive limbal epithelial stem cells

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Di Girolamo, R. Zhang, E. Pandzic, M. Park, D. Wakefield, Medical Sciences, University of New South Wales Faculty of Medicine, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) is characterized by loss of tear-film stability. Currently, desiccation stress (DS) is the predominant means for inducing DED in mice, however its effect on limbal epithelial stem cells (LESCs) has been overlooked. This study aimed to establish a DS model of DED using our in-house system to investigate the impact on the ocular surface including LESCs.

Methods: A mouse transporter unit was customized to generate a dehumidified environment in an isolated room. C57BL/6j mice were exposed to mild DS or remained untreated (UT) in our vivarium for 10 consecutive days (n=28/group). Clinical assessments included phenol red tear-thread, fluorescein staining and optical coherence tomography (OCT). Histopathology and immunofluorescence was used to evaluate tissue architecture, goblet cell (GC) status, lacrimal gland (LG) inflammation and ocular surface phenotype. Whole flat-mounted corneas were immunostained for K14, imaged by confocal microscopy and analyzed to investigate the effect of DS on LESCs.

Results: Modifications made to the animal transporter unit resulted in decreased relative humidity (RH) in cages ($43.5 \pm 4.79\%$) compared to those in the vivarium ($53.9 \pm 1.8\%$, $p=0.0243$). Under these conditions, tear production was suppressed whilst corneal permeability and corneal irregularity significantly increased. H&E staining indicated that basal corneal epithelia were stressed and increased desquamation. However, no major change in corneal thickness was detected using OCT. DS-exposed mice had reduced GC density (41.0 ± 5.10 GC/mm vs 46.9 ± 3.88 GC/mm, $p=0.0482$) and their LGs had elevated $CD4^{+}$ T-cells compared to controls. DS also elicited $K14^{+}$ epithelial cell displacement, as indicated by increased normalized fluorescence signal distanced 50-100 μm radially inwards from the limbus [$0.63 \pm 0.053\%$ (DS) vs $0.54 \pm 0.060\%$ (UT), $p=0.0317$].

Conclusions: Mild DS applied to C57BL/6 mice using a customized system generated features of DED. Following DS, ocular surface epithelial cell health decreased and LESCs appeared stressed. This suggests that downstream effects of DS on corneal homeostasis are present. The method used to induce DED in this study enables a chronic model to be developed which more closely resembles the clinical situation.

CONTROL ID: 3529662

SUBMITTER (NAME ONLY): Bingyi Wang

TITLE: Subretinal monopolar photovoltaic arrays provide pixel size-independent stimulation threshold and 40µm resolution under spatiotemporal modulation

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: High visual acuity in prosthetic vision requires effective stimulation by small pixels with little crosstalk. However, due to shallow penetration of the field with planar bipolar pixels, retinal stimulation threshold exceeds the safe charge injection limit with pixels under 40µm. To bypass such limitation, we developed arrays with deep-penetrating field and investigated their stimulation threshold and acuity in vivo.

Methods: The 1.5mm-wide hexagonal arrays of monopolar photovoltaic pixels of 20 or 40µm in size, having a common return electrode at the edge, were produced with and without 25µm tall walls surrounding each pixel. To reduce the crosstalk, the nearby pixels were converted into transient local returns by spatiotemporal modulation of their conductivity. Following subretinal implantation in rats with degenerate retina (RCS), visually evoked potentials (VEP) were recorded in response to pulsed NIR (880 nm) activation of the implants. The full-field stimulation threshold was measured with 10ms pulses at 2Hz, while acuity was measured using gratings alternating at 2Hz, under 4ms stimulation applied either at 64Hz or multiplexed into 4 sub-frames at 256Hz.

Results: The full-field stimulation threshold was $0.057 \pm 0.029 \text{ mW/mm}^2$, corresponding to a current density of 0.092 mA/mm^2 on the active electrodes, independent of pixel size and presence of the walls. This is nearly 30 times lower than that with bipolar pixels of 40µm in size. On the day of implantation, VEP amplitude typically exceeds 100µV, but it dropped to tens of µV one week later, and gradually recovered back to the initial level within 8 weeks post-op. Grating acuity matched the pixel size in 40µm arrays.

Conclusions: Photovoltaic prostheses with nearly-vertical electric field in the retina demonstrated stimulation thresholds independent of pixel size, and much lower than those with bipolar pixels. Using optical spatiotemporal modulation of the photodiode conductivity, any subset of pixels can be converted into transient local returns, thereby providing field confinement necessary for high resolution. Presence of the vertical walls did not negatively affect the retinal excitability, paving the way to honeycomb implants with local returns. Resolution of 40µm corresponds to acuity of 20/160, exceeding the threshold of legal blindness in US. Acuity studies with 20µm pixels are in progress.

CONTROL ID: 3529670

SUBMITTER (NAME ONLY): Kendall Higgins

TITLE: Identification of Candidate Ciliopathy Genes Relevant to Childhood Blindness Syndromes by Genome-wide Screening of Knockout Mice

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Higgins, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B. Moore, L. Lanoue, D. Clary, K. Lloyd, William R. Pritchard Veterinary Medical Teaching Hospital, University of California Davis School of Veterinary Medicine, University of California Davis School of Veterinary Medicine, Davis, CA, US, academic/vet, Davis, California, UNITED STATES|D. Clary, K. Lloyd, Department of Surgery, UC Davis School of Medicine, Sacramento, California, UNITED STATES|C. McKerlie, L. Nutter, The Hospital for Sick Children, Toronto, Ontario, CANADA|C. McKerlie, Department of Laboratory Medicine & Pathobiology, University of Toronto Faculty of Medicine, Toronto, Ontario, CANADA|H. Adissu, Covance Inc, Chantilly, Virginia, UNITED STATES|Z. Berberovic, M. Eskandarian, A. Flenniken, S. Newbigging, L. Nutter, The Centre for Phenogenomics, Toronto, Ontario, CANADA|Z. Berberovic, M. Eskandarian, A. Flenniken, S. Newbigging, Lunenfeld-Tanenbaum Research Institute, Toronto, Ontario, CANADA|A. Moshiri, Department of Ophthalmology & Vision Science, UC Davis School of Medicine, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We aimed to identify candidate Mendelian ciliopathy genes relevant to childhood blindness syndromes by enriching all single gene homozygote or heterozygote knockout mouse strains produced by the International Mouse Phenotyping Consortium (IMPC) with abnormal ocular phenotypes with multiple abnormal phenotypes commonly found in human ciliopathy syndromes.

Methods: We enriched the set of knocked out genes with abnormal ocular phenotypes with the genes of knockout strains with concomitant abnormalities in renal function, renal morphology, reproductive tract function, and reproductive tract morphology. The resulting set of enriched genes were then analyzed for predicted protein-protein interactions with known cilia proteins resulting in a list of "candidate ciliopathy genes". We then assessed these genes for novel association with disease by systematic literature review. From this analysis, thirty-two ciliopathy candidates were predicted to interact with known ciliopathy genes, either directly or through a secondary intermediate protein.

Results: Seven of the 32 genes have been previously identified as ciliopathy genes in non-human vertebrates, and one of these has been shown to function in human cilia. Therefore, we identified 31 novel human ciliopathy genes and 25 novel vertebrate genes with predicted roles in ciliary pathobiology. Representative histological and morphological evidence of phenotypes consistent with ciliopathies are presented from several of these ciliopathy candidates; Abi2, Wdr62, Ap4e1, Dync1li1, and Prkab1.

Conclusions: Here we present targeted deletions of 32 candidate ciliopathy genes identified by phenotyping of knockout mice, predictive bioinformatic analysis, and systematic literature review. These putative ciliopathy genes may be responsible for human syndromes including childhood blindness. Furthermore, these knockout strains are available to serve as models to test novel pre-clinical preventative or therapeutic strategies.

CONTROL ID: 3529672

SUBMITTER (NAME ONLY): Ryan Meshkin

TITLE: Effectiveness of a Telemedicine Program for Diagnosis and Triage of Common Ophthalmic Chief Complaints

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Meshkin, G.W. Armstrong, A.C. Lorch, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|R.S. Meshkin, G.W. Armstrong, N. Hall, A.C. Lorch, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The growing need for cost-effective, accessible ophthalmic care has led to an interest in telemedicine. The capabilities of telemedicine for diagnosis and triage of emergent eye complaints warrants investigation. This study assesses the utility of a tele-ophthalmology program to diagnose and triage common ophthalmic complaints presenting to an ophthalmic emergency room.

Methods: Prospective, observational study of 258 eyes of 129 patients presenting to the Massachusetts Eye and Ear Infirmary Emergency Ward (MEE EW) completed a questionnaire to gather chief complaint, history of present illness, and medical history. Anterior segment photographs with and without fluorescein dye were collected via iPhone 5C camera and posterior segment photos by a Canon non-mydratic fundus camera. Ophthalmic vital signs were collected by MEE EW physicians. All information was reviewed remotely by three MEE physicians; a diagnosis and urgency designation was recorded. Remote findings were compared to in-person clinical findings, which were treated as the gold standard. Primary outcomes included sensitivity and specificity of triage status and diagnostic accuracy via virtual examination of patients with common ophthalmic complaints: eye pain, eye redness, blurry vision, eyelid complaint. The study was not powered for subgroup analysis.

Results: 129 patients were recruited, of which 69 (53.50%) were female with mean age 56 (range 23-96). Sensitivities and specificities for telemedical triage were as follows: eye pain (n=56; sens: 0.58, CI [0.41, 0.74]; spec: 0.91, CI [0.80, 1]), eye redness (n=54; 0.68, CI [0.50, 0.86]; 0.93, CI [0.84, 1]), blurry vision (n=68; 0.73, CI [0.60, 0.86]; 0.91, CI [0.80, 1]), and eyelid complaints (n=42; 0.67, CI [0.43, 0.91]; 0.96, CI [0.89, 1]). The remote diagnostic accuracies, as stratified by chief complaint, were eye pain (27/56; 48.21%), eye redness: (32/54; 59.26%), blurry vision: (30/68; 44.11%), eyelid (24/42; 57.14%).

Conclusions: Telemedical examination of emergent ophthalmic complaints consisting of a patient questionnaire, anterior segment and fundus photos, and ophthalmic vital signs, may be able to reliably triage eye disease based on presenting complaint. Further research is needed to evaluate the diagnostic accuracy of ophthalmic telemedicine for specific ophthalmic conditions in larger pilot studies of patients with emergent eye complaints.

CONTROL ID: 3529677

SUBMITTER (NAME ONLY): John Wells

TITLE: Efficacy, durability, and safety of faricimab in diabetic macular edema (DME): one-year results from the phase 3 YOSEMITE and RHINE trials

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Data from the phase 2 BOULEVARD trial and preclinical models suggest that dual inhibition of the angiopoietin-2 and VEGF-A pathways with faricimab, the first bispecific antibody designed for intraocular use, may reduce inflammation and vascular leakage, promote vascular stability, and improve outcomes beyond anti-VEGF monotherapy for DME. The phase 3 YOSEMITE and RHINE trials were designed to compare the efficacy, durability, and safety of faricimab with aflibercept in patients with DME.

Methods: YOSEMITE (NCT03622580) and RHINE (NCT03622593) are identical, randomized, double-masked, active comparator-controlled, 100-week, phase 3 trials of faricimab in treatment-naïve and previously anti-VEGF-treated patients with center-involving DME. Patients were randomized 1:1:1 to faricimab 6.0 mg every 8 weeks (Q8W) after 6 initial Q4W doses; faricimab 6.0 mg per personalized treatment interval (PTI) after 4 initial Q4W doses; or aflibercept 2.0 mg Q8W after 5 initial Q4W doses. The PTI algorithm is a protocol-driven regimen based on the treat-and-extend concept, using prespecified BCVA and CST criteria to adjust treatment intervals at active dosing visits. Noninferiority, followed by superiority in treatment-naïve patients and then the overall population, was assessed separately for each

faricimab arm against aflibercept. The primary efficacy endpoint was mean change in BCVA from baseline averaged over weeks 48, 52, and 56. A key secondary endpoint was the proportion of patients with ≥ 2 -step ETDRS-DRSS improvement from baseline; other endpoints included the proportion of patients gaining ≥ 15 ETDRS letters from baseline, change in CST from baseline, and the proportion of patients in the PTI arm on Q4W, Q8W, Q12W, or Q16W dosing at 1 year. Safety was assessed by the incidence and severity of ocular and nonocular adverse events.

Results: In BOULEVARD, faricimab Q4W demonstrated superior vision gains and greater improvements in diabetic retinopathy severity at week 24, and showed potential for extended durability in a 16-week off-treatment observation period, when compared with ranibizumab Q4W. YOSEMITE and RHINE are ongoing trials, with year 1 results to be presented at the meeting.

Conclusions: YOSEMITE and RHINE evaluate the efficacy, durability, and safety of faricimab Q8W or per PTI, a protocol-driven regimen based on treat-and-extend, in patients with DME.

CONTROL ID: 3529705

SUBMITTER (NAME ONLY): Daniela RODRIGUES-BRAZ

TITLE: Anti-angiogenic, anti-inflammatory, and anti-edematous effects of mineralocorticoid receptor antagonism in a rat model of corneal neovascularization

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. RODRIGUES-BRAZ, C. Bonnet, M. Zhao, F.F. Behar-Cohen, Team 17, Inserm UMRS1138, Centre de Recherche des Cordeliers, Paris, FRANCE|F.F. Behar-Cohen, Ophtalmopole, Assistance publique - Hopitaux de paris, Hopital Cochin, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Corneal neovascularization (CNV) is a major cause of blindness worldwide. Topical steroids are widely used to treat CNV, but the results are highly variable. Glucocorticoids act through binding to both glucocorticoid (GR) and mineralocorticoid receptors (MR). MR overactivation contributes to retinal and choroidal neovascularization, and endothelial MR invalidation reduces CNV in mice. We thus aimed to evaluate the pharmacological effects of MR antagonism in CNV.

Methods: CNV was induced in one eye of Lewis rats by a 360° circumference total corneal de-epithelialization and limbal scratching. Rats were injected subcutaneously with MR antagonist (MRA) spironolactone 25mg/kg/day or vehicle for 14 days. Corneal morphology and thickness were assessed in vivo at day 3, 7 and 14 using Micron III optical coherence tomography (OCT). Corneal re-epithelialization was evaluated by fluorescein staining under slit lamp at day 3 and 7. Fluorescein (FA) and indocyanine green angiographies (ICG) were performed at day 14 to evaluate the surface of CNV. Rats were sacrificed at day 16 and eyes removed for immunostaining of ED1, IBA1 and GSI-B4. Peripheral cornea and tissues adjacent to limbus were also dissected at day 3 and day 7 for quantitative PCR and transcriptomic analysis. A more specific MRA eplerenone (200mg/kg/day in chew for 14 days) was also used to confirm the effect of MR antagonism.

Results: Spironolactone significantly reduced the CNV and corneal thickness compared to vehicle. There is no difference in corneal re-epithelialization between spironolactone and vehicle. Spironolactone reduced infiltration of ED1 and IBA1 positive inflammatory cells and decreased the isolectin-positive neovascular surface in the cornea. The transcriptomic signatures showed 212 differentially expressed genes (26 up-regulated and 186 down-regulated) involved in corneal wound healing and differentiation, infectious responses, inflammatory and immune responses, myogenesis and hypoxia. The qPCR showed an up-regulation of GR in spironolactone treated group tilting the GR/MR balance in favor of GR pathway. Eplerenone confirmed the anti-angiogenic effect of MRA.

Conclusions: MRA is anti-angiogenic, anti-inflammatory, and anti-edematous in rat CNV. The potential additive effect of MRA and glucocorticoids on CNV will be further tested.

CONTROL ID: 3529736

SUBMITTER (NAME ONLY): Samuel Han

TITLE: Risk factors for optical coherence tomography-assessed center-involving diabetic macular edema in a South Indian population

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Han, A. Li, W. Chan, G. Susarla, I. Lains, L. Sobrin, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|R. A N, R. Khan, V. Khetan, R. Raman, S. Mathavan, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|K. Brustoski, S.K. Iyengar, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the risk factors for center-involving diabetic macular edema (ciDME) and increased central subfield thickness (CST) assessed by optical coherence tomography (OCT) in South Indian patients with type 2 diabetes (T2D).

Methods: For this cross-sectional analysis, patients with T2D were recruited prospectively at Sankara Nethralaya Main Hospital in Chennai, South India. Both eyes of each patient were imaged with color fundus photographs (Daytona Plus Panoramic Ophthalmoscope – P200T, Optos), which were graded for presence or absence of clinically significant macular edema (CSME), and structural OCT (Cirrus HD-OCT, Model 5000). Exclusion criteria included having significant ocular disease that prevented obtaining gradable images. Demographic and clinical data were recorded. Blood was drawn for lipid, hemoglobin A1c, and genetic testing, and a urine sample was taken to measure albuminuria. CSTs were recorded from OCT retinal thickness maps of both eyes, and only the eye with the higher CST for each patient was used for analyses. ciDME was defined as being present if CST was $\geq 290 \mu\text{m}$ in women and CST was $\geq 305 \mu\text{m}$ in men. Scans demonstrating other macular pathology that could influence CST such as epiretinal membrane were excluded. Multivariate analyses were done using stepwise logistic regression to assess the effect of covariates on ciDME and CST.

Results: Of participants with gradable OCT scans (N=483), 88 had ciDME and 395 had no ciDME. The concordance between OCT assessment of ciDME and fundus photograph assessment of CSME was 89.6%. In multivariate regression with imputation, participants with ciDME were more likely to be younger, men, have a longer duration of diabetes, lower triglycerides and have albuminuria ($p < 0.028$ for all comparisons). Examining CST as a continuous outcome in multivariate regression, it was found that a higher CST was associated with male sex ($p = 1.22 \times 10^{-5}$) and albuminuria ($p = 1.09 \times 10^{-3}$).

Conclusions: OCT analysis quantitates and refines risk factors for DME, and validates observations from previous studies that have assessed DME by fundus photography alone. By clearly assessing the demographic and clinical risk factors for DME, it will be possible to better identify genes associated with the disease through ongoing genetic analyses of the collected DNA samples from these patients.

CONTROL ID: 3529784

SUBMITTER (NAME ONLY): Danial Roshandel

TITLE: Natural history of PRPF31-associated retinopathy: multimodal imaging findings

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Roshandel, R.C. Heath Jeffery, D. Zhang, T.M. Lamey, T.L. McLaren, J.N. De Roach, S. McLaren, D.A. Mackey, F.K. Chen, Centre for Ophthalmology and Visual Science, The University of Western Australia Faculty of Health and Medical Sciences, Perth, Western Australia, AUSTRALIA|D. Roshandel, R.C. Heath Jeffery, D. Zhang, S. McLaren, F.K. Chen, Ocular Tissue Engineering Laboratory, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|J.A. Thompson, T.M. Lamey, T.L. McLaren, J.N. De Roach, D.A. Mackey, Australian Inherited Retinal Disease Registry and DNA Bank, Department of Medical Technology and Physics, Sir Charles Gairdner Hospital, Nedlands, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: PRPF31-associated retinopathy (RP11, OMIM: #600138) is a common form of autosomal dominant retinitis pigmentosa (adRP). RP11 exhibits extreme variation in phenotype, ranging from non-penetrance to severe early-onset RP. Herein, we report four patterns of RP11 natural history in seven unrelated families in a prospective cohort study.

Methods: Patients underwent complete ophthalmic examination, 10-2 microperimetry (MAIA), spectral-domain optical coherence tomography and fundus autofluorescence imaging at baseline and every 6 months thereafter. Main outcome measures included age of onset of symptoms, best-corrected visual acuity (BCVA), microperimetry mean sensitivity (MS), residual ellipsoid (EZ) span and hyperautofluorescent ring (HAR) area. Genotyping was performed using targeted next-generation sequencing and Sanger sequencing.

Results: PRPF31 mutation was found in 14 members. The four patterns of disease phenotype are: (A) childhood onset with rapid progression (Figure 1A), (B) adult-onset with rapid progression (Figure 1B), (C) adult-onset with slow progression (Figure 1C) and, (D) non-penetrance (Figure 1D). Patients in group A (n=4) revealed no or barely detectable EZ with a BCVA of 20/50 or worse and MS less than 2 dB by age 50 years (n=2) or counting fingers by age 80 years (n=2). Patients in group B (n=4) presented with EZ span reduced to 4000 μ m by age 17 (n=1), 3000 μ m by age 29 (n=1) and 1500 μ m by early 60s (n=2). Group C (n=4) revealed either a mild asymptomatic phenotype (normal MS and large EZ and HAR) at age 18 (n=1) or residual EZ span greater than 3500 μ m and MS 8–19 dB by age 34–63 (n=3). Two unaffected patients were assigned to group D. Two families revealed combinations of phenotypes across and within generations. All detected mutations are predicted to lead to a loss of PRPF31 function.

Conclusions: Our findings suggest disease expression may be related to the level of wild-type PRPF31 allele expression rather than the type of the mutation. Further in vitro studies correlating wild-type PRPF31 allele expression level with clinical manifestation are necessary.

CONTROL ID: 3529816

SUBMITTER (NAME ONLY): Kayla Rudeen

TITLE: Treatment Efficacy of Dual Release of Aflibercept and Dexamethasone from a Single Hydrogel Drug Delivery System in a Laser-induced Choroidal Neovascularization Model

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is a growing subset of age-related macular degeneration patients that do not successfully respond to a monthly monotherapy treatment of anti-vascular endothelial growth factor (VEGF). Recent studies suggest that this subset may respond to a combination therapy of corticosteroid and anti-VEGF. The current combination therapy is administered in separate injections where anti-VEGF injections are repeated monthly/bimonthly. Recently, we developed a single drug delivery system that can release dexamethasone (DEX) and aflibercept (AFL) simultaneously. This study was to determine the treatment efficacy of DEX and AFL released from a single drug delivery system (DDS) in a choroidal neovascularization (CNV) rodent model.

Methods: AFL and DEX were encapsulated into poly(lactic-co-glycolic acid) particles that were embedded into a single thermoresponsive hydrogel DDS. CNV lesions were created by laser photocoagulation (50um, 0.5W) in Long-Evans rats. Animals were randomly assigned into: control (no treatment), blank-DDS (5ul, no drugs), bolus AFL intravitreal (IVT) injections (5ul, 10ug, bimonthly), AFL-DDS (5ul, 1.5ug), AFL+DEX-DDS (5ul, 1.5ug, 20ug, respectively), and DEX-DDS (5ul, 20ug). At week 0 (14 days after the laser induction), treatment was administered. Fluorescein angiography (FA) was obtained at weeks 0, 2, 6, 10, 14, 18 and 22. Multi-Otsu Thresholding was used to quantify lesion area to determine treatment efficacy.

Results: Before the treatment, FA confirmed that CNV lesions were fully developed. At week 14, increases in lesion size were seen in control($10\pm 8\%$), while slight decreases were seen in blank-DDS($-1\pm 8\%$), bolus AFL injections($-3\pm 7\%$), and DEX-DDS($-5\pm 5\%$), and larger decreases were seen in AFL-DDS($-21\pm 5\%$), and AFL+DEX-DDS($-33\pm 5\%$). At week 22, decreases were seen in bolus AFL injections($-11\pm 7\%$), DEX-DDS($-12\pm 7\%$), AFL-DDS($-33\pm 4\%$), and AFL+DEX-DDS ($-30\pm 7\%$), and increases were seen in control($2\pm 8\%$) and blank DDS($4\pm 10\%$).

Conclusions: The combination treatment of AFL and DEX released from a single DDS delivered a lower amount of overall aflibercept compared to bolus injection, with improved treatment efficacy. [MOU1] The study suggests that a combination treatment may be a viable alternative for non-responsive patients.

CONTROL ID: 3529846

SUBMITTER (NAME ONLY): Jay Stewart

TITLE: The Port Delivery System with ranibizumab (PDS)—a new paradigm for long-acting retinal drug delivery

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The PDS is an innovative, investigational, intraocular drug delivery system with the potential to reduce treatment burden in patients with retinovascular diseases. The PDS implant is a permanent, indwelling device designed to continuously deliver a customized formulation of ranibizumab. The PDS refill needle consists of a dual cannula system that allows for simultaneous exchange of implant contents with fresh drug. The characterization of ranibizumab release and refill-exchange efficiency of the PDS is reported here.

Methods: The ranibizumab release rate, active release rate, and retained ranibizumab within the implant over time were measured in vitro with various starting concentrations of ranibizumab. In the ongoing phase 3 Archway trial (NCT03677934) for neovascular AMD, PDS 100 mg/mL with fixed Q24W refill-exchanges was compared with intravitreal ranibizumab 0.5 mg Q4W.

Results: The PDS includes a surgically placed, permanent implant and ancillary devices for implant insertion, initial fill, and in-clinic refill-exchange procedures. The PDS implant was designed to be biocompatible; durable; transparent to facilitate visualization of ranibizumab within the implant; have a self-sealing, refillable septum; not interfere with the patient's field of vision; and be implanted in the superotemporal quadrant. In in vitro studies, ~73% of ranibizumab 100 mg/mL was released from the implant over 6 months after initial implant insertion and after ~450 days, levels were below the lower quantification limit. The average active release rate (SD) at 6 months was 3.95 (0.17), 3.99 (0.13), 3.85 (0.15), and 4.00 (0.17) µg/day at initial fill, first, second, and third refills, respectively, demonstrating reproducibility from implant to implant and between multiple refill-exchanges of the same implant. Changing initial ranibizumab concentration from 10 to 100 mg/mL increased starting drug release rates from ~2 to ~17 µg/day and rate of release. During a refill-exchange procedure, ~98% of the previous implant contents get replaced with fresh drug in one 100-µL injection stroke.

Conclusions: The PDS is an intraocular drug delivery system that continuously and reproducibly delivers ranibizumab over a period of months while maintaining potency. Archway phase 3 trial results support the efficacy of the PDS, as PDS 100 mg/mL Q24W had equivalent vision outcomes to ranibizumab Q4W averaged over weeks 36/40.

CONTROL ID: 3529854

SUBMITTER (NAME ONLY): Arshad Khanani

TITLE: Faricimab in Neovascular Age-Related Macular Degeneration: 1-Year Efficacy, Safety, and Durability in the Phase 3 TENAYA and LUCERNE Trials

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Dual inhibition of angiopoietin-2 and vascular endothelial growth factor-A with faricimab, a bispecific antibody designed for intraocular use, may promote vascular stability with sustained efficacy through extended durability in patients with neovascular age-related macular degeneration (nAMD). Here we report primary 1-year results of the ongoing phase 3 TENAYA and LUCERNE trials, comparing efficacy, safety, and durability of faricimab with aflibercept in patients with nAMD.

Methods: TENAYA (NCT03823287) and LUCERNE (NCT03823300) are identical, phase 3, randomized, double-masked, active comparator-controlled, 112-week studies of faricimab in nAMD. Treatment-naïve patients were randomized 1:1 to receive faricimab 6.0 mg up to every 16 weeks (Q16W) or aflibercept 2.0 mg every 8 weeks (Q8W). Patients in the faricimab arm received 4 initial every-4-week (Q4W) doses and were assessed for protocol-defined disease activity at weeks 20 and 24. Patients with no evidence of active disease at weeks 20 and 24 received Q16W dosing through week 60; those with active disease at week 20 received Q8W dosing; patients with active disease only at week 24 received every-12-week (Q12W) dosing. From week 60, faricimab-treated patients follow a personalized

treatment interval based on a protocol-driven treat-and-extend regimen through week 108. Patients randomized to aflibercept received 3 initial Q4W doses and then Q8W dosing through week 108. Efficacy and safety outcomes were assessed at Q4W study visits. The primary efficacy endpoint is mean change in best-corrected visual acuity from baseline averaged over weeks 40, 44, and 48. Secondary endpoints include the proportion of patients on faricimab Q16W, Q12W, and Q8W regimens; proportion of patients gaining ≥ 15 or ≥ 10 ETDRS letters from baseline; and changes from baseline in anatomic outcomes. Safety outcomes include incidence and severity of ocular and nonocular adverse events.

Results: In phase 2 studies, faricimab at up to Q16W dosing intervals was associated with robust vision and anatomic improvements, comparable with ranibizumab Q4W. TENAYA and LUCERNE are ongoing global phase 3 trials; year 1 study results will be presented at the meeting.

Conclusions: TENAYA and LUCERNE phase 3 trials are evaluating efficacy, safety, and extended durability up to Q16W of intravitreal faricimab in patients with nAMD.

CONTROL ID: 3529876

SUBMITTER (NAME ONLY): Nathan Steinle

TITLE: A Phase 1b Multi-Center, Open Label, Single-Arm Safety Study of Intravitreal Pegcetacoplan Supporting the Phase 3 DERBY and OAKS Studies for Geographic Atrophy: A Solution to "Tarmac Delay"

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Describe the origin and interim results of a phase 1b safety study, APL2-103, supporting two large phase 3 studies of intravitreal pegcetacoplan for geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Methods: In December 2018, the phase 3 DERBY and OAKS studies of intravitreal pegcetacoplan for GA were voluntarily paused due to transient intraocular inflammation (IOI, n=4) after dosing with a new formulation developed for phase 3 trials. An investigation to determine the exact cause was conducted. Quality review of the manufacturing process revealed an impurity in the active pharmaceutical ingredient introduced during scale up. Additional manufacturing steps to eliminate the impurity were implemented, and the resulting product was tested in several animal studies. APL2-103, a 24-month phase 1b, open-label, single-arm safety study of monthly pegcetacoplan was initiated in GA subjects with low vision (Snellen 20/200 to 20/800) before further dosing in phase 3 trials.

Results: All four patients with IOI in the phase 3 studies recovered fully (mean BCVA before: 47.5 letters [range 38-67] and after: 45.5 letters [29-68]). Phase 3 studies were re-initiated in March 2019 after a drug product lot without the impurity revealed no signs of investigator-assessed IOI in 10 subjects who completed a 7-day follow-up evaluation in APL2-103 across 4 clinical sites. APL2-103 continues supporting drug product lot evaluation before use in DERBY/OAKS. Safety findings in APL2-103 after phase 3 re-initiation were consistent with all previous and ongoing intravitreal pegcetacoplan programs. In APL2-103, one patient developed new-onset exudation, and no cases of IOI were observed with the phase 3 formulation. An exploratory interim efficacy analysis of APL2-103 in bilateral GA patients with 12 (n=9) and 18 (n=7) months of follow up revealed that the GA growth rate in pegcetacoplan-treated eyes was slower than untreated fellow eyes by 31% at month 12 and 52% at month 18.

Conclusions: The likely root cause of intraocular inflammation was identified and eliminated. These findings highlight the value of ensuring safety following manufacturing or formulation changes. APL2-103 continues to support the fully enrolled phase 3 studies, with an acceptable safety profile.

CONTROL ID: 3529958

SUBMITTER (NAME ONLY): Peter Campochiaro

TITLE: Pharmacokinetic profile of the Port Delivery System with ranibizumab (PDS) in the phase 3 Archway trial

SESSION TITLE: AMD: clinical research - new therapies and technologies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The PDS is an investigational drug delivery system that includes a pars plana implant for continuous delivery of ranibizumab into the vitreous. Ranibizumab release from the implant is mediated by passive diffusion. In the ongoing phase 3 Archway trial (NCT03677934) in patients with neovascular age-related macular degeneration (N=415), serum and aqueous humor samples were collected to characterize the PK of ranibizumab administered via the PDS refilled Q24W.

Methods: In the PDS with ranibizumab 100 mg/mL Q24W and monthly intravitreal ranibizumab 0.5 mg injection arms, serum PK samples were scheduled to be collected at randomization and at weeks 4, 24, 36, and 96 from all patients. At selected sites, samples were taken at days 2 and 7 and at weeks 12, 48, and 72 in the PDS arm, and 1–5 days after an injection in the monthly ranibizumab arm. Optional aqueous humor samples were collected from patients in either arm at weeks 24, 28, 48, 52, 72, 76, and 96; serum samples were also collected at this time. The PK-evaluable population consisted of patients who did not receive ranibizumab injections in the study eye or fellow eye after implant insertion or prior intravitreal bevacizumab treatment. Ranibizumab concentrations were measured using a validated enzyme-linked immunosorbent assay with lower limits of quantification of 15 pg/mL for serum and 20,000 pg/mL for aqueous humor.

Results: Based on Archway primary analysis data, in the PDS arm (n=94), geometric mean (coefficient of variation) serum concentrations ranged from 419 (54%) pg/mL at week 4 to 340 (94%) pg/mL at week 24. In the monthly ranibizumab arm (n=79), geometric mean serum ranibizumab concentrations ranged from 1880 (57%) pg/mL near maximum concentration (1-5 days after injection) to 58.1 (171%) pg/mL at Week 4 (C_{trough}). The aqueous humor PK profile reflected the same trends seen in serum, with PDS 100 mg/mL Q24W (n=42) maintaining concentrations above monthly intravitreal ranibizumab C_{trough} (n=46).

Conclusions: The PDS continuously releases ranibizumab over the Q24W refill interval at steady concentrations. Ranibizumab concentrations with PDS 100 mg/mL Q24W are within the range experienced with monthly intravitreal ranibizumab 0.5 mg injections. Aqueous humor PK were consistent with serum PK.

CONTROL ID: 3529966

SUBMITTER (NAME ONLY): Nazlee Zebardast

TITLE: Penetrance and characteristics of Gln368Ter Myocilin variant in UKBB

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: MYOC (myocilin) mutations account for 3-5% of primary open angle glaucoma (POAG) and 10-20% of early-onset glaucoma. We aimed to understand the true population-wide penetrance and characteristics of glaucoma among individuals with the most common MYOC variant (p.Gln368Ter) and the impact of a POAG polygenic risk score (PRS) in this population.

Methods: We used phenotype and genotype data from the UK Biobank and identified those with p.Gln368Ter variant. POAG PRS was computed based on a large POAG GWAS meta-analysis. Two masked graders reviewed fundus photographs (FPs) for disc-defined glaucoma (DDG).

Results: 200 of 73,563 participants with complete data carried the p.Gln368Ter heterozygous genotype and 177 had gradable FPs. 132 had no glaucoma, 45 (25.4%) had probable/definite glaucoma in 1+ eye and 19 (10.7%) had bilateral glaucoma. There were no differences in age, ethnicity, or gender among groups ($p > 0.05$ for all). Of those with DDG, 14 (31%) self-reported or had ICD 9/10 code for glaucoma while 31 (69%) were undiagnosed. Subjects with DDG had higher cornea corrected intraocular pressure (IOPcc) after adjustment for IOP lowering medications ($p < 0.001$) vs. those without DDG. This difference in IOPcc was more pronounced in individuals with DDG with prior glaucoma diagnosis vs. those undiagnosed ($p < 0.001$). The majority of participants with p.Gln368Ter mutation had IOP in the normal range (≤ 21 mmHg), though this proportion was lower in those with DDG ($p < 0.02$) and those with prior glaucoma diagnosis ($p < 0.03$) (Tab1). The prevalence of DDG increased with each decile of PRS. Subjects with DDG had significantly higher PRS compared to those without glaucoma (1.05 ± 0.60 vs. 0.83 ± 0.56 , $p = 0.03$). Of those with DDG, individuals with prior diagnosis of glaucoma had higher PRS compared to undiagnosed individuals (1.63 ± 0.40 vs 0.82 ± 0.50 , $p < 0.001$) and had 27.5 (95% CI 2.5-306.6) times adjusted odds of being in the top decile of PRS for POAG (Fig1).

Conclusions: Nearly 1 in 4 individuals with the p.Gln368Ter mutation had evidence of glaucoma, a substantially higher penetrance than previously estimated, with 70% of cases undetected. While IOP plays an important role, a large portion of carriers have IOP in the normal range, despite similar age, including those with DDG. PRS increases disease penetrance and severity of disease, supporting the utility of PRS in optimizing risk stratification among MYOC p.Gln368Ter variant carriers.

CONTROL ID: 3529985

SUBMITTER (NAME ONLY): Christian Mueller

TITLE: Metabolism of primary human corneal endothelial cell (HCEnC) cultures grown at ambient and 2.5% oxygen

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

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Commercial Relationships Disclosure (Abstract): Christian Mueller: Commercial Relationship: Code N (No Commercial Relationship) | Sangita Patel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Oxidative stress is central to the pathophysiology of Fuchs endothelial corneal dystrophy. Typically, HCEnC cultures are grown in 5% CO₂, room air incubators ([O₂]_A). However, [O₂] in the anterior chamber is approximately 2.5% ([O₂]_{2.5}). The purpose of our study was to investigate in vitro metabolism of HCEnC grown at [O₂]_A and [O₂]_{2.5}. We hypothesized that cells grown at [O₂]_{2.5} would have greater glycolytic activity and decreased oxidative respiration compared to cells grown at [O₂]_A.

Methods: Protocols were approved by the Univ at Buffalo and VA WNY IRBs. Donor eyes (n=5 [O₂]_A and n=6 [O₂]_{2.5}, mean age 74) were obtained within 24 hrs of death for initiating HCEnC cultures. [O₂]_A cells were grown in a humidified, 5% CO₂, 37°C incubator. [O₂]_{2.5} was created in a humidified chamber (Billups-Rothenberg, Inc., Del Mar, CA) with 2.5% O₂, 5% CO₂, balance N₂ at 37°C. Mitochondrial respiration (O₂ consumption rate [OCR]) and glycolysis (extracellular acidification rate [ECAR]) were measured with the Seahorse XFe24 (Agilent Technologies, Inc., Santa Clara, CA). OCR and ECAR measurements were performed at baseline (B) and following additions of oligomycin (O), FCCP, rotenone/antimycin A (RA) and 2DG. We calculated basal respiration (B-RA for OCR and B-2DG for ECAR), ATP-linked respiration (B-O), proton leak (O-RA), max respiration (FCCP-RA), spare capacity (FCCP-B), non-mitochondrial O₂ consumption (RA), and glycolytic reserve capacity (O-B). Mean values were compared between [O₂]_A and [O₂]_{2.5} using unpaired two-tailed t-tests with significance at p<0.05.

Results: OCR analysis showed significant differences between [O₂]_A and [O₂]_{2.5} in proton leak, spare capacity, and non-mitochondrial O₂ consumption (Table). There were no significant differences between groups for basal respiration, ATP linked respiration, and max respiration. ECAR analysis showed significant differences between [O₂]_A and [O₂]_{2.5} in basal glycolysis and glycolytic reserve capacity.

Conclusions: Our results demonstrate that in HCEnC, glycolytic activity is greater but ATP-linked respiration the same at physiologic [O₂]_{2.5} compared to [O₂]_A. Increased proton leak and non-mitochondrial O₂ consumption at [O₂]_{2.5} compared [O₂]_A suggest alternative metabolic pathways are prominent under physiologic conditions. [O₂] is an important consideration in HCEnC metabolism and FECD pathophysiology.

CONTROL ID: 3529989

SUBMITTER (NAME ONLY): Wataru Matsumiya

TITLE: Correlation between photoreceptor density in adaptive optics imaging with retinal structure and sensitivity in autoimmune retinopathy

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Matsumiya, A. Akhavanrezayat, G. Uludag, C. Yasar, H. Ghoraba, A. Mobasserian, I. Karaca, B.C. Lam, B. Pham, J.J. Hwang, R. Afridi, M. Halim, D.V. Do, Y.J. Sepah, Q.D. Nguyen, Byers Eye Institute, Stanford University, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Autoimmune Retinopathy (AIR) is a rare disease with progressive retinal degeneration which does not have a gold standard to monitor disease activity. Adaptive optics (AO) technology is recently developed to depict a photoreceptor in retina. Our aim is to evaluate utility of an AO camera in comparison with microperimetry (MP) and spectral-domain optical coherence tomography (SD-OCT) in AIR.

Methods: Three eyes of 3 patients with a confirmed diagnosis of AIR by clinical and serologic findings were assessed. AO images (rtx1, Imagine Eyes, France) of the central 4°x 4°field (not including 0.5°x 0.5° field of fovea) , MP with 4-2 staircase threshold strategy (MAIA Centervue, Italy), and OCT (Spectralis Heidelberg, Germany) were analyzed after merging images using Adobe Photoshop CS6 (Adobe Systems, San Jose, CA). A correlation was investigated among photoreceptor parameters [cone density (CD), regularity, dispersion, and spacing] in AO images, retinal sensitivity (RS) in MP, and outer retinal thickness (ORT) on OCT which were obtained at two separate time-points. AO images from 2 visits were automatically registered and parameters of photoreceptors were calculated with manual method (AO detect 3.0, Imagine Eyes), which had an excellent intraclass correlation coefficient (>0.90) in the prior study.

Results: A total of 22 regions of interest on AO, MP, and OCT images in 1 female (65 yo) and 2 males (14 yo and 56 yo) were assessed. At baseline, mean value of RS and ORT was 18.4±11.4dB and 96.2±49.9µm, respectively. Mean values of AO parameters were 1481±409/deg² (CD), 86.7±5.7% (regularity), 17.6±3.7% (dispersion), and 1.76±0.27 arcminute (spacing). Highest correlation of both RS and ORT were with CD (p=0.78, P<0.0001 and p=0.81, P<0.0001, respectively), followed by spacing (p=-0.75, P=0.0001 and p=-0.79, P<0.0001, respectively). Mean changes of CD, RS, and ORT between two time-points (range of interval: 2-5 months) were -0.9±5.1 dB, -92±157 /deg², and 15.5±26.3 µm, respectively. The correlation of changes in CD with RS, and ORT were 0.40 (P = 0.063) and 0.57 (P = 0.006), respectively.

Conclusions: Cone density appeared to have a significant correlation with retinal sensitivity (as measured by MP) and retinal structure (as measured by OCT). Therefore, measuring the cone density using manual method in AO images may be useful to assess retinal function in AIR patients.

CONTROL ID: 3529992

SUBMITTER (NAME ONLY): Briana Ebbinghaus

TITLE: Early effects of diabetes on retinal ganglion cell morphology and synaptic connectivity

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Diabetic Retinopathy (DR) is a leading cause of visual impairment in working age adults. Loss of retinal ganglion cells (RGCs) –the output neurons of the neural retina lining the back of the eye – contributes to visual impairment in this disease. Vascular changes occur with diabetes and these contribute to RGC death (Feit-Leichman et al., IOVS, 2005; Kern and Barber, The Journal of Physiology, 2008). However, little is known about the sequence of morphological and connectivity alterations in RGCs preceding their loss. Knowledge of these alterations would reveal the early impact of diabetes on RGC structure and connectivity. There are four well characterized ‘alpha’ RGC types in the mammalian murine retina with stereotypic lamination and functional profiles: ON-Sustained (ON-SUS), ON-Transient (ON-T), OFF-Transient (OFF-T), and OFF-Sustained (OFF-SUS) RGCs (Krieger et al., PLoS one, 2017). Using a mouse model of diabetes, we aimed to investigate the early effects of diabetes on the morphology and synaptic connectivity of these four RGC types.

Methods:

Male Ins2^{Akita/+} mice (Jackson labs) and littermate controls were collected at a 6-week timepoint: 2 weeks after initiation of hyperglycemia in this strain. Alpha RGCs were biolistically labeled with tdTomato as a cell-fill and fluorescently conjugated PSD-95 as a marker for excitatory synapses (Morgan et al., Neural Development, 2008). RGCs were imaged using a Leica SP8 confocal microscope and image stacks were visualized in Amira (Thermo Fisher Scientific). RGC types were determined by lamination of RGC dendrites in the retinal synaptic layer. Dendritic branching was analyzed by Sholl analyses (Fiji/Image J, NIH). PSD-95 density and asymmetric index were calculated by custom-written Matlab codes. Immunohistochemistry for RGC markers was performed at the 8-week timepoint to determine the density of RGCs across genotypes.

Results:

Average asymmetric index of RGC types was not different between genotypes. At the 8-week timepoint, RGC cell density was not affected across genotypes. RGC branching pattern and synaptic density was selectively altered in retinas from diabetic mice in a subtype-specific manner.

Conclusions:

The morphology and connectivity of RGCs is altered in a subtype-specific manner, within a short duration of diabetes before the onset of RGC loss.

CONTROL ID: 3530010

SUBMITTER (NAME ONLY): Loren Lock

TITLE: Health System Size and Rurality Predict Diabetic Eye Screening Adherence

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Most claims-based studies analyzing factors related to diabetic eye screening adherence have used single-payor databases, such as Medicare or managed care networks, and have focused on patient-level factors. In this study, we used a unique, all-payor database covering over 75% of Wisconsin residents (Wisconsin All-Payer Claims Database) to assess variability in screening rates across health systems and to identify health-system factors associated with screening.

Methods: We included adults with diabetes (18-75 years old) who had claims billed throughout the baseline (10/1/2012 - 9/30/2013) and measurement years (10/1/2013 – 9/30/2014). We excluded patients cared for by a primary care provider with fewer than 20 patients in our dataset. We performed chi-square tests and used multivariate logistic regression models to assess potential predictors of diabetic eye screening based on health system factors, patient demographics, comorbidities, and adherence with hemoglobin A1c and LDL screening guidelines.

Results: A total of 119,347 adults with diabetes from 143 Wisconsin health systems and 2,178 primary care providers met our inclusion criteria. Screening rates varied widely between health systems (31.8%-73.0%), with smaller health systems having lower screening rates. A patient's health system had substantial predictive power regarding whether a patient received diabetic eye screening (chi-square 1840.4, $p < 0.001$). In the multivariate analysis, when we excluded health system to focus on patient-level factors, patients from health systems based in small rural towns were more likely to obtain eye screening compared to patients from urban health systems (OR 1.13, 95% CI 1.08, 1.18, respectively). However, the directionality of the association reversed when health system was included in the model, with patients from health systems based in small rural towns being less likely to obtain eye screening compared to patients from urban health systems (OR 0.90, 95% CI 0.84, 0.95, respectively).

Conclusions: In this state-wide, all-payor claims database, we found significant variability in diabetic eye screening rates across health systems. Health system was a major predictor of screening adherence, with a lower likelihood of screening among patients from smaller and rural health systems. Interventions directed at the health system may be important for increasing diabetic eye screening rates.

CONTROL ID: 3530029

SUBMITTER (NAME ONLY): Majlinda Lako

TITLE: A single cell atlas of developing and adult cornea in steady state and disease conditions

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lako, J. Collin, R. Queen, D. Zerti, S. Bojic, B. Dorgau, N. Moyse, M. Moya Molina, C. Yang, L. Armstrong, F.C. Figueiredo, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|S. Dey, Technion Israel Institute of Technology, Haifa, Haifa, ISRAEL|

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ABSTRACT BODY:

Purpose: Single cell (sc) analyses of key embryonic, fetal and adult stages were performed in order to generate the first comprehensive single cell atlas of all the corneal and adjacent conjunctival cell types from development to adulthood.

Methods: Four human adult and seventeen embryonic and fetal corneas from 10-21 post conception week (PCW) specimens were dissociated to single cells and subjected to scRNA- and/or ATAC-Seq using the 10x Genomics platform.

Results: scRNA-Seq analysis of 21,343 cells from four adult human corneas and adjacent conjunctivas revealed the presence of 21 cell clusters, representing the stem, progenitor and differentiated cells in all layers of cornea and conjunctiva as well as immune cells, melanocytes, fibroblasts and blood/lymphatic vessels. A small cell cluster with high expression of limbal stem cells (LSCs) markers was identified and shown via pseudotime analysis to give rise to five other cell types representing the progenitor and differentiated corneal epithelial cells. A novel putative LSCs surface marker, GPHA2, expressed in $0.41\% \pm 0.21$ of the cultured limbal epithelial cells, was identified, based on predominant expression in the limbal crypts of adult and developing cornea and RNAi validation in cultured LECs. Combining scRNA- and ATAC-Seq analyses, we identified multiple upstream regulators for LSCs and transit amplifying (TA) cells and demonstrated a close interaction between the immune cells and corneal epithelial stem and progenitor cells. RNA-Seq analysis indicated the loss of LSCs markers and acquisition of proliferative limbal basal epithelial progenitor markers during ex vivo limbal epithelial cell expansion, independently of the culture method used. Single cell RNA-Seq of 89,897 cells obtained from embryonic and fetal cornea indicated that during development, the conjunctival epithelium is the first to be specified from the ocular surface epithelium, followed by the corneal epithelium and the establishment of LSCs/progenitor cells.

Conclusions: Our scRNA- and ATAC-Seq data of developing and adult cornea in steady state and disease conditions provide a unique resource for defining genes/pathways that can lead to improvement in ex vivo LSCs expansion, stem cell differentiation methods and better understanding and treatment of ocular surface disorders.

CONTROL ID: 3530082

SUBMITTER (NAME ONLY): Bhavna Antony

TITLE: Assessing Repeatability of Deep-Learning Based Estimation of Visual Function Test Parameters from OCT Volumes

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.J. Antony, R. Garnavi, IBM Research Australia, Southbank, Victoria, AUSTRALIA|H. Ishikawa, G. Wollstein, J.S. Schuman, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the repeatability of estimates of mean deviation (MD) and visual field index (VFI) obtained from an automated deep-learning approach that analysed raw OCT volumes.

Methods: OCT scans were acquired from both eyes of 138 healthy, 743 glaucoma suspects and 941 glaucoma patients (Cirrus HD-OCT scanner, 200x200 ONH Cubes, Zeiss, Dublin CA). The scans were acquired at multiple visits, with two or more scans acquired at each visit. Scans with signal strength < 7 were discarded, giving us a total of 19,208 OCT scans. A subset of 5207 eyes (total of 10,414 scans) had repeat scans of that met the inclusion criteria. 24-2 Humphrey visual field (VF) tests were administered at each visit. A single convolutional neural network was trained to estimate the MD and VFI (dual outputs) from downsampled OCT volumes (50x50x128 voxels). The network consisted of 5 convolutional layers, followed by a global average pooling layer and dual outputs to enable the simultaneous estimation of MD and VFI. A mean squared error loss was used to train the network using an Adam optimiser over a total of 200 epochs. A 10-fold cross-validation scheme was used, where the dataset was divided into 10 non-overlapping folds (~182 subjects per fold) – trained on 8-folds, validated on one and tested on one. Each subject was limited to a unique fold. The performance of the method was assessed by computing the median error and interquartile range. The repeatability was assessed using a set of 5207 OCT scans that had repeats available.

Results: The median absolute error (Q1, Q3) for the estimates of MD and VFI were 1.66 (0.79, 2.99) dB and 3.01 (1.48, 6.63) %, respectively. In the reproducibility test, the Pearson's correlation coefficient was 0.91 (CI: [0.91, 0.92]) and 0.91 (CI: [0.90, 0.92]), for MD and VFI, respectively. The median absolute difference between the repeated estimates for MD and VFI were 0.53 (0.21, 0.51) dB and 1.17 (0.45, 1.14)%, respectively.

Conclusions: The deep-learning based approach for estimating visual field test parameters shows repeatability better than expected test-to-test variability.

CONTROL ID: 3530110

SUBMITTER (NAME ONLY): David Berntsen

TITLE: Peripheral Defocus and Axial Eye Growth in the Bifocal Lenses In Nearsighted Kids (BLINK) Study

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.A. Berntsen, A.T. Gostovic, M.A. Chandler, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|L.T. Sinnott, A. Morrison, L. Jordan, J.J. Walline, D.O. Mutti, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Huang, School of Optometry, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: The BLINK Study was a 3-year randomized clinical trial that found +2.50 D add center-distance multifocal soft contact lenses (MFCLs) slowed myopia progression versus +1.50 D add MFCLs and single vision contact lenses (SVCLs). In this analysis, we explore the relationship between peripheral defocus and axial growth.

Methods: 294 myopic children 7-11 years old (60% female) were enrolled (mean \pm SD age = 10.3 \pm 1.2 years). Children had myopia of -0.75 D to -5.00 D (most hyperopic meridian) and <1.00 D astigmatism at enrollment (mean \pm SD spherical equivalent (M) = -2.39 \pm 1.00 D). Children were randomly assigned to one of three lenses: SVCL, +1.50 add MFCL, or +2.50 add MFCL. Autorefraction (horizontal meridian; right eye) was measured while wearing CLs centrally (line of sight) and $\pm 20^\circ$, $\pm 30^\circ$, and $\pm 40^\circ$ from the line of sight while viewing a near target (30cm) and also at distance after cycloplegia. Each child's defocus (M) profile at distance and near were fit using quadratic equations. Models of the first-year change in axial length (measured by optical biometry) were fit including the quadratic coefficient (Qc) for defocus at distance or near, central M, gender, study site, and age.

Results: After 1 year, mean axial growth was on average 0.13mm less in the +2.50 add group ($p < .001$) and 0.03mm less in the +1.50 add group ($p = .11$) versus SVCLs. Compared to SVCLs, peripheral defocus at distance was more myopic (less positive Qc) with MFCLs (Figure 1). At the 1-year visit, the average Qc in the +2.50 versus the SVCL group was .0005 D/degree² less at distance and .0004 D/degree² less at near. More myopic peripheral defocus at distance and at near in the +2.50 group was associated with less axial growth (distance: $\beta = .31$, or .016mm less axial growth, $p = .005$; near: $\beta = .49$, or .020mm less axial growth, $p < .001$).

Conclusions: More myopic peripheral defocus at distance and near in children wearing +2.50 add MFCLs compared to SVCLs was associated with less axial growth in the BLINK Study, but not by a clinically meaningful amount. The small association suggests that a linear dose-response to peripheral defocus may not fully explain the effects of MFCLs on axial growth. Exceeding a threshold amount of peripheral myopic defocus or mechanisms other than peripheral defocus may cause the significant slowing of axial growth seen with MFCLs.

CONTROL ID: 3530126

SUBMITTER (NAME ONLY): Yixin Yu

TITLE: Long-term multimodal imaging of persistent retinal neovascularization using DL-alpha-aminoadipic acid in pigmented and white rabbits

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Yu, Y. Qin, J. Fu, Y.M. Paulus, Ophthalmology & Visual Science, University of Michigan, Ann Arbor, Michigan, UNITED STATES|Y. Yu, Ophthalmology, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|X. Yang, Mechanical Engineering, University of Kansas School of Engineering, Lawrence, Kansas, UNITED STATES|X. Wang, Y.M. Paulus, Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal (IVT) injection of DL-alpha-aminoadipic acid (DL-AAA) is a new animal model for persistent retinal neovascularization (RNV) reported in rabbits. This study performs longitudinal multimodal imaging for up to 52 weeks to evaluate DL-AAA RNV in both New Zealand white (NZW) rabbits and Dutch-Belted pigmented (DBP) rabbits.

Methods: Detailed characterization and quantification of this model were performed in these two strains in 32 eyes by optical coherence tomography (OCT), fundus photography, and fluorescein angiography (FA) for up to 16 weeks following DL-AAA administration in 32 eyes and up to 52 weeks in 5 eyes. H & E histology was also performed 8 weeks after injection of DL-AAA.

Results: RNV was successfully generated using 50 µL 80mM DL-AAA solution for DBP rabbits and 80 µL 80mM DL-AAA for NZW rabbits. The incidence of persistent vascular leakage is 100% (15/15) for DBP rabbits and 70.6% (12/17) for NZW rabbits at 16 weeks. Complications with NZW rabbits ultimately decreased the efficiency in NZW rabbits to 58.8% (10/17) of NZW rabbits getting persistent (to 16 weeks) vascular leakage without ocular complications as compared with 100% (15/15) in DBP rabbits. Five eyes (2 DBP and 3 NZW) were selected from those demonstrating RNV at 16 weeks and were monitored for up to 52 weeks. All 5 demonstrated persistent RNV to 52 weeks. Quantification of the mean leakage area (MLA) in NZW rabbits is more challenging than in DBP rabbits due to reduced contrast between the leakage and background in NZW rabbits.

Conclusions: DL-AAA can induce persistent and quantifiable RNV in both DBP and NZW rabbits. DBP rabbits have a higher success rate, lower required volume of DL-AAA, and less challenging method for quantification that could be more desirable.

CONTROL ID: 3530131

SUBMITTER (NAME ONLY): Matthew Hunt

TITLE: Association of Environmental Factors with Neovascular Age-Related Macular Degeneration (nvAMD) using the Intelligent Research in Sight (IRIS)® Registry

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hunt, S. Saraf, Y. Chee, Y. Wu, C.S. Lee, A.Y. Lee, M.B. Manookin, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Known AMD risks include demographic variables such as age, sex, and race, but the impact of environmental exposures is currently unclear. We investigate associations of environmental exposures with nvAMD development across the US.

Methods: All patients ≥ 55 years in the IRIS Registry during 2016-2018 (period of interest [POI]) were analyzed. Patients undergoing treatment for nvAMD were identified by nvAMD ICD code and CPT code for anti-VEGF intravitreal injections. Patients without provider-level zip codes matching any zip code tabular area were excluded. Environmental data was obtained from public sources including the US Geological Survey, National Renewable Energy Laboratory, and National Oceanic and Atmospheric Administration. Patients were assigned environmental variables from measurements nearest their zip code. Variable selection was done using elastic-net regularization. Multivariable logistic regression quantified the association of each environmental variable with nvAMD while adjusting for age, sex, race, and phakic status.

Results: A total of 18,166,512 patients were included. All demographic variables, phakic status, elevation, latitude, solar irradiance measured in global horizontal irradiance (GHI) and direct normal irradiance (DNI), and temperature and precipitation variables were included in our model after regularization. After adjusting for demographic factors and phakic status, the strongest environmental associations were DNI (OR: 0.550, 95%CI: [0.524, 0.578]), GHI (3.874, [3.452, 4.348]), and latitude (1.099, [1.092, 1.106]), while elevation had minimal association (1.000, [1.000, 1.000]) (Figure 1). The risk of nvAMD for a 75-year-old, pseudophakic, Caucasian female was calculated for the US (Figure 2).

Conclusions: Strongest associations for environmental factors were seen for DNI, GHI, and latitude. Further studies are warranted to investigate the clinical relevance of these associations.

CONTROL ID: 3530164

SUBMITTER (NAME ONLY): Rushi Mankad

TITLE: Ethnicity/race and end-stage renal disease, but not glycemic control, are significantly associated with proliferative diabetic retinopathy

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.N. Mankad, L.A. Marek, G. Acosta, A. Cabrera, F. Monickaraj, A. Das, Ophthalmology, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|F. Monickaraj, A. Das, Surgery, New Mexico VA Health Care System, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of sight-threatening complications of diabetes, namely proliferative diabetic retinopathy (PDR), is understood to be a consequence of several modifiable and non-modifiable factors. We performed a cross-sectional, observational study to identify these factors that are significantly associated with the development of PDR.

Methods: Data was collected from two patient cohorts with type 1 or type 2 diabetes seen between February 1, 2018 and February 1, 2020: a group of 293 patients with confirmed PDR and a control group of 69 patients with confirmed mild nonproliferative diabetic retinopathy (NPDR). Patients in the PDR group were identified by ICD-10 codes and confirmed with a history of panretinal photocoagulation and/or pars plana vitrectomy for vitreous hemorrhage. Data was obtained by an extensive chart review of several systemic parameters. Statistical analysis was done via two-sample t-test for continuous variables and Chi-squared test or Fisher exact test for categorical variables.

Results: Our analysis revealed that the development of PDR was significantly associated with exogenous insulin use ($p<0.001$), elevated systolic BP ($p=0.004$), presence of macroalbuminuria ($p<0.001$), history of dialysis ($p=0.002$), and decreased GFR ($p=0.024$). In our cohort, the prevalence of PDR was higher in both Hispanics and American Indians than for Whites/Anglos. There was a lack of association between HbA_{1c} levels and PDR ($p=0.784$). The majority of PDR patients (56.8%) had good glycemic control (HbA_{1c} $<7.5\%$); similarly, the majority of mild NPDR patients (58%) had poor glycemic control (HbA_{1c} $\geq 7.5\%$). No association was found with total cholesterol ($p=0.713$), LDL ($p=0.355$), HDL ($p=0.440$), and triglyceride ($p=0.412$) levels.

Conclusions: The data suggests that glycemic control is unrelated to the development of PDR, as the majority of our PDR cohort had good glycemic control. The highest incidence of PDR was seen among American Indians and Hispanics. There is a strong association between end-stage renal disease (ESRD) and PDR. Our findings indicate that "other factors," such as genomics, may play a stronger role in development of PDR.

CONTROL ID: 3530190

SUBMITTER (NAME ONLY): Rachael Heath Jeffery

TITLE: Ultra-widfield fundus autofluorescence derived atrophy expansion rate in ABCA4-associated retinopathy is dependent on mutation severity

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate atrophy expansion rate (ER) using ultra-widfield fundus autofluorescence (UWF-FAF) in ABCA4 associated retinopathy.

Methods: Patients with biallelic ABCA4 mutations were evaluated with UWF-FAF and Heidelberg 30°×30° and 55°×55° FAF imaging. Those with atrophy secondary to STGD1 were classified into genotype groups: A (biallelic severe or null-like variants with early-onset disease), B (one intermediate variant in trans with severe or null-like variant) or C (one mild variant in trans with severe or null-like variant, or late-onset disease). The boundaries of definitely decreased autofluorescence (DDAF) were outlined manually and areas (mm²) recorded at baseline and follow-up. Bland-Altman analysis was conducted to examine agreement between observers and devices. Linear mixed modelling (LMM) was used to evaluate predictors of ER in DDAF area and square root area (SRA).

Results: Recruitment of 69 patients, 138 eyes (33 male [47%]; mean±SD age 41±20 years; range 10-83) carrying 61 unique ABCA4 variants. UWF-FAF measurements were equivalent to Heidelberg 30°×30° imaging. Baseline DDAF area was the only significant predictor of DDAF area ER (p<0.001). Age at baseline and genotype group were predictors for DDAF SRA ER. Mean DDAF area ERs were 4.65, 2.00 and 0.62mm²/year for Groups A, B and C. Mean DDAF SRA ERs were 0.25, 0.25, 0.18 mm/year.

Conclusions: UWF-FAF is a feasible and reliable modality for assessing atrophy ER in STGD1. A key novel finding in this study is the effect of genotype on DDAF SRA ER whereby the mean ER for genotype C was significantly lower than both genotypes A and B. The value of ABCA4 mutation severity in predicting atrophy ER warrants further investigation.

CONTROL ID: 3530204

SUBMITTER (NAME ONLY): Akira Hayashida

TITLE: Morphological evaluation of white spots in the granulomatous uveitis using ultra widefield OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this study was to analyze the morphological features of white spots in the peripheral fundus of patients with Sarcoidosis and Vogt-Koyanagi-Harada disease (VKH), which are classified as granulomatous uveitis.

Methods: Sarcoidosis and VKH patients in Kyushu University Hospital, who had white spots in the periphery of the fundus, were enrolled in the study. Images of the white spots were obtained using Optos® Silverstone, ultra-widefield guided swept source optical coherence tomography (OCT).

We compared the morphological characteristics of those white spots between the two diseases.

Results: OCT Images of white spots were obtained from 13 patients with Sarcoidosis and 9 patients with VKH. Atrophic lesions were observed in 10 cases of Sarcoidosis and 9 cases of VKH, all of which had retinal pigment epithelial (RPE) defects with no morphological differences between diseases. In both diseases, subretinal elevated lesions were seen in some cases (Sarcoidosis; 5 cases, VKH; 3 cases). Those lesions were Dalen-Fuchs nodule-like elevated lesions with RPE perforation or Sarcoid nodule-like lesions under the RPE without RPE perforation. In contrast, hyperreflective lesions in the retina were found only in Sarcoidosis (7 cases), but not in VKH.

Conclusions: The site of the white spots in the peripheral fundus varied, suggesting that each disease have a different morphological pattern.

CONTROL ID: 3530206

SUBMITTER (NAME ONLY): Georgie Hollitt

TITLE:

Attitudes toward glaucoma genetic risk assessment among affected individuals

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Hollitt, J.E. Craig, E. Souzeau, O. Siggs, Ophthalmology, Flinders University, Adelaide, South Australia, AUSTRALIA]

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ABSTRACT BODY:

Purpose: Despite the significant progress made in genetic risk prediction, critical gaps in knowledge pertinent to understanding barriers to the implementation of polygenic risk scores (PRS) testing persist. We performed a cross-sectional, questionnaire-based study to better understand the attitudes of individuals with glaucoma toward PRS testing for glaucoma. As the leading cause of irreversible vision loss in the world, with recognised complex heritability, few environmental risk factors, and high treatability to prevent blindness, PRS testing has strong clinical utility for glaucoma.

Methods: We surveyed 1169 individuals with glaucoma to evaluate their attitude toward polygenic risk testing for glaucoma, drawn from the Australian and New Zealand Registry of Advanced Glaucoma (ANZRAG); one of the largest databases of clinical and genetic data for primary glaucoma in the world. We assessed several factors affecting interest in testing using multivariate regression analysis.

Results: Our results show strong interest towards testing with 68.3% of individuals being likely or highly likely to have taken the test. In particular, those from an urban area (OR 1.526, CI 1.118 – 2.084, p 0.008) or with non-advanced disease (OR 1.383, CI 1.043 – 1.833, p 0.024) showed increased interest. Increased pre-diagnosis perception of risk (OR 2.007 CI 1.245 – 3.234, p 0.004) and worry of developing glaucoma (OR 2.109, CI 1.296 – 3.432, p 0.003) were associated with increased interest in testing. Those who were interested in testing indicated being more likely to change their eye health behaviour (OR 1.532, CI 1.112 – 2.110, p 0.009), recommend testing to family (OR 12.831, CI 6.334 – 25.993, p <0.001) and non-family members (OR 3.670, CI 2.660 – 5.064, p <0.001), as well as undergo testing for prognostication (OR 4.967, CI 2.467 – 10.001, p <0.001).

Conclusions:

In summary, individuals with glaucoma showed a positive attitude toward polygenic risk testing for glaucoma. These findings support the clinical implementation of polygenic risk scores for glaucoma to reduce irreversible vision loss. Further research should be performed to better understand attitudes of those who do not have glaucoma, and the attitudes and knowledge of clinicians toward PRS testing.

CONTROL ID: 3530211

SUBMITTER (NAME ONLY): Tatsuya Sobajima

TITLE: Evaluation of the effect of preloaded injector tip shapes on insertion resistance of the cornea and postoperative incision sizes in cataract surgery.

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sobajima, T. Hishida, S. Nagasaka, Y. Soda, Kabushiki Kaisha Nidek, Gamagori, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: Preloaded IOL injectors are commonplace in cataract surgery. A variety of preloaded IOL injectors have been developed with differing designs and varying clinical outcomes. Additionally, there are subtle differences in the recommended incision and the actual clinical reports. Hence, to clarify the effect of different injector tip shapes on the incision, a laboratory set up was used to determine the relationship between the insertion resistance and tip shape, and an ex-vivo study of porcine eyes was performed to determine the postoperative incision width.

Methods: The following injectors were investigated: XY-1 (HOYA), AU00T0 (Alcon), YP2.2R (KOWA), SZ-1 (NIDEK), and NSP-1 (NIDEK).

Bevel angle, slit length, tip angle, and outer circumference length of the injector tips were measured with a shape measuring device. A slit knife was used to create a 2.0 ± 0.08 mm incision in a 0.4 mm silicone rubber sheet that mimicked corneal properties. Subsequently, the tip was inserted at 2 mm/sec with a testing machine to measure the maximum insertion resistance values for each injector. Preloaded IOLs with the same power were inserted from each of the injectors into a 2.0 mm corneal incision in porcine eyes. The post-insertion incision widths were measured with intraocular calipers.

Results: The range of values for tip shapes were:

Bevel angle: 27° (SZ-1) to 48.7° (YP2.2R)

Slit length: 3.3 mm (XY-1 and YP2.2R) to 4.3 mm (NSP-1)

Tip angle: 64.1° (NSP-1) to 96.6° (AU00T0)

Outer circumference length: 5.21 mm (XY-1) to 6.09 mm (SZ-1)

The range for maximum insertion resistance was 0.155 ± 0.018 N (SZ-1) to 0.248 ± 0.022 N (YP2.2R)

Incision width on porcine eyes ranged from 2.30 ± 0.10 mm (XY-1) to 2.50 ± 0.00 mm (SZ-1).

There was no correlation between the postoperative incision width and the maximum resistance to insertion ($r=0.030$).

The circumference length had the highest correlation coefficient with respect to the postoperative incision width and tip shape ($r=0.962$).

Conclusions: The outcomes of this study indicate that shorter outer circumference can mitigate enlargement of incision width. A “sharp bevel angle” and “long slit length” of the injector tip are the main determinants for preventing enlargement. A “sharp bevel angle” is more conducive to overcoming insertion resistance of the cornea.

CONTROL ID: 3530226

SUBMITTER (NAME ONLY): Sajib Kumar Saha

TITLE: Artificial Intelligence-based Detection of Diabetic Retinopathy using Retinal Imaging and Traditional Risk Factors

SESSION TITLE: AI in the retina: Algorithms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Saha, M. Watson, C. Dehghani, S. Frost, Commonwealth Scientific and Industrial Research Organisation, Perth, Western Australia, AUSTRALIA|C. Dehghani, University of Canberra, Canberra, Australian Capital Territory, AUSTRALIA|K. Edwards, N. Pritchard, N. Efron, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|A. Russell, The University of Queensland, Saint Lucia, Queensland, AUSTRALIA|R. Malik, The University of Manchester, Manchester, Manchester, UNITED KINGDOM|R. Malik, Weill Cornell Medicine, QATAR|Y. Kanagasingam, The University of Notre Dame Australia, Fremantle, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is one of the major causes of blindness in the developed world. Early detection is crucial to reduce the risk of blindness in DR. Considering this, we have developed an artificial intelligence-based method to reliably detect DR using retinal imaging and traditional risk factors.

Methods: A deep convolutional neural network (CNN) was explicitly trained on the EyePACS dataset [<https://www.kaggle.com/c/diabetic-retinopathy-detection/data>] to perform 'disease', 'no-disease' grading of DR using color fundus photographs. A second, longitudinal dataset of retinal images and clinical data of 2~6 visits of 326 LANDMark study participants was utilised to identify the traditional risk factors most strongly associated with DR development and progression - age, HbA1c, systolic blood pressure, weight, body mass index, and waist circumference.

A support vector machine (SVM) classifier was independently trained to classify 'disease' versus 'no-disease' relying upon these traditional risk factors. In different to native SVMs that do not output probabilities, Platt scaling, a probability calibration method, was used in this work to obtain a "probability" out of an SVM.

The probabilities returned by the CNN and SVM were finally combined to detect DR.

We randomly divided the LANDMark dataset into a training set (90%) and testing set (10%). Since the dataset contained longitudinal data of multiple visits, in order to avoid reverse pair-wise bias or type-I error, we made sure same participant data were not split into training and test set.

Results: The SVM achieved an accuracy of 94% in detecting DR relying upon traditional risk factors. The CNN achieved an accuracy of 92% in detecting DR using color fundus photographs. When combined, an achieved an accuracy of 96%, with sensitivity, specificity and AUC respectively of 96%, 95% and 96% was observed.

Conclusions: A novel approach for the automated grading of DR is proposed. In comparison to state-of-the-art AI-based methods that solely use images to perform DR grading, the proposed method combines the risk factors-based assessment with the image-based assessment, providing an overall improved accuracy, sensitivity and AUC. The proposed method is found to be 4% more accurate and 2% more sensitive (without compromising specificity) than the solely image-based approach.

CONTROL ID: 3530233

SUBMITTER (NAME ONLY): Ignacio Larrayoz

TITLE: A hypothermia mimetic molecule (zr17-2) reduces ganglion cell death and prevents electroretinogram distortion following intraorbital optic nerve crush (IONC) in the rat

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ocular and periocular traumatism may result in loss of vision. Our previous work showed that hypothermia prevents retinal damage caused by traumatic neuropathy. We generated and characterized small molecules that elicit the beneficial effects of hypothermia at normal body temperature. Here we investigate whether one of these mimetic molecules, zr17-2, is able to preserve the function of retinas exposed to trauma.

Methods: Intraorbital optic nerve crush (IONC) or sham manipulation was applied to Sprague-Dawley rats. One hour after surgery, 5 μ l of 330 nmols/L zr17-2 or PBS, as vehicle, were injected in the vitreum of treated animals. Electroretinograms were performed 30 days after surgery and a-, b-wave amplitude and oscillatory potentials (OP), were calculated. Animals for TUNEL analysis were sacrificed 6 days after surgery. Western blotting was performed for cold inducible RNA-binding protein (CIRP), the target of zr17-2.

Results: Previous studies showed that zr17-2 does not cross the blood-ocular barrier, thus preventing systemic treatment. Here we show that intravitreal injection of zr17-2 results in a very significant increase in CIRP protein expression in the eye, providing mechanistic support for its pharmacological use in ocular conditions. The amplitude of a- and b-waves, as well as the OP, was significantly reduced in IONC-affected retinas ($p < 0.05$). These parameters were significantly corrected by injection of zr17-2 ($p < 0.05$) (Fig. 1). IONC resulted in a very significant increase of TUNEL-positive cells in the ganglion cell layer ($p < 0.001$) whereas injection of zr17-2 significantly reduced the number of apoptotic cells ($p < 0.001$) (Fig. 2).

Conclusions: We have shown that intravitreal injection of the hypothermia mimetic, zr17-2, increases CIRP protein expression and, as a result, significantly reduces the morphological and electrophysiological consequences of ocular traumatism and may represent a new treatment for this cause of visual loss.

*DSC, *MR-F, *RP, contributed equally

#CFL, #AM and #IML contributed equally

CONTROL ID: 3530240

SUBMITTER (NAME ONLY): Laura Cushley

TITLE: Barriers and Enablers of attendance at Northern Ireland Diabetic Eye Screening: A Qualitative Perspective from Young People aged 12-26

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the barriers and enablers of attendance at the Northern Ireland Diabetic Eye Screening Programme (NIDESP) in young people aged 12-26 years using qualitative questionnaires.

Methods: A qualitative questionnaire was distributed to young people with diabetes mellitus (YPwDM) through Diabetes clinics in the Belfast Health and Social Care Trust (BHSCT) enquiring about barriers and enablers faced for NIDESP attendance. Additionally, YPwDM were asked about their level of knowledge as to how Diabetes Mellitus (DM) might affect their eyes.

Results: The survey was completed by 25 YPwDM; 52% were male and 44% were female, one individual did not state their gender. Respondents were aged between 12 and 26 years of age, 56% were between 16-20 years. Age at diagnosis was most commonly between the ages of 8-11 years old (40%) followed by 12-15 years of age (28%). Those diagnosed between the ages of 1-3, 4-7 and 16-20 were 8%, 4% and 16% respectively, 4% did not respond. Saturation of themes was achieved by this number of responses.

Nearly all (92%) YPwDM were aware that diabetes can affect the eyes, despite this, 84% asked to receive more education on this subject. The main source of information on diabetic eye disease at present is the endocrinologist in charge of the diabetes clinic (in 72% of cases). NIDESP was known to nearly all YPwDM (88%), however 20% were unaware that attendance both at NIDESP and their high street opticians was advisable. The identified main barriers were the timing of the appointments, clash of multiple appointments and missing out on school/work being the main problems. In fact, 76% stated that they would be more likely to attend if diabetic eye screening was completed during their normal diabetes clinic appointment. One respondent strongly suggested that more encouragement from the diabetes team would be required to increase their want to attend NIDESP.

Conclusions: The study concluded that it is not necessarily the lack of knowledge that stops YPwDM attending NIDESP. Relatively modest changes in how information on diabetic eye disease is provided, and by whom; rearranging time of the eye-screening clinics and providing more detailed information could potentially have a major impact on attendance.

CONTROL ID: 3530269

SUBMITTER (NAME ONLY): Robyn Guymer

TITLE: Dual angiopoietin-2 and VEGF-A inhibition with faricimab in neovascular age-related macular degeneration: phase 3 TENAYA and LUCERNE trial design

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Guymer, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|C. Quezada Ruiz, J.R. Willis, H. Lin, Genentech Inc, South San Francisco, California, UNITED STATES|D. Silverman, J. Ives, A. Kotecha, H. Boston, Roche Products Ltd, Welwyn Garden City, Hertfordshire, UNITED KINGDOM|K. Basu, Roche Products Ireland Limited, Dublin, IRELAND|B. Swaminathan, F. Hoffmann-La Roche Limited, Mississauga, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Dual inhibition of angiopoietin-2 (Ang-2) and vascular endothelial growth factor (VEGF)-A with faricimab, the first bispecific antibody designed for intraocular use, may synergistically promote vascular stability and reduce treatment burden through extended durability in patients with neovascular age-related macular degeneration (nAMD). The phase 3 TENAYA and LUCERNE trials are designed to assess the efficacy, safety, and durability of faricimab compared with aflibercept in patients with nAMD. Here, we present the rationale for the clinical trial design.

Methods: TENAYA (NCT03823287) and LUCERNE (NCT03823300) are identical, phase 3, randomized, double-masked, active comparator-controlled, 112-week studies of faricimab in nAMD. Treatment-naïve patients are randomized 1:1 to faricimab 6.0 mg up to every 16 weeks (Q16W) after 4 initial every-4-week (Q4W) doses or aflibercept 2.0 mg every 8 weeks (Q8W) after 3 initial Q4W doses. Based on disease activity assessments (prespecified anatomical and functional criteria, and investigator discretion) at weeks 20 and 24, patients in the faricimab arm are allocated to receive Q8W, every-12-week (Q12W), or Q16W dosing until week 60. Faricimab-treated patients then follow a personalized treatment interval (PTI), a protocol-driven treat-and-extend regimen with interval adjustment based on individualized treatment response as assessed by prespecified anatomical and functional criteria at study drug dosing visits, up to week 108.

Results: The TENAYA and LUCERNE trials will evaluate the efficacy, safety, and durability of faricimab in patients with nAMD. The primary efficacy endpoint is change in best-corrected visual acuity from baseline averaged over weeks 40, 44, and 48. Secondary endpoints include the proportion of patients receiving faricimab Q16W, Q12W, and Q8W, and changes in anatomic outcomes; safety outcomes include the incidence and severity of adverse events. The PTI phase is designed to tailor treatment intervals according to patients' needs, with individualized dosing up to Q16W, to reduce treatment burden while optimizing outcomes.

Conclusions: The TENAYA and LUCERNE trials are ongoing global trials designed to evaluate the potential for dual Ang-2 and VEGF-A inhibition with faricimab to improve outcomes for patients with nAMD.

CONTROL ID: 3530280

SUBMITTER (NAME ONLY): Carolyn Pan

TITLE: Treatment for Diabetic Retinal Disease: Impact of Early/Prophylactic Treatment

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.K. Pan, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Carolyn Pan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess impact of delayed treatment in diabetic macular edema (DME) in the VISTA/VIVID trials and initiating treatment in moderately severe to severe non-proliferative diabetic retinopathy (NPDR) in the PANORAMA trial.

Methods: In this post hoc analysis in VIVID/VISTA, efficacy outcomes were compared between eyes that received intravitreal aflibercept injection (IAI) 2 mg every 4 weeks (2q4; n=290) or every 8 weeks (2q8 after 5 initial monthly doses; n=286) through 100 weeks, or laser with rescue (with 2q8 regimen) due to vision loss (from week 24 for up to ~76 weeks; n=109). Rescue initiation (RI) in VISTA/VIVID was synchronized to the baseline for initially treated patients, with outcomes assessed at week 100 from baseline. In PANORAMA, eyes with moderately severe to severe NPDR without DME received IAI every 16 weeks (2q16 after loading phase; n=135) or every 8 weeks (2q8/PRN after loading phase; n=134) or sham (n=133). All patients could receive rescue at investigator's discretion for events of PDR/anterior segment neovascularization (ASNV; 1 IAI injection and/or panretinal photocoagulation) or center-involved DME (CI-DME; IAI PRN).

Results: In VISTA/VIVID, mean best-corrected visual acuity (letters) with 2q4 and 2q8, respectively, was 59.8 and 59.1 (baseline) and 71.5 and 70.2 (week 100), and was 59.5 (baseline), 49.0 (RI), and 57.9 (week 100) for laser/rescue. Mean central subfield thickness (CST) (μm) with 2q4 and 2q8, respectively, was 493.1 and 497.6 (baseline) and 289.4 and 290.1 (week 100), and 537.5 (baseline), 538.5 (RI), and 272.9 (week 100) for laser/rescue. In PANORAMA, in the 2q16, 2q8, and sham groups, respectively, 3.0%, 3.7%, and 14.3% of patients were rescued for PDR/ASNV, and 7.4%, 8.2%, and 29.3% were rescued for CI-DME, through 100 weeks. Benefit was seen in the patients treated with IAI versus sham/rescue with respect to progression of diabetic retinal disease.

Conclusions: Patients with DME in VIVID/VISTA who received delayed IAI treatment did not achieve similar final visual acuity as those who initiated IAI at study start, despite achieving similar CST. These analyses from VIVID/VISTA and PANORAMA suggest earlier treatment could be clinically beneficial in both DME and NPDR patients.

CONTROL ID: 3530293

SUBMITTER (NAME ONLY): Rafael Peláez

TITLE: Sterculic acid treatment promotes cell survival of retinal pigment epithelium cells in a multi-pathway dependent manner.

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Peláez, A. Pariente, Á. Pérez-Sala, R. Ochoa, I.M. Larrayoz, Biomarkers and Molecular Signaling, Fundación Rioja Salud, Logroño, La Rioja, SPAIN|

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ABSTRACT BODY:

Purpose: Sterculic acid (SA) is a cyclopropene fatty acid presents in Sterculia foetida seeds, although it is also present in many other seeds. Different studies have demonstrated that this lipid has many effects over cells biological activities, generally attributed to its Stearoyl-CoA desaturase (SCD) inhibitory properties. Scd1 has demonstrated to be a new potential target for many diseases as result of the central role this gene in lipid metabolism and body weight control. Lipid accumulation in drusen deposits of retina has been also associated to age-related macular degeneration (AMD) patients. Here we pretend to evaluate the molecular pathways altered by SA treatment to prevent retinal pigment epithelium (RPE) induced cell death.

Methods: Genome-wide transcriptomic analysis were carried out in mRPE cells, exposed to SA for 24 h, and an integrative functional enrichment analysis of genome-wide expression data were made to provide insights into the cellular protective mechanisms induced by SA

Results: The expression of pivotal genes related to lipid metabolism was altered as result of the SA biological activity. Furthermore, steroid biosynthesis, cell death, actin-cytoskeleton reorganization or extracellular matrix-receptor genes were significantly modified by exposition to SA, while the specific SCD1 inhibitor did not alter the expression of these genes.

Conclusions: SA administration to RPE cells regulates crucial pathways in a SCD1 independent way that may be of interest for the treatment of ocular diseases.

CONTROL ID: 3530304

SUBMITTER (NAME ONLY): Antonia Neumann

TITLE: Effect of short-wavelength light emitting screen technologies on human contrast sensitivity

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Neumann, K. Breher, S. Wahl, Institute for ophthalmic research, University of Tuebingen, Tuebingen, GERMANY|S. Wahl, Carl Zeiss Vision International GmbH, Aalen, GERMANY|

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ABSTRACT BODY:

Purpose: Blue light (short-wavelength light) is a part of the visible electromagnetic light spectrum for the human eye. Short wavelengths have a higher energetic radiation compared to middle and long wavelengths, which might have multiple effects on retinal processes. This study was conducted to investigate whether commonly available screen technologies are able to elicit changes in contrast sensitivity (CS) and therefore may be used to control myopia eventually.

Methods: In total, 30 right eyes were randomly stimulated with light of different wavelengths: ~480 nm, ~530 nm, ~630 nm and polychromatic light ~380-780 nm, for 3 min each presented on a liquid crystal display, the ViewPixx/3D (VPixx Technologies, Saint-Bruno, Canada). Light stimulation was performed full field (FF) and only on the optic nerve head (ONH). CS was measured before any stimulation as reference and after each stimulation condition using a new and time-efficient CS test with Gabor patches and the method of adjustment for 3, 6, 12, 18 and 24 cycles per degree (cpd). Changes in CS after stimulation conditions were analyzed by three-way repeated measures analysis of variance. In a priorly conducted complementary study on a subset of five participants, the new CS test was verified to a validated CS test regarding agreement, repeatability (COR) and time.

Results: The new CS test was used with 3 trials per spatial frequency (interclass correlation coefficient = 0.94, COR = 0.1310 logCS, duration = 92 ± 17 sec). No critical change in CS after stimulation of the eye (FF or ONH) with short-wavelength light was detected (all $p > 0.05$), see Figure 1. CS measurements regarding spatial frequency differed significantly as expected from the CS function. The results showed, however, that CS differed significantly at 18 cpd after stimulation with polychromatic light from short-wavelength light ($p < 0.0001$). All other influencing factors and their interactions did not show significant effects.

Conclusions: The results of using short-wavelength light stimulation via LED screens to increase CS are inconclusive. Based on the results, melanopsin activation and thus increased levels of retinal dopamine are not easy to detect via indirect psychophysical testing. Direct and indirect links of these basic psychophysical findings to retinal signaling and eventually myopia control using short-wavelength light still require further research.

CONTROL ID: 3530305

SUBMITTER (NAME ONLY): Julian Hilmers

TITLE: Towards a more realistic visual performance assessment: The Tuebingen Visual Acuity Test at different Levels of Contrast and Ambient Luminance (VA-CAL)

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hilmers, T. Strasser, E. Zrenner, Institute for Ophthalmic Research, University of Tuebingen, Tuebingen, GERMANY|T. Strasser, K. Stingl, University Eye Hospital Tuebingen, Tuebingen, GERMANY|M. Bach, University Eye Hospital Freiburg, Freiburg, GERMANY|E. Zrenner, Werner Reichardt Centre for Integrative Neuroscience (CIN), Tuebingen, GERMANY|

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ABSTRACT BODY:

Purpose: Currently, visual acuity (VA) assessment is performed with maximum optotype contrast at moderately low luminance ($80\text{--}320\text{ cd/m}^2$), barely reflecting visual environments in daily life. Specifically, VA may not adequately assess vision in inherited retinal disorders with increased glare-sensitivity like achromatopsia (ACHM). For a more realistic assessment of patients' visual performance at different contrasts (C) and ambient luminance (AL), approximating daily life conditions, we developed a novel VA test, VA-CAL. Here we present preliminary results in ACHM patients and healthy controls.

Methods: ACHM patients (N=8; age: 16-37, mean 24.9 y) and eye-healthy controls (N=10; age: 22-29, mean 25.5 y) underwent VA-CAL. Landolt C-rings (LCR) were presented at 1m distance on a $10\times 10\text{ cm}$ field in the center of a frosted glass screen ($130\times 130\text{ cm}$), back-lit by 3,060 computer-controlled LEDs ($0\text{--}10,000\text{ cd/m}^2$, 7 steps). LCR contrast was programmable between 10-90 %. VA threshold for each condition was determined by adjusting LCR sizes using the QUEST adaptive staircase method. Participants received auditory feedback after reporting the gap position of LCR (8AFC), presented max. 10 s (ISI 1 s).

Results: As expected, VA of ACHM was well below to controls. In both, VA decreased with lower C. While VA of controls increased with AL up to a maximum between $3,000\text{--}5,000\text{ cd/m}^2$ (max. VA mean \pm SEM: $-0.5 \pm 0.03\text{ logMAR}$ @ C=90 %, AL=3,000 cd/m^2), ACHM reached their max. VA at 30 cd/m^2 (max. VA mean \pm SEM: $0.76 \pm 0.046\text{ logMAR}$ @ C=80 %). With increasing AL, VA in ACHM decreased by about 0.08 logMAR per $1,000\text{ cd/m}^2$ up to AL $3,000\text{ cd/m}^2$, followed by quite steady low VA up to AL $8,000\text{ cd/m}^2$ and a subsequent drop of VA to a minimum at AL $10,000\text{ cd/m}^2$ (min. VA mean \pm SEM: $1.41 \pm 0.08\text{ logMAR}$ @ C=10 %) (Fig. 1).

Conclusions: In this study, a novel computer-controlled method for testing of VA under different conditions of contrast and ambient luminance was developed for a more realistic visual performance assessment of visually impaired patients. Whereas in healthy subjects VA improves initially with increasing levels of AL, in patients with achromatopsia, VA decreases with increasing C and AL. Our results indicate that VA has to be measured within a broader range of C and AL to adequately assess everyday visual performance, especially in patients reporting glare sensitivity.

CONTROL ID: 3530337

SUBMITTER (NAME ONLY): Raziye Mahmoudzadeh

TITLE: Retinal Displacement Following Incisional Rhegmatogenous Retinal Detachment Repair

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Mahmoudzadeh, M. Salabati, Y. Yonekawa, A.E. Kuriyan, M. Khan, M.A. Klufas, S.J. Garg, O. Gupta, C. Regillo, M.N. Cohen, Mid Atlantic Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the incidence of post-operative retinal displacement detected on fundus autofluorescence (FAF) imaging following rhegmatogenous retinal detachment (RRD) repair with pars plana vitrectomy (PPV), scleral buckle (SB), or PPV/SB.

Methods: Single-center, prospective consecutive series conducted at Wills Eye Hospital (Philadelphia, PA, USA). Optos (Dunfermline, UK), FAF images were performed in eyes post RRD repair between April and December 2020. Images were assessed by two independent graders, masked to surgical technique. Retinal displacement was identified by imprinted retinal vessels on FAF images.

Results: Ninety-four eyes of 88 patients (73% male, mean age 62(±13) years) were included. Nineteen eyes (21%) had a macula-on RRD, 75 (79%) had a macula off RRD. Thirty-two eyes (34%) had proliferative vitreoretinopathy (PVR). Forty-four (46.8%) eyes underwent PPV alone, 9 (9.6%) underwent SB alone, and 41 (43.6%) underwent combined PPV/SB. The mean time from surgical procedure to FAF imaging was 112 days. A total of 9 eyes (9.6%) had retinal vessel imprinting on FAF consistent with retinal displacement. The mean (±SD) displacement was 0.18 mm (± 0.11; range 0.09-0.4 mm). 5 of 44 (11.3%) PPV patients and 4 of 41 (9.8%) of PPV/SB patients had displacement. No displacement was found in the SB only patients. There was no statistically significant difference in the proportion of eyes with displacement between the three surgical groups (p=0.88). All observed displacement involved the inferior vasculature. Two cases of displacement were found in patients with PVR (n=32, 9.1%), and 7 were found in patients without PVR (n=62, 11.3%; p=0.71). Mean (±SD) preoperative logMAR visual acuity was 1.46 (±0.96; Snellen equivalent 20/570) and mean (±SD) postoperative logMAR visual acuity was 0.55 (±0.37; Snellen equivalent 20/70, p<0.001). Among patients with macula-off RRD, the mean (±SD) postoperative logMAR visual acuity in the group without displacement (0.51 ± 0.34, Snellen equivalent 20/64) was significantly better than those with displacement (0.8 ± 0.37; Snellen equivalent 20/126, p= 0.035).

Conclusions: Retinal displacement after incisional retinal detachment repair occurs in approximately 10% of cases. PPV and PPV/SB showed a similar percentage of displacement. In eyes with macula-off detachments, those with displacement had worse postoperative visual outcomes compared to those without detectable displacement.

CONTROL ID: 3530339

SUBMITTER (NAME ONLY): Khaled Nassar

TITLE: Retinal vascular effects of novel soluble guanylate cyclase activator (sGCa) runcaciguat

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Xu, L. Zhou, J. Guerra, E.J. Duh, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|K. Nassar, W. Schubert, C. Terjung, K. Rheindorf, Bayer AG, Wuppertal, Nordrhein-Westfalen, GERMANY|H.M. Eilken, Bayer U.S LLC, Cambridge, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vascular degeneration can be a cause of vision loss in ischemic retinopathies including diabetic retinopathy. Targeting early microangiopathic damage might be a more effective treatment approach. sGC plays an important homeostatic role in blood vessels maintenance. However, sGC can be rendered nonfunctional by oxidative stress. The presence of sGC in retinal blood vessels, and the effect of sGC activation in retinal vascular disease has not been reported. The purpose of the study was to evaluate the effect of a novel sGC activator (runcaciguat) in the treatment of retinal vasodegeneration.

Methods: Expression of sGC α and β subunits was evaluated in post-mortem human retina specimens by immunohistochemistry. Runcaciguat was evaluated in the mouse oxygen induced retinopathy (OIR) model. Mice were treated daily with runcaciguat via oral gavage from P8 to P12. Retinal wholemounts from P12 or P18 mice were evaluated for vaso-obliteration and/or neovascularization. In STZ model and healthy rats, changes in the circumpapillary RNFL (cpRNFL) and retinal microcirculation following runcaciguat bolus intravenous therapy was evaluated with optical coherence tomography and angiography (OCT/OCTA).

Results: Immunohistochemistry demonstrated that both sGC α and β subunits were expressed in human retinal blood vessels. In OIR mice, runcaciguat treatment reduced both retinal vaso-obliteration and neovascularization in relation to the total retina compared to hyperoxic P12 retinas ($17.65\% \pm 5.35$ vs $30.65\% \pm 13.06$, $p = 0.04$ & $3.05\% \pm 1.3$ vs $8.17\% \pm 4.1$, $p < 0.0001$) and hyperoxic P18 retinas ($0.8\% \pm 0.8$ vs $3.7\% \pm 3.4$, $p = 0.002$, and $7.5\% \pm 2.9$ vs $12.12\% \pm 7.4$ vs, $p = 0.008$, mean \pm SD, one way ANOVA). 2ry to retinal vasodilation, a trend of increased cpRNFL thickness was detected in rat STZ model. The deep retinal vascular plexus diameter was increased in OCTA en Face image analysis and correlated to the runcaciguat plasma concentration (Pearson $r = 0.996$, p value: 0.004, CI. 0.82 to 0.99). The peak increase in the retinal perfusion measured by OCTA was 30 minutes following runcaciguat therapy.

Conclusions: These findings showed sGC was expressed in retinal blood vessels in humans. Together with runcaciguat's effect on retinal vascular perfusion, its protective effects on retinal vaso-obliteration in OIR suggest that runcaciguat could represent a potential novel treatment for ischemic retinopathies including diabetic retinopathy.

CONTROL ID: 3530383

SUBMITTER (NAME ONLY): Pedro Mecê

TITLE: Adaptive-glasses Full-Field OCT for high-resolution retinal imaging over a large field-of-view

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Mecê, J. Scholler, K. Groux, Y. Cai, C. Boccara, Institut Langevin, Paris, Île-de-France, FRANCE|M. Paques, K. Grieve, Quinze-Vingts National Ophthalmology Hospital, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: The highest three-dimensional (3D) resolution possible in in-vivo retinal imaging is achieved by combining optical coherence tomography (OCT) and adaptive optics. However, this combination brings important limitations, such as small field-of-view and complex, cumbersome systems, preventing so far clinical deployment. Here, we introduce Adaptive-Glasses Full-Field OCT (FFOCT), a retinal imaging system allying high-resolution, high frame rate (300Hz), 5° FOV in a compact system (footprint: 30cm by 50cm).

Methods: We used our retinal imager combining a time-domain FFOCT and an SDOCT, enabling correction of axial eye motion in real-time. We previously demonstrated the capacity of this system to achieve foveal cone mosaic imaging without the use of AO, owing to the low sensitivity to ocular aberrations of the FFOCT when using spatially incoherent light, mostly affecting the signal to noise ratio (SNR). To increase the SNR, we implemented a lens-based sensorless AO approach using a multi-actuator adaptive lens (MAL) positioned in front of the eye, like prescribed eyeglasses, in a technique we call the adaptive-glasses approach. The SDOCT signal was used as a merit function for the wavefront optimization.

Results: The FFOCT SNR was enhanced up to a factor of 10 by using the MAL for a dilated pupil. The MAL can adjust the focus axial position within the retina, to image structures in the inner retina as the nerve fiber layer with an 8 µm axial resolution. Moreover, owing to the combination of FFOCT with the adaptive-glasses approach, we can acquire high-resolution FFOCT images over a 5° FOV, without apparent anisoplanatism. This unprecedented combination of wide FOV and high-resolution facilitated important clinical tasks to diagnose retinal disorders, such as image montaging and the computation of photoreceptor-based biomarkers.

Conclusions: We showed that the combination of FFOCT, which presents a weaker sensitivity to symmetric aberrations in terms of lateral resolution [5], and the adaptive-glasses approach, to increase the SNR of FF-OCT image and to favor anisoplanatic correction, opens a new avenue to wide FOV high-resolution retinal imaging in a compact imaging system configuration, taking up essential challenges to facilitate clinical deployment of AO-OCT. The proposed system is moving to the Quinze Vingts National Ophthalmology Hospital to start clinical trials in the beginning of January 2021.

CONTROL ID: 3530417

SUBMITTER (NAME ONLY): Fethallah Benmansour

TITLE: Automated screening of moderately severe and severe nonproliferative diabetic retinopathy (NPDR) from 7-field color fundus photographs (7F-CFP) using deep learning (DL)

SESSION TITLE: AI in the retina: Algorithms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Benmansour, D. Damopoulos, A. Neubert, J. Novosel, B.G. Armendariz, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|Q. Yang, N. Anegondi, D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|D. Ferrara, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the performance of DL employing 7F-CFP in automated identification of eyes with moderately severe and severe NPDR among patients with diabetes in a US primary care setting.

Methods: Eyes of 37,358 patients with diabetes were analyzed using data, including images, collected between 1999 and 2016 (Source: Inoveon Corporation, Oklahoma City, OK). DR severity and the presence of clinically significant macular edema were assessed from 7F-CFP by professional graders at a centralized reading center, and graded using the Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale (DRSS). Prevalence of moderately severe or severe NPDR (DRSS 47–53), considering the worst DRSS score at the patient level, was 2.2% in this cohort. This set was split into 80% for model training, 10% for tuning, and 10% for testing, for a total of 29,890, 3732, and 3736 patients with 1,430,046, 180,534, and 180,135 images, respectively. A DL Inception-v3 model with transfer learning was trained at the image level on all 7 fields of view (including stereoscopy) for being either DRSS 47–53 or not. Predictions were averaged over all fields of view to provide a prediction at the eye level. We report model performance metrics in terms of area under the receiver operating characteristic (AUROC) curve, specificity, sensitivity, and positive predictive value.

Results: The best model was selected based on performance on the tuning set, as well as the optimal cutoff for specificity and sensitivity maximizing the Youden index. The model performed well on the testing set with an AUROC of 0.962 (95% CI, 0.956, 0.967), sensitivity of 0.942 (95% CI, 0.934, 0.950), specificity of 0.946 (95% CI, 0.945, 0.948), and positive predictive value of 0.281 (95% CI, 0.272, 0.290).

Conclusions: DL can support automated identification of eyes with DRSS 47–53. The model presented here can optimize screening of patients at risk of disease progression for participation in preventive clinical trials as well in clinical practice. Future research will further refine this proof-of-concept algorithm, including validation on other independent diverse datasets and in a real-world setting.

CONTROL ID: 3530420

SUBMITTER (NAME ONLY): Jelena Novosel

TITLE: A multimodal deep learning (DL) model to predict visual acuity response in the CATT study

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We developed DL models to predict visual acuity response (VAR) to ranibizumab (RBZ) by using baseline (BL) characteristics and color fundus images (CFIs) of patients with neovascular age-related macular degeneration.

Methods: VAR was formulated as a classification problem with 4 classes (<5, 5–9, 10–14, and ≥15 letters); each class was assigned based on best-corrected visual acuity (BCVA) change from BL to month 12. To solve the classification problem, we designed 3 DL models that processed data from different modalities. Single models were trained to process BL characteristics, including BCVA, age, and optical coherence tomography (OCT) imaging biomarkers (Fig 1A), or CFI (Fig 1B); the third model (multimodal model; Fig 1C) fused the 2 subnetworks to produce the final classification.

This is a retrospective analysis of BL data from 284 patients receiving RBZ monthly treatment in the CATT study (NCT00593450). The distribution across the 4 classes was imbalanced, with 64, 43, 52, and 125 patients in classes 1, 2, 3, and 4, respectively. Performance was assessed based on validation (N=56) and test (N=57) data subsets using accuracy and area under the receiver operating characteristic (AUROC) curve. As accuracy and AUROC can be misleading in an imbalanced dataset, we reported F1 score (macro [m] and per-class) and area under the precision-recall (AUCPR) curve to provide a more informative assessment of model performance.

Results: Evaluation of model performance is shown in Table 1. Performance measures varied considerably among the 3 models (eg, mF1 scores of the test dataset were 0.332, 0.236, and 0.354 for BL characteristic, CFI, and multimodal models, respectively). Additionally, individual per-class results showed large variation, reflecting the presence of a strong class imbalance in the data.

Conclusions: The 3 models showed limited ability to predict VAR to RBZ, but the BL characteristics and multimodal models outperformed the CFI model. Compared with the BL characteristics model, the multimodal model showed slightly better performance. More research is required to explore whether the predictive ability of the multimodal model can be further improved.

CONTROL ID: 3530445

SUBMITTER (NAME ONLY): Alexander Vankov

TITLE: Full Field Tissue Ablation Profilometer with Submicron Precision

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vankov, R&D, J&J Vision, Milpitas, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Alexander Vankov: Commercial Relationship(s);J&J Vision:Code E (Employment)

ABSTRACT BODY:

Purpose: Accuracy of optical change induced by laser can be achieved with OCT only in average, assuming cornea receives smooth change. Evaporation, liquid on the surface, gravity, translation to measurement bench adds tens of micrometers to measurement errors, resulting in inconsistent measurements. To evaluate laser treatment and visualize local surgical problems, profilometer should provide direct consistent measurement in each point of ablation with at least 10 micrometers of lateral resolution and submicron resolution for thickness.

Methods: Flap of porcine cornea 100 micrometers in thickness made on IFS device, J&J Vision, was placed on mirror, submerged in oil-based fluid with known refractive index 1.4700, and covered with glass cover slip. White light interferometer measures Optical Path Difference (OPD) in this cuvette with 30nm precision. We used Contour GT white light interferometer, Bruker Corp, with 2x objective. Small change in corneal refractive index allows for precise measurement of corneal thickness by OPD measurement. Thickness can be calculated as OPD divided on difference of refractive indexes between oil and tissue, 1.4700 and 1.376, respectively. After ablation with Star S4 IR, J&J Vision, flap with ablated crater was measured again. Subtraction shows laser induced difference.

Results: 8mm corneal flap, ablated with stationary top hat excimer laser beam 4mm in aperture and 19mJ in energy forms crater with central island, well known in refractive surgery. Results for ablation rate in the center was 0.36micrometers/pulse, which is in remarkable agreement with published value 0.37micrometers/pulse, measured with shadow photography. Settings for IFS flap was 100 micrometers and measured on profilometer as 106 micrometers in thickness, 10micrometers peak to valley. Lenticular extracted during SMILE procedure also can be evaluated on profilometer with same precision about 300nm. As far as tissue is embed into oil, no evaporation or hydration can occur. Specimen remain stable for at least 5 days and is not sensitive to transportation.

Conclusions: Full field tissue profilometry with at least 300nm precision is demonstrated on porcine cornea. Profilometer can be used for characterization of LASIK and SMILE laser systems on tissue and have good agreement to independent measurements.

CONTROL ID: 3530455

SUBMITTER (NAME ONLY): Nathanael Matei

TITLE: Retinal Vascular Physiology Biomarkers in a 5XFAD Mouse Model of Alzheimer's Disease

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Matei, S. Leahy, J. Burford, M. Shahidi, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|N.P. Blair, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alzheimer's disease (AD) is a neurodegenerative disorder that lacks biomarkers for early diagnosis. The retina displays many characteristics of the AD brain, such as accumulation of amyloid beta (A β) oligomers and loss of function. In AD patients, changes in retinal venous velocity (V) and vascular oxygen saturation have been reported. These parameters as well as retinal oxygen metabolism (MO₂) and delivery (DO₂) have not been investigated in animal models of AD. The purpose of the study was to test the hypothesis that alterations in retinal arterial and venous diameter (D_A, D_V), V, and total retinal blood flow (TRBF), coupled with MO₂ and DO₂ are present in the five-familial AD (5xFAD) mice.

Methods: A total of 16 5xFAD and 16 wildtype (WT) mice were evaluated (age: 3 months). D_A and D_V were measured from retinal images, and V was determined by fluorescence microsphere imaging to calculate TRBF. Phosphorescence lifetime images were analyzed to derive arterial and venous oxygen contents (O_{2A}, O_{2V}) and arteriovenous oxygen content difference (O_{2AV}). MO₂ and DO₂ were calculated from TRBF, O_{2A} and O_{2AV}. Data were available in 13 of 16 mice in each group. Retina and brain tissues were evaluated by ELISA assays to determine A β 42 levels in WT (N=4) and 5xFAD mice (N=6).

Results: In the WT group, D_A, D_V, V, and TRBF were 27 \pm 2 μ m, 30 \pm 3 μ m, 11.1 \pm 3.2 mm/s, and 1.73 \pm 0.52 μ l/min, respectively. In the 5xFAD group, D_V (33 \pm 3 μ m) was increased, while V (7.1 \pm 1.4 mm/s) was reduced (P \leq 0.04). No significant differences were detected in D_A and TRBF (P \geq 0.3). O_{2A}, O_{2V}, and O_{2AV} were 6.5 \pm 1.4 mL O₂/dL, 2.8 \pm 1.9 mL O₂/dL, and 3.7 \pm 1.3 mL O₂/dL in the WT group, respectively. In the 5xFAD group, O_{2A} (7.8 \pm 1.2 mL O₂/dL) and O_{2V} (4.3 \pm 1.6 mL O₂/dL) were increased (P \leq 0.04), while no significant differences were detected in O_{2AV} (P=0.8). In the WT group, MO₂ and DO₂ were 57 \pm 16 nLO₂/min and 107 \pm 39 nLO₂/min, respectively. No differences were detected in MO₂ and DO₂ in the 5xFAD group (P \geq 0.1). Retinal A β 42 was 2.4 \pm 0.8 pg/mg in the WT group and was increased in the 5xFAD group (5.9 \pm 2.9 pg/mg; P=0.04). In the WT group, brain A β 42 was 1.5 \pm 0.5 pg/mg and was increased in the 5xFAD group (5.4 \pm 1.3 pg/mg; P=0.0005).

Conclusions: Taken together, retinal D_V, O_{2A}, and O_{2V} were increased, while V was decreased, whereas MO₂ and DO₂ were not altered in 5xFAD mice with elevated levels of A β 42 protein in the retina and brain.

CONTROL ID: 3530500

SUBMITTER (NAME ONLY): Stefan Yohe

TITLE: In vitro characterization of ranibizumab release from the Port Delivery System

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yohe, K. Maass, J. Horvath, J. Rea, G. Barteselli, S. Ranade, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Port Delivery System with ranibizumab (PDS) is an innovative, investigational drug delivery system designed for the continuous delivery of ranibizumab into the vitreous via diffusion-mediated release kinetics. Target ranibizumab release rates were selected by leveraging clinical and pharmacokinetic (PK) data from trials with intravitreal ranibizumab injections. In vitro testing was used to verify release rates with different ranibizumab concentrations before the phase 2 Ladder trial (NCT02510794) of the PDS in patients with neovascular age-related macular degeneration.

Methods: To mimic the clinical setting in vitro, implants were filled per the clinical "Instructions for Use." Implants with ranibizumab were regularly transferred to new buffer-containing vials to mimic ocular ranibizumab clearance and to sustain similar release kinetics.

A Bradford assay was used to measure released ranibizumab concentrations in each buffer-containing vial. Concentration data were used to calculate an average daily ranibizumab release rate. The activity of ranibizumab released from implants was determined by a Biacore assay. Results from this assay were used to determine a percentage of active ranibizumab, as well as an active ranibizumab release rate. Release rate data were fit using an exponential model to mimic the expected release kinetics of diffusion and compared to predicted release rate kinetics.

Results: Release profiles of the PDS with 3 ranibizumab concentrations (10, 40, and 100 mg/mL) were determined. At day 3.5, mean (SD) ranibizumab release rates were 1.75 (0.07), 6.42 (0.35), and 16.69 (0.67) µg/day for PDS 10, 40, and 100 mg/mL, respectively. At month 6, respective mean (SD) release rates were 1.68 (0.05) and 4.16 (0.05) µg/day for PDS 40 and 100 mg/mL. PDS 100 mg/mL released 73% (SD, 1.92) of drug by month 6. Active drug release from PDS 100 mg/mL was 98%, 88%, and 75% at day 3.5, month 6, and month 12, respectively. Consistent with these data, Ladder serum PK data showed that PDS 100 mg/mL released ranibizumab through at least month 16.

Conclusions: The PDS was designed to release ranibizumab over an extended period of time. Ranibizumab release from the PDS implant was demonstrated to be highly predictable and tunable based on a simple diffusion model. These findings support the median time to first refill of 15.8 months in Ladder PDS 100 mg/mL patients.

CONTROL ID: 3530536

SUBMITTER (NAME ONLY): Karissa Wang

TITLE: Association between geographic distribution of eyecare providers and prevalence of low vision in California

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Low vision and vision impairment present national health concerns due to their association with increased systemic morbidity. Risk factors for low vision including age, gender, and education level have previously been explored, but the potential association between eye care provider availability and low vision has not been thoroughly studied. To address this gap in knowledge, we examined the prevalence and geographic distribution of eye care providers in relation to low vision prevalence in California.

Methods: Data regarding the number of eye care providers in California were obtained from the 2018 American Academy of Ophthalmology records and the 2020 Blue Book of Optometrists. The prevalence of low vision was determined from data reported in the 2014-2018 American Community Survey (ACS). For the purposes of this study, participants who were 18 years or older and reported blindness or difficulty seeing even when wearing glasses were considered to have low vision. The prevalence of eye care providers for each county and Medical Service Study Area (MSSA) in California was calculated as the number of eye care providers, including both ophthalmologists and optometrists, per 100,000 people. The prevalence of low vision at the same geographic areas was calculated as the number of subjects with low vision per 100,000 people. At the MSSA level, linear regression models were performed to determine the association between prevalence of eye care providers and low vision.

Results: Based on ACS data, the population of California who were 18 years and older was 29,594,578. There were 58 counties and 542 MSSAs in California. The prevalence of eye care providers was 22.18 per 100,000 California residents. The prevalence of low vision was 2,411 per 100,000 residents. For the increase of every one eye care provider per 100,000 residents, there was a decrease of 3.32 ± 1.71 per 100,000 in the prevalence of low vision in an unadjusted model. When adjusting for ethnicity, gender, age, income, urbanity of residence location, and access to health insurance, there was a decrease of 6.39 ± 1.35 per 100,000 in the prevalence of low vision for the increase of every one eye care provider per 100,000 residents.

Conclusions: The geographic distribution of eye care providers was widely variable in California. Higher prevalence of eye care providers is potentially associated with decreased prevalence of low vision.

CONTROL ID: 3530569

SUBMITTER (NAME ONLY): Jamie Shaffer

TITLE: Automated plexus differentiation for retinal vessels in OCTA data using deep learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: OCTA data is able to differentiate vasculature from different retinal plexuses. However, the divisions between superficial, deep, and avascular regions are typically based on segmentation of structural layers which may not perfectly correspond to the vascular plexus divisions. In this work we introduce an automated method to divide the vasculature observed in OCTA volumes according to their plexus using only the angiographic (not structural) data.

Methods: Image slabs from 235 OCTA cubes (33 patients) were handcrafted to contain only vascular data belonging to the superficial, deep, or avascular plexus. In addition to this labeled data, thin slabs from the volume were generated as unlabeled data for qualitative model evaluation. Patient-level partitioning was used to separate images into training, validation, and test sets. Two UNet models were trained and validated (Fig 1). Model 1 used single-class images with image augmentation (flip, rotate, contrast). Model 2 added single-patient synthetic images created by blending a randomly placed and sized region from an adjacent class into each image. Models were evaluated on the reserved test set: quantitatively on both single-class slab and 2-class synthetic images and qualitatively on the unlabeled images.

Results: Both models performed well on labeling single-class images ($DICE \geq 0.90$) but less well on 2-class images, particularly when distinguishing deep and avascular regions (Fig 2A). Model 2 performed only marginally better than Model 1, indicating that deep learning algorithms are robust enough to segment multi-class images even when trained only on single class images (Model 1). Predictions on unlabeled slabs were qualitatively evaluated (Fig 2B).

Conclusions: We present a deep learning model that can learn from single-class images and synthetic combinations of those images to annotate the pixels of unlabelled OCTA slabs according to their location within the superficial, deep or avascular plexus. The method looks promising for differentiating the location of different vascular plexuses within an OCTA volume independently from retinal layer structural information.

CONTROL ID: 3530575

SUBMITTER (NAME ONLY): Stuart MacGregor

TITLE: Combining glaucoma and correlated risk factors dramatically expands gene discovery for glaucoma

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Glaucoma is one of the most heritable human diseases and hence mapping the specific genes is expected to both provide insights into disease biology as well as enhance our ability to detect who will be at highest risk. While genome-wide association studies (GWAS) have identified 127 open angle glaucoma risk loci to date, these only account for a small fraction of disease heritability. Traditionally glaucoma genes were mapped using a case-control design but we recently showed (Craig et al, Nature Genetics, 2020) that power to identify genes can be dramatically increased (effective sample size increased 2.5 fold) by augmenting cases and controls with glaucoma risk factor data. Our aim here is to leverage the correlation between glaucoma, intraocular pressure (IOP) and vertical cup to disc ratio (VCDR) to identify novel glaucoma risk loci.

Methods: We conducted a multi-trait analysis of glaucoma and its risk factors, using new and existing GWASs we have collected from around the world (34,179 glaucoma cases, 349,321 controls, supplemented by 111,724 individuals with VCDR and 153,604 individuals with IOP measures, drawn from studies in the International Glaucoma Genetics Consortium, UK Biobank and the Canadian Longitudinal Study of Aging). A key novelty over previous work is that VCDR measures were derived using a machine learning approach instead of using human graders, dramatically improving accuracy and power. The input traits were combined in a multi-trait GWAS framework using the software MTAG; an important feature of the approach is that it generates results which are specific to glaucoma risk.

Results: Our analysis of European ancestry samples identified 263 genome-wide significant loci, with most showing very good concordance in other ancestries. Combining across ancestries further improved power and identified 312 independent loci associated with glaucoma. Novel loci implicated by our analysis include associations at the genes TCF7 (implicating overlapping pathways with cataract) and SYN3 (implicating overlapping pathways with macular degeneration). We are currently working on replicating the novel loci in a large case-control cohort.

Conclusions: This work dramatically expands our knowledge of glaucoma genetics by identifying a large number of new risk loci, providing new insights into glaucoma aetiology and helping enable improved prediction of who is at highest disease risk.

CONTROL ID: 3530577

SUBMITTER (NAME ONLY): Ryan Yanagihara

TITLE: Clinical Characteristics of Patients with Uveitis at Presentation: a Database Study using the American Academy of Ophthalmology (AAO) Intelligent Research In Sight (IRIS[®]) Registry

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.T. Yanagihara, M.S. Hunt, K. McKay, T. Kung, A.Y. Lee, R.N. Van Gelder, C.S. Lee, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveitis is an uncommon but significantly blinding disease. This retrospective database analysis assessed the baseline clinical characteristics of patients in the IRIS Registry presenting with uveitis.

Methods: The first uveitic eye (random eye chosen if bilateral) of each IRIS Registry patient with a new uveitis diagnosis in 2017 was included. Uveitis diagnoses and associated ocular comorbidities were determined by ICD-10 codes. Uveitis cases were anatomically subdivided into: anterior uveitis (AU), intermediate uveitis (IU), posterior uveitis (PU), panuveitis (PanU), scleritis, retinal vasculitis (RV), and “mixed” (scleritis & any intraocular inflammation). Baseline logMAR best corrected visual acuity (BCVA) was measured on the initial date of uveitis diagnosis. Baseline intraocular pressure (IOP) was defined as the maximum IOP on the earliest date within 30 days prior to diagnosis. New patients were defined as those not previously registered in IRIS prior to 2017. Established patients were those seen prior to 2017 who received a new uveitis diagnosis during 2017. Presenting BCVA and IOP were compared against IRIS Registry patients seen in 2017 without uveitis.

Results: PanU had the worst and scleritis had the best mean BCVA at presentation (20/96 and 20/28 Snellen equivalent, respectively) (Figure 1). Presenting IOP was similar among all uveitis subcategories (mean=15.97 mmHg, range=14.66-16.17 mmHg) and controls (mean=15.55 mmHg). However, there was higher variation in the distribution of baseline IOP in uveitis patients compared to controls (Figure 2). AU had the highest rates of glaucoma and cataract at baseline.

Conclusions: Baseline BCVA was worst in PanU and best in scleritis. IOP varied more among patients with uveitis than those without. Glaucoma and cataract were common baseline ocular comorbidities in patients with uveitis.

CONTROL ID: 3530580

SUBMITTER (NAME ONLY): Simon Bello

TITLE: Comparison of macular thickness analysis between a clinical SD-OCT and a low-cost OCT system

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bello, H. Bagherinia, C. Leahy, T. Shagam, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular Thickness Analysis (MTA) is a widely used tool for diagnosing and monitoring patients with ocular pathologies. The robustness of MTA is directly connected to the quality of the optical coherence tomography (OCT) system used to image the eye, which can be limited in low-cost devices. In this study we statistically compare the performance of MTA between a commercial OCT device and a low-cost OCT prototype.

Methods: A low-cost OCT prototype system (ZEISS, Dublin, CA) and a CIRRUSTM HD-OCT 5000 (ZEISS, Dublin, CA) were used to image 70 eyes with a range of ocular pathologies, including age-related macular degeneration (AMD). On each case the resulting OCT volumes were segmented to delineate the inner limiting membrane (ILM) and the retinal pigment epithelium (RPE). The prototype segmentation was used to generate macular thickness maps with 512x512 pixels over an area of 5.78mmx5.78mm. The two maps were registered to each other and the ETDRS grid was centered using the foveal location, manually selected on the CIRRUS scan (Figure 1). The ETDRS grid consists of three concentric circles with radii of 0.5, 1.5 and 2.89mm. A linear regression and Bland-Altman analysis were used to compare the two groups. The coefficient of determination (R^2), slope and intercept of the regression analysis, mean difference and 95% limits are reported for each of the 9 sectors of the ETDRS grid.

Results: A total of 70 eyes from 43 patients were imaged during this study. Table 1 shows the statistical comparison between OCT systems for each sector of the ETDRS grid. The low-cost OCT prototype measured macular thickness slightly higher than the CIRRUS, with mean differences ranging between 4 and 7 microns depending on the retinal sector. R^2 values varied between 0.90 and 0.98.

Conclusions: This study demonstrates the ability of our low-cost OCT prototype to accurately measure macular thickness with similar performance to that of a commercial OCT system. The small differences in thickness measurements are likely not clinically significant and could be compensated. This technology could be useful for monitoring patients with chronic diseases in a cost-efficient way.

CONTROL ID: 3530587

SUBMITTER (NAME ONLY): M. Ali Khan

TITLE: Evaluation of geographic atrophy secondary to age-related macular degeneration in clinical practice: analysis of the American Academy of Ophthalmology IRIS® Registry

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To study patients with geographic atrophy (GA) across clinical practices in the United States and evaluate clinical characteristics and disease progression in patients with GA.

Methods: Retrospective analysis was conducted of patients with ICD-10 codes for GA (extrafoveal or foveal) in ≥ 1 eye from 2016 to 2017 with ≥ 2 years follow-up. Neovascular AMD in the study eye before GA diagnosis was exclusionary. Presenting clinical characteristics, visual acuity (VA) change, and disease progression through 24 months were analyzed.

Results: A total of 256,635 patients were identified, of which 69,441 were eligible for inclusion. Of these, 44,120 (64%) had bilateral GA (GA:GA) and 25,321 (36%) had CNV in the fellow eye (GA:nAMD). Cohorts were balanced for age, gender, and race. In the GA:GA cohort, study eyes with extrafoveal GA had better VA at index (mean 67 letters) compared to those with foveal GA (mean 59 letters). However, over 2 years, changes in VA were similar for both the extrafoveal and foveal lesion groups with a difference of -6.8 and -6.6 mean letters, respectively. Also in this cohort, 16.7% of study eyes progressed from extrafoveal to foveal GA over a median time of 66 weeks; 11.4% of the extrafoveal study eyes and 10.2% of foveal study eyes progressed to nAMD over a median time of 74 and 66 weeks, respectively. In the GA:nAMD cohort, changes in VA values at index and after 2 years were similar to those seen in the GA:GA group. However, patients with fellow-eye nAMD progressed more often to study eye nAMD in both the extrafoveal (29.3%) and foveal (26.0%) lesion categories, over a median time of 63 and 60 weeks, respectively.

Additionally, 12.5% of study eyes in the GA:nAMD cohort progressed from extrafoveal to foveal GA over a median of 61 weeks.

Conclusions: This analysis confirms that GA is a prevalent and progressive disease with deteriorating impact on vision.

CONTROL ID: 3530603

SUBMITTER (NAME ONLY): Xiaoli Guo

TITLE: Pathogenic roles of glial ASK1 signaling in neuroinflammation

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Guo, A. Kimura, K. Namekata, C. Harada, T. Harada, Visual research project, Tokyo Metropolitan Institute of Medical Science, Setagaya, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Apoptosis signal-regulating kinase 1 (ASK1) is a mitogen-activated protein kinase kinase kinase that has been implicated in various neurodegenerative diseases. However, cell type-specific roles of ASK1 during neuroinflammation remain unknown. In the present study, we investigated the roles of ASK1 in different cell types during neuroinflammation by using an animal model of multiple sclerosis, experimental autoimmune encephalomyelitis (EAE).

Methods: ASK1^{flox/flox} mice were crossed with Lck-Cre+, Cd11c-Cre+, LysM-Cre+, GFAP-Cre+ or CX3CR1-CreER mice to generate five lines of double-transgenic mice, namely T cell-, dendritic cell-, microglia/macrophage-, astrocyte- or microglia-specific conditional knockout (CKO) lines. The resulting CKO mice were named as ASK1^{Lck} KO, ASK1^{Cd11c} KO, ASK1^{LysM} KO, ASK1^{GFAP} KO, or ASK1^{CX3CR1} KO mice for simplicity. EAE was induced in female CKO and wild-type (WT) mice at 6-8 week old by immunization with a myelin oligodendrocyte glycoprotein (MOG)₃₅₋₅₅ peptide, and clinical scores were evaluated daily. Histopathological analysis of the optic nerve and spinal cord was performed. Microglia and astrocytes were cultured and used for molecular mechanism analysis. Microarray and qPCR analysis were used to examine gene expression levels.

Results: The severity of paralytic symptoms in ASK1^{Lck} KO EAE and ASK1^{Cd11c} KO EAE mice were comparable to WT EAE mice, and the clinical symptoms observed in ASK1^{LysM} KO EAE and ASK1^{GFAP} KO EAE mice were ameliorated compared with WT EAE mice. Moreover, the ASK1^{LysM} KO EAE mice showed a reduction in clinical scores from the early stage of the disease, while ASK1^{GFAP} KO EAE mice only showed a reduction during the later stage of the disease. The levels of demyelination observed in the optic nerves of ASK1^{LysM} KO EAE and ASK1^{GFAP} KO EAE mice were milder than the level of demyelination found in WT EAE mice. We found that ASK1 signaling in microglia promoted its polarization towards pro-inflammatory microglia, macrophage infiltration into the central nervous system, and stimulated the induction of an A1 phenotype in astrocytes. Furthermore, ASK1 signaling in astrocytes recruits and activates microglia/macrophages in the later stage of EAE, which contributes, at least partly, to maintaining disease.

Conclusions: Glial ASK1 might be a promising therapeutic target for reducing neuroinflammation.

CONTROL ID: 3530604

SUBMITTER (NAME ONLY): M Dominik Fischer

TITLE: Voretigene neparvovec in patients with RPE65 mutation-associated inherited retinal dystrophy: Baseline characteristics from the real-world, prospective, observational PERCEIVE study

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Voretigene neparvovec (VN) is the first ocular gene therapy approved in multiple countries including the USA and Europe for treating patients (pts) with visual impairment due to confirmed biallelic RPE65 mutation-associated inherited retinal dystrophy having sufficient viable retinal cells. PERCEIVE, a registry-based post-authorization safety study, is designed to assess long-term safety of VN in a real-world (RW) setting. Here, baseline characteristics of participating pts treated with VN up to August 2020 are reported.

Methods: PERCEIVE is an ongoing, prospective, longitudinal, multicenter (ex-US), observational, safety study, which commenced December 2019 with the aim to enroll a minimum of 40 pts. All VN-treated pts are encouraged to participate in the study to maximize data collection, including those treated prior to study inception. After receiving VN as per local prescribing information, pts are followed-up as per the routine medical care for 5 years. The objectives are to characterize the long-term safety profile of VN via systematic collection of adverse event data, to follow pregnancy outcomes and assess visual function over time.

Results: Until data cut-off (Aug 2020), of the 15 pts enrolled, 10 pts (16 eyes) have received VN (6 bilateral; 4 unilateral). All treated pts are from Europe (Germany: 6; France: 3; Austria: 1). At the time of enrollment, the mean (standard deviation [SD]) age was 27.6 (9.81) years with a range of 15–51 years (1 adolescent; 9 adults). The majority of treated pts are female (n=7; 70%). For the treated eyes (n=16), baseline mean (SD) visual acuity was 0.96 (0.37) logMAR (n=14; range: 0.5–1.6 logMAR) and full-field stimulus threshold (white light) was –4.32 (9.40) dB (n=15; range: –34.9 to 3.2 dB). Optical coherence tomography (OCT) revealed a mean foveal thickness of 150.5 (41.07) µm (n=15; range: 76–216 µm). Central OCT showed that 11 eyes had an outer nuclear layer with a thickness range of 36–74 µm (n=9), while it was absent in 4 eyes. The ellipsoid zone line was disrupted in 9 eyes and was undetected in 6.

Conclusions: While enrollment and in person follow-up of VN-treated pts has been impacted due to COVID-19, PERCEIVE has started to provide valuable information on baseline characteristics of this vision-impaired population, and effect of VN therapy in a RW setting.

CONTROL ID: 3530624

SUBMITTER (NAME ONLY): Verena Schmid

TITLE: Effect of retinoschisin on compartmentalization on novel interaction partners of the retinal Na/K-ATPase-retinoschisin complex

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Schmid, B.H. Weber, U. Friedrich, Institute of Human Genetics, University of Regensburg, Regensburg, GERMANY|A. Bruckmann, Regensburg Center for Biochemistry (RCB), Laboratory for RNA Biology, University of Regensburg,, Regensburg, GERMANY|

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ABSTRACT BODY:

Purpose: Mutations in the RS1 gene cause X-linked juvenile retinoschisis (XLRS), a hereditary retinal dystrophy in juvenile or adolescent males. Recently, we and others showed that the retinoschisin protein encoded by RS1 binds to the retinal Na/K-ATPase and modulates its localization in the plasma membrane of photoreceptors. In this study, we aimed to identify interaction partners of the Na/K-ATPase-retinoschisin complex. Specifically, we were interested to examine an influence of retinoschisin on the localization of selected interaction partners, namely the voltage-gated potassium ion channels (Kv). This should provide new insights into the role of retinoschisin as a putative regulator of photoreceptor membrane compartmentalization.

Methods:

Porcine retinal lysates were subjected to co-immunoprecipitation targeting the $\alpha 3$ -subunit of the Na/K-ATPase (ATP1A3). Bound proteins were eluted and separated by SDS-PAGE for mass spectrometric analysis. Recognized proteins were verified in co-immunoprecipitation experiments with murine retinal lysates. Localization of Kv was investigated via immunohistochemistry in eyes from wildtype (wt) and retinoschisin-deficient (Rs1h knockout, Rs1^{tm1Web}) mice. Effect of retinoschisin on thermal stability and total protein level was investigated in Y79 cells or retinoschisin-deficient murine retinal lysates, respectively.

Results: Mass spectrometry from co-immunoprecipitates of porcine retinal lysates targeting ATP1A3 identified the Kv subunits Kv2.1 and Kv8.2. Binding to the retinal Na/K-ATPase was verified in further co-immunoprecipitations with murine retinal lysates. Immunohistochemical analyses in murine retinal cryosections revealed Kv localization to the inner segments and plexiform layers, like observed for the Na/K-ATPase. In retinae from retinoschisin-deficient mice, Kv2.1 and Kv8.2 distribution and total protein amount was altered compared to wt retinae. In contrast, no effect of retinoschisin was noted on thermal stability for Kv2.1 and Kv8.2.

Conclusions: Our data suggest that Kv subunits Kv2.1. and Kv8.2 are part of a macromolecular complex together with the Na/K-ATPase and retinoschisin. Defective compartmentalization of the retinal Na/K-ATPase and its complexing partners may be an initial step in XLRS pathogenesis.

CONTROL ID: 3530638

SUBMITTER (NAME ONLY): Mikel Aldaba

TITLE: Extended measured area tear film stability assessment method by corneal reflex image degradation.

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Aldaba, F. Diaz Douton, J. Pujol, Centre for Sensors, Instruments and Systems Development, Universitat Politècnica de Catalunya, Barcelona, Catalunya, SPAIN|

Commercial Relationships Disclosure (Abstract): Mikel Aldaba: Commercial Relationship(s);Universitat Politècnica de Catalunya:Code P (Patent) | Fernando Diaz Douton: Commercial Relationship: Code N (No Commercial Relationship) | Jaume Pujol: Commercial Relationship(s);Universitat Politècnica de Catalunya:Code P (Patent)

ABSTRACT BODY:

Purpose: Recently a new method for the tear film stability measurement based on the corneal reflex image degradation has been proposed (Aldaba et al. "Tear film stability assessment by corneal reflex image degradation". JOSA A, 36(4), B110-B115). The method on its original version is simple, objective, and non-invasive, but has a main limitation: the reduced measured area. We present a modified version of the method that extends the measured area.

Methods: A new optical design of the original setup for tear film stability measurement based on corneal degradation has been proposed. The new design is based on having normal light incidence on the corneal plane, to do so, the focus of the incident light falls on the center of curvature of the cornea. Four different lenses that theoretically provided a large measured area have been tested: 1) glass spheric lens, 50.00mm focal length, 50.00mm diameter, 2) glass aspheric lens, 50.00mm focal length, 50.00mm diameter, 3) plastic aspheric lens, 35.74mm focal length, 35.00mm diameter, 4) plastic aspheric lens, 49.80mm focal length, 51.00mm diameter. The incidence beam area at corneal plane was measured recording an image at this plane and counting the number of pixels that form the beam. The optical quality of the system was evaluated for each lens by means of the full width at half maximum of the recorded image when using an ophthalmic lens as artificial cornea (PMMA material and radius of curvature 8mm).

Results: The measured incidence beam area for the four tested lenses was: 1.79mm for lens #1, 7.72mm for lens #2, 3.36mm for lens #3 and 7.04mm for lens #4. The full width at half maximum (the lower the value the better the image quality) of the recorded image with the artificial cornea was of 8 pixels for lens #1, 4 pixels for lens #2, 5 pixels for lens #3 and 20 pixels for lens #4.

Conclusions: A new optical design for increasing the measured area of the tear film stability method based on corneal reflex image has been proposed. The new design is based on the normal incidence of the incident beam on the cornea. Four lenses were tested in the setup; two were discarded due to small beam diameter and one due to poor optical quality. One of the lenses provided the desired beam diameter and optical quality, permitting the improvement of the method.

CONTROL ID: 3530641

SUBMITTER (NAME ONLY): Werner Eisenbarth

TITLE: Algorithm based refraction – our new gold standard?

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

The determination of subjective far and near refractions is a central part of an optometric examination and its determination is yet to be challenged. Still, more and more digital and algorithm-based methods are available. This study investigated whether the algorithm-guided subjective far refraction (QuickPro) of the EyeRefract VX160 and its near refraction determination is comparable with a conventional, subjective refraction determination.

Methods: 96 persons took part in this study (spherical equivalent M = - 11.39 D to + 6.26 D, age: 39 ± 15 years). Two types of measurements were compared: QuickPro (algorithm-guided subjective far refraction) vs. conventional procedure (DNEye® Scanner 2 and subjective refraction). The near refraction (addition) was carried out both using the EyeRefract (Jackson-Cross method) and using a trial frame and Duane's figure.

Results: The differences between the two methods (QuickPro vs. DNEye® Scanner 2 + subjective refraction) showed statistically significant but clinically irrelevant differences: $\Delta M = - 0.20 \pm 0.35$ D ($p < 0.001$); $\Delta J0 = 0.07 \pm 0.14$ D ($p < 0.001$); $\Delta J45 = - 0.02 \pm 0.13$ D ($p = 0.445$). A subjective refraction based on the aberrometer measurement (DNEye® Scanner 2) took 10.55 ± 2.34 min while a QuickPro measurement 6.77 ± 2.14 min.

Statistically significant differences were found for the addition values (EyeRefract VX160: $+1.06 \pm 0.90$ D, trial frame: $+0.70 \pm 0.80$ D, $p < 0.001$) as well as its measurement time (EyeRefract VX160: 2.18 ± 0.84 min, trial frame: 4.36 ± 1.60 min, $p < 0.001$).

Conclusions: The refraction determination with the EyeRefract VX160 requires significantly less time for both the QuickPro measurement and the addition determination than a conventional procedure. In around 90% of all cases, QuickPro algorithm achieved precise measurement results across all correction values, which correspond to those of a conventional refraction determination.

CONTROL ID: 3530645

SUBMITTER (NAME ONLY): Jacob Brubaker

TITLE: Rate of bimatoprost implant biodegradation in the phase 3 ARTEMIS studies

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Bimatoprost implant 10 µg (Durysta) is a biodegradable, intracameral implant (cylindrical diameter ~200 µm, length ~1.1 mm) that releases bimatoprost steadily to lower intraocular pressure and eventually converts to water and CO₂. The implant elutes bimatoprost for ~4 months but the polymers in the implant matrix may last longer. We evaluated the rate of biodegradation of the implant in our randomized, controlled phase 3 clinical trials.

Methods: Two 20-month, phase 3 trials (NCT02247804, NCT02250651) randomized 1 eye per patient with open-angle glaucoma or ocular hypertension to an intracameral 10- or 15-µg bimatoprost implant administered on Day 1, Weeks 16 and 32 or topical timolol 0.5% BID. Estimated implant size on gonioscopy as a percentage of the initial size was recorded. We pooled data for the 10-µg implants placed on Day 1 in both trials for analysis. The population mean implant size (expressed as the percentage of the initial size) over time was modeled with a nonlinear mixed-effects model with repeated measures (MMRM) approach. The rate of biodegradation was defined as the decrease in implant size (expressed as a percentage of the initial size) per month.

Results: A total of 230 eyes were included in the analysis. Implant size data were best fit to a model that considered inter-patient variability and included an exponential function for the implant size decrease (Figure). The estimated mean (± standard error) percentage decrease in implant size from baseline was 24.1% ± 2.3% at Week 28 and 80.2% ± 1.5% at Week 52. The estimated mean rate of implant biodegradation was 3.7%/month through Week 28, 10.2%/month after Week 28 through Week 52, and 2.4%/month after Week 52 through Month 20.

Conclusions: The estimated mean size of 10-µg bimatoprost implant administered on Day 1 in phase 3 trials decreased according to an exponential function, which allows one to predict the size of a single or multiple implants in the AC. Clinical studies are in progress to further understand implant biodegradation and the ideal timing for implant re-administration.

CONTROL ID: 3530653

SUBMITTER (NAME ONLY): An-Katrien Minnaert

TITLE: Enzyme-modified nanoparticles as a possible strategy for safe and effective vitreous liquefaction

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Minnaert, K. Peynshaert, A. Harizaj, M. Wels, F. Sauvage, S. De Smedt, K. Remaut, Laboratory of General Biochemistry and Physical Pharmacy, Universiteit Gent Faculteit Farmaceutische Wetenschappen, Gent, BELGIUM|

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ABSTRACT BODY:

Purpose: When people age, liquefaction of the vitreous can result in Posterior Vitreous Detachment (PVD), routinely treated by a vitrectomy. Unfortunately, this procedure is invasive and risky since it might lead to complications such as retinal tears. As an alternative, we explored enzymatic vitreolysis both as a replacement or pre-treatment to vitrectomy. To this end, we aimed to immobilize enzymes on the surface of nanoparticles (NPs) to minimize enzyme-induced toxicity caused by retinal penetration and thus generate safe and effective vitreous liquefaction.

Methods: NPs and enzyme were incubated for 24 hours at room temperature under continuous stirring. Next, multiple centrifugation cycles were performed in order to remove the free enzyme. The activity of the enzyme-modified NPs in vitro was evaluated by measuring substrate-FITC-fluorescence with a plate-reader. The fluorescence intensity of the FITC-labeled substrate increased upon degradation by the enzyme. Additionally, ex vivo activity experiments in bovine vitreous were performed using single particle tracking (SPT). SPT measurements allow mobility tracking of fluorescent particles. We used fluorescent beads which are immobile in vitreous but are able to diffuse upon vitreous liquefaction. Finally, potential penetration of the enzyme-modified NPs into the retina upon injection in bovine vitreo-retinal explants was determined with confocal microscopy. Necessary controls with non-modified NPs and/or free enzyme were performed in every experimental set-up.

Results: We repeatedly succeeded in generating stable 300 nm NPs with an in vitro activity of 170 units/100 μ L sample. SPT experiments validated that we could generate sufficient vitreous liquefaction. Upon treatment of the bovine vitreous with enzyme-modified NPs, the mobility of injected fluorescent beads increased enormously. As expected, microscopy imaging showed clear alignment of the enzyme-modified NPs at the inner limiting membrane (ILM) while no penetration to the retina could be observed. Finally, we could not see significant structural retinal changes in the vitreo-retinal explants upon treatment with the enzyme-modified NPs.

Conclusions: This study showed that enzyme-immobilization is a promising technique for effective vitreous liquefaction. Future goals include extensive toxicity studies both ex vivo and in vivo to provide more information about the safety of this therapy.

CONTROL ID: 3530664

SUBMITTER (NAME ONLY): Dimitrios Damopoulos

TITLE: Predicting the development of clinically significant macular edema (CSME) in patients with mild nonproliferative diabetic retinopathy (NPDR) using machine learning (ML)

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Damopoulos, A. Neubert, B.G. Armendariz, R. Weikert, F. Benmansour, F Hoffmann-La Roche AG, Basel, Basel-Stadt, SWITZERLAND|L. Mendes, T. Santos, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|D. Ferrara, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop and evaluate ML models employing systemic and/or retinal imaging features for predicting whether patients with mild NPDR will develop CSME within 2 years from baseline.

Methods: Systemic and retinal imaging features (optical coherence tomography and color fundus photographs) from 348 patients (129 female; mean age, 60.9 years) with mild NPDR (Diabetic Retinopathy Severity Scale [DRSS] 20–35) and type 2 diabetes enrolled in a cohort study (NCT00763802) were pooled. Data were acquired 6 months (M6) and 2 years (M24) after baseline. Linear regression models were evaluated for predicting these events using systemic data only, imaging features only, and both combined. Area under the receiver operating characteristics (AUROC) curve was employed as a performance metric.

Results: Table 1 presents a summary of data acquired at baseline, M6, and M24. Twelve patients developed CSME in the study eye by M6, and 34 patients by M24. When using data obtained at baseline, CSME at M24 was predicted with an AUROC = 0.550 (95% CI, 0.521, 0.580) with systemic data; 0.727 (95% CI, 0.700, 0.753) with imaging features; and 0.734 (95% CI, 0.708, 0.760) with both combined. When using data from M6, CSME at M24 was predicted with an AUROC = 0.536 with systemic data, 0.734 with imaging data, and 0.713 with both combined. When using data combined from both M6 and baseline, CSME at M24 was predicted with an AUROC = 0.508 with systemic data, 0.749 with imaging features, and 0.738 with both combined. These results are summarized in Table 2.

Conclusions: Our results indicate that development of CSME in patients with mild NPDR can be more accurately predicted with retinal imaging features than with systemic data on their own. When predicting the development of CSME by M24 using data obtained at M6 only, the performance was not significantly different compared with using both baseline and M6. In the future, we plan to extend the evaluation to larger datasets, allowing more confident conclusions regarding the performance and predictive potential of the different types of data. Such predictive models of CSME in patients with NPDR could be employed to inform personalized monitoring and follow-up.

CONTROL ID: 3530675

SUBMITTER (NAME ONLY): Antonio Mateo-Orobia

TITLE: Efficacy of Artificial Tears Containing Trehalose and Hyaluronic Acid (Thealoz Duo[®]) for Dry Eye Disease (DED in Peri- and Postmenopausal Women)

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. . Mateo-Orobia, A. Blasco Martínez, E. Del Prado Sanz, L. Pablo Julvez, V. Polo Llorens, N. Lafuente Ojeda, D. Soriano Pina, M. Idoipe Corta, Ophthalmology, Hospital Universitario Miguel Servet, Zaragoza, Aragón, SPAIN|

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ABSTRACT BODY:

Purpose: Postmenopausal women have a high incidence of DED, probably due to sex hormone imbalances. This study evaluated efficacy of a 3-month daily treatment with artificial tears containing trehalose and hyaluronic acid in peri- and postmenopausal women with moderate and severe DED

Methods: This was a post hoc analysis of peri- and postmenopausal women (ages 42-54 and ≥ 55 years, respectively) with an Ocular Surface Disease Index (OSDI) ≥ 18 who had participated in a Phase III (NCT02023268) and a Phase IV (NCT02617095) studies assessing the efficacy of artificial tears containing trehalose (30 mg/mL) and hyaluronic acid (1.5 mg/mL) on the signs and symptoms of DED Patients instilled one drop of the artificial tears in each eye 3 to 6 times daily and were evaluated at baseline and after 84 ± 7 days for DED symptom severity (measured with the OSDI), visual acuity (Snellen optotype), hyperemia (MacMonnies scale), tear break-up time (TBUT, fluorescein), corneal and conjunctival staining (Oxford and Van Bijsterveld scales), tear production (Schirmer's test), and symptoms (visual analogue scale).

Results: A total of 59 women were analyzed (16 perimenopausal; 43 postmenopausal, mean \pm SD age= 48.6 ± 4.2 and 66.9 ± 8.0 years, respectively). After 84 days of treatment, the OSDI (mean \pm SD) decreased from 59.2 ± 24.7 to 22.9 ± 17.3 in perimenopausal and from 52.6 ± 20.7 to 29.1 ± 24.3 in postmenopausal women (both $p < 0.0001$). Visual acuity remained unchanged in both groups. Conjunctival hyperemia, TBUT, and corneal and conjunctival staining with fluorescein or lissamine green improved significantly in both groups (all $p < 0.0001$). Tear production also increased in peri- ($p = 0.0101$) and postmenstrual women ($p = 0.0005$). Conjunctival hyperemia, TBUT, and corneal and conjunctival staining (Oxford scale) improved more significantly in peri- than postmenopausal women. Severe symptoms at baseline and absence of symptoms at day 84 were also reported more frequently by peri- than postmenopausal women.

Conclusions: Signs and symptoms of DED improved significantly in peri- and postmenopausal women treated for 3 months with artificial tears containing trehalose and hyaluronic acid, suggesting that it is an effective treatment for eye dryness in this population. Improvement was often significantly greater in peri- than in postmenopausal women.

CONTROL ID: 3530681

SUBMITTER (NAME ONLY): Mitchell deLong

TITLE: The Synthesis and Testing of Rho Kinase Inhibitors Reversibly Coupled to Corticosteroids for the Treatment of Ocular Inflammatory Diseases

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. deLong, K. Crews, J.M. Sturdivant, A. Glendenning, M. Germann, Chemistry, Aerie Pharmaceuticals Inc, Durham, North Carolina, UNITED STATES|C. Kelly, B. Foley, D. Clancy, J. White, Biology, Aerie Pharmaceuticals Research and Development, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corticosteroids are valuable for controlling ocular inflammation. Their use is limited due to their side effects, including the induction of steroid-induced glaucoma and ocular hypertension (OHT). While the mechanism of this is unclear, fibrosis and excess collagen deposition in the trabecular meshwork (TM) have been described in patients with steroid-induced glaucoma. Compounds that inhibit Rho kinases (ROCK inhibitors) have been shown to reduce deposition of collagen in cultured TM cells. ROCK inhibition also lowers intraocular pressure (IOP) in vivo by increasing aqueous humor TM outflow. We have shown (IOVS 61(7):2953 June 2020) that a rho kinase inhibitor coupled to a corticosteroid reduces inflammation in animal models. To further investigate this new class of molecules, and to optimize activity and stability, a series of novel molecules were synthesized and tested.

Methods: Aerie successfully developed the ROCK inhibitor netarsudil as a treatment for glaucoma (Rhopressa™). Molecules from that research that contain hydroxyl groups were esterified to short chain diacids that were then coupled to steroids. To demonstrate timely enzymatic release of these two moieties, esterase assays have been performed, including with porcine-liver esterase. Retention of ROCK inhibitory activity and steroidal activity were demonstrated in kinase assays and cell lines. Compounds were evaluated for aqueous solubility and stability.

Results: Compounds A-E demonstrated considerable variability in both formulation stability and esterase sensitivity. Multiple compounds displayed potent, often single-digit nM cellular activity in one or more in vitro whole cell assays. Compound A demonstrated an extrapolated stability and activity profile that is suitable for progression. These molecules also demonstrated excellent thermal stability, and sufficient solubility to allow for ophthalmic formulation.

Conclusions: This proprietary class of ROCK inhibitor-linked corticosteroids has demonstrated potent enzymatic and cellular ROCK inhibitory activity, cellular steroidal activity, suitable in vitro and ex vivo metabolism, formulation stability under conditions needed for manufacturing, and anti-inflammatory and IOP-lowering activity in animal models. Compound A in this class of molecules is under further study for the treatment of ocular inflammatory disease.

CONTROL ID: 3530685

SUBMITTER (NAME ONLY): Varun Chaudhary

TITLE: Association between visual acuity and intraretinal (IRF) or subretinal (SRF) fluid in patients with neovascular age-related macular degeneration (nAMD) treated with intravitreal aflibercept (IVT-AFL) treat-and-extend (T&E): a post-hoc analysis of the ARIES study

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To explore the relationship between IRF/SRF and best-corrected visual acuity (BCVA) in patients with nAMD treated with IVT-AFL to guide treatment extension decisions.

Methods: ARIES (NCT02581891) was a multicenter, randomized, Phase 3b/4 study that compared the efficacy of 2 different IVT-AFL T&E dosing regimens over 2 years in treatment-naïve patients with nAMD. This post-hoc analysis explored the relationship between presence of fluid (SRF and IRF) and BCVA by describing absolute BCVA by fluid subgroups at baseline (BL) and by fluid status at fixed visits (Weeks [w] 4, 8, 16, 52, and 104).

Results: The per-protocol set comprised 210 patients (two treatment arms combined). Absence of SRF at BL was associated with lower BCVA (5–10 less letters) than if SRF was present; furthermore, at every timepoint, the absence of SRF was associated with poorer BCVA (letters) than if SRF was present (no SRF vs SRF: 64.5 vs 67.2 [w4]; 66.3 vs 68.5 [w8]; 66.4 vs 70.7 [w16]; 68.3 vs 73.6 [w52]; 65.4 vs 72.9 [w104]). Presence of IRF at BL was associated with

lower BCVA (7–9 less letters) than if IRF was absent; furthermore, at most timepoints, presence of IRF was associated with poorer BCVA (letters) than if IRF was absent (IRF vs no IRF: 61.2 vs 65.9 [w4]; 66.6 vs 66.8 [w8]; 59.0 vs 69.3 [w16]; 66.2 vs 70.0 [w52]; 70.1 vs 67.4 [w104]). The presence of both SRF+IRF at BL was associated with lower BCVA (6–8 less letters) than if only SRF was present but was associated with a higher BCVA (3–9 more letters) than if only IRF was present. Absence of SRF+IRF was not associated with better BCVA (letters) at any timepoint (no fluid vs fluid: 64.7 vs 66.8 [w4]; 66.5 vs 67.7 [w8]; 67.3 vs 69.2 [w16]; 68.5 vs 72.6 [w52]; 65.3 vs 71.9 [w104]).

Conclusions: In ARIES, IVT-AFL T&E was effective at reducing fluid and improving vision in treatment-naïve nAMD eyes regardless of fluid type. Post-hoc analyses showed that good functional outcomes were achieved in the presence of SRF, whereas IRF was consistently associated with poorer functional outcomes. These findings indicate the need to differentiate SRF and IRF as surrogate markers for BCVA, in order to guide treatment extension decisions.

CONTROL ID: 3530703

SUBMITTER (NAME ONLY): Polina Geva

TITLE: Location of photoisomerization in the rod outer segment affects photon response variability

SESSION TITLE: Photoreceptors

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Retinal rods count photons to provide for vision when the lighting is very dim. To do so, they must generate reproducible single photon responses (SPRs). The rod outer segment has a multilayered structure built from disks containing one or more incisures. We seek to understand how outer segment length, disk diameter and incisures impact SPR reproducibility

Methods: A fully space-resolved mathematical model of rod phototransduction and single cell recordings were used to analyze how the location of rhodopsin photoisomerization on the disk surface affects SPR amplitude and kinetics. In addition, the contribution of an axial concentration gradient of bicarbonate to response variability was evaluated electrophysiologically.

Results: Modeling showed that a photoisomerization at the edge of the disk edge elicits a larger, faster SPR than a photoisomerization in the disk center. This is because local depletion of cGMP at the disk rim, near the plasma membrane, closes more ion channels with a shorter delay compared to the changes that occur after a photoisomerization at the disk center. These variations, arising primarily in the rising phase of the SPR, increase in significance with disk diameter. A symmetric pattern of incisures attenuates the variability. Single cell recordings of large salamander rods confirmed that photoisomerizations at the disk edge gave rise to faster SPRs than photoisomerizations occurring randomly on the disk surface.

Bicarbonate is known to accelerate SPR recovery. It is taken up at the rod synapse, after which it diffuses to the outer segment where it is extruded by an anion exchanger.

Electrophysiology recording of long outer segment toad rods demonstrated faster rising and recovery phases at the base vs tip of outer segment without bicarbonate. Surprisingly, this difference was attenuated with bicarbonate

Conclusions: Randomness in the radial location of rhodopsin photoisomerization on the disk contributes to SPR variability, particularly for large disk diameters, but variability can be attenuated by incisures. Randomness in the longitudinal location of the photoisomerization contributes additional variability to the SPR. Bicarbonate produces the SPR less variable though the outer segment.

CONTROL ID: 3530720

SUBMITTER (NAME ONLY): John Neseemann

TITLE: Prevalence of Trachoma in Alto Amazonas, Loreto Department, Perú

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Pan American Health Organization (PAHO) has identified trachoma as a potential public health problem in Perú. We performed a cross-sectional study to determine the prevalence of trachoma in Alto Amazonas, Perú.

Methods: We selected 22 communities via probability-proportional-to-size sampling after excluding urban areas. In a random selection of approximately 30 households per community, all children aged 1-9 were examined for trachomatous inflammation—follicular (TF) and trachomatous inflammation—intense (TI), and individuals aged 15+ years were evaluated for trachomatous trichiasis (TT), i.e., upper lid trichiasis, using the World Health Organization's (WHO) 2018 amended trachoma grading system. Each child's right conjunctiva was swabbed and tested for Chlamydia trachomatis DNA.

The community level prevalence of TF, TI, and ocular C. trachomatis was adjusted for age in one-year bands and TT prevalence was adjusted using 5-year age bands. The overall prevalence of each outcome was the mean of the age-adjusted community level prevalence. 95% confidence intervals were calculated using bootstrapping methods with resampling at the community level (10,000 replications).

Results: One community refused. The location and number examined in the other 21 communities are shown in Figure 1. 617 selected households were enumerated, with 873 children aged 1-9 and 1313 adults 15+ eligible for examination of whom 778 (89.1%) and 1003 (76.4%) were examined, respectively. On average, the prevalence of TF among 1–9-year-olds was 32.6% and the prevalence of ocular C. trachomatis was 0.8% (Table 1). The prevalence of TT among individuals ≥15 years was 0.06%.

Conclusions: The overall prevalence of TF was above the WHO 5% threshold for active trachoma as being a public health problem. Consequently, the area is eligible for the implementation of trachoma elimination interventions, including annual mass administration of antibiotics for at least 5 years. The discrepancy between high TF and low ocular C. trachomatis prevalence requires further investigation.

CONTROL ID: 3530743

SUBMITTER (NAME ONLY): Ales Neubert

TITLE: Interpretable, feature-based predictive modeling of low and high treatment requirements in nAMD using SD-OCT

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Neubert, A. Thalhammer, A. Maunz, Roche Pharma Research and Early Development Informatics, Basel, SWITZERLAND|J. Dai, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an interpretable machine learning (ML) model to predict anti-VEGF treatment requirements for patients with neovascular age-related macular degeneration (nAMD).

Methods: Patients from the ranibizumab 0.5 and 2.0 mg as-needed arms of HARBOR (NCT00891735) who received monthly anti-VEGF injections during a 3-month initiation phase were included. Boundaries of five retinal layers, intra- and subretinal fluid, subretinal hyperreflective material (SHRM), and pigment epithelial detachment (PED) were automatically segmented using ML-based algorithms from spectral-domain optical coherence tomography (SD-OCT) volume scans acquired at each visit. Segmentation results were used to extract quantitative features of layer and fluid features (69 layer and 36 fluid features). BCVA and central subfield thickness (CST) measured at the 3 visits were also included. Low and high treatment groups were defined as requirement of ≤ 5 or ≥ 16 injections, respectively, in the 21 months after the initiation phase. Extreme gradient-boosting ML model was used for binary classification (low or high treatment) using stratified 5-fold cross-validation. Feature importance was analyzed using SHapley Additive exPlanations (SHAP).

Results: Data from 363 patients were analyzed. Low and high treatment groups included 82 and 83 patients, respectively, with mean (\pm SD) area under the receiver operating characteristic curve scores of 0.81 ± 0.06 and 0.80 ± 0.08 (Fig 1). Low treatment need was most strongly associated with low presence of detected PED at month 2. High treatment need was most strongly associated with low presence of SHRM at month 1, low presence of IRF at day 0 and presence of IRF at month 1 (Fig 2).

Conclusions: This exploratory study showed the feasibility of identifying low or high treatment needs for patients with nAMD using predefined imaging features from automated fluid and layer SD-OCT segmentations. Further confirmation of model performance will contribute to future development of personalized healthcare algorithms.

CONTROL ID: 3530751

SUBMITTER (NAME ONLY): Ronald Silverman

TITLE: Retrobulbar blood flow in rat eyes in acute ocular hypertension

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Silverman, R. Urs, G. Tezel, X. Yang, I. Nelson, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J.A. Ketterling, Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Most studies of the effect of acute elevation of intraocular pressure (IOP) on ocular blood-flow have focused on retinal and choroidal flow. This study determined the effect of acute changes in IOP on blood flow velocity in the retrobulbar arteries and veins supplying and draining the eye in a rat model.

Methods: We inserted a 30-gauge needle into the anterior chamber of Sprague-Dawley rats and increased IOP in 10 mm steps to 60 mmHg and then returned to 10 mmHg. After 1 minute at each pressure level (and 3 minutes after return to 10 mmHg), we used a 128-element, 18 MHz linear array probe to acquire plane wave ultrasound data at 3000 images/sec for 1.5 sec. Each image was formed by compounding transmits at 6 angles over ± 6 degrees. After applying a singular value decomposition filter to suppress echo data from slow-moving or stationary tissues, we generated color-flow Doppler images, identified retrobulbar veins and arteries and produced spectrograms from which systolic, diastolic and mean flow velocity and resistance indices were determined (Fig 1). Twenty eyes (1 eye per rat) were examined.

Results: Baseline mean arterial and venous velocities averaged 30.9 ± 10.8 and 8.5 ± 3.3 mm/sec, respectively. Arterial velocity progressively decreased at and above an IOP of 30 mmHg (Fig 2). At 60 mmHg, mean arterial velocity dropped by 55% with respect to baseline, venous velocity decreased by 20% and pulsatility index increased by 75%. Arterial and venous velocities and resistance indices returned to near baseline after IOP was restored to 10 mmHg.

Conclusions: Ocular hypertension directly compresses the retinal and choroidal vasculature, but only indirectly affects the retrobulbar circulation. Our results show progressively decreasing retrobulbar arterial velocities and increasing pulsatility at and above an IOP of 30 mmHg. Venous flow velocity decreased as well, but not as profoundly. The increase in retrobulbar arterial pulsatility index is consistent with compression of retinal vessels. Although the more moderate decrease in venous velocity could be artifactual due to reduced sensitivity to slow-flow, it may be attributable to a decrease in retrobulbar venous lumen diameter as venous blood pressure dropped with decreased volumetric outflow.

CONTROL ID: 3530778

SUBMITTER (NAME ONLY): Yusuke Kikuchi

TITLE: A pilot study using machine learning (ML) to predict treatment outcomes in patients with neovascular age-related macular degeneration (nAMD) using phase 2 trial data

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kikuchi, M. Kawczynski, N. Anegondi, J. Dai, C. Quezada Ruiz, Genentech Inc, South San Francisco, California, UNITED STATES|Y. Kikuchi, Department of Industrial Engineering and Operations Research, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop ML models to predict treatment outcomes in patients with nAMD using baseline (BL) characteristics and optical coherence tomography (OCT) imaging data from patients treated with faricimab in the phase 2 AVENUE (NCT02484690) trial.

Methods: 185 faricimab-treated eyes (80% training; 20% test) were included. 5-fold cross-validation was performed on the training set. Age, gender, best-corrected visual acuity (BCVA), central subfield thickness (CST), low-luminance visual acuity, and OCT images on study day 1, together with treatment assignment, were included in the model. Regression and binary classification models were developed to predict BCVA at month 9 and CST reduction of >35% at month 9, respectively. Symbolic models (linear model and extreme gradient boost tree) were trained on BL characteristics, and deep neural networks (DNNs; based on Inception-v3 with ImageNet weights) were trained on B-scans. Image data and BL characteristics were merged using: (1) a model stacking approach, which uses the prediction from the DNN as one of the input features for the symbolic model, and (2) a model averaging approach, which averages predictions from the DNN using OCT volume and from the symbolic model using BL characteristics.

Results: The BL linear model had an R^2 score of 0.30 and area under the receiver operating characteristic (AUROC) of 0.87. The BL DNN showed an R^2 score of 0.079 for BCVA regression and AUC of 0.70 for CST reduction binary classification. After model stacking with linear model, R^2 score and AUC were 0.32 and 0.87, respectively. The model averaging approach with linear model showed an R^2 score of 0.27 and AUC of 0.85.

Conclusions: The results suggest that the most predictive features for both BCVA and CST at month 9 were captured in BL measurements, and adding image data did not show significant improvements after stacking or averaging given the sample size. This pilot study highlights the potential for ML to support clinicians to make treatment decisions for optimal patient outcomes. To fully explore the predictive capacity of models using image data and ascertain benefits of combining image data with BL characteristics, the methodology needs to be validated on a larger data set.

CONTROL ID: 3530797

SUBMITTER (NAME ONLY): Mansour Rahimi

TITLE: Variability of Retinal Oxygen Metrics in Healthy and Diabetic Subjects

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Rahimi, S. Leahy, M. Shahidi, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|N.P. Blair, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have reported alterations in total retinal blood flow (TRBF), oxygen delivery (DO_2), oxygen metabolism (MO_2), and oxygen extraction fraction (OEF) due to various retinal diseases. The purposes of the current study were to determine intra- and inter-visit variabilities and establish normal 95% confidence intervals (CIs) for these metrics.

Methods: Twenty-two non-diabetic healthy and 14 diabetic subjects diagnosed with either no diabetic retinopathy (DR) or untreated mild non-proliferative DR participated in the study. Imaging was performed at one visit in healthy subjects and two visits in diabetic subjects. Retinal vascular oxygen saturation (SO_2) and multiple TRBF measurements were obtained using our oximetry system and Doppler optical coherence tomography, respectively. DO_2 , MO_2 , and OEF were calculated from SO_2 and mean TRBF. Intra-visit variability of TRBF was determined by the standard deviation (SD) of multiple measurements, averaged over data in each group. Normal 95% CIs for all metrics were determined in healthy subjects. Inter-visit variability was determined by the difference between measurements at two visits (6 ± 3 months apart), averaged over data in diabetic subjects.

Results: Intra-visit variability of TRBF measurements was 8 μ L/min in both healthy and diabetic subjects. Mean TRBF was 44 ± 15 μ L/min (CI: 37 to 51) in healthy subjects. Inter-visit variability in mean TRBF was 3 μ L/min (CI: -1 to 8) in diabetic subjects. DO_2 and MO_2 were 8.3 ± 2.9 μ LO₂/min (CI: 7.0 to 9.6) and 3.2 ± 0.9 μ LO₂/min (CI: 2.8 to 3.6) in healthy subjects, respectively. In diabetic subjects, inter-visit variabilities of DO_2 and MO_2 were 0.6 μ LO₂/min (CI: -0.3 to 1.5) and 0.1 μ LO₂/min (CI: -0.7 to 0.5), respectively. OEF was 0.40 ± 0.08 (CI: 0.36 to 0.43) in healthy subjects. Inter-visit variability in OEF was 0.03 (CI: -0.09 to 0.02) in diabetic subjects. Mean TRBF, DO_2 , MO_2 , and OEF measurements obtained at both visits in diabetic subjects were within normal CIs and not significantly different than those in healthy subjects ($P > 0.30$). There was an inverse correlation between mean TRBF and age in healthy subjects ($r = -0.45$; $P = 0.03$, $N=22$).

Conclusions: The findings established variabilities and normal baselines for TRBF, DO_2 , MO_2 , and OEF measurements, providing a basis for detecting and monitoring changes due to diseases.

CONTROL ID: 3530808

SUBMITTER (NAME ONLY): Thomas Callan

TITLE: Correlation of macular thickness metrics between 200 kHz and 100 kHz SS-OCT scans

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As swept-source optical coherence tomography (SS-OCT) evolves, so do the laser acquisition components. Faster laser speeds allow for shorter scan acquisition times, but one trade-off is a reduction of signal that may influence image quality. The purpose of this study was to evaluate images from both the 100 kHz and 200 kHz scanning speeds of a dual-laser SS-OCT system to verify if there were any significant differences in macular thickness measurements.

Methods: Subjects were scanned multiple times with the PLEX[®] Elite 9000 (ZEISS, Dublin, CA) SS-OCT device at both 100 kHz and 200 kHz speeds. A sample of patients from two retinal clinics, predominantly representing eyes with macular degeneration or diabetic retinopathy, were imaged using the Angio 6 x 6 mm scan pattern. Macula thickness measurements were made utilizing the internal limiting membrane (ILM) and retinal pigment epithelium (RPE) as the upper and lower thickness limits respectively. Mean thickness and SDs were determined for the regions of the standard ETDRS target centered at the fovea. Linear regression and Bland-Altman plots were used to evaluate the macular thickness values for the two speeds on the first scan taken and paired t-tests were used to determine p-values.

Results:

Macular thicknesses of 37 diseased eyes from 24 subjects were measured. The mean differences between the macular thickness measurements for the 100 kHz and 200 kHz scanning speeds were less than one micron in most ETDRS regions. No statistical difference was found in any of the regions as shown in Table 1. An example of the regression and Bland-Altman plots for the Central region can be seen in Figure 1.

Conclusions: This study demonstrated that capturing SS-OCT images with the faster scanning speed did not create any significant differences for the measurement of macular thickness in diseased retinas. The faster 200 kHz scan speed should be appreciated by both technicians and patients with shorter scan times and will not make a difference in clinical decision making.

CONTROL ID: 3530818

SUBMITTER (NAME ONLY): Lubaina Arsiwala

TITLE: Associations of visual function with cognitive measures in an older adult community-based cohort: The Eye Determinants of Cognition (EyeDOC) Study

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Understanding the coexistence of visual and cognitive impairment in older adults could inform prophylactic strategies for age-related cognitive change. Hence, we evaluated the longitudinal associations of vision with cognitive change in two community-based cohorts of older adults.

Methods: In participants of two centers of the ARIC study, presenting and corrected distance visual acuity (DVA), and contrast sensitivity (CS) were measured, for both, better- and worse-seeing eyes. Factor scores for global cognition, memory, executive function and language domains were calculated for ARIC study visits 5, 6 and 7. We quantified the associations of vision measures with cognitive outcomes, stratified by community/race, using generalized estimating equations.

Results: In our entire cohort (n=989), mean (SD) baseline age was 74 (4) years, with 37% males and 45% black Jackson community participants, with the remainder white Washington County community participants.

As hypothesized, we observed that after accounting for potential confounders, in the better-eye, worse presenting DVA was associated with a greater 10-year decline in global cognition, memory, and executive function in Washington County/white group (Table 1). Worse corrected DVA was associated with a greater 10-year decline in executive function in Washington County/white group. Better CS was associated with a less 10-year decline in global cognition, and executive function in Washington County/white group. None of these associations were confirmed in black Jackson participants, and these associations differed by community/race in the full cohort (Table 1).

Weaker associations were observed when worse-eye measurements were used (Table 2).

Conclusions: Our study supports a functional link between some vision measures and cognitive outcomes in older adults, but in only one of the two communities studied. It suggests the potential benefits of maintaining visual function for better cognitive health.

CONTROL ID: 3530877

SUBMITTER (NAME ONLY): Justin Ma

TITLE: Retinal vascular changes in Parkinson's disease on ultra-widefield retinal imaging

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Previous study of Parkinson's disease (PD) using optical coherence tomography angiography has described retinal vascular changes at the capillary level. Our cross-sectional analysis aimed to assess the larger retinal vessels in a wider field of view using ultra-widefield imaging (UWF) for retinal vascular manifestations of PD.

Methods: UWF imaging with a scanning laser ophthalmoscope (California, Optos, Marlborough, MA) was performed on 22 patients (31 eyes; mean age=68, SD=7; 64% male) with a clinical diagnosis of PD and 33 controls (51 eyes; mean age=80, SD=6; 61% male). Patients with confounding medical or ocular comorbidities were excluded. The retinal vasculature was analyzed with specialized software (Vasculature Assessment Platform for Images of the REtina; Univs. of Edinburgh and Dundee, UK) measuring vascular network complexity [fractal dimension (D_0)], tortuosity, and average rate of change of vessel width from posterior to anterior (Figure 1). D_0 was measured in a consistent region of interest (Standard ROI) in each image and further subdivided into 2 other ROI (Figure 2).

Results: Comparison of PD and control patients showed no evidence of significant differences in age or sex. No evidence of significant differences in retinal vascular network complexity in any ROI was observed in PD compared to controls. Venular tortuosity was greater in the inferonasal ($p=0.046$) and superonasal quadrants ($p=0.039$) in PD compared to controls. No evidence of statistically significant differences in tortuosity of the retinal venous system was found in any temporal quadrant, or of the arteriolar system in any quadrant. There was no evidence of changes in the average rate of change of vessel width, stratifying by arterioles and venules and by quadrant.

Conclusions: Persons with PD may have more tortuous retinal venules compared to controls. Further analyses of the retinal vasculature using UWF imaging may offer additional insight as well as the potential identification of PD by retinal vascular phenotyping.

CONTROL ID: 3530889

SUBMITTER (NAME ONLY): Xuan-Thanh-An Nguyen

TITLE: The impact of the OrCam device on the quality of life in patients with inherited retinal dystrophies

SESSION TITLE: Visual Impairment and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Nguyen, C.J. Boon, Department of Ophthalmology, Leiden University Medical Center, Leiden, NETHERLANDS|J. Koopman, Royal Dutch Visio, Center of expertise for visually impaired people, Amsterdam, NETHERLANDS|M.M. van Genderen, Department of Ophthalmology, University Medical Center Utrecht, NETHERLANDS|M.M. van Genderen, H. Stam, Bartimeus, Diagnostic Center for complex visual disorders, Zeist, NETHERLANDS|C.J. Boon, Department of Ophthalmology, Amsterdam UMC, Academic Medical Center, Amsterdam, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The aim of this study was to investigate the impact of the OrCam MyEye device on the quality of life in patients with inherited retinal dystrophies (IRD). The OrCam is a portable visual aid device, which is mounted to the frame of eyeglasses, that translates visual information to auditive feedback (e.g. text-to-speech, barcode and facial recognition).

Methods: This prospective, observational study included 20 patients with low vision (BCVA < 20/200 Snellen) due to retinitis pigmentosa (n = 9; 45%) or cone-rod dystrophies (n = 11; 55%). After receiving extensive instructions on the OrCam, patients tested the OrCam for \pm 5 weeks. Interviews were conducted before and after OrCam usage, which included the Dutch version of the NEI-VFQ-25, a modified version of the Dutch Activity Inventory (D-AI), and the OrCam Function Questionnaire (OFQ).

Results: At final visit, a significant improvement in the 'near vision' subscale of the NEI-VFQ-25 was observed ($p < 0.001$), which did not differ between retinitis pigmentosa or cone-rod dystrophy patients ($p = 0.446$). No significant changes were seen in the priority scores of the different goals of the D-AI. The OFQ showed an overall improvement in performing vision-related tasks ($p < 0.001$), although patients reported more difficulty in using the OrCam during lower light situations.

Conclusions: The OrCam MyEye is a promising low vision aid for patients with a IRD that have rehabilitation needs in reading domains. Other functionalities of the OrCam, in the current state, were reported to be less effective, suggesting that these are areas for potential improvement.

CONTROL ID: 3530911

SUBMITTER (NAME ONLY): Takashi Nishida

TITLE: Long-Term Reproducibility of Optical Coherence Tomography Angiography in Stable Glaucomatous Eyes

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Nishida, S. Moghimi, H. Hou, J.A. Proudfoot, R.C. David, A. Kamalipour, N.W. El-Nimri, C. Bowd, J. Rezapour, L.M. Zangwill, R.N. Weinreb, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess and compare long-term reproducibility of optical coherence tomography angiography (OCTA) vascular parameters and spectral-domain optical coherence tomography (OCT) thickness parameters in stable glaucoma, glaucoma suspect, and healthy eyes.

Methods: A total of 88 eyes (15 healthy, 38 glaucoma suspect, and 35 non-progressive POAG) of 68 subjects were enrolled who had at least 3 visits within 1 to 1.5 years and both OCT and OCTA (Optovue Inc, Fremont, California, USA) imaging on the same day. A series of vascular and thickness parameters were measured including macula whole image vessel density (wiVD), optic nerve head (ONH) circumpapillary capillary density (cpCD), macular whole image ganglion cell complex (wiGCC) and circumpapillary retinal nerve fiber layer (cpRNFL). Non-progressive POAG eyes were defined using Guided Progression Analysis software (Carl Zeiss Meditec, Inc., Dublin, CA) and fundus photos performed (minimum follow-up of 5 years). A random effects analysis of variance model was used to estimate intraclass correlation (ICC) coefficients and long-term variability estimates. Intra-class correlation (ICC), root mean squared error (RMSE), within-subject test-retest standard deviation (Sw), and coefficient of variation (CV) analyses were obtained to determine long-term reproducibility of OCTA and OCT measurements.

Results: No significant cpRNFL thinning, cpC loss or pfVD loss was observed ($p=0.137$, $p=0.137$, and $p=0.094$, respectively), while pfGCC thinning was detectable over time ($p<0.001$). ICC was lower for OCTA (pfVD 0.823 (95% confidence interval: 0.736, 0.888) and cpCD 0.871 (0.818, 0.912)) compared to OCT (pfGCC 0.995 (0.993, 0.997) and cpRNFL 0.975 (0.964, 0.984)). RMSE was 1.43 and 1.41 for pfVD and cpCD, and 0.65 and 1.41 for pfGCC and cpRNFL. Sw was 1.17 and 1.22 for pfVD and cpCD, and 0.57 and 1.22 for pfGCC and cpRNFL. CV was higher for OCTA parameters (pfVD 2.48 and cpCD 2.61) compared to OCT parameters (pfGCC 0.56 and cpRNFL 1.79).

Conclusions: OCTA-measured macula and ONH vascular parameters have good long-term reproducibility, supporting the use of this instrument for longitudinal analysis. OCTA long-term reproducibility is lower than OCT measured thickness parameters.

CONTROL ID: 3530912

SUBMITTER (NAME ONLY): Qin Wang

TITLE: Low-does atropine might affect alpha ganglion cell signaling in the mouse retina

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Wang, F. PAN, The Hong Kong Polytechnic University, Kowloon, HONG KONG|F. PAN, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Atropine was used to retard myopia progression in clinic, while its effect on retina is unclear. Therefore, we explored the impact of atropine from concentrations 0.05 μ M to 500 μ M on retinal ganglion cells (RGCs) in the mouse retina.

Methods: Adult C57BL/6J mice, Kcng4-YFP mice, Cx36-knockout mice were used in this study. Retinas (n=5) were removed and immersed in 800 μ M (0.05%) atropine sulfate for 30 minutes and liquid chromatography-tandem mass spectrometry (LC-MS/MS) was used to detect atropine concentration in retina. Alpha RGCs (n=10) were injected with Neurobiotin to show morphology. In electrophysiological recording, retinas were directly applied in atropine and stimulated with 525nm full-field light. ON (n=5) and OFF α RGCs (n=5) were applied with 0 μ M, 100 μ M, 300 μ M, 500 μ M atropine subsequently for does-dependent test. For time and concentration-dependent test, alpha RGCs were recorded before and after application of 0.05 μ M (n=8), 0.5 μ M (n=8), 10 μ M (n=8), 100 μ M (n=9) atropine respectively.

Results: Around 400-fold reduction was detected in retina after 800 μ M atropine applied in cornea and choroid side (1960.0 ± 524.2 nmol/L). No morphological changes were observed after superfusion in 1 μ M atropine for 30 minutes. Atropine over 100 μ M had a does-dependent inhibition effect on light-evoked response in ON α RGCs (300 μ M p=0.048, 500 μ M p=0.001) and OFF α RGCs (300 μ M p=0.048, 500 μ M p=0.003). Application of 100 μ M, 10 μ M, 0.5 μ M, 0.05 μ M atropine had no effect on spike frequency and time latency of original ON or OFF light-evoked responses. Synchronized firing pattern between OFF RGCs was not changed in 0.5 μ M atropine. However, ON responses were induced in certain OFF α RGCs (20% in 0.05 μ M, 37% in 0.5 μ M, 40% in 10 μ M, 33% in 100 μ M). Atropine of 50 μ M extended the threshold of joint inter-spike interval (ISI) distribution of α RGCs.

Conclusions: Atropine of high concentration had inhibition effect on α RGCs firing response, while low-dose atropine did not interfere with spike frequency, synchronized pattern, and threshold of joint ISI distribution of ON and OFF α RGCs. However, atropine induced ON responses from certain OFF RGCs, which suggested unintended consequences on retinal information processing.

CONTROL ID: 3530942

SUBMITTER (NAME ONLY): Oxana Pererva

TITLE: Approaches to the accuracy in ROP diagnosis

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Pererva, M. Kovalevskaya, Ophthalmology, Voronezhskij gosudarstvennyj medicinskij universitet imeni N N Burdenko, Voronezh, RUSSIAN FEDERATION|

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ABSTRACT BODY:

Purpose: To find approaches to the accuracy in retinopathy of prematurity (ROP) diagnosis.

Methods: Group #1 I stage (n=7, 7 eyes), group #2 II stage (n=6, 6 eyes), group #3 III stage (n=4, 4 eyes), group #4 IVA stage (n=3, 3 eyes), group #5 posterior aggressive ROP (PAROP) (n=2, 2 eyes), group #6 (control) - immature retina (n=6, 6 eyes). We use the best pix from RetCam Shuttle (Clarity MS, USA) video, modeling wide-field image, identifying missed the "mute" zones, the localization of the macula and checking the index of traction (Tm), the zone and extension, fractal dimension (Df) and complexity of vascular systems (CVS) (A-1 creation of a preliminary capillary plexus, B-2 normal vascularization, C-3 pathological vasculogenesis). Tm is width-to-length attitude of ellipse (optic nerve head to temporal branches of the retinal vessels). Our original method is a way of stitching images when examining children without anesthesia. Automatic wide-field fundus image algorithm: adaptive filtering, separation of the green channel, applying a Gaussian blur filter, local histogram equalization, the general transformation map. Support of the program for stitching images was at the first stage, the work was done due to the personal contribution of the researcher's. Statistical methods: Mann-Whitney U-test, Spearman's rank correlation coefficient (SPSS)

Results: Result format: Median(25%-quartile;75%-quartile). Group #1 Df 1,31(1,3;1,34), Tm 0,79(0,79;0,83), CVS 1(1;1,25). Group #2 Df 1,38(1,36;1,39), Tm 0,76(0,71;0,78), CVS 1,5(1,5;2). Group #3 Df 1,46(1,45;1,47), Tm 0,68(0,64;0,78), CVS 2,5(2,5;2,63). Group #4 Df 1,55(1,55;1,56), Tm 0,62(0,62;0,66), CVS 3(3;3). Group #5 Df 1,66(1,65;1,66), Tm 1(1;1), CVS 3(3;3). Group #6 Df 1,27(1,27;1,27), Tm 0,95(0,91;0,99), CVS 1(1;1). Strong correlation between Df and stages ($p=0,85$, $p=0,01$); negative correlation Tm and stage ($p=-0,62$, $p=0,01$) except PAROP; strong positive correlation CVS and stage ($p=0,91$, $p=0,001$) were determined. Platform modules for a wide-field image for macula area, morphometry and isolation of the vascular nodules with neural network have been developed.

Conclusions: The developed algorithm fits new ROP screening and treatment control criteria and can be used to identify the stage of the ROP as a holistic picture of the disease on one platform.

CONTROL ID: 3530989

SUBMITTER (NAME ONLY): Min Chen

TITLE: Edge-based measure for automated assessment of image quality in adaptive optics split detection images

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Split detection imaging in adaptive optics (AO) ophthalmoscopy allows for visualization of cone inner segments, even when retinal pathology disrupts photoreceptor waveguiding. Due to the small field of view of individual AO images, adjacent images are typically montaged. Overlapping images in each montage then must be sorted so that the image with the highest quality is visible and used for further analyses of the cone mosaic. This sorting is currently a laborious manual task. Here, we propose an edge-based measure that enables automated ranking of image quality in AO split detection images.

Methods: Our measure is based on the Canny edge detection algorithm, as implemented in Matlab (2020a). For each image, we run the edge detection and evaluate the proportion of the image occupied by detected edge pixels. Our method has a single threshold parameter which can be used statically to set the detection level, or adaptively chosen to produce a specified percentage of edge pixels. We compared rankings of image quality generated using the proposed approach against those of two human graders, and against two published image quality assessment methods (BRISQUE and PIQE). Using AO split detection montages from 5 choroideremia subjects, we identified 29 image locations, each with a minimum of 4 overlapping images. Each grader ranked every possible pair of images within each location (469 comparisons). The pairwise rankings were then aggregated into an overall ranking for each location using the Bradley and Terry model.

Results: For the pairwise comparisons, the inter-grader agreement was 0.75. The agreement of the automated approaches {Proposed-Threshold, Proposed-Percent, BRISQUE, PIQE} were {0.67, 0.67, 0.52, 0.59} relative to Grader 1 and {0.68, 0.71, 0.43, 0.51} relative to Grader 2. The Spearman correlation of the aggregated rankings across all 29 locations was 0.75 between Grader 1 and 2. The correlation of the aggregated rankings for the automated approaches were {0.60, 0.61, 0.20, 0.34} relative to Grader 1 and {0.59, 0.61, 0.08, 0.21} relative to Grader 2.

Conclusions: Our proposed edge-based image quality assessment generates quality rankings that are comparable to those of trained manual graders, and substantially outperforms two existing methods. This method has potential to reduce manual input to AO montages, thus enabling higher volumes of cone mosaic analyses.

CONTROL ID: 3530994

SUBMITTER (NAME ONLY): Ailin Song

TITLE: Combining artificial intelligence and robotics: a semi-automated optical coherence tomography-based approach for posterior eye disease screening

SESSION TITLE: AI in the retina: Clinical Applications

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Despite its importance in systemic diseases such as diabetes, the posterior eye is difficult to examine for non-specialists. To improve eye care in non-ophthalmology settings, we developed a semi-automated approach with potential for posterior eye disease screening, coupling a robotically-aligned optical coherence tomography system and a deep learning (DL) algorithm to classify the images.

Methods: Between August and October 2020, patients seen at the Duke Eye Center and healthy volunteers (age \geq 18) were imaged with a custom, robotically-aligned OCT (RAOCT) system following clinical eye exam (Fig 1). Using transfer learning, we adapted a preexisting convolutional neural network (Szegedy C, et al. CVPR 2016) to train a DL algorithm to classify OCT images as normal vs. abnormal. The model was trained and validated on two publicly available OCT datasets (Kermany DS, et al. Cell 2018; Srinivasan PP, et al. BOEx 2014) and two of our own RAOCT volumes. For external testing, the top-performing model based on validation was applied to a representative averaged B-scan from each of the remaining RAOCT volumes. The model's performance was evaluated against the reference standard clinical diagnosis. Saliency maps were created to visualize the areas contributing most to the model predictions.

Results: The training and validation datasets included 87,697 OCT images, of which 59,743 were abnormal. The top-performing DL model had a training accuracy of 96% and a validation accuracy of 99%. For external testing, 43 eyes of 27 subjects were imaged with the RAOCT system. Compared to clinical diagnoses, the model correctly labeled 18 out of 22 normal averaged B-scans and 18 out of 21 abnormal averaged B-scans. In the testing set, the model had an AUC for the detection of pathology of 0.92. For the correctly predicted scans, saliency maps identified the areas contributing most to the DL algorithm's predictions, which matched the regions of greatest clinical importance (Fig 2).

Conclusions: This is the first study to combine a DL model with a robotic OCT system, demonstrating a potential platform to automate eye disease screening.

CONTROL ID: 3531001

SUBMITTER (NAME ONLY): Libing Dong

TITLE: Predictors of visual recovery after post-injection endophthalmitis

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.K. Dong, Central Michigan University College of Medicine, Mount Pleasant, Michigan, UNITED STATES|R.A. Shields, Associated Retinal Consultants, Michigan, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Libing Dong: Commercial Relationship: Code N (No Commercial Relationship) | Ryan Shields: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Acute infectious endophthalmitis is a known complication following intravitreal injections, occurring at a rate of 0.016% to 0.056% per injection. Given their extensive and persistent use, we sought to evaluate factors associated with worse visual outcomes after post-injection endophthalmitis.

Methods: A retrospective, consecutive case series was conducted on patients treated for post-injection endophthalmitis at Associated Retinal Consultants (ARC) P.C. (Royal Oak, Michigan) from January 2013 thru December 2019. The main outcome measure was change in visual acuity before and after endophthalmitis. Univariate modeling was performed to assess factors associated with visual change.

Results: One hundred and forty six patients were identified who developed post-injection endophthalmitis. The median age at presentation was 78.1 years. The most common indication for treatment was neovascular age-related macular degeneration in 101 patients (69%), followed by proliferative diabetic retinopathy/diabetic macular edema in 29 (20%). Ranibizumab was injected in 68 patients (47%), Aflibercept in 56 patients (38%), bevacizumab in 10 (6.8%), dexamethasone implant in 9 (6.2%), and the remaining 3 (2%) with combination therapy. The median number of injections prior to developing endophthalmitis was 22 (range 1 to 107). The mean time from injection to endophthalmitis development was 4.5 days (range 1 to 17). The vast majority of patients (139 of 146) were treated with an immediate vitreous biopsy and intravitreal antibiotics (TAI) while 7 (of 146) underwent an immediate vitrectomy. Biopsy cultures were obtained in all 146 patients with 56 cultures (39.5%) yielding growth. The mean follow-up time after endophthalmitis development was 839 days (range 34 to 2560). Mean initial logMAR visual acuity (VA) was 0.5 (Snellen 20/63), while mean final LogMAR VA was 0.92 (Snellen 20/166). Risk factors for vision loss after endophthalmitis included culture positivity ($p = 0.017$) and need for vitrectomy ($p = 0.001$). The cumulative number of injections ($r = -0.007$, $p = 0.47$) was not associated with significant vision loss after endophthalmitis (Figure 1).

Conclusions: Although frequently done at recurrent intervals, cumulative injections are not associated with worse visual outcomes following endophthalmitis. Factors that were associated with poor visual prognosis included the culture positivity and the need for a vitrectomy in the post infection period.

CONTROL ID: 3531004

SUBMITTER (NAME ONLY): Anne Xuan-Lan Nguyen

TITLE: Correlating retinal blood vessel movements with other clinical signs in progressing retinal degenerations.

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nguyen, McGill University Faculty of Medicine, Montreal, Quebec, CANADA|A. Nguyen, C. Tardif, M. Gauthier, L. Berthiaume, P. Lachapelle, Ophthalmology, McGill University Health Centre, Montreal, Quebec, CANADA|M. Gauthier, Ecole de technologie superieure, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: We showed (Transl Vis Sci Technol. 2020;9(8):27), in a 3-decade follow-up of a patient with Retinitis Pigmentosa (RP), that while the Retinal Blood Vessel Arborization (RBVA) seemed immutable at the optic nerve head (ONH), there were suggestions of vessel movements more peripherally, as the disease progressed. We aimed at further documenting this claim.

Methods: Fundus photographs of patients (N=10) affected with a well-defined retinal degeneration were selected from our ERG databank. To be included, patients had to have at least 3 follow-up visits over a 5-year span at least. Fundus pictures were digitized (Epson Perfection v600 Photo Scanner) and processed (Adobe Photoshop) to extract the arterial and venous RBVAs. These RBVAs were compared intra-individually by overlapping the RBVAs of the 1st visit to next ones using retinal landmarks (i.e., ONH & fovea-macula). Movements were quantified using vessel overlap percentages and angular measurements of displacement at predetermined eccentricities. Results were then correlated with clinical tests such as: visual acuity (VA), visual fields (VFs) and electroretinography (ERG). Standardization of the RBVA method was tested on 18 normal subjects.

Results: The control group had a mean RBVA-overlap value (measures repeated at a 5-week interval) of $96.5 \pm 1.1\%$. In patients, the overlap % at each follow-up visits were always significantly smaller than normal ($p < .05$) and the overlap gradually decreased as the retinal degeneration progressed. As a rule, angular displacements (direction and speed of displacement) were not significantly different between arteries and veins ($p > .05$). Comparing the displacement of the RBVA (overlap % and angular displacement) with other signs of disease progression we noticed a strong correlation with the VF changes (mostly constriction) and ERG measurements [rod and cone b-waves amplitude and Hölder exponent (a Time-Frequency Domain descriptor of the ERG)]. No correlations could be obtained with the VA.

Conclusions: Our study clearly demonstrates that movements of the RBVA is a measurable clinical sign of a progression in retinal degenerative disorders similar to visual field constrictions and ERG attenuations. It remains to be determined if this new diagnostic sign could detect the onset of a retinal degenerative process at an earlier time, a finding that could be helpful in pedigree studies and genetic counseling.

CONTROL ID: 3531009

SUBMITTER (NAME ONLY): Azadeh Tavakoli

TITLE: The association between the ocular discomfort and corneal dendritic cell densities

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tavakoli, M. Markoulli, E.B. Papas, University of New South Wales School of Optometry and Vision Science, Sydney, New South Wales, AUSTRALIA|A. Tavakoli, J. Flanagan, BHVI, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Dry eye is a common, symptomatic disease which can significantly decrease quality of life. Inflammation is considered a major part of dry eye disease pathogenesis. Dendritic cells are immune cells that serve a unique role inducing primary immune responses and controlling inflammation on the ocular surface. However, the association between dendritic cell density and dry eye symptoms is not well understood. This study aimed to investigate the relationship between ocular surface discomfort and corneal inflammatory cells in individuals with no and mild to severe dry eye symptoms.

Methods: In-vivo corneal confocal microscopy (IVCM) images from 41 participants (26 females and 15 males), aged 18 to 76 years (mean: 40 ± 15 years) were analyzed. Five to eight images from the central cornea (CC) and four images from inferior whorl (IW) were analyzed for the dendritic cell densities (DCD). For assessment of ocular discomfort, participants were evaluated with the Dry Eye Questionnaire 5 (DEQ-5) and Ocular Surface Disease Index (OSDI) to measure ocular discomfort relating to 3 subcategories covering symptoms, visual function, and environmental triggers. Associations between the DCD and ocular discomfort were determined using Spearman's rho correlation. A p-value < 0.05 was considered statistically significant.

Results: The average OSDI and DEQ-5 scores were 22 ± 16 and 9 ± 5 with a range of 0 to 62 and 0 to 17, respectively. The mean DCD in the CC and IW was 35 ± 41 and 33 ± 81 with a range of 0 to 196 and 0 to 502 cells/mm², respectively. There was a moderate association between DCD at the CC and IW ($r = 0.60$, $p < 0.01$). DCD, at both locations, had no association with DEQ-5 ($r = -0.02$, $p = 0.19$), OSDI ($r = -0.08$, $p = 0.61$) or its 3 subcategories including symptoms ($r = -0.06$, $p = 0.70$), visual function ($r = -0.01$, $p = 0.95$) and environmental triggers ($r = -0.05$, $p = 0.73$). Moreover, no association was found between age, gender and DCD ($r = -0.18$, $p = 0.26$; $r = -0.10$, $p = 0.55$).

Conclusions: DCD had no relationship with ocular discomfort in this study cohort. While DCD in CC and IW indicated correlation, neither OSDI nor DEQ-5 questionnaire showed association with corneal DCD.

CONTROL ID: 3531016

SUBMITTER (NAME ONLY): Amelia Podolny

TITLE: Structural and Functional Outcomes Following Naked Versus ICG- or IVK-Assisted ERM Peeling

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Podolny, B. Quiram, P.A. Quiram, VitreoRetinal Surgery, PA, Woodbury, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many vitreoretinal surgeons elect to mark the internal limiting membrane (ILM) for removal during epiretinal membrane (ERM) peeling. While this practice is thought to reduce ERM recurrence, the reported toxicity of ILM-staining substances remains a concern given the variable visual significance of recurrent ERMs. We sought to examine structural and functional outcomes after surgery for ERM, comparing unassisted “naked” peels to assisted peels utilizing indocyanine green (ICG) or intravitreal Kenalog (IVK) for ILM marking.

Methods: A retrospective analysis was conducted on all adult patients who underwent pars plana vitrectomy and ERM peel with or without ILM marking at a single vitreoretinal surgery practice from 2014 to 2016. The primary endpoints of central macular thickness (CMT) and best-corrected visual acuity (BCVA) were pre- and postoperatively assessed, and outcomes at 1 month, 3 month, and last follow-up after surgery were compared between the two groups. Presence of residual unpeeled ERM, 3-month postoperative cystoid macular edema (CME), and ERM recurrence were evaluated secondarily.

Results: 189 eyes in 183 patients met the inclusion criteria; 120 unassisted and 69 assisted (48 ICG + 21 IVK) operations were performed. Postoperatively, CMT significantly decreased for both groups (-52.9 μ m assisted, $p < 0.001$; -37.6 μ m unassisted, $p < 0.001$), and BCVA significantly improved by the same amount in both cohorts (20/45 to 20/35 assisted, $p = 0.002$; 20/43 to 20/33 unassisted, $p < 0.001$). The instance of residual ERM was greater in the unassisted cohort, but these findings were not statistically significant (68% vs. 57%, $p = 0.054$). The assisted group demonstrated significantly higher rates of CME at 3 months after surgery (17.4% vs. 3.33%, $p < 0.001$), a trend that was observed for both ICG- (16.7% vs. 3.33%, $p = 0.002$) and IVK-assisted (19.0% vs. 3.33%, $p = 0.005$) subgroups as well. ERM recurrence, however, only occurred in the unassisted cohort (8.33% vs. 0%, $p = 0.014$).

Conclusions: Regardless of visual assistance during surgery, CMT and BCVA significantly improved after membrane peeling. Interestingly, patients who underwent ICG- or IVK-assisted peels exhibited a higher incidence of CME after 3 months. Further study is needed to determine if more extensive ERM/ILM peeling may increase the presence of postoperative CME. ERM recurrence was noted only in the unassisted cohort.

CONTROL ID: 3531055

SUBMITTER (NAME ONLY): Toke Bek

TITLE: Reduced oxygen extraction in the retinal periphery when the arterial blood pressure is increased by isometric exercise in normal persons

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Bek, S.K. Jeppesen, Ophthalmology, Aarhus Universitetshospital, Aarhus, DENMARK|

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ABSTRACT BODY:

Purpose: Recent evidence suggests that the smaller retinal vessels are significantly involved in the regulation of retinal blood flow and that this regulation may differ among the macular area and the retinal periphery. An alternative to studying blood flow regulation in smaller retinal vessels that are difficult to resolve is to assess the metabolic consequences of changes in the microcirculation using oximetry.

Methods: In twenty normal persons aged (mean \pm SD, range) 30.1 \pm 3.8, 24-37 years, the oxygen saturation and diameter of retinal arterioles and venules to the macular area and the retinal periphery were studied before and during an increase in the arterial blood pressure induced by isometric exercise.

Results: The isometric exercise increased the mean arterial blood pressure by (mean \pm SEM) 10.0 mmHg \pm 1.1 mmHg, but induced no significant changes in the diameter of the arterioles ($p=0.83$). The isometric exercise had no significant effect on the oxygen saturation in the arterioles supplying the macular area and the retinal periphery ($p>0.42$ for both comparisons). However, there was a significant increase in the oxygen saturation in venules draining the retinal periphery to reduce the oxygen extraction from (mean \pm SEM) 36.0 \pm 2.3% to 30.6 \pm 2.1% ($p=0.002$), but no significant change in the pre-existing low oxygen extraction in the macular area that changed from (mean \pm SEM) 18.2 \pm 3.0% to 16.2 \pm 1.9% ($p=0.37$).

Conclusions: Minor changes in the arterial blood pressure can induce changes in retinal rheology with significant regional variation. The finding may help explaining regional variations in manifestations of retinal vascular disease such as hyperpermeability in the macular area and capillary occlusion in the retinal periphery.

CONTROL ID: 3531069

SUBMITTER (NAME ONLY): Jingyuan Yang

TITLE: Bi-Modal Deep Learning for Recognizing Multiple Retinal Diseases based on Color Fundus Photos and OCT Images

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yang, B. Li, B. Zhang, Y. Wang, W. Yu, Y. Chen, Ophthalmology, Peking Union Medical College Hospital, Beijing, CHINA|Z. Yang, J. zhao, D. Ding, Vistel AI Lab, Visionary Intelligence Ltd., CHINA|Z. Mao, J. Liu, S. Yeh, Y. Fukuma, Topcon Medical Systems, JAPAN|H. Lin, J. Wang, X. Li, Key Lab of DEKE, Renmin University of China, Beijing, CHINA|J. Yang, B. Li, B. Zhang, Y. Wang, W. Yu, Y. Chen, Key Laboratory of Ocular Fundus Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: Artificial intelligence (AI)-based diagnosis of retinal diseases using a single imaging method of color fundus photography (FP) or optical coherence tomography (OCT) has been fully investigated.

Although bi-modal imaging examinations using both FP and OCT could provide more comprehensive retinal information than their single-modal counterparts, which might improve the accuracy of AI to detect retinal diseases, the feasibility and performance of bi-modal imaging-based AI diagnosis of retinal diseases have not been extensively investigated.

The purpose of this study is to evaluate the performance of a bi-modal imaging-based AI system in detecting multiple retinal diseases using both FP and OCT images.

Methods: The AI-based system was trained using 573 scans (from 400 patients) centered on macula, validated using 192 scans (from 140 patients), and tested using 209 scans (from another 146 patients). Each scan that captured with Topcon 3D OCT-1 Maestro (Topcon Corp., Japan) consists of one FP and one corresponding radial OCT scan, which further consists of 12 OCT B-scans. Using both images and additional summarized clinical data, at least two ophthalmologists confirmed the diagnosis of each scan, including diabetic retinopathy (DR), dry age-related macular degeneration (AMD), wet AMD, epiretinal membrane (ERM), pathologic myopia (PM), macular oedema (ME), and normal (Fig 1). Performance of this system was measured in terms of sensitivity and specificity, and average precision (AP) per diagnosis.

Results: The bi-modal image-based AI system had a mean AP for the detection of multiple retinal diseases of 0.84 (95% confidence interval [CI], 0.80 - 0.87), a sensitivity of 0.88 (95% CI, 0.84-0.93), and a specificity of 0.91 (95% CI, 0.88-0.95) (Fig 2). Compared with the bi-modal image-based AI system, the mean AP was 0.74 when the AI system was trained with only FP images (95% CI 0.69-0.78), and 0.81 when with only OCT images (95% CI, 0.77-0.84) (Fig 2).

Conclusions: AI-assisted diagnostic system based on bi-modal imaging method showed significantly better performance than that based on FP, and relatively better performance than that based on OCT. The additional information provided by bi-modal imaging method could be used for not only diagnosis, but also perhaps therapeutic decision, which needs further study.

CONTROL ID: 3531073

SUBMITTER (NAME ONLY): Ogul Uner

TITLE: A Computational Model of BAP-1 Expression in Uveal Melanoma Reveals Early-Onset Mutagenesis

SESSION TITLE: Advances in Diagnosis and Treatment of Uveal Melanoma

SESSION TYPE: Paper Session

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Commercial Relationships Disclosure (Abstract): Ogul Uner: Commercial Relationship: Code N (No Commercial Relationship) | Thonnie See: Commercial Relationship: Code N (No Commercial Relationship) | Eszter Szalai: Commercial Relationship: Code N (No Commercial Relationship) | Hans Grossniklaus: Commercial Relationship: Code N (No Commercial Relationship) | Gustav Stålhammar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is the most common primary intraocular malignancy. Mutations in BRCA1 associated protein-1 (BAP-1) is correlated with increased metastatic risk and has been assumed to occur late in tumor progression, though the latter has not been well-studied (Fig. 1). We investigated the spatial and temporal characteristics of UM BAP-1 mutagenesis using mathematical modeling.

Methods: Enucleated eyes with UM were obtained from Emory Eye Center (USA) and St. Erik Eye Hospital (Sweden). After BAP-1 immunohistochemistry, digital image analysis was used to measure each tumor cell size and grade BAP-1 immunoreactivity. Tumor size and DNA sequencing data from The Cancer Genome Atlas were added. A computational model of the proportion of BAP-1 mutant cells as a function of total tumor size was created in SPSS-26, with the ANOVA F-test used for curve fitting.

Results: A total of 156 tumors were included and 8.3 million tumor cells were measured. Tumors with a BAP-1 mutation had significantly larger mean volume than those without (2109 vs. 1552 mm^3 , $p=0.03$). Similarly, tumor cells with loss of BAP-1 expression had significantly larger mean volume than those with retained expression (801 vs. $524 \mu\text{m}^3$, $p=0.04$). The growth of the BAP-1 mutated clone was best fitted to a logarithmic curve (F-score 7, $p=0.01$), with the proportion of mutants to total number of cells described as $-73.6+18.2 \times \ln(\text{tumor volume in } \text{mm}^3)$. The mutation occurred within a UM's second mitosis at a tumor age of 0.8 to 2.8 years and volume of <1 to 37 mm^3 , depending on the UM doubling time used in the calculation. The largest volume corresponds to a lesion with 2 mm in thickness and 6 mm in diameter.

Conclusions: The BAP-1 mutation occurs within 2 tumor doublings, explaining early seeding of liver micrometastases. BAP-1 mutant cells are larger in size and the mutagenesis follows a logarithmic function, a variant of the Gompertzian tumor growth model. Our findings challenge the notion that the critical mutation occurs late in UM and underscores the importance of conducting BAP-1 testing at UM diagnosis.

CONTROL ID: 3531076

SUBMITTER (NAME ONLY): Cynthia Yu-Wai-Man

TITLE: Novel cationic targeted CL4H6 lipid nanoparticles with high silencing efficiency of MRTF-B in conjunctival fibroblasts

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Yu-Wai-Man, A. Sanghani, J. Fajardo-Sanchez, A. Tanner, King's College London Faculty of Life Sciences and Medicine, London, London, UNITED KINGDOM|K. Kafetzis, A. Tagalakakis, Department of Biology, Edge Hill University, Ormskirk, UNITED KINGDOM|Y. Sato, H. Harashima, Faculty of Pharmaceutical Sciences, Hokkaido Daigaku, Sapporo, JAPAN|C. Yu-Wai-Man, J. Fajardo-Sanchez, Department of Ophthalmology, Guy's and St Thomas' NHS Foundation Trust, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The myocardin-related transcription factor/serum response factor (MRTF/SRF) pathway is a master regulator in fibrosis. We have previously shown that MRTF-B siRNA significantly decreased fibroblast contraction in vitro and conjunctival fibrosis in vivo. Drug delivery is a major hurdle to clinical translation and our aim was to test the efficiency and safety of a novel lipid CL4H6 as a delivery system for MRTF-B siRNA.

Methods: Lipid nanoparticles (LNPs) were prepared by mixing CL4H6 with the helper lipid DOPE and DMG mPEG2k in a molar ratio of 50:50:1. The targeting peptide cY was added to the LNPs and MRTF-B siRNA or control IRR siRNA at a weight ratio of 4:1 (peptide:siRNA). Nanoparticle size, zeta potential and morphology were determined by dynamic light scattering, laser Doppler anemometry and transmission electron microscopy, respectively. SiRNA encapsulation efficiency was measured using the RiboGreen assay. We tested the effects of four LNPs (LNP+MRTF-B siRNA, LNP+cY+MRTF-B siRNA, LNP+IRR siRNA and LNP+cY+IRR siRNA) at three siRNA concentrations (25, 50, 100 nM) on MRTF-B gene expression using real-time qPCR and on cell viability in human conjunctival fibroblasts. We further assessed their functional effects using a 7-day collagen contraction assay. We analysed our results using the student's t-test.

Results: Targeted LNP+cY+MRTF-B siRNA had a size of 211.2 ± 1.9 (SEM) nm, a zeta potential of $+6.9 \pm 0.2$ mV, 0.11 ± 0.02 polydispersity index and were spherical in shape (Fig. 1). siRNA encapsulation efficiency increased from $92.5 \pm 0.7\%$ for non-targeted LNPs to $99.3 \pm 0.1\%$ for targeted LNP+cY+MRTF-B siRNA ($p=0.0005$). Both LNPs effectively silenced the MRTF-B gene in vitro, with the targeting peptide not affecting the silencing efficiency (LNP+cY: 56.5%, 62.1% and 81.5% versus LNP: 55.8%, 77.7% and 80.2%, at siRNA concentrations of 25, 50 and 100 nM, respectively). Targeted LNP+cY+MRTF-B siRNA ($p=0.857$) and LNP+MRTF-B siRNA ($p=0.219$) were not cytotoxic at 50 nM siRNA concentration compared to LNP-IRR siRNA or untreated cells. LNP+cY+MRTF-B siRNA significantly decreased matrix contraction after a single transfection by 27.2% ($p<0.0001$) at day 3 and 10.7% ($p=0.0010$) at day 7, compared to LNP-IRR siRNA.

Conclusions: Targeted CL4H6-MRTF-B siRNA-loaded LNPs represent an efficient and safe therapeutic approach to prevent conjunctival fibrosis after glaucoma filtration surgery.

CONTROL ID: 3531087

SUBMITTER (NAME ONLY): Manlong Xu

TITLE: How do RA and SLE patients differ while on long-term hydroxychloroquine therapy?

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Xu, I.M. MacDonald, Ophthalmology and Visual Sciences, University of Alberta, Edmonton, Alberta, CANADA|

Commercial Relationships Disclosure (Abstract): Manlong Xu: Commercial Relationship: Code N (No Commercial Relationship) | Ian MacDonald: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The long-term use of hydroxychloroquine (HCQ) can cause irreversible retinopathy. We performed a prospective study to investigate whether rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients differ in their resilience to HCQ toxicity.

Methods: Patients with RA and SLE referred to the Eye Institute of Alberta and screened for HCQ retinopathy were identified prospectively over a 20-month period. All patients underwent multifocal electroretinography (mfERG), fundus photography, fundus autofluorescence and spectral-domain optical coherence tomographic (OCT) imaging as part of their visits. Data collected included clinical diagnosis, age, sex, HCQ use (daily dose, total dose, duration of use), co-morbid maculopathy, and tamoxifen use. Patients with co-morbid maculopathy were excluded from the analysis. Patients who received a total dose of ≥ 2 kg of HCQ and had no evidence of retinopathy were a priori referred as the "resilient group".

Results: A total of 177 patients were recruited in the study; 8 were excluded due to co-morbid maculopathy, leaving 169 (118 RA and 51 SLE) for analysis. Thirty-six patients were in the resilient group. This group had received a significantly higher total dose (2.36 ± 0.45 vs 1.10 ± 0.54 Kg), duration of use (20.01 ± 5.23 vs 10.60 ± 5.11 years), daily dose (4.70 ± 1.53 vs 3.98 ± 1.29 mg/kg body weight), and had a higher proportion of SLE patients (50% vs 25%) compared to the rest of the cohort (all $p < 0.05$). Comparison between RA and SLE patients reveals that the SLE group had received a significantly higher total dose, duration of use, and had a higher percentage of resilient patients (all $p < 0.05$); they were also 5 years younger on average and had more females (both $p < 0.05$). Nevertheless, no significant difference was found in the percentage of resilient patients among different age groups (< 50 vs $50-69$ vs ≥ 70 years) and between genders (both $p > 0.05$). In terms of HCQ retinopathy cases, the RA group ($n=118$) had 5 (4.2%) suspect, 1 (0.8%) likely, and 3 (2.5%) confirmed cases of toxicity, whereas, the SLE group ($n=51$) had only 1 (2.0%) likely case and no suspect or confirmed cases.

Conclusions: While this is a small study, there would appear to be a significant difference between RA and SLE patients as to their relative resilience to HCQ toxicity based on their underlying clinical diagnosis.

CONTROL ID: 3531095

SUBMITTER (NAME ONLY): Brandon Kingrey

TITLE: Initial Results of the PanOptix Intraocular Lens: A Comparison of Intermediate and Near Vision Acuities of PanOptix and Monofocal Lenses

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kingrey, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|J. Boomer, T. George, University of Kansas Medical Center, Wichita, Kansas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Brandon Kingrey: Commercial Relationship: Code N (No Commercial Relationship) | Jeff Boomer: Commercial Relationship: Code N (No Commercial Relationship) | Tameka George: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the intermediate and near vision of cataract surgery patients implanted with the PanOptix intraocular lens, and to compare these visions with the acuities of patients implanted with standard monofocal IOL.

Methods: A retrospective comparative study was conducted to determine the postoperative vision in patients implanted with either the PanOptix IOL or a standard monofocal lens. The first 174 eyes implanted with the PanOptix lens from a single surgery center were included in this study. A randomly selected cohort of 103 eyes implanted with a monofocal lens from the same surgery center were included as a comparative control group. The lens power of both the PanOptix and monofocal lens was calculated with the IOL Master using the Barrett 2 formula. Three weeks after cataract surgery and lens implantation, visual acuity was measured using the Snellen chart, Jaeger chart at arm's length, and Jaeger chart at 14 inches.

Results: Among patients implanted with the PanOptix lens, 135/174 (78%) were I5 or better and 96/174 (55%) were I3 or better for intermediate vision. For near vision, 169/174 (97%) had J5 or better and 157/174 (90%) had J3 or better. Among patients implanted with the standard monofocal lens, 25/103 (24%) were I5 or better and 6/103 (6%) were I3 or better for intermediate vision. For near vision, 23/103 (22%) were J5 or better and 5/103 (5%) were J3 or better. Postoperative intermediate and near visual acuities were statistically different between both groups (p value < .001). If spectacle independence is defined as a combination of visual acuity of 20/50, I5, and J5 then 134/174 (77%) of patient's implanted with the PanOptix lens were spectacle free compared to 13/103 (13%) of patients implanted with the monofocal lens.

The preoperative refraction was not statistically significant between the PanOptix and Monofocal groups. 172/174 (99%) of patients in the PanOptix group had 20/50 distance vision or better at three weeks post-op compared with 98/103 (95%) of patients in the monofocal group, and this difference was also not statistically significant.

Conclusions: The intermediate and near vision of the PanOptix lens was far superior to that of the monofocal lens group with similar distance acuities for both. The PanOptix lens allowed for spectacle independence for a large percentage of patients.

CONTROL ID: 3531100

SUBMITTER (NAME ONLY): Adam Hanif

TITLE: Improved training efficiency for deep learning models using disease severity comparison labels

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Neural network performance relies on large, high-quality training sets. In medical image recognition tasks, small datasets and high inter-labeler variance frequently limit models' diagnostic accuracy. In this study, we compare the efficiency of training neural networks to predict disease severity using "comparison" labels versus the traditional method of using diagnostic "class" labels from a retinopathy of prematurity retinal image dataset.

Methods: 100 fundus images were each assigned "class" labels indicating plus disease severity per the majority vote of 3 experts between either "Plus", "Pre-plus" or "No Plus". Additionally, all combinations of image pairs within the set were assigned "comparison" labels reflecting relative disease severity obtained from 5 experts (4950 labels total). Deep learning models were first trained with "class" labels from up to 60 randomly sampled images, and validated on a set of 20 images with "class" labels. Then, this process was repeated using "comparison" labels. All models were then evaluated on a test set of 5561 pre-labeled fundus images in two binary classification experiments: "Normal vs. Abnormal" and "Plus vs. Non-plus". For each model, predictive performance was measured by area under the receiver operating curves (AUC).

Results: For a given number of images, models trained on "comparison" labels consistently outperformed those trained on "class" labels. For the same number of labels, the performance of "class" and "comparison" labels was similar, but models trained on class labels exhibited wider confidence intervals by up to 0.2% in "Normal vs. Abnormal" experiments and 0.4% in "Plus vs. Non-plus" experiments (Figure 1).

Conclusions: "Comparison" labels are more informative per image than "class" labels. Further, the inherent subjectivity of "class" labels generates higher variability in model performance. This offers a solution for training highly accurate image classification models with fewer data.

CONTROL ID: 3531118

SUBMITTER (NAME ONLY): David Eveleth

TITLE: High endogenous Fibroblast Growth Factor 1 levels may explain regenerative response of rabbits to endothelial damage

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Eveleth, G. Duffey, L. Myers, S. Pizzuto, J. Weant, Trefoil Therapeutics, Inc, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rabbits regenerate their corneal endothelium readily after lesioning. Humans regenerate their corneal endothelium slowly if at all. FGF1 is an important growth factor in the development of the eye and stimulates regeneration. The purpose of this study was to measure the endogenous FGF1 levels in rabbits and humans to ascertain whether differing FGF1 levels might be involved in the differing levels of regeneration.

Methods: Ocular tissues from rabbit, other species, and human eye tissues were analyzed for FGF1 content using a specific and sensitive ELISA and by western blotting.

Results: The levels of FGF1 in the aqueous humor of rabbits is significantly higher than humans (1.1 ng/ml vs 33 pg/ml, $p < 0.05$). FGF1 levels in aqueous do not appear to be correlated with age. Rabbit Descemet's membrane (+endothelial cells) contains 18 ng/g tissue. Other ocular structures in the rabbit also contain significant levels of FGF1 including the lens and iris/ciliary body.

Conclusions: Human aqueous humor has a low concentration of FGF1 while rabbit aqueous contains much higher FGF1. The levels of FGF1 in rabbit tissues are sufficient to generate a biological effect, while those in humans are not. This may help explain the differences in corneal regeneration between the two species.

CONTROL ID: 3531120

SUBMITTER (NAME ONLY): Wolfgang Fink

TITLE: VISTATM: Visual Impairment Subtle Touch AidTM

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Fink, A. Nuncio Zuniga, Visual and Autonomous Exploration Systems Research Laboratory, University of Arizona, Tucson, Arizona, UNITED STATES|B. Ramadan, N. Powers, K. Kay, Neuroscience and Cognitive Science, University of Arizona, Tucson, Arizona, UNITED STATES|S. Hong, Disability and Psychoeducational Studies, University of Arizona, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: To devise a low-tech, low-cost, robust, and minimally obtrusive navigational traveling aid - the Visual Impairment Subtle Touch Aid (VISTA) - for people with visual impairments by combining ultrasonic range detection with proportional vibrational output.

Methods: A navigational aid (Fig. 1) was devised using a sensing belt equipped with independent ultrasonic sensors (Ultrasonic HC-SR04 Distance Measuring Transducers) for distance measurements. The sensors were mounted using mobile clips to allow for user adjustability. The sensing belt was connected to a stimulation belt affixed to the ribcage. The stimulation belt used vibrating minidisc motors with vibration relating to (e.g., proportional to) the sensed distance between the belt wearer and surrounding obstacles. Each distance measuring sensor was connected to its assigned set of vibrating minidisc motors via its own Arduino Nano that performed the conversion of the sensed distance to motor vibrations. The proof-of-concept VISTA device was validated through preliminary testing on blindfolded, but fully sighted, persons and one blind person (all authors) in navigating a novel environment without any additional aids, such as a cane.

Results: While scaling the vibrational strength seemed intuitive at first, the near-field "perception" proved insufficient. Through programming the vibrational output to pulse at different intervals depending on the distance from nearby obstacles, i.e., temporal pulsecoding or frequency encoding as opposed to amplitude encoding, the need for a differentiating output was met. In preliminary tests, the devised ultrasonic-sensor-equipped belt and vibration-actuator-equipped vibration belt combination (i.e., VISTA) was capable of informing users of surrounding obstacles in real time while navigating a hallway with several turns.

Conclusions: VISTA is currently limited to level environments, especially indoors: Curbs or stairs still pose significant issues to the user without training or supplementary aids, as these obstacles are below the sensor range and therefore not detected. Miniaturization of VISTA would allow a higher density of sensors on the belt. While certainly not intended as a replacement for the widely and successfully used cane, VISTA may serve as an additional, minimally obtrusive navigational travel aid for the visually impaired to augment the spatial experience of their environment.

CONTROL ID: 3531139

SUBMITTER (NAME ONLY): Samuel Titchener

TITLE: Phosphene mapping in a 44-channel suprachoroidal retinal prosthesis

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Visual prosthesis stimulation strategies generally assume a retinotopic mapping of the stimulating electrodes. We investigated perceived phosphene locations versus retinotopic electrode positions in retinal prosthesis recipients to validate this assumption.

Methods: Three end-stage retinitis pigmentosa (RP) recipients (S1-3) of a 44-channel suprachoroidal retinal implant (NCT03406416) performed a mapping task for a subset of electrodes. In each trial a single electrode (or a shorted pair) was activated for 500ms and the subject was instructed to move their eyes (head-fixed) to the location of the phosphene. Perceived phosphene locations were expressed as the change in eye position ($^{\circ}$ of visual arc) between stimulus onset and the end-point of the resulting saccade. Predicted phosphene locations were estimated by comparing electrode locations in fundus photos with theoretical projections in the Drasdo-Fowler schematic eye. In addition, participants performed a square localisation task (10° wide targets, $n=24$) on a 42" touchscreen, and pointing precision was compared to the error between predicted and perceived phosphene locations in the mapping task.

Results: In S1 and S2, phosphene locations correlated well with retinotopic electrode locations. Variability in phosphene location for S1 and S2 was correlated with the eccentricity of the electrode from the fovea (S1: $R^2=0.69$; S2: $R^2=0.81$), suggesting more eccentric electrodes produced less spatially distinct phosphenes. For S3, phosphene locations did not correlate with electrode locations and there was little distinction between the measured locations of different phosphenes, indicating large or spatially indistinct phosphenes. This was associated with worse pointing precision in the target localisation task for S3 compared to S1 and S2 (Kruskal-Wallis $p<0.001$). Variability in phosphene location was not correlated with electrode eccentricity in S3 ($R^2=0.02$). S3 had a more clinically advanced form of RP than S1 and S2.

Conclusions: Retinotopic position was predictive of perceived phosphene location for two of three subjects in an eye-tracker mapping task. In the third subject all phosphenes appeared in a similar region of the visual field and functional performance was worse, presumably due to the distortion of retinal morphology expected with advanced RP. Accurate mapping of spatial perception may improve camera-to-electrode mapping strategies.

CONTROL ID: 3531153

SUBMITTER (NAME ONLY): Zhichao Wu

TITLE: Subthreshold Nanosecond Laser in Age-Related Macular Degeneration: Observational Extension Study to the LEAD Clinical Trial

SESSION TITLE: Dry AMD therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Wu, L.A. Hodgson, E. Caruso, C.A. Harper, S.S. Wickremashinghe, A.C. Cohn, P. Sivarajah, N. Tindill, C.D. Luu, R.H. Guymer, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|Z. Wu, C.A. Harper, S.S. Wickremashinghe, C.D. Luu, R.H. Guymer, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|F.K. Chen, Centre for Ophthalmology and Visual Science (incorporating Lions Eye Institute), The University of Western Australia, Perth, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To evaluate the long-term effect of subthreshold nanosecond laser (SNL) treatment on progression to late age-related macular degeneration (AMD).

Methods: The Laser Intervention in the Early Stages of AMD (LEAD) study is a 36-month trial where 292 participants with bilateral large drusen were randomized to receive SNL or sham treatment in one eye at 6-monthly intervals up to 30-months. After the completion of the LEAD study, the two largest recruiting sites (who recruited 212 participants) offered remaining participants an opportunity to enrol in a 24-month observational extension study, with no further treatments performed. The difference in the time to develop late AMD between those randomized the SNL or sham treatment for participants at these two sites (referred to as the “extension study”) was examined.

Results: Overall, there was no significant difference in rate of progression over a 60-month period in those randomized to the SNL compared to sham group (adjusted hazard ratio [HR] = 0.63; 95% confidence interval [CI] = 0.36 to 1.09; P = 0.098), being a similar finding seen in the 36-month LEAD study. However, there continued to be evidence of treatment effect modification based on the coexistence of reticular pseudodrusen at baseline (RPD; adjusted interaction P = 0.007). Namely, progression was significantly slowed with SNL treatment for those without coexistent RPD (adjusted HR = 0.34; 95% CI = 0.16 to 0.71; P = 0.004), but it was not significantly different for those with RPD (adjusted HR = 1.81; 95% CI = 0.67 to 4.88; P = 0.239).

Conclusions: A 24-month observational extension study to the LEAD trial confirmed that SNL treatment did not significantly reduce the overall rate of progression to late AMD. However, the persistence of a potential beneficial treatment effect in those without coexistent RPD over a longer follow-up duration of 24 months without additional treatment is encouraging. These findings provide further justification for future trials to examine the potential value of SNL treatment for slowing progression in the early stages of AMD.

CONTROL ID: 3531155

SUBMITTER (NAME ONLY): Roger Henry

TITLE: The Impact of Frailty on Perioperative Outcomes after Open-Globe Injury in the Geriatric Population

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.K. Henry, A. Uppuluri, P.D. Langer, M.A. Zarbin, N. Bhagat, Institute of Ophthalmology and Visual Science, New Jersey Medical School, Newark, New Jersey, UNITED STATES|R.K. Henry, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Frailty is a state of diminished physiological reserve limiting resolution of homeostasis following a stressor. Frailty is emerging as a powerful risk stratification tool that has been validated across multiple surgical specialties. This study tested the hypothesis that frailty is a risk-factor for perioperative complications following open globe injury (OGI) in the geriatric population.

Methods: This population-level retrospective study analyzed all cases of OGI among geriatric patients (≥ 65 years old) in the US within the Nationwide Inpatient Sample from 2002 to 2014. Patients were dichotomized as either “frail” or “non-frail” using the previously-validated Johns Hopkins Adjusted Clinical Groups (ACG) frailty-defining diagnosis indicator. Baseline characteristics, ocular complications, and clinical outcomes were compared based on frailty status. Multivariable regression tested the association of frailty with mortality and endophthalmitis.

Results: 9144 geriatric OGI patients were identified, 514 (5.6%) of whom were frail. Compared to their non-frail counterparts, frail patients were on average slightly older, (84.0 years vs 80.4 years, $P < 0.001$), female-predominant (75% versus 61%, $P < 0.001$), and of different racial profile ($P < 0.001$). Enucleation rates were higher among frail patients (10.5% versus 7.3%, $P = 0.006$), as were rates of endophthalmitis (3.1% versus 1.7%, $P = 0.022$), in-hospital mortality (5.6% versus 1.7%, $P < 0.001$), length of stay (mean LOS, 9.78 days vs 4.39 days, $P < 0.001$), and total charges billed (\$84,113 versus \$39,911, $P < 0.001$). Rates of orbital floor fracture, globe rupture, and phthisis were not significantly different. On multivariate analysis frailty was a significant independent predictor of endophthalmitis (odds ratio, OR 2.364, 95% CI 1.325-4.218) and in-hospital death (OR 4.244, 95% CI 2.772-6.499, $P < 0.001$).

Conclusions: Among the US geriatric population admitted for OGI (2002-2014), 5.6% had frailty-defining comorbidities. This cohort was slightly older (mean 84 years), predominantly female (75%), and at higher risk for enucleation (10.5%), endophthalmitis (3.1%), and in-hospital death (5.6%) while requiring greater hospital resources (mean LOS 9.78 days, mean total charges \$84,113). Awareness of the impact of frailty on perioperative complications may facilitate risk stratification, perioperative planning, and allocation of resources for this high-risk population.

CONTROL ID: 3531177

SUBMITTER (NAME ONLY): Himal Kandel

TITLE: Quality of life impact of eye diseases: a Save Sight Registries study

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Kandel, V. Nguyen, M.C. Gillies, S.L. Watson, Save Sight Institute, Sydney Medical School, Faculty of Medicine and Health, The University of Sydney, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To evaluate the quality-of-life (QoL) impact of eye diseases (keratoconus; age-related macular degeneration, AMD; retinal vein occlusion, RVO; and diabetic macular edema, DME) using the Impact of Vision Impairment (IVI) questionnaire, and to determine the relationship between the IVI scores and visual acuity.

Methods: A cross-sectional study was conducted utilizing the Save Sight Registries data. Rasch analysis was conducted on the IVI data using the Andrich Rating Scale Model. Univariate analysis included Welch's t-test, one-way ANOVA, and Pearson's correlation coefficient.

Results: The IVI was completed by 1693 patients; 336 with keratoconus, 1147 AMD, 150 RVO and 60 DME. 735 (54.2%) patients with retinal conditions had received intravitreal therapy. Participants had a mean \pm SD age of 68.0 \pm 22.2 years and 842 (49.7%) were female.

The IVI scales (overall; visual functioning, VF; emotional, EM) had robust psychometric properties including well-functioning response categories, unidimensionality (variance explained > 50%, eigenvalue of the first contrast <3.0), excellent measurement precision (person separation index > 2.0) and satisfactory fit statistics (MnSq, 0.7 to 1.3).

In a group-wise analysis, female patients had lower VF (1.8 vs 2.3), EM (2.3 vs 2.7) and overall (1.7 vs 2.1) logits IVI scores (all $p < 0.05$). The differences in mean VF scores between the diseases were not significant (Keratoconus 2.0, AMD 2.0, RVO 2.1, DME 2.1 logits; $p = 0.998$). Keratoconus patients had worse mean EM scores (Keratoconus 1.7 vs AMD 2.7, RVO 2.7, DME 2.5 logits; all pairwise $p < 0.05$). Similarly, keratoconus patients had worse mean overall IVI score in logits (1.7) than AMD (2.0), RVO (2.0), and DME (1.9), however, the differences were not statistically significant ($p = 0.06$). The IVI overall and subscale scores were similar between retinal conditions (all $p > 0.05$). Pearson's correlations of IVI scores were higher with visual acuity in the better eye (VF 0.41, EM 0.27, overall 0.37) than in the worse eye (VF 0.28, EM 0.24, overall 0.28). Correlations with visual acuity were stronger for VF than for EM subscales.

Conclusions: The IVI was a psychometrically robust QoL questionnaire. Keratoconus patients had worse IVI scores, particularly low EM scores, than patients with retinal diseases. The low strength of correlations between visual acuity and QoL scores, although statistically significant, suggested a complex relationship.

CONTROL ID: 3531234

SUBMITTER (NAME ONLY): Kohei Harada

TITLE: Toxicity of amphotericin B on corneal epithelial cells stored in Optisol-GS: corneal epithelial cell morphology and migration

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the toxicity of amphotericin B in OptisolTM-GS corneal storage media (Bausch & Lomb) on corneal epithelial cells (CECs).

Methods: Cornea specimens were dissected from Japanese white rabbit eyes, and then refrigerated at 4°C in OptisolTM-GS, with or without amphotericin B. Storage medium was divided into the following 5 groups (4 corneas per group): Group 1 (control) without amphotericin B (OptisolTM-GS only), and Groups 2, 3, 4, and 5, which included amphotericin B at the concentration of 2.5, 5, 25, and 50 µg/ml, respectively. After 7-days storage, CEC morphology and migration were evaluated. Hematoxylin and eosin staining, immunohistochemical staining (ZO-1), and terminal deoxynucleotidyl transferase-mediated dUTP-digoxigenin nick-end labeling (TUNEL) assay were performed using 7 µm cryosections obtained from the preserved corneas. For the purpose of migration assay, 3 corneal blocks (8 x 3 mm each) from 1 preserved cornea were cultured with Dulbecco's modified eagle medium and Ham's F12 nutrient mixture for 24 hours in a 12-well plate, and the area of CEC migration (2 mm at the central region) onto the stromal surface was then measured.

Results: In Groups 3, 4, and 5, CEC deformity and vacuolation was observed in all preserved specimens. However, CEC morphology was maintained in Groups 1 and 2. The expression of ZO-1 was significantly decreased in the preserved corneal specimens in Groups 4 and 5. TUNEL labelling index (mean±SD) revealed increased CEC apoptosis in Group 3 (48.6±8.7%), which was further aggravated in Groups 4 (59.9±9.0%) and 5 (60.0±7.3%), compared with the control group (33.4±5.8%). The mean CEC migration was inhibited in Group 3 (0.93±0.21mm²), and also in Groups 4 (0.73±0.27mm²) and 5 (0.66±0.12mm²) in a dose-dependent manner, compared with the control group (1.16±0.18mm²).

Conclusions: When added to OptisolTM-GS, amphotericin B was found to be toxic to CECs and inhibit CEC migration. However, our findings revealed that at a concentration of under 5 µg/ml, amphotericin B can be considered safe for use in corneal transplant surgery.

CONTROL ID: 3531242

SUBMITTER (NAME ONLY): Xiaoyong Wang

TITLE: Identification of choroidal neovascularization activity using deep learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop an automated tool for choroidal neovascularization (CNV) detection using deep learning (DL) algorithms.

Methods: We evaluated 8527 optical coherence tomography (OCT) images from 521 patients in the as-needed arms of the HARBOR trial (NCT00891735) that evaluated ranibizumab in neovascular age-related macular degeneration (nAMD). Disease activity in the study eye was defined as fluid on OCT (eg, intraretinal fluid, subretinal fluid, subretinal pigment epithelial fluid) or if a patient's visual acuity decreased by ≥ 5 letters from the previous visit. Consequently, disease activity could be defined solely by the presence of retinal fluid associated with underlying CNV on OCT without the requirement of a decrease of ≥ 5 letters relative to the previous visit. In this subset of visits, study eye OCT scans of $1024 \times 512 \times 128$ voxels collected from a Zeiss Cirrus machine were flattened toward the retinal pigment epithelium (RPE) layer, and cropped to 384 pixels above and 128 below the RPE. To accommodate the GPU memory constraints, the central 15 B-scans were selected as representatives. As such, the input size of each scan to the network was $512 \times 512 \times 15$. 3618 scans from diseased eyes and 4909 from eyes without disease were split into training and test sets in a 4:1 ratio using stratified sampling. 5-fold cross-validation was applied only using the training set to optimize parameters. A Squeeze-and-Excitation (SE)-embedded MobileNet was designed to classify eyes with and without CNV. MobileNet greatly reduces model size using depth-wise separable convolutions and the SE module contributes by adaptively recalibrating channel-wise feature response. Weighted cross-entropy was used as a loss function because the number of samples in each class was unbalanced. Data augmentation, including rotation, translation, and flipping, was applied during training.

Results: The model was evaluated on a test set of 1706 images from 102 patients and achieved an area under the receiver operating curve of 0.81 ± 0.012 , with accuracy of 0.76 ± 0.027 , sensitivity of 0.66 ± 0.028 , and specificity of 0.83 ± 0.029 .

Conclusions: Our study demonstrated that a prototype DL model can accurately detect CNV disease activity based on changes in the retinal anatomy on OCT. While this algorithm needs to be validated on other datasets, it could potentially be applied for remote and automated monitoring of nAMD.

CONTROL ID: 3531256

SUBMITTER (NAME ONLY): Melanie MARIE

TITLE: A 1-Month Toxicology and Biodistribution NHP Pilot Study Evaluating a Single Subretinal Bilateral Administration of SPVN06 - A Novel AAV-Based Gene Therapy for the Treatment of Rod-Cone Dystrophies Agnostic of the Causative Mutation

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rod-Cone dystrophies (RCD) are inherited neurodegenerative diseases characterized by an initial loss of rod photoreceptors (rods) followed by loss of cone photoreceptors (cones) eventually causing blindness. Greater than 1.5 million individuals worldwide are affected by RCD with >65 genes identified. The NXNL1 gene encodes 2 proteins produced by rods, rod-derived cone viability factor (RdCVF) and its full-length isoform, thioredoxin RdCVFL, also expressed by cones, that support cone survival by promoting glycolysis and preventing oxidative damage, respectively. SPVN06 is a novel AAV-based drug candidate encoding both human RdCVF and RdCVFL within the same vector. A single subretinal administration of SPVN06 is expected to protect against cone degeneration in RCD patients independent of the causative mutation. SPVN06 nonclinical safety was evaluated in a 1-month pilot toxicology and biodistribution study in non-human primates.

Methods: Four female cynomolgus monkeys received a bilateral subretinal injection of vehicle (n=1) or SPVN06 (n=3) at 1×10^{11} vg/eye (100 μ L). The animals were observed for one month. A limited toxicological assessment was conducted to assess systemic and ocular safety. Parameters evaluated included clinical observations, body weights, clinical pathology, organ weights and macroscopic observations. Ocular, brain, and liver tissues were microscopically assessed. A comprehensive ocular evaluation including indirect ophthalmoscopy, slit lamp biomicroscopy, intraocular pressure (IOP) measurements, fundus imaging, optical coherence tomography (OCT) and full-field electroretinography (ffERG) was conducted.

Results: There were no systemic effects on any of the parameters assessed. Ophthalmoscopic and microscopic observations were characterized by only minimal posterior uveitis and localized RPE hypertrophy confined to the dose site.

Conclusions: This one-month toxicology and biodistribution pilot study in NHP demonstrated that SPVN06 is well tolerated at 1×10^{11} vg/eye, 100 μ L, following subretinal administration. This study is informing the nonclinical development of SPVN06, a novel AAV-based drug candidate, expected to prevent cone degeneration in RCD patients independent of the causative mutation.

CONTROL ID: 3531267

SUBMITTER (NAME ONLY): Wen Shi

TITLE: Single-cell Chromatin Accessibility Identifies Pathogenic Regulatory Programs in Vogt-Koyanagi-Harada Disease and Behcet's Disease

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Previous genome-wide association studies (GWAS) show that a substantial proportion of genetic risk for autoimmune disease falls within accessible regions of the cell types associated with the disease. Chromatin accessibility provides critical information about DNA cis- and trans-regulatory elements. Despite its importance, much remains to be learned about the noncoding genome and epigenetic regulation in autoimmune eye diseases and pathogenic immune cells. Therefore, we map an epigenetic landscape of chromatin accessibility in peripheral blood from healthy individuals and patients with Vogt-Koyanagi-Harada (VKH) and Behcet's disease.

Methods: This study involved healthy individuals (N=12), patients with VKH disease (N=12), and Behcet's disease (N=13) at Zhongshan Ophthalmic Center, China. Peripheral blood mononuclear cells (PBMCs) were collected and processed using a single-cell assay for transposase-accessible chromatin sequencing (scATAC-seq). The data were aligned to the GRh38 reference genome and quantified by the Cell Ranger pipeline. We employed UMAP, a nonlinear dimensionality reduction method to visualize the data, and MACS2 to perform peak calling. We identified each cell type-specific transcription factor (TF) activity using ChromVAR.

Results: We generated high-dimensional scATAC-seq data in PBMCs and identified diverse epigenetic regulatory landscapes. A detailed analysis of the landscape of healthy individuals showed distinct transcription factor activities in double-negative B cells and unraveled the regulatory trajectory of B cell development. A significant decrease in the frequency of Th2 cells in Behcet's disease patients was noticed compared to healthy individuals ($p=0.0146$). Integration of scATAC-seq data with autoimmune disease GWAS datasets revealed target cell types as well as pathogenic TFs for VKH and Behcet's disease, such as those related to NF- κ B and STAT family.

Conclusions: The application of scATAC-seq enables unbiased identification of cell type-specific active DNA regulatory elements. This study characterizes epigenomic profiles of peripheral immunity and unveils the regulatory programs of VKH and Behcet's disease. These data represent a valuable resource for testing diagnostic and therapeutic strategies against autoimmune eye diseases.

CONTROL ID: 3531268

SUBMITTER (NAME ONLY): Pengjuan Ma

TITLE: A human circulating immune cell landscape in diabetic macular edema patients

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Inflammation plays an important role in diabetic macular edema (DME) and contribute to vascular permeability and edema by release of inflammatory cytokines, but little is known about the inflammatory roles of different circulating immune cells among DME patients. We utilized single-cell RNA sequencing (scRNA-seq), an unbiased and high-throughput single cell technology, to clarify phenotype and function of peripheral immune cells in DME.

Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from DME patients and healthy donors. Single-cell RNA libraries were prepared using the Chromium Single Cell 5' v2 Reagent (10x Genomics) kit. Raw sequence read quality was assessed using FastQC software. Cell Ranger Software was used to generate each sample's gene counts and aggregate them together. R package Seurat v3 was used for data normalizing, clustering, dimensionality reduction, differential expression analysis, and visualization.

Results: We constructed a single-cell RNA atlas comprising 62,916 PBMCs collected from 4 healthy controls and 4 DME patients. We investigated the distribution of the major immune cell lineages, including monocytes, DCs, NK and T, and B cells, using uniform manifold approximation and projection (UMAP). We characterized the expression of canonical lineage markers and other genes specifically upregulated in each cell cluster. Our differential expression gene (DEG) analysis showed that monocytes were enriched of genes participating in the cytokine pathway and inflammation activation. Compared to healthy controls, CD14++ inflammatory monocytes in DME patients had high expression levels of inflammatory genes such as IL1 β , TNF, JUN, FOS, and NF- κ B; and higher expression levels of chemokines, including CCL3, CCL4, and CXCR4. Gene Ontology (GO) and pathway analysis of the DEGs demonstrated that TNF, interleukin signaling, and NF- κ B signaling pathways were enhanced in DME patients.

Conclusions: We reveal a landscape of peripheral blood immune cell subsets in DME patients. CD14++ monocytes exhibit features of chronic stimulation and participate in chronic inflammation through producing inflammatory cytokines. Therapeutic interventions targeting chronic inflammation in monocytes may lead to improved outcomes in patients with diabetic macular edema.

CONTROL ID: 3531320

SUBMITTER (NAME ONLY): Maria de los Angeles Ramos Cadena

TITLE: Ocular Vessel Density Among Glaucoma Subjects of Different Ethnicities

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Prevalence and severity of glaucoma varies between ethnicities. It has been previously shown that ocular vessel density (VD) varies among healthy subjects of different ethnicities. To further elucidate the potential role of VD in glaucoma we examined ocular VD in Caucasian, African American (AA), and Latin at similar stages of glaucoma severity.

Methods: 150 glaucoma eyes of which 46 eyes (30 subjects) were Caucasian, 71 eyes (43 subjects) African American, and 33 eyes (19 subjects) Latin were included in the analysis. Comorbidities known to affect the systemic or local micro- or macro-vasculature and medications that are known to modify vessel diameter were excluded. Disease severity distribution was similar across ethnicity groups. All eyes had comprehensive ophthalmic examination, Cirrus HD-OCT (Zeiss, Dublin, CA) and OCT angiography (OCTA; Angioplex, Zeiss) qualified scans of the macula and optic nerve head regions (200x200 OCT cube scans and 3x3mm / 6x6mm OCTA scans). VD as provided by the device's native software in the inner vascular plexus was used for the analysis. Statistical analysis was performed using mixed-effects models accounting for ethnicity, age, axial length, visual field mean deviation (MD), OCT signal strength (SS), disc area and intra-subject correlation. Tukey-adjusted p-values for pairwise ethnicity comparisons were obtained.

Results: No significant difference was detected in age and MD among ethnicities (Table 1). Caucasian subjects had the longest AL and thinnest RNFL, and Latin subjects had the largest disc area and cup-to-disc ratio (CDR; Table 1). No significant differences were detected among ethnicities in ONH VD in any of the scan types and regions. In the macula, Caucasians had significantly higher VD in the center of both scan sizes in comparison with both AA and Latin

(Table 2). Caucasian eyes also had significantly higher VD in the full 3x3 scan in comparison with AA eyes. There were no significant differences in the rest of the macular VD measurements among the 3 groups.

Conclusions: Macular VD in glaucoma subjects varies among ethnicities and might play a role in the varying disease behavior among ethnicities. Differences in foveal avascular zone size might explain our findings but further investigation is warranted.

CONTROL ID: 3531326

SUBMITTER (NAME ONLY): Yukako Taketani

TITLE: Neurokinin-1 Receptor Antagonism Ameliorates Ocular Pain and Immune Responses in Dry Eye Disease

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ocular pain is a common symptom of dry eye disease (DED). Our previous work has demonstrated increased levels of the neuropeptide substance P (SP) in DED. SP preferentially activates the neurokinin 1 receptor (NK1R) to mediate an inflammatory response. However, the direct effects of SP in ocular pain in DED are unknown. The purpose of this study was to determine the contributions of SP to ocular pain and inflammation in DED through antagonism of NK1R.

Methods: DED was induced in 6 week old C57BL/6 female mice by housing them in a controlled environment chamber for 14 days. Eye wiping test was performed to evaluate pain after instillation of hypertonic saline (2M NaCl) on days 0, 2, 4, 7, 10, and 14 during DED induction. L-733,060 (1µg/µl), an NK1R antagonist, was administered topically twice per day from day 0 to day 14 after DED induction. Cornea, draining lymph nodes (dLNs), and trigeminal nerve ganglion (TG) were collected on day 14. SP expression in TG and cornea were measured by ELISA. The frequency of MHC-II^{high}CD11b⁺ cells in dLNs was assessed using flow cytometry.

Results: Eye wipe behavior was significantly increased in the DED group compared to the normal group ($P < 0.001$) and the peak was reached on day 4 ($P = 0.02$). Application of L-733,060 to DED mice led to significantly decreased eye wipe behavior at day 4 and 14 ($P = 0.03$). Corneal SP expression levels were 25% lower in the L-733,060 group compared to the untreated DED group ($724 \pm 24 \text{ pg}/100 \mu\text{g}$ vs. $976 \pm 82 \text{ pg}/100 \mu\text{g}$, $P = 0.051$) at day 14. In the TG, no difference in SP level was observed amongst groups ($P = 0.97$). Additionally, the L-733,060 group showed significantly fewer MHC-II^{high}CD11b⁺ cells compared to the untreated DED group at day 14 ($2.82 \pm 0.26\%$ vs. $4.46 \pm 0.24\%$, $P = 0.001$).

Conclusions: Our data demonstrate that antagonism of NK1R simultaneously reduces ocular pain and suppresses inflammation in a murine model of DED, suggesting SP blockade as a new therapeutic strategy in the management of DED.

CONTROL ID: 3531328

SUBMITTER (NAME ONLY): Jordan Reed

TITLE: An observational clinical study of the influence of phacoemulsification on choroidal neovascular membrane activity in age related macular degeneration

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Thousands of phacoemulsification surgeries are performed on eyes with exudative age-related macular degeneration (exAMD) in the United Kingdom each year. Controversy over phacoemulsification's influence on exAMD disease activity limits the information which can inform clinicians' and patients' management decisions. This observational study aims to resolve this by reporting on intravitreal injection (IVI) frequency as a pragmatic marker of exAMD disease activity in a large cohort.

Methods: A cohort of eyes with exAMD (n=327) that underwent phacoemulsification at a single tertiary centre from 2014-2019 were identified. Cases were matched by length of exAMD diagnosis at a specified 'time-zero' within the follow-up of pseudophakic eyes with exAMD (n=327). Data concerning demographics, visual acuity (VA) and intravitreal injection frequency (IVI) before and after 'time-zero'/phacoemulsification were collected. The primary outcome was change in IVI frequency following 'time-zero'/phacoemulsification which was analysed through a 2-tailed Mann Whitney U-test and univariate and multivariable linear regression.

Results: Following 'time-zero'/phacoemulsification' mean reduction in annual IVI frequency was 0.6 injections/year (95%CI 0.4,0.9) and 0.4 injections/year (95%CI 0.1,0.7) in the comparison and phacoemulsification cohorts respectively. Mean VA gain 12 months after phacoemulsification was 11.3 (95%CI 9.2,13.4) early treatment of diabetic retinopathy study (ETDRS) letters, with 214 eyes (65.4%) gaining ≥ 5 ETDRS letters after surgery. On multivariable linear regression, phacoemulsification during follow-up was found to significantly ($p=0.015$) independently increase annual IVI frequency by 0.39 (95% CI 0.07,0.71) injections, with minimal overall direct and indirect effects ($R^2=0.01$). Multivariable linear regression with final VA as the dependent variable found no significant influence from baseline demographics or length of exAMD diagnosis.

Conclusions: Whilst phacoemulsification appears to have a statistically significant independent exacerbating effect on exAMD disease activity, this effect is too small to be considered clinically significant. Phacoemulsification should be offered to patients regardless of exAMD diagnosis and independently of their gender, age and length of exAMD diagnosis.

CONTROL ID: 3531352

SUBMITTER (NAME ONLY): Yvette Schein

TITLE: Strabismus Associated with Craniosynostosis and related Craniofacial Surgery

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We sought to determine prevalence and types of strabismus in children with craniosynostosis, as well as effects of major and minor cranial suture involvement and craniofacial surgery. Limited published data describe these prevalences.

Methods: Retrospective cohort study of children with craniosynostosis over an 11-year period. Primary outcomes were prevalence and types of strabismus overall, among subtypes of craniosynostosis determined by imaging and intraoperative findings, and pre/post craniofacial surgery.

Results: 726 children with craniosynostosis were studied; mean age 2.9 years (SD 3.7), mean follow-up 3 years (SD 3), 37% syndromic/genetic association. 44% had sagittal fusion, 41% coronal, 31% metopic, 11% lambdoid, 9% minor suture(s). 82% had one major suture fused, 17% had 2-4 sutures. 56% underwent craniofacial surgery. Overall, 261 (36%) children had strabismus, of whom 18% had exotropia, 12% esotropia, 11% vertical, 20% inferior oblique overaction. Considering pre-craniofacial-surgery exams, if one major suture was fused, strabismus risk was 15-18%, except for coronal, which was 47%. Strabismus prevalence increased with number of fused major sutures (30% for 1, to 70% for all 4). Craniofacial surgery increased strabismus (26% versus 33%, $p=0.03$), but some pre-op strabismus resolved postoperatively. Vertical strabismus was associated with unilateral (36%) versus bilateral coronal synostosis (9%, $P<0.001$). Exotropia was associated with minor suture fusion (32% vs. 16%, $p=0.01$).

Conclusions: Craniosynostosis carries a 36% risk of strabismus, a 15-fold increase versus the general population, and this risk varies with number and type of sutures involved.

CONTROL ID: 3531354

SUBMITTER (NAME ONLY): Usha Chakravarthy

TITLE: Impact of Pegcetacoplan on Progression of Nascent Atrophy in Age-related Macular Degeneration (AMD)

SESSION TITLE: Dry AMD therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the potential impact of pegcetacoplan on nascent geographic atrophy (GA) lesions by analyzing their progression in patients who received either intravitreal pegcetacoplan monthly (PM) or sham treatment (S) in the phase 2 multicenter, randomized, single-masked, sham-controlled FILLY study through a post-hoc analysis.

Methods: Patients from the PM (n=42) and S (n=69) arms of the FILLY study who did not develop exudative AMD and completed the month 12 study visit were included in this analysis. The evaluation was based on examination by masked readers of optical coherence tomography (OCT) scans outside a perimeter of 500 microns from the GA border according to the Classification of Atrophy Meetings (CAM) guidelines. The primary outcome measures were a) progression from large drusen to incomplete/complete retinal pigment epithelium (RPE) and outer retina atrophy (iRORA and/or cRORA) and b) progression from iRORA to cRORA at baseline, 6 months, and 12 months.

Results: At baseline, large drusen were observed in 81% (33/41) of patients in the PM group and 74% (49/66) of patients in the S group; iRORA was present in 46% (19/41) and 55% (36/66) of patients in the PM and S groups, respectively. At 12 months, progression from large drusen to iRORA/cRORA occurred in 22.6% (7/31) and 33.3% (15/45) of the PM and S groups, respectively (p=0.31). At the lesion level, these rates were 9.1% (11/121) and 11.9% (21/177) in the PM and S groups, respectively. Progression from iRORA to cRORA was 50.0% (9/18) and 81.8% (27/33) in the PM and S groups, respectively (p=0.02), indicating a lower rate of progression from iRORA to cRORA (39% reduction) in pegcetacoplan-treated eyes. At the lesion level, these rates were 35.5% (11/31) and 64.3% (45/70) in the PM and S groups, respectively.

Conclusions: Eyes receiving monthly intravitreal pegcetacoplan had lower rates of progression from nascent GA to GA compared to sham-treated controls, suggesting a potential role for pegcetacoplan earlier in the course of GA.

CONTROL ID: 3531360

SUBMITTER (NAME ONLY): Michael Kawczynski

TITLE: Prediction of best-corrected visual acuity (BCVA) from color fundus photography (CFP) using deep learning (DL)

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Kawczynski, N. Anegondi, Q. Yang, J.R. Willis, T. Bengtsson, S.S. Gao, J. Dai, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To predict BCVA from CFP images acquired from patients with neovascular age-related macular degeneration (nAMD).

Methods: We performed a retrospective analysis of CFP images and associated BCVA measurements from the phase 3 MARINA (NCT00056836) and ANCHOR (NCT00061594) trials for nAMD. Using the Inception-ResNet-v2 convolutional neural network, a DL regression model was developed to predict BCVA at the concurrent visit from CFP images. A binary classification model was also developed to predict BCVA of < 69 letters (Snellen equivalent of < 20/40) at the concurrent visit from CFP images. Models were trained and tuned via 5-fold cross-validation on 36,541 images from 707 patients in MARINA and tested on an external validation test set of 33,591 images from 413 patients in ANCHOR. Images used for training and testing were acquired from study and fellow eyes at all available visits (screening through month 24). Internal capture fields of F1M, F2, and F3M from left and right stereo views were included, whereas external views of the eye were excluded from the analysis. To remove extraneous information, RGB images were cropped to fit the circular field of view of the CFP and resized to 299 × 299 pixels. To evaluate model performance, the coefficient of determination (R^2) was used for regression, and the area under the receiver operating characteristic curve (AUROC) was used for classification. Predictions for each image were averaged to the patient-eye-visit level. To account for the distance at which BCVA was measured, metrics were calculated for the corresponding chart distances of 2 and 4 m. Models were evaluated based on the in-sample cross-validation tuning set (MARINA) and out-of-sample test set (ANCHOR).

Results: In the regression model, R^2 for predicting BCVA at a chart distance of 2 and 4 m was 0.58 (95% CI, 0.57, 0.60) and 0.60 (95% CI, 0.56, 0.63), respectively, in the test set (Table 1). In the classification model, AUROC for predicting BCVA of < 69 letters at a chart distance of 2 and 4 m was 0.86 (95% CI, 0.85, 0.87) and 0.88 (95% CI, 0.86, 0.89), respectively, in the test set.

Conclusions: Out-of-sample, the identified DL model demonstrates a relatively strong association between the information extracted from the CFP images and visual acuity as measured by BCVA.

CONTROL ID: 3531383

SUBMITTER (NAME ONLY): Lori-Ann Christie

TITLE: Cytoprotective Effects of Brimonidine in an Induced Pluripotent Stem Cell (iPSC)-Derived Retinal Pigment Epithelium (RPE) Model of Age-Related Macular Degeneration (AMD)

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Brimonidine (brimo) drug delivery system (DDS) has been evaluated as a long-acting therapy for the treatment of geographic atrophy (GA) secondary to AMD. Our objective was to delineate the role of brimo as a cytoprotective agent using a human iPSC-derived RPE in vitro model of dry AMD.

Methods: RPE cells were differentiated from iPSC derived from healthy or albino individuals. iPSC-RPE monolayers were matured for 6 to 8 weeks using a previously published protocol that supports the development of key RPE phenotypic features, including polarized expression of RPE specific markers and cytokine secretion, transepithelial potential and resistance, fluid transport and phagocytosis (Sharma et al., 2019). The effects of melanin binding were assessed by comparing supernatant and cell-associated brimo concentrations in pigmented versus albino iPSC-RPE. Pigmented iPSC-RPE were then challenged with complement-competent human serum (CC-HS) to mimic AMD-like conditions. Challenge with CC-HS induces loss of transepithelial resistance, disrupted RPE morphology and sub-RPE lipid deposition. These changes are characteristic to the phenotypic changes of the RPE in dry AMD. We assessed brimo's ability to prevent CC-HS-induced phenotypic changes.

Results: Dose-dependent binding of brimo to melanin was observed in pigmented iPSC-RPE cells with 2- to 6-fold lower brimo concentrations in the supernatant after 24 hr incubation compared to albino RPE cells. No brimo-induced cytotoxicity was observed at concentrations up to 30 mM. Subsequent experiments were conducted at concentrations of 0.3 and 3 mM. Pretreatment of iPSC-RPE cells with brimo prevented CC-HS-induced transepithelial resistance reduction and deposition of lipid droplets. Further, we observed partial restoration of cyclic adenosine monophosphate (cAMP) and intracellular calcium levels in CC-HS-challenged iPSC-RPE cells treated with 3mM brimo. These data suggest that brimo has cytoprotective properties and preserves key functional RPE characteristics, restoring homeostatic mechanisms in cells challenged by an AMD-like insult.

Conclusions: In conclusion, our results demonstrate the cytoprotective effects of brimo in a validated model of complement-mediated RPE AMD-like physiology and support development of brimo drug delivery system (DDS) as a novel therapeutic for GA secondary to AMD.

CONTROL ID: 3531384

SUBMITTER (NAME ONLY): Kelly Nichols

TITLE: Real-world effectiveness of lifitegrast in dry eye disease patients across clinical practices in the US and Canada

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) is a chronic, multifactorial disease of the ocular surface. The purpose of this real-world clinical study was to assess the baseline characteristics and treatment outcomes in DED patients treated with lifitegrast for up to 12 months in the US and Canada.

Methods: A retrospective, non-comparative, optometrist and ophthalmologist panel-based chart review cohort study design including patients who initiated lifitegrast treatment between January 1, 2017 (US) or 1 January 2018 (Canada) and June 30, 2019 with an index date defined as the first day of lifitegrast treatment. Signs (corneal staining score; tear film break-up time) and symptoms of DED (eye dryness; blurred vision; ocular burning/stinging; foreign body sensation; ocular pain) were evaluated during the 6-month pre-index period and after 6 and 12 months of treatment with lifitegrast.

Results: A total of 600 lifitegrast-treated DED patients (76% female, mean age [standard deviation (SD)] 57 [13] years) were included in the study. Initial diagnosis of DED was determined by optometrists in 262 (44%) patients and ophthalmologists in 332 (55%) patients. Mean time from DED diagnosis to lifitegrast prescription was 23.3 months (SD 42.7) overall, and 31.5 (55.0), 23.8 (35.3) and 22.7 (48.4) for patients who initiated lifitegrast in 2017, 2018 and 2019, respectively. A total of 512 patients (92%) remained on treatment with lifitegrast at the 6-month follow-up period. Signs and symptoms of DED at the 6-month pre-index period (n=600 patients), Month 6 (n=534 patients) and Month 12 (n=320 patients) of follow-up, respectively were: (Fig. 1a-c, percentage of patients): eye dryness ([pre-index; Month 6; Month 12]: 87%; 7%; 3%); blurred vision (59%; 5%; 3%); ocular burning or stinging (55%; 3%; 1%); foreign body sensation (50%; 2%; 2%); ocular pain (12%; 1%;1%); corneal staining score (range 0–15) (median [95% Confidence Interval (CI)]: 6 [6–7]; 2 [1–5]; 2 [1–3]); tear film break-up time (median [95% CI]: 4 [3–12]; 8 [7–9]; 8 [7–8] seconds).

Mean (SD) treatment duration for these patients was 28.5 (10.6), 15.9 (5.2) and 8.8 (2.6) months for patients with index dates in 2017, 2018 and 2019, respectively.

Conclusions: Lifitegrast significantly improved several signs and symptoms of DED in this real-world observational study, with the majority of patients remaining on treatment throughout the 12-month follow-up period.

CONTROL ID: 3531414

SUBMITTER (NAME ONLY): Lenin Ochoa-de la Paz

TITLE: Neuroprotective Effect of Risuteganib on Retinal Neurons in an Excitotoxic Injury Cell Culture Model and a Mechanical Injury Rat Model

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal neuron dysfunction and cell death have been observed across many visual impairment diseases (including age-related macular degeneration, retinitis pigmentosa, glaucoma, and diabetic retinopathy) and treatment options are limited. This study aimed to determine the neuroprotective effect of the investigational drug, risuteganib (RSG), in cultured retinal neuron (RN) cells exposed to excitotoxic damage and retinal degeneration in an experimental optical nerve clamp rat model.

Methods: In RN cells, excitotoxic damage was induced by kainic acid (KA). Primary mouse neuronal cells (n=8) were exposed for 24 h to culture medium only (SSB), 50 μ M KA, or KA + 1mg/mL RSG added either 24 h before or after KA treatment. After treatment, the number and viability of cultured cells were measured using WST-8 and LDH assays. The student's t-test was used for statistical analysis. In an optical nerve clamp study, a total of eight rats were evaluated to assess the protection of ganglion cells. Animals were intravitreally injected 1.28 mg RSG (n=5) or SSB (n=3) 24 h before 60-minute optic nerves crush (ONC), followed by 48 h rest and ganglion cell survival assessment. Wilcoxon Matched-pairs signed ranks test was used for statistical analysis.

Results: Exposure to KA decreased the viability of cultured cells by 40 ± 1.0 % ($P < 0.05$). The cells treated with RSG either before or after KA showed significantly less damage (10 ± 1.5 or 18 ± 1.0 % viability reduction, respectively; $p < 0.05$). LDH assay showed none of the experimental conditions had a detectable alteration in membrane cell structure. Eyes from rats subjected to ONC and injected with vehicle had 10.09 ± 8.622 ganglion cells per field, while those treated with RSG demonstrated 19.46 ± 8.406 ganglion cells per field ($p = 0.0001$).

Conclusions: Our findings showed RSG induced a clear reduction in the cytotoxic effect generated by an excitotoxic condition in cultured retinal neurons. This effect is more prominent when RSG was applied previously to excitotoxicity generated by KA. Additionally, a statistically significant ganglion cell protective effect was observed in the ONC rat model. Altogether, these findings suggest RSG may have neuroprotective properties relevant to human retinal diseases. Nonetheless, additional studies are needed to further clarify this mechanism of action.

CONTROL ID: 3531429

SUBMITTER (NAME ONLY): Steven Saraf

TITLE: Time Series Trends for Rhegmatogenous Retinal Detachment Repair, Retinal Break Treatment, and Posterior Vitreous Detachment using the Intelligent Research In Sight (IRIS®) Registry

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Saraf, M. Lacy, M. Hunt, A.Y. Lee, C.S. Lee, Y. Chee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: We studied time series trends for incidence rates of rhegmatogenous retinal detachment (RRD) repair, retinal break (RB) treatment, posterior vitreous detachment (PVD), and cataract surgery (CS) to investigate seasonal variation and differences among age, race, and sex using the IRIS Registry.

Methods: RRD repair, RB treatment, and CS were based on CPT codes. PVD diagnosis was based on ICD-9/10 codes. Daily incidence rates were calculated during a 5 year period (2014-2018) and defined as the ratio of number of patients diagnosed with RRD, RB, PVD, and CS to the total number of patients followed on a given day. CS group was included as a comparison for seasonal variation given its elective nature. Rates were stratified by decade of life (DOL), sex, and race.

Results: A total of 2,996,982 patients were diagnosed with incident PVD. Patients undergoing RRD repair (n=248,765), RB treatment (n=367,323) and CS (n=6,132,138) were included. The mean daily incidence for RRD, RB, PVD, and CS were 0.5, 0.7, 5.1, 12.2 per 100,000 patients, respectively (Figure 1). The highest incidence of RRD was in the 5th and 6th DOL. Men had higher incidence of RRD repair than women, whereas women had higher incidence of PVD. RRD incidence was higher in Whites compared to others. Time series showing seven day moving average point incidence for RRD repair, RB treatment and PVD by sex and age demographics is shown in Figure 2. Seasonal variation in RRD repair, RB treatment, PVD, and CS corresponded to national holidays with larger fluctuations in winter months.

Conclusions: The higher incidence of RD repair and RB treatment in men compared to higher PVD incidence in women may suggest an inherent sex-related risk. The seasonal variation associated with holidays was less pronounced for RRD repair and RB treatment.

CONTROL ID: 3531433

SUBMITTER (NAME ONLY): David Eichenbaum

TITLE: Inhibition of complement C3 in geographic atrophy with NGM621: Phase 1 study results

SESSION TITLE: Dry AMD therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Complement dysregulation is implicated in geographic atrophy (GA). Complement component 3 (C3) is the convergence point for all three activation pathways. NGM621, a potent ($K_D=0.34$ nM) monoclonal antibody that inhibits C3 cleavage and blocks the complement cascade and downstream effects, is under development to reduce GA progression. The Phase 1 study (NCT04014777) evaluated the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of NGM621.

Methods: Fifteen enrolled patients had GA secondary to age-related macular degeneration in at least one eye, were ≥ 50 years of age, and had GA lesion area of ≥ 2.5 mm² and ETDRS best-corrected visual acuity (BCVA) between 54 and 4 letters in the study eye. In the single-dose cohort (n=9), intravitreal NGM621 (2, 7.5, or 15 mg) was

administered to three patients per dose; in the multidose cohort (n=6), patients received two 15-mg doses 4 weeks apart. Patients were monitored and assessed for 12 weeks. Assessments included BCVA, intraocular pressure (IOP), optical coherence tomography, fundus autofluorescence, serum NGM621 concentrations, and systemic complement activity (CH₅₀).

Results: All 15 patients completed the study; 60% were men, the median age was 80.0 years (68-90), the mean (SD) GA lesion area measured 14.9 mm² (10.8), and 86.7% of lesions involved the fovea at baseline. There were no observed drug-related AEs, no SAEs or deaths, no endophthalmitis, no intraocular inflammation, and no cases of choroidal neovascularization in any eyes. The maximum evaluated dose, 15 mg, was well tolerated in the single-dose and multidose cohorts. As expected, IOP showed acute increases 15 minutes after injection, returned to normal levels within 60 minutes, and was not meaningfully impacted over time. Serum exposures appeared dose proportional, indicating linear PK in the studied range. NGM621 serum exposure was below concentrations that produce systemic complement inhibition at the highest intravitreal dose of 15 mg, and all patients were ADA negative at all time points. GA lesion area and BCVA were generally stable over the 12-week study duration.

Conclusions: In this Phase 1 dose-escalation study, NGM621 up to 15 mg was well tolerated and had a favorable PK/PD profile in patients with GA. NGM621 is being further studied in GA in the ongoing Phase 2 CATALINA study (NCT04465955).

CONTROL ID: 3531450

SUBMITTER (NAME ONLY): Megan Lacy

TITLE: Endophthalmitis risk following same-day vs delayed sequential bilateral cataract surgery using the Intelligent Research in Sight (IRIS)® Registry

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Lacy, J. Owen, R.T. Yanagihara, M. Blazes, R.N. Van Gelder, A.Y. Lee, C.S. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|L. Hyman, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|L. Hyman, Ophthalmology, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|S. Pershing, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endophthalmitis is a rare but serious postoperative complication following ocular surgery. We performed a retrospective observational study to investigate whether same-day bilateral cataract surgery is associated with increased risk of endophthalmitis.

Methods: IRIS® Registry patients who underwent cataract surgery between 2013 and 2018 were evaluated for development of endophthalmitis within two weeks of surgery. Multivariable logistic regression models were fit to assess the risk of endophthalmitis associated with same-day surgery adjusting for age, sex, insurance type, and history of common eye disease (age-related macular degeneration, diabetic retinopathy, and glaucoma) at the subject level, and to assess whether these covariates were associated with different risk of endophthalmitis between the two surgery types. Potential cases of bilateral endophthalmitis were identified and records from these patients were reviewed to confirm endophthalmitis was bilateral.

Results: There were 5,573,639 patients who underwent cataract surgery. A total of 165,609 (3%) had same-day bilateral cataract surgery and 5,408,030 (97%) had unilateral or delayed sequential bilateral surgery. A total of 3,083 (0.055%, 95%CI [0.053, 0.057]) developed postoperative endophthalmitis. Of these patients, 74 (0.045% [0.035, 0.056]) had same-day surgeries and 3,009 (0.056% [0.054, 0.058]) had unilateral or delayed bilateral surgery. Same-day bilateral cataract surgeries were not associated with increased risk of postoperative endophthalmitis (OR: 0.79 [0.60, 1.01]). The risk profile of postoperative endophthalmitis was similar between the two surgery groups (Figure). The six (0.0001%) cases of bilateral endophthalmitis that occurred were all in the delayed sequential group.

Conclusions: Rates of postoperative endophthalmitis were similar to previous literature and the rate of bilateral endophthalmitis was low. Same-day bilateral cataract surgery was not associated with increased risk of endophthalmitis after cataract surgery and did not lead to any cases of bilateral endophthalmitis.

CONTROL ID: 3531456

SUBMITTER (NAME ONLY): Andrew Tran

TITLE: Comparing measurements of optic disc ovality index and rotation angle in myopic eyes using manual, clinical disc margin photography-based and automated, Bruch's membrane opening OCT-based techniques

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare manual measurements of optic nerve head ovality index (OI) and rotation angle based on the clinical disc margin identified on optic disc photographs with automated measurements based on Bruch's membrane opening (BMO) from optical coherence tomography (OCT) scans in healthy, non-myopic and myopic eyes.

Methods: 201 healthy or glaucomatous eyes of 166 study participants enrolled in the Diagnostic Innovations in Glaucoma Study were stratified by level of axial myopia (non-myopic, mild-myopic and high-myopic with axial length > 26 mm). Using ImageJ software, the clinical disc margin of each photograph was manually annotated and the major axis length, minor axis length and angle of major axis from horizontal axis of the annotation were measured and used to derive OI, rotation angle and direction. These derived values were compared to those generated from automated, custom-programmed BMO-based techniques using segmented OCT volumes. R^2 values from linear mixed effects models were used to describe the associations between manual, photograph-based and automated, OCT-based assessment.

Results: Average (95% CI) axial length was 23.3 mm (23.0 mm, 23.3 mm), 24.8 mm (24.7 mm, 25.0 mm) and 26.8 mm (26.6 mm, 27.0 mm) in non-myopic, mild-myopic and high-myopic eyes, respectively (ANOVA, $p \leq 0.001$). The R^2 association (95% CI) between manual photograph-based and automated OCT-based assessment of disc OI for all eyes was 0.26 (0.16, 0.36; $p < 0.001$). This association was weakest in non-myopic eyes (0.09 [0.01, 0.26; $p = 0.016$]), followed by mild-myopic eyes (0.13 [0.02, 0.29; $p = 0.004$]) and strongest in high-myopic eyes (0.40 [0.19, 0.60; $p < 0.001$]). No significant associations were found between photography- and OCT-based assessment of rotation angle with R^2 values ranging from 0.00 (0.00, 0.08) in non-myopic eyes to 0.03 (0.00, 0.21) in high-myopic eyes (all associations $p \geq 0.33$).

Conclusions: Weak associations between manual photograph-based and OCT BMO-based assessment of optic disc ovality and lack of associations between assessment of disc rotation angle indicate that measurements based on these methods cannot be used interchangeably and results should not be directly compared.

CONTROL ID: 3531477

SUBMITTER (NAME ONLY): Niranjani Nagarajan

TITLE: Impact of the COVID-19 pandemic on healthcare access and utilization for American adults who are blind or have low vision

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Flatten Inaccessibility survey was administered from April 3 to 13th, 2020 to investigate the experiences of adults with low vision or blindness during the COVID-19 pandemic. Using this data, we aimed to look at characteristics associated with concerns accessing and utilizing healthcare during the pandemic among participants.

Methods: Survey questions related to healthcare access and utilization included: (1) getting to a pharmacy for prescriptions, (2) ability to maintain their eyecare regimen, and (3) concerns regarding caregiver access should they be hospitalized for COVID. Responses of "strongly agree" or "agree" were classified as having a concern. Multivariable logistic regression was used to determine the association between demographic characteristics and age of onset of visual impairment (VI) with each concern.

Results: 1,921 participants responded to the survey, of whom 65% were blind and 35% had low vision. Table 1 presents demographic characteristics.

In regression analysis, females (OR=1.4, 95% CI=1.08-1.74) were more likely to have concerns regarding access to a pharmacy to get prescriptions than males, but no gender differences were noted for maintaining eyecare regimen or caregiver access. As compared to participants with congenital VI, participants with adult-onset VI were more likely (OR=1.8, 95% CI= 1.32-2.45) to report concerns regarding their ability to maintain their eyecare regimen, but no differences were observed for pharmacy or caregiver access. Participants with onset of VI at 2-18 years of age (OR=1.6, 95% CI= 1.16-2.14) and >18 years (OR=1.3, 95% CI= 1.00-1.69) were more likely to report concern regarding access to a caregiver if hospitalized than those who had congenital VI. Participants with additional disabilities were more likely to report concerns across all three healthcare questions (Pharmacy access: OR=1.8, 95% CI= 1.43-2.23; Eyecare regimen: OR=1.7, 95% CI= 1.32-2.23; Caregiver: OR=1.73, 95% CI= 1.39-2.14) compared to those with vision loss only.

Conclusions: Our data found that among Americans with low vision or blindness, older adults, females, people with adult onset VI, and multiple disabilities were more likely to report concerns with healthcare access and utilization during the COVID-19 pandemic. This study provides information that may aid policymakers as they shape the pandemic response for people with vision loss.

CONTROL ID: 3531488

SUBMITTER (NAME ONLY): Sarah Stuccio

TITLE: Graft Survival after Penetrating Keratoplasty in Patients with History of Incisional Glaucoma Surgery

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. Stuccio, E.J. Shiuey, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|A. Garg Shukla, W.S. Shalaby, Glaucoma, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|Z.A. Syed, Cornea, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Prior incisional glaucoma surgery is a known risk factor for graft failure and decreased visual function after penetrating keratoplasty (PK). However, little is known about the risk factors regarding specific types of glaucoma surgery and role of intraocular pressure (IOP)-lowering medications on graft outcomes. We aimed to determine an association between PK outcomes and glaucoma surgical and medical interventions.

Methods:

In this retrospective cohort study, electronic medical records at Wills Eye Hospital were queried for PKs performed between May 1, 2007 and September 1, 2018 in patients with glaucoma incisional surgery prior to PK. We obtained details of the type of glaucoma surgeries, topical and systemic treatments, and IOP before and after PK. The main outcome measures included graft failure and rejection.

Results:

We identified 148 PKs of 148 eyes (148 patients) who had glaucoma surgery prior to PK. IOP-lowering medications established by 3 months after PK and type of glaucoma surgery are shown in Table 1. The mean baseline IOP and maximum postoperative IOP for this population were 15.5 (SD=5.3) and 25.9 (SD=8.4) mmHg, respectively. Graft rejection was associated with maximum postoperative IOP ($p=0.011$) and IOP difference ($p=0.015$), defined as the difference between baseline IOP and maximum postoperative IOP. Graft failure was associated with higher maximum postoperative IOP ($p<0.001$), higher baseline IOP ($p=0.041$), IOP difference ($p=0.017$), and younger age ($p=0.006$). We did not detect a significant association between prior tube shunt surgery and graft rejection, but this relationship approached statistical significance ($p=0.093$). Other relationships that approached statistical significance include graft failure and use of topical carbonic anhydrase inhibitors (CAIs) ($p=0.070$) and the use of systemic CAIs among patients with tube shunts in the anterior chamber ($p=0.052$).

Conclusions: In patients with a history of glaucoma surgery prior to PK, increased IOP both before and after PK is associated with worse graft outcomes. Future studies are needed to determine a possible relationship between graft failure and postoperative use of CAIs or prior tube shunt placement. Our results suggest that medical and surgical risk factors should be considered when optimizing PK outcomes in patients with prior glaucoma surgery.

CONTROL ID: 3531500

SUBMITTER (NAME ONLY): Xinxing Guo

TITLE: Visual Function, Physical Function, and Activities of Daily Living in Two Aging Communities

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Visual impairment (VI) and physical limitations are common in the older population. However, their associations are yet to be explored in adults 70 years and older. We report the distribution of VI, contrast sensitivity impairment (CSI) and their associations with physical disability and quality of life (QoL) in an aging population-based sample.

Methods: In this cross-sectional analysis, participants from the Atherosclerosis Risk In Community cohort were recruited for the Eye Determinants of Cognition Study, including 494 black participants from Jackson, MS and 558 white participants from Washington County, MD. Distance presenting, corrected, and near VI was categorized as mild (20/40-20/60) and moderate or greater (<20/60) using better-eye acuity. CSI was categorized as moderate (1.04-1.50 logCS) and severe or profound (<1.04 logCS). Physical ability was assessed using the short physical performance battery (SPPB) and self-reported functional limitations, difficulty with activity of daily living (ADL) and instrumental ADL (IADL), physical QoL scores were derived from Short Form 12v2 Health Survey. Associations of VI, CSI with physical abilities were explored overall and by community.

Results: Mean age was 80 years, 63% were female, and 15% had distance presenting VI. Corrected VI (2.6% vs 5.5%), near VI (19% vs 38%), and CSI (70% vs 80%) were less prevalent in Jackson (all $P < 0.05$). Overall, moderate or greater near VI was associated with higher rates of IADL disabilities (prevalence ratios [PR]=1.54, 95% confidence interval [CI]: 1.18-2.02) and lower SPPB scores. Similarly, significant associations were found between moderate or greater presenting VI with functional limitation and lower SPPB scores; and between CSI with functional limitation, and lower physical QoL and SPPB scores. Stratified analysis showed stronger associations in Jackson than Washington County, e.g., Jackson participants with severe & profound CSI showed higher rates of IADL disabilities ($PR_{\text{Jackson}} = 2.11$, 95% CI: 1.13-3.95; $PR_{\text{Washington}} = 1.15$, 95%CI: 0.50-2.66).

Conclusions: Distance VI, near VI and CSI were associated with poor physical function and reduced QoL. These associations should be understood in the context of the communal differences. They call for public health endeavors to address VI and CSI to optimize physical ability and QoL in the older adults with poor vision.

CONTROL ID: 3531637

SUBMITTER (NAME ONLY): Michael Mbagwu

TITLE: Large Scale Cross-Vendor Linkage of Ophthalmic Imaging and American Academy of Ophthalmology IRIS® Registry Clinical Data

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ophthalmic diagnostic imaging is indispensable to clinical practice. Historically, metadata harmonization between different device manufacturers and modalities has been challenging due to insubstantial compliance with the universal Digital Imaging and Communications in Medicine (DICOM) standards, which presents hurdles to patient clinical record linkage. Here, we retrieved and integrated patient-level DICOM file meta-data from two major ophthalmic imaging manufacturers and linked them with corresponding clinical and demographic data in the American Academy of Ophthalmology IRIS® Registry (Intelligent Research in Sight).

Methods: DICOM files of six different posterior segment imaging modalities were acquired from multiple ophthalmic practices. Extracted metadata revealed both 'standards conformant' and 'private manufacturer' metadata tags. Following manual tag inspection, we implemented a programmatically scalable metadata harmonization process of consolidating the tags. This conformed to DICOM standards where possible. Adhering to HITRUST guidelines, proprietary heuristic patient matching algorithms linked these DICOM files with patient records in the IRIS® Registry.

Results: 1,842,633 DICOM files from 58,517 unique patients were available. 1,512,373 images from 48,443 unique patients were successfully linked to existing IRIS® patients. The patient match rate was 82.78%; this likely resulted from a combination of image 'test' patient exclusion, patient detail mismatch between electronic systems, and possible algorithmic parameter aberrations. Each manufacturer's DICOM files contained 127 and 77 metadata tags respectively, both consisting of standard and private tags. The resulting consolidated list consisted of 170 metadata tags.

Conclusions: Using demographic identifiers from DICOM metadata, we created an automated pipeline to comprehensively and accurately connect longitudinal real-world clinical data to various image modalities from multiple manufacturers at the patient and visit level. This curation process has produced a large, enriched and multimodal IRIS® Registry, enabling enhanced research and advanced analytics. As imaging dependence and digital data capture grows, standards compliance will be critical to advancing the virtuous cycle of data-driven clinical insights to improve quality of care and enable novel ophthalmic drug and device development approaches.

CONTROL ID: 3531639

SUBMITTER (NAME ONLY): Daniel Spiegel

TITLE: Scale-dependent improvement in contrast sensitivity with a yellow filter under light scattering conditions

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Spiegel, E. Lim, B. Drobe, Essilor Asia Pacific Pte Ltd, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Some studies show that yellow filters improve contrast processing; others fail to replicate such results. This exploratory study aimed to evaluate the effects of a yellow filter on contrast sensitivity under light scattering conditions and different spatial scales.

Methods: Twenty-four participants (19 to 46 years; mean 31.0 ± 9.5 SD; 13 females) with corrected-to-normal vision were recruited for the study. Light scattering was induced by 0.6 Bangerter foil, and Kodak Wratten 12 filter was used as an exemplar of yellow filters. Using the Freiburg Vision Test ('FrACT'), we measured monocular broadband contrast sensitivity using a 50 arcmin Landolt C under three experimental conditions: Naked eye, Bangerter foil, and Bangerter foil with Yellow filter. In a subset of subjects (13 out of 24), we repeated the measures using 25 and 100 arcmin stimuli. All testing was performed using an eight-alternative forced-choice paradigm (eight cardinal directions of the C opening). The stimuli were viewed at a gamma-calibrated CRT screen at a viewing distance of 3 meters.

Results: A repeated-measures ANOVA on the 50 arcmin data revealed the main effect of condition ($p < 0.001$) whereby Bangerter foil significantly reduced contrast sensitivity by 0.32 ± 0.07 log units ($p < 0.001$) and the addition of Yellow filter partially reversed this reduction by 0.05 ± 0.08 log units ($p = 0.003$). In addition, there was a significant correlation between the reductions of contrast sensitivity induced by the Bangerter foil and its reversal induced by the Yellow filter ($p < 0.001$). An ANOVA, conducted on the subset of subjects who completed the study on all three scales, revealed a significant interaction between the scale and condition $F_{2,24} = 3.4$, $p = 0.048$, whereby the beneficial effects of the yellow filter increased with finer scale.

Conclusions: We have demonstrated the benefit of a yellow filter on contrast sensitivity under scattering conditions. The correlation between contrast sensitivity decrease induced by the Bangerter foil and its partial reversal associated with the Yellow filter usage indicate that subjects more susceptible to scattering may benefit more from yellow filters. Finally, the scale dependence shows that the yellow filter's benefit is most relevant when the processing of fine detail is required.

CONTROL ID: 3531640

SUBMITTER (NAME ONLY): Kenneth Mandell

TITLE: Phase 1 Study of OcuRing-K™ (Ketorolac Ophthalmic Implant) in Subjects Undergoing Cataract Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for the treatment of postoperative inflammation but have known limitations with respect to their tolerability and safety. Caution is recommended in patients with dry eye disease, diabetes, and systemic immunologic disorders due to an increased risk of corneal complications. There is a need for alternative delivery mechanisms that overcome the limitations of topical NSAIDs. Here we report the first clinical results with a novel sustained-release ketorolac implant in subjects undergoing cataract surgery.

Methods: A Phase 1, open-label study was conducted to assess the safety and efficacy of OcuRing-K™ (ketorolac ophthalmic implant) for treatment of postoperative inflammation after cataract surgery. Five subjects underwent cataract extraction with intraocular lens (IOL) implantation. Prior to IOL insertion, the OcuRing-K™ was applied to one haptic of the IOL, which was then inserted into the capsular bag using the standard surgical technique. No additional anti-inflammatory medications were administered. Subjects were evaluated postoperatively 1, 7, and 28 days after surgery. Inflammation was assessed by anterior chamber cell (ACC) score using the SUN scale. Postoperative pain was assessed using a visual analog scale (VAS).

Results: OcuRing-K™ was successfully implanted in five subjects without complication. In all five subjects, IOLs were observed to be centered on the visual axis without tilt, and OcuRing-K™ implants were visualized in their proper position on the IOL haptic at all visits. The mean postoperative ACC scores were 0.6 and 0.4 at days 1 and 7, respectively, and no ACC was observed in any subjects by day 28. All subjects were pain-free at days 1, 7, and 28. No treatment-related adverse events were reported. No subjects required rescue therapy with topical anti-inflammatory medication.

Conclusions: These results represent the first evidence of the safety and efficacy of OcuRing-K™ for use in cataract surgery. Although this was an open-label study with no comparators, the minimal inflammation observed and absence of pain among all subjects are highly consistent with the known anti-inflammatory and analgesic properties of ketorolac. These findings support the potential of the OcuRing-K™ implant as a safe and effective alternative to NSAID eye drops for use in cataract surgery.

CONTROL ID: 3531648

SUBMITTER (NAME ONLY): Kai Lyn Goh

TITLE: Calcific nodules within retinal drusen in age-related macular degeneration: Association with disease progression and impact on microperimetry

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Goh, R.H. Guymer, L.A. Hodgson, Z. Wu, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|R.H. Guymer, Z. Wu, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To investigate the association between calcific nodules with progression in age-related macular degeneration (AMD) and examine their impact on visual function using microperimetry.

Methods: This study involved 280 eyes from 140 participants with bilateral large drusen. Multimodal imaging (MMI) and microperimetry were performed at baseline, and then every 6 months for 3 years. Baseline optical coherence tomography (OCT) scans covering a 20°x20° region were used to identify calcific nodules, defined as a hyporeflective core within a drusenoid lesion. The area of drusenoid lesions containing calcific nodules seen on OCT scans was then measured on color fundus photographs (CFPs). The main outcome measures were progression to late AMD determined on MMI, and mean microperimetric sensitivity. The association between the extent of drusen with calcific nodules and these outcomes was then evaluated, with and without adjustment for potential confounders.

Results: A total of 20 (7%) eyes from 12 (9%) individuals were found to have calcific nodules at baseline. The presence and extent of calcific nodules were significantly associated with an increased risk of progression to late AMD ($P = 0.034$) and lower microperimetric sensitivity at baseline ($P = 0.006$). However, these associations were no longer significant ($P \geq 0.200$ for all) after adjusting for total drusen volume from OCT imaging, presence of pigmentary changes on CFPs, and age.

Conclusions: The presence and extent of calcific nodules at baseline was not independently associated with an increased risk of progression in AMD or with lower microperimetric sensitivity, after adjusting for important confounders of AMD disease severity and risk of progression.

CONTROL ID: 3531652

SUBMITTER (NAME ONLY): Ou Tan

TITLE: Harmonizing OCT and VF parameters in the assessment of glaucoma progression speed

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Tan, D. Huang, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|D.S. Greenfield, R. Parrish, Bascom Palmer Eye Institute, University of Miami, Palm Beach Gardens, Florida, UNITED STATES|B. Francis, Doheny Eye Center and David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|R. Varma, Southern California Eyecare and Vision research Institute, Fountain Valley, California, UNITED STATES|J.S. Schuman, Langone Medical Center, New York University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Compare the speed of glaucoma progression as measured by global visual field (VF) and optical coherence tomography (OCT) metrics.

Methods: Glaucoma suspect, pre-perimetric glaucoma (PPG) and perimetric glaucoma (PG) participants of Advanced Imaging for Glaucoma study,¹ who had at least 7 visits with visual field (VF) and OCT ONH scan, were analyzed. Severity was staged by the modified Hodapp-Parrish-Anderson Criteria. Eyes with significant cataract progression were excluded. Spectral-domain OCT (RTVue, Optovue) and VF testing were performed every 6 months. The nerve fiber layer (NFL) thickness was measured from ONH scan. The NFL mean deviation (MD) were VF-equivalent dB-scale quantities based on sectorwise nonlinear regression of NFL thickness with VF deviation using cross-sectional data over a wide range of glaucoma severity.² Linear regression was used to estimate the glaucoma progression speed.

Results: Seventy-five glaucoma suspect eyes (VF MD -0.1 ± 1.2 dB), 160 PPG eyes (0.2 ± 1.3 dB), 77 early PG eyes (-0.9 ± 1.6 dB) and 20 moderate+severe PG (-10.8 ± 3.2 dB) eyes were analyzed. The follow-up duration was 54 months \pm 8 months (mean \pm SD). For both VF MD and NFL MD, the speed of progression increased monotonically with glaucoma severity (Table 1). For overall NFL thickness, the progression speed was greatest in the PPG and early PG stages, but slowed down at the moderate+severe stages. The ratios of progression speed for NFL thickness relative to VF were significantly different between stages ($p < 0.006$, one-way ANOVA). The ratios of progression speed for NFL MD relative to VF MD was generally slower (0.58-0.72), but not significantly different across disease stages ($p = 0.08$). The progression speed of both NFL-MD and VF-MD were associated with baseline parameters (faster progression in eyes with more severe disease at baseline), while progression speed of NFL thickness was not (Table 2).

Conclusions: Compared to VF MD, NFL thickness tends to overestimate the progression speed in the early stages of glaucoma and underestimate it in the later stages. Clinicians should be aware of the discrepancy in the apparent speed of disease progression as measured by structural and functional metrics, which strongly depend on the stage of disease severity. Converting the NFL thickness profile to NFL MD may provide a progression metric more consistent with VF MD over a wider range of glaucoma severity.

CONTROL ID: 3531675

SUBMITTER (NAME ONLY): Michael Lai

TITLE: Manifest Refraction Versus Wavefront Refraction in Patients with Keratoconus

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study was a retrospective, observational clinical study to compare refractive results of manifest refraction and wavefront (WF) refraction for patients with keratoconus.

Methods: The manifest and WF refractions of 613 eyes diagnosed with keratoconus were analyzed. Refractive parameters (sphere, cylinder, axis, and spherical equivalent) were compared based on stratified cohorts of increasing maximum keratometry (Kmax) (Kmax<50 diopters (D), 50-55D, 55-60D, >60D). The percentage of WF refraction axes (against-the-rule (ATR) (60-120°), with-the-rule (WTR) (0-30° and 150-180°), oblique (OBL) (30-60° and 120-150°)) that correctly corroborated with manifest refraction axes were compared, and more specifically, the percentage of patients with WF axes $\pm 10^\circ$ of manifest axes were analyzed.

Results: In the entire cohort, there was no difference between wavefront and manifest spherical refraction (P=0.07). However, cylindrical refraction and spherical equivalent were significantly different (both P<0.001). In the stratified subgroups, there was more cylindrical refraction measured on wavefront than manifest refraction for all Kmax subgroups (all P<0.001). Similarly, wavefront spherical equivalent was more myopic than the manifest spherical equivalent in the Kmax <50D, 50-55D, and 55-60D subgroups (P=0.01, <0.001, <0.001, respectively). Overall, 56.61% of WF refraction axes (ATR, WTR, or OBL) correctly corroborated with manifest refraction axes, and only 34.4% of WF refraction axes were within $\pm 10^\circ$ of manifest refraction axes. In the Kmax subgroups, 62.1%, 54.7%, 56.7%, and 48.5% of WF refraction axes correctly corroborated with manifest refraction axes in the Kmax <50D, 50-55D, 55-60D, and >60D subgroups, respectively. Additionally, 38.5%, 37.4%, 32.9%, and 18.2% of WF refraction axes were $\pm 10^\circ$ of the manifest refraction axes in the Kmax <50D, 50-55D, 55-60D, and >60D subgroups, respectively.

Conclusions: WF refraction is a convenient tool for obtaining refractive parameters of patients, but physicians should be cognizant that there can be significant differences between WF and manifest refraction for patients with keratoconus. In particular, as the severity of keratoconus increases, the reliability of the wavefront astigmatism measurements appears to decrease.

CONTROL ID: 3531713

SUBMITTER (NAME ONLY): Saki Tsutsui

TITLE: Genotype and long-term clinical features of RHO-associated retinitis pigmentosa in Japanese patients

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report the genotype and clinical features of RHO-associated retinitis pigmentosa (RHO-RP) in Japanese patients.

Methods: Multiplex polymerase chain reaction-based target sequencing of 83 known causative genes of RP or whole exome sequencing with target analysis of retinal disease-associated genes were performed in 782 patients with RP in Kyushu University Hospital. Pathogenic variants of RHO gene were detected in 19 patients. Clinical information including age, best-corrected visual acuity (BCVA), Goldmann perimetry, fundus photography, and optical coherence tomography were retrospectively obtained from the electronic medical charts. Visual outcomes were compared between classical and sector phenotypes and among variants.

Results: The mean age at the first visit was 53.9 ± 14.4 years, with the mean follow-up of 7.1 ± 3.6 years. Classical RHO-RP phenotype was associated in 16/19 (84.2%) participants, and p.Pro23Leu and p.Pro347Leu variants were noted in 4 and 2 patients, respectively. Three patients with sector RHO-RP harbored p.Ala164Val (n=2) and p.Asn78Ile (n=1) variants. In classical RHO-RP, mean BCVA decreased from 0.60 to 1.10 logarithm of the minimum angle of resolution (logMAR) over the follow-up period; whereas, in sector RHO-RP, BCVA was relatively preserved as 0.05 and 0.09 logMAR respectively at the first and last visit. Among p.Pro23Leu, p.Pro347Leu and p.Ala164Val variants, patients with p.Pro347Leu variant exhibited early onset and severe vision loss in earlier ages. Macular complications such as epiretinal membrane and cystoid macular edema was observed in 5 classical RHO-RP and 1 sector RHO-RP patients.

Conclusions: p.Pro23Leu, but not p.Pro23His, was the frequent variant causing RHO-RP in Japanese patients. As reported in previous Europe and US studies, patients with p.Pro347Leu variant showed more severe phenotype, and variants causing sector RHO-RP were associated with a good prognosis.

CONTROL ID: 3531716

SUBMITTER (NAME ONLY): Rachel Xuan

TITLE: Tear Film Osmolarity in a cohort of 1404 patients undergoing refractive surgery assessment

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Pre-operative dry eye represents a risk of sub-optimal refractive results following cataract or refractive surgery thus identification of at-risk individuals in the standard population is essential to optimising outcomes. Tear film osmolarity (TFO) is an objective measure of dry eye however minimal literature is available to provide an understanding of incidence of hyperosmolarity in the standard population and the relationship with subjective dry eye parameters and clinical variables. Our retrospective study presents a novel analysis of the largest current sample of TFO in a normal population and post-refractive subgroup.

Methods: 1404 patients (n=47 post-refractive, n=1357 standard) undergoing screening for refractive surgery from 2017 to 2020 were reviewed. Routine examination included dry eye testing with TFO (TearLab, San Diego, CA, USA) and the Ocular Surface Disease Index questionnaire (OSDI, Allergan Irvine CA, USA). Patients were instructed to refrain from topical eye drops minimum two hours before the appointment. Bivariate correlation was used to indicate a relationship between continuous variables and chi-square test between categorical variables. Mean, median and range values were provided for continuous variables.

Results: Mean TFO in the standard population was 299.1 ± 11.9 mOsm/L with 82.3% of eyes < 308 mOsm/L indicating normal tear film homeostasis. Mean inter-eye TFO difference was 8.17 ± 8.60 mOsm/L with 65.2% of eyes ≤ 8 mOsm/L. Mean TFO in the post-refractive subgroup was 299.7 ± 11.0 mOsm/L with a mean inter-eye difference of 9.0 ± 6.9 mOsm/L. Post-refractive surgery patients indicated higher mean OSDI values of 15.3 ± 14.5 compared to the remainder of the population 9.7 ± 10.6 ($p=0.012$). Significant correlation was demonstrated between TFO scores and OSDI classification for the standard population only ($p=0.005$, $r=0.077$). Contact lens use correlated inversely with TFO and OSDI scores ($p=0.000$) whilst artificial lubricants correlated with OSDI scores in the post-refractive group only ($p=0.000$, $r=0.131$).

Conclusions: TFO and OSDI scores indicate that the majority of the standard population fall within normal ranges. The impact of our findings may resonate with cataract and refractive surgeons as a reasonable percentage of individuals will be diagnosed with tear film hyperosmolarity and represent a risk for reduced post-operative outcome and ocular comfort.

CONTROL ID: 3531736

SUBMITTER (NAME ONLY): Himeesh Kumar

TITLE: The influence of Quantity and Location of Hyperpigmentary Abnormalities on the Progression of Age-related Macular Degeneration

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Kumar, L. Robman, G. Makeyeva, X. Hadoux, M. Jannaud, L.A. Hodgson, K. Goh, T. Pham, R.H. Guymer, Z. Wu, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|H. Kumar, R.H. Guymer, Z. Wu, Ophthalmology, The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To evaluate the potential added predictive value of the quantity and location of hyperpigmentary abnormalities (HP) for progression of age-related macular degeneration (AMD).

Methods: 140 participants with bilateral large drusen were followed longitudinally at six-monthly intervals for up to 36 months. They underwent multimodal retinal imaging to determine late AMD development. Baseline colour fundus photographs were graded for the presence of any pigmentary abnormalities. All pixels containing HP were then manually labelled on these baseline images, and the quantity of HP within and outside the central 3mm diameter region centred on the fovea was determined. Two predictive models that included age and any pigmentary abnormalities, one with and one without the quantitative parameters of the HP extent, were developed and evaluated.

Results: HP were detected in 81 (29%) eyes, all of which (100%) had HP inside the central 3mm region, and 41 (51%) eyes had HP outside the central 3mm region. The quantity of HP within the central 3mm region ($P = 0.036$), but not outside ($P = 0.361$), was independently associated with progression to late AMD. The addition of the quantity of HP within the central 3mm to a predictive model including presence of any pigmentary abnormalities and age did not significantly improve its performance (area under the receiver operator characteristic curve [AUC] = 0.81), compared to the model without it (AUC = 0.80; $P = 0.23$). The sensitivity of these two predictive models were 54% and 46% respectively at 90% specificity ($P = 0.32$).

Conclusions: The extent of HP within the central 3mm was associated with AMD progression at the population level. However, its addition to a model based on presence of any pigmentary abnormalities and age did not result in an improved predictive performance at the individual level in our cohort. Further analysis of spatial patterns of HP, would provide additional parameters to improve the model.

CONTROL ID: 3531740

SUBMITTER (NAME ONLY): Krunalkumar Ramanbhai Patel

TITLE: Modular Deep Neural Network (DNN) – A new paradigm for classifying optical coherence tomography (OCT) B-scans by pathology

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Macular OCT B-scans may contain various pathologies and identification of these pathologies using Artificial Intelligence-assisted technologies may help doctors diagnose macular diseases more quickly. For an accurate yet fast clinical decision support system, it is essential to develop a robust algorithm with high sensitivity that can detect the presence of multiple pathologies. This could be attempted with two different approaches such as 1) Monolithic DNN, and the proposed 2) Modular DNN. With monolithic DNN, a single DNN is involved to absorb features that are required to train all the pathologies – the usual way of handling the typical multi-label classification task. The idea of modular DNN is to dedicate a single and potentially smaller DNN for each pathology that yields individual outputs and then combines these outputs of several DNNs to arrive at conclusions.

Methods: For training and evaluating the performance of the monolithic and modular DNN based algorithms, a total of 598 CIRRUS macular OCT cubes from 598 patients were collected. The labeling was done at the B-scan level with 8 pathologies (one or more per B-scan) by two retina specialists. Ungradable B-scans were excluded from the dataset. The dataset was then divided into train and test with 80-20 split at patients' level.

Fig. 1(a) table depicts the list of 8 pathologies and their corresponding samples used for training and evaluating both algorithms while 1(b) shows the distribution of pathologies. For both methods, inception_resnet_v2 DNNs were used – 1 for monolithic DNN and 8 for modular DNN (Fig. 1(c)).

Results: The performances of both the algorithms were evaluated on the hold-out test set. The monolithic DNN achieved maximum 75.36% AUC for RPE Elevation while modular DNN achieved maximum 98.85% AUC for Intraretinal Fluid. Fig 2 shows the achieved AUCs for modular DNN for all 8 pathologies.

Modular DNN based algorithm outperforms monolithic DNN significantly for all pathologies. The proposed approach provides a flexibility to include or exclude pathologies for designing any customized workflow.

Conclusions: In this study, we determined the modular DNN architecture-based algorithm outperformed a monolithic DNN based algorithm for the multi-pathology classification task with no loss of generality.

CONTROL ID: 3531741

SUBMITTER (NAME ONLY): SANDIPAN CHAKROBORTY

TITLE: Beyond federated learning: fusion strategies for diabetic retinopathy screening algorithms trained from different device types

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) is one of the most common causes of blindness, and a screening using fundus images helps to detect DR at early stage. Various types of fundus cameras are available today, with differences in their image quality, portability, and field of view. To screen a large population, it is essential to develop an automated DR screening system that is device agnostic. We evaluate how different, device-specific solutions can be fused when the training data and underlying algorithms differ.

Methods: From previous studies, we obtained two deep learning models with different model architecture. One model (M_{HH}) was trained exclusively on fundus images captured with a low-cost hand-held fundus camera (VISUSCOUT®100; ZEISS, Jena, Germany). The second model (M_{TT}) was trained on fundus images recorded with different table-top fundus cameras manufactured by various companies.

We evaluated individual models and combination strategies on two datasets: one from hand-held cameras (VISUSCOUT®) and one from table-top cameras (seen in Messidor-2 dataset). We analyzed three fusion techniques: score level fusion, decision level combination, and system level combination. For the weighted score level combination, the optimum weights were found experimentally between 0 to 1. In decision level combination, a modified OR logic was used for referable DR. For the system level combination, the metadata of the image was used to find out whether the image was captured using VISUSCOUT or a table-top fundus camera for routing the image to the appropriate algorithm. These strategies are visualized in Fig. 1.

Results: Fig. 2 shows the diagnostic efficacy in AUC %. Every single model performs well in the data regime it was trained on (M_{HH} on data from hand-held cameras, M_{TT} on table-top camera data) but accuracy drops significantly when tested with data coming from different device. For fusing both models into a single system, we observe best screening results with score level fusion, being clearly superior to decision level or system level fusion and insensitive to the data type.

Conclusions: DR screening systems which have been trained on different device data and with different deep learning models can be fused with various combination techniques for higher system performance.

CONTROL ID: 3531744

SUBMITTER (NAME ONLY): Fang Chen

TITLE: In situ-forming semi-interpenetrating network hydrogels for corneal regeneration: in vivo biological response

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The human corneal stroma is a hydrated extracellular matrix (ECM) with 80% water, 13.6% collagen, and 0.9% glycosaminoglycans (GAGs) containing specialized fibroblast-like cells in the matrix. Its collagen is mainly type I collagen fibrils weaving together. The most abundant GAG in the normal cornea is keratan sulfate (KS), chondroitin sulfate (CS), and dermatan sulfate (DS). They form proteoglycans with a core protein in the spaces among the major collagen fibrils. GAGs can absorb and retain large amounts of water. Hyaluronan (HA) is a non-sulfated-GAG with well-known effects on corneal wound healing. We are developing in situ-forming semi-interpenetrating polymer network-based gels to mimic corneal stromal ECM for corneal regeneration and report on our recent data on the biological responses to them in vivo.

Methods: We mixed CS, DS, HA, or their combinations with type I collagen (Col) at a Col-to-GAG ratio of 2:1 and then used FDA approved NHS ester chemistry to crosslink collagen. The GAGs are therefore physically but not covalently integrated in the gel. The crosslinker for collagen here is a bifunctional PEG succinimidyl ester. The Col-to-crosslinker ratios used were 3:4 or 3:8. Gels without GAGs (Col-PEG) are also used as controls. The mixture is then added to a corneal defect of New Zealand White Rabbits under ambient conditions and allowed to gel over 5 minutes without using a catalyst or light activation. A contact lens and tarsorrhaphy were then applied. The treated cornea was monitored by OCT, topography, slit lamp, and fluorescein staining photography. The cornea was collected for immunofluorescence staining, histology, qPCR, and western blot 7 days later.

Results: No ocular inflammation or damage was found in the surrounding epithelial, stromal, and endothelial layers for all experimental eyes. Both collagen gels containing CS and HA promoted corneal epithelial wound healing compared to the collagen-only gels, and those containing HA were observed to be the most transparent. Stiffer gels (Col:crosslinker=3:4) facilitated curvatures closer to pre-operative curvatures.

Conclusions: We found that integration of CS and HA within collagen gels promoted corneal epithelial wound healing compared to collagen gels alone, while stiffer gels more closely facilitated native corneal curvature restoration. Future studies will focus on further optimization of gels in rabbit models.

CONTROL ID: 3531749

SUBMITTER (NAME ONLY): Varsha Alex

TITLE: Assessing the validity of a cross-platform retinal image segmentation tool in normal and diseased retina

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retrospective, cross-sectional study, quantitatively and qualitatively comparing automated retinal image segmentation using cross platform OrionTM software to proprietary software on retinal images captured using Heidelberg HRA+OCT

Methods: Retinal layer segmentations of normal, intermediate dry AMD and diabetic macular edema eyes were performed using Spectralis[®] HRA+OCT and automated OCT segmentation software OrionTM. Quantitative comparisons were made between the volumes of Nerve fiber layer (NFL), Ganglion cell layer (GCL), Inner plexiform layer (IPL), Outer plexiform layer (OPL), Inner nuclear layer (INL), Outer nuclear layer (ONL), total inner retinal layer (INLY) and total outer retinal layer (OUTLY). A qualitative comparison of accuracy was made by graders who compared software segmentation to manual segmentation.

Results: In normal eyes, all retinal layer volumes calculated by the two softwares were moderate-strongly correlated (Pearson correlation, $r > 0.4$) except OUTLY. However, differences were statistically significant except in GCIPL and OUTLY. Qualitative analysis done using Wilcoxon test showed that OrionTM was significantly better than Heidelberg in the segmentation of NFL and INL layers ($p \leq 0.01$). In dry AMD eyes, GCIPL, INL, ONL, INLY, TRV layer volumes were moderate-strongly correlated ($r > 0.4$) between softwares and their differences were statistically significant except GCIPL. Qualitatively, OrionTM generated significantly better segmentation only for the NFL ($p \leq 0.05$). In eyes with DME, all layer volume values were moderate-strongly correlated ($r > 0.4$) between softwares and their differences were statistically significant except OPL and OUTLY. Qualitatively, OrionTM was significantly better at segmenting INL and OPL layers ($p \leq 0.01$).

Conclusions: Layer volumes correlated well between OrionTM and Heidelberg softwares but were, in general, significantly different suggesting that they used different retinal landmarks for segmentation. Qualitatively, when comparing to the gold standard of manual segmentation, OrionTM segmented normal and diseased retina more accurately. Findings suggest that the cross-platform OrionTM retinal layer segmentation software can be used reliably to study the retinal layers in normal and diseased eyes.

Abbreviations: HB- Heidelberg, OR- Orion, TRV- Total retinal volume, GCIPL – GCL+IPL

CONTROL ID: 3531770

SUBMITTER (NAME ONLY): Yingying Wen

TITLE: Transcriptome Reveals the Potential Mechanism of Wavelength Defocus in Bidirectional Emmetropization

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wen, L. Jin, C. Xie, J. Tong, Y. Shen, Ophthalmology, Zhejiang University School of Medicine, Hangzhou, Zhejiang, CHINA]

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ABSTRACT BODY:

Purpose: Wavelength defocus plays an important role in the process of emmetropization. This study aims to explore the potential mechanism underlying retinal response to the wavelength defocus of different signs.

Methods: In this study, guinea pigs were randomly divided into 3 groups that received different lighting conditions (12:12 light cycle) for 8 weeks: white light, short wavelength light, and long wavelength light. Refraction and axial length were measured, and RNA-seq was adopted to analyze gene expression in the retina.

Results: Compared with the control group, the long wavelength light exhibited reduced refraction and increased ocular axial length, whereas the short wavelength light showed an opposite trend. RNA-seq showed that compared with the control group, 184 differently expressed genes (DEGs) in the short wavelength group were primarily enriched in the pathways including tyrosine and retinol metabolism, whereas 171 DEGs in the long wavelength group were mainly enriched in the fat digestion and absorption. There were 268 DEGs between the short and long wavelength group, which were associated with extracellular matrix remodeling. We also found that 7 DEGs in the guinea pigs retina in response to wavelength defocus were overlapped with human myopia candidate genes, suggesting functional overlap between DEGs in retina upon exposure to wavelength defocus and genes causing myopia in humans.

Conclusions: This study identified retinal targets and pathways involved in the response to wavelength defocus, as well as providing attractive targets for the development of anti-myopia drugs.

CONTROL ID: 3531779

SUBMITTER (NAME ONLY): GANESH BABU TUMKUR CHANDRA

TITLE: Evaluating the influence of data source and labelling variability on a Deep Learning (DL) based OCT B-scan abnormality classification

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. TUMKUR CHANDRA, S. CHAKROBORTY, K. Patel, Center of Application and Research in India, Carl Zeiss India (Bangalore) Pvt. Ltd., Bangalore, Karnataka, INDIA|N. Manivannan, M.K. Durbin, Carl Zeiss Meditec, Inc., Dublin, California, UNITED STATES|A. Freytag, CRT, Carl Zeiss AG, Jena, Thuringia, GERMANY|

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ABSTRACT BODY:

Purpose: DL techniques can be used to detect abnormalities in OCT B-scans. The performance of such an algorithm is dependent on quality of both data and its labels. The sources of data could be either from a clinical study or busy eye clinics. While the image quality, disease prevalence, age of subjects etc. can be well controlled within scope of a clinical study, the same may not be applicable when collected from the eye clinics. The involvement of multiple labelers may introduce inconsistencies while creating labels, because each expert has their own clinical judgment and differs depending on how and where (Primary, Secondary or Tertiary clinics) they practice. In this abstract, we discuss the effects of the above aspects on classification performance.

Methods: To assess the effect of data source, we gathered macular OCT cube data during clinical studies and from eye clinics. Next, to measure the effect of labelling variability, the data were labelled at B-scan level by five labelers. Among five labelers, two of them (labelers X & Y in Fig. 2) had similar expertise levels practicing in the same hospital, while the rest (labelers A, B & C) were from three different eye clinics. Data from each labeler was split into training and test sets. An Inception_V1 model was developed on the training set for each labeler, and the performance was evaluated on all test sets. Fig 1(a) and 2(a) show the number of samples used for trainings and evaluations.

Results: Fig 1(b) shows that evaluating a model using data from clinical trials does not always indicate good generalizability and may over-estimate the model accuracy. Training on 'uncontrolled' data sources leads overall to improved performance in a typical clinical setting, even if such a model underperforms in the clinical trial setting. From Fig 2(b), we observe that models perform well on data labelled by experts with similar background. It shows strong differences in accuracy for abnormality prediction with labelers from different backgrounds, showing significant AUC drop.

Conclusions: We conclude that prediction models are not easily transferable across labelers from different backgrounds. Furthermore, model accuracy from clinical trial model may not be transferrable to busy clinical environments.

CONTROL ID: 3531805

SUBMITTER (NAME ONLY): Aina Turull Mallofre

TITLE: Effect of the power and time of application of fogging lenses in the control of accommodation

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: An essential factor for a successful refraction assessment is the control of accommodation. Fogging is a technique for relaxing accommodation using plus power lenses instead of drugs. However, the optimal amount of power and time of application of plus lenses remain unclear. This study tested which power and time of application of fogging lenses are more adequate to achieve the maximum relaxation of accommodation (RoA).

Methods: We analyzed the accommodative response of 20 young adults, 7 males and 13 females, between 18 and 30 years old when lenses of different amount of plus power were placed in front of the patient's eye. For each patient, six different fogging lens powers relative to the manifest refraction were tested (+1D, +1.5D, +2D, +2.5D, +3D and +4D). Each lens was placed in front of the eye for 55s while the patient was looking at a VA chart placed at 6m. During that time, changes in accommodation were monitored at 10Hz frequency by means of a Hartmann-Shack aberrometer. During measurements contralateral eye was occluded. Lenses were presented in a random order, with a wash-up time between trials of 90s.

Results: The mean age of participants was 24.7 ± 3.4 years, with a mean refractive error in terms of spherical equivalent of -0.59 ± 1.37 D ranging from -4.25D to +1D. The mean RoA for all lenses was -0.05 ± 0.22 D and the mean time for achieving the maximum RoA was 24.75 ± 16.52 s.

Analyzing the cases in which the RoA was at least 0.12D, the mean RoA was 0.23 ± 0.08 D with a mean time to achieve the maximum RoA of 19.94 ± 11.52 s. Lenses that produced a better RoA were those with powers between +1D and +2.5D. Conversely, when analyzing the cases in which the RoA was under -0.12D, meaning that accommodation was activated, the mean RoA was -0.29 ± 0.17 with a mean time to get the maximum accommodation of 40.86 ± 11.18 s. Lenses that produced a higher activation of accommodation were +3D and +4D.

Conclusions: Real time monitorization permits to determine power and time of fogging lenses. Better results were obtained for powers between +1D and +2.5D and a time of application of approximately 20s. The countereffect of high-power fogging lenses was seen in lenses of +3D and +4D, that could lead accommodation to the resting state due to the high blur. Further research with a larger sample should be performed to confirm these preliminary results.

CONTROL ID: 3531808

SUBMITTER (NAME ONLY): Katharina Breher

TITLE: Metrological and refractive aspects of retinal shape estimation from 90° field of view optical coherence tomography

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal shape can be derived from distortion-corrected optical coherence tomography (OCT) scans. This parameter is of potential use in myopia research and in retina-related pathologies. The purpose of the study is to evaluate the metrological aspects of retinal shape estimation from OCT images covering a 90° field of view.

Methods: A total of 20 right eyes with refractive errors ranging from 0 to -11 diopters were imaged with a swept-source OCT system (PLEX® Elite 9000; ZEISS, Dublin, CA). Three horizontally and vertically oriented line scans were acquired. An ultra-widefield add-on lens was mounted to the system to image a 90° field of view. OCT images were adjusted to more accurately depict the anatomical structure of the retina using an image transform derived from an optical model (MATLAB 2020a; The MathWorks, Inc., Natick, MA, and OpticStudio 20.3.1; Zemax, LLC, Kirkland, WA), as seen in Fig1. The retinal radius of curvature (RRC) was calculated from the distortion-corrected scan. Median \pm interquartile range (IQR) and the coefficient of repeatability for the RRC were calculated. A simulated tolerance analysis was performed to identify the imaging parameters likely responsible for within-subject variations. Correlation analysis between axial length and RRC was conducted.

Results: Horizontal and vertical retinal curvatures calculated were 12.53 ± 1.37 mm and 12.83 ± 1.28 mm with coefficients of repeatability of 1.11mm and 0.49mm, respectively. The tolerance analysis predicted the axial length to be the most sensitive parameter in the retinal curvature calculation, which can lead to up to 28% error for 0 diopter refractive error. The working distance offset (8.2%), corneal radius (1.25%), crystalline lens refractive index (0.5%), x-offset (0.65%) and head tilt (0.33%) had less of an effect, resulting in a total root mean square error of 8.34%. Correlation analysis showed significant correlations for axial length with horizontal ($R=0.74$, $p<0.001$) and vertical RRC ($R=0.61$, $p=0.005$).

Conclusions: Calculations of retinal shape are more repeatable in the vertical than horizontal scan direction. Axial length and an offset in working distance have the biggest impact on retinal shape estimation determined with 90° field of view OCT imaging. Horizontal and vertical RRC correlate positively with axial length.

CONTROL ID: 3531835

SUBMITTER (NAME ONLY): Cristina González-Gonzalo

TITLE: Hierarchical curriculum learning for robust automated detection of low-prevalence retinal disease features: application to reticular pseudodrusen

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The low prevalence of certain retinal disease features compromises data collection for deep neural networks (DNN) development and, consequently, the benefits of automated detection. We robustify the detection of such features in scarce data settings by exploiting hierarchical information available in the data to learn from generic to specific, low-prevalence features. We focus on reticular pseudodrusen (RPD), a hallmark of intermediate age-related macular degeneration (AMD).

Methods: Color fundus images (CFI) from the AREDS dataset were used for DNN development (106,994 CFI) and testing (27,066 CFI). An external test set (RS1-6) was generated with 2,790 CFI from the Rotterdam Study. In both datasets CFI were graded from generic to specific features. This allows to establish a hierarchy of binary classification tasks with decreasing prevalence: presence of AMD findings (AREDS prevalence: 88%; RS1-6: 77%), drusen (85%; 73%), large drusen (40%; 24%), RPD (1%; 4%). We created a hierarchical curriculum and developed a DNN (HC-DNN) that learned each task sequentially. We computed its performance for RPD detection in both test sets and compared it to a baseline DNN (B-DNN) that learned to detect RPD from scratch disregarding hierarchical information. We studied their robustness across datasets, while reducing the size of data available for development (same prevalences).

Results: Area under the receiver operating characteristic curve (AUC) was used to measure RPD detection performance. When large development data were available, there was no significant difference between DNNs (100% data, HC-DNN: 0.96 (95% CI, 0.94-0.97) in AREDS, 0.82 (0.78-0.86) in RS1-6; B-DNN: 0.95 (0.94-0.96) in AREDS, 0.83 (0.79-0.87) in RS1-6). However, HC-DNN achieved better performance and robustness across datasets when development data were highly reduced (<50% data, p-values<0.05) (1% data, HC-DNN: 0.63 (0.60-0.66) in AREDS, 0.76 (0.72-0.80) in RS1-6; B-DNN: 0.53 (0.49-0.56) in AREDS, 0.48 (0.42-0.53) in RS1-6).

Conclusions: Hierarchical curriculum learning allows for knowledge transfer from general, higher-prevalence features and becomes beneficial for the detection of low-prevalence retinal features, such as RPD, in scarce data settings. Moreover, exploiting hierarchical information improves DNN robustness across datasets.

CONTROL ID: 3531865

SUBMITTER (NAME ONLY): Anja Britten

TITLE: A multipurpose SS-OCT engine – from axial eye length measurements to 4D OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The rigidity and low A-scan rate of spectral-domain optical coherence tomography (SD-OCT) is prohibiting a manifold use of OCT during ophthalmic surgery. We present a versatile swept-source OCT (SS-OCT) engine, addressing a multitude of use cases, from axial eye length measurements to live volumetric visualizations at MHz A-scan rates.

Methods: We developed a flexible SS-OCT engine and an add-on module to couple its sample arm to an ophthalmic surgical microscope. The engine includes a 1060nm tunable MEMS-VCSEL whose sweep repetition rate can be alternated between 100kHz, 400kHz or 1MHz. To increase the effective A-scan rate on cost of axial resolution, we scanned at twice the speed and mathematically divided each sweep into two halves. The 100kHz A-scan mode was used for high resolution B-scan and axial eye length measurements with an axial resolution of 6.3µm and an imaging depth of 29mm in tissue. For 4D live imaging, effective A-scan rates of 800kHz and 2MHz allowed us to realize fields of view (FOVs) of 3.1-15.7mm with imaging depths of 4.3-10.5mm and an axial resolution of 12.6µm. We imaged anterior segment and retina mimicking phantoms, as well as ex vivo porcine eyes. All data was processed and rendered live.

Results: Using the same instrument, we acquired full eye scans, anterior and posterior segment B-scans, as well as 4D-OCT scans with volume rates of up to 17vol/s. Fig.1 shows an ocular biometry scan of a test eye captured at an A-scan rate of 100kHz. Each B-scan consisted of 1024 A-scans. Sampling such enormous depths of 29mm in real-time allows for ocular distance measurements or solid state z-tracking. In Fig.2A-H an image sequence of a 17vol/s live rendered volume series can be seen. It visualizes an incision of a porcine cornea displayed at different viewing angles and zooms. An A-scan rate of 1MHz and axial resolution of 6.3µm resulted in a FOV of 3.1mm. To further enhance depth perception, depth is color-encoded from red (top) to blue (bottom) and the z-direction is indicated by an arrow.

Conclusions: We demonstrated SS-OCT's potential to address multiple ophthalmic imaging applications with a single device. 4D OCT can be used for enhancing depth perception and visualizing sub-surface structures during surgery, while imaging at lower rates enables full eye OCT for high resolution B-scan imaging and biometry scans.

CONTROL ID: 3531871

SUBMITTER (NAME ONLY): Yulia Aziza

TITLE: The Evaluation of Barrier Function in Ocular Surface Epithelium Response Mechanism via Toll-like Receptor 3 (TLR3)

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Toll-like receptor 3 (TLR3) and the retinoic acid-inducible gene I (RIG-I) like RNA helicase gene family are pattern recognition receptors in viral infection which recognize double-stranded (ds) RNA viruses and activate innate immunity. Both polyinosinic-polycytidylic acid [poly(I:C)] and polyadenylic-polyuridylic acid [poly(A:U)] are synthetic analogs of dsRNA that interact with TLR3, however, only poly(I:C) triggers the RIG-I like RNA helicase gene family. The purpose of this present study was to investigate the barrier function in immortalized human corneal epithelial (HCLE) cells and human conjunctival epithelial (HCjE) cells via stimulation of TLR3 by synthetic dsRNA.

Methods: HCLE and HCjE cells were first cultured on 12-mm Transwell[®] inserts (Corning[®]), and then stimulated with 25µg/ml poly(I:C) or 25µg/ml poly(A:U). To block TLR3, 40µM TLR3/dsRNA Complex Inhibitor (Sigma-Aldrich) was then added to the medium. After stimulation for 24 hours, transepithelial electrical resistance (TER) was measured. The flow mechanism was evaluated on poly(I:C) stimulation by dividing into the following four groups: 1) control group, 2) poly(I:C) in both apical and basal chambers group, 3) poly(I:C) in an apical chamber group, and 4) poly(I:C) in a basal chamber group. After stimulation for 1 hour, all poly(I:C) was changed into the culture medium, and measurement of TER was performed.

Results: Poly(I:C) and poly(A:U) stimulation increased TER after 24-hours ($p<0.01$). In comparison to the control group, the TER increase in the HCLE cells and HCjE cells in the poly(I:C) group was 73.6% and 94.4%, respectively, while the TER increase in the HCLE cells and HCjE cells in the poly(A:U) group was 49.2% and 12.3%, respectively. In all cells in both groups, the TER increase was blocked by TLR3 inhibitor ($p<0.01$). Evaluation of the poly(I:C) flow mechanism revealed that TER increased in all groups stimulated with poly(I:C) ($p<0.05$) at 3 hours, and that the increase remained until 24 hours.

Conclusions: The barrier function of ocular surface epithelium increased, specifically through TLR3. The reaction between poly(I:C) and TLR3 might possibly occur inside the cells. This increased barrier function acts as one of the host defense mechanisms against viral infection.

CONTROL ID: 3531887

SUBMITTER (NAME ONLY): Xoana Barcala

TITLE: Ocular dominance measurements and monovision corrections.

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To examine the role of ocular dominance on monovision corrections, using different eye dominance tests. The ultimate goal is to determine the most appropriate test to determine the dominant eye to optimize monovision.

Methods: 14 presbyopic subjects (53 ± 5 yo; SE 0.55 ± 1.33 D) participated, performing measurements at far (F, 4m) and near (N, 40cm) distances. A wearable binocular simulator (SimVis Gekko, 2Eyes Vision) was used to induce different monovision corrections. The following tests were performed: (1) Monovision Preference test (MP, best-perceived quality of grayscale natural images for 2.00 D monovision in OS/OD) at F and N; (2) Clinical Aiming Dominance (AD) at F; (3) Clinical Sensory Dominance (SD) with two levels of monocular blur, 0.50 and 1.50 D at F; (4) Binocular Rivalry (BR, fraction of predominance) using orthogonal Gabor patches at F & N (both eyes best corrected); (5) Multifocal Acceptance Score (MAS-2EV) with 4 perceptual scores (PS, 0-10 range) of perceived image quality at F/N of day/night real-world scenes for monovision (2.00 D near add in OS/OD); (6) Visual Strehl (VS) in OD/OS, from Laser Ray Tracing aberrometry.

Results: AD and SD matched in 71% of the subjects for SD1.50D (50% for SD0.50D). 78% of the subjects showed the same SD with 1.50D and 0.50D blur. VS ranged from 0.88-0.01 OS & 0.96-0.02 OD, and BR from 0.31-0.74 OS & 0.26-0.69 OD, with interocular differences >0.24 , and >0.20 in 43% and 35% of the subjects, respectively. MP at F & N were negatively correlated ($r=-0.89$, $p<10^{-4}$). Highest MP was obtained using dominant eye (far vision) selected from AD only in 36% of the subjects, SD1.50D in 65%, SD0.50D in 86% and BR in 79%. BR at F matched with subjects' preferences in AD (57%), SD0.50 (64%) and VS (50%). MAS-2EV scores were highly correlated with MP, both at F & N ($r=0.71$ & 0.82 , $p<0.004$ both). Selecting the eye for far in a monovision correction based on SD1.50, SD0.50, BR and VS (more aberrated eye) improved MP and MAS-2EV F scores by 54.9% over a flipped correction, except for AD which produced lower scores.

Conclusions: Eyes with high VS and BR interocular differences exhibited the largest differences in MP or MAS-2EV when reversing monovision. SD0.50 was the best ocular dominance predictor of optimal vision at far with monovision. Given the high discrepancies across ocular dominance tests, direct task/perception tests with simulated monovision appear most suited to select a correction.

CONTROL ID: 3531927

SUBMITTER (NAME ONLY): Yun Li

TITLE: Prediction of ranibizumab injection frequency in patients with macular edema due to retinal vein occlusion during as-needed dosing period of BRAVO and CRUISE Phase 3 trials

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Despite anti-VEGF being the standard-of-care for treatment of macular edema due to retinal vein occlusion (RVO), data show that many patients require long-term, frequent injections to maintain the gains achieved during the initial monthly treatment (tx) period, highlighting the need for more durable treatment options in RVO. Here we retrospectively investigated baseline (BL) and early tx response variables for association with ranibizumab (RBZ) tx frequency during the as-needed (PRN) dosing period of the BRAVO and CRUISE trials.

Methods: BRAVO and CRUISE compared RBZ monthly dosing vs sham during the first 6 months (M) followed by PRN RBZ dosing from M6 to M12 in patients with macular edema due to branch and central RVO (BRVO/CRVO), respectively. Post hoc statistical and machine learning methods were applied to identify features predictive of RBZ injection frequency required for vision maintenance during the PRN dosing period. We tested average of BCVA values at BL, M1, M2 and M3, BCVA change from BL to M3, and 13 pre-specified imaging features for their impact on predictive accuracy, measured by area under the receiver operating characteristic curve (AUC).

Results: BRVO and CRVO patients (overall, n = 419; 0.3 mg, n = 211; 0.5 mg, n = 208) across treatment groups received 3.3 ± 2.1 RBZ injections during the PRN dosing period. The best predictor of injection frequency was the average of BCVA values at BL, M1, M2 and M3 (overall AUC = 0.76 [0.71, 0.81]; 0.3 mg AUC = 0.80 [0.73, 0.86]; 0.5 mg AUC = 0.73 [0.66, 0.80]). Adding BCVA change from BL to M3 did not increase predictive performance significantly. Adding the pre-specified imaging variables increased performance of the statistical model (overall AUC = 0.84 [0.80, 0.88]; 0.3 mg AUC = 0.85 [0.80, 0.91]; 0.5 mg AUC = 0.82 [0.76, 0.88]).

Conclusions: The BRAVO and CRUISE RVO population was heterogeneous and required different treatment frequency following the initial 6 monthly doses. The average of BCVA values at BL, M1, M2 and M3 was associated with the greatest predictive signal of future injection need. Imaging features increased predictive performance of the model. Clinicians may find the individual modeling predictions helpful when considering options for the long-term management of patients with RVO.

CONTROL ID: 3531928

SUBMITTER (NAME ONLY): Jing Xu

TITLE: Perceived Needs and Preferences for Use of Advanced Driver Assistance Systems by Drivers with and without Age-related Macular Degeneration

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Drivers with Age-Related Macular Degeneration (AMD) may experience difficulties in many driving situations because of their vision loss. Advanced Driver Assistance Systems (ADAS) have the potential to mitigate these difficulties and maintain driving safety. Using a telephone questionnaire, we identified the driving difficulties and ADAS technology preferences of drivers with and without AMD.

Methods: To date, 19 current drivers with AMD (74 ± 10 y) and 29 drivers without AMD (71 ± 6 y) have participated. They rated their perceived driving difficulty and perceived usefulness of technology support in 15 driving situations under both good (daytime) and reduced visibility conditions. They also rated their preferences for 12 existing ADAS technologies and described their experience using those systems. To provide an understanding of the ADAS systems, we sent each participant a training document with descriptions for all ADAS systems to review before and have available during the interview.

Results: Compared with non-AMD drivers, AMD drivers reported significantly more difficulty ($p = .005$) and greater usefulness of technology support ($p = .03$) in all driving situations. Both AMD and non-AMD drivers reported significantly more difficulty ($p < .001$) and greater technology usefulness ($p < .001$) in reduced visibility conditions than in the daytime. Greater driving difficulty correlated strongly with greater perceived technology usefulness ($r = .91$, $p < .001$). Both groups perceived dealing with other road users in their blind spot, experiencing vision loss from glare, seeing unexpected pedestrians, and driving through unfamiliar areas as the most difficult tasks that would benefit from technology support. AMD drivers listed blind spot warning and pedestrian warning as their most preferred ADAS systems, while non-AMD drivers listed rearview camera and blind spot warning. The majority of AMD drivers preferred to have ADAS technologies provide both information and active intervention, while non-AMD drivers were divided between having just information or both. The perceived benefits of ADAS technologies were high in both groups.

Conclusions: This study highlights differences in technology needs and preferences between AMD and non-AMD drivers which will be used to inform future ADAS development and evaluation tailored for drivers with AMD.

CONTROL ID: 3531959

SUBMITTER (NAME ONLY): Fan Yang

TITLE: Deletion of endoplasmic reticulum (ER) Ca^{2+} efflux channel inositol-1,4,5-trisphosphate receptor type 1 or ryanodine receptor 2 promotes ER retrotranslocation/proteostasis in cyclic nucleotide-gated channel-deficient mice

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Yang, H. Ma, M. Butler, X. Ding, Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies showed that cone death in cyclic nucleotide-gated (CNG) channel-deficient mice involves endoplasmic reticulum (ER) stress-associated apoptosis and dysregulation of ER Ca^{2+} homeostasis. We also demonstrated that expression/activity of ER Ca^{2+} efflux channels inositol 1,4,5-trisphosphate receptor 1 ($\text{IP}_3\text{R1}$) and ryanodine receptor 2 (RyR2) were increased, and ER stress/cone death was reduced after deletion of the two channels. This work investigates whether deletion of ER Ca^{2+} efflux channels promotes ER retrotranslocation/proteostasis in CNG channel-deficient retinas.

Methods: $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}$ and $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}$ mice with cone-specific deletions of Itpr1 (encoding $\text{IP}_3\text{R1}$, $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}/\text{Itpr1}^{\text{fl/fl}}/\text{Hrgp}^{\text{cre}}$) or Ryr2 (encoding RyR2, $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}/\text{Ryr2}^{\text{fl/fl}}/\text{Hrgp}^{\text{cre}}$) mice were used. ER retrotranslocation/proteostasis were evaluated by examining ER retrotranslocation machinery proteins syvn 1 (E3 ubiquitin-protein ligase synoviolin 1), Sel1L (ERAD E3 ligase adaptor subunit), Herpud1 (homocysteine inducible ER protein with ubiquitin like domain 1), Derl-1 (degradation in ER protein 1), and proteasome subunits PA28 α and PSMD11 using immunoblotting. Chemical chaperone tauroursodeoxycholic acid (TUDCA, 500 mg/kg, body weight) or vehicle was given to $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}$ mice by subcutaneous injection every 3 days for 12 days, starting at P5. Retinas were collected at the end of the treatment for immunoblotting.

Results: Expression levels of syvn 1, Sel1L, and Herpud1 were unchanged in $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}$ mice, compared with $\text{Nr1}^{-/-}$ controls. However, deletion of $\text{IP}_3\text{R1}$ or RyR2 significantly increased their expression levels. Derl-1 expression level was increased in $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}$ retinas, and deletion of $\text{IP}_3\text{R1}$ completely abolished the upregulation. Expression level of PA28 α was not different between $\text{Cnga3}^{-/-}/\text{Nr1}^{-/-}$ and $\text{Nr1}^{-/-}$ retinas. Deletion of $\text{IP}_3\text{R1}$ or RyR2 significantly reduced its level. Similar findings were observed after TUDCA treatment.

Conclusions: Our results showed that ER retrotranslocation/proteostasis was increased/improved after deletion of ER Ca^{2+} efflux channels or after treatment with TUDCA. These findings suggest that promoting ER retrotranslocation/proteostasis may represent a promising strategy to reduce ER stress/cone death in CNG channel deficiency.

CONTROL ID: 3531969

SUBMITTER (NAME ONLY): Bao Tran

TITLE: Efficacy of topical application of cannabinoid receptor ligands in experimental dry eye disease

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.N. Tran, M. Maaß, J. Horstmann, G. Musial, M.E. Stern, U. Gehlsen, P. Steven, Department of Ophthalmology, Universitat zu Koln, Cologne, Nordrhein-Westfalen, GERMANY|B.N. Tran, M. Maaß, J. Horstmann, G. Musial, U. Gehlsen, P. Steven, Division of Dry Eye and ocular GvHD, Uniklinik Koln, Cologne, Nordrhein-Westfalen, GERMANY|M.E. Stern, ImmunEyez LLC, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cannabinoid receptors (CBR) 1 and 2, as part of the endocannabinoid system, were previously reported to be present in the ocular surface. Using activating or inhibiting cannabinoid ligands may affect CBR-functions such as regulating neuro-sensation, inflammation and wound healing, which are also core mechanisms of dry eye disease (DED). This study investigates the effect of several CBR ligands as a topical therapy in an experimental DED mouse model.

Methods: C57/Bl6 female mice were exposed to desiccating stress (DS) for 14 days. CBR ligands tetrahydrocannabinol (THC, agonist), SR141716A and SR144528 (selective antagonists) were formulated in aqueous solution (DMSO and Cremophore EL). Drug formulations or carrier were topically applied 3 times/day from day 1 of DS. To investigate disease severity, tear production, corneal fluorescence staining, and corneal sensitivity tests were performed at day 3, 5, 7, 10. At the end of the experiment, corneal and conjunctival tissues were analyzed regarding the expression of CBR1 and CBR2 by qPCR in naïve, DED-induced, and treated mice. Also, corneal flat mounts were stained with β 3-tubulin, then nerve density and length were semi-automatically quantified from obtained images.

Results: DS increased CBR expressions ($p < 0.05$). In treated mice, a reduced CBR expression was observed compared to DED mice ($p < 0.05$). After 10 days, all cannabinoid-ligands reduced fluorescence staining ($p < 0.01$) compared to untreated and carrier groups. Also, lower expression of IL-1 β in the cornea ($p < 0.05$) was observed. Topical application of CBR1 antagonist and THC maintained corneal sensitivity ($p < 0.05$) compared to DED mice and carrier-treated mice. In contrast to antagonists, THC protected corneal nerve density during desiccating stress ($p < 0.05$).

Conclusions: CBR1 and 2 seem to be involved in DED pathogenesis. Topical application of cannabinoid ligands reduces the expression of CBR1 and 2, which is accompanied with improvements of corneal damage and inflammation. Applying THC protected nerve density, thus maintained corneal sensitivity. Particularly, the selective CBR1 antagonist maintained cornea sensitivity without changing nerve density, which indicated a role of CBR1 in corneal neurotransmission. Therefore, this study facilitates the development of DED therapies based on cannabinoid eye drops.

CONTROL ID: 3531982

SUBMITTER (NAME ONLY): Kang-Chieh Huang

TITLE: Alterations in mTOR Signaling Result in Glaucomatous Neurodegeneration from Human Pluripotent Stem Cell-Derived Retinal Ganglion Cells

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Huang, K. VanderWall, S. Lavekar, C. Fligor, T. Cummins, Biology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|C. Gomes, J.S. Meyer, Medical and Molecular Genetics, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|K. Huang, C. Gomes, K. VanderWall, S. Lavekar, C. Fligor, Y. Pan, T. Cummins, J.S. Meyer, Stark Neurosciences Research Institute, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optineurin (OPTN) mutations contribute to neurodegenerative diseases including glaucoma, with the more severe forms resulting from an E50K mutation in the OPTN gene. However, mechanisms underlying how the OPTN(E50K) mutation leads to glaucomatous retinal ganglion cell (RGC) neurodegeneration have not been fully discovered. Here, we used human pluripotent stem cell (hPSC)-derived RGCs with the OPTN(E50K) mutation as a model to explore cellular pathways that contribute to glaucomatous neurodegeneration.

Methods: The OPTN(E50K) hPSC line was established utilizing clustered regularly-interspaced short palindromic repeats (CRISPR)/Cas9 gene editing approach, in which a knock-in E50K mutation was inserted into a wild-type H7 hPSC line. The OPTN(E50K) and isogenic control hPSCs were differentiated to retinal organoids, followed by dissociation and purification of RGCs. Morphological, functional and protein expression differences in OPTN(E50K) RGCs were identified in comparison to isogenic controls.

Results: OPTN(E50K) RGCs exhibited neurodegenerative phenotypes including reduced soma size, decreased branching and length of neurites, as well as increased excitability compared to isogenic controls. To identify mechanisms triggering disease phenotypes, western blotting demonstrated reduced expression of the OPTN protein in OPTN(E50K) RGCs, indicating a lack of OPTN protein adversely affects autophagy processing. Considering that mTOR activation promotes neural development and regulates autophagy, a downregulation of mTOR signaling was observed as a possible compensatory mechanism for autophagy deficits. To provide direct evidence that mTOR inhibition leads to degenerative phenotypes, pharmacological inhibition of mTor in wild-type RGCs resulted in shorter neurites, a smaller cell body size, and fewer primary neurites than controls. Additionally, these disease-related phenotypes were observed more rapidly in OPTN(E50K) RGCs grown in the absence of insulin, a known mTOR activator, suggesting a role for mTOR signaling deficits in neurodegeneration.

Conclusions: The results of this study indicate that deficiencies in OPTN lead to autophagy deficits and decreased mTOR activation, leading to RGC disease phenotypes. Thus, further studies of this pathway may lead to the identification of new targets for therapeutic approaches to glaucomatous neurodegeneration.

CONTROL ID: 3531999

SUBMITTER (NAME ONLY): Aindrila Saha

TITLE: Cone photoreceptors in human retinal organoids demonstrate robust light-evoked function.

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saha, R. Sinha, Neuroscience, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|A. Saha, E. Capowski, D. Gamm, McPherson Eye Research Institute, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|E. Capowski, Waisman Center, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|D. Gamm, R. Sinha, Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The first step of our high-definition central vision occurs in the cone photoreceptors in the fovea, which are tightly packed forming a dense pixel array capable of resolving fine spatial details. Death of foveal cones is the ultimate cause of central vision loss in age-related macular degeneration – a leading cause of blindness – as well as other acquired and inherited retinal degenerative diseases. Although human pluripotent stem-cell (hPSC) based replacement strategies hold promise for vision restoration in such conditions, its effective application is limited due to i) a sparse understanding of cone signaling in the primate fovea and ii) a lack of evidence that organoid cones (OCs) can exhibit light-evoked function similar to primate cones in vivo. In this study, we use primate foveal cones (FCs) as a baseline to compare the light-evoked physiology of OCs.

Methods: We used patch-clamp electrophysiology to record light-evoked responses from >100 cones across several hPSC-derived organoids (differentiated >200 days in vitro) and macaque fovea. We compared the photo-responses and membrane properties of the OCs with that of FCs.

Results: Recordings from individual OCs show robust light-evoked responses from a sizeable fraction of OCs across hPSC-organoids. OCs of different spectral types could be identified, though most of them show mid-wavelength spectral sensitivity. The response shape to brief light flashes show profiles similar to that of adult FCs. The light responses of OCs also demonstrate adaptation at higher background luminance similar to typical cones. Both the size and kinetics of light responses in OCs show variability within and between organoids. Although some of the membrane properties of OCs are comparable with that of adult FCs, a few resemble fetal FCs. These findings provide evidence that OCs mimic several physiological properties of adult FCs.

Conclusions: Our recordings from OCs show physiological light-evoked responses over a wide range of light levels. In addition, we were able to replicate several key features of primate FC photo-responses in OCs. These results provide a crucial first step in establishing hPSC-organoids as sources of bona fide human cones and as model systems for drug testing and for studying deficits in photoreceptor physiology in acquired and inherited macular degenerative diseases and cone and cone-rod dystrophies.

CONTROL ID: 3532063

SUBMITTER (NAME ONLY): Freya Mowat

TITLE: Age-related visual decline in companion dogs: a cross-sectional ERG study in a translational model species.

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.M. Mowat, M. Banghart, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|F.M. Mowat, W.K. Panek, G. Fefer, G. Wagner, H.D. Westermeyer, M. Gruen, N. Olby, Clinical Sciences, North Carolina State University, Raleigh, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is an important risk factor for visual decline and retinal disorders such as human age-related macular degeneration. Companion dogs share many aspects of the human lifestyle and environment and develop other age-related ocular disorders such as cataract and vitreous degeneration. We hypothesized that age is negatively associated with retinal function in dogs, as measured by dark- and light-adapted electroretinography.

Methods: Participants included adult companion (pet) dogs with no significant ophthalmic abnormalities. All participants underwent unilateral dark- and light-adapted electroretinography following mydriasis (RetEval, LKC Technologies). We performed statistical analysis using R version 4.0.0 to calculate correlation, R squared, and coefficients of correlation between age and ERG parameters. We calculated the strength of association between ERG measurements and age, or age adjusted for expected lifespan of the breed for purebred dogs.

Results: Median age was 11.3 years for all dogs (n = 29, 21 purebred dogs from 11 breeds, range 6.1-15.4 years). Median percentage of maximum purebred breed lifespan was 62%. (n = 20, range 41-104%). Overall, age was associated to a greater extent with ERG amplitude (P value range 0.004-0.44) than peak time (P value range from 0.13-0.97). Age was significantly associated with the dark-adapted bright-flash a-wave amplitude (R^2 .27, P = 0.004) and b-wave amplitude (R^2 .15, P = 0.04); b/a wave ratio was not significantly associated with age (P = 0.32). Age was also significantly associated with light-adapted 33Hz flicker amplitude (R^2 .25 P = 0.006). When age was represented as a proportion of maximum breed lifespan, age was also significantly associated with light-adapted flash b-wave amplitude (R^2 .09, P = 0.012).

Conclusions: Aging in companion dogs is associated with a decline in both rod- and cone-mediated ERG amplitudes. Further studies are warranted to define the relationship between age-related decline in retinal function and vision and/or retinal structure. Companion dogs could be considered a translational model for human age-related vision impairment.

CONTROL ID: 3532068

SUBMITTER (NAME ONLY): Sarah Pizzuto

TITLE: Accelerated regeneration of corneal endothelium after Descemet's stripping mediated by the engineered fibroblast growth factor TTHX1114

SESSION TITLE: Corneal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Pizzuto, J. Weant, D. Eveleth, Trefoil Therapeutics, San Diego, California, UNITED STATES|N.A. Afshari, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal endothelial dystrophy is currently being experimentally treated with limited descemet's stripping without transplantation. This work sought to test whether the regeneration of the endothelial layer after Descemet's stripping could be accelerated in corneal organ culture by treatment with an engineered form of FGF1 (TTHX1114).

Methods: Human corneas obtained from eye banks were maintained in organ culture. Descemet's stripping was performed to remove the central 4mm of endothelial cells with underlying Descemet's membrane. Corneas were then incubated in the presence or absence of TTHX1114 and the recovery of the endothelial layer evaluated by Trypan Blue and Alizarin Red staining. Lesion healing was quantitated using ImageJ. Invasion and proliferation of endothelial cells in the lesion area were evaluated by EdU incorporation and immunostaining with ZO-1.

Results: In both normal corneas and in corneas with guttae noted by the eye bank, healing of the stripped area without treatment was slow with about 30% of the stripped area healed at 14 days as judged by Trypan Blue. Healing in the presence of TTHX1114 was much more rapid, with 81% and 91% of the stripped area healed in normal and dystrophic corneas, respectively. Comparison of the lesion sizes between treated and control corneas was statistically significant (normal, $p < 0.001$, $n=10$ corneas per group; dystrophic, $p < 0.001$, $n=11$ corneas per group). In the healed areas of the treated corneas, Alizarin Red staining and ZO-1 staining revealed endothelial cells with defined ZO-1 rich cell borders covering parts of the lesion area. The endothelial cells covering the lesion area incorporate EdU indicating that they are actively proliferating.

Conclusions: The healing of Descemet's stripping lesions can be accelerated by engineered FGF1 in human corneas ex vivo in both normal corneas and corneas with signs of endothelial dystrophy.

CONTROL ID: 3532070

SUBMITTER (NAME ONLY): Heather Prior

TITLE: Effects of rosmarinic acid and β -cyclodextrin on lens clarity in adult zebrafish

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Prior, D. Van Gaalen, J. Lacroix, Biology, The King's University, Edmonton, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: This study was designed to evaluate the effect of rosmarinic acid and β -cyclodextrin on lens clarity in zebrafish with induced cataracts. As an important model organism, zebrafish offer opportunities to investigate basic as well as medical research questions in the field of cataractogenesis. Recent studies using rat and human lens tissue have shown restoration of transparency and delayed cataract formation in response to rosmarinic acid application. In addition, β -cyclodextrins have been used as stabilizers and carrier molecules when introducing antioxidants into biological systems. We have previously developed a method for the induction of cataracts in adult zebrafish which was used to produce cataracts in our study animals. We treated extracted cataractous and healthy lenses with rosmarinic acid as well as β -cyclodextrin, and assessed lens clarity in response to various treatment combinations compared to controls.

Methods: Adult zebrafish were subjected to unilateral intraocular injection of 3% hydrogen peroxide to induce cataracts. At 24 hours post-injection, fish were anesthetized for observation of cataract severity, and euthanized for extraction of both healthy and cataractous lenses. Extracted lenses were then incubated with various concentrations of rosmarinic acid and β -cyclodextrin. Lens clarity was assessed by photography of the lens placed over a grid and evaluation of opacity against a standardized scale.

Results: Using a scoring scale of 1 to 4, observations showed delayed development of opacification in healthy lenses incubated in some concentrations of rosmarinic acid and β -cyclodextrin when compared to controls, 48 to 72 hours after extraction.

Conclusions: These results support the findings in other species that rosmarinic acid may be an effective agent for preventing lens opacification. This preventative effect was detected in healthy lenses, but treatments did not significantly affect lens clarity in cataractous lenses. In addition, this study demonstrates that our method of inducing cataracts in zebrafish is a tractable experimental system.

CONTROL ID: 3532116

SUBMITTER (NAME ONLY): Alexandra Blomfield

TITLE: WNT2B deficiency leads to ectopic photoreceptor formation in mice

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Wnt/ β -catenin signaling is essential for embryonic eye development, and dysregulation of this system may lead to abnormal formation of both the anterior eye and retina. WNT2B, a ligand and activator of the Wnt/ β -catenin pathway, assists in the development of the lens and peripheral regions of the eye. Humans with WNT2B deficiency have a range of ocular defects including microcornea and colobomas. WNT2B may also assist in retinal progenitor cell differentiation, yet the potential role of WNT2B in retinal vascular or neuronal development is understudied. This project explored the effects of WNT2B on retinal neuronal and vascular formation using Wnt2b-deficient mice.

Methods: Systemic Wnt2b knockout mice were generated by crossing Wnt2b^{flox/flox} (fl/fl) mice with CMV-cre mice to deplete Wnt2b in all tissues. Adult heterozygous (Het) and homozygous (KO) Wnt2b-deficient mice (cre+) were examined and compared to fl/fl mice (cre-) as controls. Eyes were either fixed for retinal flat mount or frozen for cross sectioning. Retinal vascular morphology was assessed in flat mounts with isolectin (vascular endothelium marker) staining. Retinal neuronal morphology was assessed with H&E staining of frozen cross sections. Retinal cell type was determined via immunohistochemical staining with either rhodopsin antibody (photoreceptor marker) or isolectin, and co-stained with DAPI (nuclei marker).

Results: Both Wnt2b Het and KO mice exhibited relatively normal anterior segments with normal shape and size of the iris and lens when compared to fl/fl mice. Formation of retinal blood vessels in both Het and KO mice also appeared normal in both superficial and deep vascular layers. In retinal cross section, large clusters of ectopic cells were observed in the subretinal space around the photoreceptor inner and outer segments in both Wnt2b Het (3 out of 4 mice) and KO (2 out of 4 mice), while fl/fl retinas (from 4 mice) showed normal neuronal layers. Other neuronal layers of Het and KO eyes showed normal organization in both layer thickness and lamination, with no sign of retinal degeneration. The displaced cells were present in 2-month-old and persisted in 5-month-old Het and KO mice and stained positive for rhodopsin antibody while negative for isolectin, suggesting ectopic rod photoreceptor formation.

Conclusions: Our findings suggest that WNT2B is a novel regulator of photoreceptor formation and/or migration during eye development.

CONTROL ID: 3532122

SUBMITTER (NAME ONLY): Anthony Ewurum

TITLE: A Spectroscopic Study of the Composition and Conformation of Cholesteryl and Wax Esters Purified from Human Meibum

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Ewurum, Chemistry, University of Louisville College of Arts and Sciences, Louisville, Kentucky, UNITED STATES|A.C. Ewurum, A. Ankem, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|G. Georgiev, Complexo Interdisciplinar, IST, Universidade de Lisboa Instituto de Bioengenharia e Biociencias, Lisbon, Lisboa, PORTUGAL|D. Borchman, Ophthalmology and Visual Sciences, University of Louisville, Louisville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Anthony Ewurum: Commercial Relationship: Code N (No Commercial Relationship) | Akhila Ankem: Commercial Relationship: Code N (No Commercial Relationship) | Georgi As Georgiev: Commercial Relationship: Code N (No Commercial Relationship) | Douglas Borchman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) contributes to dry eye which affects 16 million people in the U.S. Meibum lipids are important for the stability of the tear film. The cholesteryl ester/wax ester (CE/WE) ratio decreases with MGD but it is unclear if or how CE affects meibum structure or tear film stability. The aim of this study was to bridge this gap in knowledge.

Methods: Meibum was collected from a 66-year-old Caucasian and a 29-year-old black donor and CE and WE were separated by MgO column chromatography. The esters were characterized using ¹H-NMR and the structure, conformation and phase transitional parameters of mixtures with a range of CE/WE ratios was determined using Fourier transform infrared spectroscopy.

Results: : CE and WE were completely separated. WE from the older donor A (Awe) was composed of 16 % less straight-chains and 50 % more iso-chains compared with CE from the same donor (Ace). The phase transition temperature and order (stiffness) for WE and CE from the younger donor B, Bwe and Bce, respectively, were higher, $P > 0.0001$, compared to Awe and Ace. Bwe added to Bce, decreased the hydrocarbon chain order, and phase transition temperature of Bce, $P < 0.05$. Increasing amounts of Bce added to Bwe caused the hydrocarbon chain order and phase transition temperature to increase linearly above 20 % Bce. The opposite trends were apparent for the donor A samples. The reason for the opposite trends is that Ace was more fluid, $P = 0.02$, compared to Awe, while Bce was less fluid, $P > 0.0001$, compared with Bwe.

Conclusions: Meibum CE and WE can be completely separated. CE changes the phase characteristics of meibum depending on whether it is more or less ordered, than WE. Changes in the meibum content of CE could explain changes in meibum order with age and MGD which may influence tear film stability. Studies to separate CE and WE from meibum are warranted to determine if/how meibum CE and WE conformation and composition change with age, gender, race and MGD and if the changes are related to tear film stability.

CONTROL ID: 3532126

SUBMITTER (NAME ONLY): Sai Karthik Kodeboyina

TITLE: Aqueous Humor Proteomic Changes Associated with Retinal Nerve Fiber Layer Thickness in Cataract and Glaucoma Patients

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kodeboyina, T. Lee, W. Zhi, S. Sharma, A. Sharma, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|K.E. Bollinger, L. Ulrich, D. Bogorad, A. Estes, S. Sharma, Department of Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a progressive optic neuropathy characterized by reduced retinal nerve fiber layer (RNFL) thickness. The purpose of this study was to discover aqueous humor (AH) proteomic changes associated with RNFL measurements in Cataract and Glaucoma patients.

Methods: Aqueous humor samples from 100 patients were analyzed using Liquid Chromatography-Mass Spectrometry (LC-MS/MS). RNFL parameters, including mean RNFL thickness and superior, inferior, nasal, and temporal thicknesses, were obtained from electronic medical records. Adjusting for confounding variables including age, sex, race and medications, multiple regression analyses were performed to discover the relationship between the aqueous humor protein levels and RNFL measures.

Results: We detected 356 proteins in 100 AH samples. A total of 19 proteins were significantly associated with mean RNFL thickness, 21 proteins were associated with superior thickness, 19 proteins were associated with inferior thickness, 28 proteins were associated with nasal thickness, and 5 proteins were associated with temporal thickness. There was a huge overlap in these proteins associated with different RNFL parameters. The top 10 proteins include: Limbic system-associated membrane protein, (LSAMP; $\beta = 2.23$), Immunoglobulin kappa variable 1D-33 (IGKV1D-33; $\beta = 1.96$), Testican-1 (SPOCK1; $\beta = 0.72$), matrix metalloproteinase-2 (MMP2; $\beta = -3.02$) Protein unc-45 homolog A (UNC45A; $\beta = -2.28$), Metalloproteinase inhibitor 1 (TIMP1; $\beta = -2.01$), Monocyte differentiation antigen CD14 (CD14; $\beta = -1.63$), Apolipoprotein C-III (APOC3; $\beta = -1.51$), Procollagen C-endopeptidase enhancer 1 (PCOLCE; $\beta = -1.43$), and Lysozyme (LYZ; $\beta = -1.09$).

Conclusions: In this study, we found several AH proteins associated with RNFL measures in cataract and glaucoma patients. These findings provide targets for future studies investigating precise molecular mechanisms and new therapies for glaucoma.

CONTROL ID: 3532137

SUBMITTER (NAME ONLY): Jianbo Zhou

TITLE: Post-occlusion surge and anterior chamber stability in a new phacoemulsification machine with small-bore, dual-durometer aspiration tubing

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zhou, D. Han, Research and Development, Johnson & Johnson Surgical Vison, Inc., Santa Ana, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jianbo Zhou: Commercial Relationship(s);Johnson & Johnson Surgical Vison, Inc.:Code E (Employment) | Duru Han: Commercial Relationship(s);Johnson & Johnson Surgical Vison, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: As a source of chamber instability during cataract surgery, post-occlusion surge (POS) is related to the compliance of the aspiration tubing. New fluidics packs with a small-bore, dual-durometer aspiration tubing were constructed. This study was to evaluate the performance of these fluidics packs with a new phacoemulsification machine on POS in a laboratory benchtop setting.

Methods: The inner layer of the aspiration tubing of the new fluidics packs uses a stiffer material with a smaller inner diameter than existing products, while the outer layer is soft to maintain flexibility. These packs were tested in a newly developed phacoemulsification console in peristaltic mode, along with existing packs as the control arm. A rigid body, leak-tight fixture with small internal volume and an attached pressure sensor were used to simulate the anterior chamber. A phacoemulsification handpiece with a 20G straight tip and sleeve was inserted tightly into the fixture and connected to a fluidics pack. The occlusion mechanism was created with a solenoid valve. A bottle height to generate a static irrigation pressure of 65 mmHg, an aspiration flow rate of 30 cc/min, and five vacuum presets of 200, 300, 400, 500, and 600 mmHg, were selected for this study. The intraocular pressure (IOP) waveforms were measured and recorded continuously during occlusion and occlusion break.

Results: At the vacuum preset of 400 mmHg, the new fluidics packs performed 20% better in terms of the IOP change, from the static value during occlusion to the trough of the IOP curve post occlusion, than the existing fluidics packs. For the vacuum presets from 300 to 600 mmHg, the new packs performed at least 35% better in surge area, the calculated area between the +20mmHg line and the IOP curve below this line, than the existing packs. The surge area was essentially zero at 200 mmHg vacuum for both types of fluidics packs.

Conclusions: This study demonstrated that the new fluidics pack with small-bore, dual-durometer aspiration tubing performed much better than the existing fluidics pack in post-occlusion surge in a new phacoemulsification machine in terms of the IOP change and the surge area in a laboratory setup, providing improved chamber stability.

CONTROL ID: 3532172

SUBMITTER (NAME ONLY): Eric Nguyen

TITLE: Single cell RNA-seq analysis to evaluate heterogeneity of cell populations in 3D-Bioprinted outer Blood-Retinal Barrier Models

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Song, M. Ferrer, National Center for Advancing Translational Sciences, Bethesda, Maryland, UNITED STATES|E. Nguyen, R. Quinn, T. Park, C. Malley, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Artificial outer blood-retinal barrier (oBRB) models present numerous applications in age-related macular degeneration (AMD) disease modeling. A thorough understanding of behaviors by different cell populations in the model has significant implications on the understanding of disease progression. Here, iPSC-derived epithelial cells (RPE) and endothelial cells (EC) within a 3D-bioprinted model of the oBRB were analyzed using single-cell RNA-seq to begin determining how printed choroid and RPE carry out specialized functions compared to their in-vivo counterparts.

Methods: EC, Pericytes, and fibroblasts were suspended in gelatin-based bio-ink, bioprinted onto biodegradable poly(lactic, co-glycolic) acid scaffolds and matured for one week. Afterward, RPE was seeded on the opposite sides of the membrane. The completed tissues were cultured for 6 weeks before enzymatic tissue dissociation and cell isolation using magnetic assisted cell sorting. Single-cell suspensions were used to generate barcoded single-cell gel bead-in-emulsions. Following cDNA amplification and processing, libraries were read using an Illumina HiSeq 3000. The Cellranger software package, Seurat R package, and the Biowulf computing cluster were used to process single-cell sequencing data. Gene set enrichment analysis was performed using GSEA v4.0.3, curated Gene Ontology sets and EnrichR.

Results: Differential expression (DE) analysis of RPE gene expression show a general increase in RPE signature genes in the bioprinted oBRB compared to transwell monolayer culture. tSNE analysis revealed broadly homogenous populations of RPE in oBRB and monolayer cultures. DE analysis of EC populations suggested increases in blood vessel maturation, choroidal maturation, and angiogenesis genes in the oBRB model. tSNE analysis suggested that EC in the oBRB model separated into populations at different stages of blood vessel maturation and an inflammatory population.

Conclusions: RNA-seq data suggests that the RPE monolayer acts as a homogeneous cell population within the 3D bioprinted tissue, while ECs show a greater degree of separation into differential stages of vascular maturation within the tissues. The variable stages of maturation are likely a consequence of a dynamic signaling environment within the printed choroid which would promote angiogenesis, maturation and inflammation.

CONTROL ID: 3532180

SUBMITTER (NAME ONLY): Suzanne Kirk

TITLE: MIGS, Race, and Refractive Outcomes

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kirk, A. Stefaniak, S. Griffin, N. Chung, M. Li, M. Henry, M. Chaku, Department of Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|M. Henry, Department of Ophthalmology, University of Illinois Hospital and Health Sciences System, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this research is to compare refractive outcomes of glaucoma patients who underwent phacoemulsification cataract surgery (Phaco) to those who had cataract surgery with Minimally Invasive Glaucoma Surgery (Phaco + MIGS). Previously, few studies have explored the various refractive outcomes following Phaco + MIGS procedures as compared to Phaco alone.

Methods: This is a retrospective chart review of 243 patients from Edward Hines Jr. VA Hospital and Loyola University Medical Center who had MIGS procedures (iStent® (Glaukos Corp. Laguna Hills, CA) or Kahook Dual Blade® (New World Medical, Rancho Cucamonga, CA, USA) and Phaco (Phaco + MIGS, n= 163) or Phaco alone (Phaco, n= 80). The Phaco group only includes patients from the Edward Hines Jr. VA Hospital. Subgroup analysis was performed based on the severity of glaucoma and race. We performed both independent t-tests and one-way ANOVA tests.

Results: The average difference in post-operative spherical equivalent (SE) to target refraction in Phaco + MIGS vs. Phaco was 0.462 and 0.437, respectively ($p = 0.5$). 65.5% of patients in the Phaco + MIGS group were within 0.5 D of the target refraction compared to 67.5% of the Phaco group. 89% of eyes in the Phaco + MIGS group had a post-op SE within 1 D of the anticipated target refraction vs. 92.5% of eyes in the Phaco group. The Phaco + MIGS African American subgroup ($n = 57$) had 87.8% eyes within 1 D of target vs. 88.2% in the Caucasian subgroup ($n = 110$). The Phaco African American group ($n = 27$) had 92.6% compared to the Phaco Caucasian group ($n = 53$) with 92.5% of eyes within 1 D of target refraction. We performed a one-way ANOVA to compare the effect of severity of glaucoma on refraction. In both the Phaco + MIGS and Phaco groups, there was no significant difference ($p = 0.171$ vs. $p = 0.241$), respectively. 82% of patients in the Phaco + MIGS group with refractive surprise ($> 1D$ from target) had visual acuity (VA) of 20/40 or worse vs. 100% of eyes in the Phaco group. In the Phaco group, average pre-op VA was 20/40 compared to 20/25 post-op. In the Phaco + MIGS group, average VA went from 20/60 pre-op to 20/30 post-op.

Conclusions: Our study showed no significant difference in refractive outcomes in patients who had Minimally Invasive Glaucoma Surgery with phacoemulsification compared to those who had phacoemulsification cataract surgery alone. There was also no significant difference in refractive outcomes based on race or the severity of glaucoma.

CONTROL ID: 3532189

SUBMITTER (NAME ONLY): Nasim Salimi

TITLE: Assessment of potential adverse effects of Ciprofloxacin on Müller (MIO-M1) cells

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Salimi, L. Singh, K. Schneider, M. Chwa, M. Kenney, Gavin Herbert Eye Institute, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose:

We evaluated possible adverse impacts of ciprofloxacin (CPFX) on human retinal Müller cells (MIO-M1).

Methods:

MIO-M1 cells were cultured in 96 well plates with the density of 10,000/well. The MIO-M1 cells were treated 48 hours with CPFX concentrations of 30, 60 and 120 mg/ml. 0.1 N solution of hydrochloric acid (HCl) was used as the vehicle control for CPFX. Assays measured levels of cellular metabolism (MTT), mitochondrial membrane potential (JC-1) and reactive oxygen species (ROS).

With the MTT assay, after 48 hours exposure to CPFX, 10 µl MTT assay reagent was added to each well and plates were incubated at 37°C for 2 hours. After adding 100 µl of DMSO to each well, plates were analyzed (signal at 570 nm and reference at 630 nm) with the absorbance reader.

After 48 hour treatment, the JC-1 reagent was added to each well. Plates were analyzed with a fluorescent plate reader at green (EX 485 nm and EM 535 nm) and red (EX 550 nm and EM 600 nm) to determine the red to green ratios that represent the 'live to dead' cells, respectively.

For the ROS assay, fluorescent H2DCF-DA dye was added to each well and plates read at excitation (EX, 492nm) and emission (EM, 520nm) wavelengths using the fluorescent plate reader.

Results:

The mean cellular metabolisms with 30, 60 and 120 mg/ml concentrations were: 84.5 ± 5.8 ($P=0.03$), 76.25 ± 9.1 ($P=0.03$) and 56.75 ± 4.2 ($P<0.0001$), compared to untreated cells (mean= 100 ± 0.5).

The mean of MMP in CPFX-treated cells was: 93 ± 4.8 ($P=0.19$), 85.5 ± 5.8 ($P=0.04$), and 78.75 ± 2.9 ($P=0.0004$), compared to untreated group (mean= 100 ± 0.4).

The ROS levels were not significantly changed after CPFX treatment.

Conclusions:

Exposure to CPFX decreased significantly metabolism and MMP in a dose-dependent manner in MIO-M1 cells.

Clinically relevant concentrations of CPFX impacted MIO-M1 cells in vitro.

CONTROL ID: 3532211

SUBMITTER (NAME ONLY): Jun Liu

TITLE: Heartbeat-induced corneal axial displacements are larger in keratoconus patients

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Liu, S. Kwok, N. Hazen, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Liu, D. Druzynski, A. Hendershot, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|X. Pan, Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio, UNITED STATES|N. Hazen, Biophysics Interdisciplinary Group, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure and compare heartbeat-induced corneal axial displacements (CAD) in patients with keratoconus (KCN) and normal controls (NRL) using a high-frequency ultrasound elastography method (Kwok et al, TVST, 2020).

Methods: Twenty-nine eyes in 15 KCN patients (age: 20-66; 8 males, 7 females) and 40 eyes in 20 NRLs with no known ocular diseases (age: 22-67; 6 males, 14 females) were recruited. Topographic and tomographic evaluations were obtained with an Oculus Pentacam to confirm KCN diagnosis. Intraocular pressure (IOP) and ocular pulse amplitude (OPA) were measured using a PASCAL Dynamic Contour Tonometer. A 50-MHz ultrasound probe (FUJIFILM VisualSonics) was used to acquire 1000 cross-sectional scans of the central 5-mm cornea along the naso-temporal axis at 128 frames per second. A correlation-based speckle tracking algorithm (Tang & Liu, JBME, 2012) was used to compute corneal displacements between consecutive frames. CAD was obtained as the average trough-to-peak magnitude of three heartbeat-induced axial displacement cycles.

Results: IOP and OPA were not different between KCN and NRL (IOP: 16.1 ± 3.5 vs 16.3 ± 2.5 mmHg, $p=0.85$; OPA: 2.2 ± 0.9 vs 2.6 ± 0.8 mmHg, $p=0.08$; two-sample t-tests). The CAD in KCN was 52.5 ± 20.8 μm , significantly larger than that (38.3 ± 9.1 μm) in NRL ($p<0.001$, two-sample t-test; Fig. 1). In addition, a positive association between CAD and age was observed in KCN ($r=0.42$, 95% CI= $0.063\sim0.68$, $p=0.02$, $n=29$, Fig. 2), but no significant trend was observed in NRL ($r=-0.10$, 95% CI= $-0.40\sim0.22$, $p=0.54$, $n=40$).

Conclusions: High-frequency ultrasound elastography may offer a tool for clinical biomechanical evaluation of the cornea. Our results showed a larger heartbeat-induced CAD in KCN, suggesting that CAD may be a useful parameter for KCN diagnosis. The increased difference between KCN and NRL with age may indicate progressive corneal weakening in KCN. Future studies are needed to evaluate whether CAD is associated with KCN grade and KCN progression over time.

CONTROL ID: 3532212

SUBMITTER (NAME ONLY): Dillan Patel

TITLE: The Effect of Foot Reflexology on Intraocular Pressure in Ocular Hypertension and Primary Open-Angle Glaucoma Patients

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Patel, J.D. Henderer, A. Krane, D. Yu, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|P. Kung, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|D. Cohen, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the effect of foot reflexology in primary open angle glaucoma (POAG) patients and the effect of a shoe insert to perform continuous foot reflexology in ocular hypertensive (OHTN) patients.

Methods: This is a prospective pilot study in glaucoma patients and a prospective therapeutic trial in ocular hypertensive patients. Patients were recruited from the Temple Ophthalmology outpatient clinic. Open-angle glaucoma patients were recruited from those about to have selective laser trabeculoplasty (SLT) for additional intraocular pressure (IOP) lowering. OHTN patients were recruited from the clinic. The glaucoma patients performed a 5-minute foot massage on a foot massage board (Figure 1) and the IOP was checked pre-massage, post-massage and 30, 60, 90 and 120 min post massage. OHTN patients underwent a one-month drop washout and then performed a 5-minute massage using a 3D-printed shoe insert (Figure 2) with the identical pressure checks. They then were randomly assigned to wear the shoe insert or a sham insert for one day. IOP was checked before inserting the insert and at the end of the day. The number of steps was recorded each day.

Results: For the glaucoma patients, after the 5-minute foot massage, the IOP significantly decreased up to 10% at 30, 90 and 120 min after massage in the right eye and up to 23% at all time points in the left. For the OHTN patients, IOP significantly decreased 6-13% in both eyes at all time points. For the shoe insert, there was a significant reduction in IOP of 10% for the left eye IOP but not the right eye at 6%. Two OHTN patients did not respond to the all-day shoe insert when they had responded to the 5-minute massage and one patient didn't respond at all.

Conclusions: Foot reflexology significantly lowers IOP in both glaucoma and OHTN patients. The use of this shoe insert to try and replicate the foot massage had promising, but somewhat inconsistent results. A different shoe insert might be better able to replicate the effect of the massage.

CONTROL ID: 3532213

SUBMITTER (NAME ONLY): Alison Abraham

TITLE: Associations of OCTA-based retinal microvascular markers with cognitive decline in an older adult biracial community sample: what can we learn from retinal imaging?

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Abraham, Epidemiology, University of Colorado, Denver, Colorado, UNITED STATES| A. Abraham, Y. Dong, R.A. Sharrett, J. Coresh, Epidemiology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|X. Guo, L.T. Arsiwala, A. Mihailovic, P.Y. Ramulu, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|D. Huang, Q. You, L. Liu, B.J. Lujan, A. Tomlinson, Y. Jia, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|T. Mosley, University of Mississippi, University Park, Mississippi, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accumulated vascular damage contributes to onset and progression of vascular dementia and possibly to Alzheimer's disease. Here we evaluated the feasibility and utility of using retinal imaging of microvascular markers to identify older adults at risk of cognitive disease.

Methods: The Eye Determinants of Cognition (EyeDOC) study recruited a biracial population-based sample from two sites: Jackson, MS, and Washington Co, MD. From 2017 to 2019, optical coherence tomographic angiography (OCTA) was used to capture vessel density (VD) across vascular layers and foveal avascular zone (FAZ) area from a scan of the macula. Image quality was assessed by trained graders. A neurocognitive battery of 10 tests was administered at three time points from 2011 to 2019 and incident MCI/dementia cases were ascertained. Linear mixed effects models were used to evaluate associations of retinal vascular markers with cognitive factor score change over time.

Results: 976 older adults, mean age of 78.7 (\pm 4.4) years, 44% black, were imaged. Gradable images were obtained in 55% (535/976), with low signal strength (66%) and motion artifact (22%) the largest contributors to poor quality. Both worse presenting distance visual acuity ($p < 0.001$) and worse contrast sensitivity ($p = 0.031$) were associated with poor quality images. Among the 480 participants with high quality images and no clinically significant retinal pathology, no associations of VD in any vascular layer or FAZ with longitudinal changes in either global cognitive function or with incident MCI/dementia were found.

Conclusions: In this large biracial community sample of older adults, OCTA-based retinal vascular imaging biomarkers were not associated with cognitive decline, incident MCI or dementia. Challenges with obtaining high quality OCTA images in older community-dwelling adult populations may currently limit the feasibility and utility of OCTA-retinal markers for detecting risk of cognitive disease.

CONTROL ID: 3532215

SUBMITTER (NAME ONLY): Diana Crowley

TITLE: Myo/Nog Cells are Phagocytotic and Increase in Number in Response to Photoreceptor Death in the Murine Model of Retinitis Pigmentosa

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Crowley, R. Souza, E. Tsai, S. Murad, S. Coughlan, M. Woodruff, R. Brahmabhatt, P. Lecker, G. Gorski, J. Benalcazar, L. Gugerty, J.V. Gerhart, M. George-Weinstein, A. Bravo Nuevo, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myo/Nog cells play an essential role in normal eye development. Previous studies have shown that they migrate to areas of stress and injury in the retina and are neuroprotective, but their specific role in these areas of stress is unclear. In this study, we observed the behavior of Myo/Nog cells in a congenital murine model of retinitis pigmentosa (C3H mice), which results in the loss of photoreceptor cells within the outer nuclear layer of the retina (ONL).

Methods: C57BL/6J (C57) and C3H/HeJ (C3H) mice were assessed at weeks 2.5, 3, 4, 5, and 6 using scotopic electroretinography (ERG) and histological analysis. Enucleated eyes were fixed in paraformaldehyde and cryo-sectioned. Cryosections were labeled with Myo/Nog specific monoclonal antibodies and TUNEL to detect cell death; and analyzed by fluorescence microscopy.

Results: The decreased amplitude of the A and B waves in the C3H mice in comparison to those of C57 mice was verified with ERG ($p<0.05$). Progressive thinning of the retina in the C3H mice was confirmed by microscopic analysis. While C3H mice initially demonstrated a greater number of photoreceptors at the edge of the retina, by week 4 there were significantly fewer photoreceptors at the periphery in comparison to the mid-periphery and central retina ($p<0.05$). Myo/Nog cells were significantly more numerous in C3H than C57 retinas ($p<0.05$). The majority of Myo/Nog cells were found in the diminishing ONL and choroid. Several of the Myo/Nog cells had phagocytosed apoptotic photoreceptors.

Conclusions: Progressive retinal degeneration and visual deterioration in C3H mice are accompanied by an increase in Myo/Nog cells. They accumulate in parallel with an increase in cell death in the ONL and demonstrate phagocytic properties as they engulf dying cells. These findings are consistent with Myo/Nog cells' behaviors in other forms of retinopathy and injury in other tissues. Future studies will characterize additional functions of Myo/Nog cells in this severe model of retinitis pigmentosa.

CONTROL ID: 3532231

SUBMITTER (NAME ONLY): Bahman Tahayori

TITLE: Uncertainty estimation for the feature agnostic glaucoma detection based on OCT volumes

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tahayori, B.J. Antony, R. Garnavi, IBM Research Australia, Southbank, Victoria, AUSTRALIA|H. Ishikawa, G. Wollstein, J.S. Schuman, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To improve the performance of the feature agnostic AI-based glaucoma detection algorithm by evaluating an uncertainty score for each prediction.

Methods: We previously developed a 5-layer 3D Convolutional Neural Network (CNN) in using the OCT scans from both eyes of 134 healthy, 779 glaucoma patients on a Cirrus HD-OCT scanner (200x200 ONH Cubes; Zeiss, Dublin CA). In our analysis, we excluded scans with signal strength less than 7 and downsampled the volumes to 64x64x128 voxels.

Uncertainty of AI models can be estimated by computing the effect of randomly ignoring a set of parameters within the network. We randomly zeroed 5% of each of the 5 convolutional layers and computed the entropy in the final score over 20 forward passes. The performance of the approach was assessed using a 10-fold cross validation study.

Results: Over the 10-folds, the model showed an AUC of 0.91 ± 0.027 . In analysing the uncertainty and the probabilistic scores generated by the model (Softmax function) for one fold (see Fig. 1), we observed that a threshold of 0.8 can be used to flag 75% of the false positives and false negatives for further review. On the other hand, only 25% of the healthy controls and 20% of glaucoma patients showed an uncertainty score above that threshold. Fig. 2 summarises the overall uncertainties scores and indicates that low scores are associated with the correctly identified cases while the errors show higher uncertainty scores.

Conclusions: The quantitative uncertainty measure provides supplementary information to clinicians and can be used to flag difficult cases automatically.

Given that the dataset used in this work is highly imbalanced (more positive cases compared to normal cases) the uncertainty score for true negative cases is significantly higher compared to true positive cases. We expect to achieve lower uncertainty scores for normal cases if more data for normal eyes are available.

The uncertainty analysis presented here may aid clinical interpretations of AI-based glaucoma detection outcomes. A separate study will be run to measure this improvement and compare the result with experts' level of uncertainty.

CONTROL ID: 3532234

SUBMITTER (NAME ONLY): Ai Kido

TITLE: Incidence of Central Serous Chorioretinopathy in Japan: A Nationwide Population-Based Cohort Study

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kido, M. Miyake, H. Tamura, A. Takahashi, S. Ooto, A. Tsujikawa, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: The purpose of the current study is to elucidate the epidemiological background of central serous chorioretinopathy, including its incidence and treatment pattern, using a nationwide health insurance claims database of the Japanese population.

Methods: This is a population-based cohort study using a nationwide health insurance claims database, which included the entire Japanese population aged 30 years or older (91 million people) between 2011 to 2018. The National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB) is a national claim database managed by Japan Ministry of Health, Labor, and Welfare (MHWL). As Japan employs universal health coverage, the NDB covers almost all claims issued in Japan. We accessed all data stored in the NDB under the permission of the MHWL. CSC onset was recorded by age and sex categories per year between 2011 and 2018, and the incidence rate was calculated. We identified laser photocoagulation (PC), photodynamic therapy (PDT) with verteporfin, and anti-vascular endothelial growth factor (anti-VEGF) intravitreal injection to evaluate the transition of the initial treatment pattern. In addition, geographical, climatic, and seasonal variation of incidence rate was also assessed.

Results: During the 8-year period, 247,930 incidences of CSC were identified, among which 75.9 % were male. The crude incidence rate (per 100,000 person-years) in the general population aged 30 years or older was 34.04 (95% CI, 33.90–34.17), that in males was 54.16 (95% CI, 53.91-54.40) and that in females was 15.67 (95% CI, 15.54-15.79). The mean age of onset was younger in males than in females (50.51 ± 12.48 years vs 54.67 ± 13.53 years). Most of the newly diagnosed CSC patients (86.8%) did not receive PC, PDT, or anti-VEGF. The incidence rate showed significant geographical, climatic, and seasonal variations; for example, low incidence was observed in relatively rural, cold, and snowy areas, and in summer and winter.

Conclusions: The current study provides the largest population-based evidence to clarify the detailed epidemiology of CSC. These results could help to understand the pathogenesis and mechanisms of CSC in the future.

CONTROL ID: 3532266

SUBMITTER (NAME ONLY): Chang Ho Yoon

TITLE: Aging-dependent gut microbiome dysbiosis is associated with dry eye severity in C57BL/6 male mouse model

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Emerging evidence have demonstrated that gut dysbiosis contributes to the pathophysiology or exacerbation of ocular diseases including dry eye disease. However, the relationship between aging-related changes in gut microbiota and dry eye disease have not been elucidated. We investigated the association between aging-dependent microbiome changes and dry eye severity in C57BL/6 male mice.

Methods: Eight-week-old (8W, n=15), one-year-old (1Y, n=10), and two-year-old (2Y, n=8) C57BL/6 male mice were used. Dry eye severity was assessed by corneal staining scores and tear secretion. Bacterial genomic 16s rRNA from feces was analyzed. Main outcomes were microbiome compositional differences among the groups and their correlation to dry eye severity. The Kruskal–Wallis test followed by Dunn's post hoc test was used for comparison between the three groups. Univariate analysis was used to identify the microbiome composition associated with the dry eye severity. Multivariate analysis was used to eliminate confounding age factors.

Results: In aged mice (1Y and 2Y), corneal staining increased and tear secretion decreased with statistical significance. Gut microbiome α -diversity was not different among the groups. However, β -diversity was significantly different among the groups. In univariate analysis, phylum Firmicutes, Proteobacteria, and Cyanobacteria, Firmicutes/Bacteroidetes ratio, and genus Alistipes, Bacteroides, Prevotella, Paraprevotella, and Helicobacter were significantly related to dry eye severity. After adjustment of age, multivariate analysis revealed phylum Proteobacteria, Firmicutes/Bacteroidetes ratio, and genus Lactobacillus, Alistipes, Prevotella, Paraprevotella, and Helicobacter to be significantly associated with dry eye severity.

Conclusions: Our study suggests that aging-dependent changes in microbiome composition are related to severity of dry eye signs in C57BL/6 male mice.

CONTROL ID: 3532276

SUBMITTER (NAME ONLY): Rekha Srinivasan

TITLE: Developing a new method to assess central vision using visual stimuli with natural scene statistics

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Srinivasan, A.M. McKendrick, Optometry & Vision Sciences, The University of Melbourne, Parkville, Victoria, AUSTRALIA|A. Turpin, School of Computing and Information Systems, The University of Melbourne, Parkville, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Previous studies show that some visual field (VF) defects are detectable via analysis of visual search behaviour, for example: when watching video, or performing daily living tasks. Here, we developed an alternate approach that measures the number of fixations to find targets on a background with spatial frequency content similar to natural scenes (1/f noise). We chose this approach because there is an established theoretical framework linking target detectability in the image to the predicted number of fixations[1]. We conducted a proof-of-concept experiment to test if the method can detect VF loss.

Methods: 21 older adults [aged:61-79 years] and 20 people with a clinical diagnosis of glaucoma [aged:59-84 years] participated. Participants visually searched for a Gabor (6c/°) that appeared in one of 25 possible locations within a 15° (visual angle) 1/f noise background (RMS contrast: 0.20). Gabor contrast was set at the 95% probability of seeing limit estimated from frequency of seeing curves in 28 older controls. The outcome measure was the number of fixations required to find the target, measured using a Gazepoint GP3 eye tracker. Each target was presented 20 times, in randomized and interleaved order. Normative limits (NL: 95%,98%,99%) for the number of fixations at each location was estimated. Procedure performance was assessed by calculating sensitivity (SE) and specificity (SP) for different combinations: NL, target locations with fixations outside NL (varied: 0-25) and number of repeated target presentations (varied: 1-20). The highest Area Under Curve (AUC) (computed as partial AUC (pAUC) for SP higher than 80%) was chosen; from this curve the criteria with highest SE for SP greater than 95% was selected.

Results: Older adults made a median of 2-3 fixations (Interquartile range (IQR):2-4) to locate the target on the 1/f noise for all locations. The VF was flagged “abnormal” when the fixation number was greater than the 99% NL for three or more locations (85% SE, 95.2% SP, 88% pAUC) averaged over two repeated presentations. The median time for controls to perform the task was 46 (IQR:33-65) seconds.

Conclusions: Our prototype test demonstrated effective and efficient screening of abnormal areas in central vision and was well tolerated. While we included people with glaucoma here, the method is designed to generalize to any form of central VF loss.

1.Najemnik & Geisler. Nature, 2005:434.

CONTROL ID: 3532288

SUBMITTER (NAME ONLY): Andrew Lam

TITLE: Fixation stability using soft contact lenses versus built-in auto-focus in OCTA of myopes

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Lam, K.K. Lau, H. Wong, J.P. Lam, M. Yeung, Center for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Kowloon, HONG KONG|

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ABSTRACT BODY:

Purpose: High myopia has been found to be associated with reduced retinal capillary vasculature. Optical defocus could lead to erroneous OCTA measurement. Some OCTA systems have built-in ocular lenses to compensate refractive defocus. We hypothesized that inadequate optical correction could lead to fixation instability, hence affecting OCTA measurements.

Methods: Seventy eyes of 70 myopes (35: spherical equivalent $>-3D$, 35: spherical equivalent $<-6D$) had OCTA measured using a Cirrus SD-OCT. Three measurements were obtained using a 6x6 mm scan (350x350 pixels) centered at the fovea, first with soft contact lens correction, followed by using the built-in Auto Focus correction after removal of contact lenses. Valid OCTA scans had signal strength of ≥ 7 and no obvious artefacts. Fixation stability of the 3 OCTA scans was analyzed in terms of deviation (in pixel) of the fovea from the centre of the 350x350 grid (Figure 1). OCTA metrics, namely vessel length density (VD) and perfusion area density (PD) using the ETDRS format, and foveal avascular zone (FAZ) were averaged from the three OCTA scans and compared between different correction methods.

Results: Low myopes ($-1.89D \pm 0.75D$) and high myopes ($-8.10D \pm 1.34D$) had similar age. Fixation stability of low myopes from three OCTA scans (test-retest repeatability) was similar between the two correction modes (contact lens: 10 pixels vs Auto Focus: 7 pixels). High myopes had poor fixation stability when corrected with Auto Focus (test-retest repeatability: 17 pixels) compared with using contact lenses (12 pixels). Signal strength was higher in low myopes than high myopes when corrected with contact lenses (8.96 vs 8.40) and Auto Focus (8.82 vs 8.17). When combining the two groups, only VD at the outer ring and PD of the entire 6mm circle showed significant difference between the two correction methods. VD and PD results were smaller when using Auto Focus. No significant difference in FAZ was found.

Conclusions: Fixation was more stable in OCTA measurement when myopes were corrected with soft contact lenses, especially high myopes. In general, VD, PD, and FAZ were similar using different correction methods that could be due to using averaged results from three OCTA scans. Multiple OCTA scan averaging approach is recommended.

CONTROL ID: 3532291

SUBMITTER (NAME ONLY): Kazutaka Hirabayashi

TITLE: Changes in retinal sensitivity, thickness, and perfusion density following treatment for branch retinal vein occlusion (BRVO)

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the relationship between retinal sensitivity (RS), retinal thickness (RT), perfusion density (PD), and the effect of laser treatment over 1 year in patients with BRVO treated with intravitreal ranibizumab injection (IVR) or IVR with laser treatment.

Methods: Patients with BRVO who received IVR at Shinshu University Hospital between 2017 and 2018 were assessed at baseline and 12 months after initial treatment. RS in 34 stimulus locations in the central 10° were assessed using microperimetry (Microperimeter MP-3; Nidek Co., Ltd., Gamagori, Japan). From these same RS locations, RT by optical coherence tomography (OCT) (PLEX Elite 9000; Carl Zeiss Meditec, Inc, Jena, Germany) and PD by OCT angiography were measured. In addition, the presence of superficial and deep hemorrhage in each region was evaluated. Focal laser (MC-500 Vixi; Nidek Co., Ltd.) was applied (multiple times if needed) to areas with residual edema after IVR. Relationship between application of laser treatment and changes in RS, RT, and PD were assessed.

Results: Fourteen eyes of 14 patients (5 men and 9 women aged 72.0 ± 7.7 years, 7 IVR alone and 7 combination) were analyzed. At baseline, RS showed a significant negative correlation with RT ($r = -0.68$, $p = 3.35e-71$, Pearson's correlation coefficient) and a positive correlation with PD ($r = 0.72$, $p = 1.16e-42$). RT and PD were negatively correlated ($r = -0.64$, $p = 1.14e-40$) with each other.

At 12 months, RS showed a significant positive correlation with RT and PD (RT: $r = 0.56$, $p = 5.72e-36$; PD: $r = 0.60$, $p = 2.12e-46$). PD and RT showed a positive correlation ($r = 0.61$, $p = 2.49e-46$) with each other.

Areas with superficial hemorrhage had significantly lower RS than those with deep hemorrhage at baseline and at 12 months (baseline: $p = 0.0025$; 12M: $p = 0.0208$, Mann Whitney test).

There was a significant improvement in RS at 12 months in the IVR monotherapy group ($p < 0.0001$, One-way ANOVA) but not in the combination group ($p = 0.675$). RS was significantly higher in the IVR monotherapy group than in the combination group at 12 months ($p < 0.0001$).

Conclusions: In eyes with BRVO, regions with low PD at baseline had thicker retinas. Twelve months after initiation of therapy, RS improved in the IVR monotherapy arm but not in eyes requiring combination therapy. These findings may be of value in assessing prognosis in eyes with BRVO.

CONTROL ID: 3532294

SUBMITTER (NAME ONLY): Priya Kulkarni

TITLE: Bilateral macular edema (ME) at baseline and 1 year due to diabetic retinopathy (DR), neovascular age-related macular degeneration (nAMD), and retinal vein occlusion (RVO)

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The most common causes of ME (DR, nAMD, and RVO) can affect both eyes. Bilateral ME significantly impacts a patient's visual function and ability to perform tasks of daily living. This study aims to understand the prevalence of bilateral ME at initial diagnosis (baseline) for patients with DR, nAMD and RVO, and second eye involvement at 1 year (1yr) for patients with unilateral ME at baseline.

Methods: A retrospective observational claims database study, using Truven® marketscan, in adults (≥ 18 years) with at least one diagnosis of ME between Oct 2016 to Jun 2018 as ascertained by the ICD-10 codes. Patients were categorized into three groups according to ME involvement at initial diagnosis: unilateral (right or left), bilateral or unspecified. Patients with unilateral ME at baseline were followed for 1yr to estimate the bilateral involvement (Figure 1).

Results: Out of 37,827 patients with DR, 23,250 (61%) had an initial diagnosis of bilateral ME, 13,492 (36%) had unilateral involvement; and 1085 (3%) unspecified. Of 13,492 with unilateral ME at baseline, only 2490 had at least 1-yr follow-up. Of these, 573 (23%) developed bilateral involvement at 1yr as follows: 14% within the first 3 months, 5% between 4-6 months, 2-3% between 7-9 months and 2% between 10-12 months.

Extrapolating the observed bilateral involvement rate to all patients with unilateral involvement (36%), 8% developed bilateral macular edema at 1yr.

Bilateral rates for nAMD and ME secondary to RVO estimated in an analogous manner are given in Table 1. Of 30,548 nAMD and 11,953 RVO patients, 9,097 (30%) and 473 (4%) had an initial diagnosis of bilateral ME respectively, with additional 9% and 2% developing bilateral ME by 1yr.

Conclusions: At the initial diagnosis, DR patients had a greater proportion of bilateral ME (61%) compared to nAMD (30%) and RVO (4%). Fewer RVO patients developed bilateral ME by 1yr compared to DR and nAMD patients. In summary, ME secondary to DR and nAMD frequently affect both eyes and regular bilateral monitoring is necessary. Evaluation of risk factors associated with more severe disease and vision threatening complications such as ME is warranted.

CONTROL ID: 3532308

SUBMITTER (NAME ONLY): Alina Miron

TITLE: Endothelial cell viability after DMEK graft preparation

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Miron, G. RJ Melles, S. Oellerich, R&D, NIOS, Rotterdam, South Holland, NETHERLANDS|A. Sajet, E. A Groeneveld, J. Kok, M. Dedeci, M. de Jong, V. Amo-Addae, G. RJ Melles, J. van der Wees, Amnitrans EyeBank, NIOS, Rotterdam, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To evaluate the effect of graft preparation and organ-culture storage on endothelial cell density (ECD) and viability of Descemet membrane endothelial keratoplasty (DMEK) grafts.

Methods: DMEK grafts (n=27) were prepared at Amnitrans EyeBank Rotterdam from 27 corneas (15 donors) that were eligible for transplantation but could not be allocated due to the Covid-19-related cancellation of elective surgeries. Cell viability (by Calcein-AM staining) and ECD of 5 grafts originally scheduled for transplantation, were evaluated on the originally planned surgery day, whereas 22 grafts from paired donor corneas were evaluated either directly post-preparation or after 3-7 days of storage.

Results: Light microscopy (LM) evaluation of all grafts showed an unremarkable endothelial cell monolayer directly after preparation. However, median viable ECD for the 5 grafts initially allocated for transplantation was 18% (range 9-73%) lower than median LM ECD. For the paired DMEK grafts, viable ECD determined by Calcein-AM staining on the day of graft preparation and after 3-7 days of graft storage showed a median decrease of 1% (mean, 5(\pm 11)%) and 2% (mean, 16(\pm 33)%), respectively. Median % graft area populated by viable cells after preparation and after 3-7 days of graft storage was 88% (mean, 85(\pm 12)%) and 92% (mean, 88(\pm 14)%), respectively.

Conclusions: Loss of viable cells may be observed for some grafts within hours after preparation with insignificant additional ECD changes during 3-7 days of graft storage. Implementing an additional post-preparation step in the eye bank to evaluate cell density before graft release for transplantation may help to reduce postoperative DMEK complications.

CONTROL ID: 3532312

SUBMITTER (NAME ONLY): Md Asif Khan Setu

TITLE: Deep Learning-based Segmentation and Quantification of Nerve Fibers and Dendritic cells in Confocal Microscopy of the Cornea

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Setu, G. Musial, V. Tahmaz, M.E. Stern, P. Steven, Department of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|M. Setu, G. Musial, V. Tahmaz, P. Steven, Division of Dry Eye and Ocular GvHD, Uniklinik Koln, Koln, Nordrhein-Westfalen, GERMANY|S. Schmidt, Heidelberg Engineering GmbH, Heidelberg, Baden-Württemberg, GERMANY|M.E. Stern, ImmunEyez LLC, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In vivo confocal microscopy (IVCM) is a non-invasive optical imaging modality that enables a histological visualization and provides morphometric information about corneal nerve fiber (CNF) and dendritic cell (DC), that aid clinicians to diagnosis of inflammatory corneal diseases. Quantification of CNF and DCs requires manual annotation or semi-automatic approaches, which are time consuming, non-reproducible, and laborious. The purpose of this research study was to develop deep learning-based models to segment and quantify CNF and DC in IVCM automatically, therefore reducing inter-or intra-observer variability and time associated with manual perception to analyze larger volumes of clinical images.

Methods: A CNF segmentation and DC detection model were developed based on deep learning algorithms U-Net and Mask R-CNN respectively. The CNF segmentation model was trained with 1036 and tested on 183 images while the DC detection model was trained with 446 and tested on 50 images. To analyze CNF morphology, number of nerves, number of branching points, nerves density, nerves length, and tortuosity were measured. An automatic Python-based software was written to compute the morphometric parameters directly from the binary segmented image produced by deep learning model. Moreover, Bland-Altman's statistical analysis was performed to determine the consistency between automatic segmentation and manual annotation.

Results: The CNF segmentation model reliably segments the testing images with an average 83% sensitivity and 91% specificity while the DC detection model detects DCs with an average 92% precision, 95% recall, and 93% F1 score. In Bland-Altman's analysis, the mean of automatic and manual segmentation for all morphometric parameters was close to 0, and more than 95% of the values were within the limit of agreement. To segment and morphometric evaluation of CNF, our developed software took on average 4.5 seconds per image while to detect and count the DCs took on average 3 seconds.

Conclusions: Our developed deep learning-based models demonstrated high consistency between automatic and manual segmentation of IVCM images with rapid speed. The results show that the system has the potential to be implemented into clinical practice for CNF segmentation and DC detection in IVCM.

CONTROL ID: 3532323

SUBMITTER (NAME ONLY): Wolf-Dieter Vogl

TITLE: Topographic Effects on AI-Quantified Regional Progression in the FILLY Trial of Pegcetacoplan (APL-2) for Treatment of Geographic Atrophy Secondary to AMD

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Vogl, H. Bogunovic, J. Mai, G.S. Reiter, S. Riedl, D. Lachinov, U. Schmidt-Erfurth, Department of Ophthalmology and Optometry, Medizinische Universität Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To investigate treatment effects on local progression of Geographic Atrophy (GA) with respect to topographic growth patterns quantified from SD-OCT images by deep learning in age-related macular degeneration (AMD).

Methods: 334 SD-OCT scans of 57 eyes with monthly (AM), 52 eyes with every-other-month (AEOM) treatment and 58 eyes with sham (SM) injection from baseline and 1 year follow up of a Phase 2 clinical trial evaluating pegcetacoplan in patients with GA secondary to AMD (FILLY, NCT02503332) were included. Retinal pigment epithelium loss were automatically segmented using deep learning. Local GA growth rate was determined from the delineated en-face projections of GA as the distance of baseline border points to the closest border point at 1 year. Growth direction was categorized into “towards fovea” when angle between growth direction and direction to fovea was less than $\pm 90^\circ$ and “away from fovea” otherwise.

Mixed effects models grouped by eyes and distance as random factor were used to regress growth speed for each GA lesion border point using treatment and growth direction as covariates.

Results: Using 321,946 GA border points, mean growth for SM was 64 $\mu\text{m}/\text{year}$ (95%CI: 39 to 87), with 18 $\mu\text{m}/\text{year}$ less(95% CI: 5 to 32, $p=.0103$) and 6 $\mu\text{m}/\text{year}$ less(95% CI: -8 to 20, $p=.39$) for AM and AEOM, respectively. For the 195,396 points showing GA growth, the mean growth was 108 $\mu\text{m}/\text{year}$ (95%CI: 86 to 132) for SM and additional reduced growth by 26 $\mu\text{m}/\text{year}$ (95%CI: 6 to 47, $p=.0135$) and 4 μm (95%CI: -16 to 25, $p=0.72$) for AM and AEOM, respectively. Growth towards fovea is reduced by 4 μm (95%CI: 2 to 5, $p<.001$) for SM and additionally by 13 μm (95%CI: 11 to 15, $p<0.0001$) and 12 μm (95%CI: 11 to 14, $p<0.0001$) for AM and AEOM treatment.

Conclusions: Eyes treated with pegcetacoplan showed a significantly slower GA lesion growth rate compared to sham, and an even slower growth rate towards fovea. By assessing local GA growth and direction, the heterogeneity in GA progression is captured in more detail and enables observation of treatment effects with respect to topography. Using deep learning to automatically quantify atrophy in in-vivo OCT images allows for precise and accurate assessment and analysis of GA progression at a large scale and may provide new insight into disease mechanisms and response to novel treatment.

CONTROL ID: 3532325

SUBMITTER (NAME ONLY): Hong Qi

TITLE: Quantification of Increased Corneal Subbasal Nerve Tortuosity in Dry Eye Disease and Its Correlation with Clinical Parameters

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study quantified corneal subbasal nerve tortuosity in dry eye disease (DED) and investigated its correlation with clinical parameters by proposing an aggregated measure of tortuosity (Tagg).

Methods: The sample consisted of twenty-six eyes of patients with DED and Twenty-three eyes of healthy volunteers, which represented separately the dry eye group and the control group. Clinical evaluation of DED and in vivo confocal microscopy analysis of the central cornea were performed. Tagg incorporated six metrics of tortuosity including LC, Cur_max, TC, TSC, DCI, and ICM. Corneal subbasal nerve images of subjects and a validation data set were analyzed using Tagg. Spearman's rank correlation was performed on Tagg and clinical parameters.

Results: Tagg was validated using 1501 corneal nerve images. Tagg was higher in patients with DED than in healthy volunteers ($P < 0.001$). Tagg was positively correlated with the ocular surface disease index ($r = 0.418$, $P = 0.003$) and negatively correlated with tear breakup time ($r = -0.398$, $P = 0.007$). There was no correlation between Tagg and corneal fluorescein staining, the Schirmer I test or corneal sensation.

Conclusions: Tagg was validated for quantification of corneal subbasal nerve tortuosity, and was higher in patients with DED than in healthy volunteers. A higher Tagg may be linked to ocular discomfort and tear film instability.

CONTROL ID: 3532333

SUBMITTER (NAME ONLY): Nancy Holekamp

TITLE: Barriers to adherence to age-related macular degeneration and diabetic macular edema management plans:
A multi-national qualitative study

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Research has shown that patients in the real world with neovascular age-related macular degeneration (nAMD) or diabetic macular edema (DME) treated with anti-vascular endothelial growth factor (VEGF) achieve lower vision improvements compared to patients in clinical trials. This has been partly attributed to treatment burden, which can impede a patient's ability or willingness to follow their management plan (i.e., adherence). This study aims to better understand the treatment experience of intravitreal anti-VEGF injections from the patient, caregiver, and physician perspectives.

Methods: Patients with nAMD/DME treated with anti-VEGF injections, their caregivers, and retina specialists (RSs) participated in 1:1 exploratory phone interviews in Canada, France, Germany, Italy, Spain and the United States. Interview transcripts were analyzed qualitatively to identify concepts related to treatment experience and drivers of and barriers to following a management plan.

Results: We interviewed 62 RSs, 95 patients (49 nAMD, 46 DME) and 79 caregivers (of 47 nAMD, 32 DME patients). In our sample, RSs estimated the non-adherence rate among their patients to range from 0 to 20%. The majority of nAMD patients and approximately half of DME patients reported never missing an injection visit. All respondents reported similar drivers for following a management plan. Treatment effectiveness was reported as a key driver by ~30-40% of all respondents. The most commonly reported driver by RSs and patients/caregivers were patient education (34%) and the doctor-patient relationship (~60%), respectively. Various barriers to following a management plan were reported: fear of injection, health-related (vision loss, lack of treatment effectiveness), time and travel-related (waiting time, visit frequency, distance to site), and education-related (lack of understanding treatment purpose and procedures). RSs reported additional barriers (comorbidities, insurance coverage) taken into account when making anti-VEGF prescribing decisions.

Conclusions: There was a consensus among patients, caregivers, and RSs regarding drivers of and barriers to anti-VEGF treatment. New therapies offering improved or longer-acting effectiveness along with enhanced patient education may improve nAMD/DME patient adherence to their management plan and achieve better real-world vision outcomes.

CONTROL ID: 3532338

SUBMITTER (NAME ONLY): Mhd Hasan Sarhan

TITLE: The effect of dataset size on pretraining and transfer learning for diabetic retinopathy in narrow field to widefield domain shift

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To study the effect of the pretraining dataset on the transferred model performance. It has been established that pretraining a deep learning system (DLS) on narrow field (NF) fundus images then transfer the model to widefield (WF) fundus images enhances the performance on WF fundus diagnosis for diabetic retinopathy (DR). We studied the effect of the pretraining dataset size on the transferred model.

Methods: We collected smaller (32k) and larger (120k) NF images datasets using VISUSCOUT® 100 (ZEISS, Jena, Germany) handheld fundus camera. The images were annotated for referable DR (more than mild DR). A DLS (Resnet-50) for each dataset was developed to detect referable DR from the images. For the transfer learning, we collected WF fundus images from 361 subjects (77% normal, 23% referable DR) using tabletop CLARUS™ 500 (ZEISS, Dublin, CA). The images were annotated for referable DR. We split the WF dataset into train/validation/test (80/10/10) sets and evaluated the final model on the test set. The two NF models were fine-tuned on the same training split of WF data and compared together and with directly evaluating WF images on NF models without fine-tuning. Augmentation techniques were used for robustness. We compared accuracy, sensitivity (Sen), specificity (Spc), and area under the curve of the receiver operating characteristics curve (AUC) for evaluation of the performance. Fig. 1 overviews the performed experiments

Results: The pretrained model on the larger NF dataset produced marginally better results on the WF dataset after transfer compared with the pretrained model on the smaller NF dataset on the considered metrics. We observed large confidence intervals for Sen and Spc because of the dataset size limitations. The best model achieved 86.5% AUC, 84.4% accuracy, 90% Sen (95%CI [71%, 100%]), and 83% Spc (95%CI [70%, 95%])

Conclusions: Increasing the NF pretraining dataset size potentially enhances the fine-tuning on the WF dataset. However, this enhancement is limited by the size of the WF dataset. This suggests that increasing the NF pretraining dataset size improves the prediction on WF dataset up to a certain limit where collecting more WF data is required for further improvements.

CONTROL ID: 3532343

SUBMITTER (NAME ONLY): Quint Medley

TITLE: In-vitro and In-vivo pharmacology of SAF312 as a TRPV1 inhibitor for ocular surface pain

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The transient receptor potential cation channel subfamily V member 1 (TRPV1) plays a key role in ocular surface pain. The use of SAF312, a potent non-competitive antagonist of TRPV1, is a novel steroid sparing approach for treatment of ocular surface pain. The study evaluated the in-vitro and in-vivo pharmacology of SAF312.

Methods: Expression of TRPV1 was evaluated in donor human cornea by immunostaining of TRPV1, along with β -tubulin, a marker for corneal neurons. The selective action of SAF312 on TRPV1-mediated Ca^{2+} -flux was assessed by the fluorescent FLIPR assay. The inhibitory action of SAF312 was evaluated in CHO cells expressing human TRPV1 using fluorescent Ca^{2+} -sensitive indicator dyes. The ocular tissue and plasma pharmacokinetic (PK) parameters (C_{max} , AUC, and T_{max}) of SAF312 were described in New Zealand white rabbits following a single dose of bilateral ocular administration (0.5, 1.0, 1.5, and 2.5%; 0.175, 0.350, 0.525, and 0.875 mg/eye/35 μ L, respectively).

Results: TRPV1 was expressed in superficial nerves, nerves in the mid-stroma, and deep stroma indicating a potential role for TRPV1 in nociception within the cornea (Fig 1). TRPV1 is also expressed at a high level in the corneal epithelium. SAF312 was >150-fold selective for TRPV1 when tested against a panel of 18 TRP channels. SAF312 inhibited capsaicin, low pH 2-(n-morpholino)ethanesulfonic acid (MES, pH 5.5), anandamide (AEA), and N-arachidonoyl dopamine (NADA) stimulated human TRPV1 with IC_{50} values of 12, 16, 7.3 and 36 nM, respectively in a selective, non-competitive, and reversible manner. PK analysis of SAF312 in the rabbit ocular tissues and plasma showed the highest exposure in cornea and conjunctiva, followed by aqueous humor, lens, retina, plasma and vitreous humor. The exposure for SAF312 in cornea 12 h after single bilateral 0.5% administration was at least 69-fold and 23-fold higher than the IC_{50} assessed in the cellular assays for capsaicin (12nM) and NADA (36nM), respectively.

Conclusions: SAF312 has been shown to be a selective and potent inhibitor of TRPV1, a key mediator of ocular pain process which is expressed in the corneal neurons, and has potential for further investigation in clinical trials.

CONTROL ID: 3532344

SUBMITTER (NAME ONLY): Tilman Schmoll

TITLE: Imaging the choriocapillaris with SS-OCT at MHz A-scan rates

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Resolving individual capillaries of the choriocapillaris with swept source optical coherence tomography (SS-OCT) angiography is challenging and has so far been limited to very small field of views (FOV). We present a MHz SS-OCT prototype, which provides high-contrast choriocapillaris (CC) images over FOV of up to 12mm x 12mm.

Methods: We developed a 1060nm SS-OCT prototype, capable of A-scan rates up to 1.7MHz. Its lateral resolution was 7.8µm and its axial resolution was 9 µm in tissue. We acquired Angio 12mm x 12mm scans with a sampling of 1024 (A-scans) x 1024 (B-scans) x 4 (B-scan repetitions) and Angio 2.2mm x 2.2mm scans with a sampling of 320x300x10. To create CC en face images, we segmented the RPE and integrated over 3 pixels, corresponding to a 20µm slab below the RPE fit. To compare our image quality to state of the art images, we acquired Angio 12 mm x 12 mm and Angio 3 mm x 3 mm scans of the same eye, using the 100 kHz mode of the Plex® Elite 9000 (ZEISS, Dublin, CA).

Results: In Fig. 1a&b Angio 12 mm x 12 mm scans of the CC acquired at 100 kHz (a) and 1.7 MHz (b) are presented side by side. Especially when comparing the magnified views in the blue boxes, one can appreciate significantly more contrast in the higher resolution 1.7MHz images. Fig. 1c-f show Angio scans over smaller FOV with higher sampling density. The Angio 3mm x 3mm scan with the commercial instrument is shown in c&d for the superficial and CC slab respectively. A corresponding Angio 3mm x 3mm image of the superficial slab is shown in Fig. 1f. Fig. 1e shows a 2.2mm x 2.2mm MHz Angio image of the CC at the location indicated by the yellow box in Fig. 1b. This illustrates that not only the sampling rate and lateral resolution, but also the sampling density strongly impact the ability to resolve individual capillaries of the CC.

Conclusions: We demonstrated that MHz A-scan rates paired with improved lateral resolution, can significantly improve the resolution of individual capillaries in the CC over a large FOV. We further show that increasing the lateral sampling and the number of B-scan repetitions can again significantly enhance the contrast of CC images.

CONTROL ID: 3532355

SUBMITTER (NAME ONLY): Maureen Farrell

TITLE: Genetic testing yield among patients with suspected primary heritable optic atrophy

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The clinical and genetic heterogeneity of suspected primary heritable optic atrophy (phOA) poses genetic diagnostic challenges. Patients with suspected phOA were retrospectively analyzed to determine genetic testing yield and clinical correlates.

Methods: Medical records of patients with genetic testing for suspected phOA were reviewed. Sex, age at vision symptom onset (VSO) and OA diagnosis (OAD), clinical diagnosis subgroup, presence of syndromic features, and positive family history were analyzed. Clinical diagnosis subgroups included 1) Dominant Optic Atrophy (DOA) (OPA1 or OPA3), 2) Leber Hereditary Optic Neuropathy (LHON), 3) unspecified isolated OA, and 4) syndromic OA. Probands underwent Sanger Sequencing, Next Generation Sequencing, and/or whole exome sequencing. Molecular confirmation indicated presence of pathogenic variants

Results: Fifty unique probands with suspected phOA were identified (32 male, 18 female). Mean ages were 22±20 years (standard deviation) for VSO and 26±21 years for OAD. Testing confirmed molecular causes in 30% of cases (15/50), including 11/32 males and 4/18 females (not significant; Fisher's exact test). Molecular testing result stratified by clinical diagnosis subgroup confirmed disease-causing genotypes in 6/23 with suspected DOA, 4/6 with suspected LHON, 2/8 with unspecified isolated OA, and 3/13 with suspected syndromic OA. Age at VSO and OAD between molecularly confirmed vs. unconfirmed cases were not statistically different. Isolated OA was reported in 42 probands (84%) and suspected syndromic OA in 8 probands (16%); genetic testing yield was not different between these groups (31% vs. 25% respectively; Fisher's test). Genetic testing yield was 60% for probands with positive family history (9/15) and 19% for singletons (6/32) (p=0.0077; Fisher's test).

Conclusions: Consistent with prior studies, family history was positively associated with testing yield, but was not significantly affected by sex, clinical diagnosis subgroup, or presence of syndromic features. A large prospective phOA cohort is needed to identify and refine clinical associations and drive gene discovery required to improve genetic diagnostic yield among unconfirmed patients.

CONTROL ID: 3532392

SUBMITTER (NAME ONLY): Michael Schneider

TITLE: Visual performance declines in 24 mo C57BL/6J mice are unrelated to outer retina oxidative stress in vivo

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schneider, B.A. Berkowitz, R. Roberts, B. Schilling, A. Orchanian, E. Graffice, K. Sinan, A. Berri, L. Harp, Department of Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|R.H. Podolsky, K.L. Childers, Beaumont Research Institute, Beaumont Health, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related declines in visual performance increase the risk of morbidity and mortality from falls in humans and are so far untreatable; rats and mice also show reduced vision with age. The cause of age-related declines in visual performance is unclear but evidence ex vivo suggests a link to photoreceptor / retinal pigment epithelium oxidative stress.

Methods: 2 and 24 mo male C57BL/6J mice were non-invasively evaluated for excessive production of paramagnetic free radicals based on whether R1 (= 1/T1) in retinal laminae are reduced after acute anti-oxidant (AO) administration [QUEnch-assiSTed (QUEST) magnetic resonance imaging (MRI)]. Superoxide production was measured in excised retina (lucigenin assay). Acute AO administration was also used to test for age-related oxidative stress-induced thinning of subretinal space (QUEST optical coherence tomography [OCT]) and cone-based visual performance declines (QUEST optokinetic tracking [OKT]).

Results: At 2 mo, no evidence was found in vivo for oxidative stress in any retinal layer. At 24 mo, oxidative stress was localized only to superior outer retina. Yet, no age-related change in retinal superoxide production was noted suggesting that free radical species other than superoxide contributed to the positive QUEST MRI signal at 24 mo. Subretinal space did not show age-related thinning and was unresponsive to AO's. Finally, visual performance declined with age and was not restored by AO's that were effective in QUEST MRI.

Conclusions: Outer retinal oxidative stress appears to be insufficient to explain the reduction in visual performance in 24 mo C57BL/6J mice.

CONTROL ID: 3532421

SUBMITTER (NAME ONLY): Girish Valluru

TITLE: Anthropometric measures and their relationship to a keratoconus-like trait in the US population, NHANES 1999-2008

SESSION TITLE: Keratoconus and Corneal Biomechanics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To determine the relationship between anthropometric measures and a keratoconus (KCN)-like trait of high spherical dioptric power (≥ 48.0 D).

Methods: Participants of the 1999-2008 NHANES visual exam with demographic, ocular, and anthropometric data were included (Unweighted 20,165; Weighted 173,695,441). Cases had a KCN trait of spherical dioptric power ≥ 48.0 D ($n = 171$) and controls < 48.0 D ($n = 19,994$). Multivariable analyses were performed for pooled and sex-stratified populations accounting for NHANES complex survey design. 3 separate models assessed an outcome of KCN trait with primary predictors of (1) BMI, (2) height, and (3) weight. The independent effects of height were assessed by adjusting for weight residuals in multivariable analysis and similarly for weight adjusted for height residuals.

Results: There was a strong inverse relationship between height and KCN trait in the pooled population ($P < 0.0001$ for trend) and women ($P < 0.0001$ for trend). In pooled analysis, the inverse relationship between height and KCN trait found that for every 1-inch increase in height, there was a 16% reduced odds (OR, 0.84; 95% CI: 0.78-0.91) of KCN trait. In women there was a 19% reduced odds of KCN trait for each 1-inch increase in height (OR, 0.81; 95% CI: 0.74-0.88), but the inverse association was borderline in men (OR, 0.88; 95% CI: 0.76-1.01).

Conclusions: Shorter height is associated with a higher risk of KCN trait of high spherical dioptric power (≥ 48.0 D). Gender plays a role in this relationship with a greater association seen in women than in men. These findings can contribute to improved understanding of the pathogenesis of keratoconus.

CONTROL ID: 3532429

SUBMITTER (NAME ONLY): Julie Wallin

TITLE: Remodeling of inhibitory synapses at retinal bipolar cell terminals after loss of afferent input.

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Bipolar cells in the retina receive photoreceptor information and are responsible for transferring this information to amacrine cells and ganglion cells in the inner retina. The axon terminals of bipolar cells make specialized ribbon synapses with amacrine and ganglion cell processes. Output at these ribbon sites is regulated by distinct subsets of inhibitory synapses. In this study our purpose was to determine the impact of photoreceptor loss on the organization of inhibitory synapses at retinal bipolar cell terminals.

Methods: To understand how retinal bipolar cells alter their inhibitory synaptic connections in response to loss of their primary input partners, we utilized the rd1 photoreceptor degeneration mouse line (mice homozygous for the rd1 mutation) and performed immunolabeling for distinct GABA receptor types. To visualize individual ON bipolar cells, we crossed the rd1 line to the Grm6-tdtomato line, where the mGluR6 promoter drives tdtomato expression in ON bipolar cells. We quantified receptor levels at the one-month and two-month time-point. Images were acquired on a Leica SP8 confocal microscope and stacks were analyzed with Image J (Fiji/NIH) and Amira (Thermo Fisher Scientific). Receptor amounts were determined within individual bipolar cell terminals and protein expression was correlated to mRNA levels by qPCR. We performed single-cell electrophysiology to determine the bipolar cell receptor type-specific responses to GABA puff applications. Markers for OFF bipolar cell types were used to compare synaptic protein levels in the ON vs OFF laminae of the degenerating retina.

Results: We observed bipolar cell type-specific changes in inhibitory synaptic proteins across terminals of the rd1 retina. We also observed compartment-specific alterations in bipolar cell axon terminals as compared to their dendrites in the outer retina. Protein levels of GABA receptor types showed differences across the receptor subsets and across the time points studied.

Conclusions: During retinal degeneration, bipolar cells undergo significant changes in their inhibitory synaptic connectivity and receptor organization. These changes are receptor-type specific, bipolar cell type-specific and compartment-specific.

CONTROL ID: 3532435

SUBMITTER (NAME ONLY): Tae Jin Lee

TITLE: The abundance of Serine Protease Inhibitors in Human Aqueous Humor and Race and Gender-Specific Alterations in Glaucoma Patients

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Serine protease inhibitors (SERPINs) are a family of protease inhibitors known to be involved in the pathogenesis of several ocular diseases. In this study, we analyzed the levels of serpin proteins in human aqueous humor (AH) and their association with glaucoma in Caucasian and African American patients.

Methods: Human AH samples from 148 subjects were analyzed using Liquid Chromatography-Mass Spectrometry (LC-MS/MS). There are 36 known members in the SERPIN superfamily. The abundance of each SERPIN was detected, and differential expression analysis was performed in patients with and without glaucoma, and the data stratified by gender and race.

Results: A total of 13 SERPIN proteins, including SERPINA1, SERPINA3, SERPINA4, SERPINA5, SERPINA6, SERPINA7, SERPINA8, SERPINC1, SERPIND1, SERPINF1, SERPINF2, SERPING1, SERPINI1 were reliably detected in human AH. Six SERPIN proteins, including SERPINA4, SERPINA5, SERPINA6, SERPINA8, SERPINC1, and SERPIND1, were found to be differentially expressed in glaucoma patients. Additionally, SERPINA1, SERPINA3, and SERPINA7 were differentially expressed in glaucoma only in male subjects, whereas SERPINA5 was differentially expressed in glaucoma only in female subjects. Similarly, dividing the data based on race revealed three proteins, including SERPINA1, SERPINA8, and SERPING1, were differentially expressed in Caucasian glaucoma patients. In contrast, four proteins, including SERPINA4, SERPINA5, SERPINA6, and SERPIND1, were significantly altered in African American glaucoma patients. SERPINC1 was differentially expressed in both Caucasian and African American glaucoma patients.

Conclusions: A total of 13 out of 36 SERPINs were found in the human AH. Several of these proteins were found to be altered in glaucoma patients in addition to displaying race and gender specific variations.

CONTROL ID: 3532437

SUBMITTER (NAME ONLY): David Ngan

TITLE: Ocular Signs and Symptoms of Post-Concussion Syndrome

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Ngan, E. Peterson, G. Tan, Loma Linda University School of Medicine, Loma Linda, California, UNITED STATES|J. Pyun, E. Hawy, Department of Ophthalmology, Loma Linda University Medical Center, Loma Linda, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision deficits and oculomotor dysfunction have been previously reported in association with concussions or mild traumatic brain injuries. We aim to identify the visual manifestations of post-concussion syndrome using a retrospective, observational clinical study.

Methods: A retrospective chart review study was performed. All patients referred to a neuro-ophthalmology clinic over two years with a post-concussion syndrome diagnosis were included. Patients with abnormal CT or MRI neuroimaging suggestive of moderate or severe traumatic brain injury were excluded. All ocular signs and symptoms, visual field, and OCT imaging of the RNFL and GCL were evaluated. The Circle test assessed stereoacuity. Analysis of the data was performed to determine the prevalence of the studied elements.

Results: Fifty-two patients were eligible for the study. The mean age was 49.65 ± 14.08 years and were predominantly female (69.2%), not Hispanic or Latino (75.6%), and White or Caucasian (79.5%). 50.0% of the patients had multiple office visits. The most common modes of injury were motor vehicle accidents and falls, and 50.0% had multiple concussions, including 13.6% having three or more. 76.3% of the subjects had pre-existing migraines, and 26.9% were taking prescribed opioid medications. Headaches (92.3%) and light sensitivity (91.3%) were the most significant symptoms, and 36.5% of the total subjects had convergence insufficiency or reading difficulties. Severe or moderate loss of stereopsis was found in 72.2% of patients, who tended to be older than those with mild or no stereopsis loss (52.69 ± 13.87 years vs. 40.00 ± 13.15 years; $p = 0.0148$). Visual field testing was unreliable in 42.6% of subjects, while OCT imaging of the RNFL and GCL was normal (95.9% and 88.2%, respectively). The average RNFL thickness was found to be 97.37 ± 10.78 μm .

Conclusions: Headaches and light sensitivity are the most prevalent symptoms in post-concussion syndrome, while the loss of stereopsis and convergence insufficiency are the most common ocular signs.

CONTROL ID: 3532440

SUBMITTER (NAME ONLY): Cherie Nau

TITLE: Corneal Swelling after One Hour of Small and Large Diameter Scleral Lens Wear

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.B. Nau, M. Schornack, Ophthalmology, Mayo Foundation for Medical Education and Research, Rochester, Minnesota, UNITED STATES|E. Shorter, University of Illinois Hospital and Health Sciences System, Chicago, Illinois, UNITED STATES|J.S. Fogt, The Ohio State University, Columbus, Ohio, UNITED STATES|A.C. Nau, Korb and Associates, Boston, Massachusetts, UNITED STATES|J.S. Harthan, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure corneal thickness after short-term small and large diameter scleral lens wear.

Methods: Twenty healthy participants were fit on their right eye according to manufacturers' fitting guides with a 15.2mm OneFit 2.0 lens (Blanchard Contact Lens Inc., Manchester, NH) and a 18.0mm BostonSight lens (BostonSight, Needham, MA). Lenses were each worn on the same day for one hour with the order of wear randomized. Central corneal thickness was measured using Pentacam rotating Scheimpflug photography system (Oculus Inc, Wetzlar, Germany) both prior to lens wear and immediately after lens removal. Differences in central corneal thickness are compared before and after lens wear using a paired t-test.

Results: The average age of participants was 29 ± 9 (SD) years old (Range: 22-57 years), with 5 males and 15 females. Corneal thickness after one hour of small diameter lens wear ($554 \pm 30 \mu\text{m}$, $n=10$) compared to before lens wear ($548 \pm 28 \mu\text{m}$, $n=10$), was statistically increased ($P=0.02$, 1.2%). Corneal thickness after one hour of large diameter lens wear ($544 \pm 34 \mu\text{m}$, $n=10$) compared to before lens wear ($531 \pm 30 \mu\text{m}$, $n=30$) was also increased and had statistical significance ($P=0.02$, 2.4%). Small lens wearers then wore the large lens for one hour and had a further, but not statistically significant increase in corneal thickness ($547 \pm 37 \mu\text{m}$, $P=0.5$, 1.4%). Similarly, large lens wearers had a non-statistically significant increase in corneal thickness after an hour of small lens wear ($545 \pm 31 \mu\text{m}$, $P=0.3$, 1.0%).

Conclusions: After one hour of lens wear, both small and large diameter lens wearers experience an increase in central corneal thickness. An additional hour of lens wear in a different lens design also increased central corneal thickness, but not as much as the first hour. Differences in lens diameter and design may influence cornea physiology differently.

CONTROL ID: 3532445

SUBMITTER (NAME ONLY): Jeremy Benson

TITLE: Random Forests with Retinal Biomarkers for Diabetic Peripheral Neuropathy

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Benson, X. Guo, S.C. Nemeth, P. Soliz, VisionQuest Biomedical, Albuquerque, New Mexico, UNITED STATES|J. Benson, T. Estrada, Computer Science, University of New Mexico, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: This work uncovers relevant biomarkers in digital fundus photographs for classifying Diabetic Peripheral Neuropathy (DPN).

Methods: Our dataset consists of 104 digital fundus photographs from 52 patients that have been graded with the Singapore "I" Vessel Assessment (SIVA) software. Using 75 features obtained with SIVA, we train and test a series of random forest classifiers. We perform 10-fold cross validation and 80/20 split of the data. Monofilament, vibration, nerve conduction study (NCS), and pinprick are alternately used for the reference standard. We report on the classification accuracy of the random forests for each as they serve as ground truth. The top 5 relevant retinal features per reference standard are presented.

Results: For our random forest classification, the average errors across the 10-fold runs were 3.33%, 23.33%, 35.24%, and 29.52%, for monofilament, vibration, NCS, and pinprick, respectively. We provide a sample decision tree using the monofilament-based random forest as an example of the classification subprocess. In this tree, we choose between normal or DPN through a series of Gini index splits on the SIVA retinal features. Our forest is comprised of a thousand trees, where a random subset of all SIVA features is employed. The resulting classifier is the aggregation of these trees (i.e., a forest). We highlight the top SIVA biomarkers across the various reference standards that are present in the forests.

Conclusions: We establish a baseline comparison between digital fundus biomarkers, obtained from the SIVA software process, and various clinical tests for DPN. The Quantitative Sensory Tests (QSTs) of monofilament and vibration show the closest relation in terms of raw classification of DPN, and perform the best when using the features from SIVA in our random forest experimentation. While the performance of the various reference standards ranges in accuracy, there remains a consistent subset of SIVA features that appear throughout the models and lead to the model decision of DPNs versus controls. The insight gained from this work will serve as the foundation for future automated approaches in feature extraction for risk assessment of DPN using retinal images, as there are specific biomarkers that are clearly relevant, regardless of the ground truth.

CONTROL ID: 3532509

SUBMITTER (NAME ONLY): Francis Price

TITLE: Evaluating Vision-related Reading Ability With a de Novo PRO Instrument in a Phase 3 Study of AGN-190584 (Pilocarpine 1.25%) for Presbyopia

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Price, Price Vision Group, Indianapolis, Indiana, UNITED STATES|M. Moshirfar, Hoopes Vision, Utah, UNITED STATES|J. Stokes, X. Niu, E. Shirneshan, Allergan, an AbbVie company, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: An optimized formulation of pilocarpine (AGN-190584) was developed as a pharmacologic treatment for presbyopia. In a phase 3 efficacy and safety study, a new Patient Reported Outcome (PRO) instrument, the Near Vision Presbyopia Task-based Questionnaire (NVPTQ), was used to evaluate vision-related reading performance and associated satisfaction.

Methods: In this multicenter, double-masked, 30-day study (NCT03804268; n=323), individuals with presbyopia were randomized to bilateral AGN-190584 or vehicle (placebo) once daily. Secondary efficacy endpoints included mean change from baseline in mesopic NVPTQ Performance (range: 0-5) and Satisfaction (range: 0-4) domain scores on 4 paper-based reading tasks at Day 30 Hour 3. Cumulative distribution of change scores was depicted (intent-to-treat population). Proportion of responders to AGN-190584 (participants achieving individual-level meaningful change thresholds of ≥ 0.75 and ≥ 1.00 point improvement from baseline in Performance and Satisfaction scores, respectively) at Day 30 Hour 3 (3 hours after dosing) was assessed.

Results: At Day 30 Hour 3, statistically significant improvements from baseline in both scores were reported with AGN-190584 versus vehicle: the mean score difference (95% confidence interval [CI]) between groups was 0.8 (0.6, 1.1) in vision-related reading performance and 0.8 (0.5, 1.1) in associated satisfaction ($P=.011$ for each). The AGN-190584 group showed consistent separation in improvement compared with the group receiving vehicle. Of the AGN-190584 group, 24.0% (95% CI: 13.0, 34.9) and 26.8% (95% CI: 16.2, 37.5) more individuals reported improvements at individual-level meaningful change thresholds in mesopic Performance and Satisfaction scores, respectively ($P<.001$ for each), versus vehicle.

Conclusions: Analyses of these PRO efficacy endpoints demonstrated significant treatment benefit in patient-centric outcomes in presbyopia. Participants who received AGN-190584 reported greater ability and satisfaction related to near-vision reading compared with participants receiving vehicle supporting the role of a pharmacologic treatment for this condition.

CONTROL ID: 3532519

SUBMITTER (NAME ONLY): Eric Desjarlais

TITLE: Pentosan Polysulfate Sodium Maculopathy: A Big Data Study of Patients with Interstitial Cystitis

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.B. Desjarlais, J.E. Kim, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Eric Desjarlais: Commercial Relationship: Code N (No Commercial Relationship) | Judy Kim: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Recent studies describe a novel association between pentosan polysulfate sodium (PPS), an oral glycosaminoglycan used for symptomatic control of interstitial cystitis (IC), and pigmentary maculopathy. We used multivariate logistic regression analysis to investigate this relationship in a multicenter cohort of patients with IC.

Methods: The TriNetX Research Network was queried for patients from 30 healthcare organizations who had a diagnosis of IC. The primary outcome measure was any one of six retinopathy diagnoses that may have been used clinically to document PPS-related maculopathy. These included non-exudative age-related macular degeneration (AMD), exudative AMD, drusen, hereditary retinal dystrophy, toxic maculopathy, and unspecified macular degeneration. Logistic regression models comparing groups with and without PPS exposure were fitted, adjusting for covariates including demographics, systemic comorbidities, and exposure to hydroxychloroquine (HCQ), another drug that can cause maculopathy.

Results: There were 18,154 patients in the study, including 1,437 men and 16,717 women with IC. Average age was 54.2 (17.1 SD) years. A total of 4,147 (22.8%) patients had at least one order for PPS. Average duration of PPS therapy was 1.37 (2.37 SD, range 0.00 to 14.33) years. In multivariate logistic regression analysis, there was a statistically significant increase in the odds of retinopathy diagnosis associated with PPS duration (OR = 1.11 per year, 95% CI 1.05 to 1.17, $p = 0.0001$), HCQ duration (OR = 1.20, 95% CI 1.11 to 1.29, $p < 0.0001$), age (OR = 1.08, 95% CI 1.07 to 1.09, $p < 0.0001$), history of smoking (OR = 1.46, 95% CI 1.16 to 1.84, $p = 0.0011$), essential hypertension (OR = 1.75, 95% CI 1.37 to 2.25, $p < 0.0001$), diabetes mellitus (OR = 1.31, 95% CI 1.03 to 1.65, $p = 0.0244$), and significant kidney disease (OR = 1.41, 95% CI 1.11 to 1.77, $p = 0.0040$). Repeat regression with PPS duration as a categorical variable in two-year increments revealed a significant association starting at 5 to 6 years of PPS therapy (OR = 2.23, 95% CI 1.14 to 3.96, $p = 0.0109$).

Conclusions: After adjusting for covariates known to increase the risk of retinopathy, there was a statistically significant increase in the odds of retinopathy diagnoses corresponding with duration of PPS therapy. These findings strengthen the body of evidence suggesting an ocular toxicity related to duration of PPS usage.

CONTROL ID: 3532528

SUBMITTER (NAME ONLY): Theodore Leng

TITLE: AAO IRIS Registry data replicates VIEW 1 and VIEW 2 clinical trial outcome data

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The VIEW 1 and VIEW 2 studies led to FDA approval of aflibercept for the treatment of neovascular age-related macular degeneration (nAMD) in 2011. In this electronic health record (EHR) based registry study, we replicated the study design from an observational research perspective and evaluated the outcomes using real-world data (RWD) contained in the American Academy of Ophthalmology IRIS[®] Registry (Intelligent Research in Sight), the world's largest single-specialty clinical database.

Methods: The IRIS Registry was queried for eyes older than 50 years with nAMD that were treatment-naïve on the index date. Using structured data (ICD coded, CPT codes, etc.) we excluded a prior diagnosis of nAMD, DME, DR, uncontrolled glaucoma, causes for CNV besides nAMD, prior RD, prior uveitis, prior vitrectomy surgery, prior corneal transplantation and those with missing gender/race information. Cohorts emulated the study arms of the VIEW 1 and VIEW 2 trials: cohort 1 received 2 mg of aflibercept every 4 weeks (2q4), cohort 2 received 2 mg of aflibercept every 8 weeks after 3 monthly injections (2q8) and cohort 3 received 0.5 mg ranibizumab every 4 weeks (rq4). We allowed a buffer of +/- 7 days for treatment schedules. By definition, the number of injections in each cohort was 12 (2q4), 7 (2q8) and 12 (rq4).

Results: The cohorts corresponding to the three arms of the VIEW 1 and VIEW 2 studies included 348 (2q4), 331 (2q8), and 460 (rq4) eyes. We found that 92.5% (2q4), 95.2% (2q8) and 92.6% (rq4) of eyes maintained vision (losing < 15 ETDRS letters), compared to 95.1 to 95.6 (2q4), 95.1 to 95.6% (2q8), and 94.4% (rq4) of eyes in the VIEW studies. We also found that 19.8% (2q4), 28.1% (2q8) and 25% (rq4) of eyes gained 15 or more ETDRS letters and had a mean gain of +3.9 (2q4), +6.9 (2q8) and +5.8 (rq4) ETDRS letters at 12 months. In the VIEW studies, mean BCVA gains were 8.3 to 9.3 letters at 12 months.

Conclusions: This is the first time that RWD has been used in an attempt to replicate the primary outcomes of a clinical trial in ophthalmology. The proportion of eyes losing <15 across the VIEW 1 and VIEW 2 studies was similar to our registry cohort, indicating proof-of-concept, although the mean gains in letters varied across the studies. Benchmarking real-world endpoints versus randomized controlled trials could be a valuable tool in validating the predictive ability of these endpoints as a measure of effectiveness.

CONTROL ID: 3532585

SUBMITTER (NAME ONLY): Arsany Yassa

TITLE: Epidemiologic Analysis of Mucinous Adenocarcinoma of the Eyelid: A Population-Based Analysis, 2000-2017

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Yassa, M.T. Mikhael, M. Tadrosse, A. Tadrosse, S.T. Mikhael, J. Eloy, Department of Ophthalmology & Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|M. Tadrosse, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|S.T. Mikhael, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|J. Eloy, Department of Otolaryngology – Head and Neck Surgery, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: There are limited studies on mucinous adenocarcinoma of the eyelid (MAE) in the literature. Using a large database, we explore the epidemiologic trends of this entity.

Methods: A retrospective, population-based analysis was conducted using the Surveillance, Epidemiology, and End Results Registry. All patients diagnosed with MAE from 2000-2017 were included. Incidence rate (IR) was calculated in number of cases/million/year. Overall survival (OS) was calculated using the Kaplan-Meier method.

Results: 222 cases were identified, 58.1% of whom were female and 73.8% were white. Overall IR of MAE was 0.14. Annual percent change was 7.34 ($p < 0.001$). There was no difference in IR between males (0.13) and females (0.14) [$p = 0.34$]. IR in the black race (0.247) was significantly higher than in the white (0.12) [$p < 0.001$] and in the Asian/Pacific Islander (0.10) [$p < 0.001$] races. IR in patients older than 65 years old (y/o) [0.74] was significantly higher than in those 22-64 y/o (0.083) [$p < 0.001$] or in those younger than 21 y/o (0.002) [$p < 0.001$]. Stratification based on stage showed that 78.1 % of cases were localized, 4.5 % were regional and 17.4 % were distant. Only 1 bilateral case was identified and the rest of the cases were unilateral.

Conclusions: Mucinous adenocarcinoma of the eyelid incidence is highest in the elderly and black populations and is not affected by sex. Incidence is increasing over the timeframe studied. Most of the cases are diagnosed at a localized stage.

CONTROL ID: 3532587

SUBMITTER (NAME ONLY): Niles Raval

TITLE: An Evaluation of Commercially Available Ophthalmic Surgery Simulators for Continuous Curvilinear Capsulorrhexis Training

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Raval, A. Shrivastava, Ophthalmology, Montefiore Medical Center, Bronx, New York, UNITED STATES|V. Hawn, M. Kim, X. Xie, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: We aim to provide objective and subjective assessments of three commercially available continuous curvilinear capsulorrhexis (CCC) simulators formally evaluated by cataract surgeons on a variety of task-specific metrics.

Methods: The study was carried out under standard operating room conditions using video-enabled Zeiss Lumera™ microscopes. Expert (>1000 cases) cataract surgeons (N=7) were tasked to perform a 5.5-mm CCC on three simulators (Bioniko™, Kitaro™, and SimulEYE™) in randomized order for a total of three trials on each model. Surgeons were asked to subjectively rate on a modified Likert scale (1-7) how well each simulator approximated human tissue. The duration, size, and number of capsular forceps manipulations ("grabs") were examined and analyzed with multiple regression analyses.

Results: There were statistically significant differences among the simulators and across the three trials for all outcome measures. With respect to grabs, Bioniko required a greater number (6.53 ± 3.14) than both Kitaro (4.90 ± 2.47 , $p=0.01$) and SimulEYE (3.90 ± 1.34 , $p<0.0001$). Trial 1 (6.19 ± 3.57) had a greater number of grabs than both trials 2 (4.33 ± 2.01 , $p=0.002$) and 3 (4.81 ± 1.63 , $p=0.02$). With respect to CCC size (maximum diameter in mm), Kitaro (8.00 ± 0.84) had the largest average compared to Bioniko (5.24 ± 0.60 , $p<0.0001$) and SimulEYE (5.11 ± 0.41 , $p<0.0001$). CCC size was overall larger in trial 3 (6.29 ± 1.56) than in trial 1 (5.94 ± 1.39 , $p=0.003$). Surgeons spent more time (seconds) performing the CCC on Bioniko (41.95 ± 26.70) than on Kitaro (32.05 ± 14.99 , $p=0.02$) and SimulEYE (28.90 ± 15.18 , $p=0.002$) and more time on trial 1 (42.24 ± 25.23) than on trials 2 (28.48 ± 15.87 , $p=0.001$) and 3 (32.19 ± 16.44 , $p=0.01$). Kitaro (4.56 ± 0.84 , $p<0.0001$) and SimulEYE (4.19 ± 0.92 , $p<0.0001$) were rated as more realistic than Bioniko (1.38 ± 0.80) on a Likert scale (1-7).

Conclusions: Each simulator confers its own unique advantages. SimulEYE and Kitaro were thought to most closely approximate real capsular tissue, and surgeons performed the CCC faster on these kits than on the Bioniko model. Surgeons created a 5.5-mm CCC most accurately on the Bioniko and SimulEYE models. In general, surgeons performed faster CCCs across the three trials, suggesting a learning curve. Larger validation studies will help residency programs best utilize training tools for novice surgeons.

CONTROL ID: 3532592

SUBMITTER (NAME ONLY): anqi LYU

TITLE: Which factors affect the reading of Chinese characters in normal peripheral vision?

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. LYU, H. Kwong, A.M. Cheong, School of Optometry, The Hong Kong Polytechnic University, HONG KONG|A.E. Silva, B. Thompson, Optometry & Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|L.A. Abel, School of Medicine, Deakin University, Burwood, Victoria, AUSTRALIA|S. Cheung, Department of Psychology, University of Hong Kong, HONG KONG|B. Thompson, A.M. Cheong, Centre for Eye and Vision Research Limited, HONG KONG|

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ABSTRACT BODY:

Purpose: Patients with central vision loss have to use their peripheral vision to read. For English text, visual span in both the temporal and spatial domains limits reading speed in peripheral vision. It is unknown whether the same is true for Chinese reading. Individual Chinese characters contain more information than individual English letters and can be sequenced horizontally or vertically. This study examined the relationship between visual span and reading of Chinese characters in normal central and peripheral vision.

Methods: 13 young Chinese native readers were recruited. Reading performance in terms of maximum reading speed (MRS) and critical print size (CPS) was examined using the rapid serial visual presentation paradigm at three visual field locations: central vision, 10° left and 10° below fixation. Temporal visual span was measured using trigram character-recognition as described by Cheong et al. (2007), with strings of three-randomly selected Chinese characters presented at a range of exposure durations. Spatial visual span was measured by presenting trigrams at different character position away from the fixation for 200ms. Visual span measurements were made for all three central (horizontal and vertical presentations), 10° left (vertical) and 10° lower (horizontal) visual field locations.

Results: MRS was significantly faster and CPS smaller at central vision than left and inferior vision ($p < 0.001$). No significant differences for MRS or CPS were observed between the two peripheral visual field locations. Temporal visual span in terms of temporal threshold (TTT) was significantly shorter in central vision than inferior or left visual field. Spatial visual span in terms of average recognition accuracy (ARC) at central 5-character positions was significantly higher for central vision than inferior or left visual field. No differences in visual span were found between inferior and left visual field. MRS was significantly correlated horizontal TTT and horizontal ARC for central and inferior vision ($r_s > -0.60$) but not for the left visual field.

Conclusions: Our results support the hypothesis that visual span contributes to reading performance for Chinese characters in central vision and in the inferior field. Surprisingly, this hypothesis does not apply when they read at 10° left visual field, suggesting that other factors might better explain the reduced reading performance at left visual field.

CONTROL ID: 3532601

SUBMITTER (NAME ONLY): Brian Peng

TITLE: Is myopia prevalence related to outdoor green space? A pilot study

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.A. Peng, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|M. Jong, T.J. Naduvilath, BHVI, Sydney, New South Wales, AUSTRALIA|M. Jong, University of Canberra, Canberra, Australian Capital Territory, AUSTRALIA|I. Flitcroft, University College Dublin, Dublin, IRELAND|I. Flitcroft, Technological University Dublin, Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: There is now substantial evidence to indicate that environmental factors including time outdoors can influence the development of myopia, particularly in school-aged children. It is well known that urban and rural differences in myopia prevalence exist, but few studies have attempted to characterise the built or natural environment using objective means. The aim of this study is to investigate the relationship between the prevalence of myopia and the quantity of green spaces across different regions of the world, using an objective satellite imaging technique.

Methods: The prevalence of myopia in the 15 to 19 year age group in Australia, Brazil, China, Finland, India, Iran, Japan, Oman, Singapore, South Africa, and the United Kingdom were collected from study data obtained from a systematic review and meta-analysis by Holden et al. (2016). Normalised Difference Vegetation Index (NDVI), an indicator of vegetation density, was derived from Landsat 7 Enhanced Thematic Mapper Plus (ETM+) satellite data. Green space (mean NDVI) was quantified using a 30-kilometre radius buffer surrounding point coordinates corresponding to locations mentioned in the Holden et al. prevalence studies (n = 12) that contributed most to prevalence data. Simple linear regression was used to analyse yearly data, whilst a generalised linear model (GLM) was fit to analyse aggregated NDVI and prevalence data. A mixed effects model was applied to assess the significance of green space when study was a random effect.

Results: The results indicated a negative cubic relationship between surrounding green spaces and myopia prevalence, although the association was weak. The results of the mixed effects model suggested that green space was not significant when the study effects were considered as a random factor (p = .099).

Conclusions: There was no statistically significant association between green space and myopia prevalence in the 15-19-year-old group. Use of a larger sample and standardisation of green space data may improve the robustness of the data. Additionally, use of buffer zones with smaller radii should be considered as they may be more applicable to real life daily green space exposure and potentially reveal a different relationship.

CONTROL ID: 3532603

SUBMITTER (NAME ONLY): Amanda Carpenter

TITLE: Comparison of automated and manual operation of an ophthalmic device

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Carpenter, A. Bender, K.G. Foote, A. Millan, K. Arianta, N. Manivannan, L. Rothmann, J. Straub, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acquiring high quality ophthalmic images typically requires a trained operator in close proximity to a patient. Motorized alignment can enable remote operation, e.g. for physical distancing during a pandemic, and automated alignment can enable quality imaging when a trained operator is not readily available, e.g. in low-resource environments. We evaluated and compared manual and automated operation of an ophthalmic device on a motorized stage.

Methods: We acquired data on 5 normal subjects (10 eyes) by both manual (via a trained operator) and automated operation using a prototype with three off-axis iris cameras (one below and on each side of the device) and a 3-axis motorized stage (Fig. 1). The motorized stage allowed all data to be acquired with a plexiglass shield between the subject and operator for remote operation during the COVID-19 pandemic. Auto-alignment was achieved using custom software to align the device to the patient pupil, with real-time pupil detection via a deep-learning algorithm. Auto-capture was triggered once the pupil was detected at the target location. We evaluated alignment success rate (alignments that triggered a capture), mean \pm SD time to align, and accuracy of alignment (mean \pm SD distance between detected pupil center and target).

Results: Of 24 auto-alignments (1-3 per eye), 23 successfully triggered a capture; 1 failed due to a software bug. All 14 manual alignments (1-3 per eye) proceeded to capture. Time to align for auto-alignment (29 ± 15 s) was significantly faster than for manual alignment (72 ± 37 s). The accuracy of alignment was 0.94 ± 0.59 mm for auto and 0.97 ± 0.41 mm for manual operation. A two-sample t-test assuming independent alignments for auto and manual results did not demonstrate a statistically significant difference in accuracy ($p > 0.05$).

Conclusions: This comparison of manual and auto-alignment and capture for a motorized device indicated that this auto-alignment method is 2.5x faster than motorized manual alignment, saving an average of 40 s per alignment. Auto-operation was comparable in accuracy, and reliable on normal eyes. While further investigations are needed for a clinical population, this method shows promise for utility in a clinical setting.

CONTROL ID: 3532606

SUBMITTER (NAME ONLY): Isabelle Audo

TITLE: Qualitative exploration of patient and caregiver experiences of visual function impairments and impacts on vision-dependent activities of daily living and health-related quality of life associated with Retinitis Pigmentosa and Leber Congenital Amaurosis in Germany and France

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Audo, Sorbonne Université, INSERM, CNRS, Institut de la Vision, CHNO des Quinze-Vingts, DHU Sight Restore, INSERM-DGOS CIC1423, Paris, FRANCE|N. Williamson, H. Bradley, M. Barclay, J. Sims, R. Arbuckle, Adelphi Mill, Bollington, Cheshire, SK10 5JB, UNITED KINGDOM|F. Patalano, C. Spera, C. Naujoks, J. Banhazi, Novartis Pharma AG, Basel, SWITZERLAND|N. Afroz, Novartis NBS, Hyderabad, INDIA|M. Fischer, Nuffield Laboratory of Ophthalmology, NDCN, University of Oxford, Oxford, UNITED KINGDOM|M. Fischer, Oxford Eye Hospital, Oxford University NHS Foundation Trust, Oxford, UNITED KINGDOM|T. Durham, Foundation Fighting Blindness, Columbia, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) and Leber Congenital Amaurosis (LCA) are rare inherited retinal degenerative disorders (IRD). Visual impairments associated with these disorders have significant impacts on patients' vision-dependent activities of daily living (ADL) and broader health-related quality of life (HRQoL). There is a paucity of evidence exploring the patient experience of RP/LCA and how these impairments impact on patients' lives across different genotypes in Europe. This study aimed to explore the experience of RP/LCA from patient and caregiver perspectives, across different genotypes and ages in Germany and France.

Methods: Thirty semi-structured qualitative concept elicitation interviews were conducted with 9 adults, 5 adolescents, 5 children, and 11 caregivers of children aged 3-11 years in Germany and France. All patients had a clinical and genetic diagnosis of RP/LCA. The sample included different gene mutations linked to RP/LCA: RPE65 (n=11), RPGR (n=5), CEP290 (n=3), AIPL1 (n=2), LRAT, PDE6B, RDH12 and RP2 (n=1 each). Thematic analysis of verbatim interview transcripts was performed.

Results: There was consistency across age groups and RP/LCA genotypes in terms of the most relevant concepts. Night blindness, peripheral vision and contrast sensitivity limitations were the most frequently reported visual function symptoms. Severity of impairments depended on lighting conditions and familiarity of environment. Proximal vision-dependent impacts included limitations to mobility and ADLs. Visual aids used included a white cane and assistive devices. Participants reported impacts on broader HRQoL domains, most commonly emotional well-being, social and work/school functioning. Similar concepts were reported by caregivers of children with RP/LCA.

Conclusions: Visual function symptoms and impacts on vision-dependent ADLs and HRQoL reported by participants were consistent across age groups and genotypes, suggesting the same measures may be appropriate for use in all RP/LCA types. Findings increase the understanding of the qualitative experience of RP/LCA and supported the development of fit-for-purpose patient- and observer-reported outcome measures for use in RP/LCA clinical trials.

CONTROL ID: 3532652

SUBMITTER (NAME ONLY): Elena Ivanova

TITLE: Selective Micropulse Individual Retinal Therapy development based on the analysis of the micropulse mode testing and computer simulation

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Ivanova, P. Volodin, Laser retinal surgery, FGAU Nacional'nyj medicinskij issledovatel'skij centr Mezotraslevoj naucno-tehniceskij kompleks Mikrohirurgia glaza imeni akademika S N Fedorova, Moscow, RUSSIAN FEDERATION|

Commercial Relationships Disclosure (Abstract): Elena Ivanova: Commercial Relationship: Code N (No Commercial Relationship) | Pavel Volodin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The micropulse mode of serial lasers with short-pulse duration and duty cycle allows one to exert selective impact on the retinal pigment epithelium (RPE). However, there are no standard micropulse modes for treatment, it is difficult to control the level of retinal damage, and individual pre-testing is required. In this study, the development of the Selective Micropulse Individual Retinal Therapy (SMIRT) with a low level of retinal damage and the assessment of the therapeutic effect of CSC (central serous chorioretinopathy) without preliminary testing are addressed.

Methods: This study has been conducted on 73 patients with acute CSC, transparent optical media, aged 30 to 65, with type 1-4 on the Fitzpatrick scale (FS). The testing of the micropulse mode (50 μ s, 2.4%, 10 ms, 100 μ m, 0.4-1.9 W) was performed in 33 patients with 1584 spots analyzed using the autofluorescence (AF) method (488 nm). Another 40 patients were divided into 4 equal groups (10 eyes). In groups 1-3, CSC was treated in the same micropulse mode with the predicted power for the ED of the RPE damage according to AF data of 50%, 70%, and 90%, respectively. The 4th was the control group with no treatment. The testing and treatment were performed with a Navilas577s laser system. Computer simulation was built with the Arrhenius integral to assess the heating and protein denaturation of the RPE and adjacent structures. The Fisher's exact test was used for statistical analysis.

Results: A logistic regression function EDlevel with 3 parameters such as power, age, and FS was constructed based on the AF results for 33 patients. The reverse function was used to predict the required power based on the individual properties according to the chosen ED level. According to computer simulation, for the modes used in groups 1-3, harmful damage to retina and choroid was 35%, 37% and 49% of the damage to the RPE, respectively. Three months later, in groups 1-3 complete resorption of subretinal fluid was observed in 5 ($P<0.35$), 8 ($P<0.023$) and 10 eyes ($P<0.0008$) out of 10, respectively.

Conclusions: In the developed SMIRT, the required power is selected without prior testing, based on the age and FS of the patient. The SMIRT has shown efficacy in the treatment of CSC.

CONTROL ID: 3532658

SUBMITTER (NAME ONLY): Yu-Yen Chen

TITLE: Patients with retinitis pigmentosa may have a higher risk of developing primary angle-closure glaucoma and open-angle glaucoma

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, Department of Ophthalmology, Taichung Veterans General Hospital, Taichung, TAIWAN|T. Lo, Department of Medical Education, Taichung Veterans General Hospital, Taichung, TAIWAN|

Commercial Relationships Disclosure (Abstract): Yu-Yen Chen: Commercial Relationship: Code N (No Commercial Relationship) | Tzu-Chen Lo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate whether patients with retinitis pigmentosa (RP) have a higher proportion of primary angle-closure glaucoma (PACG) and open-angle glaucoma (OAG) development.

Methods: Using the Taiwan National Health Insurance Research Database from 2001 to 2013, patients with RP were enrolled into the RP group and age- and gender-matched individuals without RP (1:4 matched) were enrolled into the control group. Kaplan-Meier curves were generated to compare the cumulative hazard of subsequent PACG and OAG between the two groups. A Cox regression analysis was performed to estimate the crude and adjusted hazard ratios (HRs) for PACG and OAG.

Results: 6223 patients with RP and 24892 controls were enrolled. During the 13-year study period, 1.61% of RP patients and 0.81% of controls developed PACG (p value < 0.0001). Besides, more proportion of RP patients developed OAG than controls did (1.57% vs. 0.58%, p value < 0.0001). RP group had a significantly higher cumulative hazard of PACG and OAG compared to the control group (p value < 0.0001). The Cox regression model indicated that the RP group had a significantly higher risk for PACG and OAG (adjusted HR= 2.04 and 2.83, respectively).

Conclusions: Patients with RP are at significantly greater risk of developing PACG and OAG.

CONTROL ID: 3532672

SUBMITTER (NAME ONLY): Jessica Yang

TITLE: Utility of post-operative review following Nd:YAG laser capsulotomy

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.F. Yang, L. Vander Woude, M.K. Mansfield, M.B. Sherwood, S.S. Iyer, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|A. Walia, Washington University in St Louis, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nd:YAG laser capsulotomy (YAG) is a common procedure with infrequent adverse events. We reviewed intraocular pressure (IOP) measurements 30 minutes after YAG in glaucomatous and non-glaucomatous eyes and a one-week post-op dilated fundus exam (DFE) to detect retinal tear (RT) and detachment (RD). We are interested in the utility of these same day and one-week visits, especially in glaucoma patients and in this COVID-19 era.

Methods: We analyzed 1,406 eyes from 1,138 patients who received YAG from 2011 to 2020 at the University of Florida. Exclusion criteria included YAG performed for reasons other than posterior capsular opacification, IOP not recorded and glaucoma status not analyzed. IOP (pre-op, 30 minutes post-op and at follow-up), follow-up DFE and glaucoma history were recorded. Primary outcome measures were change in IOP at same day and one-week post-op visits and incidence of RT and RD.

Statistical analyses were conducted in IBM SPSS Statistics. Pre-op and same day post-op IOP in all patients (N=578) and in glaucoma patients (N=93) were compared with paired t-test. Univariate regression analysis was performed to assess if glaucoma history predicted which patients would have a rise in IOP of 5mmHg or more. ANOVA was used for comparison of intergroup difference between pre-op, same day post-op, and follow-up.

Results: There was no significant change in mean pre-op and post-op IOP in all patients ($p = 0.557$), nor in the glaucoma patients ($p = 0.194$). Many patients (68.9%, N=404) were given a drop of brimonidine prior to YAG procedure. 69 patients had a rise in IOP of 5 mmHg or more at 30 minutes following YAG, including 13/93 (14%) of glaucoma eyes and 56/485 (12%) of non-glaucoma eyes. An IOP spike of 10mmHg occurred in 9 of these eyes of which 1 eye had glaucoma (1%) and 8 did not (89%). Using binary logistic regression, we found that glaucoma was not predictive for rise in IOP of 5mmHg or more following YAG (OR 1.23; 95% CI=0.64-2.34). No patients had RT or RD detected during one-week follow-up visit.

Conclusions: There is no significant change in IOP in all patients and in glaucoma patients. Glaucoma was not considered a risk factor for rise in IOP. YAG does not seem to increase the risk of RT or RD. In this COVID-19 era, when all practitioners aim to decrease in-person visits, small changes on a large scale can make an impact. If validated, our results bring into question the necessity of post-op visits after YAG.

CONTROL ID: 3532673

SUBMITTER (NAME ONLY): Shrinivas Pundlik

TITLE: Area under the Curve as an Alternative Outcome Measure of Dark Adaptation Response

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Pundlik, G. Luo, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Pundlik, A. Nigalye, I. Lains, R. Katz, J. Kim, V.P. Douglas, A. Marmalidou, I.K. Kim, J. Miller, D.G. Vavvas, J.W. Miller, D. Husain, G. Luo, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Nigalye, I. Lains, K. Mendez, R. Katz, V.P. Douglas, A. Marmalidou, I.K. Kim, J. Miller, D.G. Vavvas, J.W. Miller, D. Husain, Retina Service, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|K. Mendez, Brigham and Women's Hospital Channing Division of Network Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rod intercept time (RIT) is commonly used as a measure of dark adaptation (DA) response. However, in some age-related macular degeneration (AMD) patients, the sensitivity fails to recover to the requisite threshold within the testing duration for a valid RIT determination. This precludes proper quantification of the DA response. We evaluated whether DA response in such eyes can be quantified using the area under the dark adaptation curve (AUDAC), which can serve as an alternative measure of DA response within the same testing time frame.

Methods: DA was measured using the AdaptDx (Maculogix, Harrisburg PA) 20-minute protocol (which output RIT value) in 136 eyes (AMD: 98, Control: 38). The RIT criterion was 3 log units sensitivity recovery, failing which, the RIT was set at maximum of 20 minutes per protocol. Separately, normalized AUDAC was computed from the DA curve using the trapezoid method with respect to the same measurement limits. Association between AUDAC and RIT in eyes with RIT < 20 minutes was computed using a linear model, which was then used to predict the RIT values in eyes that failed to record a valid RIT value. Furthermore, the AUDAC was evaluated for predicting AMD presence using a logistic regression model, and the accuracy and the F score were compared with that for the AdaptDx threshold (RIT=6.5 min.).

Results: In 101 eyes with RIT < 20 minutes, the median [IQR] values of RIT and AUDAC were 5.8 [6.4] minutes and 0.063 [0.054], respectively, with a strong linear association between the two measures ($p < 0.001$, $R^2 = 0.87$). In 35 eyes that failed to record a valid RIT (RIT set at 20 minutes; 34 AMD, 1 control), there was a large variation in the AUDAC (median [IQR]: 0.276 [0.091]) due to the differences in the underlying DA curves, indicating that DA response can still be measured in these eyes. As expected, the RIT was projected to be >20 minutes in 33 out of the 35 eyes (median [IQR] RIT was 24.1 [7.8] minutes) using the linear model between RIT and AUDAC. When predicting AMD presence, the performance of AUDAC (76.5% accuracy; $F_1=0.84$) was comparable to RIT (78% accuracy; $F_1=0.83$).

Conclusions: In eyes where sensitivity fails to recover to the requisite criterion, including many AMD patients, the DA response cannot be quantified using RIT. AUDAC offers a reliable alternative analytic approach to measuring DA response for all eyes, even those that fail to record a valid RIT value.

CONTROL ID: 3532675

SUBMITTER (NAME ONLY): James Regun Karmoker

TITLE: Ocular phenotype of RORgt promoter-driven AhR knockout mice in response to RPE injury

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Karmoker, S. Bounds, J. Farriester, J. Cai, Department of Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|K. Youngsil, Y. Chen, Dean McGee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported that choroidal $\gamma\delta$ T cells protected the retinal pigment epithelium (RPE) from oxidative injury. Aryl hydrocarbon receptor (AhR) is a key transcription factor for the differentiation and function of interleukin 17 (IL-17)-producing T cells. The goal of the current project is to examine the roles of AhR and IL-17⁺ $\gamma\delta$ T cells in acute and chronic toxicity models of RPE injury.

Methods: AhR-floxed mice were crossed with transgenic mice with Cre expression driven by the RAR-related orphan receptor gamma (Rorc) promoter, to generate AhR knockout in IL-17-producing T cells (Rorc-Ahr KO). Flow cytometry analysis was conducted to verify the IL-17⁺ $\gamma\delta$ T deficiency. Rorc-Ahr KO mice were either treated with sodium iodate or fed on a high-fat, cholesterol-rich diet for 6 weeks to induce acute or chronic RPE injury. Optical coherence tomography (OCT), fundus photography, and electroretinogram (ERG) were used in live animals to determine ocular phenotype. Microglia activation was assessed by immunofluorescence staining of cryosections or RPE flat mounts.

Results: AhR deficiency led to impaired IL-17 production in $\gamma\delta$ T cells. In the chronic RPE toxicity model, the conditional knockout mice had a higher number and more extensive area of subretinal IBA-1⁺ microglia infiltration as indicated by immunostaining on RPE flat-mounts or retinal cryosections. Rorc-Ahr KO had focal RPE pigment loss and atrophy, especially in the peripheral region. Consistent with the pathology findings, Rorc-Ahr KO had reduced scotopic a- and b-wave responses. In the acute toxicity model, fundus photography, OCT, and quantification of RPE flat mounts showed more severe damage in the conditional knockouts.

Conclusions: Deficiency in IL-17 production in choroidal $\gamma\delta$ T cells increased the sensitivity to RPE injury, suggesting IL-17 plays a protective role by controlling microglial activation.

CONTROL ID: 3532679

SUBMITTER (NAME ONLY): Miho Tagawa

TITLE: Deterioration of Phagocytosis in induced Pluripotent Stem Cell-Derived Retinal Pigment Epithelial Cells established from Patients with Retinitis Pigmentosa Carrying Mer Tyrosine Kinase Mutations

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tagawa, H. Ikeda, Y. Inoue, S. Iwai, Y. Iida, M. Hata, A. Tsujikawa, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, JAPAN|I. Asaka, Center for iPS Cell Research and Application (CiRA), Kyoto Daigaku, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the mechanism of onset and progression of retinitis pigmentosa (RP) due to mutations in Mer tyrosine kinase (MERTK) gene using induced pluripotent stem cells of the retinal pigment epithelium (iPSC-RPE) derived from patients.

Methods: iPSC-RPE were derived from two patients with RP with MERTK gene mutations (MTK) and three normal (NOR) individuals. Morphological differences in the diseased (MTK) and normal (NOR) iPSC-RPE were evaluated using bright field microscopy, transmission electron microscopy, and immunochemistry analyses. Phagocytosis was analyzed with fluorescent bovine photoreceptor outer segments (POS) using flow cytometry and POS-derived protein, rhodopsin, in the iPSC-RPE cells fed POS using western blotting.

Results: There were no morphological differences between MTK and NOR iPSC-RPE. Flow cytometry analysis revealed that the percentage of FITC-positive MTK iPSC-RPE (15.5 ± 6.6 %) was significantly lower ($P = 0.046$) than that of NOR iPSC-RPE (27.3 ± 14.2 %). The relative intensity of rhodopsin in MTK iPSC-RPE (0.51 ± 0.18) was significantly lower ($P = 0.016$) than that in NOR iPSC-RPE (0.82 ± 0.20).

Conclusions: We successfully developed a human cell-based in vitro model of retinal degeneration. In the diseased iPSC-RPE, phagocytosis of POS was found to be deteriorated.

CONTROL ID: 3532689

SUBMITTER (NAME ONLY): Joshua Ong

TITLE: Acute and Long-Term Visual Recovery Following Optic Nerve Sheath Fenestration for Severe Vision Loss

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Ong, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|E. Massicotte, S.T. Stefko, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joshua Ong: Commercial Relationship: Code N (No Commercial Relationship) | Erika Massicotte: Commercial Relationship: Code N (No Commercial Relationship) | S Stefko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic nerve sheath fenestration (ONSF) is a surgical procedure that acutely relieves the pressure from cerebrospinal fluid around the optic nerve to preserve vision in patients with papilledema. Decision to utilize ONSF or ventriculoperitoneal (VP)/lumboperitoneal (LP) shunts or to combine both procedures largely remains institution/surgeon dependent. This study tested the hypothesis that ONSF acutely reverses vision loss after surgery and continues to improve months after the surgery.

Methods: Retrospective chart review was performed on 11 years of data from a single hospital system database utilizing current procedural terminology (CPT) for ONSF (2009 – 2020). Patients aged 18 and older who had undergone ONSF procedure for elevated intracranial pressure with severe vision loss were included in the study. Data was reviewed for a reduction in blindness (defined as logMar \geq 1) and Humphrey/Goldmann visual fields immediately post-op, 3-9 months post-op, and at the latest visit.

Results: 34 eyes (24 patients) were included in this study. The average age was 36.0 years old (SD +/- 10.0 years). Nineteen patients were female (79.2%) and seventeen were Caucasian (70.8%). Seventeen of patients had a documented risk factor of obesity (70.8%), and the mean BMI of all patients was 34.2. The mean opening pressure at diagnosis was 39.4 cm H₂O. Average pre-op LogMar was 1.30 and 19 eyes (56%) were legally blind pre-operatively (LogMar \geq 1). Average mean deviation on Humphrey visual field was -21.36 (16 eyes) pre-operatively. 26 eyes (76.5%) had combined ONSF with VP shunt, 2 eyes (5.9%) with ventriculostomy, and 2 eyes (5.9%) with stenting of venous sinus. Immediately after surgery, 45.5% (15) of patients had improved visual acuity, 24.4% (8) had stable visual acuity, and 30.3% (10) had decreased visual acuity. The average post-operative change in LogMar visual acuity was +0.23. There was a 28% reduction in blindness (LogMar \geq 1) immediately after surgery post-op and a 56% reduction in blindness in the most recent exam (average days from surgery to most recent visit: 690 days).

Conclusions: Visual recovery and reduction in blindness (LogMar \geq 1) after an ONSF procedure increases over the postoperative period. It may be that as many as 50% of eyes blinded by IIH will recover useful vision with this surgery.

CONTROL ID: 3532690

SUBMITTER (NAME ONLY): Dhanach Dhirachaikulpanich

TITLE: A transcriptome based computational drug repurposing analysis to target the RPE/choroid abnormality in advanced age-related macular degeneration

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Dhirachaikulpanich, L.I. Paraoan, Eye and Vision Science, Institute of Life Course and Medical Sciences, Faculty of Health & Life Sciences, University of Liverpool, Liverpool, Merseyside, UNITED KINGDOM|D. Dhirachaikulpanich, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, THAILAND|

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ABSTRACT BODY:

Purpose: Advanced age-related macular degeneration (AMD) is a devastating blinding disease centring on the retinal pigment epithelium (RPE)/choroid. The current treatments can only slow the progress of the disease. The current big data era affords comparisons of large gene expression datasets generated from large drug perturbation response studies aiming to explore the repurposing of currently available drugs for different diseases. Here, we exemplify the application of such an integrating transcriptomic method to find potential drugs for advanced AMD.

Methods: The publicly available microarray transcriptome (GSE29801) of advanced AMD RPE/choroid was combined with RNAseq (GSE135092) by an integrating quantitative method to extend the assessment of the differential gene expression in advanced AMD RPE/choroid. The resulting significant genes were subjected to over-representation analysis of KEGG pathways to highlight crucial biological processes in advanced AMD. For the purpose of this study, the differentially expressed genes in the significant pathways were then compared with the drug perturbation profile from the L1000 Connectivity Map (CMap), querying the correlation of a predicted response with the differential gene expression profile in advanced AMD RPE/choroid.

Results: We furthered our previous integrative transcriptomic analysis of RPE/choroid to combine transcriptomic data of 35 advanced AMD RPE/choroid samples. The analysis showed 427 genes differentially expressed ($p < 0.05$) with advanced AMD (276 upregulated and 151 downregulated). Among the differentially expressed genes, over-representation analysis highlighted extracellular matrix (ECM)-receptor interaction and focal adhesion as two significant KEGG pathways ($FDR < 0.05$). The 11 significant upregulated genes in ECM-interaction pathway were used to query the correlated drug perturbation in CMap database and identified dihydrofolate reductase inhibitor, vitamin D receptor agonist and MTOR-PI3K inhibitor as potential drug classes by this computational method (CMap enrichment score > 99).

Conclusions: Integrative RPE/choroid transcriptome analysis against the drug perturbation response database predicted three potential drug classes, based on dihydrofolate reductase inhibitor, vitamin D receptor agonist and MTOR-PI3K inhibitor, with potential for repurposing for advanced AMD.

CONTROL ID: 3532716

SUBMITTER (NAME ONLY): Asael Papour

TITLE: Acoustic power measurements of ultrasonic vitrectomy device and the effects in pig eyes

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Papour, J. Taylor, A. Zulkifli, A. Skinner, B. McCary, Surgical R&D, Bausch and Lomb, St. Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acoustic power measurements of ultrasonic vitrectomy devices and the tissue interaction have not been fully characterized to-date and the unique close ended needle with side port configuration cannot be accounted for in the theoretical calculations. Computational fluid dynamics (CFD) simulations and measurements in water and pig eye reveal the non-linear effects and behavior. This is a significant step in characterizing the power, energy-tissue interaction, and safety of ultrasonic vitrectomy devices.

Methods: Acoustic pressure of 23, 25, and 27 gauge vitrectomy needles was measured in a degassed water tank using a hydrophone (B&K 8103) according to the IEC 61847 standard.

The ocular tissue measurements used a whole pig eye with infusion for IOP control and aspiration of 50 mmHg, with the hydrophone external to the eye.

Whole eye ANSYS simulations estimated the; phase transition, velocity, and pressure with the following parameters: No-slip boundary conditions, saline solution viscosity 1.02×10^{-3} Pa.s, density 1005.3 kg/m^3 , with a transient timesteps of 1 μs .

Results: Pressure decrease was measured with the 23g ported and smaller diameter needles compared to the unported 23g needle ($p < 0.01$), and a decrease in average pressure was observed with the pig eye while increase in pressure variability was measured with higher strokes ($p > 0.05$) (Fig.1).

CFD simulations (Fig. 2) show high pressure increase at the inner needle tip during retraction motion (3157 mmHg) compared to the outer needle tip at extraction motion (< 1200 mmHg), with phase change volume fraction of $> 60\%$ and $< 10\%$, respectively.

Conclusions: The results indicate that ocular tissue has low acoustic energy absorption properties while the IOP may reduce the occurrence of cavitation events which in turn lowers the average power. The CFD simulations further bolster these results by showing that inner needle cavitation events to be the main contributor to the measured acoustic power.

The low acoustic energy-tissue interaction within the low ultrasonic frequency range (< 100 kHz) and power (< 100 mW), further promotes the safety of a posterior ultrasonic vitrectomy device.

CONTROL ID: 3532725

SUBMITTER (NAME ONLY): Naoko Kato

TITLE: Predicting keratoconus progression using deep learning

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We aimed to determine the need for corneal crosslinking (CXL) among keratoconus cases using deep learning (DL).

Methods: Two hundred and seventy-four corneal tomography images taken by Pentacam HR[®] of 158 keratoconus patients were examined. All patients were examined two times or more, and divided into two groups; the progression group included eyes showing keratoconus progression that underwent CXL, and the non-progression group consisted of eyes showing no progression. An axial map of the frontal corneal plane, a pachymetry map, and a combination of these two maps were examined and assessed according to the patients' age. Training with a convolutional neural network on these learning data objects was conducted. The area under the curve (AUC), sensitivity, and specificity were examined for detecting the need for CXL.

Results: Ninety eyes showed progression and 184 eyes showed no progression. The axial map, the pachymetry map, and their combination combined with patients' age showed mean AUC values of 0.783, 0.784, and 0.814 (95% confidence interval [0.721 - 0.845], [0.722 - 0.846], and [0.755 - 0.872], respectively), with sensitivities of 87.8%, 77.8%, and 77.8% ([79.2 - 93.7], [67.8 - 85.9], and [67.8 - 85.9]) and specificities of 59.8%, 65.8%, and 69.6% ([52.3 - 66.9], [58.4 - 72.6], and [62.4 - 76.1]), respectively.

Conclusions: Using the proposed DL neural network model, keratoconus progression can be predicted with high sensitivity and specificity on corneal tomography maps combined with patients' age.

CONTROL ID: 3532728

SUBMITTER (NAME ONLY): Tiffany Lau

TITLE: Functional and Structural Outcomes of Patients with Diabetic macular oedema treated with multiple Ozurdex implants at 24 months – Real Life Data

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Lau, A.E. Ghareeb, M. Kishikova, A. Kotagiri, I. Masri, J. Smith, D. Varma, D. Steel, M. Habib, Sunderland Eye Infirmary, Sunderland, Tyne and Wear, UNITED KINGDOM|A.E. Ghareeb, D. Steel, Bioscience Institute, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diabetic macula oedema (DMO) remains one of the most common causes of visual loss in the industrial working-age population. Intravitreal Ozurdex Implant (dexamethasone 0.7 mg) is an established treatment option for management of DMO with favorable long-term outcomes, however, one of its side effects is increase in intraocular pressure (IOP). The duration of Ozurdex action varies from 3-6 months. The purpose of this study is to investigate the differences in functional and structural outcomes as well as effect on IOP for patients receiving 1, 2 or 3 Ozurdex intravitreal implants in the first 12 months of treatment at 24-month post-treatment initiation in a real-life setting.

Methods: Retrospective study of patients with DMO treated with Ozurdex implants between January 2016 and October 2019, at Sunderland Eye Infirmary, UK. The number of Ozurdex implants injected in the first 12 months of treatment were calculated for each patient.

The primary outcome measures were mean changes from baseline in best-corrected visual acuity (BCVA), central macular thickness (CMT) and IOP at 24 months. Secondary outcomes included proportions of patients with ≥ 10 letters gain or loss; $\geq 20\%$ of CMT gain or loss and final BCVA and CMT.

Results: 89 eyes (74 patients) were included in the study, with 43, 35 and 11 eyes receiving 1, 2 or 3 implants, respectively, in the first 12 months. The baseline BCVA was similar in all 3 groups (55.2, 54.1, 54.8 letters, respectively, $p=0.80$). At 24 months, the group receiving 3 Ozurdex implants demonstrated the highest increase in BCVA of 9.88 letters compared to 1.23 and -1.20 letters for group 1 and 2, respectively, although significance was limited by small sample size ($p=0.24$). Reduction in CMT was $-78.91\mu\text{M}$, $-102.53\mu\text{M}$ and $-189.00\mu\text{M}$ for 1, 2 and 3 Ozurdex implants, respectively ($p=0.08$). There has been a minor IOP change from baseline of -0.76mmHg , 2.47mmHg , 2.13mmHg ($p=0.973$) in 1, 2 and 3 Ozurdex implant groups, yet this was clinically insignificant.

Conclusions: The results of our real-life study showed that early treatment with multiple frequent Ozurdex implants in the first year (3 implants) yielded better functional and structural outcomes at 24 months as compared to patients' groups treated less frequently (1 or 2 implants) though this hasn't reached statistical significance levels with no clinical significant safety concerns.

CONTROL ID: 3532758

SUBMITTER (NAME ONLY): Daniel Hass

TITLE: In vivo ^{13}C -succinate infusion reveals gluconeogenesis in the mouse retina and eyecup

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Hass, C. Bisbach, J. Hurley, Biochemistry, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|E. Giering, T. Munding, VA Puget Sound Health Care System, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gluconeogenesis is a process wherein metabolites are diverted from the Krebs cycle to become glycolytic intermediates. Gluconeogenesis is critical for blood glucose homeostasis, and is thought to be restricted to liver, kidney, intestine, and muscle tissue. Previous literature suggests that amphibian retinas are capable of this process, and our goal is to determine whether gluconeogenesis occurs in the mammalian retina.

Methods: We infused male and female C57BL6/J mice with 100mg/kg $^{13}\text{C}_4$ -succinate through jugular catheters and euthanized mice 1, 2, 3, 5, and 12 minutes following the infusion, dissecting and snap-freezing retina and eyecup tissue (EC; a complex of choroid, sclera, and RPE; n=3-5/tissue/time point). Un-infused mice served as a '0 minute' control. At 0 and 5 minutes post-infusion, we also collected liver tissue (n=3).

Frozen samples were derivatized with methoxyamine and TBDMS, and analyzed by gas-chromatography mass spectrometry to determine the abundance of ^{13}C -labeled metabolites in the Krebs cycle (succinate, fumarate, malate, and citrate) and glycolysis (pyruvate, phosphoenolpyruvate, and 3-phosphoglycerate).

Results: Infused $^{13}\text{C}_4$ -succinate populated the bloodstream (>95% of blood succinate was labeled) and led to succinate infiltration in to retina (8% of pool) and EC (57% of pool). Surprisingly, ^{13}C from infused succinate was incorporated into $^{13}\text{C}_3$ -pyruvate, $^{13}\text{C}_3$ -phosphoenolpyruvate, and $^{13}\text{C}_3$ -3-phosphoglycerate in both tissues. These metabolites respectively accumulated at a rate of 0.2 (0.96), 0.13 (0.96), and 0.14 (0.92) % pool/minute (mean slope; R^2) in the retina, and 0.1 (0.59), 0.07 (0.68), 0.09 (0.97) % pool/minute in the EC. There was no observable accumulation of ^{13}C on glycolytic intermediates in liver, thus our observations are not explained by gluconeogenesis in the liver.

Conclusions: Retina succinate pools are far less labeled by succinate than ECs, yet in both tissues the diversion of Krebs cycle intermediates (succinate) to ^{13}C labeled glycolytic metabolites occurred at a similar rate. These data suggest that (a) both tissues are capable of gluconeogenesis and (b) the retina diverts a larger fraction of ^{13}C from succinate to gluconeogenesis than EC tissue. These findings are not recapitulated in liver tissue or ex vivo retina or EC tissue supplied with $^{13}\text{C}_4$ -succinate, suggesting that the cellular environment may dictate the activity of this pathway.

CONTROL ID: 3532768

SUBMITTER (NAME ONLY): Masahiro Miura

TITLE: Choroidal melanin thickness measurement in healthy Japanese subjects by polarization-sensitive optical coherence tomography

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Miura, T. Iwasaki, Ophthalmology, Tokyo Ika Daigaku Ibaraki Iryo Center, Inashiki-gun, Ibaraki, JAPAN|S. Makita, Y. Yasuno, Computational Optics Group, Tsukuba Daigaku, Tsukuba, Ibaraki, JAPAN|S. Azuma, T. Mino, T. Yamaguchi, Kabushiki Kaisha Topcon Kenkyu Kaihatsu Center, Itabashi-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: To evaluate choroidal melanin distribution in healthy subjects by polarization-sensitive optical coherence tomography (PS-OCT).

Methods: This study involved 57 eyes of 57 healthy Japanese subjects. The presence of melanin in the choroid was determined by using the degree of polarization uniformity (DOPU) obtained by 1 μ m Jones-matrix PS-OCT. Choroidal melanin thickness was evaluated for 5 mm circular region from the foveal center, and compared with age (26 – 84 years), axial length (22.0 – 28.5 mm), choroidal thickness, and choroidal luminal/stromal ratio. To evaluate the distribution of choroidal melanin thickness, circular region was divided into five sectors (center, upper, lower, nasal, and temporal) by modified ETDRS layout.

Results: The mean choroidal thickness and choroidal melanin thickness (mean \pm SD) at 5 mm circular region were $202.5 \pm 80.8 \mu$ m and $68.3 \pm 24.2 \mu$ m, respectively. Mean choroidal thickness showed significant negative correlation with age ($\beta = -0.30$, $P = 0.004$) and axial length ($b = -0.21$, $P = 0.03$), and significant positive correlation with luminal/stromal ratio ($\beta = 0.62$, $P < 0.001$). Mean choroidal melanin thickness showed significant negative correlation with axial length ($\beta = -0.26$, $P = 0.045$) and luminal/stromal ratio ($\beta = -0.60$, $P = 0.001$), and significant positive correlation with choroidal thickness ($\beta = 0.85$, $P < 0.001$). The mean choroidal thickness and choroidal melanin thickness of the nasal sector were significantly thinner than that of all other sectors ($P < 0.001$).

Conclusions: PS-OCT provides an in vivo objective choroidal melanin distribution. Choroidal melanin thickness varies significantly with location, axial length, and choroidal morphology.

CONTROL ID: 3532772

SUBMITTER (NAME ONLY): Rohit Sharma

TITLE: Sensimed Triggerfish® contact lens sensor for 24-hour intraocular pressure profile-safety and validity.

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sharma, Consultant Ophthalmic Surgeon, Eye Department, University Hospitals Derby & Burton NHS trust, Burton, UNITED KINGDOM|R. Sharma, Asstt Professor (Honorary), University of Nottingham, Nottingham, Nottinghamshire, UNITED KINGDOM|Z. Ong, Nottingham university, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose:

Sensimed Triggerfish® contact lens sensor (CLS), a relatively new device, is designed to monitor 24-hour intraocular pressure (IOP) profile. Currently, the safety, tolerability and validity of triggerfish CLS remains controversial. We performed a prospective observational study (the first such study in the NHS UK) to evaluate the safety, tolerability of CLS in glaucoma patients and whether the CLS measurement can be correlated to IOP measured using Goldmann applanation tonometry (GAT).

Methods: This was an observational single-facility study. 24 voluntary patients (9 females, 15 males) with glaucoma underwent 24-hour continuous measurement of IOP with a Triggerfish® CLS. Clinic letters and communications to the GP (general practitioner) were reviewed to identify any objective and subjective reports of eye symptoms during or after the usage of CLS.

IOP were measured immediately before and after CLS usage using GAT by ophthalmologists. We then compared the changes of IOP measurements (end-initial IOP in mVeq) from CLS and changes of IOP (end-initial IOP in mmHg) from GAT among the 24 patients to look for correlation.

Results: All patients successfully completed the 24-hour measurement of IOP with CLS. The mean age was 69.83 (SD: 7.8). No patient needed emergency visit or discontinuation or removal of the CLS before the prescribed period. The reporting rate of side effects, watering, redness, pain, blurring or discomfort was 0%. At the 3-week follow up clinic, the overall incidence of objective and subjective report of eye symptoms such as ocular pain and blurred vision was 0%. The Pearson correlation coefficient between the difference of IOP measurement from CLS and GAT was $r = -0.173$ ($p = 0.43$), which represented a weak negative correlation.

Conclusions: Our study showed that IOP measurement with 24-hour CLS is safe & well-tolerated in glaucoma patients. There were no short term or permanent complications or side effects reported. Our results showed a weak correlation between Triggerfish data changes and IOP measurements using the GAT. Though CLS cannot totally replace GAT for IOP measurement, this complements & adds useful insight on the innovative continuous 24 hour IOP profile and nocturnal measurements not covered by the static clinic GAT. Bigger, well-designed studies shall help in this exciting topic.

CONTROL ID: 3532773

SUBMITTER (NAME ONLY): Poria Dorali

TITLE: Location-Based Analysis on Optimizing Teleretinal Imaging Accessibility in a Large Safety-Net System

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Dorali, R. Limongi, T. Lee, Department of Industrial Engineering, University of Houston, Houston, Texas, UNITED STATES|C.Y. Weng, Baylor College of Medicine Department of Ophthalmology, Houston, Texas, UNITED STATES|C.Y. Weng, Department of Ophthalmology, Ben Taub Hospital, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: With the growing adoption of teleretinal imaging (TRI), it is important to design a TRI-based screening program that is easily accessible over a large geographic area. This study develops a modeling framework that identifies locations to place future TRI screening centers that maximize TRI visits for in-need census tracts in a large, county-wide safety-net system.

Methods: A location-based Monte Carlo discrete event simulation model was developed including all census tracts in Harris County to evaluate patient visits to current TRI screening centers. A total of 500,000 hypothetical patients were generated and tracked over their lifetime under annual TRI screening recommendations. Patient compliance rates were varied based on factors such as race, poverty level, and travel time. The top 20% of census tracts with the greatest need was identified by factors such as total number of visits and minimum travel time to the nearest center. A new potential center was then identified based on a weighted centroid of the top 20% census tracts where the weights are assigned proportional to census tract-specific needs. The simulation was then run again with the new center added to analyze the benefits for patients within the in-need census tracts.

Results: For the top 20% of census tracts, the model identifies a new potential TRI screening center in northwest Harris County in an area that is currently not covered by existing centers (See Fig 1&2). For census tracts in the top 20% that are impacted by the placement of the new center, yearly TRI visits increase by 32.81% (95% CI; 32.21-33.48%) with a reduction in average travel time per impacted patient of 7.96 minutes (95% CI; 7.93-7.99 minutes). Furthermore, average cost (\$)/QALY per impacted patient decreased by \$19.06 (95% CI; \$15.42-\$22.70).

Conclusions: The location model can be a useful tool in designing a TRI-based screening program that maximizes TRI visits for a heterogeneous population over a large geographic area. TRI screening locations can be identified that account for patient-specific compliance data and geodemographic factors. Positive benefits in cost/QALY can be seen on a county-level when new locations are placed strategically.

CONTROL ID: 3532782

SUBMITTER (NAME ONLY): Manas Biswal

TITLE: Buspirone is protective against oxidative stress induced changes in cell culture and animal models of RPE oxidative injury

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.R. Biswal, R.J. Paulson, R. Vichare, Department of Pharmaceutical Sciences, Taneja College of Pharmacy, University of South Florida, Tampa, Florida, UNITED STATES|M.R. Biswal, Department of Ophthalmology, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|A.S. Lewin, Department of Molecular Genetics and Microbiology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|A.S. Lewin, Department of Ophthalmology, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Preservation of central vision is an unmet clinical need in dry age-related macular degeneration (AMD). Chronic oxidative stress impairs the normal functioning of RPE and causes RPE atrophy, leading to loss of macular photoreceptors. The purpose of our study is to determine if buspirone, a partial 5-HT_{1A} agonist receptor agonist, is protective against oxidative stress-induced changes in the RPE.

Methods: The effect of buspirone was evaluated in the sodium iodate model (NaIO₃) of RPE oxidative injury and paraquat-induced oxidative damage in differentiated human ARPE-19 cell culture model. Protection of RPE and photoreceptors in NaIO₃-treated C57BL/6J mice with or without buspirone treatment was characterized by the preservation of outer nuclear layer thickness (mean ± standard error of mean), measured by spectral-domain optical coherence tomography (SD-OCT). RPE/choroid from mice was analyzed by ZO-1 (a phosphoprotein present at tight junctions) and immunostaining of RPE flat-mounts. Quantitative RT-PCR was performed to investigate the effect of buspirone on inducing the expression level of protective enzymes. In response to paraquat-induced cellular toxicities and RPE junctional abnormalities in ARPE-19 cells, the impact of buspirone was assessed by MTT assays and ZO-1 immunocytochemistry, respectively.

Results: Daily intraperitoneal injection (i.p.) of buspirone (30mg/Kg) for 12 days mitigated the thinning of the outer nuclear layer (p<0.0001) in the NaIO₃ model (88.04µm ± 8.009, n=12) compared to vehicle treated eyes (32.83 µm ± 3.861, n=10) determined by SD-OCT. Fluorescent images of RPE flat-mounts stained with ZO-1 tight junction protein revealed the structural preservation of RPE from oxidative damage in buspirone treated mice. Furthermore, buspirone treatment showed an increased trend of expression of key cytoprotective antioxidant genes (Nqo1, Cat, Sqstm1, Gstm1, and Sod2) in the RPE/choroid compared to untreated eyes. MTT assay showed dose-dependent protection of viability in buspirone-treated ARPE-19 cells in culture and preservation of RPE junctional integrity in differentiated ARPE-19 cells in response to paraquat-induced cellular toxicities.

Conclusions: Buspirone provided structural protection of RPE cells from oxidative injury by inducing antioxidant survival pathway. As an FDA-approved drug, repurposing buspirone may be useful in treating dry-AMD.

CONTROL ID: 3532783

SUBMITTER (NAME ONLY): Yunlu Xue

TITLE: AAV-Txnip prolongs cone survival and vision in mouse models of retinitis pigmentosa

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is an inherited retinal disease, affecting >20 million people worldwide. Loss of daylight vision typically occurs due to the dysfunction/loss of cone photoreceptors, the cell type that initiates our color and high acuity vision. Currently, there is no effective treatment for RP, other than gene therapy for a limited number of specific disease genes. Therefore, we would like to develop a gene-agnostic therapy, aimed at preserving cone photoreceptors and daylight vision, independent of the specific genes that are involved.

Methods: We used adeno-associated virus (AAV) to deliver candidate genes to the eyes of neonatal RP mice. The AAV8 capsid employing cone-specific promoters was used for cell type-specific expression. AAV delivery was via subretinal injections. The initial screen was done in rd1 mice, the fastest RP degeneration strain, followed by infections of the rd10 and rho^{-/-} strains. Rd1 retinas were harvested at P50, flat-mounted and the surviving cones within the central half of radius were quantified. To test for an effect on visual function, optomotor behavioral assays were used on treated rd10 and rho^{-/-} mice.

Results: We found that AAV-Txnip prolongs the survival of cone photoreceptors and improves visual acuity in RP mouse models. The rescue effect of Txnip depends upon lactate dehydrogenase b (Ldhd), and correlates with the presence of healthier mitochondria. A Txnip allele, C247S, which blocks the association of Txnip with thioredoxin, provides an even greater benefit. Moreover, the combination of Txnip.C247S and Nrf2, a therapeutic transcription factor which regulates the oxidative stress response, provides a synergistic effect in rescue.

Conclusions: These and additional observations lead to a model wherein Txnip shifts cones from their normal reliance on glucose, to enhanced utilization of lactate for mitochondrial metabolism, thus benefiting the cones in a condition where the glucose supply is limiting.

CONTROL ID: 3532785

SUBMITTER (NAME ONLY): Itika Garg

TITLE: Vascular Metrics and Non-Perfusion Area Measured by Wide-Field Swept-Source OCT-Angiography (WF-SSOCTA) in Different Stages of Diabetic Retinopathy

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Garg, C. Uwakwe, E.S. Lu, R. Katz, J. Moon, K.M. Wai, Y. Lu, J.W. Miller, L.A. Kim, D. Husain, D.G. Vavvas, J. Miller, Retina Service, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|Y. Cui, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|R. Le, Department of Ophthalmology, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|Y. Zhu, Department of Ophthalmology, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|I. Garg, C. Uwakwe, Y. Cui, E.S. Lu, R. Katz, R. Le, Y. Zhu, J. Moon, K.M. Wai, Y. Lu, T. Elze, J.W. Miller, L.A. Kim, D. Husain, D.G. Vavvas, J. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies with smaller cohorts have shown decreased vessel density with increasing diabetic retinopathy (DR) severity. Recently, there has been increasing interest in WF fundus photography and fluorescein angiography in the management of diabetic eye disease. We explore the added value of WF SS-OCTA in a large prospective observational study of diabetic patients compared to controls.

Methods: We imaged 402 eyes of 241 patients (70 eyes of 55 control patients and 332 eyes of 186 diabetic patients) using WF SS-OCTA between December 2018 to September 2020. 6x6mm and 12x12mm scans centered on the fovea were analyzed using ARI Network (Zeiss Portal) for vessel density (VD), vessel skeleton density (VSD), foveal avascular zone (FAZ) raw size, circularity and perimeter; and ImageJ for non-perfusion area (NPA) on 12x12mm scans only. Mixed-effects multivariate regression models were used to test for significance.

Results: Among patients with diabetes (median age 59 years), 45 eyes of 24 patients had no DR, 71 eyes of 40 patients had mild non-proliferative DR (NPDR), 45 eyes of 28 patients had moderate NPDR, 28 eyes of 16 patients had severe NPDR, and 133 eyes of 78 patients had proliferative DR (PDR). Trend analysis revealed a progressive decline in VD and VSD with increasing DR severity ($p < 0.05$). PDR patients had an increased FAZ raw size ($\beta = 0.14$, $p = 0.03$), perimeter ($\beta = 0.83$, $p = 0.03$), and irregularity ($\beta = -0.10$, $p < 0.001$). Also, the mild ($\beta = -0.07$, $p = 0.047$) and moderate NPDR ($\beta = -0.10$, $p = 0.01$) group had irregular FAZ on 12x12mm scans. Controlling for DR severity and age, diabetic macular edema was associated with a more irregular FAZ on 6x6mm scans ($\beta = -0.06$, $p = 0.004$). NPDR and PDR had greater NPA versus controls ($p < 0.001$). On receiver operating curve (ROC) analysis, wide-field NPA was the best test to detect the presence of DR, area under the curve (AUC) 0.97.

Conclusions: Herein, we present a comprehensive study of a large cohort of DR patients imaged on the WF SS-OCTA. The enhanced resolution and larger area coupled with a bigger sample size validates prior work that indicated VD reductions with increased DR severity. Furthermore, our work highlights the importance of NPA which can be more readily and repeatedly measured with WF SS-OCTA.

CONTROL ID: 3532796

SUBMITTER (NAME ONLY): Si Chen

TITLE: Identification of mechanisms underlying retinal ganglion cell survival in zebrafish after optic nerve injury

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: During glaucoma, retinal ganglion cell (RGC) axons are damaged, causing the RGCs to die, resulting in the irreversible loss of visual function. There are no FDA-approved drugs or therapies to protect RGCs from death in glaucoma. Unlike in mammals, zebrafish maintain most RGCs after optic nerve injury; however, the molecular underpinnings of RGC neuroprotection are unknown. Here, we sought to identify neuroprotective factors in zebrafish RGCs after injury and determine if macrophages/microglia are required to survive RGCs after optic nerve transection.

Methods: isl2b:GFP zebrafish, in which ~60% of RGCs are labeled, was utilized at ~3 months. Animals underwent an optic nerve transection surgery in the left eye, while the right eye of the same fish went through a sham surgery. To quantify RGC survival after transection, retinal flat mounts were made and imaged using confocal microscopy at 1-14 days post-injury (dpi) and RGC survival over time was quantified using ImageJ software. Retinae were dissociated at 6, 12 and 24 hours post transection and RGCs were sorted and collected by fluorescence-activated cell sorting. RNA-Seq was performed in biological triplicate, and gene expression changes after injury were quantified. After analyzing the RNA-seq data, several pathways were identified to be possibly involved in RGC survival. Pharmacological experiments were performed and the results on RGC survival quantified. Immunofluorescence imaging of transgenic lines labeling specific leukocyte populations was performed to assess the interaction of immune responses and RGC survival after optic nerve transection.

Results: After injury, RGC survival was: $94.44 \pm 5.45\%$ (1dpi); $92.52 \pm 3.54\%$ (3dpi) and $76.35 \pm 2.58\%$ (7dpi), with levels returning to $98.71 \pm 4.82\%$ at 14dpi. Analysis of RNA-seq data indicate JAK/STAT signaling pathway and immune responses were activated after optic nerve transection, amongst other pathways. Local inhibition of the JAK/STAT pathway leads to the reduction of RGC survival, while local suppression of immune responses by dexamethasone rescued RGCs after injury. Furthermore, depletion of macrophages/microglia increased RGC survival after injury.

Conclusions: Zebrafish maintain most RGCs after optic nerve injury. JAK/STAT signaling pathway regulates RGC survival after optic nerve injury. Immune responses play a critical role in RGC survival after injury.

CONTROL ID: 3532820

SUBMITTER (NAME ONLY): Jackson Moran

TITLE: Supervised reduction of antiviral and steroid therapy in herpetic interstitial keratitis

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Herpetic interstitial keratitis (IK) caused by herpes simplex virus (HSV) or varicella zoster virus (VZV) can cause sight-threatening corneal scarring. This retrospective chart review describes the outcomes of a supervised reduction protocol (SRP) – in which topical steroids and systemic antivirals are only reduced under direct physician supervision, to ensure quiescence before further reduction – for treatment of herpetic IK.

Methods: A cohort of 50 patients with HSV or VZV IK, all treated with SRP between September 2016 and March 2020, were included in the study. Baseline characteristics and details related to ocular outcomes were collected. The primary outcome measures were time from IK diagnosis to quiescence, time from quiescence to IK recurrence, incidence of IK recurrence, and the change in logMAR visual acuity pre-and post-treatment.

Results: The mean follow-up period was 2.7 ± 0.8 years. Quiescence of IK was achieved within 10 weeks of treatment for 47% and 81% of patients in the HSV IK and VZV IK cohorts respectively. Recurrent IK was observed in 38.6% and 50% of patients in the HSV IK and VZV IK cohorts. The mean time from quiescence to recurrence was 170 ± 130 days in the HSV cohort and 300 ± 289 days in the VZV IK cohort. Complete cessation of topical steroids preceded recurrence of IK in 69% and 63% of patients who experienced at least one recurrence in the HSV IK and VZV IK cohorts, respectively. No statistically significant changes in logMAR visual acuity between IK diagnosis and quiescence were detected in either cohort.

Conclusions: The time periods from herpetic IK diagnosis to quiescence and from quiescence to recurrence, as well as the rates of IK recurrence, may be helpful to clinicians attempting to determine a long-term treatment strategy for this patient population. The proportion of patients achieving quiescence within 10 weeks in the HSV IK group was higher than was seen in the seminal Herpetic Eye Disease Study (HEDS), as was the observed IK recurrence rate. The relatively high IK recurrence rates in this study may reflect increased detection of mild, pre-symptomatic IK with the SRP, due to close follow-up. Lack of change in logMAR pre- and post-treatment suggest that patients treated with SRP experienced mild, visually insignificant episodes of IK.

CONTROL ID: 3532830

SUBMITTER (NAME ONLY): Marta Alonso Plasencia

TITLE: Relationship among retinal vessel density, foveal avascular zone and diabetic retinopathy severity degree.

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Alonso Plasencia, R. Abreu-Gonzalez, Ophthalmology, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|M.A. Gomez-Culebras, Paediatric Surgery, Hospital Universitario Nuestra Senora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: Optical Coherence Tomography Angiography (OCTA) is a new diagnostic technology that can help us to a better understanding of diabetic retinopathy (DR) therefore validation of its results is needed.

We tested the hypothesis that DR severity is directly related with the vessel density (VD) and foveal avascular zone (FAZ) parameters measured with OCTA in a prospective observational study.

Methods: We performed a comprehensive ophthalmic examination including best corrected visual acuity (BCVA), anterior and posterior slit-lamp biomicroscopy, retinography, OCTA with RS-3000 Advance AngioScan (Nidek, Gamagori, Japan) and microperimetry with MP-3 (Nidek, Gamagori, Japan) in diabetic mellitus and healthy subjects. Diabetic retinopathy severity was graded following the International clinical diabetic retinopathy disease severity scale. Mean vessel density in the 4,5 x 4,5 mm centered in fovea protocol, FAZ area and FAZ perimeter were calculated and correlated with the DR severity. Also VD was calculated in smaller sectors (in a 9-grid-chart) and correlated with DR severity with Spearman correlation test.

Results: Between healthy and diabetic retinopathy eyes, 210 eyes we analyzed. The severity of the DR was correlated with de mean vessel density in the superficial plexus with a strength of - 0,507 (95% CI=[(-0,601)-(-0,398)]; $p<0,001$) and in the deep plexus with a strength of - 0,606 (95% CI=[(-0,684)-(-0,512)] ; $p<0,001$). By sectors, in the superficial plexus the nasal superior and nasal inferior were correlated with higher strength than the other sectors. In the deep plexus, the most correlated sectors were temporal to fovea, central sector and nasal to fovea.

The severity of the DR was also correlated with de FAZ area and perimeter with a strength of 0,276 (95% CI=[0,146-0,396]; $p<0,001$) and 0,335 (95% CI=[0,189-0,464]; $p<0,001$), respectively.

Conclusions: Diabetic retinopathy is a diabetic microvascular complication that can damage macular capillaries and perifoveal anastomotic arcades along the time. As a result, the vessel density is reduced in the macular area and FAZ area and perimeter are enlarged. This changes can be measured with OCTA and are more obvious as the severity of the DR increases.

Moreover, deep plexus is correlated with higher strength with the severity of the DR, as in previous studies is pointed, the injury of this plexus could be earlier and more severe.

CONTROL ID: 3532858

SUBMITTER (NAME ONLY): Jerome Garneau

TITLE: Anatomical and functional outcomes of retinal detachment associated with giant retinal tears compared to simple rhegmatogenous retinal detachment

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Garneau, M. Hébert, E. You, A. Lachance, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Faculté de médecine, Université Laval, Québec, Québec, CANADA | M. Hébert, E. You, A. Lachance, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Département d'ophtalmologie et ORL - Chirurgie cervico-faciale, Centre Universitaire d'Ophtalmologie, Hôpital du Saint-Sacrement, CHU de Québec-Université Laval, Québec, Québec, CANADA |

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ABSTRACT BODY:

Purpose: Retinal detachment (RD) associated with giant retinal tear (GRT) is a cause of rapidly developing and important vision loss especially in men. The surgical management is challenging for these patients as proliferative vitreoretinopathy (PVR) is often present. The single surgery anatomical success (SSAS) appears to be lower than in patients with simple rhegmatogenous RD (RRD) and the visual recovery is limited. The purpose of our study is to compare the functional and anatomical outcomes of primary surgery in patients with GRT-associated RD to patients with RRD.

Methods: We conducted a retrospective study at CHU de Québec – Université Laval. Medical records of all consecutive patients operated for primary RRD between 2014 and 2018 at our center were reviewed. Among the total cohort of 2247 patients, we included patients with simple RRD and patients with non-traumatic GRT-associated RD. We analyzed pre-, intra- and postoperative data, such as extension of giant tears, number of quadrants affected by the RD, macula and lens status, type of surgeries and best corrected visual acuity (BCVA) during follow-ups and compared them between both groups. We also compared the anatomical success rate of first surgery between GRT-associated-RD and RRD groups.

Results: There were 39 patients (1.7%) with GRT-associated RD and 1661 patients (74%) with RRD. Mean ages were 57.2 ± 8.3 years and 61.8 ± 11.9 years ($p=0.29$), while mean number of affected quadrants were 2.4 ± 0.8 and 2.4 ± 0.9 ($p=0.24$) in the GRT and RRD patients, respectively. In GRT patients, GRT size was 125 ± 39 degrees. Final BCVA was 0.25 ± 0.19 logMAR and 0.31 ± 0.47 logMAR ($p=0.76$) in GRT and RRD patients respectively. The SSAS was 82% (32/39) in the GRT-associated-RD group and 90% (1495/1661) in the RRD group ($p=0.10$). After correcting for other preoperative factors, GRT was an independent risk factor for worse SSAS (odds ratio: 0.422, $p=0.047$).

Conclusions: Our study compares the anatomical and functional results of GRT-associated RD and RRD patients. GRT-associated RD is still a challenge to treat as our results suggest that it may be associated with poorer SSAS than RRD.

CONTROL ID: 3532859

SUBMITTER (NAME ONLY): Blanca Molins

TITLE: Modelling retinal disease with a blood-retinal-barrier in vitro system combining human pluripotent stem cells and decellularized retinal tissue

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Molins, A. Adan, Institut d'Investigacions Biomediques August Pi i Sunyer, Barcelona, Catalunya, SPAIN|E. Garreta, C. Hurtado del Pozo, N. Montserrat, Institut de Bioenginyeria de Catalunya, Barcelona, Catalunya, SPAIN|A. Adan, Hospital Clinic de Barcelona, Barcelona, Catalunya, SPAIN|N. Montserrat, Institutio Catalana de Recerca i Estudis Avancats, Barcelona, Catalunya, SPAIN|

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ABSTRACT BODY:

Purpose: Reductionist approaches into mechanisms underlying diseases of the outer blood-retinal-barrier (oBRB), such as age-related macular degeneration and diabetic retinopathy (DR) have been hampered by the lack of optimal in vitro models utilizing human cells to provide the 3-D dynamic architecture and allow expression of the in vivo phenotype for both the retinal pigment epithelium (RPE) and the choroidal endothelium (EC). The main limitations of the current oBRB models also arise from the cell sourcing, the lack of a proper Bruch's membrane (BM) analogue, and lack of choroidal microvasculature with flow. Therefore, we aimed to develop an oBRB-on-a-chip biomimetic system to emulate the cellular interactions that occur in retinal inflammatory disorders.

Methods: We have generated a microfluidic device that allows the simultaneous co-culture of RPE with perfusable EC. Taking advantage of the differentiation potential of human pluripotent stem cells (hPSC), we optimized differentiation protocols to obtain hPSC-RPE and hPSC-EC from hPSC. On the other hand, by combining biomaterial engineering and decellularization protocols we designed a BM analogue that favors the co-culture of hPSC-RPE and hPSC-EC.

Results: Differentiated hPSC-RPE showed a phenotype similar to that of mature RPE, while differentiated hPSC-EC showed a mature endothelial phenotype as they showed tubulogenesis properties and expressed endothelial markers. The co-culture of EC with hPSC-RPE cells increased the RPE barrier functional activity, significantly increasing TEER and decreasing the basolateral secretion of VEGF. On the other hand, we developed a decellularization protocol to obtain decellularized BM (dECM-BM) that guarantees DNA removal while preserving collagen and elastin fibers. Moreover, the BM analogue successfully allowed the co-culture of EC and hPSC-RPE cells. Finally, we challenged the oBRB model with glucose oscillations and recapitulated the DR microenvironment.

Conclusions: Our oBRB biomimetic co-culture system recapitulates the complex cellular interactions of the oBRB, inducing an increased RPE barrier functional activity, and allowing for the emulation of inflammatory microenvironments occurring during retinal disease. Overall, this human oBRB in vitro model represents an optimal platform to study the inflammatory processes underlying retinal pathologies.

CONTROL ID: 3532864

SUBMITTER (NAME ONLY): Ofira Zloto

TITLE: Peripapillary and Fovea Avascular Zone OCT Angiography Parameters in Exfoliation Glaucoma vs Primary Open Angle Glaucoma vs Healthy Eyes

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Zloto, R. Veksler, I. Moroz, H. Goldberg, H. Levkovitch-Verbin, Sheba Medical Center The Goldschleger Eye Institute, Tel Hashomer, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To examine the differences in the peripapillary vascular parameters and foveal-avascular-zone (FAZ) vascularity parameters between primary open-angle-glaucoma (POAG) patients vs. exfoliation-glaucoma (XFG) patients vs. healthy subjects.

Methods: :This is cross-sectional study, comparative clinical-study. POAG and XFG patients and healthy subjects underwent a comprehensive ophthalmic examination, including visual field, optical-coherence-tomography (OCT) and OCT-angiography (OCTA) of the optic-disc and FAZ. Differences in peripapillary vessel-density (VD), perfusion-density (PD), and FAZ area and circularity were examined between groups, as well as correlations between clinical parameters and vascularity parameters for each glaucoma group.

Results: A total of 109 subjects were analyzed, including 45 with POAG, 30 with XFG, and 34 controls. The average peripapillary VDs were lowest among the XFG patients and highest among the controls ($P < 0.05$, ANOVA). The average peripapillary PD of the central ring was lowest in the PXF group and highest in the control group ($P = 0.02$, ANOVA). A significant negative correlation was found between the average peripapillary VDs and PDs of the inner ring and full ring and disease severity of the POAG patients. There was a significant positive correlation between the average peripapillary PDs of the central rings and full ring and the central-macular-thickness of the XFG patients ($P < 0.01$ and $P < 0.04$, respectively, Pearson correlation).

Conclusions: Peripapillary vascular parameters of the POAG and XFG patients were lower compared to those of normal participants. Investigations into the roles of OCTA as a diagnostic parameter for predicting the risk of glaucoma development and progression are warranted.

CONTROL ID: 3532870

SUBMITTER (NAME ONLY): Rita Laiginhas

TITLE: Persistent Hyper-Transmission Defects Detected on En Face Swept Source OCT Images are a Risk Factor for Geographic Atrophy in Eyes with Intermediate AMD

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Laiginhas, Y. shi, M. Shen, W.J. Feuer, G. Gregori, P.J. Rosenfeld, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if choroidal hyper-transmission defects (hyperTDs) with a greatest linear dimension (GLD) $\geq 250\mu\text{m}$ detected on en face swept source OCT (SS-OCT) images could serve as a risk factor for progression to geographic atrophy (GA) in eyes with intermediate AMD (iAMD).

Methods: This is a retrospective review of a prospective observational case series that included eyes with iAMD imaged with SS-OCT imaging (PLEX Elite 9000, Carl Zeiss Medics, Dublin, CA) at the Bascom Palmer Eye Institute. All subjects underwent 6X6mm scans and en face images were prepared using a slab positioned 64 to 400 μm beneath Bruch's membrane. Two graders independently evaluated all en face images for the presence of hyperTDs. Based on a previous study that defined persistent hyperTDs as having a GLD $\geq 250\mu\text{m}$, all hyperTDs $\geq 250\mu\text{m}$ were identified and tracked. Progression of these eyes to GA, nonexudative macular neovascularization (MNV), and exudative MNV were recorded and graded.

Results: A total of 182 eyes from 134 patients were included with a median follow up of 28 months (range 6-55). At baseline, 29 eyes had at least one hyperTD $\geq 250\mu\text{m}$ and all hyperTDs were found to be persistent. In those eyes without a hyperTD $\geq 250\mu\text{m}$ at baseline, 33 developed hyperTDs $\geq 250\mu\text{m}$ during follow-up and only one was found to be non-persistent. At the last available visit, 17 eyes progressed to GA, 14 eyes progressed to exudative MNV, and 4 eyes had nonexudative MNV. All foci of GA detected on B-scans were previously detected as hyperTDs $\geq 250\mu\text{m}$. A Kaplan-Meier analysis showed that the cumulative risk of developing GA reached 52% following the appearance of hyperTDs $\geq 250\mu\text{m}$. In a time-dependent Cox-survival regression sensitivity analysis, the increased risk of forming GA after detecting a hyperTD $\geq 250\mu\text{m}$ was 45 times greater compared with eyes without a hyperTD $\geq 250\mu\text{m}$ (hazard ratio=45, 95%CI 6-337; $p<0.001$).

Conclusions: Choroidal hyperTDs detected on en face SS-OCT images with a GLD $\geq 250\mu\text{m}$ were found to be persistent and associated with the development of GA. The detection of these lesions may serve as a useful biomarker for assessing eyes at risk for progression from iAMD to late AMD.

CONTROL ID: 3532876

SUBMITTER (NAME ONLY): Judith Goldstein

TITLE: Inconsistencies in Visual Acuity Data in Electronic Health Records

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Goldstein, X. Guo, Ophthalmology, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|M.V. Boland, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Challenges exist in harmonizing electronic health record (EHR)-derived data for secondary analysis, yet the problem is rarely studied. We aim to characterize data quality and quantify inconsistencies in EHR-derived visual acuity (VA) data during ophthalmology encounters.

Methods: Retrospective analysis of all VA entries from all eye care encounters across nine clinical locations and 9 subspecialties of the Wilmer Eye Institute between August 1, 2013 and December 31, 2015. Using the pre-defined VA menu options as the standard, we compared the VA entries to the menu options to determine their agreement on an overall and subspecialty level. VA entries were classified into 3 categories: (1) exact match of the VA entry to one of the 24 menu options; (2) partial discordance between the VA entry and the menu options but the entry could be converted to an accepted VA value; (3) total discordance between the VA entry and the menu options and not able to convert it to an accepted VA value.

Results: All VA entries from 513,036 encounters representing 166,212 patients were included. Of the 1,573,643 VA entries, 1,142,738 (72.6%) were an exact match to one of the menu options, 295,943 (18.8%) were partially discordant, and the remaining 134,962 (8.6%) were totally discordant, and classified as missing data. Documented VA entries with providers from comprehensive eye care (86.5%), oculoplastics (81.2%), and pediatrics/strabismus (77.1%) yielded the highest proportions of exact match with the menu options. VA entries during visits with providers from retina (17.5%), glaucoma (14.0%), neuro-ophthalmology (8.8%), and low vision (8.8%) had the highest rates of total discordance / missing VA data.

Conclusions: Inconsistencies exist in VA entries by ophthalmology subspecialty, affecting data quality measures of completeness, correctness and concordance. Transparency regarding data quality may reveal potential biases in VA documentation and should be considered before analyzing data between providers or institutions.

CONTROL ID: 3532879

SUBMITTER (NAME ONLY): Mervyn Thomas

TITLE: Genotypic and phenotypic spectrum of foveal hypoplasia

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Foveal hypoplasia (FH) is characterised by the continuation of inner retinal layers posterior to the foveola. Varying degrees of FH represent the different stages of arrested development of the fovea. The Leicester Grading System for FH divides typical FH into four grades and an additional grade for atypical FH. The grading system has been applied to various disorders including albinism, idiopathic infantile nystagmus (with or without FRMD7 mutations), PAX6 mutations, SLC38A8 mutations and AHR mutations. The grading system is used as a diagnostic and prognostic tool.

To date, it is unclear whether mutations of certain genes are associated with worse foveal morphology and prognosis. Thus, we aimed to perform a comparative study to characterise the genotypic and phenotypic spectrum of FH in the aforementioned genetic aetiologies.

Methods: In this multi-centre study, patients with known genetic associations with FH (n=288) were identified from one centre in UK and two centres in South Korea. Genetic diagnosis was achieved using targeted panel-based sequencing or exome sequencing. Due to the rarity of AHR mutations, we only included cases reported in the literature. Optical coherence tomography of the fovea was obtained in all subjects. Grades of FH (Leicester Grading System) were: Grade 1: shallow foveal pit, presence of outer nuclear layer widening, presence of outer segment (OS) lengthening; grade 2: grade 1 but absence of foveal pit, grade 3: grade 2 but absence of OS lengthening; grade 4: grade 3 but absence of ONL widening.

Results: The most common genetic aetiology for typical FH was albinism (74%), followed by PAX6 mutations (15%) and SLC38A8 mutations (9%). AHR and FRMD7 mutations were rare causes of FH. All grades of FH were seen in albinism and PAX6 mutations. In SLC38A8 mutations, we only observe grade 3 (80%) and grade 4 (20%) FH. In AHR mutations only grade 3 FH has been reported. In cases of FH and FRMD7 mutations only grade 1 FH was observed.

Conclusions: Albinism and PAX6 mutations are associated with much wider spectrum of arrested retinal development, however SLC38A8 mutations, AHR mutations and FRMD7 mutations have much narrower spectrum. Our data suggests that arrested retinal development occurs earlier in development in SLC38A8 and AHR mutations and much later in FRMD7 mutations. However, with albinism and PAX6 mutations the defined time period of foveal developmental arrest is more variable.

CONTROL ID: 3532885

SUBMITTER (NAME ONLY): Jahnvi Bansal

TITLE: VFQ Responses in Patients with Argus II Retinal Prosthesis System and the relationship with postoperative visual function testing

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this study is to analyze responses to the visual function questionnaire (VFQ) given to patients with the Argus II Retinal Prosthesis. Our primary objective is to assess whether the Argus II retinal prosthesis improved the quality of life of patients with profound retinal dystrophy over two years. We also aim to assess whether the VFQ scores correlated with visual function outcomes.

Methods: Five patients with profound retinal dystrophy were enrolled in this single institution cohort study. All surgeries were completed by a single surgeon at Stony Brook University Hospital. A VFQ was given to patients at baseline prior to implantation of Argus II Retinal Prosthesis and at year 1 and year 2 post implantation. Visual function data (Direction of Motion (DOM) and Square Localization (SL)) and OCT images (Cirrus-SD-OCT) were extracted from the Argus II Retinal Prosthesis Post Approval Study. Distances between electrode array-retina gap were measured at each electrode on the array with the Cirrus SD-OCT caliper measurement tool. Visual function tests were performed with the device OFF and ON at each visit. Data analysis was completed using IBM SPSS.

Results: 'VFQ-Social Functioning' score showed a statistically significant increase from M0 to M24 (paired t-test, $p < 0.05$). Spearman's correlation tests showed a strong positive association between direction of motion (DOM) and 'VFQ-Dependency' from M12 to M24 ($r_s = 0.745$, $p < 0.05$). There was additionally a strong negative association between square localization (SL) and 'VFQ-Ocular Pain' from M12 to M24 ($r_s = -0.701$, $p < 0.05$). Finally, a strong, positive association between electrode array-retinal gap distance and 'VFQ-Dependency' was found ($r_s = 0.778$, $p < 0.05$).

Conclusions: This study demonstrates that results on portions of the visual function questionnaire for the Argus II Retinal Prosthesis patients were significantly predicted by visual function outcomes. The VFQ thus can serve as a bridge between the patient's satisfaction with the implant and the clinical data in the form of square localization and direction of motion test accuracy. It is also essential to fully consider the VFQ results when assessing patients postoperatively, and can be helpful when used in long-term management.

CONTROL ID: 3532906

SUBMITTER (NAME ONLY): Rhys Ishihara

TITLE: NOVEL TACTILE BOTTLE TOP ADAPTORS TO FACILITATE MEDICATION COMPLIANCE IN VISUALLY IMPAIRED PATIENTS

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Eye drop compliance is five times worse in patients with impaired vision than normal vision despite the availability of current visual aids, such as colored bottle caps. The aim of the study is to test a novel 3D tactile label on the neck of the bottle, intended to increase accurate identification of medication and facilitate improved treatment compliance in low vision patients.

Methods: A 3D tactile bottle adaptor was designed in red, blue, green, and yellow color. Each adapter has a square or sphere shape on protruding spikes that varies in number of protrusions, 1, 2, or 3. In phase 1 clinical trial 20 healthy adults (ages 18 – 100 years) were enrolled and asked to wear a low vision simulator. Fogged goggles were used to simulate 20/200 or worse visual acuity, binocularly. Each subject was randomized to a preset group of six combinations of varying colors, protrusions, and shapes. The subjects were asked to identify the characteristics of the tactile devices in three presentations. The evaluations included color, number of protrusions, and shape at the end of the protrusions. Responses and the time to identify each characteristic were recorded.

Results: Accuracy of color identification was 100%, with an average time of 2.13 ± 1.03 seconds to identify. All subjects correctly identified the number protrusions when of one or two protrusions were presented (100%). The mean time taken was 3.13 ± 2.63 and 3.93 ± 4.48 seconds, respectively. Ninety-five per cent of the subjects identified 3 protrusions correctly with an average time taken of 4.53 ± 6.06 seconds. The identification success for square and sphere end pieces were 91.67% and 73.33%, with average time for identification of 9.87 ± 7.56 and 10.87 ± 8.96 seconds, respectively.

Conclusions: The novel 3D tactile adaptor on medication bottles was identified with great accuracy and speed by our low vision simulated subjects. Particularly, the color and number of protrusions were identified with the most accuracy. Although, patients more easily identified the square shaped end piece when compared to spheres, both were still identified relatively accurately and quickly. This data provides the basis for the phase II trial, in which patients with low vision will be tested for accurate medication identification.

CONTROL ID: 3532912

SUBMITTER (NAME ONLY): Eiji Murotani

TITLE: A computational approach to deriving the empirical frequency-of-seeing curves in patients with glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Murotani, Kahoku Eye Clinic, Kahoku, Ishikawa, JAPAN|

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ABSTRACT BODY:

Purpose: To derive the empirical frequency-of-seeing (FOS) curves in patients with glaucoma from longitudinal visual field data using a probabilistic modeling.

Methods: Series of 15 visual fields were taken from 130 glaucoma patients in the Rotterdam Eye Study (in the public domain). Smooth regression was used to prepare test-retest data for a hypothetical glaucoma patient. The author modeled the test-retest data as a multinomial distribution generated from a biased die with 42-faces (<0 , 0, 1, ..., 40dB). FOS curves, defined as cumulative gaussian function, were incorporated into the bias, based on the possible response sequences at four primary points ($\pm 9^\circ$, $\pm 9^\circ$) during the Humphrey Full Threshold testing. The parameters of FOS curves (luminance of inflection point, slope, and asymptotic maximum response probability) were estimated by a computer program written in the probabilistic programming language stan.

Results: FOS curves corresponding to each sensitivity from 0 to 35dB were successfully derived. As glaucoma progresses, the asymptotic maximum response probability declined monotonically from 99% (35dB) to 14% (0dB). In contrast, the horizontal shift of inflection point stopped spontaneously when the luminance reached approximately 19dB. Consequently, the psychophysical threshold for luminance increment was not changed substantially in moderate to severe stages (Fig. 1).

Conclusions: These results show that visual dysfunction in glaucoma patients is distinctly different from previously proposed. Interestingly, the luminance increment threshold appears to be inherently limited.

CONTROL ID: 3532915

SUBMITTER (NAME ONLY): Marina Tadrosse

TITLE: Socioeconomic Disparities and Survival Patterns Based on Geographic Location in Patients with Conjunctival Melanoma

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Tadrosse, A. Tadrosse, A. Yassa, M.T. Mikhael, M. Tadrosse, M. Mounir, S. Sadek, P.D. Langer, Rutgers New Jersey Medical School Institute of Ophthalmology and Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The impact of geography on survival rates in patients with conjunctival melanoma (CM) is unknown. Using a population-based study, we analyzed socioeconomic differences and survival outcomes in CM patients based on region of residence in the U.S.

Methods: Data on CM patients were extracted from the Surveillance, Epidemiology, and End Results U.S. database from 1975 to 2016. Patients were stratified based on geography depending on whether they resided in the Eastern, Western, or Southern U.S. Contingency table analyses followed by a post-hoc test were used to compare demographic and socioeconomic factors among CM patients. Cancer-specific relative survival (RS) and overall survival (OS) analyses were performed using the Kaplan-Meier method.

Results: A total of 664 patients were identified from the West (68.2%), the East (16.4%), and the South (15.4%). The proportion of patients presenting with a localized disease stage was comparable among all regions: 76.3% (West), 75% (East), 76.1% (South) [$p>0.05$]. The South had the largest proportion of patients who were black (4%) compared to the West (1.5%) and the East (0%) [$p<0.001$]. Mean patient income levels were significantly different across all regions: South (\$44,130), East (\$73,880), West (\$66,970) [$p<0.0001$]. The proportion of patients residing in metropolitan areas was similar in the East (94.5%) and the West (93.1%) but was statistically lowest in the South (62.7%) [$p<0.0001$]. The South had the greatest proportion of patients who were uninsured (8.5%) compared to the West (4.7%) and the East (0%) [$p<0.001$]. Five-year RS significantly differed based on region [East, 88.3%; West, 88.9%; South, 80.8%; $p=0.04$], so did the five-year OS [East, 78.4%; West, 81%; South, 70.1%; $p=0.03$].

Conclusions: The South had the greatest proportion of CM patients who were black, uninsured, had the lowest mean income level, and resided in non-metropolitan areas. Although disease stage profiles were similar among all three regions, both RS and OS were lowest for patients in the South. Clinicians should be cognizant of these geographic and socioeconomic trends while managing patients with CM.

CONTROL ID: 3532919

SUBMITTER (NAME ONLY): Marjean Kulp

TITLE: Prescribing Patterns for Hyperopia

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Hyperopia is the most common vision diagnosis in children. However, there are no evidence-based prescribing guidelines for managing hyperopia. The purpose of this study was to survey pediatric eye care providers to identify current patterns of prescribing for bilateral hyperopia when considering magnitude of hyperopia as well as other factors.

Methods: Pediatric eye care providers who were members of professional organizations or listservs were invited via email to participate in a Qualtrics survey study of current pediatric spectacle prescribing practices. Participants answered questions on "What factors influence whether or not you prescribe for bilateral hyperopia" and "At what level of bilateral hyperopia would you typically prescribe correction for a child with age-normal distance visual acuity (VA) and near visual function, and no strabismus (manifest deviation) or symptoms (select the lowest level in spherical equivalent [SE])". The distribution of responses given by ophthalmologists and optometrists was compared using Kolmogorov-Smirnov CDF test (after excluding "would not prescribe" responses).

Results: As shown in Table 1, eye care providers reported that symptoms, presence of astigmatism and/or anisometropia, reading problems, and accommodative function were most commonly considered when prescribing for hyperopia; cost and possibility of teasing by peers were least commonly considered. When considering factors for prescribing glasses for hyperopia, ophthalmologists and optometrists differed significantly for every factor except symptoms and possibility of teasing. Among factors showing the greatest differences were stereoacuity, emmetropization, and near visual acuity, where optometrists were more likely to consider these factors than ophthalmologists (Table 1). The level of hyperopia at which more than 50% of all eye care providers reported prescribing decreased with patient age from +5D at age 6 to <11 months (54.9%) to +4.5D for 1 to <2 years (53.9%) to +4D for 2 to <4 years (65.5%) to +3D for 4 to <7 years (51.1%) and for ≥7 years (59.2%). The distribution between ophthalmologists' and optometrists' responses was significantly different ($p < 0.0001$).

Conclusions: Disagreement remains among eye care providers in prescribing for children with low and moderate hyperopia.

CONTROL ID: 3532927

SUBMITTER (NAME ONLY): Mohamed Estai

TITLE: Incentives and barriers to diabetic retinopathy screening in Australian general practices

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Despite the appeal of retinal photography in facilitating retinal screening including incentives through Medicare Benefits Schedule (MBS) items (12325 and 12326), comprehensive diabetic retinopathy (DR) screening has not been achieved in Australia. This study aimed to identify the incentives and barriers to conducting DR screening in general practices.

Methods: A qualitative study, involving in-depth interviews, was conducted between November 2019 and March 2020. Fifteen general practitioners (GPs) from urban and rural practices in Australia were recruited. Data were collected using a semi-structured interview guide. All interviews were conducted over the phone, and each interview lasted up to 45 minutes. Recorded data were transcribed verbatim. The thematic analysis was carried out using NVivo to organise data and classify recurrent themes.

Results: Thirteen male and two female GPs aged 54.7 ± 15.5 years completed the interviews. Seven participants were practising in urban areas, while eight were practising in rural areas. All participants had access to a direct ophthalmoscope, but none owned retinal cameras. None of the participants performed DR screening in their general practices. Only three participants were aware of the MBS items that allow GPs to bill for retinal photography and image reporting. Seven themes (a combination of incentives and barriers) emerged, namely (i) GPs awareness of MBS items; (ii) optometrists are perceived as ideal for DR screening; (iii) GPs are not competent in DR detection; (iv) costs; (v) time constraints; (vi) the need for dedicated staff to take the responsibility of DR screening; (vii) the use of artificial intelligence in DR detection.

Conclusions: The study identified specific strategies to enable the wider implementation of DR screening in general practice, notably investing in a nationwide awareness campaign to maximise the use of MBS items, improve GPs' competency in DR detection, subsidising equipment costs, particularly for small or rural practices, and the need for a champion ace to integrate DR screening into practice workflow. Findings can guide the current clinical guidelines and policymakers to develop a better framework of key enablers that underpin the successful implementation of DR screening. Future research is needed to identify other barriers from the patients' perspectives.

CONTROL ID: 3532959

SUBMITTER (NAME ONLY): Ali Ghareeb

TITLE: Real-life outcomes of dexamethasone intravitreal implant (Ozurdex) in diabetic macular oedema for treatment-naive eyes compared to anti-VEGF non-responders at three months post-treatment

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Ghareeb, T. Lau, M. Kishikova, A. Kotagiri, I. Masri, J. Smith, D. Varma, D. Steel, M. Habib, Sunderland Eye Infirmary, Sunderland, Tyne and Wear, UNITED KINGDOM|A.E. Ghareeb, D. Steel, Biosciences Institute, Newcastle University, Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diabetic macular oedema (DMO) is a common cause of vision loss in the working-age population. Ozurdex is used as a first or second line treatment for DMO. The functional and structural outcomes of treatment have been reported, however its relative efficacy after anti-VEGFs have failed is yet to be determined. The purpose of our study is to present real-life data of functional and structural outcomes in patients with DMO treated with Ozurdex first line as compared to Anti-VEGF non-responders at 3 months after first Ozurdex injection.

Methods: Retrospective analysis for all patients with DMO treated with Ozurdex implant between January 2016 to October 2019, at Sunderland Eye Infirmary, UK. The full cohort was subclassified to treatment-naive eyes and anti-VEGF non-responders' eyes. The primary outcome measures were observed at 3 months post implant for the 2 groups, and included mean changes in best-corrected visual acuity (BCVA) and central macular thickness (CMT) from baseline. Secondary outcomes included proportions of patients with ≥ 10 letters gain or loss; $\geq 20\%$ of CMT gain or loss and final BCVA and CMT. Baseline characteristics of both treatment-naive eyes and Anti-VEGF non-responders were compared including age, sex, diabetes duration, DMO duration, comorbidities, baseline vision and CMT.

Results: We included 89 eyes (74 patients), with 30 treatment naïve eyes and 59 anti-VEGF non-responders. The improvement in VA in the first group was 5.7 and 5.3 letters in the second group ($p=0.85$), with the final VA of 63.9 and 58.2 letters, respectively ($p=0.13$). CMT decreased in the naïve and previous anti-VEGF groups at three months ($-83.21\mu\text{M}$ vs $-88.47\mu\text{M}$, respectively; $p=0.85$). In the treatment naïve versus previous anti-VEGF groups, we found ≥ 10 letters gain was experienced in 26.67% and 20.69% ($p=0.82$), ≥ 10 letters loss in 3.33% and 5.17% ($p=0.82$), and $\geq 20\%$ of CMT reduction in 48.28% and 44.07% ($p=0.82$), respectively.

Conclusions: Our study shows no statistically significant difference in functional or structural outcomes between treatment-naïve and previous anti-VEGF groups at three months. These results confirm that the short-term efficacy of Ozurdex implant is comparable both as a first or second line of treatment in patients with DMO.

CONTROL ID: 3532960

SUBMITTER (NAME ONLY): Jordan Deaner

TITLE: Reduction in Cystoid Macular Edema and Ellipsoid Zone Reconstitution in Non-paraneoplastic Autoimmune Retinopathy Treated with Anti-Interleukin-6 Monoclonal Antibodies

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Deaner, G.J. Jaffe, D. Grewal, Ophthalmology, Vitreoretinal Surgery, Duke University, Durham, North Carolina, UNITED STATES|R.T. Keenan, L. Carnago, Medicine, Division of Rheumatology and Immunology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the effect of anti-interleukin-6 (IL-6) receptor monoclonal antibodies tocilizumab and sarilumab eyes with non-paraneoplastic autoimmune retinopathy (npAIR) with cystoid macular edema (CME)

Methods: Retrospective case series including 14 eyes of 8 patients with npAIR and CME treated with anti-IL-6 medications. Visual acuity (VA) and central subfield thickness (CST), total macular volume (TMV), and ellipsoid zone integrity change as measured optical coherence tomography were extracted from charts prior to and at 3, 6, 12, 18, and 24 months after anti-IL-6 therapy was initiated. Eyes that had a >20% reduction in CST were defined as treatment responders, >20% increase in CST as failures, and ≤20% change in CST as stable.

Results: Eleven eyes of six patients had failed multiple prior immunosuppressive therapies. There was a significant reduction ($P<.05$) in CST baseline ($473.1\text{ }\mu\text{m}$) after initiation of anti-IL-6 therapy that began at 3 months ($389.2\text{ }\mu\text{m}$) and continued through 24 months ($348.7\text{ }\mu\text{m}$). Similarly, there was a significant reduction ($P<.05$) in TMV baseline ($10.15\text{ }\mu\text{m}^3$) after initiation of anti-IL-6 therapy that began at 3 months ($8.91\text{ }\mu\text{m}^3$) and continued through 24 months ($7.67\text{ }\mu\text{m}^3$). VA improved from 0.84 to 0.52 at 24-month follow-up, a change that did not reach statistical significance ($P=.157$). Nine of 14 eyes (64.3%) were treatment responders, 4 eyes (28.6%) were stable, and 1 eye (7.1%) was a treatment failure. See Table 1 for full results. Prior to starting anti-IL-6 therapy, 9 of 14 eyes (64.3 %) of eyes had EZ integrity loss which was evident on macular OCT with an average loss of $30.0\text{ }\mu\text{m}$ per month. After starting IL-6 therapy, there was a significant decrease in rate of EZ change, experiencing an average restoration of $22.7\text{ }\mu\text{m}$ per month ($P=.008$). It was possible to discontinue rituximab in all 4 patients who were on this therapy for AIR, and at least one eye of all patients responded to anti-IL-6 treatment. No patient had adverse events or required discontinuation of therapy while on anti-IL-6 medication.

Conclusions: In this cohort of patients with npAIR and CME, treatment with anti-IL-6 medications tocilizumab and sarilumab, was associated with reduced CME, partial restoration of the ellipsoid zone, and a trend towards improved VA, while reducing burden of prior immunosuppressive therapies.

CONTROL ID: 3532998

SUBMITTER (NAME ONLY): Francine Behar-Cohen

TITLE: Role of corticoids in retinal pigment epithelium physiopathology

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.F. Behar-Cohen, M. Zhao, E. Gelize, From physiopathology of retinal diseases to clinical advances, Centre de Recherche des Cordeliers, Sorbonne Université, Université de Paris INSERM, Paris, FRANCE|F.F. Behar-Cohen, Ophthalmopole, stance Publique Hôpitaux de Paris, Hôpital Cochin, Paris, FRANCE|L. Kowalczyk, Y. arsenijevic, J. Canonica, Ophthalmology, University of Lausanne, Jules Gonin Eye Hospital, Fondation Asile des Aveugles., Lausanne, SWITZERLAND|E. Pussard, U1185, Inserm, Le Kremlin-Bicêtre, Paris, FRANCE|D. Le Menuet, Inserm UMRS1124 Université Paris Descartes, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Corticoids bind to glucocorticoid (GR) and mineralocorticoid receptor (MR), both expressed in the RPE but the transcriptional regulations induced by corticoids have not been fully explored.

The purposes are: - to analyzed corticoids-induced transcriptional regulations in human RPE derived from iPS (iRPE), - to measure corticoids in human ocular media, - to analyze the retinal phenotype of P1hMR mice that over express human MR.

Methods: GR and MR expression was analyzed in iRPE cells and corticoid-induced nuclear translocation was quantified. Corticoids were measured in human ocular media using a liquid chromatography-tandem mass spectrometry. iRPE cells were exposed to aldosterone, the MR-specific agonist, cortisol and cortisol + RU-486, a direct GR antagonist . Transcriptomic analysis identified genes differentially regulated at 24 hrs after stimulations. Validation was performed by RT-PCR, western-blot and immunohistochemistry. In order to evaluate the biological consequence of MR overactivation in the retina, the retinal phenotyping of mice overexpressing the human MR (P1hMR) was analyzed.

Results: iRPE cells stably express functional MR and GR. They do not produce or metabolize corticoids. In human aqueous humor and vitreous, cortisol and cortisone were measured at salivary levels but aldosterone was detected, suggesting that cortisol activates GR and MR in RPE cells. Genes regulated similarly by aldosterone and by cortisol + RU-486 represent MR activated genes. They encodes proteins involved in extracellular matrix remodeling, epithelia-mesenchymal transition (EMT) and RPE cell migration (Itgb3, Plaur and Fosl1), immune balance (Tnfsf18, Ptrx3), and in RPE phagocytosis (Mrp3, Gfra2, Ptrx3). Down-regulated genes (Cnn1, Mgp, Amtn) encodes proteins involved in extracellular matrix remodeling and choroid innervation.

P1hMR mouse showed choroidal vasodilation, elongation of photoreceptors outer segments, focal alteration of the RPE/ choroid interface, migration of RPE cells and focal choroidal excavations, mimicking human pachychoroid phenotype

Conclusions: The human RPE is a mineralo-sensitive epithelium. Activation of MR pathway in the RPE induces the regulation of genes involved in RPE differentiation, immune regulation, synaptic transmission and angiogenesis, and extracellular matrix remodeling. P1hMR mouse confirmed the pathogenic role of MR overactivation and its possible link with pachychoroid epitheliopathy.

CONTROL ID: 3533001

SUBMITTER (NAME ONLY): Hursuong Vongsachang

TITLE: The impact of weather and seasons on falls and physical activity among older adults with glaucoma: a prospective cohort study

SESSION TITLE: Visual Impairment and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Vongsachang, A. Mihailovic, P.Y. Ramulu, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|J. E, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Identifying environmental risk factors is important to prevent falls in elderly with visual impairment. We examined the relationship between weather and seasons on falls and physical activity in a prospective cohort of older patients with visual field (VF) loss.

Methods: Older patients with glaucoma were recruited from the Wilmer Eye Institute to participate in a three-year longitudinal study. Monocular VF results were combined to generate integrated VF sensitivity for each patient. Participants recorded the occurrences of falls and injurious falls using a monthly calendar over the three-year period. Steps and active minutes were recorded for 7 days consecutively at baseline and in each study year using an accelerometer. Average daily temperature and precipitation data were merged with corresponding study dates (National Centers for Environmental Information). Study dates were assigned to Northern Hemisphere astronomical seasons. Using multivariable logistic and negative binomial regression models incorporating generalized estimating equations, we analyzed the association between weather/season with 1) the odds of falling and having an injurious fall and 2) average daily steps and active minutes.

Results: Across 240 participants (Table 1), there were 406 falls recorded over 7569 person-months, of which 163 were injurious (40%). The odds of falling did not vary with temperature, precipitation, or seasons. However, every ten-degree Celsius increase in average daily temperature was associated with 24% higher odds of having an injurious fall, as opposed to non-injurious (OR=1.24, 95% CI [1.01, 1.53], p=0.04). Injuries resulting from a fall were more likely to occur outdoors, as opposed to indoors, with higher average temperatures (OR per 10 degrees C=1.46, 95% CI [1.03, 2.07], p=0.03) and summer season (OR=2.69 vs winter, 95% CI [1.12, 6.50], p=0.03). Temperature, precipitation, and seasons were not significantly associated with average daily steps or activity (Table 2).

Conclusions: Although overall falls and physical activity did not vary with weather or seasons, warmer weather may be linked with conditions that lead to injurious falls among older individuals with visual impairment. Falls should be understood as a year-round problem in the visually impaired, though the likelihood of injury and the location of fall-related injuries may change with season/temperature.

CONTROL ID: 3533003

SUBMITTER (NAME ONLY): Amisha Dave

TITLE: Comparison of Cone Density Measurements in Patients with Retinitis Pigmentosa and Healthy Controls using Adaptive Optics

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Dave, C. Malley, R. Mays, M. Arango, L. Huryn, W.M. Zein, B.P. Brooks, T. De Silva, C. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics (AO) is a retinal imaging technique with potential to characterize the photoreceptor mosaic and improve current diagnostics. However, variability in acquisition protocols, instrumentation, and image quality require studies to measure and interpret pathology in AO images. This work analyzes cone density (CD) measurements in a clinical setting between healthy controls (HC) and retinitis pigmentosa (RP) patients.

Methods: AO images were acquired using the rtx1 flood-illuminated AO camera (Imagine Eyes, Orsay, France) from the right eyes of 10 RP patients and 3 HC. All subjects had five 4°x4° images acquired centered at the following locations relative to the fovea: (0°,0°), (2T°,0°), (2N°,0°), (0°,+2°), and (0°,-2°). Intrasession repeatability of CD measures was investigated using three images in four overlapping 2°x2° quadrants. Automation facilitated counting of ~190 densely sampled regions of interest using AOdetect per 4°x4° image. Comparisons of CD were made between healthy eyes and eyes with different severities of RP as determined by 24-2 Humphrey visual field mean deviations.

Results: HC had statistically higher CDs (mean 21275 ± 2890 cones/mm²) across the sampled region when compared to all RP patients (mean 12903 ± 3001 cones/ mm², p = <.0001).

There was a significant decrease in CD in all severities of RP compared to HC. Within the RP patients, the CD of severe RP patients (mean 7357 ± 1703 cones/mm²) was significantly decreased compared to mild and moderate RP patients. Within a single image of a patient, there was no statistically significant difference between CD within a 1° radius versus a 3° radius from the fovea.

Within each patient population, there was no statistically significant difference in repeated CD measurements in overlapping 2°x2° quadrants. HC showed fair intrasession repeatability (mean 21348 ± 1998 cones/ mm²), while RP patients showed good to excellent intrasession repeatability (mean 13269 ± 1146 cones/ mm²).

Conclusions: CD measurements in AO images acquired in a clinical setting reveal gradual changes that correlate with the disease severity of RP. The measured variability of the cone counting algorithms was not a substantial contributor to the changes measured due to disease. Quantitative measurements from AO imaging could help effectively measure and interpret the changes due to RP.

CONTROL ID: 3533013

SUBMITTER (NAME ONLY): Stephen LoBue

TITLE: Risk Factors for Acute Elevated Intraocular Pressure after Intravitreal Anti-VEGF Injections

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. LoBue, A. Michael, Ophthalmology, SUNY Downstate Health Sciences University, New York, New York, UNITED STATES|S. LoBue, A. Guagliardo, T. Chang, M. Davis, S. Fish, Ophthalmology, Acuity Eye Group & Retina Institute Pasadena, Pasadena, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study the effects of intravitreal injection (IVI) on intraocular pressure (IOP) and to predict the patient population which may be most susceptible to acute elevations in IOP.

Methods: A three-month, prospective study of patients receiving IVI of anti-VEGF at the Acuity Eye Group. IOP was measured pre-injection as well as post-injection at 10-minute intervals up to 50 minutes. Patients with an IOP greater than 35mmHg at 30 minutes received an ACP. Patients with an IOP below 35mmHg were monitored without intervention.

Results: 617 patients were included, with a mean age of 73 years. Patients received IVI for diabetic retinopathy (n = 199), age-related macular degeneration (n= 355), and retinal vein occlusion (n = 63). Average pre-injection IOP was 16 +/-5 mmHg. Average post-injection IOP was 25, 27, 28, 27, and 29 mmHg at 10, 20, 30, 40, and 50 minutes respectively (P<.0001). The ACP group (n=17) had a pre-injection average IOP of 24 +/- 7 mmHg (p<.0001), and post-injection IOP of 47 +/- 10 and 44 +/- 9 mmHg at 10 and 20 minutes respectively (p<.0001). Overall, 33% of patients with a pre-injection IOP > 25 mmHg and 50% with a pre-injection IOP > 30 mmHg required ACP. A diagnosis of glaucoma was higher in the ACP group compared to the non-ACP, 82.3% vs 14.2% (p<0.0001), and a diagnosis of glaucoma suspect was also higher in the ACP group vs non-ACP, 17.6% vs 9.0 respectively (p>0.05). Patients with a pre-injection IOP > 25 mmHg and a history of glaucoma had a 58.3% rate of ACP. The number of IVI were similar between the ACP and non-ACP group at 22 +/- 10 vs 19 +/- 11 injections, respectively. A 31-gauge needle had a higher incidence of ACP when pre-injection IOP > 25 versus 30-gauge, 42.9% vs 29.4% respectively (p>0.05).

Conclusions: IVI of anti-VEGF medication is associated with a transient but significant increase in IOP. Patients with a pre-injection IOP of 25mmHg or greater, combined with a history of glaucoma, may be at a higher risk of prolonged IOP increases and may benefit from prophylactic ACP.

CONTROL ID: 3533022

SUBMITTER (NAME ONLY): Muneeb Faiq

TITLE: Effects of chronic intraocular pressure elevation on cerebrospinal fluid dynamics in the optic nerve

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.A. Faiq, V. Adi, J. Zhu, S. Khoja, A. Sainulabdeen, C. Parra, G. Hamilton-Fletcher, G. Wollstein, J.S. Schuman, K. Chan, Department of Ophthalmology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|J. Zhu, Department of Ophthalmology, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing, CHINA|C.H. Lee, J. Zhang, K. Chan, Department of Radiology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|C.K. Leung, Department of Ophthalmology, The Chinese University of Hong Kong, Hong Kong, CHINA|G. Wollstein, J.S. Schuman, Department of Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Though chronic intraocular pressure (IOP) elevation and glymphatic disturbances have been implicated in various optic neuropathies, the relation between IOP and optic nerve (ON) cerebrospinal fluid (CSF) dynamics has not been sufficiently investigated. We employed contrast-enhanced MRI (CE-MRI) for in vivo investigation of CSF dynamics in the ON with and without chronic IOP elevation.

Methods: IOP was elevated unilaterally in adult C57BL/6J mice (n=15, Group 1) by intracameral injection of in situ cross-linking hydrogel. Chronic IOP elevation in the injected eye (Group 1a) was confirmed at 4 weeks post-injection, at 19.37 ± 3.41 mmHg (mean \pm SEM) relative to the fellow, untreated eye (Group 1b) at 11.39 ± 3.74 mmHg. Another 20 healthy naive mice received no intervention to either eye (Group 2). A polyethylene tubing was inserted intrathecally at the lumbar region (L4-L5) followed by CE-MRI using a 7-Tesla Bruker BioSpec scanner. Contrast dynamics was monitored using 3D T1-weighted FLASH sequence with an isotropic resolution of $78 \times 78 \times 78 \mu\text{m}^3$. Twelve 10-min continuous scans were acquired, beginning with 3 baseline acquisitions followed by 30 min of Gd-DTPA contrast infusion while the scanning continued till the 12 timepoint. Change in contrast intensity (CI) over time was quantified in 6 anatomical regions of interest (ROIs) viz. posterior ON subarachnoid space (ONSAS-P), anterior ON SAS (ONSAS-A), posterior ON parenchyma (ONP-P), anterior ON parenchyma (ONP-A), olfactory bulb (OB, positive control), and muscle tissue (MT, negative control).

Results: Between group ANOVAs were significant for each ROI in the ON (all p's<.001), and not significant for control regions. Post-hocs revealed that for ONSAS-A, Group 1a had lower CI than Group 1b (p<.001) and Group 2 (p<.001), while Groups 1b and 2 also differed (p=.011). For ONP-A, Group 1a had lower CI than Group 1b (p=.003) and Group 2 (p<.001), with no difference between Groups 1b and 2. For ONSAS-P, Groups 1b and 2 CI differed significantly (p=.011), and for ONP-P, Group 1a had lower CI than Group 1b (p<.001) and Group 2 (p=.003), while Groups 1b and 2 CI also differed (p=.004).

Conclusions: Chronic IOP elevation is associated with significant decrease in the CSF flow into the ON SAS and ON parenchyma. CSF dynamics is also altered in the contralateral ON projected from the fellow eye with normal IOP.

CONTROL ID: 3533023

SUBMITTER (NAME ONLY): Brandon Pham

TITLE: Oral montelukast is associated with decreased odds of diabetic retinopathy

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Pham, W. Matsumiya, A. Akhavanrezayat, G. Uludag, C. Yasar, H. Ghoraba, J.J. Hwang, S. Lajevardi, B.C. Lam, J. Regenold, N. Yavari, V. Bazojo, I. Karaca, A. Mobasserian, H. Nguyen, Q.D. Nguyen, Ophthalmology, Byers Eye Institute at Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent research using experimental animal models has suggested that montelukast, a leukotriene receptor antagonist, may play a role in preventing diabetic retinopathy (DR). However, few studies have investigated its potential efficacy in humans. This case-control study was conducted to investigate whether use of oral montelukast was associated with decreased odds of DR in patients with diabetes mellitus.

Methods: Medical records of subjects presenting to a tertiary eye center between November 1, 2019 and November 1, 2020 were collected using the Institutional Cohort Finder tool and analyzed. ICD codes were used to identify patients with diabetes mellitus (E08-E13) and DR (E08.31-35/E11.31-35). Control patients (with diabetes mellitus but without DR) who presented to our center during a similar time period were used to calculate crude and adjusted odds ratios for oral montelukast. Only subjects with no missing data were analyzed in this study. Using available clinical records, patients were also assessed for the presence of DR risk factors, including elevated hemoglobin (Hb)A1c levels, smoking history, end-organ damage (i.e. diabetic nephropathy and neuropathy), hypertension, hyperlipidemia, and non-Caucasian race.

Results: A total of 563 patients with DR were evaluated at our center during the study period. In our study, 14 of the 210 (6.6%) patients were identified to have used oral montelukast prior to the diagnosis of DR, compared to 60 of 353 controls (16.9%) (univariable OR: 0.38, 95% CI: 0.21-0.68, P = 0.0012). In the multivariate logistic regression analysis, use of oral montelukast was significantly associated with decreased odds of DR (adjusted OR: 0.32, 95% CI: 0.16-0.62, P = 0.0009), as well as identification as a "never smoker" (adjusted OR: 0.49, 95% CI: 0.30-0.79, P = 0.004). Several risk factors were significantly associated with increased odds of DR, including hypertension (adjusted OR: 5.81, 95% CI: 3.62-9.33, P < 0.0001), hyperlipidemia (adjusted OR: 5.51, 95% CI: 3.39-8.95, P < 0.0001), and higher HbA1c (OR 1.35, 95% CI: 1.21-1.51, P < 0.0001).

Conclusions: Use of oral montelukast is associated with decreased odds of DR in patients with diabetes mellitus; subjects with DR are less likely to have consumed oral montelukast. Given the role of chronic inflammation in the pathophysiology of DR, these protective benefits may be related to montelukast's anti-inflammatory properties.

CONTROL ID: 3533026

SUBMITTER (NAME ONLY): Huy Nguyen

TITLE: kinematics of novel intravitreal steroid implant injector in simulated vitrectomized and non-vitrectomized eyes

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Intravitreal implants are routinely used for depots of sustained drug delivery. Injections of current market devices have been reported to cause retinal hemorrhages and macular holes from direct mechanical forces during injection. We provide kinematic analysis in simulated vitreous and saline to confine the range of safe injection velocities from novel intravitreal implant delivery devices.

Methods: 10 proprietary Aerie Pharmaceutical intravitreal delivery systems were recorded at 240 frames-per-second at 1024×1024 pixel resolution. 396µg implants of dimensions 265 x 265 x 4500µm were injected with fast and slow velocities into an open top chamber at room temperature and pressure. 4 implants were launched with slow velocity into normal saline. 4 implants were launched with high velocity into vitreous substitute - hyaluronic acid 1%. 2 implants were launched with high velocity into saline. Empiric initial velocity coming out of the injector barrel (v_o) was derived by launching implants straight vertically into air and assumed negligible air resistance. Adult eye retina to retina diameter is assumed to be between 19.4mm to 25.8mm (22.9mm average).

Results: Injection velocity (v_o) was 3431 ± 50 mm/s for fast injections. The 4 slow velocity injections delivered the implants exactly at the site of injection in both media. In hyaluronic acid, fast injections delivered implants to a maximum displacement (x_{max}) of 16.7 ± 3.2 mm in 25 ± 5 ms. In saline, fast injections delivered implants to x_{max} of 28.5 ± 5 mm in 50ms.

Conclusions: Slow speed injections would likely be best used for local implant placement (at site of injection) in any medium. V_o of 3431 mm/s is approximately the upper limit of injection velocity for these implants in non-vitrectomized eyes as the x_{max} range encompasses maximum retina-to-retina distance, however could be further optimized to account for injection angles that direct toward shorter paths. Smaller v_o should be used for vitrectomized eyes as modeled by saline. Empiric drag coefficients for these implants would help calculate force transmitted to the retina upon contact.

CONTROL ID: 3533030

SUBMITTER (NAME ONLY): Noraliz Garcia-O'Farrill

TITLE: Modified-dropless protocol (nil intraocular) for Micro-incision Vitrectomy Surgery (MIVS)

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Garcia-O'Farrill, G.T. Brown, A.A. Hunter, Oregon Eye Consultants, LLC, Eugene, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prophylactic topical eye drops to be instilled by the patient after undergoing vitreoretinal surgery can be inconvenient and expensive. We performed a retrospective clinical study to evaluate the outcomes of a novel, modified-dropless protocol for 25-gauge and 27-gauge (27G) micro-incision vitrectomy surgery (MIVS) that omits any intraocular injections of antibiotics or steroids.

Methods: The Institutional Review Board approved a database review of all patients with any surgical indication for MIVS that underwent the modified-dropless protocol performed by a single surgeon at Oregon Eye Consultants, LLC. Eighty-nine patients who had surgery between February to November 2020 were eligible from 108 total surgeries. Only patients who underwent a surgical peritomy were not candidates for the modified-dropless protocol. Instead of pre- or post-operative drops, at the time of surgery patients were given a 0.5cc subconjunctival injection of a 1:1 Cefazolin (50mg/cc):Dexamethasone (10mg/cc) in the inferior fornix and 0.5cc of posterior Sub-Tenon's Kenalog (STK). No intravitreal injections were administered. Fourteen patients who had a penicillin allergy were instead given separate subconjunctival injections of 0.25cc each of Vancomycin (10mg/cc) and Dexamethasone. Mean follow up was 69 days.

The primary endpoint was postoperative cases of endophthalmitis within 3 months. Secondary endpoints consisted of Best-Corrected Distance Visual Acuity (BCVA), intraocular pressure (IOP), and postoperative complications (retinal detachments, inflammation, need for additional surgery) within 3 months of surgery.

Results: The study comprised 89 eyes from 46 females and 43 males (mean age 69.9±9.7; range 37-93 years). Pre-operatively there were 41 phakic and 48 pseudophakic eyes. All surgeries were performed with the 27G MIVS platform.

There were no cases of postoperative endophthalmitis. Mean logMAR BCVA improved from 0.65±0.64 to 0.54±0.58 postoperatively (p=0.03). Excluding patients who had silicone oil tamponade, postoperative BCVA improved from 0.58±0.60 to 0.46±0.50 (p=0.01). Mean IOP increased from 14.3±3.7 to 15.1±4.1 postoperatively (p=0.12).

Conclusions: A modified-dropless postoperative protocol involving subconjunctival and posterior sub-Tenon's injections only may be a safe and convenient alternative to topical eye drops for patients undergoing MIVS but additional and larger studies are needed.

CONTROL ID: 3533043

SUBMITTER (NAME ONLY): Golnoush Sadat Mahmoudi Nezhad

TITLE: Comparison of GCL and GCIPL Measures for Detection of Early Glaucoma

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Mahmoudi Nezhad, V. Mohammadzadeh, J. Martinyan, K. Edalati, D. Yaldazadeh, M. Mirzaei, J. Caprioli, K. Nouri-Mahdavi, Glaucoma Division, Stein Eye Institute, David Geffen School of Medicine, Los Angeles, California, UNITED STATES|B. Zhou, N. Amini, Department of Computer Science, California State University Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Test the hypothesis that macular ganglion cell layer (GCL) measurements are able to detect early damage better than ganglion cell/inner plexiform layer (GC IPL) thickness.

Methods: First cohort included 84 glaucoma eyes with visual field (VF) mean deviation (MD) ≥ -6 dB and 129 normal eyes. 8x8 GCL and GC IPL macular grids were exported and 5 superior and inferior macular sectors were defined (Figure 1). Areas-under-ROC curves (AUC) for sectoral GCL and GC IPL measures were compared.

A second cohort of 98 glaucoma and 48 normal/glaucoma suspect (GS) eyes with GMPE macular scans had GCL/GCIPL deviation maps analyzed. Proportion of areas with abnormal ($<5\%/1\%$ cutoffs) and supernormal thickness ($>95\%/99\%$ ile cutoff) was estimated on deviation maps (Figure 2). Differences in extent of abnormal and supernormal regions were compared in glaucoma and normal/GS subjects.

Results: In the first cohort, average VF MD was -3.0 ± 1.8 dB in glaucoma eyes. Inferior sector 2 thickness performed best for detection of glaucoma with both GCL and GC IPL (AUCs=0.895; $p>0.05$). VF MD was -2.3 ± 1.7 dB in glaucoma eyes in the second cohort. In the central elliptical area, extent of GCL damage at $<5\%$ and 1% cutoffs was $27.4\% \pm 26.0\%$ and $15.2\% \pm 20.6\%$ vs. $26.7\% \pm 26.4\%$ and $14.6\% \pm 20.6\%$ for GC IPL, respectively, in glaucoma eyes ($p=0.01$ and $=0.02$, Figure 2a); the extent of GCL and GC IPL supernormal regions were similar ($p=0.87$). In normal eyes, extent of GCL abnormality at 5% and 1% cutoffs were $16.0\% \pm 18.9\%$ and $5.9\% \pm 10.7\%$ vs. $15.0\% \pm 18.4\%$ and $5.3\% \pm 10.5\%$ for GC IPL ($p=0.07$ and $=0.01$); GCL and GC IPL supernormal areas were similar ($p=0.93$). Results for the entire scan area were similar (Figure 2b). Extent of abnormality at $<1\%$ cutoff best predicted glaucoma (AUC=0.730 vs. 0.700 for GCL vs. GC IPL).

Conclusions: Macular GCL deviation maps are more likely than GC IPL to flag abnormality with acceptable specificity; however, the difference is clinically unremarkable. GCL and GC IPL sectoral thickness are equivalent for detection of glaucoma.

CONTROL ID: 3533048

SUBMITTER (NAME ONLY): Frank Spors

TITLE: Relationship Between Add Power of Multifocal Soft Contact Lenses and Higher-Order Wavefront Aberrations in the Context of Myopia Management

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study investigated changes in higher-order wavefront aberrations (HOA) in eyes wearing Proclear multifocal soft contact lenses with two different add powers in the context of myopia management.

Methods: Using the Pathfinder II module of a Zeiss Atlas corneal topographer, HOA, up to the 6th Zernike order, were measured with and without Proclear multifocal D soft contact lenses for 6 mm pupil diameters in the right eyes of 40 subjects. Contact lenses with add powers of +1.50 D and +2.50 D were evaluated. Root-mean-square (RMS) values of combined HOA, as well as individual spherical-like (Z4,0 and Z6,0) and coma-like (Z3,-1, Z3,1, Z5-1 and Z5,1) HOA, were evaluated. In addition, Zernike coefficients of spherical aberration (Z4,0) were analyzed. Statistical analysis was carried out using repeated-measures ANOVA and Dunnett's multiple comparisons test.

Results: Mean RMS values of combined HOA increased by 0.09 μ m (SE 0.03) for 1.50D add power and 0.28 μ m (SE 0.03) for 2.50D add power. ($p < 0.0001$) Mean RMS values of spherical-like HOA increased by 0.11 μ m (SE 0.02) for 1.50D add power and 0.23 μ m (SE 0.02) for 2.50D add power. ($p < 0.0001$) Mean RMS values of coma-like HOA decreased by 0.01 μ m (SE 0.02) for 1.50D add power and increased by 0.13 μ m (SE 0.03) for 2.50D add power. ($p < 0.0001$) Mean spherical aberration coefficients were 0.26 μ m (SE 0.02) without contact lenses and further increased by 0.11 μ m (SE 0.02) for 1.50D add power and 0.22 μ m (SE 0.02) for 2.50D add power ($p < 0.0001$).

Conclusions: Proclear multifocal D contact lenses increase higher-order aberrations of the eye, especially spherical-like and coma-like aberrations. The effects are greater the higher the contact lens add power. Several studies reported significant negative associations between the RMS of total HOAs and axial eye growth and suggested that increased HOAs acted as an inhibitory signal for axial elongation and myopia progression. Especially the impact of spherical aberration on retinal image blur has been proposed to play a pivotal role in this process. Since Proclear multifocal D contact lenses demonstrated their efficacy in slowing myopia progression, it is possible that the increase in the aforementioned higher-order aberrations plays an important role in this process.

CONTROL ID: 3533061

SUBMITTER (NAME ONLY): Swati Singh

TITLE: Morphological Variants of Meibomian Glands: Correlation of Meibography Features with Histopathology Findings

SESSION TITLE: Lacrimal gland and Meibomian gland

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Singh, S. Basu, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: This study describes the histopathological findings of different morphologies of human meibomian glands (MG) seen on infrared imaging.

Methods: Tarsal plates dissected from 7 cadaveric upper eyelids were imaged using infrared meibography and then studied histopathologically using hematoxylin-eosin and peroxisome proliferator-activated receptor-gamma (PPAR γ) antibody (for meibocyte differentiation) staining. The different morphological characteristics of MG (varying size and shape) on meibography were correlated with histopathology using image analysis software.

Results: Of the total 127 glands, the observed morphological variants on meibography based on size were: normal (n=62), short (n=18), severely short (n=6), and dropout (n=12) glands, and on shape were hooked (n=2), tortuous (n=5), overlapping (n=1), thick (n=15) and fluffy (n=6) glands. Short, hooked, tortuous, overlapping glands had similar histological structure as seen in normal glands whereas thick, and fluffy glands had increased acinar diameter. In normal glands, the ductal epithelium was 2-3 layers thick of nucleated non-keratinized squamous cells and more multilayered in thick and fluffy glands. The areas where acini were emptying their contents into the lumen had multilayered ductal epithelium, whereas areas with no actively secreting acini had a single cell layer ductal epithelium. The mean thickness of the periacinar acellular matrix zone in normal glands was 4.21.2 microns, whereas it was 6.70.98 microns in severely shortened glands. The glands with morphology other than severely short type demonstrated strong nuclear, and weak cytoplasmic PPAR γ expression limited to the basal acinar cells similar to normal glands, whereas severely short glands showed atrophic acini with weak cytoplasmic expression of PPAR γ . Gland dropout areas showed no evidence of any glandular tissue and had normal tarsal architecture on histology.

Conclusions: Hooked, tortuous, short glands have similar acinar histology as normal glands, whereas severely short glands show atrophic acini with decreased PPAR γ expression. A larger study is warranted to validate the findings in a clinical setting with various pathologic conditions.

CONTROL ID: 3533077

SUBMITTER (NAME ONLY): vahid mohammadzadeh

TITLE: Ganglion Cell Complex: The Optimal Macular Outcome Measure for Detection of Glaucoma Progression across The Glaucoma Severity Spectrum

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. mohammadzadeh, G. Mahmoudi Nezhad, S. Heydar Zadeh, S.K. Law, A.L. Coleman, J. Caprioli, K. Nouri-Mahdavi, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|E. Su, R. Weiss, Biostatistics, University of California Los Angeles, Los Angeles, California, UNITED STATES|N. Amini, Computer Science, California State University Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To demonstrate that ganglion cell complex is the optimal outcome for detection of structural progression regardless of glaucoma severity within a Bayesian hierarchical framework.

Methods: 8×8 superpixel arrays from longitudinal macular volume scans of 112 eyes were exported. A hierarchical Bayesian random intercept and slope (RIAS) model with random superpixel variance was fit to full macular thickness (FMT), outer retinal layers (ORL), ganglion cell complex (GCC), ganglion cell/inner plexiform layer (GCIPL), and ganglion cell layer (GCL) measurements for each superpixel. We estimated population and individual superpixel slopes and intercepts. The primary outcome measure was the proportion of significant negative (worsening) and positive (improving) slopes at superpixels defined as slopes with $p < 0.1$. We compared subgroups of superpixels with mild and severe damage based on the total deviation (TD) of corresponding 10° visual field locations ($TD > -8$ and < -8 dB, respectively).

Results: Mean (SD) follow-up time and baseline 10° visual field mean deviation were 3.6 (0.4) years and -8.7 (5.8) dB, respectively. Thicker baseline measurements were associated with faster rates. A higher proportion of negative slopes was observed for FMT (54.9%), followed by GCC (36.5%), ORL (35.6%), GCIPL (30.6%), and GCL (19.8%) (Figure 1); the proportion of significant positive rates was small and comparable among various measures (Table 1). Out of 925 superpixels detected as progressing by only FMT, 79% also demonstrated significant ORL slopes. The proportion of significant negative rates was lower in the severe group for all inner macular measures; GCC identified the highest proportion of negative slopes among inner macular measures regardless of severity.

Conclusions: GCC is the optimal macular outcome measure for detection of change across the macula at all stages of glaucoma. The higher proportion of negative slopes for FMT is substantially explained by observed rates of ORL change.

CONTROL ID: 3533078

SUBMITTER (NAME ONLY): Varshini Varadaraj

TITLE: Post-cataract surgery health outcomes in frail older patients

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Varadaraj, O.D. Schein, B.K. Swenor, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|S. Chung, O.C. Sheehan, D. Roth, K. Bandeen-Roche, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: For frail patients, even low-risk procedures increase postoperative mortality risk. In a study population comprising older adults who underwent cataract surgery, we examined associations between frailty and non-vision-related health outcomes after cataract surgery, the most common procedure among Medicare beneficiaries.

Methods: We used National Health and Aging Trends Study (2010-2014) data linked to Centers for Medicare and Medicaid Services claims. Frailty (criteria: exhaustion, low physical activity, weakness, slowness, shrinking), the predictor variable, was assessed at the visit prior to cataract surgery, and participants were classified as frail (≥ 3 criteria), prefrail (1-2 criteria) or robust (0 criteria). Multivariable models, adjusted for age, gender, race, smoking, diabetes, and number of comorbidities, were used to examine associations between frailty and hospitalization rate, emergency department (ED) visits, and hospital length of stay (LOS) over the 12-months after cataract surgery.

Results: A total of 557 participants who underwent cataract surgery during the study period (2011-2014) were included in the analysis. Participants were a mean age of 76 (SE=0.3) years, and the majority were female (58%) and white (77%), and 11% were classified as frail, 49% prefrail, and 40% robust, prior to cataract surgery. In regression analysis, the odds of hospitalization in the year following cataract surgery were greater among pre-frail (OR=1.8; 95% CI=1.0, 3.2) and frail older adults (OR=3.8; 95% CI=1.8, 8.1), as compared to robust older adults. Prefrail (OR=1.5; 95% CI=0.9, 2.4) and frail (OR=2.8; 95% CI=1.5, 5.5) older adults also had greater odds of an ED visit, as compared to robust older adults. In addition, prefrail (IRR=2.4; 95% CI: 1.1, 4.8) and frail (IRR=3.8; 95% CI=1.3, 11.1) older adults had greater LOS when hospitalized, as compared to robust older adults.

Conclusions: Prefrail and frail older adults undergoing cataract surgery were more likely to be hospitalized and have an ED visit, as well as have longer LOS in the following year, suggesting that frailty may be a risk factor for these negative outcomes following cataract surgery.

CONTROL ID: 3533082

SUBMITTER (NAME ONLY): John Lin

TITLE: Characteristics of first-year residents in top ranked United States ophthalmology residency programs: a 10-year study

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the characteristics of first-year residents in top ranked United States (US) ophthalmology residency programs over the past decade.

Methods: Data from first-year ophthalmology residents in 2009, 2013, 2016, and 2019 was obtained from institutional websites, Doximity, and LinkedIn and the Wayback Machine. For each resident, publications were obtained from Scopus and Google Scholar, research productivity was measured using the h-index, and medical school rank and region were based on 2021 US News and World Report (US News) and US Census Bureau designations, respectively. The 20 ophthalmology residency programs ranked as 'Top 13' or 'High Performing' by the 2021 US News were labeled Tier 1; the 100 unranked as Tier 2. One-way ANOVA and χ^2 tests were used to analyze trends and odds ratios (OR) were calculated using logistic regression.

Results: Data was obtained on 81% (1496/1850) of the residents; 43% (644/1492) were female; 5% graduated from medical schools outside the US or Canada; 10% (155/1492) had other graduate degrees; 21% (317/1492) attended a top 20 medical school; and 41% (616/1496) had an h-index of one or more. Over the decade, the mean h-index increased (0.87 to 1.26; $p < 0.05$) and the proportion of residents who attended top 20-ranked medical schools decreased (28 to 18%; $p < 0.05$). Independent factors associated with being a resident in a Tier 1 program were having a master's degree [OR: 2.08, 95% CI: 1.18–3.69] or PhD [OR: 2.13, 95% CI: 1.25–3.64], attending a top 20 [OR: 8.02, 95% CI: 5.12–12.55] or top 40 [OR: 2.45, 95% CI: 1.56–3.85] school, attending a school in the Northeast [OR: 1.86, 95% CI: 1.27–2.70] or having an h-index of one or more [OR: 1.84, 95% CI: 1.40–2.41].

Conclusions: Graduate degrees, attending a highly ranked medical school or a medical school in the Northeast, and research experience were key characteristics of first-year residents in top ranked US ophthalmology residency programs.

CONTROL ID: 3533084

SUBMITTER (NAME ONLY): Karen Wai

TITLE: Application of a Digital Green Filter for Improved Visualization of Retinal Breaks on Ultra-Widefield Fundus Imaging

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.M. Wai, J. Moon, M. Dahrouj, J. Miller, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultra-widefield fundus photos have enabled eyecare professionals to better visualize and document retinal pathology. Optos (Optos P200DTx icg, Optos, Marlborough, MA, USA) is an ultra-widefield imaging system that creates pseudocolor photos by combining red (633 nm) and green (532 nm) laser sources. We hypothesize that applying an additional digital green filter overlay relative to the traditional settings of an Optos fundus photo may better highlight retinal breaks. Green light, given its shorter wavelength, will focus on the retina more superficially at the level of retinal vessels, relative to red light, which is focused on the retinal pigment epithelium and choroid.

Methods: Seventeen ophthalmology residents from a single institution were tested. Residents were presented with fundus photos of 10 eyes from 10 patients taken on the Optos system with either a retinal tear or hole. Participants were shown each fundus photo twice in a randomized order – once with traditional color settings and once with the addition of a green filter overlay. Participants were asked to identify the retinal break. Participants were scored on whether the break was correctly identified and timed on how long it took to identify the pathology, with a maximum of 20 seconds to examine each photo.

Results: On average, residents were able to identify more breaks on fundus photos with the green filter overlay compared to the standard settings (8.6/10 vs. 6.8/10, $p<0.01$). Residents were also able to correctly identify breaks on the fundus photos more quickly on images with green filter overlay relative to standard settings (7.5 seconds vs. 9.1 seconds, $p<0.05$). On a post-test survey, fifteen residents (88.2%) felt that the green filter overlay made it easier to identify retinal breaks, while two (11.8%) could not tell a difference. Fifteen residents (88.2%) felt a green filter overlay would be a useful tool in ophthalmology clinics and for telemedicine application.

Conclusions: Fundus ultra-widefield imaging has become an essential tool in identifying and documenting retinal pathology, especially in the era of teleophthalmology. Application of a green filter overlay may help in identifying retinal breaks for eyecare providers at all levels of training.

CONTROL ID: 3533099

SUBMITTER (NAME ONLY): Viswa Ramasubramanian

TITLE: Do Multi-zone Contact Lenses Reduce Peripheral Hyperopic Defocus during Accommodation?

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Ramasubramanian, D.M. Schneider, M.T. Jaskulski, M. Rickert, P.S. Kollbaum, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|A. Bradley, Coopervision Inc, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hyperopically defocused retinal image is thought to provide signal for the eye to grow. Multi-zone contact lenses (CL) could potentially reduce hyperopic defocus or introduce myopic defocus. This study measured the refractive states across the pupil of subjects wearing multi-zone CL designs during on-axis and off-axis accommodation.

Methods: Five young myopic subjects aged 21 to 24 years were fit bilaterally with Comfilcon A single vision (SV), center-distance (CD) multifocal with +2D add, and center-near (CN) multifocal with +2D add CLs. While subjects accommodated binocularly to electronically displayed (iWatch) letter stimuli at 0D and -4D target vergences (TV), wavefront measurements (right eye) were acquired using a custom modified COAS-HD aberrometer along the visual axis, 30⁰ nasal and 30⁰ temporal fields. Raw wavefront slope data from each lenslet of COAS were used to develop a pupil map of axial refractive error.

Results: Mean \pm SD spherical equivalent refraction was -4.77 ± 1.77 D. As stimuli approached, the distribution of refractive states across the pupil after correcting for the TV, shifted towards hyperopia for all lenses indicating accommodative lag. With the multi-zone lenses, the distributions were wider and had more myopic defocus and less hyperopic defocus. In the fovea, the mean % increase in myopically defocused pupil area (relative to SV lens) with CD and CN lenses at 0D TV was 38% and 26%, and at -4D TV was 6% and 5%, respectively. Likewise, mean % decrease in the hyperopically defocused pupil area was 5% for both CD and CN at 0D TV, and 12% and 3%, respectively, for the -4D TV. In the nasal retina (30⁰), the mean % increase in myopically defocused pupil area with CD and CN lenses at 0D TV was 28% and 8%, and at -4D TV was 5% and 1%, respectively. Mean % decrease in the hyperopically defocused pupil area was 27% and 3% for CD and CN at 0D TV, and 17% and -4%, respectively, for the -4D TV. In the temporal retina (30⁰), the mean % increase in myopically defocused pupil area with CD and CN lenses at 0D TV was 38% and 4%, and at -4D TV was 4% and -3%, respectively. Likewise, mean % decrease in the hyperopically defocused pupil area was 27% and 10% for CD and CN at 0D TV, and 12% and -15%, respectively, for the -4D TV.

Conclusions: Comfilcon A CD lens effectively reduced the hyperopic defocus and increased the myopic defocus at the pupil plane during on-axis and off-axis accommodation.

CONTROL ID: 3533184

SUBMITTER (NAME ONLY): Christopher Anthony

TITLE: Teleophthalmology in the United States Army: A Review from 2004 through 2018

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.M. Anthony, A. Altman, B. Otte, C. Lappan, G.L. Legault, Ophthalmology, San Antonio Military Medical Center, Fort Sam Houston, Texas, UNITED STATES|M.J. Mines, R. Mazzoli, Ophthalmology, Madigan Army Medical Center, Tacoma, Washington, UNITED STATES|R. Mazzoli, Ophthalmology, Uniformed Services University of the Health Sciences, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe results of the United States Army Ocular Teleconsultation program from 2004 through 2018 and the current condition, benefits, barriers, and future opportunities for teleophthalmology in the clinical settings and disease areas specific to the United States military.

Methods: 653 ocular teleconsultations were reviewed; 76 concerned general policy questions and were not further analyzed while 577 were examined in more depth. The main outcome measures included diagnostic category, evacuation recommendation status by the consultant, the association of the request with trauma, the presence of photographs or advanced imaging, and which specialties participated in answering a request. The secondary outcome measures included the month and year each consult was requested, the average and median response time of consultants annually, the country from which the request originated, the military status and branch of service of each military patient, and the nationality, age, and military status of foreign patients.

Results: The average response time in 2018 was 2.27 hours compared to 9.73 hours in 2004. 60% of consults originated from Iraq and Afghanistan. U.S. Army personnel comprised the largest percentage of consults (38.6%). Non-military patients from the US accounted for 19% of consults. Non-U.S. patients including coalition forces, contractors, detainees, and non-combatants accounted for 14.4% of consults, of which 22% were children. Anterior segment consults accounted for 45.1% of all consults with corneal surface disease being the largest subset within this diagnostic category. Dermatology and neurology were the most commonly co-consulted specialties. Photographs accompanied 37.4% of consults, with the likelihood requesters included photographs being greatest in cases involving pediatric ophthalmology (77.8%) and oculoplastics (71.7%). Evacuation was recommended in 22.7% of overall cases and 41.1% of trauma cases.

Conclusions: Army teleophthalmology has been an indispensable resource in supporting and advancing military medicine, helping to optimize ophthalmic care for American military personnel, beneficiaries, allied forces, and local nationals worldwide. A dedicated ophthalmic care and coordination system which utilizes new advances in teleconsultation technology could further enhance our capability to care for the ophthalmic needs of patients abroad, with opportunity for improving domestic care as well.

CONTROL ID: 3533209

SUBMITTER (NAME ONLY): Natacha Villegas

TITLE: Efficacy of Netarsudil as an Additional Therapy for Glaucoma in Patients Already on Maximally Tolerated Medical Therapy

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Villegas, W. Lee, Ophthalmology, Stanford University, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although the pivotal trials for netarsudil demonstrated that it was effective in lowering IOP as a primary monotherapy, in clinical practice it is more commonly used as an adjunctive treatment for patients on multiple topical medications. It is not clear how well netarsudil performs as an adjunctive therapy in these circumstances. This study seeks to evaluate the efficacy of netarsudil in glaucoma patients with inadequately controlled IOP on otherwise maximally tolerated medical therapy.

Methods: This is a retrospective, observational clinical study of patients started on netarsudil at Stanford University. All subtypes of glaucoma and pre-treatment IOPs were included. Exclusion criteria included glaucoma surgery or laser within 6 months of starting netarsudil and other modifications to the patient's medication regimen within 4 weeks. The primary outcome measure was treatment success, defined as IOP reduction from pre-treatment baseline below a pre-determined, patient specific target, and no further medication, laser, or surgery recommended subsequent to starting netarsudil. Other outcome measures included extent of IOP reduction and adverse effects.

Results: 62 eyes of 45 patients were included. Most patients had a diagnosis of primary open angle glaucoma (59%). Most eyes were on 3 or more drops (88%). 36 eyes (58%) achieved treatment success at first follow up. The mean change in IOP for all patients at first follow up was -3.53 mmHg (-17%). In patients who achieved treatment success, mean IOP change was -5.22 mmHg (-28.0%). Of the eyes with baseline IOP of ≤ 20 mmHg, 69% achieved treatment success, compared to only 17% of eyes with baseline IOP ≥ 21 (Figure 1). All patients that failed treatment were offered surgery. 20% of patients reported an adverse reaction to netarsudil, which led to discontinuation in 4 (6%) of the patients with initial treatment success.

Conclusions: Netarsudil is effective in lowering IOP for patients on otherwise maximally tolerated medical therapy, achieving treatment success in most patients for which glaucoma laser or surgery would be the only remaining therapeutic options, especially in eyes with baseline IOP under 20 mmHg. In addition, Netarsudil was overall well tolerated, with few patients opting to discontinue therapy due to local side effects.

CONTROL ID: 3533215

SUBMITTER (NAME ONLY): Vickery Trinkaus-Randall

TITLE: Epithelial abrasion induces distinct changes in interaction of 2 ion channel proteins Pannexin1 and P2X7 in diabetic mice

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.E. Trinkaus-Randall, K.L. Segars, C.B. Rich, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Epithelial wound healing is essential to repair the barrier function of the cornea after injury. We found that Pannexin1 (Panx1), a channel that moves ATP into the extracellular space, is localized along cell borders in unwounded tissue and becomes concentrated near the wound margin. We propose that the region of intense localization of Panx1 is where Ca²⁺ mobilization occurs and hypothesize that the interaction of Panx1 and P2X7 is important in corneal wound healing. Our goal is to determine if the interaction is altered in moderately obese NONcNZO10/LtJ mice that model type 2 diabetes in humans.

Methods: Epithelial debridement wounds were performed on corneas from C57BL/6J and from NONcNZO10/LtJ mice. Immunohistochemical assays were performed before and after injury and imaged using confocal microscopy. Corneas were incubated in the presence or absence of inhibitors against Panx1 and P2X7 to examine Ca²⁺ mobilization and communication between cells. Proximity ligation assays (PLA) were performed to determine the interaction of the proteins before and after injury. Analyses were performed using ImageJ and CellProfiler.

Results: Panx1 was present along cell borders in unwounded tissue in both models with more diffuse staining in NONcNZO10/LtJ mice. An epithelial abrasion induced a striking difference in the localization of Panx1 and there was intense staining near the leading edge where Ca²⁺ mobilizations were detected. However, Panx1 was not intense in the epithelium of NONcNZO10/LtJ female and male mice near the wound. Inhibition caused a change in cell shape distal to the wound. It also attenuated calcium mobilizations near the leading edge that led to a fold reduction in cell-cell communication. PLA revealed a reduction in the interaction between P2X7 and Panx1 in epithelium of NONcNZO10/LtJ mice.

Conclusions: Injury induces a change in localization of Panx1 that is not detected in the epithelium from the moderately obese type 2 diabetic mice suggesting that the protein is dysregulated. The decreased interaction of the two channel proteins suggests that both are critical for the migration of epithelium and suggest that the decrease in cell-cell communication depends on this interaction. The results demonstrate that Panx1 is a critical component to the healing response, and suppression is associated with cell-cell communication and migration.

CONTROL ID: 3533270

SUBMITTER (NAME ONLY): Jia Yin

TITLE: Corneal Nerves Modulate Angiogenesis via Secreted Neuropeptides

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yin, S. zhu, L. Liu, K. Pang, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiogenesis in the normally avascular cornea underlies common corneal diseases. Corneal nerves, derived from trigeminal ganglion (TG), are master regulators of ocular surface homeostasis. Here we seek to determine whether corneal nerves directly modulate angiogenesis and investigate the role of nerve-derived neuropeptides.

Methods: TG neurons were isolated from BALB/C mice and cultured in Neurobasal A medium. Conditioned media (CM) of TG neurons was collected between Day 3 and 4 of culture. A co-culture system was set up by placing TG neurons in the top chamber of a transwell and culturing vascular endothelial cells (VEC, MILE SVEN1 cell line) in the bottom chamber. VEC proliferation, migration, and tube formation were determined with and without TG neurons or their CM. *in vivo* corneal angiogenesis was induced by placing intrastromal sutures in BALB/C mouse corneas. Expression of neuropeptides were determined using immunofluorescence.

Results: Presence of TG neurons in co-culture decreased VEC proliferation by 35% ($P=0.008$) and migration by 20% ($P=0.046$). Similarly, conditioned media (CM) of TG neurons reduced VEC proliferation ($P<0.0001$), migration ($p=0.017$), and the number of junctions ($P=0.004$) and length of tubes ($P=0.001$) formed by VEC. Topical application of neuron CM led to a 76% reduction in suture induced-corneal angiogenesis *in vivo* ($P=0.025$). TG neurons and corneal nerves express neuropeptides substance P (SP) and calcitonin gene-related peptide (CGRP). In addition, more than 80% of TG neurons and 90% of subbasal corneal nerves express alpha-melanocyte-stimulating hormone (α -MSH). Exogenous SP (1 μ M) and CGRP (100nM) promoted VEC proliferation and tube formation *in vitro*, and local application of their antagonists Spantide I and CGRP837, respectively, led to decreases in corneal angiogenesis *in vivo*. In contrast, α -MSH (100nM) reduced VEC proliferation, migration, and tube formation *in vitro* and subconjunctival injection of α -MSH reduced corneal angiogenesis by 56% ($P=0.008$) *in vivo*. Antagonizing α -MSH signaling with Agouti-signaling protein or siRNA knock-down in TG neurons reversed the inhibitory effects of neuron CM on VEC proliferation, migration, and tube formation.

Conclusions: TG neurons and corneal nerves express pro-angiogenic neuropeptides SP and CGRP, and anti-angiogenic peptide α -MSH, which plays a critical role in the direction modulation of corneal angiogenesis by corneal nerves.

CONTROL ID: 3533285

SUBMITTER (NAME ONLY): Alan Kong

TITLE: Corneal imaging practices for keratoconus patients at an academic medical center

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.W. Kong, T. Ahmad, M.L. Turner, N.D. Pasricha, M. Indaram, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|N.D. Pasricha, Department of Ophthalmology, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal tomography, such as Pentacam®, provides both corneal pachymetry and posterior corneal curvature data in addition to anterior corneal curvature data provided in corneal topography, aiding in the diagnosis and detection of keratoconus. The purpose of this study is to characterize the corneal tomography usage for keratoconus at a tertiary care center.

Methods: Single-institution retrospective study of patients treated for keratoconus from January 2012 through December 2019. Patients were categorized by age (pediatric: < 18 years, adult: ≥ 18 years) and intellectual disability status (diagnosis of Down syndrome and/or autism) at their first clinic visit. Student's t-test was used to calculate statistical differences between groups.

Results: 611 subjects were identified, 55 of which were pediatric patients. Only 11% of patients underwent corneal tomography at their first visit in 2012, which increased to 70% by 2019. Over this time period, pediatric patients were significantly more likely to have corneal tomography at their first visit compared to adult patients (42% vs. 24%, $P = 0.01$). The majority of patients had corneal topography, regardless of age ($P = 0.41$). 9 subjects with intellectual disability were identified, all of whom were adults at their first visit. 67% had corneal topography, however only one had corneal tomography, which was for the right eye only ($P = 0.22$ right eye; $P < 0.001$ left eye). Finally, patients with corneal tomography imaging at the first visit were more likely to undergo corneal collagen cross-linking (24% vs. 6%, $P < 0.001$) and less likely to require a corneal transplant (5% vs. 16%, $P < 0.001$) by their most recent visit compared to those without corneal tomography imaging.

Conclusions: Our study demonstrates greater use of corneal topography compared to corneal tomography, although tomography use is increasing. Furthermore, corneal tomography usage was more prevalent in younger populations, likely reflecting known keratoconus progression in adolescence as well as provider practice differences. We also demonstrate minimal use of corneal tomography in disabled patients, which warrants further investigation. Subjects with earlier corneal tomography imaging also had fewer corneal transplantations, suggesting the importance of obtaining earlier corneal tomography. Thus, future research may provide insight into optimal monitoring and consequences of corneal imaging in keratoconus.

CONTROL ID: 3533317

SUBMITTER (NAME ONLY): Christopher Schiefer

TITLE: Machine Learning Assisted Quantification of New Vessels on the Disc in Proliferative Diabetic Retinopathy

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Schiefer, N. Barrett, B. Blodi, A. Domalpally, Department of Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|E.T. Dobson, K.W. Eliceiri, Laboratory for Optical and Computational Instrumentation, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Early Treatment Diabetic Retinopathy Study (ETDRS) severity scale has been the gold-standard for grading diabetic retinopathy (DR) in clinical research for decades. Graders determine ETDRS severity from fundus photographs by comparing lesions to standard photographs. Grading of new vessels on the disc (NVD) is based on the area involved by the new vessels compared to standard 10A (Figure 1) which has NVD equal to $\frac{1}{3}$ disc area (DA) or 0.85mm^2 . Then, an eye is categorized as $<\frac{1}{3}$ or $\geq\frac{1}{3}$ DA. However, this binary classification may be insufficient to measure regression of NVD as a potential outcome for therapeutic studies. Our goal is to use a machine learning (ML) tool to quantitatively analyze images

Methods: Fundus photographs from 66 eyes with NVD were included. Images were calibrated using disc to macula distance. Of these, 40 images were randomly selected to train a classifier with Trainable Weka Segmentation, a Fiji plugin which combines ML algorithms to perform pixel-based segmentation. The classifier was applied to the remaining images, and a segmented mask was generated for each. Artificially-segmented pixels outside the area of NVD were not excluded in the current version of our classifier. NVD area (mm^2) and vascular length (mm) were documented for each eye. All images were independently reviewed by two graders and categorized as NVD $<\frac{1}{3}$ or $\geq\frac{1}{3}$ DA.

Results: Graders categorized 31 (46.9%) eyes as $<\frac{1}{3}$ DA and 35 (53.1%) eyes as $\geq\frac{1}{3}$ DA. There was equal distribution of both categories in training and validation images. In eyes categorized as NVD $<\frac{1}{3}$ DA, the mean area of NVD with ML quantification was 0.099mm^2 (SEM=0.025), compared to 0.501mm^2 (0.159) in eyes categorized as $\geq\frac{1}{3}$ DA ($p=0.02$) Mean vascular length of NVD was 0.010mm (0.003) and 0.048mm (0.016) in both categories respectively ($p=0.026$).

Conclusions: There is strong correlation between ML quantification of NVD and subjective binary classification. Quantification of NVD using ML provides a finer measurement and ability to assess change over time. Employing this tool in longitudinal data will help describe the natural history of change in area and length of NVD over time.

CONTROL ID: 3533334

SUBMITTER (NAME ONLY): Shannon Chen

TITLE: Comparison of outcomes of Ahmed Glaucoma Valve alone versus Ahmed Glaucoma Valve combined with phacoemulsification in Black and Latino patients

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.X. Chen, N. Tan, SUNY Downstate Health Sciences University College of Medicine, New York, New York, UNITED STATES|N.M. Radcliffe, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|N.M. Radcliffe, New York Eye Surgery Center, The Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Controversy exists regarding whether the Ahmed Glaucoma Valve combined with phacoemulsification (AGV-phaco) is as safe and effective as standalone AGV surgery. We sought to compare these techniques in an understudied, Black and Latino population.

Methods: We reviewed charts of eyes from Latino or Black patients followed for 12 months after AGV-phaco or AGV surgery. A single surgeon conducted all procedures in the Bronx, NY from 2014-2019. Baseline demographics, intraocular pressure (IOP), number of glaucoma medications, and visual field mean deviation were compared using Pearson's Chi-squared and Wilcoxon rank-sum tests. To evaluate postop outcomes, we used rank-sum tests or Chi-square tests on the following: 1-year change in IOP and number of medications, vision loss of 2 lines or more, slit lamp procedures, reoperation for glaucoma, shallow or flat anterior chamber, corneal complications, retinal or choroidal complications, and presence of hypertensive phase (HP). For any significant findings, we conducted linear or logistic regression and adjusted for preop IOP. HP described an IOP reading > 21 mmHg within the first 3 postop months after reduction of IOP to less than 22 in the first week, without tube malfunction. Sterling IRB deemed this study to be exempt.

Results: We studied 78 AGVs and 125 AGV-phacos from 203 eyes. At baseline, mean IOP was 7.9 mmHg higher in standalones ($p < 0.0001$). Mean change in IOP was greater for AGVs ($-15.9 \text{ mmHg} \pm 10.9$) than AGV-phacos ($-8.9 \text{ mmHg} \pm 9.6$; $p < 0.0001$). However, surgery type did not predict change in IOP after adjusting for preop IOP ($p = 0.57$). Medications decreased by approximately 1 in both groups ($p = 0.77$). Vision loss occurred in 29.5% of AGVs and in 14.4% of AGV-phacos ($p = 0.015$). HP occurred in 65.4% and 38.4%, respectively ($p = 0.00032$). After preop IOP adjustment, surgery type did not predict vision loss ($p = 0.062$), but it did predict HP. AGV-phacos were 53.6% less likely to undergo a hypertensive phase post-adjustment ($p = 0.017$). Differences in other studied events were not significant ($p > 0.05$).

Conclusions: AGV-phaco in Black and Latino patients may be as effective in treating glaucoma as standalone AGV after adjusting for preop IOP. AGV-phaco may also be slightly safer, with lower odds of HP after preop IOP adjustment. This may be due to differences in AGV pocket pathophysiology in combined surgery.

CONTROL ID: 3533339

SUBMITTER (NAME ONLY): Lynn Sun

TITLE: Reliability of Intraocular Pressure Measurements in a Low Contact Drive-Through Setting

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.W. Sun, D. SALAZAR, Y. Zhou, J.D. Stein, J.S. Weizer, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has spurred innovation beyond traditional healthcare.¹ At our institution, a drive-through intraocular pressure (IOP) measurement protocol using the iCare tonometer was established to facilitate low-contact monitoring of select glaucoma patients. However, the iCare may be prone to error due to variable measurement technique and local air currents.² We endeavored to assess the reliability of drive-through IOP measurements by comparing them with recent measurements taken in clinic settings.

Methods: Inclusion criteria were all patients with drive-through IOP measurements performed from May 11-Aug. 11, 2020; exclusion criteria were any patients with IOP medication change or ophthalmic procedure between the studied IOP measurements. Drive-through IOP measurements were compared with the most recent prior in-clinic IOP measurements. Data was gathered using the Sight Outcomes Research Collaborative (SOURCE) data repository.²

Results: The study group consisted of 338 patients receiving drive-through IOP measurements. Significant differences were found between drive-through IOPs and prior in-clinic measurements. The mean drive-through vs. in-clinic IOP OD was 17.0 mmHg (SD 5.3) vs. 14.5 mmHg (SD 4.2), and OS was 17.8 mmHg (SD 5.6) vs. 15.1 mmHg (SD 4.5), a difference of 17.6% OD and 17.8% OS. Differences between individual measurements ranged from -5.5 mmHg to +12 mmHg. 71.4% of drive-through IOPs were higher than corresponding in-clinic IOPs; 22.7% were lower. 30.5% of drive-through IOPs were higher than >5 mmHg. In 18.4% of cases, drive-through IOP measurements resulted in management changes (typically, the addition of an IOP-lowering drop). In comparison, only 10.5% of in-clinic measurements resulted in management changes--the equivalent of a 75% increase in intervention.

Conclusions: Low-contact forms of IOP monitoring will continue to play a role in tele-ophthalmology. However, our data reveals potential inaccuracies in drive-through iCare IOP measurements which tend to overestimate IOP, thus triggering interventions in more drive-through cases than typically seen in clinic.

CONTROL ID: 3533349

SUBMITTER (NAME ONLY): S. Priya Narayanan

TITLE: Fingolimod demonstrates neuroprotective properties in an experimental model of optic neuritis

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Narayanan, A. Candadai, F. Liu, M. Alfarhan, M. Adil, S. Fagan, P. Somanath, Clinical and Experimental Therapeutics, The University of Georgia, Augusta, Georgia, UNITED STATES|S. Narayanan, A. Candadai, F. Liu, M. Alfarhan, Vision Discovery Institute, Augusta University, Augusta, Georgia, UNITED STATES|M. Adil, S. Fagan, P. Somanath, Augusta VA Medical Center, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision impairment associated with optic neuritis (ON) is prevalent in approximately 20% of patients with multiple sclerosis (MS). All the approved disease-modifying therapies (DMTs) available for MS function by suppressing inflammation, however, the impact on the long-term neurodegenerative phase is not completely known. Any agent with additional neuroprotective properties may offer advantages over existing therapies in reducing ultimate MS disability. The current study was undertaken to determine the neuroprotective properties of fingolimod (FTY), a sphingosine-1-phosphate receptor modulator, and its potential as a therapy for ON.

Methods: Utilizing the rat retinal neuronal cell (R28) line, an in vitro model to assess MS-induced neurodegeneration was established. Neuronal damage was induced by treatment with tumor necrosis factor (TNF α). Cell viability was quantified using Trypan blue method. Changes in signaling molecules were elucidated using Western blot and alterations in neuronal morphology were assessed by immunofluorescence studies.

Results: Treatment of R28 cells with TNF α caused significant cell death, while FTY treatment increased cell survival. Neuronal damage was induced by treating R28 cells with TNF α for 24h at a dose of 10 ng/mL. Dose-dependent studies showed that FTY concentration at 25 nM significantly reduced TNF α -induced cell death compared to the control group (N=5, p<0.01). The upregulation observed in phospho-p38 MAPK in response to TNF α treatment was significantly reduced in the presence of Fingolimod (N=3, p<0.05). Further, the level of cell survival marker, Bcl-xL was decreased, while the expression of cleaved caspase-3 (a cell death marker) was increased in TNF α -treated R28 cells. These changes were reversed significantly in response to Fingolimod treatment (N=3, p<0.05). Immunofluorescence studies using antibodies against neuronal markers, Tuj1 (neuron-specific class III beta-tubulin), and neuronal enolase demonstrated that FTY treatment protected the retinal neurons against the TNF α -induced neurodegenerative changes.

Conclusions: In conclusion, our study suggests that Fingolimod exhibited neuroprotective properties in an experimental model of optic neuritis.

CONTROL ID: 3533381

SUBMITTER (NAME ONLY): Tatiana Rosenblatt

TITLE: Discontinuation and Loss to Follow-Up Rates in Clinical Trials of Intravitreal Anti-Vascular Endothelial Growth Factor Injections

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Rosenblatt, N. Rayess, A. Al Moujahed, P. Mruthyunjaya, Ophthalmology, Byers Eye Institute, Stanford University School of Medicine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Clinical trials are often designed to include homogenous, highly specific patient populations with many resources to reduce patient dropout. Results may not translate to real-world settings. We performed a retrospective meta-epidemiological study to evaluate discontinuation and loss to follow-up (LTFU) rates in clinical trials of intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections for diabetic macular edema (DME), age-related macular degeneration (AMD), and retinal vein occlusion (RVO).

Methods: Clinicaltrials.gov was queried for all completed trials of anti-VEGF injections for DME, AMD, or RVO. Of the 658 trials identified, 582 were excluded for being non-interventional (n = 90), having fewer than 100 patients (n = 207), terminating early (n = 6), or missing study results (n = 279). The remaining 76 trials (DME n = 33, AMD n = 33, RVO n = 10) of 27,823 patients were analyzed for discontinuation and LTFU rates.

Results: Mean discontinuation rate was 12.44% (SD 8.12%, range 0 – 54.12%) (Figure 1A), with higher rates among control (18.87%) than treatment arms (10.78%, p = .006). Subject withdrawal was the most common reason for discontinuation, followed by adverse events and LTFU (Table 1). Mean LTFU rate was 1.84% (SD 1.78%, range 0 – 7.76%) (Figure 1B), with no significant differences when stratified by disease, treatment type, or treatment frequency.

Conclusions: Discontinuation rates of major intravitreal anti-VEGF clinical trials were highly variable, suggesting even trials struggle with overall patient retention. Though trial LTFU rates were low, real-world outcomes may differ due to higher reported LTFU rates, which should be considered when extrapolating trial results to clinical practice.

CONTROL ID: 3533384

SUBMITTER (NAME ONLY): Sunny Kwok

TITLE: Mechanical Deformation of Peripapillary Retina during Intraocular Pressure Elevation

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kwok, M. Pan, N. Hazen, J. Liu, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|Y. Ma, J. Liu, Department of Ophthalmology and Visual Science, The Ohio State University, Columbus, Ohio, UNITED STATES|N. Hazen, Biophysics Interdisciplinary Program, The Ohio State University, Columbus, Ohio, UNITED STATES|X. Pan, Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To map and quantify the peripapillary retina (PPR) deformation during intraocular pressure (IOP) elevation in human donor eyes using high-frequency ultrasound elastography.

Methods: Inflation tests were performed in 10 donor globes (age: 20-74 years old, 4 male and 6 female) while IOP was raised in 0.5 mmHg steps from 5 to 30 mmHg. Each eye was inflated twice to capture 2D scans of the posterior eye centered at the optic nerve head (ONH) along the nasal-temporal (NT) and superior-inferior (SI) axis using a 50MHz ultrasound probe (Vevo2100, VisualSonics). A correlation-based speckle tracking algorithm (Tang & Liu, JBME 2012) was used to compute displacements, and strains were calculated using least squares estimation. Radial, tangential, and shear strains were obtained by coordinate transformation. Peripapillary sclera (PPS) and PPR were manually segmented for regional analysis (Fig 1A, tan and pink, respectively). Regional strain analysis was conducted at IOP = 30 mmHg using paired t-test.

Results: Localized high tangential and shear strains were present in PPR during IOP elevation (up to 5%, Fig 1B). On average, PPR had less radial compression ($-0.55 \pm 0.25\%$ vs $-2.32 \pm 0.74\%$, $p < 0.001$), greater shear ($1.49 \pm 0.65\%$ vs $1.13 \pm 0.32\%$, $p = 0.029$), and similar levels of tangential stretch ($0.29 \pm 0.19\%$ vs $0.38 \pm 0.19\%$, $p = 0.13$, Fig 2A) as compared to the PPS. Exploratory analysis showed no significant differences in strains between quadrants in either PPR or PPS (Fig 2B).

Conclusions: Peripapillary retinal damage is characteristic of glaucoma progression. Our findings showed that although PPR experienced minimal radial compression during IOP elevation, localized shear and stretch were substantial, which could contribute to mechanical damage in this region during IOP elevation. These results provide new insights into IOP-related mechanical insults to the neural tissue near the ONH, where glaucomatous damage initiates.

CONTROL ID: 3533393

SUBMITTER (NAME ONLY): Ignacio Rodriguez-Una

TITLE: Early lensectomy in patients with pseudoexfoliation: long-term outcomes of effectiveness and safety

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Fernández-Vega, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|I. Rodriguez-Una, A. Fernández-Vega, M. Garcia-Diaz, P.P. Rodriguez-Calvo, L. Fernandez-Vega-Cueto, J. Alfonso, J. Merayo-Llves, Instituto Universitario Fernández-Vega. Fundación de Investigación Oftalmológica. University of Oviedo, Oviedo, SPAIN|I. Rodriguez-Una, M. Garcia-Diaz, P.P. Rodriguez-Calvo, L. Fernandez-Vega-Cueto, J. Alfonso, Instituto Oftalmológico Fernández-Vega, Oviedo, SPAIN|J. Merayo-Llves, Instituto de Investigación Sanitaria del Principado de Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Capsular pseudoexfoliation (PEX) is a heterogeneous syndrome that can present as a wide variety of clinical scenarios and early lensectomy may help to reduce comorbidity in some of them. This study aimed to assess the long-term effectiveness, predictability and safety of cataract surgery in patients presenting whether symmetric or asymmetric PEX.

Methods: A retrospective, observational clinical study was designed, including PEX patients that underwent phacoemulsification with hydrophobic acrylic intraocular lens (IOL) implantation in both eyes at one centre between 2001 and 2015. Multifocal IOL were only implanted in selected cases of asymmetric PEX. A postoperative follow-up ≥ 5 years, ≥ 3 preoperative reliable visual field (VF) tests and the presence of periodical VF tests until the analysis visit were required.

322 eyes of 161 patients were included (mean age: 71.4 ± 5.7 years), with a mean follow-up time of 8.5 ± 2.8 years (range: 6-17 years). Patients were classified in two groups: 102 patients with symmetric PEX (PEX material seen in both eyes with the slit lamp), and 118 patients with asymmetric PEX (only one eye presented clinically apparent PEX). Preoperative and postoperative visual acuity, intraocular pressure (IOP), number of hypotensive drugs and VF mean deviation (MD) were registered, as well as the appearance of intraoperative and postoperative complications. Wilcoxon test was used for statistical analysis.

Results: Before surgery, no statistical differences were found between both groups. Postoperatively, 95%, 96% and 96% of eyes were within ± 1.00 D in symmetric PEX, asymmetric PEX with monofocal IOL, and asymmetric PEX with multifocal IOL groups, respectively.

At the final follow-up visit, IOP remained stable in the main two groups ($p=0.08$; $p=0.06$) with a reduction of the number of medications ($p<0.001$). MD worsened from -8.8 dB to -11.6 dB in the symmetric group ($p<0.001$), and remained stable in the asymmetric group (from -5.0 dB to -7.1 dB; $p=0.42$). No intraoperative complications were registered in the asymmetric group, in comparison with the symmetric group: 7 (3.4%; $p=0.05$). Ten cases (4.9%) of late IOL dislocation were found, only in the symmetric group ($p=0.04$).

Conclusions: Early lensectomy with IOL implantation in patients with PEX before its symmetric presentation results effective, safe and predictable in the long term.

CONTROL ID: 3533397

SUBMITTER (NAME ONLY): Barbara Wirostko

TITLE: Systemic and Ocular Toxicology and Pharmacokinetic Profiles of QLS-101, a Novel Topical IOP-Lowering Therapeutic

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.M. Wirostko, H. Sookdeo, T. Htoo, R. Casale, M.P. Fautsch, C. Steel, Qlaris Bio, Inc, Massachusetts, UNITED STATES|U. Roy Chowdhury, M.P. Fautsch, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|B.M. Wirostko, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: QLS-101, a water-soluble phosphate ester prodrug of an ATP-sensitive potassium channel opener, is being developed by Qlaris Bio as an ocular hypotensive agent with a novel mode of action that affects distal outflow resistance and episcleral venous pressure. This summarizes the potential toxicity and pharmacokinetic (PK) profiles of QLS-101 in beagle dogs.

Methods: To assess ocular toxicity and PK, beagle dogs (age 5-7 months) were dosed topically (OU) once daily for 28 days with 2.0%, 4.0%, or 8.0% QLS-101 (n=3 males and 3 females per group). To evaluate systemic maximum tolerated dose (MTD), single escalating doses of QLS-101 (0.05-5.0 mg/kg/day) were administered by i.v. bolus to one male and one female beagle dog, with a 48h minimum observation period between doses. Plasma samples were collected at various timepoints in both studies, concentrations of QLS-101 and its active moiety QLS-100 were determined by LC/MS-MS, and data used to generate PK parameters. Mortality, clinical observations, body and organ weights, and food consumption were assessed in each study. Necropsy examinations were performed and select tissues were isolated and prepared for histopathology.

Results: QLS-101 was well-tolerated at all dose levels except 5 mg/kg/day i.v. When dosed topically, the no-observed-adverse-effect level (NOAEL) was determined to be 8.0%. At this dose, the mean C_{max} and $AUC_{T_{last}}$ values on day 28 were 147 ng/mL and 1.26 ug*h/ml, respectively, for males, with similar results in females. QLS-100 C_{max} and $AUC_{T_{last}}$ levels at NOAEL were 31 ng/ml and 166 ng*h/ml in males, with similar results in females. Using dogs administered single escalating i.v. doses, the MTD was determined to be 3 mg/kg. Side effects were limited to non-adverse skin redness at all dose levels, consistent with vasodilation. Unexpectedly, the observed skin redness initially presented peripherally in the distal limbs (fore and hindpaws) and in the pinnae rather than the trunk, neck, or face. The MTD corresponded to sex-combined C_{max} and $AUC_{T_{last}}$ values of 16.4 µg/mL and 106.55 µg*h/mL for QLS-101, and 35.5 ng/mL and 431 ng*h/mL, for QLS-100. No mortality, change in body weight or food consumption were noted. Histological examination showed no systemic toxicity as a result of QLS-101 treatment.

Conclusions: QLS-101 is well-tolerated in beagle dogs and suitable for clinical development as an IOP-lowering therapeutic.

CONTROL ID: 3533437

SUBMITTER (NAME ONLY): Rahul Iyengar

TITLE: Imaging Biomarkers of Diabetic Retinopathy Treatment and Progression Using Quantitative Ultra-widefield Fluorescein Angiography

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.S. Iyengar, Ophthalmology - Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|G. Yu, C. Powell, A. Tran, C. Miranda, E. Young, K. Demetriou, L. Devisetty, Y.M. Paulus, Ophthalmology - Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan, UNITED STATES|M. Aaberg, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|T. Patel, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultra-widefield (UWF) fluorescein angiography (FA) is widely used in the evaluation of diabetic retinopathy (DR), but further study is necessary to explore how quantifiable biomarker areas on FA images may relate to DR treatments. This study seeks to determine if associations exist between areas of nonperfusion (NP) and neovascularization (NV) in eyes of patients with diabetes and treatment with panretinal photocoagulation (PRP) or intravitreal (IVT) injections, and if calculated areas and demographic factors are associated with DR progression.

Methods: In this retrospective, cross-sectional study, a total of 363 patients (651 eyes) who were treated at the University of Michigan Kellogg Eye Center between January 2009 and May 2018 were included. Eligible participants were 18 years or older with diagnoses of type 1 or 2 diabetes who received UWF FA. Patients with previous PRP or poor-quality images were excluded. Our main outcome measures included comparison analyses of measured surface areas (biomarkers) in millimeters squared (mm^2), number of IVT injections and PRP treatments, and DR progression.

Results: Our cohort of 363 patients (651 eyes) received a total of 3,041 IVT injections and 878 PRP treatments with a mean follow-up time of 915 days ($\text{SD} \pm 714$). IVT injections were positively associated with posterior NP (difference, 1.15 mm^2 ; 95% CI, 0.43 – 1.86; $P = 0.0017$). PRP treatments were positively associated with total NP (difference, 27.24 mm^2 ; 95% CI, 14.68 – 39.79; $P = 2.1 \times 10^{-5}$), mid-periphery NP (difference, 10.34 mm^2 ; 95% CI, 4.43 – 16.26; $P = 6.1 \times 10^{-4}$), far-periphery NP (difference, 18.67 mm^2 ; 95% CI, 10.24 – 27.09; $P = 1.4 \times 10^{-5}$), total NV (difference, 1.75 mm^2 ; 95% CI, 0.84 – 2.65; $P = 1.6 \times 10^{-4}$), mid-periphery NV (difference, 1.23 mm^2 ; 95% CI, 0.51 – 1.96; $P = 8.4 \times 10^{-4}$), and far-periphery NV (difference, 0.37 mm^2 ; 95% CI, 0.14 – 0.61; $P = 0.0019$). While DR progression was not associated with biomarker areas, it was positively associated with a pre-existing diagnosis of type 2 (147% increase; 95% CI, 7% – 473% increase; $P = 0.03$) as compared to type 1 diabetes.

Conclusions: Areas of NP and NV on UWF FA demonstrated associations with IVT injections and PRP treatments. Quantifiable biomarker areas in UWF FA may assist with patient prognostication and management.

CONTROL ID: 3533443

SUBMITTER (NAME ONLY): Cynthia Steel

TITLE: Ocular Tissue Conversion and Activity Profile of QLS-101, a Novel Topical IOP-Lowering Therapeutic

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Steel, H. Sookdeo, T. Htoo, R. Casale, B.M. Wirostko, Qlaris Bio, Inc., Wellsley, Massachusetts, UNITED STATES|U. Roy Chowdhury, M.P. Fautsch, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|B.M. Wirostko, Ophthalmology, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: QLS-101, a water-soluble phosphate ester prodrug of an ATP-sensitive potassium channel opener in preclinical development, has shown potent IOP reduction in multiple normotensive and glaucomatous animal models. The purpose of this study was to determine the conversion profile and activity of QLS-101 and its active moiety (QLS-100) using human tissue.

Methods: Conversion of QLS-101 (200 μ M-5.0 mM) was examined by LC/MS-MS following incubation at pH 7.4 with either human alkaline phosphatase (ALP), acid phosphatase, or 5'-nucleotidase (2.0 nM-1.0 μ M) for up to 2h. Further dose- and time-dependent analysis of QLS-101 (0.01-40.0 mM) conversion to QLS-100 was determined following incubation with human ALP (0.0002-0.2 U/ μ l) for up to 72h. Tissue-specific conversion of QLS-101 was assessed in fresh human ocular tissues and fluids over 24h. To quantify channel activity, HEK-293 cells stably expressing human Kir6.2/SUR2B ATP-sensitive potassium channel subunits were incubated with increasing concentrations (0.003-100 μ M) of either QLS-101 or QLS-100. Pinacidil (100 μ M), a commercially-available ATP-sensitive potassium channel opener, was used as a positive control. Cell membrane potential was measured on a FLIPR fluorescence plate reader.

Results: Human ALP, but not acid phosphatase or 5'-nucleotidase, converted QLS-101 to QLS-100 in vitro, with K_m and k_{cat} values of 630 μ M and 15 min⁻¹, respectively. In a separate study at a fixed QLS-101 concentration, approximately 21% of QLS-101 was converted by ALP in a concentration-dependent manner. Similarly, ALP at a fixed concentration converted QLS-101 to QLS-100 in a QLS-101 inverse concentration-dependent manner. In human ocular tissues, 24h conversion of QLS-101 was most robust in samples of iris, ciliary body, trabecular meshwork, and sclera. Treatment of HEK-Kir6.2/SUR2B cells with QLS-100 resulted in a concentration-dependent hyperpolarization of the cell membrane, with a mean EC_{50} value of 0.53 μ M \pm 0.05, consistent with pinacidil (EC_{50} = 5.49 μ M \pm 0.99). In contrast, application of QLS-101 did not result in any significant hyperpolarization, confirming QLS-101 as an inactive prodrug.

Conclusions: QLS-101 is activated by human ALP to QLS-100, which promotes cell membrane hyperpolarization through ATP-sensitive potassium channels composed of Kir6.2/SUR2B.

CONTROL ID: 3533452

SUBMITTER (NAME ONLY): Vanessa Rave

TITLE: Real-world analysis of brolucizumab in neovascular AMD

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Rave, K. Sharma, A. Wagner, K. Kapoor, Wagner and Kapoor Research Institute, Norfolk, Virginia, UNITED STATES|V. Rave, K. Sharma, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent clinical trials have explored the efficacy of intravitreal brolucizumab (IVB) for wet AMD in treatment-naïve patients, but little is known about its use in treatment-experienced patients. The purpose of this study is to evaluate patient response to IVB in a real-life clinical setting with a focus on successful extension of treatment interval while maintaining visual acuity (VA) and central foveal thickness (CFT).

Methods: This was a retrospective, single-center study. We included 144 patients with wet AMD who received their first treatment of IVB between 11/1/20 and 4/20/20, and these patients were followed through 12/4/20. All patients were previously treated with intravitreal anti-VEGF. Using the treat and extend regimen, patients were observed closely to ensure that they achieved optimal treatment intervals. All patients underwent eye examinations at each visit and optical coherence tomography imaging at least every other visit. Key outcome measures were VA, CFT, and treatment interval.

Results: 144 eyes that received IVB for wet AMD were included in this study (64 men and 80 women, average age 77.56 ± 11.84). Prior to the study period, patients had an average baseline logMAR VA of 0.6050 ± 0.4635 , average baseline CFT of 281.84 ± 81.63 μm , and average baseline treatment interval of 33.93 ± 9.85 days. During the study period, patients received an average of 4.37 ± 1.74 (range 1-8) treatments, with 84.0% of the population having received 3 or more treatments. Changes in VA and CFT from baseline to final treatment were of statistical nonsignificance, but average treatment interval was extended from 33.76 days to 60.37 days ($p < .001$). Average baseline treatment interval increased significantly to 43.99 ± 20.17 , 42.69 ± 15.05 , 64.60 ± 16.75 , 61.24 ± 11.83 , 62.48 ± 11.23 , and 52.70 ± 14.48 after 1, 2, 3, 4, 5, and 6 treatments, respectively ($p < 0.001$). 106 (81.54%) patients extended their treatment intervals by at least seven days, 21 (16.15%) maintained their previous interval, and 3 (2.31%) tightened their previous intervals by at least seven days. 99 (76.15%) patients achieved an interval of 56 days or longer.

Conclusions: The results of this study showed that IVB is a promising treatment option for patients with suboptimal response to other anti-VEGF agents. Our study cohort maintained VA and CFT within one standard deviation of baseline while, on average, extending their treatment intervals and therefore reducing treatment burden.

CONTROL ID: 3533454

SUBMITTER (NAME ONLY): Mohib Khan

TITLE: Investigating the Development of Psychiatric Disorders After a New Diagnosis of Glaucoma

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Khan, D. Belyea, Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|H. Pakhchanian, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We performed a retrospective cohort study to evaluate the temporal association between a new diagnosis of glaucoma and the subsequent onset of psychiatric disorders.

Methods: TriNetX (Cambridge, MA, USA), a federated electronic health records research network was used to identify a total of 468,480 individuals with the diagnosis of glaucoma using a series of ICD-10 codes (H40 category) and were stratified into cohorts based on age at the time of diagnosis. Each subject was then matched to a control without the diagnosis of glaucoma based on age, sex, race, BMI, and the presence or absence of essential hypertension, diabetes mellitus, cerebrovascular disease, heart failure, nicotine dependence, and alcohol related disorders. The primary endpoint of the study was the incidence of a new psychiatric disorder within 90-days of being diagnosed with glaucoma compared to matched controls. Data compilation and analysis were done through Microsoft Excel.

Results: Subjects in the 25-35 and 36-49 years of age cohorts did not show a statistically significant increase in the incidence of psychiatric disorder within 90-days of being diagnosed with glaucoma compared to matched controls. Subjects in the 50-64 years of age cohort showed a statistically significant higher risk of developing generalized anxiety disorder [RR 1.23, 95% 1.04-1.45] and adjustment disorder [RR 1.21, 95% 1.02-1.43] in the first 90-days after a new diagnosis of glaucoma compared to matched controls. Subjects in the 65 years of age and over cohort showed a statistically significant higher risk of developing generalized anxiety disorder [RR 1.550, 95% 1.41-1.7], adjustment disorder [RR 1.62, 95% 1.47-1.79], persistent mood disorders [RR 1.24, 95% 1.11-1.38], and panic disorders [RR 1.24, 95% 1.05-1.47] in the first 90-days after a new diagnosis of glaucoma compared to matched controls.

Conclusions: Patients over the age of 50 with a new diagnosis of glaucoma are at a significantly higher risk of developing new psychiatric disorders shortly after receiving a new diagnosis of glaucoma. Increased awareness of these associations can lead to improved patient care by employing an early multidisciplinary approach to address these comorbidities.

CONTROL ID: 3533455

SUBMITTER (NAME ONLY): Jennifer Nadelmann

TITLE: Effect of Autologous Platelet-rich Plasma Eye Drops in the Treatment of Dry Eye Disease (DED)

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.B. Nadelmann, V.Y. Bunya, G. Ying, P. Hua, M. Massaro-Giordano, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Platelet rich plasma (PRP) is an autologous preparation that concentrates platelets in a small volume of plasma that has been used to treat ocular surface diseases. The purpose of this study was to determine if treatment with autologous PRP eye drops improved symptoms and signs of dry eye disease (DED).

Methods: A retrospective case series was conducted of patients who were prescribed autologous PRP eye drops for treatment of ocular surface disease. Subjects were excluded if they did not have a follow-up visit, underwent intraocular surgery prior to their follow-up visit, previously received nerve growth factor treatments or did not have a baseline examination with photography. Symptoms were assessed using the Ocular Surface Disease Index (OSDI) and subject report. Patients also underwent a slit lamp exam, which included ocular surface staining with fluorescein and lissamine green.

Results: The charts of 47 patients with a history of ocular surface disease were included who had been prescribed PRP drops. 64 eyes of 32 patients had evaluable photographs of lissamine green staining taken at the baseline and at follow-up. The mean age at the baseline visit was 60 years (SD 13.3) and there were 39 (83%) females. Thirteen patients (28%) had a history of ocular graft-versus-host disease. Sixteen patients (34%) had a history of Sjögren's syndrome and four patients (8.5%) had Rheumatoid arthritis. The average time of follow-up was 182.7 days, and 162.6 days for those who had follow-up photographs done. There was a statistically significant decrease in OSDI score from baseline to follow-up (39.5 vs 30.8 points, $p=0.02$). Among the 64 eyes included, 9 (14.1%) eyes had an improvement in conjunctival lissamine green staining (by ≥ 1 point) at follow-up, 49 (76.6%) eyes had stable staining and 6 (9.4%) eyes had increased staining (by ≥ 1 point) at follow-up. Among the 20 eyes with Schirmer testing, there was a borderline significant increase in score from baseline to follow-up visit (5.9 vs. 9.7, $p=0.06$).

Conclusions: We found that treatment with PRP drops was associated with a significant improvement in OSDI score for patients with ocular surface disease. The majority of eyes treated had stable or decreased lissamine green conjunctival staining at follow-up. Future larger prospective studies are needed to further evaluate the efficacy of PRP drops for treating ocular surface disease.

CONTROL ID: 3533457

SUBMITTER (NAME ONLY): Varun Reddy

TITLE: Neovascular Glaucoma Management and Outcomes at a Large County Hospital

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Reddy, Ophthalmology, Weill Cornell Medicine, New York, New York, UNITED STATES|B. Winward, H. Bhalli, C. Goodrich, J.T. Whitson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neovascular glaucoma (NVG) is a debilitating disease secondary to retinal ischemia. This study aims to examine NVG cases at Parkland Memorial Hospital and assess patient characteristics that may have impacted the types of management employed and ultimately the visual acuity (VA) and intraocular pressure (IOP) outcomes. In doing so, we hope to gain helpful insight for the management of future NVG cases.

Methods: This was a retrospective chart review of neovascular glaucoma cases at Parkland Memorial Hospital with at least 6 months of follow up. Outcome metrics included number of glaucoma medications utilized, IOP, VA, and number of surgeries performed.

Results: We found that proliferative diabetic retinopathy (PDR) was by far the most common cause of NVG in our patient population (84.62%), followed by retinal vein occlusion (RVO) (12.09%).

75% of patients with a presenting VA of 20/400 or better underwent primary tube shunt while 50% of patients with presenting VA worse than 20/400 underwent primary cyclophotocoagulation (CPC). For patients who underwent a single surgery, there was no significant difference in IOP outcomes at 1 month ($p=0.92$), 6 months ($p=0.51$), or 1 year ($p=0.70$) after surgery, or at the final follow up ($p=0.13$) between CPC vs. tube shunt. There was also no significant difference in number of surgeries required to control IOP between primary CPC vs. tube shunt cases ($p=0.31$).

Patients with presenting VA of 20/400 or better had significantly better VA at 1 month, 6 months, and 1 year post diagnosis, and at the final follow up visit than those with presenting VA worse than 20/400 ($p<0.05$).

Patients with a presenting systolic blood pressure less than 130 mm Hg had a lower IOP at 1 year post diagnosis than those with a higher systolic pressure ($p=0.02$), but otherwise there was no difference in IOP between the two groups at any of the other measured timepoints ($p>0.05$).

Conclusions: Similar to the general population, we observed that PDR and RVO are the two leading causes of NVG. Our practice pattern is consistent with commonly implemented patterns in that the majority of eyes 20/400 or better visual acuity underwent primary tube shunt while eyes with poorer presenting visual acuity underwent primary CPC. Presenting visual acuity appears to provide insight into a patient's long term visual prognosis. Blood pressure control at presentation also seems to be a modifiable risk factor for progression of NVG.

CONTROL ID: 3533460

SUBMITTER (NAME ONLY): Mark Grogan

TITLE: Analysis of the Protein Profile of Congenital Hereditary Endothelial Dystrophy Corneal Stroma after Keratoplasty

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.P. Grogan, Ophthalmology, Summa Health System, Akron, Ohio, UNITED STATES|R. Bouhenni, Center for Vision Science Research, Akron Children's Hospital, Akron, Ohio, UNITED STATES|R. Bouhenni, Pharmaceutical Sciences, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|D.P. Edward, P. Patel, Ophthalmology, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|R. Mittal, Ophthalmology, Dalmia Ophthalmic Pathology Services, Bhubaneswar, INDIA|

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ABSTRACT BODY:

Purpose: Chronic corneal stromal changes in corneal endothelial dystrophies such as congenital hereditary endothelial dystrophy (CHED) can cause poor visual recovery despite endothelial replacement by endothelial keratoplasty (EK). The poor recovery of visual acuity has been attributed to the persistent corneal haze despite restoration of normal corneal endothelial function after EK. In this pilot study, we sought to investigate whether the persistent corneal haze in CHED is due to alterations in the protein content of the corneal stroma by comparing the proteomic profile of the corneal stroma in CHED to that of healthy corneas.

Methods: Protein profiles of archived formalin fixed paraffin embedded corneas [n=6], 3 CHED and 3 healthy age matched control corneas, age range 12-20 years, were analyzed by liquid chromatography followed by tandem mass spectrometry (LC/MS-MS). Relative protein abundances were determined by spectral counting. G test followed by post hoc Holm Sidak was used for statistical analyses to determine significance in the differential expression of proteins between CHED and the control group. Proteins were classified into functional groups using Protein ANALysis THrough Evolutionary Relationships (PANTHER) classification system.

Results: Using stringent filtering criteria, 11 and 19 proteins were detected at significantly lower and higher levels respectively in the CHED compared to control corneas ($p < 0.05$). Alpha-enolase (3.69-fold), Collagen alpha-2(I) chain (3.29-fold) and a protein similar to Mimecan (3.16-fold) were the top 3 proteins detected at lower levels, whereas the top 3 proteins detected at higher levels were Collagen alpha-2(V) chain (~4.5 fold), Heat shock protein 90kDa alpha (3.84 fold) and Thioredoxin (3.2 fold). The altered proteins are involved in the integrin signaling angiogenesis, cytoskeleton regulation in addition to inflammation and oxidative stress pathways.

Conclusions: CHED eyes using LC/MS-MS revealed significant differences in their corneal stromal protein profile compared to control. Alteration of the different collagens that are involved in the integrin signaling pathway may play a role in the corneal stromal changes and reduced cornea clarity after EK in CHED.

CONTROL ID: 3533492

SUBMITTER (NAME ONLY): John Garcia

TITLE: Assessment of Oblique Penlight Exam to Estimate Anterior Chamber Depth

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Garcia, Meharry Medical College School of Medicine, Nashville, Tennessee, UNITED STATES|A. Chomsky, VA Tennessee Valley Healthcare System, Nashville, Tennessee, UNITED STATES|A. Chomsky, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): John Garcia: Commercial Relationship: Code N (No Commercial Relationship) | Amy Chomsky: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to compare the estimated anterior chamber depth (ACD) by oblique penlight examination (OPE) when compared to ACD measured by partial coherence interferometry (PCI).

Methods: The study compromised a retrospective chart review of 172 eyes of 86 patients at VA Tennessee Valley Healthcare System who received an OPE and PCI as part of cataract surgery work-up. These patients had their eyes assessed with OPE by technician staff prior to dilation and received measurements that include ACD by PCI. All technicians received standardized training in performing OPE and had a standardized grading sheet available. Grading was from 1-4 (Grade 1 > ¾ Anterior chamber shadow (ACS), Grade 2 = 1/3-3/4 ACS, Grade 3 < 1/3 ACS, Grade 4 = no shadow). Patients who had prior intraocular surgery or ocular trauma were excluded from the study. One-way ANOVA and correlation analysis of the data was performed to assess statistical significance. The data was also analyzed by t-test as to whether a dichotomous OPE result showed deeper average ACD by PCI in grade 4s versus all grades 1-3.

Results: There were no grade 1s, eight grade 2s, five grade 3s and 159 grade 4s by OPE. The mean and median ACD by PCI were 3.43 and 3.28; with a range of 2.11 to 5.69.

When comparing all data, the one-way ANOVA analysis resulted in a p-value of 0.440014.

The correlation analysis resulted in a p-value of 0.496349. When comparing average ACD by PCI of all grade 4s (3.45) to all grades 1-3 (3.15), the results showed a p value of 0.203082 by t-test.

Conclusions: The results of the one-way ANOVA and correlation analysis reveal no statistical significance that the OPE properly estimates the ACD in comparison to PCI. Additionally, when looking at average ACD of grade 4s versus grades 1-3, there was also no statistical significance. Although this study is limited by its sample size, this study shows OPE does not reliably estimate ACD. Further studies of larger sample sizes are likely to reveal similar results due to the user-error associated with the OPE technique.

CONTROL ID: 3533505

SUBMITTER (NAME ONLY): Hila Epstein-Barash

TITLE: Keratolytic and Keratostatic activity of Selenium Disulfide and its disease modifying role in Meibomian Gland Disease

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Epstein-Barash, H. Rapaport, Y. Alster, O. Rafaeli, R&D, Azura Ophthalmic, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) is the leading cause of dry eye disease (DED). Research over the past decade has pointed to hyperkeratinization, or the build-up and shedding of keratin protein in the Meibomian gland ducts and at the gland orifice, as the root cause of obstructive MGD. Selenium disulfide (SeS₂), a potent keratolytic agent used in dermatologic shampoos for severe dandruff and seborrheic dermatitis, may be used to target meibomian glands' hyperkeratinization and thus be useful in restoring their normal function in patients with MGD. The objective if this in-vitro study was to determine mechanism of action by which SeS₂ effect keratinization, cellular differentiation, proliferation, and adhesion.

Methods: The keratolytic effect (breakdown of disulfide bonds) of SeS₂ was investigated in an ex vivo study of human skin using concentrations of SeS₂; 0.1, 1, or 10 mM. The study measured free thiol levels, which are indicative of a decrease in the number of the disulfide bonds that determine the strength of keratin filaments. The keratostatic effect measured by cell turnover was evaluated using a keratinocyte cell line and human skin. Keratinocytes in an in vitro model were incubated with SeS₂ (500 µM, 1 mM, and 5 mM). Cell turnover was measured using the FACS propidium iodide (PI) and BrdU incorporation assay.

Results: SeS₂ was shown to cause significant keratolytic activity in human skin with a 60% increase in free thiols relative to control at 10 mM ($p < 0.05$). In vitro keratinocyte proliferation 28 hours following first exposure was reduced by up to 90%, ($p < 0.05$) at all concentrations. Similarly, the ex vivo studies, measuring BrdU incorporation at 100 µM, 1 mM, and 10 mM showed that the compound significantly reduced cell turnover by up to 35%, ($p < 0.05$), with accumulation of cells in S phase and G2/M phase during cell cycle (decreased cell division).

Conclusions: The pathogenesis of MGD is a result of accumulation of excess keratin in the gland's canal and within the lipid. The results suggest that Selenium disulfide works in multiple pathways that are involved in MGD including reduced cell turnover and activity of keratinocytes and softening of keratin through the reduction of disulfide bonds. Hence both in vitro and ex vivo models indicate that Selenium disulfide is a promising candidate for the treatment of MGD.

CONTROL ID: 3533512

SUBMITTER (NAME ONLY): Jose Villa-Carpes

TITLE: VISUAL ACUITY CHANGES WITH TIME FOLLOWING VISION THROUGH BANGERTER FILTERS

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Villa-Carpes, J. Marin-Sanchez, Ophthalmology, Hospital Clinico Universitario Virgen de la Arrixaca, El Palmar, Murcia, SPAIN|J. Villa-Carpes, E. Fernandez, J. Bueno, Laboratorio de Óptica, Instituto Universitario de Investigación en Óptica y nanofísica, Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To analyze whether any type of visual adaptation induced by Bangerter Filters (BF) exists, beyond changes in the blur perception, in terms of Visual Acuity (VA) measured with the Freiburg VA test.

Methods: 25 young healthy adults were enrolled in the experiment, 18 females and 7 males (mean age: 26.2 ± 2.0 years). VA was measured with the Freiburg test at 4 metres, C-Landolt optotype during 0.3 s of exposure time, 4 orientations and 30 repetitions. The BFs (density 0.6) were mounted on top of neutral spectacles. The VA was retrieved at four time points: natural viewing conditions before wearing BF (AV1); immediately after the incorporation of BF (AV2); after 40 min of vision through BF (AV3); and finally, right after returning to natural vision without BF (AV4). A control group underwent the same experimental procedure under natural vision, without filters. Objective refraction and keratometry values were also assessed before and after the use of the BFs. Regression models were used to fit the variables before and after BF use with statistical software.

Results: The Shapiro-Wilk test yielded a normal distribution for the VA values, although the parameters describing the distributions slightly changed among the 4 measurements. A statistically significant (paired T-student test) increase of 16.7% in VA was found after 40 minutes of vision through the BFs. In contrast, the average VA in the control group exhibited no change with time. The values of objective refraction and keratometry remained constant before and after the use of BFs.

Conclusions: A statistically significant increase in VA was measured after 40 min of continuous vision through BFs, with changes neither in refraction nor in ocular biometry. The results obtained from the control group showed that the VA improvement could not be credited to a learning effect. The VA improvement obtained in the experiment shows a quantitative enhancement in vision after an adaptation time.

CONTROL ID: 3533514

SUBMITTER (NAME ONLY): Yair Alster

TITLE: Lipogenic activity of Selenium Disulfide and its role in enhancing lipid production in Meibomian Glands

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Alster, H. Epstein-Barash, H. Rapaport, O. Rafaeli, R&D, Azura Ophthalmic, ISRAEL|

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ABSTRACT BODY:

Purpose: Meibomian Gland Dysfunction (MGD) is the leading cause of Dry Eye Disease (DED). Reduced secretion of lipids due to MGD leads to instability of the tear film and drying of the ocular surface. Meibomian glands share strong similarities with sebocytes in terms of their embryologic development, structure and holocrine mode of lipid secretion. Treatment of seborrheic dermatitis and Dandruff using Selenium disulfide (SeS₂) shampoo results in about 30% of treated patients complaining of excessive oil on their scalp and sebumeter testing indicated increased amount of sebum over the skin following treatment with SeS₂ shampoo. The objective of this work was to test the hypothesis that SeS₂ can directly induce lipid production in glands producing cells such as meibocytes and sebocytes.

Methods: The ability of SeS₂ to enhance lipid secretion was evaluated in a 3-D cultures of human sebocytes (human cell line SEBO662; BioAlternative, France). First, using a 2-D Sebocyte model, SeS₂ concentration range which did not induce apoptosis of the immortalized sebocyte cell line was determined. Following that, the lipogenic effect was tested in the 3-D culture treated with two Selenium disulfide concentrations and a carrier control. The treated cultures were incubated for 14 days. Oil-red-O stained tissue sections were evaluated to determine lipid production based on the extent of lipid accumulation which was quantified by calculating the lipid droplet surface area in the samples.

Results: When compared to control, lipid production was shown to be significantly increased by 282% (P<0.05) with 0.01 µM and by 348% (P<0.05) with 0.1 µM SeS₂.

Conclusions: Through their lipid secretion the Meibomian glands play a crucial role in maintaining a healthy ocular surface and its optical quality. Located in the upper and lower eyelids, these oil-producing glands are modified sebaceous glands and are responsible for secreting the lipid layer (meibum) that forms the outermost layer of the tear film. The in-vitro results suggest that Selenium disulfide has the potential to improve Meibomian Glands' function by increasing their lipid production. Such outcome may have significant therapeutic effects in patients with MGD

CONTROL ID: 3533518

SUBMITTER (NAME ONLY): Dario Rusciano

TITLE: EFFECTS OF TOPICAL GABAPENTIN ON OCULAR PAIN AND TEAR SECRETION

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Rusciano, M. Olivieri, S. Pezzino, Research, Sooft Italia SpA, Montegiorgio, Marche, ITALY|M. Dal Monte, M. Cammalleri, P. Bagnoli, Biology, Università degli Studi di Pisa, Pisa, Toscana, ITALY|

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ABSTRACT BODY:

Purpose: Neuropathic ocular pain is a frequent occurrence in medium to severe dry eye syndrome (DES). Only palliative treatments, such as lubricants and anti-inflammatory drugs, are available to alleviate patients' discomfort. Anesthetic drugs are not indicated, because they may interfere with the neural feedback between the cornea and the lacrimal gland, thus impairing tear production and lacrimation. Aim of this study has been to address the analgesic and not anesthetic activity of gabapentin (GBP), given as eye drops on the ocular surface, and to show that it does not decrease lacrimation.

Methods: GBP (2%) or oxybuprocaine (BNX: 0.4%) eye drops were given to rabbits' eyes. Sensibility was estimated by a Cochet-Bonnet esthesiometer and lacrimation measured by Schirmer strips. Pharmacokinetics (PK) was studied by HPLC/MS/MS in eye tissue extracts. Expression of neurotransmitters and aquaporin-5 (AQP5) was detected in lacrimal glands in vivo, and corneal epithelial cells in vitro.

Results: Analgesic effects obtained by GBP instillation were distinct from anesthetic effects after BNX. PK analysis showed that the most part of GBT (97.7% at 30 minutes, and 96.7% at 2 hours) remains in the conjunctiva, and the cornea contains most of the remaining amount (2.1% at 30 minutes, and 2.5% at 2 hours). Schirmer test showed that BNX indeed decreased lacrimation in the first 30 minutes, whereas GBP – unexpectedly – even stimulated it, with an effect lasting 90 minutes. Correspondingly, the neuro-mediators Ach and Ne were decreased in the lacrimal glands after BNX treatment, while they were dramatically increased after GBP treatment. Similar findings were made for AQP5 expression. Notably, GBP also increased AQP5 expression in corneal epithelial cells in vitro.

Conclusions: GBP appears to be endowed with anti-inflammatory (published), analgesic and secretagogue properties. Therefore, topic administration of GBP as eye drops could be the ideal treatment for neuropathic pain caused by severe dry eye.

CONTROL ID: 3533523

SUBMITTER (NAME ONLY): Janice Kim

TITLE: Association of Human Plasma Metabolomics with Delayed Dark Adaptation in Age-Related Macular Degeneration

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Dark adaptation (DA), a functional outcome measure, is impaired early in age-related macular degeneration (AMD) prior to visual acuity loss. Metabolomics, the qualitative and quantitative analysis of metabolites, have provided insight on multifactorial diseases including AMD. In order to better understand AMD pathogenesis, we performed a study to analyze the association between plasma metabolite levels and DA in AMD.

Methods: Cross-sectional study including both eyes of 71 subjects, 53 with AMD (13 early AMD, 31 intermediate AMD, 9 late AMD) and 18 controls. Participants were imaged with color fundus photographs for AMD classification (Age-Related Eye Disease Study classification). Fasting blood samples were collected and used for metabolomic profiling with ultra-performance liquid chromatography-mass spectrometry (LC-MS). Patients were also tested with the AdaptDx (MacuLogix, Harrisburg, PA) DA 20 minutes protocol. Rod-intercept time (RIT) was assessed and area under the dark adaptation curve (AUDAC) were calculated. Associations between RIT and metabolite levels were tested using multilevel multivariate mixed-effects linear modelling. An alternative analysis was performed using AUDAC as the outcome.

Results: Prolonged RIT was significantly associated ($P < 0.01$) with lower levels of fatty acid-related lipids and higher levels amino acids related to glutamate, leucine, isoleucine, and valine metabolism. Specifically, 8 plasma metabolites were associated with RIT, including 2 amino acids (N-acetylglutamine [$P = 0.005$], +r and N-acetylleucine [$P = 0.008$], +r), 1 carbohydrate (mannitol/sorbitol [$P = 0.003$], +r), and 5 fatty acid-related lipids ([$P < 0.008$], -r). Similar results were found for 14 significant plasma metabolites when AUDAC was used as the outcome, with the addition of 2

nucleotides (beta-alanine [P= 0.002], +r, and xanthine [P= 0.008], -r).

Conclusions: To our knowledge, this is the first report to study the association of metabolites with DA. Our results suggest that reduced levels of fatty acid-related lipids and elevated levels of amino acids may be associated with worse DA (prolonged RIT or increased AUDAC), suggesting that oxidative stress and mitochondrial dysfunction may play a role in AMD and its visual impairment.

CONTROL ID: 3533536

SUBMITTER (NAME ONLY): Biyue Guo

TITLE: Treatment zone characteristics in children with slower axial elongation after orthokeratology treatment

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Guo, S. Cheung, P. Cho, School of Optometry, The Hong Kong Polytechnic University, Hong Kong, CHINA]

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ABSTRACT BODY:

Purpose: To determine the treatment zone characteristics in children with slower axial elongation (AE) after orthokeratology (ortho-k) treatment and potential correlation with myopia control effect

Methods: Pertinent data was retrieved from 34 children (ROMIO: 13; TOSEE: 21) were retrieved: 18 subjects with the slowest AE (0.03 ± 0.12 mm) and 16 subjects with the fastest AE (0.70 ± 0.11 mm) after 24-month lens wear. The subtractive tangential corneal topographical map (24-month visit) was used to determine the treatment zone (TZ), defined as the central flattened area enclosed within points showing no refractive change. Measurements were taken with the cross-sectional line aligning with the horizontal axis and passing through the approximate geometric center of the TZ. The size and depth (maximum dioptric change) of the TZ were determined. Induced myopic defocus was defined as differences between the points with greatest dioptric changes for both temporal (difference between AD) and nasal (difference between BE) as shown in Figure 1. The slopes of corneal power changes (eg. AD/DC or BE/EC in Figure 1) on temporal and nasal sides (along the horizontal cross-sectional line) were estimated manually using print-outs of the graphs. Only data from the right eye were analysed and compared.

Results: Baseline data (refraction, vision, and axial length) did not differ between the fast and the slow progression subjects, but the former were younger (8.68 ± 0.82 vs 9.95 ± 1.49 years; $p = 0.004$). Smaller TZ size were noted in the slow progression group (2.98 ± 0.58 mm vs 3.56 ± 0.80 mm, $p = 0.024$), but no significant correlation between TZ size and axial elongation was found ($r = 0.317$, $p = 0.068$). No significant differences were found in TZ depth, slopes of corneal power change and induced myopic defocus between the two groups.

Conclusions: Slower progressors after ortho-k treatment has statistically smaller TZ size compared to fast progressors. However, no correlation was found between TZ size and axial elongation.

CONTROL ID: 3533544

SUBMITTER (NAME ONLY): Micaela Gobeille

TITLE: Rasch Analysis and Validation of a Timed Instrumental Activities of Daily Living Instrument in Low Vision Patients

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.R. Gobeille, K. Fujiwara, R.W. Massof, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Assess internal and external validity of a Timed Instrumental Activities of Daily Living (TIADL) instrument to evaluate visual ability based on task performance time and error rate for patients with low vision when the instrument is administered in patients' homes.

Methods: Data were collected within patients' homes from patients with low vision receiving home care from an occupational therapist (n=144). Patients completed a series of ADL tasks as quickly and accurately as possible. Tasks included: 2 telephone tasks, 8 cash transaction tasks (i.e. making change), 3 search tasks (i.e. finding items on a shelf), 3 short reading tasks (i.e. reading package information), and a medication management task. Completion time and number of errors were recorded for each task. Data were then quantized and underwent Rasch analysis to estimate the latent visual ability variable based on observed time and accuracy. The Activity Inventory (AI) was also administered and data underwent Rasch analysis to estimate self-reported visual ability.

Results: At baseline, average TIADL task performance time was 26 seconds (range 1-441 seconds), and 72% of the 2561 tasks performed were completed without error.

Pseudo- R^2 was large for TIADL item measures estimated by time (0.996) and error (0.954), as well as for person measures estimated by time (0.929). Pseudo- R^2 for TIADL person measure estimated by error was small (0.16). The distribution of TIADL person measure infit mean squares approximated the expected χ^2/df distribution for both time and error. Item infit z-scores fell within 2 standard deviations of 0 except for one item corresponding to medication management. TIADL item measures estimated from time versus those from error were well correlated ($R=0.73$), while person measures estimated from time versus those from error showed a more moderate correlation ($R=0.38$). Visual ability based on TIADL time was moderately correlated ($R=0.34$) with visual ability based on the AI.

When rehabilitation outcome measures were compared between TIADL time and the AI, change scores were positive (0.65 logit for AI, 0.54 logit for TIADL time) and Cohen's effect sizes were moderate ($d=0.78$ for AI, $d=0.53$ for TIADL time). Weak agreement was seen between AI and TIADL time change scores ($R=0.16$).

Conclusions: Valid outcome measures can be estimated from TIADL performance time when observed in the patient's home environment.

CONTROL ID: 3533551

SUBMITTER (NAME ONLY): Mathew Mitchell

TITLE: A Comparison of Short-term Efficacy and Post-operative Management of Xen Gel Stents to Glaucoma Drainage Devices in a Private Practice Setting.

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mitchell, J. Nolan, M. Latina, Advanced Glaucoma Specialists, Massachusetts, UNITED STATES|M. Latina, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mathew Mitchell: Commercial Relationship: Code N (No Commercial Relationship) | John Nolan: Commercial Relationship: Code N (No Commercial Relationship) | Mark Latina: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The XEN gel stent is touted as comparable to the trabeculectomy, however, many surgeons prefer glaucoma drainage devices (GDD) as a primary glaucoma surgical procedure. To our knowledge there have been no studies comparing XEN to GDD procedures. This study evaluates short-term efficacy and post-op management of the XEN compared to GDD in a real-world private practice setting.

Methods: We performed a retrospective chart review of 123 patients treated with either glaucoma shunt surgery, using Baerveldt, Molteno, or Ahmed valves, or XEN surgery with ab-interno or ab-externo implantation. The IOP, number of glaucoma medications, visits, and needling interventions were determined for the groups over 3 months. Two-tailed Mann-Whitney U Test was used for statistical analysis.

Results: A total of 123 patients were included, 35 males, 24 females with a mean age of 75 in the glaucoma shunt group (GSG)(n=59) and 24 males, 40 females with a mean age of 74 in the Xen stent group (XEN)(n=64). GSG used Baerveldt 250mm (n=4), Molteno 3 185mm (n=15), and Ahmed FP7 (n=27) or S2 (n=13) valves. XEN was inserted internally (n=36), and externally (n=27). Pre-op IOP of GSG (26.2 ± 8.95 mmHg) was not significantly different from XEN (24.0 ± 7.21 mmHg) ($p=0.3$). XEN had greater percent post-op IOP reduction at 1 month (XEN= $37.5\% \pm 28.4\%$, GSG= $23.7\% \pm 30.8\%$, $p=0.008$), however, the reduction was not significantly different at 1 day (XEN= $61.7\% \pm 37.3\%$, GSG= $45.1\% \pm 48.1\%$, $p=0.07$), 1 week (XEN= $57.9\% \pm 23.2\%$, GSG= $44.0\% \pm 35.5\%$, $p=0.06$), and 3 months (XEN= $36.2\% \pm 23.5\%$, GSG= $31.9\% \pm 26.3\%$, $p=0.3$). XEN required more post-op visits over 3 months (XEN= 11.9 ± 4.1 , GSG= 9.53 ± 3.3 , $p=0.0002$). GSG required more IOP-lowering medications at 3 months (3.12 ± 1.08 vs. 2.14 ± 1.46 , $p=0.0003$). Post-op interventions were not significantly different between GSG (1.02 ± 1.23) and XEN (1.34 ± 1.54) ($p=0.3$).

Conclusions: Both the GSG and XEN achieved similar percent reduction in IOP at 3 months of 31.9-36.2%. XEN required significantly more post-op visits, while GSG required significantly more post-op medicines to achieve the reduction in IOP. Although there were more post-op visits in the XEN group, this could be due to lack of experience with the relatively new procedure. In a private practice setting, the two procedures produced a similar IOP reduction at the end of the global period with a slight variation in post-op management.

CONTROL ID: 3533556

SUBMITTER (NAME ONLY): Amirmohsen Arbabi

TITLE: Sociodemographic and Economic Factors in Outcomes of Tube Shunts for Neovascular Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Arbabi, W.S. Shalaby, J. Myers, M. Moster, R. Razeghinejad, L. katz, A. Shukla, Ophthalmology, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the potential impact of sociodemographic and economic factors on the neovascular glaucoma (NVG) tube shunt surgery outcomes

Methods: This retrospective, single center, comparative case series included consecutive patients who underwent tube shunt surgery for NVG and had ≥ 6 months of follow-up. Regional average adjusted gross income (AGI) was determined by cross-referencing self-reported residential zip codes with average AGI per zip code supplied by the Internal Revenue Service. Two groups were created: 1) lower income - individuals from neighborhoods with the lowest 10% of AGI (near the United States poverty line), 2) higher income – the remaining 90% of individuals. Main outcome measures were visual acuity (VA), intraocular pressure (IOP), and glaucoma medication number at 6 months and the most recent visit.

Results: Mean annual AGI in the higher income group (130 patients) was \$69,596 \pm 39,700 and the lower income group (16 patients) was \$27,487 \pm 1,600 ($P < 0.001$). Age, sex, distance to the clinic, language, and all baseline clinical variables (including VA and IOP) were comparable between groups. Lower income was associated with non-white race (81.3% vs. 52.3%; $P = 0.024$). At month 6, VA in the lower income group (median: HM, range: 20/70 – NLP) was worse than the higher income group (median: CF, range: 20/25 – NLP) (logMAR VA : 2.32 ± 0.8 vs. 1.77 ± 1.1 ; $P = 0.02$); these trends persisted through the most recent visit ($P = 0.043$) (Figure 1). Follow-up IOP and medications were similar between groups.

Conclusions: Our study analyzed a possible relationship between income and outcomes after surgery for NVG and found that despite similar preoperative characteristics in the two groups, those with lower income had significantly worse VA at postoperative month 6 and at their most recent visit. Furthermore, the lower income group had a higher proportion of non-white race, which may have affected surgical outcomes. Additional study on this potential association is warranted and may help guide clinicians in counseling patients and provide further insight regarding reasons for worse visual outcomes in the most vulnerable populations.

CONTROL ID: 3533564

SUBMITTER (NAME ONLY): Xiangxiang Liu

TITLE: Transcleral Cyclophotocoagulation Using Slow Burn Technique in Glaucoma Secondary to Vitreoretinal Surgeries: One-Year Results

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Liu, M. Khodeiry, H. Sheheitli, M. Sayed, R.K. Lee, Bascom Palmer Eye Institute, Department of Ophthalmology, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|X. Liu, Beijing Tongren Eye Center, Beijing Tongren Hospital, Capital Medical University, Beijing, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: The management of secondary glaucoma following vitreoretinal surgeries is challenging as postoperative conjunctival scarring and subconjunctival migration of silicone oil may limit the success of conventional filtration and tube surgeries. We report the treatment outcomes of slow burn transscleral cyclophotocoagulation (TSCPC) as a primary glaucoma surgical technique in the management of secondary glaucoma attributed to prior vitreoretinal surgeries.

Methods: A retrospective study of 18 eyes of 18 patients with medically uncontrolled glaucoma secondary to pars plana vitrectomy (PPV) with silicone oil injection (SOI) and no history of previous incisional glaucoma or cyclodestructive procedures, who underwent TSCPC using slow burn settings (1250-milliwatt power and 4-second duration). The primary outcome: surgical success at 1 year defined as intraocular pressure (IOP) 6 - 21 mmHg and reduced $\geq 20\%$ from baseline, no incisional glaucoma reoperation, and no loss of light-perception vision. Secondary outcomes included glaucoma medication use, visual acuity (VA) changes, and surgical complications.

Results: The mean age of the patients at time of surgery was 52.0 ± 17.4 years, and the mean follow-up duration was 18.1 ± 4.7 months. At 1 year, IOP decreased from 29.7 ± 9.6 mmHg to 14.6 ± 6.5 mmHg with mean IOP reduction of 45.8 % ($p < 0.001$). The baseline number of glaucoma medications was 4.2 ± 0.9 at baseline and 1.9 ± 1.3 at 1 year after TSCPC ($p < 0.001$). A non-significant change in logMAR VA from 1.36 ± 6.8 at baseline to 1.29 ± 0.79 at 1 year was reported ($p=0.722$). The success rate at 1 year was 72.2 %. Two eyes (11.1%) had TSCPC retreatment. One eye (5.6%) required incisional glaucoma reoperation. Complications included: iritis in 2 eyes (11.1%), macular edema in 1 eye (5.6%), hypotony transient in 1 eye (5.6%) and hyphema in 1 eye (5.6%).

Conclusions: Slow burn TSCPC as a primary glaucoma surgical procedure in patients with secondary glaucoma following PPV and SOI has high efficacy and minimal complications. Prospective studies with a larger number of participants are needed to confirm our encouraging results.

CONTROL ID: 3533575

SUBMITTER (NAME ONLY): Samantha Madala

TITLE: The association between retinal vascular occlusions and cardiovascular disease subtypes

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Madala, M.H. Goldbaum, M. Bakhoun, The Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|C. Bakhoun, Pediatric Nephrology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vascular occlusions are associated with cardiovascular disease. However, the association of retinal vascular occlusions with different subtypes of cardiovascular disease is not well defined. Additionally, whether retinal vascular occlusions are associated with higher risk of stroke independent of underlying cardiovascular disease is unknown.

Methods: In this cross-sectional study, we reviewed the records of 98,202 individuals who were evaluated by an ophthalmologist or an optometrist at our institution for different clinical indications from July 1, 2015 until July 1, 2020. We identified individuals with retinal vascular occlusions, stroke and cardiovascular diseases including hypertension, diabetes mellitus (DM), carotid disease, coronary heart disease (CHD) and atrial fibrillation (AF) through billing diagnosis codes. All statistical analyses were performed using IBM SPSS version 26. Logistic regression models were used to analyze odds ratios for retinal vascular occlusions and stroke with 95% confidence intervals. Differences between two and three groups were analyzed with Pearson-Chi Square and one-way ANOVA tests, respectively.

Results: The following cardiovascular diseases were significantly associated with retinal vascular occlusion: carotid disease (OR, 3.0; CI 2.5 – 3.6), hypertension (OR, 2.1; CI 1.9 – 2.4) and DM (OR, 1.5; CI 1.3 – 1.7). CHD and AF were not significantly associated with retinal vascular occlusion. Females had lower odds of retinal vascular occlusion (OR, 0.88; CI 0.79 – 0.98). After adjusting for age, sex and underlying cardiovascular co-morbidities, we found that presence of retinal vascular occlusion was associated with an odds ratio for stroke of 2.2 (CI 1.9 – 2.7). The association between retinal vascular occlusion and stroke was significantly higher in individuals younger than 40 years of age, with an odds ratio for stroke of 8.4 (CI 3.6 – 19.6, $p < 0.001$), even after adjusting for sex, hypertension, DM, carotid disease, AF and CHD.

Conclusions: Our findings demonstrate a strong association between retinal vascular occlusion and carotid artery disease, hypertension and DM. Our results also demonstrate that retinal vascular occlusion is significantly associated with stroke, and more strongly so in younger subjects. Individuals who present with retinal vascular occlusion warrant further evaluation for underlying cardiovascular disease and stroke prevention.

CONTROL ID: 3533579

SUBMITTER (NAME ONLY): Natalie Bick

TITLE: Step-to-step gait symmetry in glaucoma

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.A. Bick, M. Redfern, R. Cham, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|I. Conner, R. Cham, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|G. Wollstein, K. Chan, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|K. Chan, Radiology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Falls risk increases with glaucoma. Gait impairments occur in people with glaucoma; however, they do not fully explain why greater visual field loss results in higher fall rates (Mihailovic 2020). Harmonic ratios, which are derived based on the frequency analysis of trunk acceleration signals, quantify step-to-step gait symmetry and have been associated with falls risk in older adults (Bellanca 2013). Harmonic ratios have not been examined in glaucoma. This pilot study tested the hypothesis that gait symmetry will be reduced with worse visual field loss in glaucoma, particularly under sensory challenging conditions and increased attention demands.

Methods: Ten adults with glaucoma (6F/4M, 67±8 years), instrumented with motion capture markers (Vicon Motion Systems Ltd, UK) and accelerometers (Delsys Inc., MA), were asked to walk in 8 conditions with varying floor (hard floor, carpet), light (well-lit, dim) and concurrent information processing (IP) task conditions (no task, auditory IP choice reaction time task). Glaucoma severity was determined using the visual field mean deviation (VF MD) assessed by automated Humphrey perimetry (Zeiss, CA). The VF MD measured in the better/worse eye and averaged across the 10 participants was equal to -2.9±3.8 / -7.5±6.7 dB, respectively. The analyses used mixed linear models with the fixed effects including VF MD either in the better eye or worse eye, floor/light condition, IP condition and the first order interaction of these factors. Subject was added as a random effect. The dependent gait measure was the anteroposterior (AP) harmonic ratio (Bellanca 2013). Statistical significance was set at 0.05.

Results: Visual field MD in the better eye was associated with the AP harmonic ratio ($F(1,8)=11.9$, $p=0.009$), i.e. step-to-step gait symmetry in the anteroposterior direction was reduced with worse visual field loss in the better eye. In addition, the main effect of floor/light condition was associated with the AP harmonic ratio ($F(3,58)=8.4$, $p<0.0001$). Post-hoc analyses found this effect was driven by a change in floor condition. All other effects included in the analyses did not reach statistical significance ($p>0.1$).

Conclusions: Gait symmetry is reduced in glaucoma and thus may be an important metric. Further research is needed to determine if reduced gait symmetry is associated with increased falls risk in this population.

Mihailovic. Invest Ophthalmol Vis Sci. 2020;61(3):30.

Bellanca. J Biomech. 2013; 46(4):828.

CONTROL ID: 3533602

SUBMITTER (NAME ONLY): Yukihiro Shiga

TITLE: Live two-photon calcium imaging in retinal ganglion cells: characterization of early changes in a mouse glaucoma model.

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Shiga, L. Alarcon-Martinez, N. Belforte, H. Quintero, D. Villafranca-Baughman, F. Dotigny, A. Di Polo, Department of Neuroscience, University of Montreal Hospital Research Center (CRHUM), Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Calcium plays a critical role in the regulation of neuronal activity. Our current understanding of calcium dynamics in living retinal ganglion cells (RGCs) and how they are altered in glaucoma is limited. Here, we used two-photon laser scanning microscopy (TPLSM) to investigate i) real-time light-triggered calcium responses in ON and OFF RGCs and their compartments (dendrites, soma, axons), and ii) alterations in light-evoked calcium responses during ocular hypertension damage.

Methods: Live calcium imaging in RGCs was performed by TPLSM in transgenic mice carrying the calcium indicator CGaMP6 (Thy1.GCaMP6) or after intraocular administration of an adeno-associated virus (AAV) encoding GCaMP6. Ocular hypertension was induced by intracameral injection of magnetic microbeads. The following light-evoked calcium responses were measured: i) baseline fluorescence (F_0), ii) peak fluorescence ($\Delta F/F_0$), iii) rise time (T_r : time to reach 1/3 peak $\Delta F/F_0$), and iv) decay time (T_d : time to fall to 1/3 peak $\Delta F/F_0$). Student's t-test or ANOVA were applied (significance = $p < 0.05$).

Results: TPLSM imaging demonstrated distinct light-evoked calcium dynamics among RGC subtypes, with ON cells characterized by higher peak ($\Delta F/F_0$) fluorescence and faster (low T_r) responses than OFF cells (N=8 mice/group, n=~70 cells/group, $p < 0.001$, $p < 0.01$). TPLSM also revealed distinct compartment-dependent calcium responses including lower baseline (F_0) in axons and dendrites relative to soma, and higher peak fluorescence ($\Delta F/F_0$) in axons relative to soma (N=5 mice/group, n=5-7 cells, ANOVA, $p < 0.001$, $p < 0.05$). RGC calcium responses were altered soon after induction of ocular hypertension. For example, ON RGCs transduced with AAV.GCaMP6 displayed a significant increase in T_d values relative to controls (N=4-8 mice/group, n=48-61 cells/group, $p < 0.05$) suggesting delayed calcium signal decay in glaucoma. These results were consistent with those observed in Thy1.GCaMP6 mice (N=7-8 mice/group, n=76-90 cells/group, $p < 0.05$).

Conclusions: Our data support that: i) TPLSM is a powerful tool to assess calcium dynamics in living RGCs with unprecedented spatiotemporal resolution, ii) calcium responses differ among RGC subtypes and subcellular compartments, and iii) calcium dynamics are altered in glaucoma indicating impaired calcium homeostasis in vulnerable RGCs.

CONTROL ID: 3533616

SUBMITTER (NAME ONLY): Mark Bullimore

TITLE: The Underestimated Role of Myopia in Projected Visual Impairment in the United States

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Bullimore, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|N.A. Brennan, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The projected prevalence of visual impairment (VI) in the USA has been estimated but has not accounted for the increasing prevalence of myopia, particularly in older individuals. We estimate the USA prevalence of VI in 2050 accounting for the changing distribution of both age and myopia.

Methods: 1. Age projections of the USA population in 2050 were taken from the USA census website.
2. Overall prevalence of myopia (−0.50 D or worse) of 49.8% was used, based on Vitale et al. (2008) and Holden et al. (2016).
3. The distribution of myopia, by severity, was calculated using the model of Brennan et al. (2020)
4. VI as a function of age and refractive error was modelled by multiple linear regression from a large data set of an advanced European population (Tideman et al. 2016). This data set is agnostic with respect to the disease condition associated with VI.
5. Finally, by convolving the distributions of myopia and age with the cumulative risk of VI, the number of individuals in the USA with VI in 2050 was calculated.

Results: Of the estimated 2050 USA population of 399.8 million, 199.1 million will be myopic and 29.5 million will have high myopia (< -5D). The cumulative odds of visual impairment (20/40 or worse) is $10^{(0.057\text{Age} - 0.122\text{Rx} - 4.03)}$ and the projected total number with VI is 19.1 million. Of these, 12.6 million will be myopes compared with 6.5 million non-myopes. Given approximately equal numbers of myopes and non-myopes, an estimated 6 million cases of VI will therefore be directly attributed to increased risk of eye disease associated with myopia (= 12.6 – 6.5). Among individuals 65 years and younger, myopes will comprise 75% of individuals with VI, while representing only half of the population. At 82 years, myopes will still account for two-thirds of VI.

Conclusions: Assuming that the data from Tideman et al. are applicable to the USA, we predict that some 30% of VI in the US population in 2050 will be attributable to myopia. Failure to account for the increasing prevalence of myopia among the aging population leads to a substantial underestimate of the prevalence of VI. Approaches that treat disease-states associated with myopia are needed to reduce the threat of VI in the USA.

CONTROL ID: 3533621

SUBMITTER (NAME ONLY): Michael Chua

TITLE: Amniotic membrane subretinal placement to promote closure of persistent full-thickness macular holes

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chua, J. Lee, M. Jansen, J. Giovinnazzo, B. Powell, R. Gentile, A. Deobhakta, G. Landa, A. Dayan, R.B. Rosen, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: We report a case series of patients with persistent macular holes who underwent human amniotic membrane (hAM) subretinal placement to achieve successful anatomic macular hole closure.

Methods: This is a retrospective review of a non-consecutive case series conducted at New York Eye and Infirmary of Mount Sinai. There were 10 patients from March 2019 to May 2020 who presented with persistently open full-thickness macular holes. All patients underwent subretinal hAM subretinal placement to promote closure of recalcitrant, full-thickness macular holes.

Results: Ten patients, 6 females and 4 males were included in the series. The mean age was 56.7 years (range 20-77 years). Eight of the patients had already undergone pars plana vitrectomy with internal limiting membrane peeling and gas or silicone oil tamponade. One patient's previous surgical history was unknown. One patient had a chronic full-thickness macular hole for over a decade. The mean preoperative BCVA was 1.6 logMAR (20/800) ranging from 2 to 0.8 logMAR (20/2000 – 20/150). Eight patients received gas as tamponade, of which 5 patient received SF6 20-25% and 3 patients received C3F8 10-14%. Two patients received silicone oil as tamponade. Patients were examined 1 day, 1 week, 1 month, 3 months and 6 months. An optical coherence tomography scan was performed at every visit. BCVA improved from mean 1.6 logMAR preoperatively (20/800) to 1.4 logMAR (20/500) 1-month after the surgery. At the 3-month post-operative visit, the BCVA improved to 1.1 logMAR (20/250), for 9 of the 10 patient records available. In all 10 cases, the macular hole appeared closed at the 1 week post-operative visit and remained closed at their last follow-up exam. OCT showed macular hole closure in all the cases. No adverse events such as increase in intraocular pressure or intraocular inflammation were reported during the post-operative period.

Conclusions: For large, chronic, recurrent, or persistent macular holes, the use of amniotic membrane subretinal transplantation may serve as a useful surgical adjunct to promote macular hole closure.

CONTROL ID: 3533632

SUBMITTER (NAME ONLY): Brendan Kenyon

TITLE: Topical Recombinant Human Nerve Growth Factor Improves Outcomes in Murine Model of Neuropathic Corneal Pain

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Kenyon, D.L. Harris, F. Qiu, C. Chao, Y. Seyed-Razavi, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|B. Kenyon, Program in Neuroscience, Tufts University Graduate School of Biomedical Sciences, Boston, Massachusetts, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Since its discovery, nerve growth factor (NGF) has sparked widespread interest in possible therapeutic utility across neurologic diseases. NGF and other neurotrophic factors are upregulated in neuropathic pain, although their precise role remains to be fully understood. Herein, we assess the possible therapeutic benefit of recombinant human NGF (rhNGF) in the ciliary nerve ligation model of neuropathic corneal pain.

Methods: Adult 7- to 8-week-old male C57BL/6J mice underwent ciliary nerve ligation for the induction of NCP and were treated with six 10 µL drops/day of 0.02mg/mL rhNGF or vehicle (n=6/group). Clinical outcomes were assessed at 7-, 10-, and 14-days post-ligations. Outcomes included corneal fluorescein staining (CFS), Cochet-Bonnet esthesiometry, and challenge with 10 µL of [5M] saline, cold saline, and L-menthol for assessment of pain by the paw wipe response. At day 14, trigeminal ganglia (TG) were excised for qRT-PCR analysis of neurotrophic factors and cytokines.

Results: Ligation did not significantly alter CFS or corneal sensitivity between groups at any time point ($p>0.05$). Animals did not differ in their baseline or post-ligation responses to [5M] saline prior to treatment initiation (16.0 vs 13.0, $p>0.05$; 31.0 vs 31.6, $p>0.05$). There was a persistent decrease in response to [5M] saline in the rhNGF-treated group (Day 7: 21.7 vs 30.2, $p<0.001$; Day 10: 18.0 vs 27.4, $p<0.001$; Day 14: 16.2 vs 28.3, $p<0.0001$). Responses to cold saline were slightly, although not significantly, reduced in the NGF group (Day 7: 5 vs 8.6, Day 10: 5.2 vs 7.8, Day 14: 4.4 vs 7.2; all $p>0.05$). Similar results were obtained with responses to L-menthol (Day 7: 5.0 vs 9.0, $p<0.05$; Day 10: 5.2 vs 7.4, $p>0.05$; Day 14: 2.8 vs 5.8, $p>0.05$). rhNGF treatment reduced levels of several neurotrophic factors in the TG compared to vehicle treatment (BDNF: 0.78 vs 1.00, $p<0.05$; NT-3: 0.25 vs 1.00, $p<0.01$; NT-4/5: 0.11 vs 1.00, $p<0.05$), but did not show increase in pro-inflammatory cytokines (IL-1b: 0.50 vs 1.00, IL-6: 0.92 vs 1.00, TNF-a: 0.69 vs 1.00; all $p>0.05$).

Conclusions: These findings suggest that topical rhNGF treatment improves pain outcomes in our neuropathic corneal pain and warrant future studies in the clinic. Furthermore, qRT-PCR results indicate that topical rhNGF treatment alters expression of neurotrophic factors, but not pro-inflammatory cytokines within the TG.

CONTROL ID: 3533651

SUBMITTER (NAME ONLY): Danny Jokl

TITLE: Uniocular peripheral retinal laser stabilizes AMD visual outcomes binocularly

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.H. Jokl, R. Allikmets, W. fan, M. busuioc, Columbia University Irving Medical Center, New York, New York, UNITED STATES|R. Smith, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|D.H. Jokl, S. Amarakoon, S. Yzer, J. van meurs, Rotterdam Ophthalmic Institute, Rotterdam, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Purpose: Can uniocular, peripheral retinal laser influence AMD vision outcome long term?

Methods: Methods: 14 patients with AMD with IRB approval (Rotterdam, The Netherlands (ISRCTN 967546)- and baseline vision (20/20-20/40 OU), consented to uniocular, 200 argon laser 200 μ spots at 200 mV to the superior temporal retina, with the untreated eye as control. At termination, binocular changes in drusen volume and visual acuity were observed. In place of a control, AREDS AAMD long term visual outcomes were used.

11/14, patients, (5 M, 6F; ages 58-83), 3 patients had deceased, were examined a mean of 58 months (12-74 months) with digital fundus photos and drusen images. DNA of 11/14 patients was analyzed for ARMS2 and CFH with AMD-associated SNPs. Masked clinical and genetic data were correlated.

Results: At a significance level of 0.05 - a significant interaction beneficial effect between increasing time from the initial laser treatment was found.

In the treated eye, coefficient for time was 0.0013 ($p=0.0016$) - for every month increase, the average VA increases by 0.0013 units, adjusting for eyes (whether it's the right eye or the left eye).

In the control eye, coefficient for time was 0.0040 (p -value < 0.0001) - for every month increase, the average VA increases by 0.0040 units.

- 64% of the cohort displayed little visual loss after 10 years;

- 27% had uniocular visual loss;

- 9% (one case) had bilateral visual loss.

The two genetic risk alleles showed no correlation with the final visual acuity.

Uniocular retinal laser had a binocular effect on vision outcomes:

91% (10/11subjects) maintained baseline visual acuity in one or both eyes.visual acuity in one or both eyes.

A significant interaction between treatment and time ($p=0.0028$), with better VA for the treated eye was found.

Conclusions: In the presence of alleles for ARMS2 and CFH, functional long term binocular visual outcomes compared favorably to AREDS AAMD long term visual acuity findings,

The mean net change in drusen area in the treated (resp., control) eye was +1.5 resp., -1.1) mm sq, was not significant (paired t test ($p= 0.13$)).

- These serendipitous findings suggests a systemic immune system activation to inflammation induced by uniocular retinal laser.

- Despite limitations of a pilot study, confirmation from a larger controlled study is warranted.

CONTROL ID: 3533686

SUBMITTER (NAME ONLY): Samuel Novo

TITLE: Transcription factors mediating the post cataract surgery response

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.G. Novo, A. Garg, A. Faranda, M.H. Shihan, Y. Wang, M.K. Duncan, Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cataract surgery is known to induce ocular inflammation, which if left untreated, can result in damage to other ocular tissues. We have previously reported that the lens epithelial cells (LECs) retained in the eye post cataract surgery (PCS) initiate the expression of inflammatory cytokines 1-2 days prior to their phenotypic transition into the myofibroblasts and aberrant lens fiber cells that cause posterior capsular opacification (PCO). However, the mechanism driving the initiation of inflammatory gene expression in LECs and its relationship to PCO pathogenesis is unknown.

Methods: RNA isolated from wildtype (WT) mouse LECs at 0 and 6 hours after lens fiber cells removal to simulate cataract surgery was used for RNAseq. FosB^{tm1.Nes} mice that carry a floxed FosB allele were bred to MLR10Cre mice, which express Cre recombinase in the lens, to generate a FosB lens conditional knockout (cKO) mice. RNAseq was conducted on the FosB cKO mice similarly to the wildtype (WT) mice. The transcriptomic changes observed were validated by immunostaining WT and FosB cKO mice at various times PCS.

Results: RNAseq revealed that remnant LECs upregulate numerous genes known to contribute to the inflammatory response, smooth muscle cell proliferation, and cell migration by 6 hours PCS. Further, the top most upregulated differentially expressed gene in LECs at 6 hours PCS was FosB, a member of the AP1 complex of transcription factors and an immediate early gene (IEG), which drives the inflammatory, fibrotic, and proliferation response of cells in other systems. FosB protein levels upregulate in LECs by 6 hours PCS and slowly downregulate over the next 5 days PCS. We generated a FosB lens cKO mouse to test the hypothesis that FosB upregulation PCS is important in LEC response to surgery. These lenses develop normally and are transparent into adulthood. Initial analysis of the upregulation of TNC, a classic fibrotic marker, and CXCL1 and COX2, 2 classic inflammatory markers, did not reveal any major changes, however, RNAseq is ongoing to determine globally the role of FosB PCS.

Conclusions: IEGs, including FosB upregulate robustly within 6 hours PCS. FosB is not necessary for lens development or transparency, while its roles in PCO are under active investigation.

CONTROL ID: 3533707

SUBMITTER (NAME ONLY): Kunpeng Pang

TITLE: Perfluorodecalin-based oxygenated emulsion mitigates ocular hypoxia and inflammation after alkali burn

SESSION TITLE: Blood flow, ischemia, reperfusion

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Pang, S. Li, S. zhu, J. Yin, Schepens Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|K. Pang, Department of Ophthalmology, Qilu Hospital of Shandong University, Jinan, Shandong, CHINA|K. Pate, Coruna Medical, LLC, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chemical injury to the eye leads to ocular hypoxia and inflammation, which in turn contribute to tissue damage and decrease in vision. We have previously demonstrated that a perfluorodecalin-based supersaturated oxygen emulsion (SSOE) reduces optical opacity and tissue fibrosis after alkali burn to mouse corneas. Herein, we aim to determine the effects of SSOE on ocular hypoxia and tissue inflammation after alkali burn.

Methods: SSOE containing 25% oxygen-carrier perfluorodecalin was manufactured in hyperbaric condition. Alkali burn was induced by placing a 2-mm-diameter filter paper disc soaked with 1M sodium hydroxide solution onto the central cornea of BALB/C mouse for 20 seconds, followed by irrigation with PBS until the pH level of the ocular surface returned to 7. 50 μ l SSOE or non-oxygenated emulsion (vehicle control) was applied to the cornea immediately after burn for 30 minutes. The anterior chamber oxygen concentration was recorded using the DP-PSt7-2 oxygen sensor. Cell apoptosis was determined with TUNEL staining. The expression of inflammatory markers IL-1 β and MMP9 was determined with real-time PCR, and the infiltration of CD45⁺ cells to the cornea and conjunctiva was evaluated by immunostaining and flow cytometry, respectively.

Results: Alkali burn led to a 60% decrease (165 vs 66 μ mol/L, $P < 0.0001$) in the anterior chamber oxygen concentration, which was reversed and further increased (535 μ mol/L, almost 3 times over atmospheric level) by topical application of SSOE, but not the vehicle control. Alkali burn led to cell apoptosis in all layers of the cornea at 1 hour, whereas in SSOE-treated eyes, apoptotic cells were only seen at the superficial epithelial layer (TUNEL-positive cell 100% in control vs 45% in SSOE group, $P = 0.025$). Moreover, SSOE reduced apoptosis of lens epithelial cells (60% in control vs 17% in SSOE group, $P = 0.004$). SSOE treatment reduced the expression of IL-1 β in the cornea ($P = 0.003$) and of MMP9 in the iris/ciliary body ($P = 0.049$). In addition, SSOE treatment decreased the infiltration of CD45⁺ inflammatory cells in the cornea and conjunctiva (27.8% in control vs 19.9% in SSOE group, $P = 0.002$) at 24h after alkali burn.

Conclusions: Topical application of SSOE reduces tissue hypoxia, cell apoptosis, and inflammation after alkali burn. These are the potential mechanisms underlying the therapeutic efficacy of SSOE in treating chemical injury.

CONTROL ID: 3533711

SUBMITTER (NAME ONLY): Michael Berry

TITLE: Corneal laser procedure for vision improvement in patients with late stage age-related macular degeneration and other retinal disorders

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Berry, Optimal Acuity Corporation, Austin, Texas, UNITED STATES|R. Devenyi, S. Markowitz, University of Toronto, Toronto, Ontario, CANADA|M. Berry II, Princeton University, Princeton, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the safety and efficacy of corneal photovitrification (CPV), a new corneal laser procedure, for vision improvement in patients with late stage age-related macular degeneration (AMD) and other retinal disorders involving central vision loss.

Methods: In this retrospective observational cohort study, 60 treated (46 wet AMD - most of which continued to receive anti-VEGF injections, 8 dry AMD, 6 other) and 24 untreated eyes of 42 patients (22F, 20M, 77.7 ± 10.4y) received pre-Tx best corrected distance visual acuity (BCDVA) and potential visual acuity (PVA) examinations and post-Tx BCDVA examinations at 1 month (1m), 3m, 6m and 12m follow-up times. Analyses included descriptive statistics (mean ± SD), Wilcoxon signed rank tests (p-values for post- vs. pre-Tx) for BCDVA, and Pearson correlation coefficients (PCCs) for logMAR values of post-Tx BCDVA vs. pre-Tx PVA.

Results: Safety - No complications or adverse events occurred.

Efficacy - Mean (± SD) BCDVA of treated eyes improved significantly (p=0.0022) from 20/316 (1.20 logMAR) at baseline to 20/200 (1.00 logMAR) at 12m post-Tx, corresponding to 16.7 (± 9.3) letters gained. Mean (± SD) BCDVA of treated eyes also improved significantly with 8.4 (± 11.2), 12.7 (± 15.9) and 9.3 (± 9.3) letters gained at 1m, 3m and 6m, respectively. BCDVA changes of untreated eyes were as large as 2.9 ± 5.1 letters gained at 12m post-Tx, but were not statistically significant.

PVA - At baseline, the mean (± SD) PVA value of treated eyes was 20.8 (± 10.6) letters better than the mean (± SD) BCDVA value, indicating great potential for improvement, but actual mean BCDVA improvements were in the range of 40 to 80% of the PVA "prediction". PCCs for post-Tx BCDVA logMAR values of treated eyes vs. pre-Tx PVA logMAR values were positive and large: 0.71, 0.56, 0.80 and 0.63 at 1m, 3m, 6m and 12m, respectively.

Conclusions: The CPV corneal laser procedure provides significant vision (BCDVA) improvements in patients with late stage AMD and other retinal disorders with central vision loss. The BCDVA improvements correlate well with PVA "predictions".

CONTROL ID: 3533725

SUBMITTER (NAME ONLY): Douglas Brown

TITLE: Ophthalmology and COVID-19: A Snapshot of Clinical Practice in the US

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Brown, E. Jennings, J. Lam, Y. Zhang, Ophthalmology, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a respiratory virus that initially appeared in Wuhan, China in December of 2019. It quickly spread around the globe with the World Health Organization declaring the outbreak a pandemic on March 11, 2020. With rapidly changing national and global guidelines researchers at Temple University (Philadelphia, PA) surveyed ophthalmologists across the United States to examine their response to the pandemic during the months of April 2020 to July 2020.

Methods: The survey is a population based, cross-sectional study. Participants were identified on April 21, 2020 with the "Find an Ophthalmologist" feature on the American Academy of Ophthalmology's website allowing for random retrieval of contact information across the 50 states, ensuring a random sampling of participants by state and general demographics. We distributed the survey via email with responses collected between April and July 2020. We sent 2,299 emails and collected 147 responses (response rate of 6%). Results were compiled and analyzed using the Google Survey Tool.

Results: Ophthalmologists of every specialty, practice type, and geographic region responded. Patient visits across the country fell with 41.8% of respondents seeing less than 25% of their usual volume. Only 20.5% of ophthalmology practices were seeing 26-50% of their patients, 12.3% of practices were seeing 51-75% of patients, and 11.6% of practices were still seeing 76-100% of their patients; 13.7% of ophthalmology practices saw no patients at all. The most common changes implemented were physicians and staff masking (97.29%), decreasing ancillary staff (96.66%), patients masking (95.24%), and cleaning rooms between patients (91.84%). In the office, 61.0% of respondents implemented telemedicine software with another 47.1% indicating they plan to use telehealth at a later date. In our survey, 42.9% of respondents indicated they were performing elective procedures with 68% of respondents stating surgical masks were appropriate for short, low risk procedures compared to 80% of respondents stating N95 was most appropriate for high risk, short cases of less than one-hour duration.

Conclusions: The majority of respondents followed national trends and adhered to CDC and AAO recommendations. Significant financial burden and unpredictable viral trends further emphasize the importance of continual monitoring and adherence to established guidelines.

CONTROL ID: 3533737

SUBMITTER (NAME ONLY): Elia Duh

TITLE: Neuroprotective and Anti-Inflammatory Effects of a Novel Soluble Guanylate Cyclase Activator Runcaciguat in Ischemic Retinal Disease Animal Models

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.J. Duh, Z. Xu, H. Cho, L. Zhou, L. Wu, J. Guerra, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|W. Schubert, C. Terjung, K. Nassar, Bayer AG, Wuppertal, GERMANY|

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ABSTRACT BODY:

Purpose: Neuroinflammatory processes and neurodegeneration are important elements of ischemic retinopathies including diabetic retinopathy (DR). There is a great need for therapies targeting earlier disease before irreversible damage. Soluble guanylate cyclase (sGC) exhibits neuroprotective effects in the central nervous system, but its expression and role in the retina remains unclear. sGC activators might be of potential benefit, especially since they can act on sGC rendered nonfunctional by oxidative stress. The purpose of this study was to evaluate the effect of a novel sGC activator, runcaciguat, in retinal ischemia-reperfusion (I/R) and DR animal models.

Methods: Expression of sGC alpha and beta subunits was evaluated in post-mortem human retina specimens by immunohistochemistry. Transient retinal ischemia-reperfusion was induced in rats by elevation of the intraocular pressure for 20-45 minutes. Streptozotocin injection was used to induce diabetes in other rats. Genome wide expression and RNA Sequencing analyses were performed following I/R. Oral runcaciguat (0.1-10 mg/kg PO QD) was evaluated in a prophylactic and/or interventional setting. Treatment effect on retinal morphology and function were evaluated by histological staining, optokinetic testing (OKT), and electroretinography (ERG).

Results: In addition to retinal blood vessels, multiple human neuronal elements expressed both sGC alpha and beta subunits, including retinal ganglion cells. I/R upregulated multiple inflammatory chemokines, including Ccl2, Cxcl10, Ccl3, Ccl4, and Timp1, at 1 hour after reperfusion and peaking by 6 hours. Runcaciguat-treated rats exhibited better visual acuity compared with vehicle (0.17 ± 0.03 cycle/degree vs. 0.02 ± 0.01 cycle/degree, p value < 0.0001) as measured by OKT, and neuroretinal function as measured by ERG. Runcaciguat-treated rats had improved morphology including increased inner plexiform layer thickness. Runcaciguat-treated diabetic rats exhibited superior neuroretinal function by ERG (312.3 ± 65.5 μ v vs 182.3 ± 60.4 μ v) and increased inner plexiform layer thickness (31.95 ± 11.94 μ m vs 27.93 ± 10.21 μ m) and ganglion cell count, compared to vehicle treatment.

Conclusions: The anti-inflammatory and neuroprotective effects of runcaciguat support sGC as a novel early therapeutic target for diabetic and other ischemic retinopathies.

CONTROL ID: 3533745

SUBMITTER (NAME ONLY): Karine Bojikian

TITLE: Projection-Resolved Optical Coherence Tomographic Angiography of the Macular Ganglion Cell Layer Plexus

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.D. Bojikian, J. Wang, P. Wei, L. Liu, Y. Jia, D. Huang, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K.D. Bojikian, Ophthalmology, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the macular ganglion cell layer plexus (GCLP) boundaries using projection-resolved optical coherence tomographic angiography (PR-OCTA) in healthy eyes.

Methods: Participants were scanned using a commercial OCTA system (RTVue-XR Avanti; Optovue Inc, Fremont CA) in a 6×6-mm area centered on the foveal avascular zone. The split spectrum amplitude decorrelation angiography algorithm (SSADA) was applied to detect flow signal. The GCLP anterior boundary was marked at the nerve fiber layer (NFL)-GCL junction. PR-OCTA algorithm was used to remove flow projection artifacts. Ganglion cell and inner plexiform layer (GCIPL) was divided into 20 equal slabs. In each slab, vessel density (VD) in each polar coordinate sector (Figure 1) were measured using a custom software with automatic shadow exclusion and reflectance compensation. Fifth-degree polynomial fit was used to analyze the correlation between VD and depth in the GCIPL and estimate the boundary between GCIPL and intermediate capillary plexus.

Results: 38 normal participants (78.9% female) were enrolled, and one eye in each participant was studied. Mean age and standard deviation was 59.6±10.7. The watershed (depth of minimum VD) between the GCLP and the intermediate capillary plexus (ICP) is located at 75% depth within the GCIPL (Figure 2) throughout the macula. GCLP VD was significantly ($p<0.0001$) correlated with GCIPL and macular ganglion cell complex (GCC) thickness ($r=0.443$, and $r=0.857$, respectively). The correlation was significantly stronger for macular GCC compared to GCIPL ($z=-3.3$, $p<0.001$).

Conclusions: Macular GCLP supplies the anterior 75% of the GCIPL. Its density is better correlated with GCC, which also contain the NFL, than with the GCIPL, suggesting that it also supplies the posterior aspect of the NFL. Mapping the macular GCLP may be useful in evaluating ganglion cell perfusion in glaucoma and optic neuropathies.

CONTROL ID: 3533751

SUBMITTER (NAME ONLY): Kayshaliya Sharma

TITLE: Cost Efficacy and Challenges of Real-world Brolucizumab use for Neovascular AMD

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sharma, V. Rave, Eastern Virginia Medical School, Norfolk, Virginia, UNITED STATES|K. Sharma, V. Rave, A. Wagner, K. Kapoor, Wagner Kapoor Research Institute, Norfolk, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uncertainty exists regarding the safety of intravitreal brolucizumab (IVB) in patients with nAMD post hoc clinical trials. We performed a retrospective clinical analysis to investigate the relative risk of adverse events and adjunctive treatment costs in a year-long cohort study designed to analyze pre-treated anti-VEGF eyes that converted to IVB.

Methods: We performed a chart review of 144 patients (64 male, mean age 77.6 ± 11.8) who received treatment between 10/1/2019-12/4/2020. Qualifying criteria were: IVB initiated between 11/2019-4/2020 and previous anti-VEGF treatment. Random selection of 155 patients (mean age 82.14 ± 9.8) treated with intravitreal aflibercept (IVA) for nAMD at the same institution in this time period was used for comparison. Patients underwent eye exams aided by optical coherence tomography. Additional diagnostics were given upon clinical judgment. Adverse events were classified as Uveitis, Retinal Artery Occlusion (RAO), or Anterior chamber inflammation (ACI). Number of follow-ups and associated healthcare expenditures were used to assess costs. Key outcome measure for safety evaluation was best-corrected visual acuity (BCVA).

Results: Total of 16 eyes (11.1%) with IVB had adverse events versus 1 uveitis case in the IVA group (0.64%). Eyes that switched to IVB were significant for higher inflammatory rates ($p < 0.0001$) with relative risk of 17.2 compared to IVA. Of the IVB events, 4.9% were Uveitis, 2.8% RAO, and 4.2% ACI. Mean baseline ETDRS letters was 52.58 vs 45.37 at the last examination with an overall decreased BCVA (-7.20 ETDRS). BCVA ± 2 lines were maintained in 68.8% of patients at the last exam. Total treatment costs were \$14,128 to \$1,336 in IVA. On average, the adjunct cost was \$883 per patient on IVB.

Conclusions: Use of IVB was significant for increased risks versus IVA in eyes with prior anti-VEGF. With \$883 per event added to the marketed q12W cost, IVB is still cost efficient by \$3237 versus an q8W IVA regimen in 1 year. While lower costs make IVB an attractive alternative for nAMD treatment, increased risks compounded by higher individual treatment costs is dramatic compared to IVA. Additional follow-ups with potential irreversible vision loss increase patient burden and warrant extra caution with IVB use. Prospective study >1 year would aid this evaluation.

CONTROL ID: 3533768

SUBMITTER (NAME ONLY): Clayton Santiago

TITLE: Comparative analysis of single-cell and single-nucleus RNA-sequencing in a rabbit model of induced proliferative vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Santiago, M. Gimmen, S. Blackshaw, Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|Y. Lu, M. McNally, C. Eberhart, J. Qian, M.S. Singh, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|T. Zollner, W. Schubert, K. Nassar, Bayer AG, Wuppertal, GERMANY|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is the most common cause of failure of retinal reattachment surgery. There is no available pharmacologic treatment for PVR. The molecular pathways involved in the initiation and progression of PVR are poorly understood. In this study, we sought to identify the genes and transcriptional networks involved in PVR progression.

Methods: All animal procedures were conducted in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by the Johns Hopkins Animal Care and Use Committee. PVR was induced unilaterally in specific pathogen free Dutch Belted rabbits by vitrectomy, retinotomy, retinal detachment, platelet-rich plasma injection, and cryotherapy. At different time points after PVR induction, extracted retinas were dissociated into either single cells or single nuclei. Samples were processed to assess the transcriptional profile using single cell or single nucleus RNA sequencing (sc-RNAseq or sn-RNAseq). Fellow eyes were used as non-PVR controls.

Results: Retinas (N=9) were harvested at time points ranging from four hours to 30 days after PVR induction. We profiled >40,000 single cells and nuclei in this study. Retinal pigment epithelium cells, glial cells, and neural retinal cell types were identified in the sc-RNAseq and sn-RNAseq data sets using selected marker genes. The data identified several candidate genes involved in PVR progression, including inflammatory response and cellular proliferation genes. Pseudotime analysis was performed to examine progression from control conditions to early and late stage PVR.

Conclusions: Our high throughput analysis identified several genes that were differentially expressed between control and disease states. SnRNA-seq may have an advantage over scRNA-seq as it can reduce dissociation-induced cellular stress responses. These studies support snRNA-seq and sc-RNAseq as useful tools to study transcriptional networks in animal models of PVR and to identify novel molecular targets for potential pharmacologic modulation.

CONTROL ID: 3533776

SUBMITTER (NAME ONLY): Jonathan Holmes

TITLE: Rasch calibrated Symptom Questionnaire for Childhood Intermittent Exotropia

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.M. Holmes, Ophthalmology and Visual Sciences, University of Arizona, Tucson, Arizona, UNITED STATES|D.A. Leske, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|A. Hercinovic, D.L. Chandler, B.M. Melia, Z. Li, R.T. Kraker, Jaeb Centre for Health Research, Tampa, Florida, UNITED STATES|A.M. Chen, S.A. Cotter, Southern California College of Optometry, Fullerton, California, UNITED STATES|S.A. Erzurum, Northeastern Ohio Medical University, Rootstown, Ohio, UNITED STATES|E.R. Crouch, East Virginia Medical School, Norfolk, Virginia, UNITED STATES|E. Jenewein, Salus University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To Rasch calibrate and evaluate performance of a previously developed questionnaire evaluating symptoms of childhood intermittent exotropia (IXT).

Methods: An initial 22-item questionnaire was developed based on interviews of children with IXT and their parents. The questionnaire had been previously reduced to 7 items by selecting items associated with reduced health-related quality of life (Hatt SR et al,2016). In the present study, the 7-item child IXT symptom questionnaire, with 3 response options, was completed by 386 children age 3 to 10 years old who were enrolled in an RCT comparing overminus to non-overminus glasses, with follow-up exams at 6 and 12 months on treatment and at 18 months (after overminus had been weaned). Factor analysis was performed to determine dimensionality, and Rasch analysis was performed to evaluate questionnaire performance and obtain logit values(converted to a 0 (no symptoms) to 100 scale). Overall differences between time points were assessed using the paired t-statistic. Differences between treatment groups and 95% confidence intervals (CIs) were estimated using ANCOVA, adjusted for baseline scores.

Results: The childhood IXT symptom questionnaire was unidimensional. Response ordering was appropriate. There was no notable local dependence, no significant differential item functioning for sex or age, but suboptimal targeting (mean -1.62 logits) and poor person separation (0.95). Overall, 6-, 12-, and 18-month scores were similar, and all showed significant improvement from baseline (Mean differences from baseline: -5.3 pts, 95% CI -7.2 to -3.4 at 6 months, -6.6 pts 95% CI -8.6 to -4.6 at 12 months, -5.7 pts 95% CI -8.1 to -3.4 at 18 months). There was no significant difference in the IXT symptom score between children treated with overminus and non-overminus glasses while on treatment (mean 28.8 vs 31.1 points; mean difference -3.0, 95% CI -6.2 to 0.1 at 6 months, and 28.4 s vs 28.1 points; mean difference 0.2, 95% CI -2.9 to 3.4 at 12 months).

Conclusions: The Rasch scored childhood IXT symptom questionnaire showed reasonable psychometric performance and was able to detect improvement in symptoms after 6, 12, and 18 months of either overminus or non-overminus glasses treatment. Overminus glasses treatment does not appear to reduce child-reported symptoms of IXT more than non-overminus.

CONTROL ID: 3533804

SUBMITTER (NAME ONLY): Wei-Chun Lin

TITLE: Medication List Extraction Using Natural Language Processing for Glaucoma Patients

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Lin, M. Hribar, Medical Informatics & Clinical Epidemiology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|J. Kaluzny, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|J.S. Chen, School of Medicine, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accuracy of medication data in electronic health records (EHRs) is essential for patient care and research. Previous work has shown frequent errors in medication lists include incomplete records, duplicated prescriptions, and failed discontinuation of medications. Since medication lists are inaccurate, physicians often record medication information in progress notes, which is difficult to automatically extract since notes are written as free-text narratives. The purpose of this study is to develop a natural language processing (NLP) model for automatically extracting medication information from free-text notes for glaucoma patients. Medication is a crucial part of glaucoma treatment and is important for glaucoma research such as predicting disease progression.

Methods: We used an NLP technique called Named Entity Recognition (NER) to extract medication information from clinical notes. First, we sampled a dataset of 296 progress notes from office visits at OHSU in 2019 with ICD10 codes associated with glaucoma. Next, we manually annotated text in each note for six entities related to medication. Figure 1 displays an example of the annotation. Next, we developed and evaluated an NER model with the Python spaCy package, using the annotated dataset randomly split into 75% for training and 25% for testing. Finally, we evaluated the results of the NER model's extraction for the test set comparing the manually annotated and the NER model's extracted entities using F1 score, precision, and recall.

Results: Table 1 shows the overall and per-entity performance for the NER model on test data. The NER model had an overall F1 score = 0.949, precision = 0.944, and recall = 0.953. The F1 scores for the entities ranged from 0.97 for the "Route" and 0.91 for the "Dosage". An error analysis was performed for false negative and positive on all entities. Several causes of errors were identified, including differences in note formatting, ambiguous annotation, and misclassification when medication information was contained in multiple short sentences.

Conclusions: This study shows that NLP can be used to accurately extract glaucoma medication information from free-text EHR data; the performance of our model is similar to the best performing published NLP models for medication extraction studies. This has implications in improving the data quality and usefulness for medication data in glaucoma research.

CONTROL ID: 3533818

SUBMITTER (NAME ONLY): Daniel Zhu

TITLE: Patterns of Cataract Surgery Related Litigations in the United States from 2000-2020

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Zhu, A. Wong, R. Gupta, A.S. Li, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the characteristics of cataract surgery-related malpractice between 2000 and 2020.

Methods: All U.S. medical malpractice civil trials involving patients who suffered complications of cataract surgery were retrospectively searched in the LexisNexis legal database between January 1, 2000 and December 1, 2020. Available data was collected on each case. Monetary amounts were inflation-adjusted to 2020 dollars. Data collection and descriptive statistical analyses were conducted using the Statistical Package for the Social Sciences with $p < 0.05$ for significance.

Results: Over the past 20 years, 482 cataract surgery litigations were identified in the LexisNexis database, filed in 37 states. New York (27.5%), Florida (8.9%), and California (8.3%) were the top three states with the greatest number of cases. Of the cases where the age was known, the majority of plaintiffs were between the ages of 60-79. 48.5% of verdicts were for the defendant, 11.8% were for the plaintiff, and 30.5% were settled. The remaining cases were either dismissed, pending, discontinued, mediated, or other/unknown. The leading reasons for litigation were retinal detachment and endophthalmitis. The average amounts demanded, offered, and awarded were \$1,224,061, \$241,314, and \$1,350,600 respectively. When comparing between the decades of 2000-2010 and 2011-2020, there was a significant increase in the amounts demanded ($p = 0.039$, Mann Whitney U test) in the second decade compared to the first with no significant increase in the amounts awarded ($p = 0.118$, Mann Whitney U test).

Conclusions: Almost half of reviewed cataract-related malpractice litigation resulted in a defendant verdict.

Settlements or plaintiff verdicts were very costly with amounts awarded averaging above \$1 million. Over the past decade, while plaintiffs are demanding significantly more, there was no significant increase in awarded amounts.

CONTROL ID: 3533832

SUBMITTER (NAME ONLY): Ehtesham Shamsher

TITLE: Resveratrol nanoparticles are neuroprotective in a rat model of glaucoma

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Shamsher, L. Guo, B.M. Davis, V. Luong, N. Ravindran, M. Cordeiro, Institute of Ophthalmology, University College London Faculty of Brain Sciences, London, London, UNITED KINGDOM|E. Shamsher, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|M. Cordeiro, Western Eye Hospital, London, London, UNITED KINGDOM|S. Somavarapu, University College London School of Pharmacy, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Resveratrol is a natural polyphenol found in red wine and dark chocolate known for its antioxidant, anti-inflammatory and anti-apoptotic properties. All these properties can be used to treat neurodegenerative diseases such as glaucoma. To date, resveratrol low solubility in water and bioavailability limits its clinical use. The goal of this study was to develop a novel nanoparticle formulation of resveratrol and to assess it in an ocular hypertension (OHT) rat model of glaucoma.

Methods: Resveratrol nanoparticles (RNs) were formulated using a thin film rehydration technique. OHT rat model was induced with the injection of 1.85 M normal saline solution in two episcleral veins of the left eye of 10 Dark Agouti rats. The right eye was used as an internal control. RNs (n=5) or vehicle (n=5) were given topically as an eye drop daily for 3 weeks from induction. After 3 weeks, rats were imaged with the Detection of Apoptosing Retinal Cells (DARC) technology. DARC count was defined as the number of apoptosing retinal cells counted by a masked investigator. Next, all rats were sacrificed, and their retinas immunostained with Brn3a antibody. Retinal Ganglion Cell (RGC) density ratio was defined as the ratio between the left treated and the right untreated eye (control).

Results: RNs were formulated with an encapsulation efficiency >70% and a stability >90 days. They were well-tolerated without any sign of ocular irritation. RN treatment was found to significantly reduce RGC loss compared to the vehicle (1.02 ± 0.05 vs 0.70 ± 0.11 RGC density ratio, $p < 0.05$). RNs did not reduce the Intraocular Pressure (IOP) suggesting that their neuroprotective effect was independent of IOP, although this effect was not found to be significant in the DARC count compared to the vehicle (493 ± 83 vs 612 ± 84 DARC count, $p > 0.05$).

Conclusions: These promising results show that topical administration of RNs was neuroprotective and well-tolerated in an OHT glaucoma rat model by reducing significantly RGC loss. This effect appears to be independent of IOP, but was not seen in the DARC count. We suggest larger studies are needed to confirm these encouraging results.

CONTROL ID: 3533838

SUBMITTER (NAME ONLY): Alexander Vorperian

TITLE: Intrасession Repeatability and Intersession Reproducibility of Macular Vessel Parameters by Optical Coherence Tomography Angiography

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vorperian, N. Khan, J. Lee, B. Burkemper, D.J. Grisafe, V. LeTran, B. Song, B. Wong, B.Y. Xu, G. Richter, USC Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|X. Zhou, Z. Chu, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using optical coherence tomography angiography (OCTA), this study seeks to compare intrасession repeatability and intersession reproducibility of macular vessel parameters in glaucoma and non-glaucoma subjects.

Methods: A series of 6x6mm macular optical coherence tomography angiography scans (Cirrus HD-OCT 5000) were acquired from both glaucomatous and non-glaucomatous subjects as part of an observational, longitudinal study. Next, vessel area density (VAD), vessel skeleton density (VSD), and flux were calculated using a research-based quantification software. Additionally, perfusion density (PD_Z) and vessel density (VD_Z) were calculated using commercially developed software (Cirrus 11.0, Carl Zeiss Meditec). Finally, the intrасession repeatability and intersession reproducibility of these macular parameters were determined using the following statistical parameters: within-eye standard deviation (S_W), within-eye coefficient of repeatability (CR_W), within-eye coefficient of variation (CV_W), and intraclass correlation coefficients (ICC).

Results: The intrасession CV_W from the non-glaucoma group (n=75) was 1.466 for VAD, 1.150 for VSD, 5.203 for PD_Z , and 4.836 for VD_Z while the intersession CV_W from the non-glaucoma group (n=53) was 2.245 for VAD, 1.411 for VSD, 6.971 for PD_Z , and 6.564 for VD_Z . The intrасession CV_W from the glaucoma group (n=60) was 1.294 for VAD, 1.006 for VSD, 4.910 for PD_Z , and 4.516 for VD_Z while the intersession CV_W from the glaucoma group (n=40) was 1.899 for VAD, 1.228 for VSD, 5.858 for PD_Z , and 5.532 for VD_Z . Non-glaucomatous intrасession ICC ranged from 0.561 for PD_Z to 0.795 for VAD while non-glaucomatous intersession ICC ranged from 0.334 for PD_Z to 0.740 for VSD. Glaucomatous intrасession ICC ranged from 0.728 for PD_Z to 0.894 for VAD while glaucomatous intersession ICC ranged from 0.541 for PD_Z to 0.780 for VSD.

Conclusions: Macular OCTA parameters had greater intrасession repeatability than intersession reproducibility for both glaucomatous and non-glaucomatous eyes. Additionally, the macular parameters analyzed by the research-based software demonstrated higher repeatability than the commercial parameters across both non-glaucomatous and glaucomatous eyes.

CONTROL ID: 3533848

SUBMITTER (NAME ONLY): William Bloom

TITLE: Ultra-wide field imaging to assess the optic nerve and retina in Boston type I and II keratoprosthesis patients

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.R. Bloom, S. Smith, A. Hendershot, R. Kuennen, T. Oostra, W. Terrell, T.F. Mauger, C.M. Cebulla, Department of Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|W.R. Bloom, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|W. Terrell, Mary Lanning Healthcare, Hastings, Nebraska, UNITED STATES|T.F. Mauger, Department of Ophthalmology and Visual Sciences, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The ability to view the posterior segment in keratoprosthesis (Kpro) implanted patients is limited. The purpose of this retrospective, observational study was to investigate the use of ultra-wide field (UWF) scanning laser ophthalmoscopy imaging and its utility for serial evaluation of the retina and optic nerve in patients with either a Boston type I or II Kpro.

Methods: A retrospective chart review of patients with Boston type I or II Kpro seen at The Ohio State University Wexner Medical Center between 2009 and 2020 was performed under an IRB-approved protocol. Twenty-eight Kpro patients were identified. Fifteen eyes from 14 patients implanted with a Boston type I or II Kpro underwent UWF imaging (UWFI) as standard of care using the Optos imaging system and were consecutively enrolled into this study. A total of 35 patient visits included UWFI. Images were graded for quality by a single masked reader on a defined 4-point scale ("Poor", "Fair", "Good", or "Very Good") and assessed for clinical pathology of the retina and optic nerve. Clinical characteristics and examination findings were described using descriptive statistics.

Results: Fourteen of the 15 eyes (93.3%) had a type I Kpro, while one eye (6.7%) had a type II Kpro. UWFI from 35 patient visits were reviewed for quality and clinical pathology. 2.9% of images (1/35) were graded as "poor" and provided no visualization of posterior segment structures. 97.1% of images (34/35) were deemed "fair", "good", or "very good" and provided at least some clinical utility. Clinically useful images were obtained on both type I and type II Kpro implanted patients. The optic nerve and macula were both visible in 94.3% of images (33/35). Clinical pathology included glaucoma, macular degeneration, and repaired retinal detachment. In 4 eyes, UWFI was performed serially at multiple visits (range: 3-9 individual visits), allowing for longitudinal follow up (range: 3-46 months).

Conclusions: UWFI provides adequate visualization of the posterior segment in Kpro implanted patients. Importantly, this imaging modality allowed noninvasive longitudinal monitoring of retinal and optic nerve clinical pathology in this select patient population. To the best of our knowledge, this is the first study to report the use of UWFI in a patient implanted with a type II Kpro.

CONTROL ID: 3533854

SUBMITTER (NAME ONLY): Arathi Ponugoti

TITLE: Evaluation of chronic effects of e-cigarette aerosol inhalation on macular perfusion using OCT-Angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Electronic cigarette (e-cig) use in young adults has increased dramatically, the long-term effects of which are largely unknown. Acute impaired microvascular function and endothelial vascular dysfunction have been observed during e-cig use but chronic vascular effects of use remain underexplored, especially in the delicate and highly metabolically active retina where such effects might present earlier. We performed a cross sectional clinical observational study to determine if there are differences at baseline in the microvasculature and central retinal thickness (CRT) between e-cig users and age matched non-user controls using OCTA.

Methods: We obtained 10x10 scan angle images of right and left maculae in 26 adult daily e-cig users and right eye maculae in 25 age matched controls using an OCTA integrated Spectralis SD-OCT tabletop system (Heidelberg Engineering, Germany). A customized MATLAB algorithm was used to calculate foveal avascular zone (FAZ), vessel area density (VAD), and vessel length density (VLD) for the superficial and deep vascular complexes (SVC and DVC). Spectralis software was used to calculate foveal, superior, inferior, nasal, and temporal CRT. Wilcoxon rank sum tests were used to assess variability of FAZ, VAD, VLD, and CRT parameters between groups and differential contribution of e-liquid concentration and years of e-sig use.

Results: Images were acquired in 52 e-cig user eyes (n= 26, mean age 27.8 ± 6.72 yrs) and 25 non-user age matched controls (n=25, mean age 28.04 ± 4.53 yrs). FAZ, VAD, VLD, and CRT were measured in all 77 eyes. No statistically significant difference was found between users and non-users for FAZ, SVC VAD, SVC VLD, or DVC VAD. A statistically significant difference was found for DVC VLD ($p=.0003$), with e-cig users having a slightly higher VLD on average. Inferior CRT was significantly thinner in users compared to non-users ($p=.012$). E-liquid concentration significantly correlated with thinner inferior CRT in e-cig users ($P > F .0408$).

Conclusions: Overall, no significant negative differences were found in the retinal microvasculature parameters between e-cig users and non-users. Decreased inferior CRT in e-cig users might not be clinically meaningful at this time but warrants further assessment of retinal effects as this population ages and continues to use e-cigs.

CONTROL ID: 3533863

SUBMITTER (NAME ONLY): Michael Beyeler

TITLE: An explainable AI model to predict electrode deactivation in retinal prostheses from routine clinical measures

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Beyeler, Psychological & Brain Sciences, University of California Santa Barbara, Santa Barbara, California, UNITED STATES|M. Beyeler, Z. Hu, Computer Science, University of California Santa Barbara, Santa Barbara, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To provide appropriate levels of stimulation, retinal prostheses must be calibrated to an individual's perceptual thresholds ("system fitting"). Nonfunctional electrodes may then be deactivated to reduce power consumption and improve visual outcomes. However, thresholds vary drastically not just across electrodes but also over time, thus calling for a more flexible electrode deactivation strategy. Here we present an explainable artificial intelligence (XAI) model fit on a large longitudinal dataset that can 1) predict at which point in time the manufacturer chose to deactivate an electrode as a function of routine clinical measures ("predictors") and 2) reveal which of these predictors were most important.

Methods: We analyzed a longitudinal dataset of 5496 perceptual thresholds and electrode impedances measured on 627 electrodes in 12 Argus II patients (Second Sight Medical Products). The data was collected from 2007-2018 during 285 sessions conducted at 7 different implant centers. To prepare the raw data for machine learning, we combined threshold and impedance values with clinical data crowd-sourced from the literature, and split the features into three different categories: 1) Routinely collected data (e.g., age at blindness onset, age at implant surgery), 2) System fitting (e.g., thresholds, impedances, charge density limits), and 3) Follow-up examinations (more recent threshold and impedance measurements). We then used gradient boosting (XGBoost), a powerful XAI model based on decision trees, to predict electrode deactivation as a function of these features.

Results: The model predicted electrode deactivation from routinely collected data with 60.8% accuracy. Performance increased to 75.3% with system fitting data, and to 84% when thresholds from follow-up examinations were available. The model further identified subject age and time since blindness onset as important predictors of electrode deactivation.

Conclusions: On the one hand, these findings highlight the importance of periodical threshold measurements to continuously monitor device performance. On the other hand, in the absence of such measurements, our work demonstrates that routinely collected clinical measures and a single session of system fitting might be sufficient to inform an XAI-based electrode deactivation strategy for retinal prostheses.

CONTROL ID: 3533867

SUBMITTER (NAME ONLY): Shudan Wang

TITLE: The effect of blocking substance P in reducing ocular redness

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Various clinical conditions may cause dilation of the conjunctival vessels, leading to ocular redness (OR), among which allergic conjunctivitis is the most common cause, followed by dry eye disease and infectious conjunctivitis. Herein, using animal models of both allergic and non-allergic OR, we evaluated the therapeutic efficacy of topical blockade of substance P (SP) in treating the red eye.

Methods: Allergic OR was induced in Guinea pigs with topical 1.5 mg/mL histamine, and non-allergic OR was induced in rabbits with topical 5% dapiprazole. Once topical histamine or dapiprazole was applied, animals immediately received topical treatment of L-703,606, a SP receptor antagonist, or vehicle. Animal eyes were thereafter examined by a slit lamp, and images were taken every 30 seconds in the first 2 minutes, and then at 6, 10, 20, 30, 40, 50, and 60 minutes post treatment. The severity of redness was analyzed using ocular redness index (ORI) which is a continuous numerical score from 0 to 100.

Results: In the vehicle control group, the ORI reached peak at 10 minutes in allergic OR and the maximal increase from baseline was 17.04. In the non-allergic OR model, maximal increase in ORI score is 13.07 at peak time of 20 minutes post-induction. Topical treatment of L-703,606 significantly reduced ORI at each time point evaluated in both allergic and non-allergic OR models. At peak time, L-703,606 treated group showed ORI reduction of 8.21 in allergic model and 5.76 in non-allergic model, respectively.

Conclusions: Topical blockade of SP is effective for treating allergic and non-allergic red eye.

CONTROL ID: 3533893

SUBMITTER (NAME ONLY): Kit Ying Choy

TITLE: Deepening of the anterior chamber may impair the aqueous outflow system in guinea pigs

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Choy, S. Shan, R. Chun, C. To, School of Optometry, The Hong Kong Polytechnic University, Kowloon, HONG KONG|C. To, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Myopia is a refractive condition that increases the risk of glaucoma. Studies have shown that the risk of developing glaucoma, especially primary open angle glaucoma (POAG), is more pronounced in high myopes. We hypothesized that excessive myopic eye growth may cause structural changes of the outflow system, leading to IOP elevation.

Methods: Myopia was induced in healthy albino guinea pigs (n=24) by form deprivation (FD). A translucent plastic diffuser goggle was attached and randomly assigned to one of the guinea pig eyes. The ocular parameters including axial length (AXL), anterior chamber depth (ACD) and vitreous chamber depth (VCD); refractive error (Rx) and IOP were monitored regularly. After 3 to 8 weeks of FD, both eyes were removed and outflow facility was measured using constant flow method with perfusion system (iPerfusion).

Results: The treated eyes became significantly more myopic ($-4.63 \pm 0.67D$, $P < 0.01$), elongated ($0.23 \pm 0.04mm$, $P < 0.01$) and with higher IOP ($0.73 \pm 0.29mmHg$, $P = 0.02$) than fellow control eyes. In general, the IOP correlated well with the outflow facility ($r = -0.40$, $P = 0.05$). Pearson correlation analysis revealed that myopic refraction was significantly correlated with axial elongation, but not with IOP and outflow facility. However, when the correlations in both eyes were studied together, intraocular change of ACD (δACD) was found to correlate moderately and significantly with δIOP ($r = 0.40$, $P < 0.01$) and outflow facility ($r = -0.39$, $P = 0.01$).

Conclusions: Axial elongation in albino guinea pigs correlated well with changes in the IOP and outflow facility. Specifically, eyes with deepened ACD showed significantly higher IOP and lower outflow facility. It indicated that ACD deepening may cause structurally changes that lead to gradual blockage of the aqueous outflow system and elevation of IOP.

CONTROL ID: 3533915

SUBMITTER (NAME ONLY): Wen-Tao Deng

TITLE: Disease mechanisms of X-linked cone dystrophy caused by missense mutations in the red and green cone opsins

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Deng, P. Zhu, F.M. Dyka, W.W. Hauswirth, University of Florida, Gainesville, Florida, UNITED STATES|W. Baehr, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Red/green cone opsin missense mutations N94K, W177R, P307L, R330Q and G338E have been identified in subjects with congenital blue cone monochromacy or color-vision deficiency. Studies on disease mechanisms due to these cone opsin mutations have been previously carried out exclusively in cell culture. Here we expressed these cone opsin mutants specifically in mouse cones via AAV in M-opsin knockout ($Opn1mw^{-/-}$) mice to investigate their subcellular localization, the pathogenic effects on cone morphology, function, and cone viability.

Methods: AAV8-733 vectors expressing the above cone opsin mutants driven by the cone-specific PR2.1 promoter were injected subretinally into one eye of 1 month old $Opn1mw^{-/-}$ mice, while the contralateral eyes remained untreated. AAV-mediated transgene expression was analyzed by western blots. L/M-opsin mediated retinal function was analyzed 6 weeks post-injection by photopic electroretinography (ERG). Subcellular localizations of each cone opsin mutant and the other cone outer segment specific proteins were examined by immunohistochemistry. Cone viability in each mutant treated eyes was examined by retinal whole mounts stained with peanut agglutinin (PNA).

Results: Expression of N94K and W177R was barely detectible while P307L, R330Q, and G338E showed expression levels comparable to that of endogenous M-opsin. N94K and W177R were misfolded and localized exclusively in cone inner segments and endoplasmic reticulum. In contrast, P307L, R330Q and G338E were detected exclusively in cone outer segments. Expression of R330Q and G338E, but not P307L, also partially restored expression and correct localization of the remaining cone outer segment proteins and resulted in partial rescue of M-cone mediated light responses. ERG amplitudes in R330Q and G338E injected eyes were $54.5 \pm 15.5 \mu V$ and $56.3 \pm 18.1 \mu V$, respectively (average \pm STD, $n=8$), significantly higher than the unrecordable M-cone ERGs from untreated contralateral control eyes ($P < 0.0001$). Expression of W177R and P307L caused severe cell toxicity resulting in rapid cone loss, while N94K, R330Q and G338E were only modestly toxic.

Conclusions: Although the underlying biochemical and cellular defects caused by these mutants are distinct, we predict they all present a gain-of-function phenotype, resembling autosomal dominant retinitis pigmentosa associated with the majority of rhodopsin missense mutations.

CONTROL ID: 3533961

SUBMITTER (NAME ONLY): Michael Niederleithner

TITLE: Single shot wide field MHz swept source optical coherence tomography angiography

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Niederleithner, A. Britten, P. Matten, R.A. Leitgeb, W. Drexler, T. Schmoll, CMPBME, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|H. Ren, R. Williams, S. Kubach, T. Schmoll, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Several retinal diseases show vascular pathologies in the periphery first. Although widefield fluorescein angiography (FA) fundus cameras can image these areas, they require contrast agents and a lengthy patient setup procedure. In this work, we present how MHz swept-source OCT angiography (SS-OCTA) can provide similar information non-invasively and faster.

Methods: We developed a SS-OCTA system using a frequency-domain mode locked laser operating at an A-scan rate of 1.7 MHz with a central wavelength of 1060 nm and a tuning range of 75 nm, translating to 9 μm axial resolution in tissue. The lateral resolution is 20 μm ($1/e^2$) and the imaging depth in tissue is 6 mm. To compensate for eye motion, the retina is tracked during acquisition using an additional line scanning ophthalmoscope. If motion occurs, the scan location is corrected, and the scans acquired since motion detection are rescanned. The single shot field of view (FOV) of 18 mm by 18 mm (~65 degrees) on the retina is sampled laterally with 2048x2048 A-scans and 4 repetitions per slow scanning axis position. After SS-OCTA processing using the complex signal, projections from the inner limiting membrane to the IS/OS junction are generated. In this study, we imaged 5 healthy subjects, and 20 patients with diabetic retinopathy, choroidal neovascularization, and retinal occlusion.

Results: We acquired single shot SS-OCTA images with a FOV of 65 degrees from healthy subjects and patients with retinal diseases. The acquisition time with tracking enabled was well below 30s in patients. The image quality was sufficient to resolve capillaries over the entire FOV. Figure 1 shows the widefield SS-OCTA projection of a diabetic eye. SS-OCTA's motion contrast allows for identification of areas of non-perfusion. Because the full level of detail cannot be appreciated in the widefield image as displayed in Fig. 1, Fig. 2 shows magnified views of the same acquisition at the locations indicated by the orange boxes. In Fig. 2II), even the capillaries around the foveal avascular zone can be resolved.

Conclusions: We demonstrated that SS-OCTA is approaching the FOV of widefield FA fundus cameras. This has reduced chair time and lack of need for contrast agents, which makes widefield SS-OCTA a potential replacement for many FA exams.

CONTROL ID: 3533971

SUBMITTER (NAME ONLY): Gerhard Garhofer

TITLE: Effect of topical oestradiol eye drops on signs and symptoms of dry eye disease in post-menopausal women

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Garhofer, L. Schmetterer, D. Schmidl, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|M. Vidaeus, H. Ageland, Redwood Pharma AB, SWEDEN|

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ABSTRACT BODY:

Purpose: Previous evidence indicates that topical oestradiol may be beneficial for patients with dry eye disease (DED), especially in post-menopausal women. The current phase II study was performed to investigate the effect of a recently developed formulation of oestradiol eye drops on signs and symptoms of DED.

Methods: In this randomized, controlled, parallel-group study, 104 post-menopausal women with moderate to severe dry eye were included. 17- β -oestradiol-3-phosphate eye drops (RP101) were administered in three different dosage groups (group 1: 0.5% twice daily, group 2: 0.1% morning and vehicle in the evening, group 3: 0.1% twice daily) and compared to control (group 4: vehicle IntelliGel, twice daily). Treatment was administered for a total period of three months. Schirmer's test II, corneal staining and SANDE symptom score were assessed at baseline and at day 14, 30, 60 and 90 after treatment start. Safety was determined via frequency of adverse events.

Results: Schirmer's test II wetting distance significantly increased in all 4 groups from baseline to day 90 without significant difference between groups (group 1: $+5.6 \pm 6.7$; group 2: $+3.7 \pm 4.2$; group 3: $+4.8 \pm 4.5$, group 4: $+4.0 \pm 5.3$ mm/5min). Statistical significance versus baseline occurred earlier in the treatment groups versus the control group. Corneal staining score was significantly reduced after the three-month treatment period with no significant difference between treatment groups ($p < 0.001$ vs baseline in all groups). Staining of the inferior cornea, however, showed a significantly more pronounced decrease in the highest dose group compared to vehicle ($p = 0.0463$). Symptoms as assessed with the SANDE test decreased at the end of the treatment period in all 4 groups (between -18.7 ± 23.5 and -26.3 ± 28.0 mm for frequency of symptoms and between -13.1 ± 26.8 and -24.1 ± 40.2 mm for severity of symptoms). Topical RP101 eye drops were well tolerated on the ocular surface and showed a favorable safety profile.

Conclusions: The results of the study indicate that topical RP101 eye drops improve signs and symptoms of DED in post-menopausal women. The results of the study showed a good safety profile of the topical ophthalmic formulation. Further adequately powered phase III studies are required to assess therapeutic efficacy of topical oestradiol in the treatment of DED.

CONTROL ID: 3533979

SUBMITTER (NAME ONLY): Ursula Schmidt-Erfurth

TITLE: AI-based quantification of photoreceptor maintenance in the treatment of Geographic Atrophy Secondary to AMD in the FILLY trial

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To quantify the therapeutic effect of pegcetacoplan (APL2) on inhibition of photoreceptor (PR) loss on conventional OCT images using deep learning in GA.

Methods: SD-OCT scans (Spectralis) in a raster of 512x49x496 voxels were obtained at monthly intervals during the phase II FILLY trial of APL2, an investigational complement C3 inhibition, in patients with geographic atrophy (GA) secondary to AMD. Patients with complete outer retinal atrophy (cRORA) were randomized into a sham group (SM), a group receiving monthly (AM) and another group receiving bimonthly (AEOM) intravitreal injections of APL2. Using expert manual annotation at an A-scan level, a deep learning segmentation algorithm was developed based on a convolutional neural network (CNN). Fully automated delineation of the area presenting with complete photoreceptor (PR) loss was performed at baseline, at 2, 6 and 12 months. The associated retinal pigment epithelial (RPE) loss was measured via a previously established algorithm.

Results: A total of 31,752 B-Scans of 648 volumes of 162 study eyes (SM:56, AM:54, AEOM:54) were evaluated from baseline to month 12. The square-root lesion area based on PR loss was 0.108, 0.111, 0.106 mm at baseline in the SM, AEOM and AM groups. While the mean PR defect size increased to 0.110, 0.112, 0.116 mm over months 2,6,12 in the SM group, the AM group presented a significantly smaller lesion extension with 0.105, 0.106, 0.110 mm, respectively over time, which was also seen as a trend for the AEOM group (Table 1). Moreover, the PR lesion sizes were found to consistently exceed the underlying borders of RPE loss by 73, 64, 61, and 60 % at the subsequent intervals.

Conclusions: Deep-learning based algorithms are able to distinctly and reliably quantify the extension and growth of photoreceptor loss and appear to represent ideal tools to evaluate disease activity as well as therapeutic efficacy of slowing GA progression. Based on standard OCT imaging, automated monitoring of RPE and PR loss and maintenance should be considered for an optimized management of patients with GA.

CONTROL ID: 3533983

SUBMITTER (NAME ONLY): Mariko Shirane

TITLE: Polymorphisms of cytomegalovirus UL40 protein signal peptides in Cytomegalovirus-associated uveitis

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shirane, N. Yawata, S. Yamana, A. Hayashida, T. Ito, K. Shibata, E. Hasegawa, A. Takeda, K. Sonoda, Ophthalmology, Kyushu University, Fukuoka, JAPAN|T. Kaburaki, Ophthalmology, Jichi Medical University Saitama Medical Center, Saitama, JAPAN|

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ABSTRACT BODY:

Purpose: Cytomegalovirus (CMV) is latently infected in more than 80% of Asian population and recurs subclinical reactivation over the life time. Virus reactivation induces clinical issues such as viremia and retinitis only in severely immunocompromised hosts. Recently, however, it has been revealed that CMV can cause various ocular inflammation such as anterior uveitis (CMV-AU) and chronic retinal necrosis (CRN) in hosts without apparent immunosuppression and with mild to moderate immunosuppression, respectively. The signal peptides (SP) of CMV UL40 protein are polymorphic and are presented on HLA-E molecules which are directly recognized by NK cells and CD8⁺T cells. The antiviral immune responses differ depending on the polymorphisms, and two SP polymorphisms (SP1 and SP2) are frequently observed in CMV viremia. We analyzed the polymorphisms of UL40 SP sequences in the intraocular fluids of the three different CMV-associated uveitis and compared them among the diseases.

Methods: gDNA was extracted from the intraocular fluids of 25 cases of CMV-AU, 7 cases of CRN, and 16 cases of CMV retinitis. The UL40 SP region was amplified by PCR and the SP sequences were determined by direct sequencing.

Results: Two UL40 SP sequences (SP1 and SP3) were detected in intraocular fluids of CMV-associated uveitis. SP1 was the dominant type in CMV retinitis (14/16 cases, 88%), whereas it was less frequent in CMV-AU (20/25 cases, 80%) and CRN (3/7 cases, 43%). In contrast, SP3 was more frequent in CMV-AU (5/25 cases, 20%) and CRN (4/7 cases, 57%, $p=0.045$) compared to that in classical CMV retinitis. SP2, which is the 2nd most frequent type in CMV viremia, was not detected in the intraocular fluids.

Conclusions: The distributions of CMV UL40 SP sequences in intraocular fluids of CMV-associated uveitis were different among the CMV-associated diseases, suggesting that polymorphisms of UL40 may be involved in the pathogenesis of intraocular inflammation and the variations of the ocular diseases.

CONTROL ID: 3533989

SUBMITTER (NAME ONLY): Enrico Borrelli

TITLE: Three-year OCT Predictive Factors of Disease Recurrence in eyes with Successfully Treated Myopic Choroidal Neovascularization.

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Borrelli, M. Battista, G. Vella, R. Sacconi, L. Querques, D. Grosso, F. Bandello, G. Querques, Università Vita Salute San Raffaele, Milano, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: Choroidal neovascularization (CNV) is a frequent and sight-threatening complication in high myopia. The anti-vascular endothelial growth factor (VEGF) therapy is the current standard of treatment in newly diagnosed myopic CNV. However, after exudation is resolved, patients may experience recurrences that were demonstrated to significantly impact the long-term visual outcomes. The aim of this study is to assess the relationship of demographics, clinical characteristics and structural optical coherence tomography (OCT) findings to disease recurrence in a cohort of patients with newly diagnosed myopic CNV.

Methods: In this IRB-approved retrospective analysis, we collected data from 64 participants (64 eyes) with successfully treated myopic CNV who had obtained resolution of exudation after treatment (study baseline) and with 3 years of regular follow-ups. At baseline, several OCT qualitative features and quantitative measurements were graded by two readers and included in the analysis. Main outcome measures included incidence of disease recurrence and hazard ratio (HR) for demographics, clinical characteristics and OCT risk factors.

Results: At month 36, 40 eyes (62.5%) developed disease recurrence (active CNV). Multivariate linear regression analysis revealed that final visual acuity (at 36 months - dependent variable) was associated with visual acuity at baseline visit ($p<0.0001$), baseline size of patchy atrophy ($p=0.010$), baseline subfoveal choroidal thickness ($p=0.008$), baseline maximum CNV height and width ($p=0.011$ and $p=0.003$), and recurrence of CNV exudation ($p=0.007$). The following factors were associated with an increased risk of disease recurrence: size of patchy atrophy had an HR of 1.14 (95% CI, 1.01-1.29; $p=0.036$); maximum CNV width had an HR of 1.02 (95% CI, 1.01-1.04; $p<0.0001$).

Conclusions: We identified OCT risk factors for the disease recurrence in eyes with successfully treated myopic CNV. Assuming that disease recurrence is a sight-threatening event, our findings may help in the identification of high-risk patients and eventually ameliorate their outcome.

CONTROL ID: 3534029

SUBMITTER (NAME ONLY): John Petrie

TITLE: Comparative study of the effects of nicotinamide on cultured iPSC-derived human RPE cells from normal and Smith-Lemli-Opitz Syndrome (SLOS) donors

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the effects of nicotinamide (Nic) on differentiation and protein expression profiles of cultured iPSC-derived RPE cells from normal human donors (Dys0100; DYS), vs. mildly (CWI) and severely (A2) affected SLOS donors.

Methods: DYS, CWI and A2 iPSC-RPE cells were derived as previously described (Ferrer M et al., 2014; Ramachandra Rao et al., 2018). Cells (passage #6) were seeded in low-Ca²⁺ medium on tissue culture plastic, grown to confluence, and switched to high-Ca²⁺ medium containing either basal (~33 mM; vehicle control (VC)) or 10 mM Nic. Cell morphology was monitored by phase-contrast and confocal fluorescence microscopy. After 1.5 mo., monolayers were harvested in RIPA buffer and processed for Western blot (WB) analysis. Blots were probed with antibodies to RPE65, CRALBP, and Best-1, normalized to b-actin levels. CWI and A2 RPE cells cultured on poly-L-ornithine-coated RINZL plastic coverslips ± Nic, were probed with anti-Occludin MAb (clone OC3F10); F-actin was detected with Alexa Fluor® 568-Phalloidin. Statistical analysis: Student's t-test, with significance threshold P<0.05.

Results: DYS and CWI cells exhibited relatively normal RPE-like morphology; however, A2 cells appeared markedly unhealthy and hypertrophic. Supplementation of culture media with 10 mM Nic improved iPSC-RPE differentiation, polygonal morphology, monolayer uniformity, phase-bright border and anti-Occludin staining continuity, and F-actin organization, relative to VC. While the effects were modest for DYS and CWI cells, A2 cells showed profound improvement. By WB analysis, RPE65 expression levels increased in all cell lines (+Nic, vs. VC): by ~2.5X (DYS) and ~2.2X (CWI), vs. ~5.8X (A2). Similarly, CRALBP expression increased (+Nic, vs. VC) by ~1.4X (DYS) and ~1.5X (CWI), vs. ~7.4X (A2). Also, Best-1 expression increased (+Nic, vs. VC) by ~2.5X (DYS) and ~3.7X (CWI), vs. ~9X (A2).

Conclusions: Culture medium supplementation with 10 mM Nic promotes up-regulation of RPE cell markers and normal RPE-like morphology and cytology of cultured iPSC-RPE cells, particularly those derived from severely-affected SLOS donors. Nic supplementation may augment therapeutic efficacy of current standard-of-care treatment for SLOS patients.

CONTROL ID: 3534033

SUBMITTER (NAME ONLY): Philip Zhou

TITLE: Impact of the COVID-19 Pandemic on Diabetic Macular Edema Patient Outcomes at a Tertiary Care Veterans Affairs Hospital

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zhou, J. Gao, K. Biggerstaff, S. Orengo-Nania, R. Channa, Baylor College of Medicine, Houston, Texas, UNITED STATES|R. Channa, UW Health, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retina clinic volumes declined during the COVID-19 pandemic, and there have been limited studies on how this impacted patient outcomes. Optimal management of diabetic macular edema (DME) requires adherence to regular treatment schedules. We aimed to evaluate the impact of the pandemic on visual and anatomic outcomes in patients with DME requiring anti-VEGF injections at our institution.

Methods: Data was collected from the retina clinic at the Michael E. DeBakey VA Medical Center in Houston, Texas. Patient charts from April 2020 were compared to April 2019 to determine changes in attendance. To evaluate outcomes, we reviewed DME patients with appointments scheduled from April 1 - 30, 2020. Data from the last visit prior to April 1, 2020 was compared to the first follow-up visit between April 1, 2020 to December 1, 2020. Ocular surgery or absence of injections within the 3 months prior to scheduled appointment excluded patients from this study. Central foveal thickness (CFT) was measured from optical coherence tomography images and Snellen visual acuity (VA) measurements were obtained from the medical record. Poor outcome was defined as VA decrease of one or more lines or a CFT increase of 10% or more. Analysis included the eye with the worse VA from each patient.

Results: Total visits to the retina injection clinic decreased by 54% from 533 patient visits in April 2019 to 247 visits in April 2020. Of 562 unique patients scheduled for April 2020, 185 patients were on anti-VEGF injection schedules for DME treatment. 51 patients were excluded. Of the remaining 134 patients, the mean age was 64.7 ± 8.8 years. 86% (115/134) were rescheduled, and of these, 26/115 were lost to follow-up until the end of our study period. The remaining 89/115 were seen with an average follow-up interval of 115.2 ± 50.0 days. At follow-up, 37/89 (42%) had worsened vision, 24/89 (27%) had worsened edema, and 54% (48/89) had a poor outcome of either worsened vision or worsened edema.

Conclusions: Pandemic related rescheduling of patients with DME delayed follow-up care and treatment. On average, patients were rescheduled to a visit that was 2.4 months later than their usual visit and about half the patients experienced worsening of vision or edema. Additional studies are needed to identify patients at highest risk of vision loss so that those patients can be triaged and evaluated appropriately.

CONTROL ID: 3534043

SUBMITTER (NAME ONLY): Haydn Walker

TITLE: Conditional Deletion of AP-2 β in the Periocular Mesenchyme of Mice Promotes Corneal Conjunctivalization

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Walker, A. Taiyab, M. Akula, J.A. West-Mays, Pathology and Molecular Medicine, McMaster University, Hamilton, Ontario, CANADA|T. Williams, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: The corneal endothelium and stroma derive from the periocular mesenchyme (POM), which originates from neural crest cells (NCCs), while the corneal epithelium stems from the anterior surface ectoderm. Signalling between the POM and surface ectoderm regulates epithelial proliferation and cell fate. Activating Protein-2 beta (AP-2 β), encoded by *Tfap2b*, is a transcription factor expressed in the POM. We have previously shown that conditional knock out AP-2 β generates a unique anterior segment phenotype that includes a closed iridocorneal angle, absent corneal endothelium and reduced corneal epithelial stratification. The purpose of this investigation was to further determine the impact of AP-2 β deletion in the POM on the corneal epithelial phenotype.

Methods: To generate the AP-2 β NCC KO model, male mice heterozygous for *Tfap2b*, *Tfap2b*^{+/-}, and the *wnt1-cre* transgene, *Wnt1Cre*^{+/-}, were bred with female mice in which the *Tfap2b* gene was floxed, *Tfap2b*^{lox/lox}. AP-2 β expressing offspring from this breeding scheme were used as age-matched controls. Eyes were enucleated from euthanized 2-3-month-old mice and processed before being embedded in paraffin. Immunohistochemistry was conducted using primary antibodies specific to Keratin-12 (K12), a corneal epithelial marker, and Keratin-15 (K15), a marker of conjunctival and limbal epithelia.

Results: Mature AP-2 β NCC KO mice have a distinct corneal phenotype, with significantly reduced stratification, an absent endothelium and disorganized, vascular stroma. 2-3-month-old eye sections from wild-type mice demonstrated consistent immunostaining of K12 across the corneal epithelium, while K15 was confined to the limbal region and continued throughout the conjunctival epithelium. In contrast, AP-2 β NCC KO mice demonstrated significantly reduced expression of K12 across the corneal epithelium, while K15 was observed consistently across the entire corneal epithelium, continuous with the conjunctiva.

Conclusions: The observed phenotypic changes in keratin expression indicate a shift towards conjunctival cell fate during development as a result of AP-2 β NCC KO. This change to the epithelial phenotype is consistent with other signs of corneal conjunctivalization seen in the AP-2 β NCC KO model, including stromal neovascularization.

CONTROL ID: 3534065

SUBMITTER (NAME ONLY): Onkar Sawant

TITLE: Histological Characterization of Retinal Degeneration in Mucopolysaccharidosis Type IIIC

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Heparan- α -glucosaminide N-acetyltransferase (HGSNAT) participates in lysosomal degradation of heparan sulfate. Mutations in the gene encoding this enzyme cause mucopolysaccharidosis IIIC (MPS IIIC) or Sanfilippo disease type C. MPS IIIC patients exhibit progressive neurodegeneration, leading to dementia and death before adulthood. Although some MPS IIIC patients exhibit incidences of non-syndromic retinitis pigmentosa and early signs of night blindness, majority of ocular phenotypes are not well characterized. The goal of this study was to investigate retinal degeneration phenotype in the Hgsnat knockout (KO) mouse model and correlate this phenotype with human ocular findings to understand the effects of Hgsnat mutation on the retina.

Methods: Heterozygous mice carrying mutation in the Hgsnat were crossed and offspring were sacrificed at 6 months of age. Cone and rod photoreceptors were analyzed using cone arrestin, S-opsin and rhodopsin antibodies. Outer nuclear layer (ONL) thickness and number of nuclei in the ONL layer were measured. Retinal OCT and fundus imaging was performed on an 11 year old MPS IIIC patient as a routine ophthalmic evaluation. Retinal histology was performed on the eye from 35 year old MPS IIIC donor and compared it to the age-matched control donor-eye.

Results: Our data suggest that loss of Hgsnat severely affects rod photoreceptors while cone photoreceptors are mainly unaffected at 6 months of age. We observed more than 30% reduction in the thickness and number of nuclei in the ONL in the Hgsnat KO retinas compared to those of the controls, indicating rod photoreceptor degeneration ($P < 0.05$). We also observed thinner outer segment length in Hgsnat KO retinas indicating reduced levels of rod photopigment rhodopsin. An 11 year old patient showed intraretinal cystic macular edema with myelinated nerve fiber. Severe retinal degeneration was observed in a 35 year old eye-donor.

Conclusions: To our knowledge, these are the first reports characterizing ocular phenotypes arising from deleterious variants in the Hgsnat gene associated with MPS IIIC clinical phenotype. Together our findings indicate that retinal manifestations of MPS IIIC are present even before cerebral manifestations. Thus, ophthalmological evaluations could be used as early diagnostic indicators of disease progression as well as end-points for evaluation of future therapies for MPS IIIC patients.

CONTROL ID: 3534072

SUBMITTER (NAME ONLY): Walter Wittich

TITLE: Graduate training in vision impairment & rehabilitation: The breadth of education and research possibilities to increase evidence-based practice

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wittich, L. Michaud, J. Renaud, O. Overbury, School of Optometry, Université de Montréal, Montréal, Québec, CANADA|W. Wittich, Centre de recherche interdisciplinaire en readaptation du Montréal métropolitain, Montréal, Québec, CANADA|

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ABSTRACT BODY:

Purpose: To initiate an international discourse on consensus towards optimal training environments for highly qualified personnel, including practitioners and researchers interested in vision impairment and rehabilitation. Current training options are typically incomplete, segmented or absent from many academic environments. Using the Graduate Program for Vision Science at the Université de Montréal (UdeM) as an example, we present an education model to address this need that provides both applied and research training under one roof.

Methods: In 2016, and in consultation with 1 national and 2 local vision rehabilitation centers, UdeM developed and established a bilingual Master's degree program in Vision Science to specifically train rehabilitation professionals in orientation & mobility (O&M), low vision (LV) and vision rehabilitation therapy (VRT). The hierarchical structure and development timeline of the program options are presented in Figure 1. Trainees may choose between a professional track, leading to employment as clinician-scientists, or the research track, leading towards academia, research and/or industry (Figure 2). Enrolment and graduation data were extracted from the UdeM administrative database.

Results: Since Sept. 2016, 63 students have enrolled in the professional Master's, 31 (8 O&M, 20 LV, 3 VRT) have graduated and 25 are in progress. Additionally, 1 Basic-Science Master's thesis was completed, with 1 in progress, and 3 PhD students have graduated, with 2 in progress (the first PhD on vision rehabilitation graduated in 2017). One postdoctoral fellowship has been completed, with 2 in progress. In total, 66 trainees have completed or are currently concentrating their practicum and research efforts on Vision Impairment & Rehabilitation.

Conclusions: The presented program structure has been extremely productive in generating highly qualified personnel. The parallel tracks facilitate cross-fertilization of relevant ideas, and support integrated knowledge translation through collaboration with clinic-based internship supervisors. This training structure of clinicians as potential future collaborators allows the field of vision impairment & (especially) rehabilitation to move forward where evidence-based practice is concerned.

CONTROL ID: 3534087

SUBMITTER (NAME ONLY): Venkatkrish Kasetty

TITLE: Complications, Compliance and 3-Year Outcomes after Endolaserless Vitrectomy with Aflibercept Monotherapy for PDR-Related Vitreous Hemorrhage

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.M. Kasetty, D. Starnes, H. Frazier, H. Singh, D.M. Marcus, Ophthalmology, Southeast Retina Center, Augusta, Georgia, UNITED STATES|V.M. Kasetty, Ophthalmology, Henry Ford Health System Department of Ophthalmology, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the 3-year visual and anatomic outcomes, safety, and compliance for patients undergoing endolaserless vitrectomy with intravitreal aflibercept injection (IAI) monotherapy for proliferative diabetic retinopathy (PDR)-related vitreous hemorrhage (VH).

Methods: Eyes underwent endolaserless vitrectomy and received one preoperative and intraoperative IAI followed by randomization to a q8week or q16week IAI group. Additional IAI for PDR progression or DME was administered as needed. Non-compliance was defined as missing >3 consecutive or >6 mandatory appointments. Q8week eyes were evaluated at week 104 for PDR stability and were transitioned to q16week IAI dosing for year 3 if appropriate. Q16week eyes were subject to q8week conversion at any time point if they experienced 2 episodes of recurrent VH.

Results: 31/40 eyes were randomized (14 and 17 eyes in q8week and q16week groups, respectively) with 25/31 (81%) randomized eyes completing 152 weeks. Compliance criteria was met by 10/14 (71%) and 9/17 (53%) eyes in the q8 and q16week groups, respectively. Through 104 weeks, q8 and q16week eyes received an average of 14.4 and 8.8 IAI, respectively. At week 104, 8/14 (57%) q8week eyes were converted to q16week IAI and 3/17 (18%) q16week eyes were converted to q8week IAI. Q8week eyes observed an increase in visual acuity (VA) of 34 letters from 41 to 75 letters (20/160 to 20/32) ($p=0.003$) compared to an increase of 27 letters from 48 to 75 letters (20/100 to 20/32) in the q16week group ($p=0.013$). Adverse ocular events in compliant patients included worsening VA > 30 letters at any timepoint (3 q8week eyes, 6 q16week eyes) and VH (2 q8week eyes, 6 q16week eyes). One case of neovascular glaucoma was seen in the q16week group and 1 retinal detachment occurred in both q8 and q16week groups. In addition, recurrent VH was experienced by 1 compliant q8week eye compared to 3 compliant q16weeks eyes.

Conclusions: Endolaserless vitrectomy with aflibercept monotherapy for PDR-related VH has shown to provide significant long-term visual gains. Frequent IAI is required to achieve fewer proliferative consequences. Non-compliance remains a patient-centered issue, further indicating the need for persistent and frequent postoperative anti-VEGF therapy. This data may provide a foundation for evaluating longer acting anti-VEGF treatment modalities with this approach.

CONTROL ID: 3534101

SUBMITTER (NAME ONLY): Olivia Cundy

TITLE: Genetic and environmental contributions to the variance of the Belin-Ambrósio Enhanced Ectasia Display "D" score explored in a classic twin study

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Belin-Ambrósio Enhanced Ectasia Display "D" (BAD-D) score is a summary corneal tomographic parameter shown to be sensitive in detecting subclinical keratoconus. We explored heritability of this parameter in a largely healthy twin cohort.

Methods: Scheimpflug corneal imaging was performed using the Oculus HR (High-Resolution) Pentacam (Oculus, Wetzlar, Germany) in adult volunteers recruited from the TwinsUK registry based at St Thomas' Hospital in London. Images from the right eye were used for analysis. Only complete twin pairs were included. The BAD-D parameter was noted, and coefficients of intra-pair correlation were calculated for monozygotic (MZ) and dizygotic (DZ) twin pairs. Heritability was estimated by maximum likelihood structural equation modelling using the OpenMx package.

Results: Images from 136 twin volunteers (37 MZ and 31 DZ pairs) were included. Mean (SD) age was 61 (11) years. The majority (93%) were female, reflecting the demographics of the registry. The mean (SD) value of the BAD-D parameter was 1.27 (0.73). Tests of normality did not detect significant deviation from a normal distribution. Pearson coefficients of intra-pair correlation were 0.68 ($p = 4.1 \times 10^{-6}$) and 0.33 ($p = 0.066$) for MZ and DZ pairs respectively. The age-adjusted estimate of heritability was 66.4% (95% CI, 46.6-79.2).

Conclusions: The calculated intra-pair correlation coefficient for MZ twins was double that for DZ twins, indicating that the majority of the variance in this parameter is determined by genetic factors. We estimated that approximately two thirds of the variance was attributable to genetic factors. Further studies can seek to identify associated genes.

CONTROL ID: 3534109

SUBMITTER (NAME ONLY): Liangbo Shen

TITLE: Sepsis and Necrotizing Enterocolitis are Associated with Thinner Retinal Nerve Fiber Layer in Preterm Infants at 36 Weeks Postmenstrual Age

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.L. Shen, Department of Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|S. Mangalesh, S. Michalak, N. Sarin, L. Vajzovic, S.F. Freedman, M. El-Dairi, C.A. Toth, Department of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|B. McGeehan, G. Ying, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|J. Finkle, E.J. Benner, N. Younge, C.M. Cotten, S.F. Freedman, Department of Pediatrics, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neonatal insults from systemic diseases have been implicated in the pathway of impaired neurodevelopment in preterm infants. Thinner retinal nerve fiber layer (RNFL) assessed by optical coherence tomography (OCT) has been associated with poorer neurodevelopment in preterm infants, suggesting RNFL thickness may reflect the brain as a whole in preterm infants. However, it remains unknown if RNFL thickness can serve as a noninvasive biomarker for the impact of systemic diseases on the central nervous system in preterm infants. We aimed to investigate associations between systemic health factors and RNFL thickness in preterm infants.

Methods: The STudy of Eye imaging in Preterm infantS (BabySTEPS) prospectively enrolled infants eligible for retinopathy of prematurity screening based on standard guidelines. We imaged both eyes of these infants at 36 ± 1 weeks postmenstrual age (PMA) using a handheld OCT system at the bedside in the Duke intensive care nurseries. RNFL thickness of the right and left eyes was averaged for each infant. We evaluated associations between RNFL thickness and 27 systemic health factors using multivariable regression models.

Results: We included 83 infants with RNFL thickness measures in this study. Of the 83, 16 infants had sepsis or necrotizing enterocolitis (NEC). These events occurred before the OCT imaging (time interval = 50 ± 22 days). Among 27 systemic factors, infant weight at imaging and sepsis/NEC were independently associated with RNFL thickness. RNFL was 10.4 µm thinner in infants with sepsis/NEC than without sepsis/NEC (52.7 ± 9.0 vs. 63.1 ± 10.2 µm; $P < 0.001$). This difference remained statistically significant after adjustment for confounding variables (birth weight, birth weight percentile, gestational age, infant weight at OCT imaging, and growth velocity). A 250-g increase in infant weight at OCT imaging was associated with a 3.1 µm (95%CI = 2.1 to 4.2) increase in RNFL thickness ($P < 0.001$).

Conclusions: Low infant weight and sepsis/NEC were independently associated with thinner RNFL in preterm infants at 36 weeks PMA. To our knowledge, this study is the first to suggest that sepsis/NEC may affect retinal neurodevelopment. OCT-measured RNFL may offer a noninvasive biomarker to assess the negative impact of sepsis/NEC on the central nervous system in preterm infants.

CONTROL ID: 3534120

SUBMITTER (NAME ONLY): Moonjung Choi

TITLE: Molecular chaperones are direct binding partners in mitochondrial targeting of SLC4A11.

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Choi, J.A. Bonanno, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Moonjung Choi: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Bonanno: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: SLC4A11 is an ammonia-sensitive mitochondrial uncoupler suppressing glutamine induced oxidative stress. Our preliminary data indicate that SLC4A11 might traffic to the mitochondria of corneal endothelium through a "chaperone-mediated carrier-pathway". The purpose of this study is to investigate direct physical interaction between molecular chaperones and SLC4A11.

Methods: In situ protein interactions between SLC4A11 and either HSP90 or HSC70 was examined and visualized using Proximity Ligation Assay (PLA), which uses a pair of oligonucleotide-labeled secondary antibodies (PLA Probes). Anti-HA was paired with either anti-HSP90 or anti-HSC70 primary antibodies in PS120 fibroblasts transfected with either HA epitope-tagged human SLC4A11 (PS120-hSLC4A11-HA) or empty vector (PS120-EV) cells. When the primary antibodies are in close proximity to each other (< 40nm), PLA-fluorescence spots are quantified using a Zeiss LSM 800 confocal microscope with Airyscan (63X objective, 1.8X zoom). In order to validate whether the chaperones guide SLC4A11 to the mitochondrial surface receptor to import the pore of the translocase of the outer membrane (TOM) complex, mitochondria of the cells were labeled with MitoTracker CMXRos prior to PLAs: 1) HA/TOM70 (outer mitochondrial membrane marker), 2) HA/HSP90, and 3) HA/HSC70. Incubation with no primary antibody and each separate primary antibody was done as negative controls for the PLAs.

Results: Significant PLA signals of SLC4A11 with HSP90 or HSC70 were observed in PS120-hSLC4A11-HA cells, but not in PS120-EV cells. Furthermore, PLA: HA/TOM70 revealed that SLC4A11 directly binds to the mitochondrial surface receptor, TOM70. The PLA: HA/TOM70 signals were colocalized with the mitochondria labeled with MitoTracker CMXRos. Like the distribution of HA/TOM70 PLA signals to the mitochondria, fewer than half of HA/HSP90 and HA/HSC70 PLA signals closely overlapped mitochondria. More than half of the PLAs signals appeared in the cytoplasm, which indicates where SLC4A11-chaperone complexes are initially recruited.

Conclusions: We found that HSP90 and/or HSC70 are the chaperones as physical binding partners with SLC4A11, which, in turn, allows SLC4A11 to traffic across the mitochondria.

CONTROL ID: 3534134

SUBMITTER (NAME ONLY): Michael Osterman

TITLE: Investigation of the use of drusen as a biomarker for age-related macular degeneration reveals shared genetic risk in the Amish

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. Osterman, Y.E. Song, J.L. Haines, Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|M.D. Osterman, Y.E. Song, J.L. Haines, Cleveland Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|M. Nittala, S.R. Sadda, Doheny Imaging Reading Center, Doheny Eye Institute, Los Angeles, California, UNITED STATES|W.K. Scott, M.A. Pericak-Vance, Hussman Institute for Human Genomics, University of Miami, Coral Gables, Florida, UNITED STATES|D. Stambolian, Ophthalmology and Genetics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of vision loss nationwide and accounts for 8.7% of blindness. Detailed GA and drusen measurements may be promising biomarkers for staging and monitoring of AMD. However, the genetic relationship between these traits and AMD is not fully understood. Here, we investigate the genetics of quantitative measures of drusen and GA in an Amish population using genetic risk scores (GRSs) derived from a previous large AMD genome-wide association study (GWAS).

Methods: We performed chip genotyping using an Illumina Multi-Ethnic Genotyping Array with custom content. GA and drusen measures were obtained from macular optical coherence tomography (OCT) volume scans. 1,117 Amish adults with a family history of AMD from Ohio, Pennsylvania, and Indiana were included in the analyses after quality control and assurance. GRS were constructed using summary statistics of genome-wide significant SNPs for AMD from Fritsche et al. (2016). We tested the impact of the GRS for both the presence/absence of GA and drusen and, for those with GA and/or drusen, the impact on the measures. Traits included geographic atrophy, drusen area, and drusen volume within 3 and 5mm circles centered on the fovea. Logistic regression models were used to test the added utility in predicting the presence each of these drusen traits beyond a basic covariate-only model including age, sex, and smoking status. Similarly, linear models were constructed to investigate prediction of the quantitative measures of each of these traits by using the same predictors on subsets of individuals with presence of each of the traits.

Results: Results indicated a small, but statistically significant ($p < 0.05$), effect of the GRS to improve model performance for presence of each of the five traits. Area under curve (AUC) for drusen area and volume in a 3mm circle improved from 0.797 and 0.831 to 0.825 and 0.864, respectively, by adding the GRS to a covariate-only model. Further, it had a significant effect in improving prediction of the quantitative measures of drusen area and volume.

Conclusions: These results suggest that drusen development and AMD share underlying risk loci, helping to elucidate the relationship between drusen and AMD, potentially allowing for future use of drusen traits as a biomarker.

CONTROL ID: 3534144

SUBMITTER (NAME ONLY): Alison Teo

TITLE: Prevalence of Demodex Colonization in Patients Presenting to an Outpatient Clinic

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Teo, A. Jacobson, Ophthalmology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|E. Rosenberg, SightMD, Babylon, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Demodex follicularis and demodex brevis are microscopic ectoparasites known to cause blepharitis. However, there is limited knowledge regarding the prevalence of Demodex in asymptomatic healthy individuals versus those with symptomatic pathologic demodicosis.

Methods: This was a prospective, cross-sectional study examining the prevalence of and risk factors for Demodex colonization in all patients 18 years and older presenting to two large, tertiary care outpatient ophthalmology clinics. Demographic information, prescription and non-prescription ocular medications, and concurrent pathologies such as pterygia, blepharitis, and dry eye disease was also recorded. Each patient underwent epilation of four eyelashes, one from each eyelid. Each eyelash was examined underneath a compound light microscope looking for the presence of Demodex species or eggs. For patients positive for Demodex, appropriate treatment was initiated with routine follow up.

Results: 199 patients were examined, with an average patient age of 59.4 ± 2.1 years. Demodicosis was newly diagnosed in 55.3%, with 61.8% and 68.3% noted to have blepharitis and dry eye, respectively. Only 1% of those with confirmed Demodex were previously diagnosed and treated. The presence of Demodex was found to be independent of sex, number of clinic visits, self-administered lid hygiene regimen, or prescription ophthalmic drops. There were statistically significant associations noted between the presence of Demodex and age ($p=0.005$), history of pterygium surgery ($p=0.01$), dermatochalasis ($p=0.001$), blepharitis ($p<0.001$), and dry eye disease ($p=0.001$). Patients using alpha-agonist eyedrops showed a decreased risk of Demodex colonization ($p<0.05$).

Conclusions: In the clinical setting, Demodex is grossly under-diagnosed and responsible for both acute and refractory blepharitis in a large subset of patients. In agreement with prior studies, we found a positive correlation between presence of Demodex and age as well as presence of blepharitis and dermatochalasis. However, in contrast to previous studies, there was little association with pterygia and a decreased incidence of demodicosis in patients using alpha-agonist drops. Over 50% of the entire study population and over 60% of patients with blepharitis were found to have Demodex. Ongoing investigations into appropriate diagnosis and treatment regimens have great potential to improve quality of life for our patients.

CONTROL ID: 3534162

SUBMITTER (NAME ONLY): Matthew McKay

TITLE: Assessing the uniformity of uveitis clinical concepts and associated ICD-10 codes across healthcare systems sharing the same electronic medical records system

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. McKay, M. Blazes, M. Lacy, K.L. Pepple, A.Y. Lee, C.S. Lee, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|M. Dahrouj, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|A. Reddy, University of California San Francisco, San Francisco, California, UNITED STATES|N. Apostolopoulos, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|H. Nguyen, Ophthalmology, Stanford Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the degree of uniformity in mapping of uveitis clinical concepts to International Classification of Diseases, Tenth Revision (ICD-10) code across healthcare systems using the same electronic health record (EHR) system.

Methods: Researchers from five different healthcare systems (University of Washington, Harvard University, Stanford University, Yale University, University of California San Francisco), each of which employ the Epic EHR, queried 54 uveitis related diagnostic terms and recorded associated ICD-10 codes. The main outcome measure was the degree of uniformity for uveitis ICD-10 code associations.

Results: Fifty-four uveitis related diagnostic terms were queried within the Epic EHR at five different healthcare systems. There was perfect agreement among all five centers for 52 out of 54 diagnostic terms. The proportion of uveitis diagnoses with identical ICD-10 mapping on pair-wise comparison between centers was greater than 96% for all comparisons (Table). Two diagnostic terms were observed to have differences in ICD-10 coding: (1) juvenile idiopathic arthritis associated chronic uveitis and (2) intermediate uveitis. Intermediate uveitis was associated with H20.1x (ICD-10 description: 'chronic iridocyclitis') or H20.9 (ICD-10 description: 'unspecified iridocyclitis') in three centers while being associated with H30.2x (ICD-10 description: 'posterior cyclitis') at the two remaining centers. The discrepancies appear to be related to a recent update in diagnostic mapping in the Epic EHR. Further, considerable overlap was observed for multiple diagnostic terms with the same code, creating anatomic, etiologic, and infectious non-specificity in identifying diagnosis by ICD-10 code. Fifteen diagnostic terms had no ICD-10 association at any of the centers.

Conclusions: ICD-10 mapping to uveitis diagnostic terminology appears to be highly uniform at different centers with the Epic EHR. However, temporal changes in diagnosis mapping to ICD-10 code and lack of one-to-one mapping of diagnosis to ICD-10 code add additional sources of complexity to interpretation of big data studies in uveitis.

CONTROL ID: 3534164

SUBMITTER (NAME ONLY): Matthew Starr

TITLE: Development of cystoid macular edema following rhegmatogenous retinal detachment surgery

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Starr, L. Cai, M. Ammar, L. Patel, A. Obeid, O. Gupta, C. Regillo, J. Hsu, Y. Yonekawa, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|E. Ryan, C. Ryan, VitreoRetinal Surgery, PA, Minnesota, UNITED STATES|A. Capone, Beaumont Health, Royal Oak, Michigan, UNITED STATES|G. Emerson, The Retina Center, Minnesota, UNITED STATES|D. Joseph, Barnes Retina Institute, Saint Louis, Missouri, UNITED STATES|D. Elliott, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cystoid macular edema (CME) following cataract surgery is a well-known phenomenon. Less is known regarding the risk factors, though, of developing CME following repair of rhegmatogenous retinal detachments (RRD).

Methods: This is a subgroup analysis of the Primary Retinal Detachment Outcomes (PRO) study, a multi-institutional study of consecutive primary RRD surgeries from 1/1/2015 through 12/31/2015. The primary outcome was development of post-operative CME following RRD surgery. The analysis was limited with those with post-operative optical coherence tomography imaging and at least 3 months of follow up following RRD repair.

Results: There were 1,466 eyes that met the inclusion criteria, and 140 (9.6%) developed post-operative CME following primary RRD repair. Multivariate analyses with statistically significant associations were older patient age (OR 1.03 per year, 95% CI 1.01 to 1.05), pre-operative proliferative vitreoretinopathy (PVR, OR 1.74, 95% 1.03 to 2.95), and cataract surgery following RRD repair (OR 2.18, 95% CI 1.47 to 3.25). Of the 843 (57.7%) phakic eyes, 76 (9.0%) developed post-operative CME. Multivariate analysis showed that cataract surgery following RRD repair was an independent risk factor ($p < 0.0001$) in this subset. Of the 623 (42.3%) pseudophakic eyes, 60 (9.9%) developed post-operative CME. Older age was an independent risk factor ($p = 0.0075$). When examining only eyes that underwent successful retinal re-attachment with a single surgery, 77 of 1211 (6.4%) eyes developed CME. Post-operative cataract surgery ($p = 0.0005$) and pre-operative PVR ($p = 0.0011$) were the independent risk factors for CME based on multivariate analyses in this subgroup. Of note, vitrectomy and vitrectomy with scleral buckle resulted in higher rates of CME compared to scleral buckle alone on univariate analyses, but did not remain statistically significant on multivariate regression analysis.

Conclusions: CME occurred in nearly 10% of eyes following RRD repair. The biggest risk factors were recurrent retinal detachment, preexisting PVR, older age, and cataract surgery following RRD repair.

CONTROL ID: 3534168

SUBMITTER (NAME ONLY): David Boyer

TITLE: Systemic Antisense Oligonucleotide Inhibition of Complement Factor B for Treatment of Geographic Atrophy: Results of a Placebo-controlled Phase 1 Dose-Escalation Study

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sahni, S. Fauser, Hoffman-La Roche, Basel, SWITZERLAND|R. Geary, E. Schneider, M. McCaleb, Ionis Pharmaceuticals Inc, Carlsbad, California, UNITED STATES|D.S. Boyer, Retina-Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: An over-active alternative complement pathway (ACP) is implicated in geographic atrophy (GA) pathophysiology and ACP end products are present in the choriocapillaris (CC), drusen and Bruch's membrane of eyes with AMD. In monkeys, a systemic Factor B antisense oligonucleotide (ASO) reduced ocular factor B (FB) protein >99%. We determined clinical safety, pharmacokinetic (PK) and pharmacodynamic (PD) activity of IONIS-FB-L_{Rx}, an ASO specifically targeting human complement factor B gene (CFB) and subsequent factor B (FB) production in the liver, as a means to decrease ACP activity in the CC.

Methods: In a phase 1 masked, randomized placebo-controlled single and multiple ascending dose study, healthy volunteers (HV) were randomized to either placebo or IONIS-FB-L_{Rx} (ACTRN12616000335493). The drug was administered (8 administrations in 6 wk – twice wk for 2 wk then once wk for 4 wk) at doses of 10 mg or 20 mg in the multiple ascending dose study. Endpoints assessed throughout the study: ocular and systemic safety, pharmacokinetic (PK) and pharmacodynamic (FB and ACP activity (AH50)).

Results: 54 HV (age range 27- 65 yrs) were enrolled and all subjects completed study (wk 19). There were no safety signals or clinically-relevant changes in ocular endpoints (BCVA, IOP, comprehensive examination), blood chemistries, hematology or vital signs following IONIS-FB-L_{Rx} dosing. The maximum tolerated dose (MTD) was not reached. The systemic PD markers of plasma FB levels reduced in a dose dependent manner by approximately 56% and 72% after multiple administrations of 10 mg and 20 mg, respectively. The mean (+/- SE) % reductions of FB, ACP activity (AH50) and classical complement pathway activity (CH50) levels for the 20 mg dose on Day 43 (7d post last administration) was -72 (+/-3), -62 (+/-5) and -12 (+/-5)%, respectively.

Conclusions: IONIS-FB-L_{Rx} is a novel antisense oligonucleotide drug, administered subcutaneously with a potential for monthly dosing. This first-in-human IONIS-FB-L_{Rx} study found the antisense drug to exhibit robust lowering of systemic FB and excellent safety profile. Based on these data, a Phase 2 double-masked, randomized placebo-controlled trial (N=330), the GOLDEN study, is currently underway to determine the potential of systemic IONIS-FB-L_{Rx} in reducing progression of GA (NCT03815825).

CONTROL ID: 3534170

SUBMITTER (NAME ONLY): Alicia Canalejo

TITLE: Myopic choroidal neovascularization: prognostic factors with a PRN regimen of Anti-VEGF therapy

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Canalejo, M. Lopez-Galvez, M. Muñoz Moreno, Hospital Clinico Universitario de Valladolid, Valladolid, Castilla y León, SPAIN|M. Lopez-Galvez, Instituto de Oftalmobiología Aplicada, Valladolid, Castilla y León, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the short and long-term efficacy of Anti-Vascular Endothelial Growth Factor (VEGF) intravitreal therapy with a Pro Re Nata (PRN) approach in the treatment of myopic choroidal neovascularization (CNV) and to investigate the correlation of basal risk factors with treatment outcomes, in order to individualize treatment.

Methods: Observational, retrospective study of 91 patients (28 men and 63 women) treated with Anti-VEGF therapy due to neovascularization secondary to pathologic myopia for a 1 to 6 years period. Best Corrected Visual Acuity (BCVA) and Central Retinal Thickness (CRT) before and after treatment were analyzed. The mean number of injections in the first year, and during the whole treatment period was assessed. Additionally, prognostic factors for Anti-VEGF treatment were identified such as age, baseline visual acuity, localization and anatomic features of CNV studied by OCT, as well as treatment considerations.

Results: Mean (SD) age at onset was 67.9 (14.4) years. The BCVA (logMAR) improved from 0.72 at baseline to 0.53 one month after the first injection, it remained stable in 0.53 after three months. BCVA after 6 years was 0.58 ($p < 0.05$ in all cases). A reduction of 47.96 μ m ($p < 0.05$) in CRT was observed in OCT three months after treatment. The mean number of injections during the first year was 3.05, and 3.65 for the complete follow-up period. BCVA improved 3 lines in young patients, compared to 1 line in patients over 60 years ($p = 0.115$). One month after treatment, BCVA in subfoveal CNV changed from 0.85 to 0.66 ($p < 0.05$), whereas in juxtafoveal CNV it improved from 0.58 to 0.39 ($p < 0.05$). Type 2 CNV demonstrated a better response to treatment (from 0.71 to 0.56) than type 1 CNV (from 0.75 to 0.62), $p < 0.05$.

Conclusions: Anti-VEGF therapy has demonstrated efficacy in the short and long-term with a significant improvement in BCVA and in CRT. The PRN regimen or "as needed" is appropriate and includes a more individualized treatment approach. Advanced age, poor baseline visual acuity and subfoveal localization worsen prognosis. However, further studies are needed in order to identify which patients would benefit from a more intensive therapy in the long term.

CONTROL ID: 3534176

SUBMITTER (NAME ONLY): George Sanchez

TITLE: Patient's age as a prognostic factor of the visual outcome after surgical repair of primary macula-off rhegmatogenous retinal detachment (RRD)

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Sanchez, A.H. Sohn, J. McGinnis, D. Mantopoulos, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, UNITED STATES]

Commercial Relationships Disclosure (Abstract): George Sanchez: Commercial Relationship: Code N (No Commercial Relationship) | Ashley Sohn: Commercial Relationship: Code N (No Commercial Relationship) | Jacob McGinnis: Commercial Relationship: Code N (No Commercial Relationship) | Dimosthenis Mantopoulos: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To determine whether the patient's age correlates with the final best corrected visual acuity (BCVA) following surgical repair of a macula-off RRD. To look for signs of accelerated retinal atrophy after RRD in elderly patients using Optical Coherence Tomography (OCT).

Methods: Retrospective, consecutive case series. The medical records of patients who presented with RRD at an academic medical center anytime between January 2012 and October 2020 were reviewed. These patients were divided into three age groups: (A) ≤ 60 years-old, (B) 61-75 years-old, and (C) ≥ 76 years-old. Differences in postoperative BCVA between these age groups were assessed. Secondary outcome was differences in the central retinal thickness (CRT) based on OCT.

Results: From the 412 patients that were screened, 106 met the inclusion criteria (Figure 1). Eighty of them were male. Thirty-four of them were in group A, 49 in group B, and 23 in group C. The mean age \pm SD was 66.7 ± 10.3 years-old. The mean follow-up period was 22.1 ± 18.1 months. The mean logMAR (Snellen) BCVA \pm SD, pre-operatively and post-operatively, were 1.5 ± 0.8 (20/630) and 0.5 ± 0.5 (20/60), respectively. At final follow-up, logMAR (Snellen) BCVA was 0.25 (20/35), 0.57 (20/74) and 0.62 (20/83) in groups A, B, and C, respectively ($p < 0.05$ between the different subgroups). The difference in final CRT on OCT between the subgroups was not statistically significant (316.9 μ m in group A, 313.2 μ m in group B, and 310.2 μ m in group C).

Conclusions: In elderly patients who undergo successful surgery for macula-off primary RRD the visual recovery might be more limited compared to that in younger patients. In the current study the difference between the CRT in different age subgroups was not statistically significant.

CONTROL ID: 3534183

SUBMITTER (NAME ONLY): Yang Liu

TITLE: The therapeutic effect of Roxadustat in a mouse model of meibomian gland dysfunction

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, S. Yang, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Yang, Ophthalmology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, CHINA|

Commercial Relationships Disclosure (Abstract): Yang Liu: Commercial Relationship(s);Schepens Eye Research Institute:Code P (Patent) | Shan Yang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We recently discovered that meibomian glands (MGs) exist in a relatively low oxygen environment in vivo, and that hypoxia inducible factor 1 α (HIF1 α) plays a very important role in the regulation of MG function. We hypothesize that Roxadustat (Roxa) could serve as a treatment for MG dysfunction (MGD) by activating the HIF1 α pathway in MGs. To test our hypothesis, we used a newly identified MGD animal model--the Apolipoprotein E-deficient (ApoE KO) mouse--in our study. The ApoE KO mice present the clinical and pathological changes seen in MGD patients, and are also characterized by a marked increase in total plasma cholesterol levels.

Methods: Sixteen adult male ApoE KO mice were used in this study. Four sex- and age-matched wild type (WT) C57BL/6J mice were used as phenotype controls. The ApoE KO mice were treated with vehicle or Roxa for 12 weeks. Ocular surface and adnexal evaluations, and tear volume and body weight measurements were made before and after Roxa treatment. Mouse eyelids were removed and processed for histology and MG area quantification. MG sections were subjected to MG area quantification, LipidTox staining, and immunostaining for HIF1 α and its associated proteins, including glucose transporter 1 (Glut1), carbonic anhydrase 9 (CA9), peroxisome proliferator-activated receptor gamma (PPAR γ), and the adhesive protein desmoglein (Dsg). Total serum cholesterol was measured at the end of the treatment. Experiments were approved by the Institutional Animal Care and Use Committee of The Schepens Eye Research Institute and adhered to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Results: Roxa significantly reduced MG dropout, decreased corneal fluorescein staining, and increased the tear volume. Roxa also enhanced HIF1 α activation, changed the expression pattern of Glut1, CA9 and PPAR γ , and significantly increased the expression of Dsg in the MGs. In addition, Roxa significantly decreased the percentage of weight gain and total serum cholesterol level in these mice.

Conclusions: Roxa may serve as a potential new therapy for the treatment of MGD.

CONTROL ID: 3534196

SUBMITTER (NAME ONLY): William Ridder

TITLE: Saccade Latencies are Longer for Early/Intermediate AMD than Age-Matched Normal Patients.

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.H. Ridder, L. Centeno, Southern California College of Optometry, Marshall B Ketchum University, Fullerton, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): William Ridder: Commercial Relationship: Code N (No Commercial Relationship) | Lani May Centeno: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previous literature has shown that fixation stability and reading performance is poor in patients with advanced stages of age-related macular degeneration (AMD). However, little research has been conducted to determine oculomotor characteristics in patients with early/intermediate AMD. The aim of this study was to determine saccade latency differences between early/intermediate AMD patients and age-matched controls.

Methods: Thirteen subjects with early/intermediate AMD (age 75.1 ± 10.29) and fourteen age-matched controls (age 70.5 ± 6.42 , $p = 0.18$) were enrolled in the study. All participants underwent a clinical comprehensive eye examination including refraction, best corrected visual acuity, optical coherence tomography, color fundus photography, and fundus autofluorescence photos. The logMAR visual acuities were 0.03 ± 0.105 and -0.007 ± 0.119 for the AMD and control patients, respectively ($p = 0.35$). The simplified AREDS scale was used to classify the AMD patients (2.5 ± 1.17). Saccade latency was obtained utilizing the screen-based Tobii TX300 eye tracker (Tobii Technology, Sweden) to determine eye position. Testing procedures were conducted monocularly. The stimulus for testing was an "X" subtending 2 degrees vertically and horizontally. Initially, the cross appeared in the center of the display. The cross was displayed for 30 seconds before the stimulus was removed and an identical cross was displaced 5 degrees horizontal to the right or left of the initial cross. The second cross was displayed for 30 seconds and then removed. Saccade latency was defined as the time in milliseconds between when the cross moved and the subject's first saccade to the new cross location. The average saccade latency was determined for five forward (i.e., to the right) and backward saccades (i.e., to the left).

Results: Saccade latency was statistically increased for early/intermediate AMD (326.1 ± 91.6) compared to age-matched controls (252.3 ± 80.3) for forward saccades (two-tailed t-test, $T_{25} = 2.229$, $p = 0.035$) but not backward saccades (AMD 299.2 ± 95.7 , Control 293.1 ± 164.7 , $p = 0.37$).

Conclusions: Forward saccade latency was significantly greater for early/intermediate AMD subjects compared to age-matched controls. This increase in saccade latency for early/intermediate AMD patients may account for their increase in reading complaints.

CONTROL ID: 3534198

SUBMITTER (NAME ONLY): Stephanie Cote

TITLE: Perioperative management of antithrombotic agents in glaucoma surgery: a survey

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma surgery in anticoagulated patients poses unique challenges. There is currently no consensus on perioperative management of antithrombotics for glaucoma surgeries, and the new non-vitamin K antagonist oral anticoagulants (NOACs) have introduced further uncertainty. Our purpose was to survey the practice patterns of glaucoma specialists on perioperative management of antithrombotic agents in patients undergoing glaucoma surgery.

Methods: An anonymous cross-sectional survey was sent to members of the American Glaucoma Society (AGS) to investigate ophthalmologists' usual practice regarding antithrombotic therapy prior to, during and after trabeculectomies and glaucoma drainage implantations (GDI).

Results: One hundred and six surgeons responded to our survey. For trabeculectomies, majority of surgeons reported stopping P2Y12 inhibitors, NOACs, and warfarin (55%, 56% and 64% respectively) while 49 out of 104 (47%) surgeons routinely stop aspirin (ASA) before surgery (Figure 1). Similarly, for GDI, warfarin (54%) was most commonly stopped pre-operatively, followed by P2Y12 inhibitors and NOACs (both 49%), and ASA (42%). The majority of the surgeons who discontinue antithrombotic therapy reported doing so 6 days prior to surgery for aspirin, 3-5 days before surgery for P2Y12 inhibitors and warfarin, and either 48 or 72 hours before surgery for NOACs. Of those who stop warfarin and NOACs, the majority routinely liaise with patient's internist or general practitioner. Most surgeons resumed each antithrombotic within 1-day post-operatively, however almost half of those same surgeons (55% and 42% for warfarin, 46% and 53% for NOACs, for trabeculectomies and GDI respectively) said they will occasionally delay resuming greater than 1-day. The type of glaucoma surgery affects the decision to stop an antithrombotic in 53% of surgeons. Of those surgeons, 78% are more likely to stop an antithrombotic for trabeculectomies, 7% for GDI, and 15% for minimally invasive glaucoma surgeries (MIGS).

Conclusions: There is variability in the perioperative management of antithrombotic therapy among glaucoma surgeons with a considerable proportion reporting not stopping these agents pre-operatively. Further evidence-based guidelines are required to provide recommendations and address variations in practice.

CONTROL ID: 3534228

SUBMITTER (NAME ONLY): Sara Vaz-Pereira

TITLE: Sensitivity and specificity of MultiColor imaging in detecting proliferative diabetic retinopathy

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the accuracy of MultiColor imaging (MC) compared to fluorescein angiography (FA) in detecting proliferative diabetic retinopathy (PDR) and associated diabetic retinopathy features.

Methods: Fifty-nine eyes from 38 PDR patients were included. MC images were reviewed by 2 independent masked graders. A qualitative analysis based on the following features was performed: neovascular complexes (NVC), disc neovascularization (NVD), neovascularization elsewhere (NVE), microaneurysm (MA), intraretinal hemorrhage (IRH), vitreous hemorrhage (VH), preretinal hemorrhage (PRH), fibrosis, hard exudates (HE), epiretinal membrane (ERM), diabetic macular edema (DME), ischemia and laser spots (LS). Measures of diagnostic accuracy compared to FA were determined.

Results: The sensitivity for the detection of NVC using MC was 95.1%, with a specificity of 40.0%, positive predictive value (PPV) of 92.9% and negative predictive value (NPV) of 50.0%. Sensitivity and specificity were higher in detecting NVD (88.9% and 76.9%) while NVE registered higher PPV (88.9%). MC was highly sensitive in detecting IRH, HE, ERM and LS (100%), MA (98.0%) and fibrosis (95.5%). Highest specificity was found for VH (100.0%), DME (100.0%), PRH (98.1%) and LS (89.5%). The area under the receiver-operating characteristic analysis of MC was excellent in NVD (0.83, 95% confidence interval (CI), 0.71-0.95, $p<0.001$), IRH (0.89, 95% CI 0.74-1.00, $p<0.001$), VH (0.81, 95% CI 0.60-1.00, $p=0.005$) and PRH (0.89, 95% CI 0.68-1.00, $p=0.004$) and outstanding in LS detection (0.95, 95% CI 0.87-1.00, $p<0.001$). These results are likely due to the contrast and quality of the MC, since a better discrimination is enabled by the green wavelength. The intergrader agreement for the MC features assessed was almost perfect with a weighted kappa of 0.86 (standard error: 0.02, 95% confidence interval: 0.82–0.88).

Conclusions: MC detected some PDR features such as NVD, VH, PRH, IRH and laser spots, more accurately than FA. These findings make MC a useful test for the diagnosis and follow-up evaluation of PDR, complementing the noninvasive imaging of this disease.

CONTROL ID: 3534231

SUBMITTER (NAME ONLY): David Mundy

TITLE: In vitro characterization of a novel in situ-forming semi-interpenetrating polymer network of crosslinked collagen and glycosaminoglycans for corneal defect repair

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In situ-forming hydrogels are promising new candidates to treat corneal injury and disease, as global corneal donor shortages leave millions at risk for or affected by corneal blindness without effective treatment. The extracellular matrix of the corneal stroma consists of collagen type I and glycosaminoglycans (GAGs) which together provide biomechanical and biochemical cues that modulate cellular behavior. We have developed and characterized a novel semi-interpenetrating polymer network (SIPN) of crosslinked collagen and GAGs that can potentially treat corneal stromal defects and promote wound healing.

Methods: The SIPN was formed by crosslinking collagen type I with succinimidyl glutamic acid ester difunctionalized polyethylene glycol (PEG) using N-hydroxysuccinimide (NHS) ester chemistry, which was then mixed with hyaluronic acid (HA), chondroitin sulfate (CS), or both. To determine gel stiffness, storage (G') and loss (G'') moduli were measured. Transparency was evaluated by UV/Vis spectroscopy as transmittance after gelation. Gel cytocompatibility was assessed by live/dead assay using human corneal epithelial cells seeded on the gels.

Results: The collagen-PEG NHS gel and its SIPNs with HA and/or CS started to form within 1 minute, reaching 50% gelation within 10 minutes under ambient conditions. Mechanical properties were tunable by changing the concentration of PEG and the ratio of collagen:GAGs. 4% PEG (v/v PEG to collagen) gels had higher storage moduli than 8% PEG gels, whereas addition of GAGs decreased gel stiffness. The collagen-PEG and SIPN gels all showed over 95% transparency from 380 to 700 nm. Transmittance remained over 95% at 48 hours, whereas transmittance of non-crosslinked collagen decreased significantly over time. All gels were cytocompatible, with the SIPN with HA and/or CS demonstrating improved cell viability over collagen-PEG NHS alone.

Conclusions: We have developed a novel, collagen-PEG SIPN with GAGs that forms quickly in situ under ambient conditions. The hydrogel displays tunable mechanical properties, maintains excellent transparency, and promotes corneal epithelial cell viability, demonstrating the potential to promote wound healing and advance the treatment of corneal injury and disease.

CONTROL ID: 3534240

SUBMITTER (NAME ONLY): Nikolaos Katsinas

TITLE: Olive pomace phenolic compounds can inhibit inflammatory and oxidative-related diseases of human ocular surface epithelium

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Katsinas, C. García-Vázquez, M. González-García, A. Enriquez-De-Salamanca, IOBA-University of Valladolid, Valladolid, Castilla y León, SPAIN|N. Katsinas, S. Rodríguez Rojo, Institute of Bioeconomy, University of Valladolid, Valladolid, Castilla y León, SPAIN|M. González-García, A. Enriquez-De-Salamanca, Centro de Investigacion Biomedica en red en Bioingenieria Biomateriales y Nanomedicina, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To determine the antioxidant and anti-inflammatory activity of crude extracts and their two major phenolic compounds (Oleuropein – OL and Hydroxytyrosol – HT), derived from the olive oil's industry main environmentally hazardous by-product, the Olive Pomace (OP), in human corneal (HCE) and conjunctival (IM-ConjEpi) epithelial cells.

Methods: Two OP extracts were produced: extract 1 (E1) by a conventional extraction, and 2 (E2) by a Design of Experiments extraction optimization. Their anti-inflammatory and antioxidant effects were tested in vitro in HCE and IM-ConjEpi cells. Cells were pre-treated for 2h with E1 (0.05-0.80 mg/mL) and E2 (0.005-0.400 mg/mL) and then stimulated with TNF- α (25 μ g/ml) for 24h in the presence/absence of treatments. IL-1 β , IL-6, IL-8 and IP-10 secretion was analysed by an immune bead-based array. Intracellular Reactive Oxygen Species (ROS) production was determined by H2DCF-DA dye assay in ultraviolet (UV)-B radiation-exposed cells in the presence/absence of treatment for 1h (with 1h pre-treatment). The effect of OL (5–300 μ M), HT (1–100 μ M) and their mixture (5 μ M OL + 10, 25 or 50 μ M HT) was also tested. Cells not exposed to TNF- α or UV-B, and vehicle-treated cells were used as control. Data were normalized to corresponding protein content.

Results: TNF- α stimulated IP-10-secretion was significantly decreased in a dose-dependent way by E2 and HT in IM-ConjEpi and HCE cells, and by E1 and OL in IM-ConjEpi cells. IP-10 secretion was also decreased in HCE cells by 5 μ M OL + 10 μ M HT ($P < 0.001$). IL-6 secretion was inhibited dose-dependently by HT and E1, and by 0.2 and 0.4 mg/mL of E2 in HCE ($P < 0.05$). E1 (0.6 and 0.8 mg/mL), E2 (0.2 and 0.4 mg/mL) and 100 μ M of HT decreased IL-8 secretion in HCE cells. IL-1 β production in HCE was inhibited by E1 dose-dependently. UV-B stimulated ROS production was significantly inhibited in both cell lines by E1, E2, OL and HT dose-dependently and by 5 μ M OL + 10 μ M HT ($P < 0.01$).

Conclusions: Extracts from OP, an environmentally hazardous agro-industrial by-product, as well as their major phenolic compounds, HT and OL, may be used as therapeutic agent for inflammatory and oxidative-related ocular surface diseases. The results of this work consist an essential baseline for the treatment of these diseases in the future, while are paramount for the sustainable growth of related industries. Results are patent pending.

CONTROL ID: 3534264

SUBMITTER (NAME ONLY): Hidenori Takahashi

TITLE: Detecting keratoconus severity from corneal data of different populations with machine learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop a machine learning model to detect keratoconus severity from corneal topography, elevation and pachymetry parameters and to assess the generalizability of the model using an independent dataset from a different population.

Methods: We developed a machine learning model to detect different keratoconus severity levels from corneal parameters and compared it to four other machine learning models. The base model was trained and tested using 5881 cases in Brazil We then evaluated the model using a dataset with 1351 cases. We included only 50 raw corneal parameters and excluded all parameters that were generated by Pentacam to assess keratoconus. We utilized a 5-fold cross validation of the area under the receiver operating characteristic curve (AUC) to evaluate machine learning models.

Results: A total of 1726 eyes from the Brazil dataset were diagnosed as normal and 4155 were abnormal based on the Pentacam KCN index. A total of 400 eyes from Japan dataset were normal and 951 eyes diagnosed as KCN based on the Pentacam KCN index. The Random Forest classifier achieved the best AUC of 0.96 compared to four other classifiers once tested on the eyes from the Brazil dataset (Fig. 1). This model also achieved a high AUC of 0.87 once independently tested on all eyes from the Japan dataset (Fig. 2, left panel). Most of the confusions in the model tested on Japan dataset was between normal eyes and eyes with the mild stage of keratoconus (Fig 2, right panel).

Conclusions: The proposed machine learning algorithm provided a highly specific and sensitive model that can detect normal and four stages of keratoconus, with only raw Pentacam corneal parameters, without the machine generated keratoconus indices. The proposed model was generalizable to other cohorts from different races and has the potential to be used in cornea research and clinical practice to automatically detect keratoconus severity from corneal parameters.

CONTROL ID: 3534285

SUBMITTER (NAME ONLY): Jana D'Amato Tothova

TITLE: A porcine cornea model for testing corneal storage media formulations

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. D'Amato Tothova, L. Giurgola, C. Gatto, Alchimia srl, Ponte San Nicolò, ITALY|S.

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic further increased the lack of human donor corneas for research purposes. In this study we established a porcine cornea model for testing corneal storage media formulations.

Methods: 14 corneas were extracted from porcine eye globes obtained from local slaughterhouse after povidone-iodide 5% disinfection. The tissues were stored in standard corneal culture medium Eusol-C (AL.CHI.MI.A. SRL) at 4°C. After 0, 3, 7, and 14 days the tissues were analyzed in quintuplicate at T0 and in triplicate for the other timepoints with Optical coherence tomography (OCT) for central corneal thickness (CCT). The corneal transparency was evaluated by measurement of optical density using a homemade instrument. At each timepoint corneal endothelium was stained with trypan blue and alizarin red and evaluated with an inverted microscope with 100 X magnification (Nikon) for endothelial cell density (ECD) and morphology in both whole cornea and in dissected corneal lamellas consisting of Descemet's membrane (DM) and endothelial cells (EC).

Results: The corneal transparency diminished along storage time of approximately 10%. Corneal thickness increased of approximately 100 µm at day 14. ECD decreased of approximately 10% from T0 to the final T14 timepoint leading to an average of 2800 cells/mm² at T14. The dissected DM corneal lamellas allowed good EC morphology evaluation which was well preserved after 14 days at 4°C. The flaccidity of porcine corneas made OCT measurements difficult and CCT showed slight variability.

Conclusions: We established a porcine cornea model that allowed reproducible corneal evaluation of ECD, endothelial morphology CCT and transparency in whole porcine corneas and dissected DM corneal lamellas. In conclusion, the evaluation of porcine corneal tissues allowed to compensate to the lack of human donor tissues for research use, providing a reliable tool for testing corneal storage media formulations.

CONTROL ID: 3534308

SUBMITTER (NAME ONLY): Shahin Nasr

TITLE: Impact of Amblyopia on the Function of Stereo- and Motion-Selective Clusters in Human Extrastriate Cortex

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Nasr, B. Kennedy, A. Nabasaliza, R.B. Tootell, Radiology, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|S. Nasr, R.B. Tootell, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Nabasaliza, D.G. Hunter, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|P. Bex, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|D.G. Hunter, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Amblyopia is a developmental disorder caused by disruption of symmetric binocular visual input early in life. Most amblyopic individuals suffer from impairments in stereopsis and motion perception, especially in the central visual field. We studied the impact of amblyopia on the functional organization of fine-scale stereo- and motion-selective clusters across human extrastriate visual cortex.

Methods: We localized stereo- and motion-selective clusters across areas V2, V3, V3A and MT in 5 amblyopic (3 strabismic and 2 anisometropic) subjects and 14 controls using high-resolution (1 mm isotropic) fMRI in a 7T scanner. In separate scan sessions, we also measured speed, direction, and coherence sensitivity of the response in the motion-selective clusters. We also localized color-selective clusters in the same subjects as an internal control.

Results: Controls (≈ 50 arc sec randot stereoacuity) showed stereo-selective clusters across extrastriate visual areas (Fig. 1A), while amblyopic individuals (>250 arc sec) showed no significant stereo-selective response (Fig. 1B). Nevertheless, interdigitated clusters of motion- and color-selective responses were still found in areas V2/V3 of amblyopic individuals, as detected in controls. In both groups we also detected motion-selective responses within areas V3A and MT.

Despite the overall similarity in the distribution of motion-selective clusters between the two groups, the level of motion-selective response, especially to higher speeds and lower coherency levels, was weaker in amblyopic compared to control subjects. In V2 and V3, this between-groups difference: (i) was confined to those regions that represented the central (0° - 3°) visual field and (ii) accompanied a weaker direction-selectivity in amblyopic compared to control subjects.

Conclusions: Amblyopia affects the functional organization and the response selectivity of stereo- and motion-selective clusters across human extrastriate visual cortex. The spatial distribution of this effect is consistent with behavioral reports of a stronger amblyopia impact on central compared to peripheral vision.

CONTROL ID: 3534333

SUBMITTER (NAME ONLY): Tsutomu Yasukawa

TITLE: Autologous iris pigment epithelial cell sheet implants for chorioretinal diseases with retinal pigment epithelial atrophy

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yasukawa, Y. Hirano, A. Kato, Y. Ogura, Ophthalmology and Visual Science, Nagoya City University Graduate School of Medical Sciences, Nagoya, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) plays an essential role in maintenance of photoreceptors. RPE dysfunction may cause several diseases including retinitis pigmentosa, age-related macular degeneration, and pathologic myopia. Strategies for regenerative medicine are divided into autologous and allogeneic, somatic and stem cell-derived, an epithelial cell sheet and cell suspension. Iris pigment epithelium (IPE) is an alternative candidate because of relatively easy access for sampling. The purpose of this study is to prepare an IPE cell sheet for autologous implantation and evaluate neuroprotective effects in vivo.

Methods: Using our own technology to produce an RPE cell sheet with Bruch's membrane, a cell sheet of IPE cells, which were isolated from the iris and cultured, was prepared and implanted into the subretinal space of the right eye in 10 nude rats to evaluate possible adverse events histologically and in 13 royal college surgeons (RCS) rats under immunosuppression to assess neuroprotective efficacy. As the control group, only the sham surgery was performed in 10 nude rats and 10 RCS rats. At week 2, all of the right eyes of nude rats were enucleated to evaluate any adverse events histologically. In months 1 and 3, the right eyes of RCS rats were enucleated to assess both neuroprotective effects and any adverse events. To evaluate neuroprotective effects, the remaining outer nuclear layer (ONL) was graded from 1 to 5 (1: totally missing, 2: very slightly remaining, 3: slightly remaining, 4: moderately remaining, 5: largely remaining).

Results: There were no adverse events both in and outside of the implanted site in nude rats and RCS rats. In the control group of RCS rats, 3 of 5 eyes in month 1 and all of 5 eyes in month 3 showed the totally missing ONL (grade 1). In contrast, the ONL was somewhat remaining in all of 8 eyes (in grades 2-4) in month 1 and 4 of 5 eyes (in grades 2 and 3) in month 3 in the group with the IPE cell sheet implantation.

Conclusions: An IPE cell sheet implantation showed neuroprotective efficacy, suggesting the potential for regenerative medicine. We will plan to perform a phase I/IIa clinical study for regenerative medicine for diseases related to RPE dysfunction.

CONTROL ID: 3534336

SUBMITTER (NAME ONLY): Dongyi Wang

TITLE: Neural network aided erythrocyte stasis characterization based on erythrocyte mediated angiography (EMA)

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Wang, Y. Tao, University of Maryland at College Park, College Park, Maryland, UNITED STATES|J. Pottenburgh, W. Lai, C. Simon, O. Saeedi, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: EMA is a novel imaging technique permitting direct erythrocytes visualization. With EMA, erythrocytes can be observed in motion or in stasis. One cause of the transient stasis is hypothesized to be a manifestation of status of vasomotion. Erythrocytes in stasis could serve for characterizing hemodynamics status of retinal/choroidal vasculature in systemic and ocular diseases including primary open-angle glaucoma (POAG). This research has two main goals 1) developing a network model to quantify paused erythrocyte densities in EMA; 2) studying differences of relative paused erythrocyte densities for the control and POAG/POAG suspects.

Methods: 1) To train a network, we labelled 3752 cells in 24 temporally averaged (TA) images from 6 eyes (4 POAG/POAG suspects, 2 controls) which can visualize erythrocytes in stasis. Two trained researchers labelled pausing erythrocytes, and consensual labellings were used for network training. A regressional network was designed and trained in the manner of leave-one-eye-out cross validation to count pausing erythrocytes. 2) The trained model was applied to 22 eyes (16 POAG/POAG suspects, 6 controls) from 15 subjects. For each eye, EMA imaged both its peripapillary and macula area with duration of 5-15 seconds. The detected paused erythrocyte densities are 106.6 ± 159.27 cells/TA image and 191.25 ± 98.08 /TA images in the peripapillary and macula area. We defined peripapillary to macular ratio (PMR) as the paused cell count ratio between peripapillary and macula area. Generalized estimating equation (GEE) was used to compare PMR between controls and POAG/POAG suspects.

Results: 1) The cross validated f1-score of trained network is 0.938, which showed no significant difference compared to two trained researchers ($p < 0.05$). 2) The PMR value was 0.94 ± 0.23 in controls and 0.49 ± 0.18 in POAG/POAG suspects. POAG is statistically significant related to the PMR value ($p < 0.001$).

Conclusions: 1) Regression based neural network is a reliable model to quantify paused erythrocytes in EMA videos. 2) Our results showed differing PMR values between control and POAG/POAG suspects. This new finding manifests PMR can be potentially considered as a pathophysiological biomarker of early stage glaucomatous damage. Further studies are needed to determine the axial location of paused erythrocytes to better explain the phenomenon.

CONTROL ID: 3534338

SUBMITTER (NAME ONLY): Ryan Somogye

TITLE: Predicting Pulsatile Ocular Blood Volume Non-invasively

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Somogye, C.J. Roberts, R. Small, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|C.J. Roberts, Department of Ophthalmology & Visual Science, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|E. Spoerl, K.R. Pillunat, L.E. Pillunat, Department of Ophthalmology, Universitätsklinikum Carl Gustav Carus, Dresden, Sachsen, GERMANY|R. Small, Department of Anesthesiology, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a method of estimating pulsatile ocular blood volume (POBV) from measurements taken during an ophthalmic exam with a tonometer capable of measuring intraocular pressure (IOP) and ocular pulse amplitude (OPA).

Methods: A data set compiled from a previous accuracy study (Boehm 2008) on the PASCAL dynamic contour tonometer (DCT) provided central corneal thickness (CCT) and axial length (AL), as well as IOP and OPA using DCT and intracameral (ICM) measurements for 60 cataract patients. Briefly, once supine intracameral pressure was set to 15, 20, and 35 mmHg (randomized sequence) using a fluid-filled manometer, the system was closed by a stopcock, and IOP and OPA measurements were acquired at each manometric set-point (DCT and ICM simultaneously). The statistically significant correlation of ocular rigidity (OR) to the natural log of AL from a previously published study invasively measuring ocular rigidity through fluid injection was applied to the data set to estimate OR from AL. Friedenwald's original pressure volume relationship was used to derive the estimated blood volume delivered to the choroid with each heartbeat (POBV) as a function of OR, IOP, and OPA, according to the equation $POBV = \log((OPA+IOP)/IOP) / OR$. Linear regression analyses were performed comparing OPA to OR and calculated POBV at each of the three manometric set-points. POBV was also compared to the factor OPA/IOP with all data points combined. Significant threshold was $p < 0.05$.

Results: OR estimated from AL showed a significant positive correlation to OPA for both DCT ($p < 0.011$) and ICM ($p < 0.006$) at all three manometric pressure set-points, with a greater slope for lower IOP. Calculated POBV also showed a significant positive correlation to OPA ($p < 0.001$) with greater slope at lower IOP. In the combined analysis, POBV showed a significant positive correlation to OPA/IOP ($p < 0.001$) in both ICM and DCT measurements with $R^2 = 0.9685$, and $R^2 = 0.9589$, respectively (see Figure).

Conclusions: POBV provides a straight-forward method to estimate pulsatile ocular blood volume noninvasively. Higher IOP with lower OPA results in the lowest values of POBV. The OPA/IOP factor may provide a useful clinical tool for evaluating changes in ocular blood flow in diseases with a vascular component, such as diabetic retinopathy and normal tension glaucoma. Future studies are warranted.

CONTROL ID: 3534341

SUBMITTER (NAME ONLY): Jonathan Ibinson

TITLE: Aerosolization Detection with Noncontact Tonometry in Corneal Phantoms using an Air Quality Indicator

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.T. Ibinson, C.J. Roberts, M.A. Reilly, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|C.J. Roberts, M.A. Reilly, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|A. Yousefi Koupaei, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the performance of a static air quality monitor to measure aerosolization of a dynamic air puff from a noncontact tonometer (NCT) using cornea phantoms.

Methods: Three rubber corneal phantoms of different stiffnesses were used to represent intraocular pressure (IOP) values of 6, 13, and 43 mmHg. No liquid components and therefore no aerosol-generating potential was present. Reported concentrations of particulate matter (PM) less than 2.5 and 10 μ m, respectively PM_{2.5} and PM₁₀, were recorded using a static air quality indicator (AQI; LKC 1000S+) during an air puff generated using an Ocular Response Analyzer G3. The phantoms were mounted in a styrofoam head with eye socket locations. The AQI was set in four locations around the phantom. Depending on indicator position with respect to the phantom, the locations were defined as "upper/lower" and "same/opposite." Tests were performed in an isolated room. Baseline AQI values were recorded prior to each test with a one-minute delay between tests to allow the device to recalibrate. An ANOVA was performed to assess the effect of covariates IOP and location on changes to AQI measurements from the baseline, Δ PM_{2.5} and Δ PM₁₀. A Monte Carlo simulation with 10,000 replicates was undertaken to determine the likelihood of observing published trends by chance. The statistical significance threshold was $p < 0.05$.

Results: No correlations were found between PM_{2.5} and IOP ($p = 0.3943$) or location ($p = 0.3049$). Reported concentrations of PM₁₀ depended significantly on both IOP ($p = 0.0241$) and location ($p = 0.0167$), specifically the lower opposite location ($p = 0.0031$). Monte Carlo simulations using these results suggest that the likelihood of finding a spurious positive correlation between IOP and PM at the upper same location are 53% and 92% for PM_{2.5} and PM₁₀, respectively.

Conclusions: While a statistically significant correlation was found between reported PM₁₀ and IOP/location, even the highest reported PM values were far below the AQI sensitivity of ± 10 and $\pm 15 \mu\text{g}/\text{m}^3$ for PM_{2.5} and PM₁₀, respectively. The AQI updates every 3 seconds, yet the NCT puff is approximately 30 ms in duration. Since these experiments were conducted in the absence of any aerosol source (i.e., tear film), published IOP-PM correlations are likely a result of air pressure magnitude. (Tang 2020) Therefore, the AQI is not capable of quantifying aerosolization with an NCT air puff.

CONTROL ID: 3534357

SUBMITTER (NAME ONLY): Michael Moussa

TITLE: Impact of Carrier Graft Thickness on Intraoperative Aqueous Leak after Boston Keratoprosthesis Implantation

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Moussa, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|P. Agarwal, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|P. Agarwal, Mid Yorkshire Hospitals NHS Trust, Wakefield, Wakefield, UNITED KINGDOM|R.R. Sayegh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R.R. Sayegh, Ophthalmology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Various carriers for the Boston Keratoprosthesis (KPro) have been proposed including xenografts, autografts, collagen constructs, as well as fresh, frozen, dehydrated and γ -irradiated allografts. One potential limiting factor in the use of these carriers is the discrepancy in thickness. We examine the impact of corneal thickness on aqueous leak after KPro implantation.

Methods: Using a femtosecond laser, ethanol-preserved corneal donor buttons were mounted on an artificial anterior chamber and cut to various thicknesses. Anterior segment OCT was used to measure the thickness before and after the cut creation. A dermatologic punch was used to make a central hole and the KPro was assembled in the standard fashion. The assembled corneal construct was mounted onto the anterior chamber which was attached to a phacoemulsification machine with the intraocular pressure (IOP) set at the lowest setting of 20 mmHg. The IOP was gradually increased and a fluorescein strip was used to check Seidel positivity.

Results: Three corneas were cut with resulting post-cut thicknesses of 168 μm , 346 μm , and 413 μm , and a fourth cornea was left uncut with a thickness of 858 μm . When connected to the phacoemulsification machine, the three cut corneas were Seidel positive at 20 mmHg, while the fourth remained Seidel negative even at maximal IOP (80 mmHg).

Conclusions: A minimal corneal carrier graft thicknesses between 413 μm and 858 μm is required to avoid intraoperative leak during KPro implantation. Additional experiments are needed to further narrow down this range.

CONTROL ID: 3534371

SUBMITTER (NAME ONLY): Fuqiang Zhong

TITLE: In-vivo evidence of increased lamina cribrosa compliance at onset of experimental glaucoma in nonhuman primates

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Zhong, Y. Hua, J. Wei, M. Bansal, I.A. Sigal, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J. Reynaud, B. Fortune, Devers Eye Institute Legacy Health Research, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure acute lamina cribrosa (LC) deformations induced by elevated intraocular pressure (IOP) when healthy and at onset of experimental glaucoma (EG).

Methods: The optic nerve heads (ONHs) of four eyes of four rhesus macaque monkeys were imaged using optical coherence tomography (OCT, Spectralis) in three imaging sessions before (baselines 1 and 2) and at the onset of laser-induced EG. Onset was defined as confirmed peripapillary RNFL loss from OCT. In each session, the ONHs were scanned after IOP was set for 10 minutes to 10 mmHg and to 40 mmHg. Digital volume correlation (DVC) analysis was then used to determine the LC changes between scans. LC changes represent either acute (between IOP levels) or chronic deformations (between sessions at the same IOP, Fig. 1).

Results: LC deformations between baseline 1 and baseline 2 at low IOP (10 mmHg) were the smallest (compression 2-3%) in all four eyes, indicating good repeatability (Fig. 2, Step 4). During baseline, acute IOP-induced LC deformations were substantially larger (8-12%) and consistent in all four eyes at both tests (Fig. 2, Steps 1 and 2), indicating stable LC compliance. Compared with the acute IOP effects at baseline, the acute IOP effects at onset (Fig. 2, Step 3) were larger in three monkeys (up to 17%) and smaller in one monkey (5%). Interestingly, chronic changes induced by onset of EG (Fig. 2, Step 5, 8-15%) were larger than the acute IOP-induced LC deformations at baseline.

Conclusions: Acute and chronic IOP-induced LC changes can be reliably measured using OCT and DVC. At EG onset, three of four monkeys exhibited substantial changes in the LC and increased LC compliance, suggesting that the damage and remodeling processes are already advanced.

CONTROL ID: 3534380

SUBMITTER (NAME ONLY): Tasneem Sharma

TITLE: Pathogenesis of Space Associated Neuro-Ocular Syndrome examined using the Ex-Vivo Human Translaminar Autonomous System

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.P. Sharma, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Tasneem Sharma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The chronic dysregulation between intracranial pressure (ICP) and intraocular pressure (IOP) in space may restructure the posterior eye to a condition that is maladaptive to Earth and can cause Space Associated Neuro-ocular Syndrome (SANS). We will employ our novel ex-vivo translaminar autonomous system (TAS) to effectively recreate the ex-vivo mechanical and pathological IOP/ICP microenvironment to study SANS pathogenesis.

Methods: To recapitulate SANS conditions, dissected human posterior cups (PCs) (N=3) were cultured in the TAS model for various translaminar differentials (IOP: ICP chambers; 16:12; 16:15, 21:12, 21:15 mmHg) and maintained over 14 days. In addition, the ONs were placed in 6- and 10-degree tilts with IOP: ICP at 16:15 mmHg. Posterior globe changes were determined via photomicrographs. We identified retinal, inflammatory and apoptotic markers through TAQMAN arrays. The FN and COLIV expression were examined from conditioned medium of various groups by Western analysis. Degeneration of ON axons from various experimental conditions was assessed by paraphenylenediamine staining. The morphological reorganization and gliosis of optic nerve head (ONH) was studied by expression of LAM and GFAP. TUNEL staining was used to assess apoptosis. Transport and functional analyses were performed by Cholera-toxin B and electroretinograms respectively.

Results: We successfully maintained all translaminar differentials (N=3) over 14 days. Post culture, visual micrograph depicted a general bulging at the ONH for all groups. The 6-degree tilts with IOP: ICP at 16:15 mmHg had elevated expression of all retinal markers compared to control. The tilting of the ON caused highest increase in GFAP, BAX and TLR4 expression. Compared to control, all groups displayed elevated FN and COLIV. Experimental conditions depicted greater degenerated axons. Extensive glial scarring and cupping was also observed due to ON tilting. Increased TUNEL positive cells were identified within experimental groups. Minimal expression of CTB was detected within control and certain experimental groups. Compared to control, ERGs from experimental groups showed varying amplitudes at 1000mcd.s/m².

Conclusions: Our novel TAS model characterized the SANS pathogenesis. This model can be utilized for future preclinical studies and a unique tool to test new therapeutics that can target SANS pathogenesis in astronauts.

CONTROL ID: 3534381

SUBMITTER (NAME ONLY): Nicholas Hazen

TITLE: Regional Mechanical Deformation of Human Corneal Stroma during Intraocular Pressure Elevation

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Hazen, K. Clayson, S. Kwok, J. Liu, Department of Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|N. Hazen, K. Clayson, Biophysics Interdisciplinary Group, The Ohio State University, Columbus, Ohio, UNITED STATES|X. Pan, Department of Biomedical Informatics, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Liu, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify and analyze regional variations of mechanical strains within the corneal stroma in human donor globes during intraocular pressure (IOP) elevation using high-frequency ultrasound speckle tracking.

Methods: Ten globes from 9 human donors were obtained (age: 41-76 years old, 5 male and 4 female). Treatment with poloxamer 188 (3.5-4.25%) was used to return corneas to their physiological hydration as described previously (Clayson et al, EER, 2019). The globes were inflated from 5 to 30 mmHg in intervals of 0.5 mmHg. At each IOP level, an ultrasound scan was acquired using a 50 MHz probe (MS700, FujiFilm VisualSonics) from the central 9.73 mm of the cornea along the nasal-temporal meridian. Tissue displacements were calculated using ultrasound speckle tracking and strains were calculated using least squares estimation (Tang and Liu, JBME, 2012). The corneal stroma was divided into two regions, central and paracentral as shown in Fig 1a. The deformation of these two regions was compared using paired t-tests.

Results: Strains measured at 30 mmHg were recorded for all 10 globes. Tangential strain in the corneal stroma was significantly larger in the paracentral ($1.8 \pm 1.5\%$) than the central ($0.40 \pm 1.1\%$) zone ($p = 0.0022$, Fig 1b, Fig 2a). Radial strain was not significantly different between these two zones ($-2.1 \pm 1.9\%$ vs $-1.9 \pm 1.0\%$, $p = 0.73$, Fig 1c, Fig 2b). Shear strain magnitude was also not significantly different between zones ($2.7 \pm 1.2\%$ vs $3.1 \pm 2.2\%$, $p = 0.49$, Fig 1d, Fig 2c).

Conclusions: High-frequency ultrasound elastography enabled quantification of the different types of deformation through corneal stroma, showing tangential stretch, radial compression, and shear during IOP elevation. The central cornea was subject to lower tangential stretch but similar radial compression and shear as compared to the paracentral cornea. The finding of lower tangential strain in the central cornea was consistent with previous reports of corneal surface deformation using optical methods.

CONTROL ID: 3534390

SUBMITTER (NAME ONLY): Alejandro Juarez

TITLE: Cell-free liquid hydrogel sealant/filler restores long term corneal integrity and shape after perforating and non-perforating trauma in feline eyes

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate long term in vivo functionality of corneas regenerated using a cell-free, liquid hydrogel sealant/filler (LiQD Cornea; McTiernan et al., Sci. Adv. 2020) following deep corneal ablation with or without perforation in the feline model.

Methods: Two healthy cats underwent 3 and 1,5 mm diameter x stepwise 250/450 μ m deep surgical corneal ablation with and without needle perforation of the wound bed. The filler, made of 10% (w/w) CLP-PEG mixed with 1% fibrinogen and crosslinked with 2% (w/w) DMTMM, was applied to the wound bed that had been pre-coated with thrombin (250 U/ml). In situ gelation occurred within 5 min and a temporary tarsorrhaphy was performed. Examinations were performed weekly for 1 month and then monthly for 12 months. In vivo Outcome parameters included: slit-lamp assessment, Scheimpflug tomography, optical coherence tomography (OCT), confocal microscopy (CM), and endothelial cell morphometry, and ex vivo: transmission electron microscopy (TEM) and immunohistochemistry, including study of extracellular vesicles and exosomes.

Results: A smooth epithelial layer re-grew over the filled defects. The gelled filler remained stably integrated through the entire 12 months, without swelling, neovascularization, inflammation, infection, or rejection. Slit lamp, OCT (Fig.1), and CM showed progressive replacement of the filler by a more reflective tissue smoothly filling the wound bed, while keratocytes and nerves began to be seen, suggesting remodeling of the gel. The mild haze, maximum at 2-3 months, seen at the wound interface and within the remodeling tissue, disappeared with time. Host stroma and endothelium remained normal at all times. Tomography confirmed restoration of smooth and normal corneal surface curvature (Fig.2).

Conclusions: Biointegration of this hydrogel filler allowed stable restoration of normal corneal shape and transparency in the feline model, with less inflammation and no neovascularization compared to previous reports in the minipig and rabbit models. It offers a promising alternative to cyanoacrylate glue and corneal transplantation for ulcerated and traumatized corneas in human patients.

CONTROL ID: 3534392

SUBMITTER (NAME ONLY): Zachary Harbin

TITLE: Comparison of Pterygium Recurrence Rates between Attending and Resident Surgeons

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Harbin, S. Seale, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|J. Thompson, Louisiana State University Health Sciences Center, New Orleans, Louisiana, UNITED STATES|A. Kheirkhah, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|L. Deschner, Pediatrics, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|H. Das, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recurrence is a major complication of pterygium surgery. There is limited data on how much the surgeon's experience contributes to recurrence rates, specifically as it pertains to trainee ophthalmology residents. We performed a retrospective, cohort study to compare recurrence rates after pterygium surgery performed by attending physicians and trainee residents in our institution.

Methods: We analyzed data of pterygium surgeries performed by trainee residents and attending physicians in an academic institution in South Texas in the years 2008-2019. All residents' surgeries were performed under direct supervision of an attending physician. Only primary pterygium cases with a minimum postoperative follow-up of six months were included. Patients' demographics, primary surgeon, use of conjunctival autograft (CAU) or amniotic membrane graft (AMG), recurrence of pterygium, follow-up length, and complications were recorded.

Results: This study included 240 eyes of 229 patients with a mean age of 55.6 ± 12.3 years (range, 28-91 years). Of these eyes, 100 surgeries were performed by attending physicians (including 87 with CAU and 13 with AMG) and 140 surgeries by trainee residents (including 119 with CAU and 21 with AMG). There were no significant differences between the attending and resident groups regarding age, sex, and surgical technique (CAU versus AMG). Patients were followed for an average of 19.8 ± 15.2 months. No statistically significant differences were found between attending physicians and residents when comparing the rate of pterygium recurrence for either CAU (6.8% vs 10.0%, respectively, $p=0.42$) or AMG (69.2% vs 47.6%, respectively, $p=0.22$). Moreover, there were no significant differences in other postoperative complications between the groups.

Conclusions: Our results suggest that pterygium recurrence rates are similar between attending physicians and supervised trainee residents. Thus, acceptable outcomes can be expected when pterygium surgery is performed by a supervised ophthalmology resident.

CONTROL ID: 3534405

SUBMITTER (NAME ONLY): Sze Wan Shan

TITLE: The Role of Thrombospondin-1 in Rho-kinase Inhibitor Mediated Changes in Outflow Facility

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rho-kinase (ROCK) inhibitors is a novel class of anti-glaucoma agents, which act by increasing the aqueous humor outflow through conventional trabecular meshwork (TM) pathway. The downstream signaling consequences of ROCK inhibition in the TM are not fully understood. In this study, we evaluated the role of thrombospondin-1 (TSP-1) in triggering ROCK inhibitor-mediated increase in outflow facility.

Methods: Primary cultures of human TM (hTM) cells were used. Cell migration assay was conducted with or without Y39983 (1 μ M, a selective ROCK inhibitor), LSKL (a TSP-1 antagonist), and TSP-1 siRNA knockdown. Differential protein expression was quantified by LC-MS/MS using SWATHMS technologies. Expression of TSP-1 protein and mRNA was confirmed by Western blot analysis and qPCR, respectively. Conventional outflow facility was measured in ex vivo mouse eyes.

Results: Proteomic analyses identified 20 proteins whose expression were significantly altered after hTM cells were treated with Y39983 for 2 days. Of these, thrombospondin-1 (TSP-1) was downregulated 5-fold following Y39983 treatment. In addition, Y39983 elicited a dose-dependent inhibition of hTM cell migration. Similarly, LSKL and TSP-1 siRNA knockdown significantly reduced TSP-1 gene expression (~50% reduction and ~80% reduction, respectively) and hTM cell migration, respectively. In the presence of Y39983, no further inhibition of cell migration was observed after LSKL treatment and TSP-1 gene silencing. Likewise, LSKL increased the outflow facility in mouse eyes by 74%, similar to that of Y39983 (increase by 82%). There were no additive effects with simultaneous treatment with LSKL and Y39983.

Conclusions: Y39983 down-regulated the TSP-1 expression in hTM and silencing TSP-1 gene expression improved the outflow facility. Since there was no additive effect with combined treatment of Y39983 and TSP-1 blockade, the results suggests that TSP-1 is a downstream effector of ROCK inhibition that regulates outflow facility.

CONTROL ID: 3534412

SUBMITTER (NAME ONLY): Zhe SUN

TITLE: Low frequency ultrasound-mediated transcorneal delivery of riboflavin for corneal collagen crosslinking in treating keratoconus

SESSION TITLE: Keratoconus and Corneal Biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. SUN, M. Aresdhayana, Z. LU, J. Chung, L. Lau, Y. Chau, Department of Chemical and Biological Engineering, The Hong Kong University of Science and Technology, Kowloon, HONG KONG|

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ABSTRACT BODY:

Purpose: To investigate the feasibility of using low-frequency US to break through the epithelial barrier for the delivery of riboflavin to corneal stroma. To determine the effect of US-mediated delivery of riboflavin in ultraviolet A collagen crosslinking (UVA-CXL) on the biomechanical property of ex-vivo porcine cornea.

Methods: Riboflavin solution (0.5%) was applied to the fresh porcine corneal surface for 30 min as shown in Fig 1. In US-treated group (n=10), fresh porcine eyes with intact epithelium were treated with low-frequency US continuously. Temperature increase was maintained to be less than 1°C. In Epi-on control group (n=10), no US was applied while epithelium remains intact. In the Epi-off control group (n=10), epithelium was removed to mimic the conventional practice for corneal riboflavin delivery. Fluorophotometer(OcuMetrics) was used to quantify the amount of stromal riboflavin by the detection of fluorescence intensity. Half of each group received UVA irradiation (365nm, 3mW/cm², 30min) for CXL. Young's modulus of the corneal strip was measured by rheometer (TA, G2) to determine the change in corneal stiffness post CXL.

Results: The fluorescence intensity in the cornea of US-treated group was at least two orders of magnitude higher than Epi-on group. Fig.2A and 2B indicate that the amount of riboflavin transported to the cornea by US treatment is similar to that attained by scarping off the corneal epithelium in Epi-off group. The values of Young's modulus of US-treated and Epi-off samples were increased by UVA-CXL by 1.40 and 1.44 fold, respectively, which was in contrast to the negligible difference observed in the Epi-on samples (Fig.2C).

Conclusions: Low frequency US enhanced the absorption of riboflavin in corneal stroma via transcorneal route in the absence of thermal effect. US-mediated delivery of riboflavin to the cornea is sufficient to enable effective CXL by UVA for increasing the stiffness of porcine cornea. The study supports that low-frequency US may provide a less invasive alternative to modulate transcorneal barrier for delivering riboflavin into corneal stroma, potentially benefiting the treatment of keratoconus.

CONTROL ID: 3534417

SUBMITTER (NAME ONLY): Stewart Lake

TITLE: Merging retinal optical coherence tomography images in three dimensions

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Lake, K. Williams, College of Medicine and Public Health, Flinders University, Adelaide, South Australia, AUSTRALIA|S.R. Lake, M. Bottema, K. Reynolds, College of Science and Engineering, Flinders University, Adelaide, South Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) provides high resolution cross-sectional two dimensional retinal images, with the ability to reconstruct local retinal shape from these sections in three dimensions. OCT is capable of sampling a limited area of retina in a single image. Wider field images have become available with developing technologies including swept source (SS) OCT, as well as through the merging in series of individual B scans in two dimensions. Merging SS OCT images in three dimensions (3D) has not previously been reported. Here, overlapping SS OCT cubes were reconstructed in 3D and merged via two different methods to explore the utility and limitations of composite images for retinal shape analysis.

Methods: From three eyes of three human participants, overlapping pairs of 9 x 9 mm SS OCT cubes were taken. Twenty five B scans were sampled from each cube, and used to reconstruct local retinal shape within the area covered by the scanning laser ophthalmoscope (SLO). For each eye, three pairs of corresponding points were identified in the SLO images from each cube. The reconstructed 3D images were merged via two different methods, using a rigid transformation to preserve shape features:

[1] sequential rotations using the axis-angle method

[2] via calculation of, then rotation with a quaternion.

Results: Composite images from one eye are shown in Figure 1. The two methods produced similar images, with no overall difference in alignment (mean (standard deviation) axial difference within en face overlapping area was 30.8 (23) pixels (quaternion rotation) versus 30.9 (23) pixels (axis angle rotation), where 1536 pixels = 3 mm, two sample t-test, $p < 0.005$).

Conclusions: Merged OCT images provided a good qualitative description of wide field retinal shape in three dimensions. Each rotation induced small errors, although the single rotation quaternion method performed no better than the sequential rotation required for the axis angle method. Although the magnitude of induced error was low with both rotation methods, care should be taken in performing quantitative analyses of composite images.

CONTROL ID: 3534438

SUBMITTER (NAME ONLY): Susana del Olmo Aguado

TITLE: Plasma rich in growth factors protects retina against blue light in an in vivo model.

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To study the effect of plasma rich in growth factors (PRGF) under blue light conditions in an in vivo model of retinal degeneration after a medium-long term light exposure.

Methods: Male Wistar rats were exposed to dark/blue light conditions for 30 days. At day 7, right eyes were injected with saline and left eyes with PRGF. Electroretinography (ERG) and intraocular pressure (IoP) measurements were performed before and after the experiment. After sacrifice, retinal samples were collected. Haematoxylin-eosin staining was performed to analyse the structure of retinal sections. Immunofluorescence for Brain-specific homeobox/POU domain protein 3A (Brn3a), Choline acetyltransferase (ChAT), Rhodopsin, Heme oxygenase-1 (HO-1) and Glial fibrillary acidic protein (GFAP) was performed to study the retinal conditions.

Results: The results obtained by ERG showed that blue light reduced the retinal functionality. The use of PRGF at day 7 decreased the harmful effect of blue light after 30 days of light exposure. IoP measurements did not show significant differences among treatments. The immunohistological analysis performed showed that blue light changed the retinal structure and markers expression, which was counteracted by the treatment with PRGF.

Conclusions: Blue light causes retinal degeneration. PRGF blunted the injury, restoring the functionality of these cells and maintaining the tissue integrity.

CONTROL ID: 3534445

SUBMITTER (NAME ONLY): Noushin Zibandeh

TITLE: The Regulatory Effect of IFN- γ or IL-17A Primed Limbal Mesenchymal Stem Cells on Lymphocytes Immune Response

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Zibandeh, E. Kusan, A. Sahin, Research Center for Translational Medicine, Koc Universitesi, Istanbul, Istanbul, TURKEY|A. Sahin, Ophthalmology, Koc Universitesi, Istanbul, Istanbul, TURKEY|

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ABSTRACT BODY:

Purpose: The cornea is a transparent, avascular tissue that covers the front portion of the eye. In pathologic and highly inflammatory conditions, the entire ocular surface is at risk for persistent scarring and visual loss. Despite all the treatment strategies, no effective solution has been found for patients with severe corneal injuries. Mesenchymal stem cells (MSCs) are of particular interest for the treatment of immune-related diseases owing to their immunosuppressive properties. Priming with proinflammatory cytokines improve the immunosuppressive function of MSCs. The purpose of our study is to identify the immunosuppressive effect of interferon (IFN)- γ and Interleukin (IL)17A primed Limbal-MSCs (LMSCs) on lymphocyte response.

Methods: LMSCs were isolated from cadaveric corneoscleral rims and cultured in DMEM with penicillin-streptomycin and fetal bovine serum. LMSCs were characterized and differentiated in passage 3. The lymphocytes were isolated from peripheral venous blood of healthy controls (n=10). LMSCs were stimulated with IFN- γ or IL-17A for 48 hours. At the end of this period, peripheral blood mononuclear cells of healthy individuals were isolated and cultured with or without stimulated LMSCs for 72 hours. The cultures were stimulated with anti-CD3 and anti-CD28 antibodies. After 72 hours, lymphocytes were collected and analyzed for proliferation assay, cell viability assay with AnnexinV/PI, Fas, FasL and CD4⁺CD25⁺FoxP3⁺T regulatory cell ratio via flow cytometry.

Results: Our results demonstrated that IFN- γ or IL-17A stimulated LMSCs suppressed the proliferation of T lymphocytes compared to unstimulated LMSCs cultures and it was statistically significant (P<0.05, P<0.05, respectively). IFN- γ stimulated LMSCs suppressed the Annexin V and Fas expression compared to unstimulated LMSCs cultures (P<0.05) but IL-17A stimulated LMSCs did not reduce the AnnexinV and Fas expression significantly compared to unstimulated LMSCs cultures (P>0.05). IFN- γ stimulated LMSCs increased T regulatory cell frequency compared to unstimulated LMSCs cultures (P<0.05).

Conclusions: Our data showed that stimulated LMSCs especially IFN- γ decreased lymphocyte proliferation and apoptosis while increased the T regulatory cell ratio. We believe that LMSCs could potentially be a source for future treatment strategies of inflammatory conditions particularly corneal disease.

CONTROL ID: 3534457

SUBMITTER (NAME ONLY): Gabriella Acosta

TITLE: High throughput screening of a small molecule chemical library reveals novel therapeutic potential drugs in treatment of diabetic retinopathy

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Acosta, Ophthalmology, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|A. Das, Ophthalmology, New Mexico VA Health Care System, Albuquerque, New Mexico, UNITED STATES|F. Monickaraj, A. Das, Ophthalmology, University of New Mexico Hospital, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alteration of the blood-retinal barrier is the hallmark of diabetic retinopathy that results in damage to cell junctional proteins ultimately leading to vision loss. Current anti-VEGF treatments are effective only in 33-45% patients with diabetic macular edema (DME). To overcome challenges associated with existing therapies, we used a previously approved, small molecule drug library to check the efficacy on the functionally promising candidate molecules.

Methods: We used the Prestwick chemical library (PCL) consisting of off-patent compounds approved by FDA with diverse chemical and pharmacological characters, and well characterized bioavailability and safety information in humans. We performed a high throughput screening (HTS) assay platform to check the in vitro monolayer permeability in human retinal endothelial cells (HRECs) with the electrical cell substrate impedance sensing (ECIS) system. HRECs (approx. 8000 cells/well) were plated into fibronectin-coated 96-well plates and grown for 16 hours until maximum resistance was attained (1200 V). Human recombinant VEGF (50 ng/ml) was added to the wells along with each of 250 drug library compounds (10 uM). Changes in trans-endothelial electrical resistance were monitored for 24 hours. We used a cutoff range of > 75% viability using MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay with concentration of 10 uM. Resistance values were normalized to the identical starting resistance value at time 0 and presented as normalized resistance versus time.

Results: Several compounds showed toxicity and were eliminated from the trial. The ECIS assay identified 5 drugs that decreased in vitro permeability in VEGF treated HRECs. Five drugs, namely rufinamide, etofenamate, mexenone, melengestrol acetate, and sulfaquinoxaline sodium salt showed significantly increased resistance after the addition of VEGF compared to controls without drugs, while other drugs resulted in no change to mild change in resistance.

Conclusions: In this study we have identified several drugs that can decrease in vitro permeability in human retinal endothelial cells. The identified chemical probes can be directly used for anti-diabetic retinopathy drug development or serve to discover novel disease targets for future drug discovery.

CONTROL ID: 3534461

SUBMITTER (NAME ONLY): Or Shmueli

TITLE: cRORA progression and its baseline predicting factors

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Shmueli, J. Levy, Ophthalmology, Hadassah Medical Center Department of Ophthalmology, Jerusalem, Jerusalem, ISRAEL | R. Yehuda, A. Szeskin, L. Joskowicz, School of Computer Science and Engineering, Hebrew University of Jerusalem Faculty of Science, Jerusalem, ISRAEL |

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ABSTRACT BODY:

Purpose: To quantitatively evaluate progression rate and the baseline predictors of progression of complete retinal pigment epithelium and outer retinal atrophy (cRORA) in cases of dry age-related macular degeneration (AMD).

Methods: Two ophthalmologists retrospectively annotated cRORA. Two-thirds of the scans were annotated by one grader and validated by a second-grader. A third of the scans were independently annotated by both graders. Primary outcomes: 1) cRORA area progression (mm^2/year); 2) cRORA square root area progression (mm/year); and 3) radial progression towards the fovea (mm/year).

The effects of the different baseline predictors on the primary outcomes were analyzed, including 1) the total area; 2) area at a diameter of 1 mm around the center; 3) focality; 4) circularity; 5) total lesion perimeter; 6) minimal feret (Feret_{\min}); 7) maximal Feret (Feret_{\max}); 8) minimal distance from the center at baseline; 9) sex; 10) age; 11) hypertension and 12) lens status.

Results: cRORA was annotated on a dataset of 37 baseline and follow up pairs of OCT scans 16 patients with dry AMD. Inter-grader variability was tested on 1989 standalone OCT B-scans and resulted in a DICE coefficient of 0.75 ± 0.16 .

Mean area progression was $1.34 \pm 0.80 \text{ mm}^2/\text{year}$ ($p < 0.0001$). Mean square root area progression was $0.32 \pm 0.18 \text{ mm}/\text{year}$ ($p < 0.0001$). Mean radial progression towards the fovea was $0.06 \pm 0.12 \text{ mm}/\text{year}$.

A multiple linear regression model (adjusted $r^2 = 0.665$) showed baseline focality (estimated $\beta = 0.101$; $p = 0.0008$) and baseline circularity (estimated $\beta = -1.789$; $p = 0.0076$) were significant factors associated with cRORA area progression. The lesions' baseline minimal distance from the center correlated with radial growth rate towards the center on univariate linear regression analysis ($p < 0.0001$; $r = 0.686$).

Conclusions: This study quantitatively measured cRORA area progression rate in dry AMD patients, as compared to traditional fundus autofluorescence measurements. cRORA area progression varied with respect to baseline focality and circularity indices. Radial progression correlated with the lesion's baseline minimal distance from the center. These results may be used in the research of treatments for retinal atrophy secondary to dry AMD.

CONTROL ID: 3534465

SUBMITTER (NAME ONLY): Divya Rao Parthasarathy

TITLE: Development and performance of a novel 'offline' deep learning (DL)-based glaucoma screening tool integrated on a portable smartphone-based fundus camera

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Rao Parthasarathy, Remidio Innovative Solutions Pvt Ltd, Bangalore, Karnataka, INDIA|C. Hsu, F.M. Savoy, Medios Technologies, Remidio Innovative Solutions Pvt Ltd, SINGAPORE|M. Eldeeb, Department of Ophthalmology, University of Toronto, Toronto, Ontario, CANADA|D. Jinapriya, Department of Ophthalmology, Queen's University, Kingston, Ontario, CANADA|S. Shroff, S. S, Z. Pradhan, Narayana Nethralaya, Bangalore, Karnataka, INDIA|S. Deshmukh, Thorat Eye Hospital, Akola, Maharashtra, INDIA|

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ABSTRACT BODY:

Purpose: There exists no ideal screening tool for glaucoma. We developed and assessed the performance of a novel automated screening tool using DL on monoscopic fundus images. It is deployed on-the-edge on a portable smartphone-based fundus camera, and assesses presence of referable glaucoma.

Methods: We trained a binary classifier for referable glaucoma (glaucoma suspect and likely glaucoma) using DL with a diverse dataset of 5716 images from Asian and Caucasian populations. This included 58% images of referable glaucoma. Five glaucoma specialists were involved in grading. The ground truth came from both the images themselves as well as from a comprehensive glaucoma evaluation. The resulting algorithm was validated on two datasets. Validation set A comprised of 626 images (63% referable glaucoma) captured on the target device on Asian eyes. The reference standard was optic disc assessment on these images. An independent Test set B comprised of 389 images (62% referable glaucoma) captured on Caucasian eyes. The reference standard was the diagnosis of glaucoma made following a complete glaucoma evaluation. The ground truth for both datasets was the interpretation made by glaucoma specialists. The activation maps generated by the algorithm highlight the regions of the input images which contributed most to the automated diagnosis.

Results: The DL algorithm had a sensitivity of 97% (CI 96%-99%), a specificity of 92% (CI 88%-95%) and an AUC of 0.97 in detecting referable glaucoma on validation set A. Sensitivity in detecting likely glaucoma was 0.97. On test set B, the sensitivity for detecting referable glaucoma was 96% (CI 93%-98%) the specificity was 82% (CI 76%-88%) and the AUC 0.93. Sensitivity in detecting likely glaucoma was 0.98. Activation maps showed that the AI relied on key glaucoma features like vertical cup-to-disc ratio, neuroretinal rim abnormalities, disc hemorrhages and retinal nerve fibre layer (RNFL) defects to make a diagnosis.

Conclusions: The DL algorithm based on monoscopic fundus images deployed 'offline' on a portable fundus camera has high sensitivity and specificity in screening for referable glaucoma. Further work includes validation in prospective clinical trials.

CONTROL ID: 3534466

SUBMITTER (NAME ONLY): Mengxi Shen

TITLE: Swept Source OCT Angiographic Characteristics of Treatment-Naïve Nonexudative Macular Neovascularization in AMD Prior to Exudation

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shen, J. Yang, W.J. Feuer, X. Jiang, Y. shi, G. Gregori, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|Q. Zhang, H. Zhou, Z. Chu, X. Zhou, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|L. De Sisternes, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if there are any characteristic changes in treatment-naïve nonexudative macular neovascularization (MNV) in age-related macular degeneration (AMD) when imaged using swept source optical coherence tomography angiography (SS-OCTA) that may be predictive of near-term exudation.

Methods: AMD patients with treatment-naïve, nonexudative MNV were identified and underwent SS-OCTA imaging (PLEX® Elite 9000; Carl Zeiss Meditec, Inc, Dublin, CA) using 6X6mm and 12X12mm scans by the same technician at all visits. The patients were divided into two groups based on whether the nonexudative MNV developed exudation. If the nonexudative MNV developed exudation, then the last two visits before the visit when exudation was documented were selected for analysis. If the MNV did not develop exudation, then the two consecutive visits 6 months before their last follow-up visits were used for analysis to be sure no near-term exudation developed. MNV area, choriocapillaris (CC) flow deficits (FDs), MNV vessel area density (VAD), MNV vessel skeleton density (VSD), retinal pigment epithelial detachment (PED) volume, mean choroidal thickness (MCT), and choroid vascularity index (CVI) measurements were measured at the two visits prior to exudation. The en face area measurements of the MNV were obtained by using a previously described validated automated algorithm that detected angiographic flow within the outer retina to CC slab.

Results: Twenty-one eyes with nonexudative MNV were identified and followed. Twelve eyes did not develop exudation, while nine eyes developed exudation. There were no significant differences between the two groups in the MNV area, the percentages of surrounding CC FDs, or the rate of change in any of the measurements (all P values ≥ 0.052). The eyes that did develop exudation had smaller MNV-VAD ($P=0.002$), MNV-VSD ($P=0.005$), and MNV-PED volume ($P=0.04$) measurements at the visit prior to exudation. The CT and CVI measurements over the final two visits were not significantly different between the two groups (all P values >0.19).

Conclusions: The onset of exudation was associated with lesions with less vascularity and smaller PED volume measurements, but measurements of MNV area, CC FDs, CT, and CVI or the change in any measurements did not show statistically significant differences between the two groups over the final two visits.

CONTROL ID: 3534469

SUBMITTER (NAME ONLY): Swarup Swaminathan

TITLE: Rapid initial OCT RNFL thinning is predictive of large visual field loss during extended follow-up in glaucoma

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.S. Swaminathan, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|S.S. Swaminathan, A.A. Jammal, S. Berchuck, F.A. Medeiros, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the relationship between the rate of retinal nerve fiber layer (RNFL) loss during initial follow-up and the magnitude of associated visual field loss during an extended follow-up period.

Methods: This was a retrospective cohort study. A total of 1,150 eyes of 839 glaucoma patients extracted from the Duke Glaucoma Registry. Rates of RNFL loss were obtained from global RNFL thickness values of the first 5 optical coherence tomography (OCT) scans. Rates of visual field loss were assessed using standard automated perimetry mean deviation (SAP MD) during the entire follow-up period. Joint longitudinal mixed effects models were used to estimate rates of change. Eyes were categorized as fast, moderate or slow progressors based on rates of RNFL loss, with cutoffs of $\leq -2\mu\text{m}/\text{y}$, -2 to $-1\mu\text{m}/\text{y}$ and $\geq -1\mu\text{m}/\text{y}$, respectively. Univariable and multivariable regressions were completed to identify significant predictors of SAP MD loss.

Results: The rate of RNFL change was $-0.76 \pm 0.85\mu\text{m}/\text{y}$ during initial follow-up, which occurred over 3.7 ± 1.5 years. 765 (66%) eyes were slow, 328 (29%) moderate, and 57 (5%) fast progressors, with corresponding rates of SAP MD loss of $-0.16 \pm 0.35\text{dB}/\text{y}$, $-0.32 \pm 0.43\text{dB}/\text{y}$, and $-0.71 \pm 0.65\text{dB}/\text{y}$ over the extended follow-up period of 6.1 ± 1.9 years ($P < 0.001$). Age, OCT progressor group, and baseline SAP MD were all significantly associated with the rate of SAP MD loss ($P < 0.001$).

Conclusions: Rapid RNFL thinning during an initial follow-up period was predictive of concurrent and subsequent rates of visual field decline over an extended period. Patients with fast OCT thinning may be at high risk for developing functional disability.

CONTROL ID: 3534470

SUBMITTER (NAME ONLY): Shaikha Al Jneibi

TITLE: Outcomes of Intracorneal Ring Segments for Keratoconus at a Tertiary Care Center in the United Arab Emirates

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Al Jneibi, P. Agarwal, Cleveland Clinic Abu Dhabi, Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|R.R. Sayegh, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|R.R. Sayegh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the visual, refractive and keratometric changes after INTACS implantation for keratoconus.

Methods: Retrospective chart review of records between March 2016 and September 2019 at the Cleveland Clinic Abu Dhabi. All INTACS SK rings were inserted using a femtosecond laser according to the manufacturer's recommendations. Visual, refractive and keratometric changes, along with surgical complications, were analyzed.

Results: Sixty seven eyes of 67 keratoconus patients aged 18 to 47 (average 29) years were included. Thirty-eight were male and 38 had their right eyes operated on. Seventeen had prior collagen cross-linking and 2 had previous PRK. The mean follow-up duration was 7.5 months. Statistically significant improvement was noted in uncorrected visual acuity (preop LogMAR 1.00 to postop 0.55), best-corrected acuity (0.30 to 0.20), spherical equivalent (8.29D to 5.43D), sphere (-6.59D to -3.94D), and cylinder (3.52D to 3.16D). On keratometry, SimK improved from 49.08D to 46.58D ($p<0.001$) and Kmax from 55.19D to 52.30D ($p,0.001$), however corneal astigmatism improved from 4.15D to 3.85D which was not significant ($p=0.27$). No complications were noted.

Conclusions: INTACS implantation resulted in significant improvement in visual, refractive, and keratometric outcomes in our patients.

CONTROL ID: 3534481

SUBMITTER (NAME ONLY): Yannis Paulus

TITLE: Retinal Hypoxia Evaluation Using Organic Room-Temperature Phosphorescent Nanoparticles

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.M. Paulus, V. Nguyen, Y. Li, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|Y. Zeng, J. Kim, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yannis Paulus: Commercial Relationship(s);University of Michigan:Code P (Patent) | Yingying Zeng: Commercial Relationship(s);University of Michigan:Code P (Patent) | Van Phuc Nguyen: Commercial Relationship(s);University of Michigan:Code P (Patent) | Yanxiu Li: Commercial Relationship: Code N (No Commercial Relationship) | Jinsang Kim: Commercial Relationship(s);University of Michigan:Code P (Patent)

ABSTRACT BODY:

Purpose: Ischemia-induced hypoxia is a common complication associated with numerous diseases including retinal vein occlusions. No effective solution exists to evaluate extravascular tissue oxygen tension. This report demonstrates a novel lipid-polymer hybrid organic room-temperature phosphorescence (RTP) nanoparticle (NP) platform that optically detects tissue hypoxia in real-time with high signal-to-noise ratio.

Methods: A lipid-polymer hybrid, core-shell RTP NP was fabricated with Br6A metal-free organic phosphor embedded within the polymer matrix core coated with an amphiphilic lipid shell. Poly(4-bromostyrene) (PS4Br) was chosen as the host polymer for intravitreal injection (Br6A-LPS4Br) and polystyrene-b-poly(4-vinylpyridine) (PS4VP) for intravenous injection. This was injected into 11 rabbits with a Rose Bengal dye-enhanced thrombosis retinal vein occlusion model, laser photocoagulation, or controls and evaluated with multimodal imaging post NP administration via intravenous and intravitreal administration.

Results: The fabricated RTP NPs exhibit bright RTP and high sensitivity toward oxygen quenching with desirable colloidal and optical stability. The RTP NPs were tested as a hypoxia imaging probe in vivo using rabbit RVO and photocoagulation models via intravitreal and intravenous injection respectively. The RTP NP signal is exclusively generated where tissue hypoxia is present with a signal-to-noise ratio of 12.5. Longitudinal phosphorescence imaging in Rose-Bengal RVO and control rabbits demonstrated significant phosphorescent signal peaking at 2h post-intravitreal injection of NP that persisted for at least 7 days (Figure). No ocular or systemic complications are observed with either administration route.

Conclusions: This organic RTP NPs allows for biocompatible, non-destructive, sensitive detection of tissue hypoxia longitudinally and has potential to evaluate hypoxia-driven retinal vascular diseases.

CONTROL ID: 3534491

SUBMITTER (NAME ONLY): Gulfidan Bitirgen

TITLE: Structural alterations of macular inner retinal layers in patients with Fabry disease

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Bitirgen, Department of Ophthalmology, Necmettin Erbakan Universitesi Meram Tip Fakultesi, Konya, TURKEY|K. Turkmen, Department of Internal Medicine/Nephrology, Necmettin Erbakan Universitesi Meram Tip Fakultesi, Konya, TURKEY|

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ABSTRACT BODY:

Purpose: Fabry disease (FD) is a rare X-linked lysosomal storage disorder characterized by the accumulation of globotriaosylceramide in various tissues, leading to renal, vascular, and neurological complications. Although structural changes in central and peripheral nervous system have been previously reported in FD, little is known on the alterations of retinal layers. This study aims to evaluate macular inner retinal layer changes in patients with FD using spectral domain optical coherence tomography (SD-OCT).

Methods: Twelve consecutive patients with FD and 12 age- and sex-matched healthy control participants were included in this cross-sectional study. The Mainz Severity Score Index (MSSI) was used to measure the severity of FD. All participants underwent SD-OCT (Heidelberg, Germany) imaging, and retinal layer segmentation was performed automatically. Total macular volume (TMV) and central macular thickness (CMT) were recorded, and the average thicknesses of nerve fiber layer (NFL), ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL) and total inner retinal layers (IRL) were measured at the central fovea (1 mm) and four quadrants (superior, inferior, nasal, temporal) of the parafoveal region (1-3 mm).

Results: Intraretinal hyperreflective dots and increased retinal vessel tortuosity were observed in the OCT images of patients with FD (Figure 1). Compared to healthy control subjects, patients with FD had significantly reduced total IRL thickness at superior ($P=0.005$), inferior ($P=0.016$), temporal ($P=0.005$), and nasal ($P=0.011$) quadrants. Additionally, INL thickness was reduced at superior ($P=0.038$), temporal ($P=0.006$), and nasal ($P=0.022$) parafoveal regions. No significant differences were observed in TMV, CMT, NFL, GCL, and IPL thickness between patient and control groups. The MSSI inversely correlated with the thickness of INL at central ($\rho=-0.666$; $P=0.018$) and inferior ($r=-0.627$; $P=0.029$) regions.

Conclusions: This study demonstrates significant structural alterations in the macular inner retinal layers in patients with FD. Further studies are required to identify potential pathophysiological mechanisms of inner retinal changes in FD.

CONTROL ID: 3534496

SUBMITTER (NAME ONLY): Victor Sendra

TITLE: Distinct Plasmacytoid Dendritic Cell-T Cell Contacts in Draining Lymph Nodes Define T Cell Responses during Acute Herpes Simplex Virus Keratitis

SESSION TITLE: Corneal immunology and neovascularization I

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.G. Sendra, A. Jamali, B. Kenyon, D.L. Harris, P. Hamrah, ophthalmology, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|P. Hamrah, Ophthalmology, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Plasmacytoid dendritic cells (pDCs), are specialized immune cells residing in the cornea and play a key role in linking innate and adaptive immunity. In this study, we investigated the dynamic changes of pDCs-T cell interactions in draining lymph nodes (dLNs) that define the T responses in acute herpes simplex virus (HSV)-1 keratitis

Methods: Intravital multiphoton microscopy (IV-MPM) was performed in living mice to image dLNs in bone marrow chimera mice from Tred (T cells are red) x pDC-GFP (pDCs are green) mice during steady state and after corneal inoculation with TLR-9 agonist or HSV-1 to study the kinetics of pDC/T cell interactions. Number of contacts (N), short (<5min) and long contact time (>5min or >30min) were analyzed. Local pDCs were depleted by subconjunctival injections of diphtheria toxin or PBS (sham) in BDCA-2-DTR Tg mice. dLN were excised and assessed for T cell phenotype by flow cytometry with CD45 (pan-leukocytes marker), CD3 (T cells), CD8, and CD4, and production of IL-6 and TGF- β 1

Results: IV-MPM imaging in dLNs showed pDC-T cells interactions after corneal inoculation of TLR-9 agonist compared to steady state with a high percentage having long contact time >5min (53.8% vs. 19.2%) and >30min (23.1% vs. 0%)($P<0.01$). Interestingly, we identified dLNs areas with T cell clusters after HSV-1 keratitis, where pDCs interacted with high number of T cells ($N=3.0$) compared to steady state ($N=1.5$, $p<0.01$); and a high percentage having long contact time >5min (50.0%) and >30min (15.4%) compared to areas without T cell clusters (15.4% and 0%, respectively; $P<0.01$) or during steady state (20.0% and 0% respectively; $P<0.01$). dLNs from corneal pDC-depleted mice showed an increased density of CD4 and CD8 T cells (2.1-fold and 2.3-fold) compared to sham group ($P<0.001$), as well as increased IL-6 secreting T cells (3.4-fold) and reduced TGF- β 1 secreting T cells (0.58-fold) during HSV-1 keratitis

Conclusions: Intravital imaging of dLNs demonstrates distinct pDCs-T cell interaction patterns, predominantly in areas with T cell clusters during acute HSV-1 keratitis. Moreover, pDC limit IL-6, but enhance TGF- β expression by T cells in concordance to the increase in Th17 over Tregs response previously observed by our group. Together, our data suggests that pDCs are involved in the T cell fate through direct interaction with T cells in HSV-1 keratitis

CONTROL ID: 3534505

SUBMITTER (NAME ONLY): Omar Singer

TITLE: Pediatric Ocular Injury as a Result of Toy Gun Injury 2010-2019: An Observational Study

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Singer, A. Uppuluri, M.A. Zarbin, N. Bhagat, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to report demographic data and outcomes among pediatric patients with ocular trauma due to toy guns with projectiles. Toy guns with projectiles include toys such as BB guns, airsoft guns, pellet guns, dart guns, etc. There have been studies in the past which have reported demographic data specific to one of these categories of toy guns, this study has been conducted to assess the safety of all projectile toy guns.

Methods: Data were computed from the National Electronic Injury Surveillance System (NEISS), maintained by the Consumer Product Safety Commission (CPSC). Using product code 1399 (toy guns with projectiles) we were able to analyze injury data from 2010-2019 weighted to represent the US population. We restricted our analysis to include children aged 0-20 and analyzed eye injuries specifically. Our analysis included diagnosis of injury, location of injury, race, sex, month, day of the week, as well as disposition. We further subdivided our data by age (0-9 and 10-20) as well as analyzed the data by gender.

Results: There were a total of 6,617 cases included in the NEISS database for ocular trauma between 2010 and 2019. The more common age group was aged 0-9, making up 61.1% of those included in the study. Males were also more commonly injured, making up 79.3% of those in the study. By far the most common diagnosis was ocular contusion (51.5%), other diagnoses included hematomas, laceration, sprain, hemorrhage, conjunctival trauma, and other (encompassing all other diagnoses). The most serious cases resulted in an open globe injury, in 1.5% of all cases, and all were in the 10-20 age subgroup. 92.1% of cases were treated and released within the same visit. Of the remaining 7.9% of patients, 7% were triaged and transferred to another facility. The most common time of the year for ocular injury with toy guns was December, with 18.7% of cases occurring during this month, followed by November with 9.7% of cases. Saturday and Sunday had the highest number of eye injuries to the ED with toy guns, together the weekend accounted for 46.3% of all injuries.

Conclusions: Toy gun injuries were more common among young male patients. Injuries in the last decade were more commonly seen in the month of December and presented to the ED more frequently during the weekend (Saturday and Sunday). Only 1.5% of injuries were severe with OGIs and were seen among older children (10-20).

CONTROL ID: 3534519

SUBMITTER (NAME ONLY): Jordan Miller

TITLE: iLids: Virtual oculoplastics in the COVID-19 pandemic

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Miller, D. Pennipede, Ophthalmology, University of Kansas Medical Center, Kansas City, Kansas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jordan Miller: Commercial Relationship: Code N (No Commercial Relationship) | Dante Pennipede: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: During COVID-19 many adjustments have occurred within medicine. Notably, telehealth has become a ubiquitous tool for providing safe care. Past studies have looked at integration of telehealth into oculoplastics (Elishai, 2020). However, no literature exists regarding the best use of this modality; this study aims to fill that gap.

Methods: 395 men and women, aged 3-95, seen April to September 2020 in the oculoplastic department at KU Eye were included. Via chart review, subjects were categorized based on age, gender, encounter type, appointment format, whether the patient presented for their appointment, and complications experienced. The data were then analyzed using chi-square testing and linear regression models.

Results: Most patients seen were females over 60 years old (Image 1) . The most common encounter types were new patient and follow up (Image 2). There was statistical significance between encounter type and appointment format, with most telehealth visits being post-ops or follow ups ($X^2=22.94$, $df=4$, $p=0.00013$). Expectedly, there was a significant difference in the number of appointment related complications and appointment format ($X^2=60.448$, $df=2$, $p=7.481e-14$). Telehealth visits had a higher association with complications including: delay in appointment time due to connectivity issues, and having to resort to a different appointment format (i.e. rescheduling for a different day in-person, or resorting to phone due to issues with the telehealth interface). There was a positive correlation with age and complications, however this was not found to be significant ($p=0.747$). There was also no significant difference in "no-shows" among telehealth versus in-person visits ($X^2=2.6769$, $df=1$, $p=0.1018$).

Conclusions: Tried during the COVID-19 pandemic at KU Eye, and supported by Elishai et al., telehealth has proven to be a safe and effective way to provide care to patients in an oculoplastic practice. It useful for post-operative visits, pre-operative evaluation, new patient visits, and routine follow up. Patients of various ages can utilize the technology to attend a telehealth visit with minimal complications. To reduce the frequency of these complications, it may be prudent to implement an interactive tutorial for patients prior to their appointment time. Further research investigating outcomes of patients seen via telehealth versus in-person is warranted.

CONTROL ID: 3534521

SUBMITTER (NAME ONLY): Evan Dackowski

TITLE: Glaucoma in Guyanese patients seen in Montefiore ophthalmology clinics in the Bronx, New York

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.K. Dackowski, V. Hawn, J. Moon, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|S. Patel, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|W. Yao, Montefiore Medical Center, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The majority of Guyanese Americans live in the metropolitan New York City area. Prompted by anecdotal evidence of a higher rate of primary open-angle glaucoma (POAG), we set out to determine the risk of POAG and closed-angle glaucoma (CAG) among Guyanese patients compared to other racial and ethnic groups seen at a major hospital system in the Bronx.

Methods: Unique medical record numbers of patients (age ≥ 40) across all comprehensive and subspecialties at the Montefiore ophthalmology department were obtained for patients whose country of origin was Guyana as well as self-identified White, Black, and Hispanic patients from 2018-2020. Glaucoma-related ICD-10 diagnostic codes associated with each unique MRN were fitted to a logistic regression and the odds ratios of POAG and CAG for Guyanese patients, adjusting for age and sex, were calculated.

Results: A total of 409 Guyanese, 2787 White, 13,655 Black, and 13,713 Hispanic patients were included in this study. The mean \pm SD ages for each population were: 64.1 \pm 11.1 years in Guyanese, 67.8 \pm 12.9 years in Whites, 64.4 \pm 12.3 years in Hispanics, and 64.9 \pm 12.2 years in Blacks. For POAG, there were 37 (9.0%) cases in Guyanese patients, 145 (5.2%) cases in Whites, 910 (6.6%) cases in Hispanics, and 1725 (12.6%) cases in Blacks. After adjusting for age and sex, POAG was more common in Guyanese than in Whites (OR=2.38, 95% CI=1.62-3.50, $p<0.01$) and Hispanics (OR=1.39, 95% CI=0.98-1.98, $p=0.07$), but less common than in Blacks (OR=0.67, 95% CI=0.47-0.95, $p=0.02$). For CAG, there were 5 (1.2%) cases in Guyanese patients, 14 (0.5%) cases in Whites, 113 (0.8%) cases in Hispanics, and 116 (0.8%) cases in Blacks. Adjusting for age and sex, CAG was more common in Guyanese patients than in Whites (OR=3.07, 95% CI=0.99-8.12, $p=0.03$), while the odds ratios were not significantly different compared to the Hispanic and Black populations. Although males had significantly higher odds of both POAG and CAG, there was no heterogeneity by sex on the association between race and these glaucoma types.

Conclusions: Patients from Guyana had higher odds of POAG versus the White and Hispanic groups as well as higher odds of developing CAG compared to the White patients in our sample. These results may suggest that Guyanese patients should be referred for full eye exams to screen for glaucoma.

CONTROL ID: 3534522

SUBMITTER (NAME ONLY): Tiffany Chen

TITLE: Resident-performed immediate sequential bilateral cataract surgery during the COVID-19 pandemic

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.A. Chen, S.P. Chen, T. Ahmad, N. Parikh, S. Ramanathan, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|N.D. Pasricha, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Minimizing healthcare-related exposures for patients and providers are paramount during the coronavirus (COVID-19) pandemic. We performed a retrospective cohort study to compare visual outcomes and patient satisfaction in senior resident-performed immediate sequential bilateral cataract surgery (ISBCS) versus delayed sequential bilateral cataract surgery (DSBCS).

Methods: All ISBCS and DSBCS patients who underwent senior resident-performed cataract surgery in the Comprehensive Ophthalmology division of a single academic institution from May to September 2020 were included. Outcome measures were final corrected distance visual acuity (CDVA), final manifest refraction (MRx), incidence of intraoperative and postoperative complications, total number of clinical and surgical visits, and patient satisfaction, assessed postoperatively by telephone questionnaire.

Results: Fourteen (22 eyes) and 28 (56 eyes) patients underwent senior resident-performed ISBCS and DSBCS, respectively. Final CDVA was 20/25 or better in 21 (95%) ISBCS eyes and 51 (91%) DSBCS eyes ($p=0.670$). The deviation of final MRx from target refraction was within 0.50 D in 17 (77%) ISBCS eyes and 47 (84%) DSBCS eyes ($p=0.522$). There was no significant difference in intraoperative ($p=1.000$) or postoperative ($p=1.000$) complications. ISBCS patients averaged 3.5 fewer visits than DSBCS patients (5.9 vs 9.5, $p<0.001$). All ISBCS and 20 DSBCS patients (87%) reported they were overall "very satisfied" or "satisfied" with their experience ($p=0.701$), and there was no significant difference in the overall visual function 7 score, where 0 indicates the worst possible functional impairment and 100 indicates no disability ($p=0.561$). Finally, five of the six senior residents who performed the ISBCS cases included in this study reported that they preferred performing ISBCS over DSBCS.

Conclusions: This early experience demonstrates that senior resident-performed ISBCS is as safe and effective as DSBCS, with the added benefit of averaging fewer in-person visits for patients. Residency programs should consider offering senior resident-performed ISBCS to select patients during the COVID-19 pandemic.

CONTROL ID: 3534538

SUBMITTER (NAME ONLY): Samuel Lee

TITLE: Associations between Niacin Intake and Glaucoma in the National Health and Nutrition Examination Survey

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.Y. Lee, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|V.L. Tseng, F. Yu, J. Caprioli, A.L. Coleman, Ophthalmology, Stein and Doheny Eye Institutes, David Geffen School of Medicine, University of California Los Angeles, California, UNITED STATES|T.J. Avallone, Ophthalmology, Naval Medical Readiness and Training Command San Diego, California, UNITED STATES|F. Yu, Department of Biostatistics, Fielding School of Public Health, University of California Los Angeles, Los Angeles, CA, USA, California, UNITED STATES|A.L. Coleman, Department of Epidemiology, Fielding School of Public Health, University of California Los Angeles, Los Angeles, CA, USA, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine associations between niacin intake and glaucoma in the National Health and Nutrition Examination Survey (NHANES).

Methods: The study population included adults in the 2005-2008 NHANES. Dietary intake of niacin was analyzed both as a continuous variable and at a cutoff point of 16 mg per day, the recommended daily value for adult males. Glaucoma was defined as 2+ abnormal points on visual fields and cup-to-disc ratio or asymmetry $\geq 97.5\%$ of the NHANES population. Covariates included age, gender, ethnicity, level of education, income, body mass index, smoking status, alcohol intake, steroid intake, diabetes mellitus, cataract surgery, macular degeneration, and myocardial infarction. Logistic regression modeling was used to examine the associations between niacin intake and glaucoma in the study population, adjusting for all study covariates. Analyses were weighted using NHANES multistage sampling design.

Results: The weighted study population included 82,415,936 individuals, of whom 3,021,541 (3.7%) had glaucoma. There were no statistically significant associations between continuous levels of dietary niacin intake and glaucoma in any models: unadjusted odds ratio [OR] = 0.99, 95% confidence interval [CI] = 0.97, 1.01 per 1 mg increase in niacin intake; adjusted (aOR) = 1.01, 95% CI = 0.98, 1.03 per 1 mg increase. When comparing dietary niacin intake was greater versus less than 16 mg, there was a statistically significant association between niacin intake and glaucoma in the unadjusted model (OR = 0.69, 95% CI = 0.49, 0.96 for >16 mg vs ≤ 16 mg), but not in the adjusted model aOR = 0.75, 95% CI = 0.48, 1.18 for >16 mg vs ≤ 16 mg.

Conclusions: In the 2005-2008 NHANES population, there was no association between continuous levels of dietary niacin intake and glaucoma, but a possible association at a cut point of 16mg intake per day. These findings suggest the need for further study of associations between niacin and glaucoma.

CONTROL ID: 3534542

SUBMITTER (NAME ONLY): Diego Ogando

TITLE: Inducible Slc4a11 knock out in adult mice produces corneal edema through alteration of pump and barrier functions

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.G. Ogando, R. Shyam, E.T. Kim, Y. Wang, C. Liu, J.A. Bonanno, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: The conventional Slc4a11 knock out (KO) shows significant corneal edema at eye opening; a fact that complicates the study of the initial events leading to edema. We have reported that Slc4a11 is a NH_3 -activated mitochondrial uncoupler that facilitates glutamine catabolism and suppresses mitochondrial superoxide production. Here we tested the hypothesis that inducible Slc4a11 KO in the adult mouse leads to progressive corneal edema characterized by oxidative stress and alterations of pump and barrier functions of the corneal endothelium (CE).

Methods: Slc4a11 Flox (SF) mice were crossed with mice expressing the estrogen receptor–Cre Recombinase fusion protein and at 8 weeks of age were fed Tamoxifen (Tx) enriched chow (0.4 g/Kg) for 2 weeks, followed by normal chow; and controls were fed normal chow. Corneal thickness (CT) was measured by OCT. Oxidative damage was detected by nitrotyrosine staining, tight junctions by ZO-1 and adherens junctions by F-actin staining. Pump function was tested by stromal lactate concentration and barrier function by paracellular permeability to fluorescein. To generate inducible Slc4a11 KO mice strictly in keratocytes, SF mice were crossed with Kera-rtTA;tetO-Cre driver mice (IOVS 2017, 58: 4800–4808) and were fed DOX since embryonic day 0 until test at 3 months of age.

Results: Tx induced a 98% decrease in Slc4a11 expression in corneal tissue. Tx produced gradual corneal edema with an increase in CT of 34% at 2 weeks and 49% at 8 weeks of treatment. Cell density was not changed but morphology was significantly altered. Oxidative stress was evident as nitrotyrosine abundance increased. Tx induced a decrease in the CE pump function evidenced by an increased stromal lactate accumulation (Ctrl: 4.24 ± 1.19 nmol/mg tissue vs Tx: 9.71 ± 1.36 , $p=0.02$, $n=5$), and down regulation of MCT2 and Atp1b2. However, Tx increased CE ATP levels by 12%. Tx increased paracellular permeability (decreased barrier function) by 16% and altered tight and adherens junctions. No significant differences in CT were found between WT mice and Slc4a11 KO in keratocytes only.

Conclusions: These data confirm that oxidative stress and perturbation of pump and barrier functions of the CE are early events following diminution of Slc4a11 expression. Slc4a11 expression is also high in keratocytes, however specific KO did not lead to corneal edema.

CONTROL ID: 3534547

SUBMITTER (NAME ONLY): Kunal Malik

TITLE: Reference Standards for Assessment of Fluid in Neovascular Age-Related Macular Degeneration (nAMD)

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Malik, M. Lanser, J.W. Pak, M. Banghart, B. Blodi, A. Domalpally, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: In nAMD, intraretinal (IRF) and subretinal fluid (SRF) on spectral domain optical coherence tomography (SDOCT) are used to tailor anti-VEGF treatment. Automated quantification of fluid on SDOCT using artificial intelligence (AI) may allow clinicians to identify patients requiring treatment. However, studies have shown poor agreement between assessment of fluid between AI and retina specialist. This study is designed to develop better reference standards to train AI algorithms with a robust qualitative and quantitative assessment of fluid related to nAMD.

Methods: SD OCT cube scans of 20 patients with nAMD undergoing anti-VEGF treatment were included. Experienced reading center graders assessed the following qualitative fluid variables: presence, grid location, center subfield (CSF) involvement, and type of IRF (cystoid vs non-cystoid) and SRF (presence of sub-retinal hyperreflective material or SHRM). Both IRF and SRF were categorized as mild or more than mild (mtmIRF/mtmSRF) based on subjective assessment. For quantitative assessment, volumes of IRF (internal limiting membrane to inner segment/outer segment (IS/OS)) and SRF (IS/OS to retinal pigment epithelium) were documented using custom segmentation software. All images were independently reviewed by two expert graders.

Results: IRF was evaluated in 10 (50%) eyes and categorized as mtmIRF in 6 (60%) eyes. IRF was located within CSF in 8 (80%) eyes and was associated with cysts in 10 (100%) eyes. SRF was evaluated in 14 (70%) eyes and categorized as mtmSRF in 9 (64.2%) eyes. SRF was located within CSF in 13 (92.8%) eyes and associated with SHRM in 14 (100%) eyes. The mean IRF volume was 6.3 (SD=0.27) in eyes with mild IRF and 7.9 (SD=1.2) in eyes with mtmIRF ($p=0.03$). The mean SRF volume was 0.7 (SD=0.1) in eyes with mild SRF and 1.3 (SD=0.85) in eyes with mtmSRF ($p=0.07$). Agreement on fluid severity between the two graders was 93% ($k=0.85$ SE= 0.14; 95% CI=0.57-1) for SRF and 89% ($k= 0.73$ SE= 0.25; 95% CI= 0.24-1) for IRF.

Conclusions: Detailed and reproducible evaluation of fluid on SDOCT in nAMD can be performed to provide qualitative and quantitative evaluation of SRF and IRF. Employing these methods in a dataset to correlate with physician decision to treat and patients' visual outcomes will further refine the reference standards and help train clinically useful AI algorithms.

CONTROL ID: 3534549

SUBMITTER (NAME ONLY): Liat Gantz

TITLE: Digital eye strain symptoms during online university learning in Israel and the USA during the COVID-19 pandemic

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Gantz, Department of Optometry and Vision Science, Hadassah Academic College, Jerusalem, Jerusalem, ISRAEL|M. Rosenfield, College of Optometry, SUNY The State University of New York, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Liat Gantz: Commercial Relationship: Code N (No Commercial Relationship) | Mark Rosenfield: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Due to the COVID-19 pandemic, online university studies resulted in extended hours spent by students in front of digital displays. These displays differ significantly from printed materials and often result in symptoms known as “digital eye strain” (DES). This study examined the symptoms of DES in university students in Israel and in the USA during online learning.

Methods: The English and Hebrew translated DES and Ocular Surface Disease Index (OSDI) dry eye questionnaires were inserted into Google Forms and sent to university students by email and social media. The OSDI determined if the symptoms were due to pre-existing dry eye disease. Non- university students, participants with self-reported ocular infections or prior ocular surgery, and those not attending online studies were excluded. Results were analyzed using descriptive statistics, with DES survey scores above 5 considered symptomatic. Mann Whitney U-test was applied to compare the samples.

Results: The Israeli and USA cohorts comprised 160 (38 optometry students, 24 male, mean age: 26±8) and 163 State University of New York optometry students (34 male, mean age: 24±2), respectively. Respondents spent 18±9 and 15±5 weekly hours in online studies, with 7±7 and 9±3 daily hours on the computer, and 6±9 and 4±3 daily hours on cell phones in the Israeli and USA cohorts, respectively. 98% and 96% of the cohorts reported mainly using computer monitors for studying. The most frequently reported symptoms during or immediately after online studies in the Israeli and USA cohorts included eye fatigue (60% and 48%), eye strain (58% and 31%), ocular discomfort (44% and 31%), headaches (43% and 26%), dry eyes (39% and 34%), and burning eyes (40% and 22%). The prevalence of ocular eye strain, burning eyes, headaches, ocular discomfort and photophobia was significantly higher in the Israeli cohort ($p<0.05$). The prevalence of DES symptoms far surpasses the typical prevalence of mild to severe dry eye (15% in the Israeli cohort, 7% in the USA cohort).

Conclusions: Results demonstrate a high prevalence of DES symptoms in university students. In the future, a causative relationship with digital displays can be established by comparing responses to symptoms reported during live learning. Healthcare providers should educate patients about ways to reduce DES.

CONTROL ID: 3534582

SUBMITTER (NAME ONLY): Nicholas Palmer

TITLE: Patient preferences in retinal drug delivery

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Palmer, B. Jacobs, T. Shetty, A.R. Hajrasouliha, D. Jusufbegovic, T.W. Corson, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|H. Dimaras, SickKids Research Institute, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Intravitreal (IVT) injections of anti-vascular endothelial growth factor drugs are currently a mainstay of pharmacological treatment for many retinal diseases but have shown relatively low patient compliance in previous studies, reducing treatment efficacy. New developments in small molecule anti-angiogenic drugs provide the future possibility of alternative drug delivery routes such as eye drops or oral tablets. This survey study aimed to determine what factors influence patient views of IVT injections and how future treatments might be administered to increase patient compliance and satisfaction with treatment.

Methods: An IRB-approved patient survey was designed to explore patient preferences, demographics, and perspectives on treatment compliance. Inclusion criteria consisted of any patient who received IVT injections for a retinal disease at the Glick Eye Institute from 2016 through July 2020. Respondent demographics and diagnosis were collected from medical records. Participants were stratified by number of IVT injections received (≤ 4 vs. ≥ 4) and by sex. Survey responses were evaluated on a five level Likert scale and differences between groups assessed using the Student's t-test.

Results: Respondents (n=54; response rate 5%) ranged in age from 27 to 91 and came from a diverse pool of education and income levels. Retinal disease diagnoses included macular degeneration, diabetic retinopathy, ocular histoplasmosis, and central serous retinopathy. Responses revealed that 83.3% of participants agreed or strongly agreed that they were apprehensive prior to receiving their first IVT injection, but that 79.6% were willing to receive injections indefinitely to preserve their vision. However, when questioned about future alternative treatment routes, 75.5% of participants preferred eye drops over IVT injections and 65.4% preferred oral tablets over IVT injections. Despite this, a majority of patients still preferred ophthalmologist visits spaced every 1–3 months. Responses did not differ between sex or between number of IVT injections received.

Conclusions: A majority of retinal disease patients are willing to receive IVT injections indefinitely in order to preserve their vision. However, if new treatments were available, most participants would prefer eye drops or oral tablets over IVT injections. This finding underscores the value of developing new therapeutics with alternative delivery routes.

CONTROL ID: 3534593

SUBMITTER (NAME ONLY): kotaro tsuboi

TITLE: Three-dimensional quantification of intraretinal cystoid space in patients with macular hole

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. tsuboi, D. Huang, Y. Jia, T.S. Hwang, S.T. Bailey, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|K. tsuboi, M. Kamei, Aichi Ika Daigaku, Nagakute, Aichi, JAPAN|Y. Guo, J. WANG, D. Huang, Y. Jia, Oregon Health & Science University Department of Biomedical Engineering, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize and quantify intraretinal cystoid spaces in patients with macular hole (MH).

Methods: We conducted a retrospective, observational study which included consecutive, MH patients who underwent successful MH closure after a primary surgery with 12-month follow-up postoperatively. We obtained 3×3-mm macular optical coherence tomography scans with a commercial device preoperatively and processed with a custom software. The software detected the intraretinal cystoid spaces in each of B-scan images and quantified as fluid volume (FV) (Figure). We defined inner FV as cystoid spaces in the inner nuclear layer and outer FV as cystoid spaces between the outer plexiform layer and the Henle's fiber layer. MH was classified with the International Vitreomacular Traction Study (IVTS) classification. Spearman's correlation coefficient was used for univariate analysis. In multivariate analyses, variables that were a P value less than 0.10 in the univariate analysis were selected by forward stepwise selection for linear regression models.

Results: Forty-two eyes of 39 patients were included. Eleven eyes (26%) were small MH, 12 eyes (29%) were medium MH, and 19 eyes (45%) were large MH. Sixteen eyes (38%) had vitreomacular traction (VMT). Of 42 eyes, 39 eyes (93%) underwent combined phacovitrectomy and all eyes were pseudophakia postoperatively. Large MH was associated with increased inner FV compared to small MH ($P = 0.0026$), while there were no differences in the outer FV between MH size. Inner and outer FV was similar in eyes with and without VMT. Postoperative VA was significantly associated with the inner FV ($p = 0.39$, $P = 0.0097$), while minimum MH size ($p = 0.29$, $P = 0.063$), basal MH size ($p = 0.20$, $P = 0.21$), and outer FV ($p = -0.053$, $P = 0.74$) were not. In multivariate analysis, the inner FV was the only significant factor for postoperative 12-month VA ($\beta = 0.44$, $P = 0.0033$).

Conclusions: Inner FV is associated with larger MH size based on IVTS classification and worse postoperative VA. These suggest inner FV represents retinal degenerative change associated with more advanced MH.

CONTROL ID: 3534603

SUBMITTER (NAME ONLY): Ian Pitha

TITLE: Dendrimer-based nanoparticles for early detection and therapeutic targeting of microglia in a rat glaucoma model

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I.F. Pitha, S. Kambhampati, A. sharma, R. Sharma, L. McCrea, K. Rangaramanujam, Center for Nanomedicine/Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal and optic nerve (ON) microglia were identified previously as early indicators of damage and therapeutic targets in glaucoma models. Hydroxyl dendrimer nanoparticles selectively target activated microglia in the brain and retina. Here, we assess dendrimer-based nanoparticles for their ability to label activated microglia and therapeutically target microglia in laser-induced experimental rat glaucoma.

Methods: Unilateral, translimbal laser treatment was performed to induce glaucoma in Wistar rats and IOP was monitored serially by rebound tonometry. Cy5-labelled dendrimer (D-Cy5) was administered either intravitreally or systemically at 3, 7, or 28 days following laser treatment. Retinal biodistribution and microglial uptake was determined by immunofluorescence microscopy and Iba-1 labelling at 3-28 days following dendrimer treatment. N-acetylcysteine-conjugated dendrimer (D-NAC) or free NAC (20µg/eye) was injected intravitreally 7 days after translimbal laser and retinal transcription of TNFα, IL-1b, MCP-1, ICAM-1, iNOS, and NRF2 was determined by RT-PCR (n=6 per group) on day 28.

Results: In the laser induced glaucoma eyes, activated microglia were increased in the retina and ON compared to contralateral control eyes. Intravitreally administered D-Cy5 was selectively localized and retained in activated microglia of laser-treated eyes for up to 28 days. D-Cy5 colocalization with Iba-1 positive retinal microglia was 90% at 7 days after injection and 55% after 28 days. Retinal cross sections demonstrated nerve fiber layer and inner plexiform layer dendrimer uptake in laser-treated eyes, with minimal dendrimer uptake in healthy eyes. Following laser treatment and systemic D-Cy5 administration, dendrimer uptake was not seen in retina, however, was present in the ON. A single dose of intravitreal D-NAC reduced significantly retinal transcription of inflammatory markers TNFα, IL-1b, MCP-1, ICAM-1, and iNOS compared to untreated ($p < 0.01, 0.01, 0.01, 0.05,$ and 0.01 respectively) and NAC-treated eyes ($p < 0.05, 0.05, 0.01, NS,$ and NS respectively).

Conclusions: Hydroxyl dendrimer nanoparticles labeled activated microglia at early timepoints and reduced transcription of inflammatory genes in laser-induced glaucoma. These results highlight the potential of dendrimers for early glaucoma detection and as targeted therapeutics for glaucoma treatment.

CONTROL ID: 3534607

SUBMITTER (NAME ONLY): Lara Skelton

TITLE: Evaluation of tauopathy in rat retinas following acoustic blast overpressure exposure

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Skelton, S. Ramachandra Rao, S.J. Fliesler, Ophthalmology and Biochemistry, University at Buffalo, Buffalo, New York, UNITED STATES|L.A. Skelton, S. Ramachandra Rao, S.J. Fliesler, Research Service, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|M.T. Pardue, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Atlanta, Georgia, UNITED STATES|M.T. Pardue, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Several neurodegenerative diseases involve accumulation of misfolded tau, which leads to neurofibrillary tangle formation. Also, tau hyperacetylation promotes tau accumulation and aggregation. Here, we examined the levels and distribution of acetylated (Ac) and total tau in rat retinas following acoustic blast overpressure (ABO) exposure, relative to unexposed controls.

Methods: Anesthetized adult male Long-Evans rats were subjected to ABO exposure, twice, with 1-mo. recovery between exposures. Eyes/retinas were harvested at 48 h post-2nd ABO exposure; non-exposed, age/sex-matched rats served as controls. Immunohistochemistry (IHC) was performed on cryosections of PFA-fixed eyes, probing with polyclonal antibodies (Abs) against Ac-tau (9AB or AC312) or a pan-tau rabbit mAb (EP2456Y). Average % IPL area occupied by pan-tau-labelling was calculated in thresholded z-stack images using ImageJ. Ab specificity was tested by Western blot (WB) analysis, using in vitro-acetylated recombinant rat tau (Ac-rat-tau) as a standard. Statistical analysis: Student's t-test, with significance threshold $P < 0.05$ ($N = 7/\text{group}$).

Results: IHC with Ac-tau Abs showed immunolabelling of nuclei within the GCL INL, ONL and RPE-choroid, and diffuse-to-punctate IPL labelling. A filamentous labelling pattern in the IPL and INL was evident using Ab AC312. However, pan-tau mAb EP2456Y labelled the inner retina, with a diffuse-to-punctate pattern in the GCL, IPL, and perinuclear labeling in the INL, consistent with prior studies. Tau puncta in the IPL varied in size and density. Thresholded image analysis of the IPL region revealed a ~2.8 fold increase in %Area occupied by pan-tau- labelled puncta in ABO-exposed retinas compared to controls. WB analysis revealed that both anti-Ac-tau Abs detected Ac-rat-tau, but not non-Ac-rat-tau. However, both Abs exhibited cross-reactivity with the catalytic domain of p300 acetyltransferase, required for tau acetylation in vitro. EP2456Y detected both Ac and non-Ac forms of tau, but not p300, and was tau-specific.

Conclusions: Visual dysfunction following ABO exposure may be due, in part, to retinal tauopathy caused by tau accumulation, aggregation, and inclusion body formation. However, IHC results obtained using 9AB and AC312 anti-Ac-tau Abs should be interpreted with caution, due to potential cross-reactivity with p300.

CONTROL ID: 3534622

SUBMITTER (NAME ONLY): Prem Patel

TITLE: Surgical Outcomes of Pars Plana Vitrectomy with Scleral Buckle versus Vitrectomy alone for Primary Retinal Detachment

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.N. Patel, P. Williams, D. Callanan, Ophthalmology, The University of Texas Southwestern Medical Center Medical School, Dallas, Texas, UNITED STATES|W. Solley, P. Williams, D. Callanan, Texas Retina Associates, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: This retrospective study aimed to compare single surgery anatomic success (SSAS) between pars plana vitrectomy (PPV) and vitrectomy with scleral buckle (PPV/SB) for primary retinal detachment repair.

Methods: Charts of patients who presented to Texas Retina Associates between August 2010 to February 2020 for retinal detachment were reviewed. An initial cohort was randomly generated for preliminary analysis. The primary outcome measure was single surgery anatomic success (SSAS), defined as attachment at 3 months after primary surgery without any additional surgeries during that interval. Patients with <90 days of follow-up data were excluded. Other collected data included pre-operative and final visual acuity, detachment morphology, macular status, lens status, demographic information, and length of follow-up. Group comparison of categorical data was performed with Pearson's chi-square and Fisher's exact test.

Results: 2,103 eyes were identified in our cohort, which were treated with PPV (n = 1791) or PPV/SB (n = 312). Overall, PPV/SB had significantly higher single surgery success rate (94.2%) compared to PPV (87.8%, p = 0.001). In 909 phakic eyes, the SSAS was significantly higher with PPV/SB (94.9%, 187/197) compared to PPV alone (87.2%, 621/712, p = 0.002). In contrast, there was no statistically significant difference in SSAS between PPV/SB and PPV among the 1,167 pseudophakic eyes (92.9% vs 88.8%, p = 0.18). In phakic eyes with inferior pathology, those undergoing PPV/SB reported significantly greater SSAS than PPV (96.9% vs 79.7%, p < 0.001), however the difference was not significant in superior pathology (p = 0.53). Mean change in visual acuity was similar for PPV/SB and PPV (logMAR Snellen 0.48 and 0.44 respectively, p = 0.73).

Conclusions: The addition of scleral buckle to vitrectomy may improve surgical outcomes in patients with primary retinal detachments, particularly in phakic eyes and in those with inferior detachments. We report higher single surgery anatomic success rates than previously described in literature. Despite the differences observed in surgical outcomes, visual recovery was similar for PPV and PPV/SB in our cohort.

CONTROL ID: 3534655

SUBMITTER (NAME ONLY): Timothy Xu

TITLE: Cancer Risk in Patients with Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.T. Xu, Alix School of Medicine, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|K.H. Baratz, M.P. Fautsch, M.A. Mahr, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|D.O. Hodge, Health Sciences Research, Mayo Clinic's Campus in Florida, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is the most common trinucleotide repeat (TNR) expansion disorder, involving a CTG repeat in the widely expressed transcription factor 4 gene. It is unknown whether patients with FECD are at variable risk of systemic disease, but several other TNR expansion disorders such as myotonic dystrophy type 1 are associated with increased cancer risk. We sought to quantify the risk of malignancy in patients with FECD.

Methods: Using the Medicare Limited 5% Data Sets, U.S. Medicare fee-for-service beneficiaries (age ≥ 65 years old) with FECD and cancer were identified via International Classification of Diseases (ICD), 9th and 10th Revision diagnostic codes from January 1, 2014 to December 31, 2016. Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated to compare risk of various cancers in Medicare beneficiaries with FECD compared to those without FECD. The main outcome measure was OR of cancer at various anatomic locations in patients with and without FECD. In order to evaluate the potentially confounding variable of intensity of medical care between groups, the Charlson comorbidity index for systemic diseases, such as diabetes and cardiovascular disease, was applied.

Results: Of the 1,462,740 beneficiaries in the Medicare Limited 5% Data Set, 15,534 (1.1%) patients had an ICD code for FECD. Compared to U.S. Medicare beneficiaries without FECD, FECD patients were at increased risk for the following malignancies after adjustment for age, sex, race, tobacco use, and Charlson comorbidity index: breast (OR: 1.32; 95% CI: 1.22 to 1.43; $p < 0.001$), cutaneous basal cell (OR: 1.42; 95% CI: 1.35 to 1.49; $p < 0.001$), cutaneous squamous cell (OR: 1.45; 95% CI: 1.38 to 1.53; $p < 0.001$), and ovarian (OR: 1.84; 95% CI: 1.48 to 2.30; $p < 0.001$). Conversely, FECD cases were at decreased risk for lung (OR: 0.81, 95% CI: 0.71 to 0.93, $p = 0.003$) and prostate cancer (OR: 0.88; 95% CI: 0.81 to 0.96; $p = 0.002$).

Conclusions: Patients with FECD ≥ 65 years old may be at increased risk for cancer at several anatomic locations. Further studies are needed to confirm this association, elucidate potential disease mechanisms, and identify genetic and/or environmental risk factors.

CONTROL ID: 3534657

SUBMITTER (NAME ONLY): Max Williger

TITLE: Influence of optical blur on light and dark perimetric stimuli scaled for changes in eccentricity

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Williger, M.W. Dul, V. Moore-Stoll, H. Rahimi, J. Jin, J. Alonso, SUNY College of Optometry, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Standard clinical perimetry uses 0.43 degree stimuli which are influenced by optical blur and retinal eccentricity. We assessed the influence of optical blur on light and dark perimetric stimuli scaled for changes in eccentricity.

Methods: Three eyes of 3 control subjects were tested using full optical correction followed by 3 levels of optical blur (+1, +3, +5) at the corneal plane with contact lenses. To mitigate the effects of learning, 3 tests preceded the introduction of optical blur. Each test was comprised of 579 trials, including 51 catch trials at 90 different positions in the visual field, each position was repeated 3 times for each the light and dark trials with 6 repeats in each of two blind spot positions.

Hardware consisted of a head mounted display equipped with an eye tracker (HTC VIVE embedded Tobii) with a refresh rate of 90 Hz, a max luminance of 200 cd/m² and a horizontal field of view of 100 degrees. Unity (version 2017) software was used to generate the stimuli and a library provided by Tobii Pro was used to measure eye movements at 120 Hz. Eye movement was restricted within a central 2.5 degree radius circle. Stimuli were light or dark squares superimposed on a spherical binary noise background. Stimulus size was increased as a function of eccentricity using a power law relationship: $\text{stimulus size} = \text{minimum scale} * (\text{eccentricity}/5)^\alpha$, where the minimum scale is the size in degrees of the stimulus 5 degrees from the fovea, eccentricity is the distance from the fovea in degrees, and alpha is the exponential scale in which the size of the stimulus increases as a function of eccentricity. The minimum scale was set at 2.5 with an alpha of 0.26.

Results: Response accuracy was recorded as a percentage for each visual field location and intrasubjective comparisons were made between light and dark stimuli as well as between magnitudes of optical blur. Consistent with previous work, subjects were more accurate for darks (~10% error rate) vs. light (~20% error rate) stimuli. There was no change in percentage accuracy with the introduction of optical blur for either lights ($p = 0.17$) or darks ($p = 0.15$) (Figure 1).

Conclusions: Both light and dark perimetric stimuli scaled in size for retinal eccentricity are resistant to blur up to +5 diopters. Scaling perimetric stimuli may be useful in clinical practice.

CONTROL ID: 3534662

SUBMITTER (NAME ONLY): Lidia Cardelle

TITLE: Dopamine Receptor Agonists Selectively Benefit Visual Deficits at Early Stages of Diabetic Retinopathy in Rats

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Cardelle, R.S. Allen, K. Chesler, M.T. Pardue, Center for Visual and Neurocognitive Rehabilitation, Atlanta VA Healthcare System, Decatur, Georgia, UNITED STATES|L. Cardelle, R.S. Allen, K. Chesler, M.T. Pardue, Department of Biomedical Engineering, Georgia Institute of Technology/Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Treating healthy and diabetic mice with dopamine receptor agonists selectively enhanced visual function; the D1R agonist increased spatial frequency thresholds, while the D4R agonist increased contrast sensitivity thresholds (Jackson et al., J Neurosci 2012; Aung et al., J Neurosci 2014). Here we investigated the benefits of three dopamine receptor agonists (D1R, D2R, D4R) on visual function at various stages of diabetic retinopathy (DR) in rats.

Methods: Hyperglycemia was induced in 2-month-old male Long-Evans rats using streptozotocin (STZ; blood glucose > 250 mg/dL). Optomotor responses (OMR) were measured in diabetic and control rats before and 30 minutes after a single intraperitoneal injection of SKF38393 hydrobromide, a dopamine D1R agonist (1 mg/kg); Bromocriptine mesylate, a dopamine D2R agonist (5 mg/kg); or PD168077 maleate, a dopamine D4R agonist (1 mg/kg). Each agonist was injected 2-3 days apart. OMR was assessed at 8 weeks post-STZ (n=10-11/group) and at 16 and 20 weeks post-STZ in a subset of rats (n=4-6/group). OMR thresholds were compared pre- and post-agonist between diabetic and control rats at 8 weeks post-STZ and then all agonists compared across time using three-way repeated ANOVAs.

Results: At all timepoints, spatial frequency and contrast sensitivity thresholds were significantly decreased in diabetic rats ($p < 0.0001$; Figure). At 8 weeks post-STZ, the D1R agonist selectively increased spatial frequency thresholds in diabetic rats ($p < 0.0001$), but not in control rats. Additionally, the D4R agonist selectively increased contrast sensitivity thresholds in diabetic rats ($p = 0.0003$) but not in control rats. These differences were not detectable at 16 or 20 weeks post-STZ. The D2R agonist did not show significant effects at any timepoint.

Conclusions: These results show that acute dosing of the D1R agonist selectively benefits visual acuity, while D4R selectively benefits contrast sensitivity at early stages of DR. Therefore, dopamine receptor agonists may benefit visual deficits associated with diabetes if they are administered early in disease progression.

CONTROL ID: 3534679

SUBMITTER (NAME ONLY): Jordan Bell

TITLE: Development of a Deep Learning-Enhanced Automated Image Quality Assessment Platform for Spectral Domain Optical Coherence Tomography: The Segmentation Confidence Score

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Bell, J. Whitney, D. Sevgi, J. Hach, S. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accuracy of automated retinal layer segmentation is dependent on image quality. The purpose of this study is to assess the feasibility of an automated quality SD-OCT assessment tool through a “segmentation confidence score” as a predictor of image quality and segmentation accuracy.

Methods: Eighty-six SD-OCT scans (Cirrus, Zeiss) were included in this study. Following review of each of the 128 slices, two expert readers assigned each scan a quality grade based on manual segmentation feasibility: good - gradable with minimal defects, fair - gradable despite notable defects, or poor - ungradable. Using an automated image feature assessment platform, traditional image quality parameters related to signal intensity including signal intensity mean, median, variance, skew, kurtosis, and homogeneity were calculated for each slice and averaged for each scan.

Utilizing an automated machine learning (ML) enhanced retinal layer segmentation platform, the following layers were segmented: internal limiting membrane, outer nuclear layer, ellipsoid zone, retinal pigment epithelium, and Bruch’s membrane. A segmentation confidence score for each layer of each slice was obtained, ranging from 0-100 based on the percentage of x-axis pixels where the ML platform was able to detect a layer. Confidence scores for all layers and slices were averaged to obtain a mean confidence score for each scan. The performance of a random forest ML classifier was assessed with traditional image quality parameters and also with the segmentation confidence scores. AUC values were obtained from 10 iterations of 5-fold cross-validation [reported: mean (variance)].

Results: Using the image parameters related to signal intensity measures alone, the AUCs for classifying good, fair, and poor quality scans were 0.951 (0.001), 0.874 (0.005), and 0.931 (0.007), respectively. The addition of the ML-derived segmentation confidence scores to the ML scan quality classifier increased the AUCs for good, fair, and poor quality scans to 0.975 (0.0005), 0.929 (0.003), and 0.992 (0.0001), respectively.

Conclusions: The ML-based segmentation confidence score enabled a highly discriminating tool for assessing OCT quality. Automated quality assessment could enable rapid feedback for optimizing automated image analysis, clinical trial inclusion, and clinical feedback for photographers.

CONTROL ID: 3534685

SUBMITTER (NAME ONLY): Joseph Juliano

TITLE: Acquired vitelliform macular degeneration, characteristics and challenges of managing subretinal fluid

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Juliano, S. Patel, H. Ameri, Department of Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the characteristics of sub-retinal fluid (SRF) in acquired vitelliform macular degeneration (AVMD) and highlight diagnostic challenges in this entity given the similarity to age-related macular degeneration. We examined the spectrum of image findings in patients with AVMD and provide a treatment approach in cases that are difficult to differentiate from wet age-related macular degeneration (AMD) when SRF occurs.

Methods: A retrospective review of electronic medical record and clinical imaging of 22 eyes of 16 patients with AVMD at a single institution from 2015 - 2020. The rates of SRF, drusen, pigment epithelial detachment (PED), and patient clinical information such as age, length of follow-up, and BCVA was determined.

Results: The mean age at diagnosis with AVMD was 72 years old with a mean follow-up time of 29 months. Median best corrected visual acuity (BCVA) was 20/29 at presentation and 20/29 at final follow-up. Drusen was a prevalent clinical feature, found in 13 of 22 eyes (59.1%) in our study. Four of 22 eyes (18.2%) had the presence of PEDs. SRF was found in 10 of 22 eyes (45.5%) at some point during their follow-up. Of these 10 eyes, in 7 eyes the SRF was located underneath the fovea (70%), recurrence occurred in 4 of 10 eyes. All recurrences of SRF were in the same location as the initial presentation of sub-retinal fluid. The average time of the occurrence of SRF in AVMD was 2.4 ± 3.6 months, and the average time of SRF disappearance was 7.6 ± 5.6 months. Three eyes received an anti-vascular endothelial growth factor injection for SRF. In 66% of cases receiving an injection the fluid later relapsed and remitted without further injections during the course of follow-up.

Conclusions: AVMD remains a diagnostic challenge in the context of SRF, particularly when associated with drusen. In our case series, SRF tended to be central involving and recurred with or without the use of anti-VEGF injections. Proper differentiation of AVMD may prevent unnecessary long-term treatment with intravitreal anti-VEGF injections.

CONTROL ID: 3534686

SUBMITTER (NAME ONLY): Alisha Khambati

TITLE: Comprehensive Analysis to Uncover Determinants of Patient Appointment Compliance in Ophthalmology at the Kresge Eye Institute

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Appointment compliance (AC) has a significant impact on physician-patient relationship and overall patient care. However, determinants of AC in Ophthalmology and its subspecialties remains elusive.

Methods: We performed a five-year, January 2014 to December 31, 2018, retrospective analysis across Kresge Eye Institute (KEI) and its affiliated 24 outpatient Michigan locations. A total of 597,364 appointments across >13 subspecialties were included, in which cancellations, testing, pediatric, and spontaneous emergency appointments were excluded. AC was the primary outcome of interest. Compliant (CO) and non-compliant (NC) groups were compared to the following variables: patient characteristics (gender, race, age, insurance), appointment rank (relative to patient history), scheduling location, month, and ophthalmic specialty, in regard to arrival and no-show.

Results: Among all appointments, 59.77% were associated with a female patient and 79.16% of the total number of appointments were compliant. The mean patient age across all appointments was 58.01 years (SD: 20.07 years) with a range of <1 year to 118 years (IQR: 48.09-71.52 years) and depicted a CO of 59.61%. AC differed concerning specialty, with retina representing the highest compliance across all appointments at 23.84%. Among 200+ insurance providers, Medicare was most frequently used and represented the greatest CO at 44.41%. African Americans were the primary ethnicity served by KEI at 61.02% and had the highest number of NC appointments at 73.36%. Appointment month depicted significant compliance in the month of March at 9.02% ($p < 0.0001$). Among appointment locations, KEI General, which had the highest frequency of appointments represented the least compliance with an NC of 36.06%.

Conclusions: Our study demonstrates the impact of patient demographics, appointment characteristics, and ophthalmic subspecialty on AC. A better understanding of these determinants could allow for an increased CO for Ophthalmology practices.

CONTROL ID: 3534688

SUBMITTER (NAME ONLY): Sarah Michalak

TITLE: Topical ripasudil for the treatment of canine corneal endothelial dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Michalak, S. Park, S. Kim, M. Casanova, M.A. Bowman, M. Ferneding, S.M. Thomasy, Department of Surgical and Radiological Sciences, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|S.M. Thomasy, Department of Ophthalmology & Vision Science, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Canine corneal endothelial dystrophy (CED) represents a spontaneous model for Fuchs endothelial corneal dystrophy (FECD). Current therapies for CED are palliative, warranting investigation of new therapeutics addressing the underlying endothelial degeneration. This study evaluates the tolerability and efficacy of the topical rho-kinase inhibitor, ripasudil, in the treatment of a canine model of FECD through a prospective, single-arm clinical trial.

Methods: Twenty-four eyes of 14 client-owned CED-affected dogs received topical ripasudil 4 times daily. Ophthalmic examination, intraocular pressure (IOP) measurement, ultrasonic pachymetry, in-vivo confocal microscopy, and Fourier-domain optical coherence tomography were performed at baseline and at 1, 3, and 6 months after enrollment. Central corneal thickness, percentage of cornea affected by edema, and corneal endothelial cell density at each time point were determined by a masked analyst. One-way repeated measures analysis of variance or Friedman's test were used to evaluate the effect of treatment on disease progression. Due to high variability in disease severity and response to therapy, individual eyes were also classified as improved, progressed, or stable at the 6-month time point based on defined clinical response criteria (Table 1).

Results: During the treatment period, all 14 dogs developed some degree of conjunctival hyperemia, 4 dogs demonstrated reticulated intraepithelial bullae, and 2 dogs developed corneal stromal hemorrhage. These adverse events did not necessitate permanent cessation of ripasudil treatment in any dog. No significant differences were found in corneal endothelial cell density, corneal thickness, extent of corneal edema, or IOP between baseline, 3-month, and 6-month measurements. When considered individually, 5 eyes improved, 14 eyes remained stable, and 5 eyes progressed during the treatment period.

Conclusions: Topical ripasudil was well-tolerated in the eyes of dogs with CED. As previously reported, conjunctival hyperemia and reticulated intraepithelial bullae were the most common adverse events encountered. Variable response to therapy was observed, with some eyes, particularly those with early disease, showing a favorable response while others progressed during the treatment period. Further studies are needed to investigate factors that influence the response to ripasudil therapy in a canine model of FECD.

CONTROL ID: 3534691

SUBMITTER (NAME ONLY): Victoria Wang

TITLE: Fluctuations in Macular Thickness in Patients with Diabetic Macular Edema treated with Anti- Vascular Endothelial Growth Factor Agents

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.Y. Wang, B. Kuo, A.X. Chen, R.P. Singh, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|K. Wang, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A.X. Chen, T. Greenlee, T.F. Conte, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: There are currently no dependable ways to predict visual outcomes in patients with diabetic macular edema (DME) who are being treated with anti-vascular endothelial growth factor (VEGF) injections. Identification of biomarkers that are predictive of visual outcomes is crucial for the clinical management of DME. The purpose of this study was to test the hypothesis that patients with greater retinal thickness fluctuations have worse visual outcomes.

Methods: This retrospective cohort study analyzed 270 DME patients seen at the Cleveland Clinic Cole Eye Institute from 2012 to 2019 based on the following inclusion criteria: initiation of anti-VEGF therapy during the study period without prior anti-VEGF treatment, follow-up for at least 12 months after first injection, no concomitant maculopathies, and no concurrent steroid injections or focal laser photocoagulation treatment received. Visual acuity (VA) and central subfield thickness (CST) were collected at 0, 3, 6, 9, and 12 months for each patient. Retinal thickness fluctuation was quantified by the standard deviation (SD) of CST across 12 months. Eyes were stratified into quartiles based on CST SD, and 12-month VA was compared. A mixed effects regression model was also used to evaluate the relationship between CST SD and VA at 12 months.

Results: Mean baseline and 12-month VAs were 63.3 ± 15.7 and 68 ± 13.8 ETDRS letters ($p < 0.001$). Mean baseline and 12-month CST were 401.8 ± 124.9 and 337.1 ± 101.0 μm ($p < 0.001$). Mean CST SD was 61.8 ± 52.5 μm . CST SD was a significant negative predictor of 12-month VA ($p < 0.001$) when adjusting for baseline factors, demographics, injections, DR stage, HbA1c, and insulin dependence.

Conclusions: Larger retinal thickness fluctuations are associated with poorer visual outcomes in eyes with DME treated with anti-VEGF injections. Retinal thickness variability may be an important prognostic biomarker for DME patients and may aid in the evaluation of these patients' progress in clinical practice.

CONTROL ID: 3534692

SUBMITTER (NAME ONLY): Steven Kymes

TITLE: Economic Evaluation of Treatment of Macular Edema Due to Central or Hemiretinal Vein Occlusion in the SCORE 2 Trial

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kymes, The Medwin Group, Saint Louis, Missouri, UNITED STATES|N.L. Oden, P.C. Van Veldhuisen, EMMES Group, Rockland, Maryland, UNITED STATES|I.U. Scott, The Pennsylvania State University, University Park, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The main outcome results of the SCORE2 trial demonstrated that, among patients with macular edema due to central (CRVO) or hemi-retinal vein occlusion (HRVO), intravitreal bevacizumab was non-inferior to aflibercept with respect to visual acuity after 6 months of monthly injections. The current study evaluates the cost-effectiveness of treatment initiation with bevacizumab versus aflibercept.

Methods: We modeled two algorithms: 1) initiate bevacizumab, switching to aflibercept if a patient does not respond to treatment; 2) initiate treatment with aflibercept,. A microsimulation model was constructed simulating 10,000 participants in TreeAge Pro using SCORE 2 data. Parameter estimates were drawn from an a priori distribution creating 100 independent simulations to be pooled. Cost of treatment with bevacizumab and aflibercept was taken from the literature. Patient-centered effectiveness was measured using quality adjusted life years (QALYs) estimated in a two-stage process. First, baseline utility scores were estimated for all participants from NEI-VFQ scores applying a mapping algorithm by Payakachat. Next, utility scores were mapped to visual acuity and other factors using a mixed model method (SAS PROC MIXED). ETDRS best-corrected visual acuity (BCVA) in the best-seeing eye and asymmetry in ETDRS BCVA between eyes had the best fit. The incremental cost-effectiveness ratio for the simulation is reported.

Results: In the simulation, participants initiated with aflibercept gained 1.7 more letters in the treated eye at 6 months than patients initiated with bevacizumab and 3.9 more letters at 12 months. Approximately 20% of simulants who initiated treatment on bevacizumab switched to aflibercept within six months. The difference in QALYs (a person-based measure) was 0.001 QALY favoring those initiated with bevacizumab due to modest differences in the untreated eye. Treatment of those initiated with aflibercept was \$20,029 more after 12 months than those initiated with bevacizumab.

Conclusions: Initiating treatment with bevacizumab in patients with CRVO- or HRVO-associated macular edema, and reserving treatment with aflibercept for those who do not respond to initial treatment, is likely to be a preferred strategy from the perspective of payors considering benefits in the broader health sector.

CONTROL ID: 3534705

SUBMITTER (NAME ONLY): Katherine Dalzotto

TITLE: Wide-Field Fundus Autofluorescence Can Facilitate Bardet-Biedl Syndrome Diagnosis

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Dalzotto, M. Schmitt, K.E. Stepien, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|E. Kellom, Waisman Center Medical Genetics Clinic, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bardet-Biedl Syndrome (BBS) is a syndromic disease characterized by obesity, hypogonadotropic hypogonadism, polydactyly, developmental delay, genitourinary abnormalities, renal disease, and retinal degeneration. Despite syndromic findings, patients often are misdiagnosed with nonsyndromic retinitis pigmentosa (RP). Fundus autofluorescence (FAF) imaging can be especially helpful in diagnosing inherited retinal degenerations (IRDs) by detecting outer retinal degeneration. Here we analyze wide-field FAF in adult patients with BBS to determine if unique patterns exist.

Methods: Nine patients with genetically-confirmed BBS (6 females, 3 males; age range 18-65) were identified. Electronic medical records were reviewed for medical and ocular history, ocular clinical exam findings, and ocular imaging.

Results: Past medical history revealed syndromic findings in all patients and suspicious family history elements in several patients. Prior to their BBS diagnosis, 4 of 9 patients had been diagnosed with nonsyndromic RP and one with Leber congenital amaurosis (LCA). Three patients had mutations in BBS1, one in BBS2, one in BBS4, one in MKKS, one in TTC8, and two in BBS10. Visual acuity varied from 20/50 to no light perception (NLP), but generally decreased with increasing age. Advanced cataracts prevented fundus visualization in one patient. Macular atrophy was present in 8 patients. Optical coherence tomography (OCT) showed macular loss of outer retinal structure in 8 patients. Seven patients displayed foveal hypoautofluorescence with concentric hyper- and hypoautofluorescence in a bullseye pattern. Six of 8 patients had few to no peripheral pigmentary changes/bone spicules on clinical exam, however wide-field FAF of these patients revealed extensive speckled or diffuse peripheral hypoautofluorescence.

Conclusions: Despite other syndromic findings (which can be life-threatening), patients with BBS are often misdiagnosed with nonsyndromic RP. We conclude that, along with detailed medical and family history, specific imaging findings on wide-field FAF can aid in the diagnosis of BBS in adult patients with suspected IRDs by better delineating macular degeneration patterns and unearthing extensive peripheral hypoautofluorescence not always evident on clinical exam.

CONTROL ID: 3534723

SUBMITTER (NAME ONLY): Jaycob Avaylon

TITLE: Intraoperative Retinal Changes May Predict Surgical Outcomes After Epiretinal Membrane Peeling

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mukkamala, R. Welch, A. Yazdanyar, P. Emami-Naeini, S. Wong, A. Morshiri, S.S. Park, G. Yiu, Department of Ophthalmology and Vision Science, University of California Davis, Sacramento, California, UNITED STATES|J. Avaylon, J. Storkersen, California Northstate University College of Medicine, Elk Grove, California, UNITED STATES|J. Loo, D. Cunefare, S. Farsiu, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate if intraoperative retinal changes during epiretinal membrane (ERM) peeling affect anatomic or functional outcomes after surgery.

Methods: We measured retinal thickness using an intraoperative optical coherence tomography (iOCT) device in patients undergoing pars plana vitrectomy with membrane peeling for idiopathic ERM. Changes in intraoperative central macular thickness (iCMT) were compared with postoperative improvements in CMT and best-corrected visual acuity (VA).

Results: 27 eyes from 27 patients (mean age 68 years) underwent iOCT-assisted ERM peeling surgery. Before surgery, mean VA was logMAR 0.50±0.36 (Snellen 20/63) and mean baseline CMT was 489±82 µm. Mean iCMT before peeling was 477±87 µm, which correlated well with preoperative CMT (P<0.001). Mean change in iCMT was -39.6±37µm (range -116 to +77µm). After surgery, VA improved to logMAR 0.40±0.38 (Snellen 20/50) at month 1 and logMAR 0.27±0.23 (Snellen 20/37) at month 3, while CMT decreased to 397±44µm and 396±51µm at months 1 and 3. Eyes that underwent greater amount of iCMT change (absolute value of iCMT change) were associated with greater CMT reduction at month 1 (P<0.001) and month 3 (P=0.010), while those with greater intraoperative thinning (actual iCMT change) showed a trend toward better VA outcomes at months 1 (P=0.054) and 3 (P=0.036).

Conclusions: Intraoperative changes in retinal thickness may predict anatomic and visual outcomes after idiopathic ERM peeling surgery.

CONTROL ID: 3534751

SUBMITTER (NAME ONLY): Chandana Papudesu

TITLE: Physical Activity in Functionally Monocular Patients in the United States, 2003-2006

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Papudesu, S.W. van Landingham, Ophthalmology, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|J.R. Willis, Ophthalmology, Genentech Inc, South San Francisco, California, UNITED STATES|P.Y. Ramulu, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Real-world physical activity patterns in monocular persons have not been previously characterized. This study uses a nationally representative sample to compare the physical activity levels of functionally monocular to binocularly sighted persons in the United States.

Methods: This cross-sectional study uses data from the 2003-2004 and 2005-2006 National Health and Nutrition Examination Survey (NHANES) to compare differences in physical activity between functionally monocular and binocular participants. Functionally monocular is defined as visual acuity of better than 20/200 in one eye and 20/200 or worse in the other eye after auto-refraction. The main outcome measures were accelerometer-measured mean steps per day and mean daily minutes of moderate or vigorous physical activity (MVPA). Statistical analysis was conducted using multivariable negative binomial regression models, which included age, gender, race/ethnicity, better-eye visual acuity, educational attainment, and obesity as covariates. Sample weights were used according to guidelines from the National Center from Health Statistics.

Results: 7,967 NHANES participants had complete visual acuity and accelerometer data. The mean age at baseline was 44.5 years, and a majority were Caucasian (73%) and female (52%). In unadjusted analysis, functionally monocular participants (n=102) took fewer steps (7,254 vs 10,012, $p<0.01$) and engaged in fewer minutes of MVPA (13.6 vs 26.8, $p<0.01$) per day compared to binocularly-sighted participants (n=7,846). When adjusted for age and better-eye visual acuity, however, these between-group differences were not statistically significant. These results may be explained by the age disparity between groups: the mean age of the monocular group was 65.5 (CI 50.8-70.2) compared to the binocular group, which was 44.2 (CI 43.2-45.3). In our final model, monocular participants took 17% fewer steps per day ($p=0.15$) and engaged in 26% fewer minutes per day of MVPA ($p=0.12$).

Conclusions: Functionally monocular persons have similar physical activity levels compared to those with binocular eyesight in the United States. Additional work is needed to determine if particular types of activity are impacted by monocular status, and if the timing of vision loss has an impact on activity levels.

CONTROL ID: 3534758

SUBMITTER (NAME ONLY): Yayu Chen

TITLE: The effect of wearing progressive addition lenses on visual symptoms and binocular vision functions in Taiwanese non-presbyopia adults

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, C. Lin, C. Yang, Department of Optometry, Da-Yeh University, Dacun, Changhua, TAIWAN|

Commercial Relationships Disclosure (Abstract): Yayu Chen: Commercial Relationship: Code N (No Commercial Relationship) | Chi-Fong Lin: Commercial Relationship: Code N (No Commercial Relationship) | Cheng-Jan Yang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: With the rapid development of technology, the frequency and duration of using digital devices have increasing in daily life, including mobile phone, tablet and computer. Near work for prolonged time can have negative effects for binocular vision. Therefore, this study evaluated the visual symptoms and binocular vision functions after wearing progressive addition lenses (PALs) in Taiwanese non-presbyopia adults.

Methods: 51 healthy non-presbyopia adults aged from 20 to 30 years old were recruited in this study. All participants were measured visual symptoms and binocular vision functions before and after wearing PALs (+0.85 D) for 6 months. Convergence insufficiency symptom survey (CISS) was to use for quantifying the visual symptoms. Near point of convergence (NPC), amplitude of accommodation (AA) and near positive fusional vergence (NPFV) were measured for evaluating binocular vision functions.

Results: After wearing PALs for 6 months, the scores of CISS were statistically significantly reduced (before: 16.86 ± 6.69 ; after: 12.35 ± 7.18 , $p < 0.001$). There was no significant difference before and after wearing PALs for 6 months in the results of NPC, AA and NPFV. However, the mean values of NPC (before: 4.94 ± 4.56 cm; after: 4.40 ± 3.51 cm, $p = 0.285$), AA_{OD} (before: 10.38 ± 3.75 D; after: 10.52 ± 2.80 D, $p = 0.710$), AA_{OS} (before: 10.22 ± 3.75 D; after: 10.43 ± 2.98 cm, $p = 0.588$) and NPFV (before: $7.10 \pm 9.34^\Delta$; after: $7.78 \pm 9.96^\Delta$, $p = 0.597$) were slightly improved.

Conclusions: Our results showed that PALs could significantly ameliorate visual symptoms and slightly improved the binocular vision functions for Taiwanese non-presbyopia adults.

CONTROL ID: 3534759

SUBMITTER (NAME ONLY): Manjulatha Sara

TITLE: Synergistic activity of a peptide mimic with quinolones and cephalosporins against Staphylococcus aureus

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sara, R. Kuppusamy, M. Afzal, M. Khan, M. Yasir, P. Kalaiselvan, A. Hui, M.D. Willcox, University of New South Wales School of Optometry and Vision Science, Sydney, New South Wales, AUSTRALIA|R. Kuppusamy, N. Kumar, University of New South Wales School of Chemistry, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Antibiotic resistance is a global crisis. Antimicrobial peptides are being developed to provide new therapeutic options to reduce resistance. Some of these antimicrobial peptides have broad-spectrum antimicrobial activity and act rapidly on bacteria reducing its resistance. However, the half-life of peptides in the body is compromised due to proteolysis. In order to overcome this degradation, peptide mimics are developed to retain the benefits of the antimicrobial activity. This study investigated whether an antimicrobial peptide mimic could work in synergy with quinolones and cephalosporins against a multidrug-resistant strain of Staphylococcus aureus.

Methods: The antimicrobial peptide mimic 758 was used together with the first line antibiotics ciprofloxacin and ceftazidime. The minimum inhibitory concentration (MIC) of each drug was determined by the microtitre broth dilution method. Subsequently, a checkerboard assay was performed to examine the interaction between antibiotics and peptide mimic. The results were expressed as the fractional inhibitory concentration index (FICI). FICIs of ≤ 0.5 indicate synergism; 0.6-1 indicates additive effect; 1-4 - no interaction and ≥ 4 - antagonism.

Results: Peptide mimic 758 had a MIC of 2.5µg/ml for multidrug-resistant S. aureus strain. Compound 758 produced synergism with both ciprofloxacin and ceftazidime with a FICI of < 0.2 and 0.3 respectively. The MIC of ciprofloxacin was reduced from 2.5µg/ml to 0.15µg/ml and of the peptide mimic from 2.5µg/ml to 0.03µg/ml. The MIC of ceftazidime was reduced from 32µg/ml to 10µg/ml and of the peptide mimic from 2.5µg/ml to 0.03µg/ml.

Conclusions: The peptide mimic was able to significantly enhance the antimicrobial activity of the first-line antibiotic ciprofloxacin and third-generation cephalosporin ceftazidime. Future research will examine other strains and bacteria, as well as the mechanism of the synergy.

CONTROL ID: 3534767

SUBMITTER (NAME ONLY): Kathleen Dyer

TITLE: The relationship between fetal growth and retinal nerve fibre layer thickness measured in a cohort of young adults

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Retinal nerve fibre layer (RNFL) thinning is an important early marker of glaucoma. It is known that RNFL thickness is associated with birth weight and head circumference at birth, both markers of intrauterine growth. We explored relationships between patterns of fetal anthropometric growth, as reflective of early life influences on fetal wellbeing, and global RNFL thickness measured in young adulthood.

Methods: A subset of Caucasian participants (n = 485) from the Raine Study, a pregnancy cohort study based in Western Australia, were included in the analysis. Participants underwent serial ultrasound scans at 18, 24, 28, 34 and 38 weeks' gestation, with fetal biometry measured at each scan. An eye examination including measurement of optic disc parameters via spectral-domain optical coherence tomography imaging was undertaken at a 20-year follow-up. Growth trajectories based on measurements of fetal head circumference (FHC), abdominal circumference (FAC), femur length (FFL) and estimated fetal weight (EFW) were explored via group-based trajectory modelling. Generalised estimating equations (GEEs) were used to evaluate differences between groups of participants with similar growth trajectories with respect to global RNFL thickness.

Results: Participants with consistently large FHCs throughout gestation had thicker RNFLs than those with small, moderately small or moderately large FHCs, after adjusting for fetal sex, maternal smoking during pregnancy, gestational age at birth, and intraocular pressure and axial length at the 20-year follow-up ($p = 0.005$, 0.005 and 0.003 , respectively). This model showed better fit according to the quasi-information criterion when compared to similarly adjusted GEE models analysing associations between RNFL thickness and either birth weight or head circumference at birth. There were no significant differences in RNFL thickness between trajectory groups in the FAC, FFL or EFW models, although similar trends to those in the FHC model were demonstrated.

Conclusions: FHC growth is strongly correlated with RNFL thickness in young adulthood and is moreover a better predictor than birth weight or head circumference at birth. This indicates that adverse early life conditions may predispose towards thinning of the RNFL in child and adult life. There may therefore be implications for the long-term risk of glaucoma in individuals with restricted FHC growth.

CONTROL ID: 3534772

SUBMITTER (NAME ONLY): Reiko Arita

TITLE: Factors affecting blink number and incomplete blink rate in the population-based Hirado-Takushima study

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Arita, Ophthalmology, Ito Clinic, Saitama, Saitama, JAPAN|R. Arita, T. Mizoguchi, M. Kawashima, S. Fukuoka, S. Koh, R. Shirakawa, T. Suzuki, N. Morishige, LIME working group, Tokyo, JAPAN|T. Mizoguchi, Ophthalmology, Mizoguchi Eye Clinic, JAPAN|M. Kawashima, Keio University, JAPAN|S. Fukuoka, Omiya Hamada Eye Clinic, JAPAN|S. Koh, Ophthalmology, Osaka Daigaku Igakubu Fuzoku Byoin, Suita, Osaka, JAPAN|R. Shirakawa, Ophthalmology, University of Tokyo, JAPAN|T. Suzuki, Ophthalmology, Toho University, Oomori hospital, JAPAN|N. Morishige, Ohshima Eye Hospital, JAPAN|

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ABSTRACT BODY:

Purpose: The quantity and quality of blinking are key determinants of homeostasis at the ocular surface. However, few epidemiological studies have examined the characteristics of blinking. We therefore determined the number of blinks (BN) and incomplete blink rate (IBR) according to sex and age in a population-based study (Hirado-Takushima study). We also investigated factors related to the ocular surface or lifestyle that might influence these parameters.

Methods: The study subjects were residents of Takushima Island, Nagasaki Prefecture, Japan, who gave informed consent and for whom BN and IBR were measurable with a LipiView interferometer (Johnson&Johnson). Generalized additive model (GAM) analysis was performed separately according to age and sex. Systemic illness (hypertension, diabetes, dyslipidemia, collagen disease, depression), lifestyle-related factors (BMI, visual display terminal [VDT] time, TV time, time spent outside, use of eye makeup or contact lenses, having a pet, sleep time), ocular symptoms, and tear film– and meibomian gland–related parameters (15 items) were evaluated, and factors potentially affecting BN and IBR were examined with a mixed-effects model.

Results: A total of 356 subjects (133 men and 223 women; mean age \pm SD, 55.5 ± 22.4 years) and 701 eyes were enrolled in the study. BN was 3.17 ± 1.72 over 20 s and decreased with age in both men and women ($p=0.017$). Individuals with dyslipidemia had a reduced BN ($p=0.015$). The fluorescein staining score ($p=0.044$) and meiboscore ($p=0.027$) were positively and the thickness of the lipid layer of the tear film ($p<0.0001$) was negatively related to BN. Mean IBR was 41.1% for all ages. IBR decreased with age ($p=0.015$). VDT time ($p=0.017$) and eye makeup use ($p=0.006$) were positively and time spent outside ($p=0.036$) and TV time ($p=0.022$) were negatively related to IBR.

Conclusions: BN may increase to compensate for disturbance of the ocular surface, including when the lipid layer of the tear film is deficient as a result of meibomian gland dysfunction, whereas IBR may be susceptible to lifestyle factors such as eye makeup use and VDT time.

CONTROL ID: 3534781

SUBMITTER (NAME ONLY): Kristina Hess

TITLE: Postreceptor Neuronal Degeneration in Pseudoxanthoma Elasticum

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the association of age, presence of optic nerve head drusen (ONHD) and number of previous intravitreal anti-VEGF injections with inner retinal layer thicknesses in patients with pseudoxanthoma elasticum (PXE).

Methods: In this retrospective study, longitudinal spectral domain optical coherence tomography (OCT) imaging data from patients with PXE were compared to controls. A custom deep-learning-based segmentation algorithm was trained and validated to quantify the retinal nerve fiber layer (RNFL), ganglion cell layer (GCL), inner plexiform layer (IPL) and the inner nuclear layer (INL) for each ETDRS-subfield. The association of age, number of anti-VEGF injections and ONH drusen with the RNFL/GCL/IPL/INL thickness as dependent variable were investigated using mixed model regression. The model was applied for a macular ring including all outer ETDRS subfields with an ETDRS grid centered to the fovea.

Results: Fifty-three eyes of 30 patients with PXE were compared to 100 eyes of 100 controls. The mean age was (median [IQR]) 54.0 [46.3, 61.7] years for patients vs. 58.1 [36.6, 37.8] years for controls. In patients, ONHD were visible in 15 eyes from 13 patients and the number of anti-VEGF injections ranged from 0 to 55. In the multivariable analysis, age ($-0.09 \mu\text{m}/\text{year}$, $p < 0.001$), the diagnosis of PXE ($-1.80 \mu\text{m}$, $p = 0.022$) and an interaction term between age and the presence of ONHD ($-0.22 \mu\text{m}/\text{year}$, $p = 0.002$) were significantly associated with the GCL thickness in the ring of all outer ETDRS subfields. Including the number of intravitreal injections did not improve the model fit. The RNFL was solely dependent on age without any influence of other parameters. The IPL showed significantly decreased thickness in patients ($-4.79 \mu\text{m}$) compared to controls ($P = 0.015$), but with a significant interaction of group and age ($+0.11 \mu\text{m}/\text{year}$, $P = 0.003$) compatible with gliotic remodeling in older patients with concurrent atrophic changes.

Conclusions: This study demonstrates a significant association of ageing and ONHD with GCL thinning in patients with PXE. Given the severity of postreceptor neuronal degeneration in a subset of patients, neuroprotective therapy once available would warrant consideration. Further, emerging anti-VEGF agents, which allow for less frequent intravitreal injections and/or smaller injections volumes, may be considered to minimize transient intraocular pressure elevations with potential adverse effects on the GCL.

CONTROL ID: 3534786

SUBMITTER (NAME ONLY): Susan Luo

TITLE: Follow-up for in-person eye care after teleophthalmology diabetic eye screening in a U.S. academic medical center

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Luo, M. Wingelaar, B. Xing, B. Burckhard, Y. Liu, Ophthalmology & Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teleophthalmology provides evidence-based diabetic eye screening in primary care, but U.S. studies have reported low follow-up rates (e.g. 30%) for in-person eye care among screen positives. In this study, we evaluated follow-up outcomes after teleophthalmology in an academic U.S. medical center.

Methods: We retrospectively reviewed medical records of adults with diabetes who had teleophthalmology performed using a Topcon NW400 retinal camera (Topcon Medical Systems, Inc., Oakland, NJ, USA) at 2 primary care clinics in Madison, WI between Jan 2018 and Oct 2020. Single-field 45° images of the fundus and anterior photos of each eye were reviewed by eye care providers. Patients needing further in-person eye care were contacted by letter and by phone from schedulers to make an eye appointment. The primary outcome was chart documentation of a completed follow-up eye appointment within 1 year of imaging.

Results: Among 361 patients, the average age was 58.4 years, 54% were men, and 98% had health insurance. 332 patients (92%) had gradable images, including 15% with diabetic retinopathy that was severe or worse in 0.6%. A total of 74 patients (21%) were referred for follow-up eye care due to either abnormal findings (13%) or ungradable images (8%). Patients referred for follow-up eye care were more likely to be insured by Medicare or Medicaid ($p<0.001$) than Commercial insurance. Pathologic findings were identified among 58% ($n=19$) of patients with ungradable images. No uninsured patients were referred for follow-up. There was a 65.5% follow-up rate ($n=58$) among patients imaged between Jan 2018 and Dec 2019, with 48.3% following up within the recommended timeframe. Patients with higher hemoglobin A1c ($p=0.04$) were less likely to follow-up. Among those that did not follow-up ($n=20$), 75% had made an eye appointment, but either cancelled (45%) or no-showed (30%). A total of 8 patients (21%) among those who followed up underwent treatment (e.g. laser, intravitreal injection, and/or cataract surgery).

Conclusions: We found higher follow-up rates (65.5%) for in-person eye care compared to prior reports. While lack of insurance has been cited as a major barrier, follow-up rates remain limited even among patients with insurance. Interventions to further increase follow-up are needed to more effectively improve visual outcomes after screening.

CONTROL ID: 3534796

SUBMITTER (NAME ONLY): Waleed Alsarhani

TITLE: Characteristics and Recurrence of Pterygium: A Single Center Study with a Long Follow-up

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To describe the clinical features of patients with pterygium and analyze the recurrence rate of conjunctival autografting alone, conjunctival autografting combined with intraoperative mitomycin C, and amniotic membrane grafting.

Methods: A retrospective study of primary pterygium was conducted between January 2017 and February 2020. The number of patients who presented with pterygium was 292, while the number of operated cases was 94 (32.19%). The main outcome measured was recurrence over an average follow-up period of 29.3 ± 11.9 months.

Results: Pterygium involving the cornea was observed in 55% of the cases. In the multivariate regression analysis, female gender was the only independent risk factor for a pterygium to encroach on the cornea. The overall rate of recurrence for the three procedures was 17% over an average time of 14.19 ± 11.9 months, with 37% of the recurrences occurring after the first year. The only factor associated with a significant risk of recurrence was dry eye disease. The recurrence rates following conjunctival autografting with and without mitomycin C were 15.6% and 15.8%, respectively. The recurrence rate following the amniotic membrane graft was almost double (27%) that following the conjunctival autograft (15.6%); however, this difference was not statistically significant. For conjunctival autografts, adding fibrin glue to sutures did not result in a lower recurrence rate ($p=0.747$).

Conclusions: The only factor associated with the recurrence of pterygium was dry eye disease. More than one-third of recurrences developed after the first year, which stresses the importance of a long follow-up.

CONTROL ID: 3534807

SUBMITTER (NAME ONLY): Katy Coggins

TITLE: Association between poor oral health and risk of glaucoma

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Coggins, J.T. Whitson, Ophthalmology, The University of Texas Southwestern Medical Center Medical School, Dallas, Texas, UNITED STATES|A. Husain, K. Parsegian, Dentistry, The University of Texas Health Science Center at Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary open angle glaucoma (POAG) and periodontitis have both been shown to be inflammatory-driven processes, with several previous studies suggesting that there may be a link between periodontal disease and an increased risk of glaucoma. The purpose of our study was to explore further the association between chronic periodontitis and glaucoma in a retrospective case-control study design. Our null hypotheses stated that POAG did not affect the prevalence of periodontitis, prevalence of tooth extraction, or average number of tooth extractions as compared with healthy, age-matched patients without POAG.

Methods: Patient information was extracted from charts in the BigMouth Dental Data Repository for UTHealth School of Dentistry from 2006-2019 among patients between ages 18-80 years old. Patients that had identified as having a diagnosis of glaucoma on a medical questionnaire were selected for the glaucoma case group and randomly selected, age-matched patients who had reported as having no diagnosis of glaucoma on the same medical questionnaire were selected for the controls. There were 330 patient charts in the BigMouth database that met the inclusion criteria for the glaucoma group. For the controls, 330 age-matched healthy patients were selected. The three main outcome measures that we identified during data extraction were periodontal disease, history of tooth extraction, and number of teeth extracted. Chi-square, Student's t-test, and one-way ANOVA calculations were performed for statistical analysis purposes, as appropriate.

Results: There was a statistically significant increased prevalence of patients with periodontal disease among older glaucoma patients aged 70-79 years vs. controls ($p=0.035$). This was the only age range in which we found a statistically significant difference in the prevalence of periodontal disease between test and control groups. There was no statistically significant difference in the prevalence ($p=0.800$) or average number ($p=0.653$) of tooth extractions between the two groups.

Conclusions: Our study found a statistically significant increased prevalence of periodontal disease among older glaucoma patients aged 70-79 years old compared to controls, although this association was not found to be similarly significant within the other age ranges. This finding corroborates previous studies that concluded that there is in fact an association between periodontal disease and an increased risk of glaucoma.

CONTROL ID: 3534810

SUBMITTER (NAME ONLY): Yi Hua

TITLE: 3D eye-specific analysis of factors influencing lamina cribrosa oxygen concentration

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Hua, P. Lee, B. Brazile, I.A. Sigal, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|P. Lee, I.A. Sigal, Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.A. Walker, Department of Biomedical Informatics, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxygen in the lamina cribrosa (LC) is essential for maintaining functioning retinal ganglion cell axons and vision. Measuring LC oxygen experimentally is not yet possible and thus it is usually studied using numerical models. LC oxygen models have been highly simplified and generic (Chuangsuwanich et al., 2016), or eye-specific but 2D (Hua et al., 2020). Our goal was to leverage new 3D eye-specific models of the LC vessel network to identify the factors with the largest influence on LC oxygen.

Methods: We reconstructed a detailed 3D model of the monkey LC vessel network based on histological sections (Fig. 1). Hemodynamics boundary conditions were defined to simulate blood flow from the circle of Zinn-Haller, drainage through the central retinal vein, and interactions with the pre and retrolaminar regions. Using a Monte Carlo approach, 500 models were generated with varying (baseline \pm 20%) microvessel diameter, pressures (arteriole, venule, prelaminar, and retrolaminar), inflow hematocrit, and oxygen consumption rate. Models were simulated to estimate LC neural tissue oxygen concentration. Regression analysis was used to determine factor influences on the minimum (10th percentile) oxygen concentration in the LC.

Results: The factors influencing the minimum oxygen concentration the most were: the microvessel diameter, oxygen consumption rate, and arteriole pressure; and to a less extent: the venule, retrolaminar, and prelaminar pressures, and the inflow hematocrit (Fig. 2).

Conclusions: Our models predict that the microvessel diameter, oxygen consumption rate, and arteriole pressure have the largest influence on the oxygen concentration in the LC. To understand the susceptibility to ischemia in retinal ganglion cell axon damage and vision loss, the influential factors should be better characterized.

CONTROL ID: 3534825

SUBMITTER (NAME ONLY): Mckenzee Chiam

TITLE: Sex Differences in Scholarly Productivity, Academic Promotion, and NIH Funding of Academic Glaucoma Specialists

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chiam, M.L. Camacci, S. Pantanelli, Department of Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|E. Lehman, Department of Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma specialists represent the fourth largest subspecialty within academia. To our knowledge, this is the first study to investigate sex differences in scholarly productivity, academic promotion, and NIH funding within this sub-group.

Methods: This was a cross-sectional study of glaucoma specialists employed across 113 US academic institutions. Using institutional websites, data on gender, residency graduation year, and academic rank were collected between January-March 2019. The Scopus database was used to obtain each faculty member's h-index, which is a measurement of publication productivity, and m-quotient, which adjusts for an individual's career length. The NIH Research Portfolio Online Reporting Tool database was queried for data on NIH funding. Chi-square testing was used to analyze categorical values and Wilcoxon Rank Sum testing was used for continuous variables.

Results: A total of 431 glaucoma specialists were identified, of whom 157 (36.4%) were female and 274 (63.6%) were male. A greater proportion of females vs. males were assistant professors [101 (64.3%) vs. 126 (46.0%); $p=0.003$] and a smaller proportion of females were full professors [20 (12.7%) vs. 80 (29.2%); $p=0.001$]. No difference was found among associate professor positions [female: 36 (22.9%) vs. male: 66 (24.1%); $p=1.000$] and department chair positions [3 (1.9%) vs. 22 (8.2%); $p=0.103$]. Females had lower median h-indices compared to their male counterparts (4.0 vs. 8.0; $p<0.001$), but similar median m-quotients (0.4 vs 0.5; $p=1.000$). Females had a shorter median career length based on their residency graduation year compared to males (13.0 vs 21.0 years; $p<0.001$). Among NIH-funded investigators, females had a median grant funding of \$1.1M compared to \$1.4M for males ($p=1.000$).

Conclusions: Shorter career length among female glaucoma specialists likely contributes to the difference seen in scholarly productivity and composition of senior academic ranks between sexes. Career length should be considered when comparing scholarly productivity between sexes.

CONTROL ID: 3534832

SUBMITTER (NAME ONLY): Anna Camos-Carreras

TITLE: Functional tests and ganglion cell complex measured with optical coherence tomography in Autosomal Dominant Optic Atrophy.

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Camos-Carreras, M. Figueras-Roca, S. Alba-Arbalat, M. Dotti-Boada, B. Sanchez-Dalmau, Ophthalmology, Hospital Clinic de Barcelona, Barcelona, Barcelona, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) with optical coherence tomography (OCT) and functional tests as visual acuity (VA) and Hardy Rand and Rittler (HRR) Standard Pseudoisochromatic Test in patients with Autosomal Dominant Optic Atrophy (ADOA).

Methods: Prospectively defined, cross-sectional study of 38 eyes of 19 patients with diagnosis of ADOA. All patients underwent a complete functional examination with VA and colour test, and a structural examination with OCT (Cirrus®, Zeiss).

Results: Analysis of OCT results was done and correlated with functional tests. Results show that temporal sectors of GCC and inferior and superior RNFL sectors were directly correlated with VA measured with ETDRS and with HRR in eyes with ADOA.

Conclusions: Functional and morphologic changes observed in ADOA eyes are helpful to understand the physiology of the disease. Analyzing OCT, VA and colour test could be a future tool to select patients who can take benefit of receiving future treatments.

CONTROL ID: 3534836

SUBMITTER (NAME ONLY): Marta Sacchetti

TITLE: Validation of a novel single-use esthesiometer to test corneal sensitivity

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Sacchetti, F. Giovannetti, A. bruscolini, M. marenco, G. firmani, A. chicca, A. lambiase, Department of Sense Organs, Università degli Studi di Roma La Sapienza, Roma, Lazio, ITALY

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ABSTRACT BODY:

Purpose: Assessment of corneal sensitivity (CS) allows to identify alterations of ocular surface sensory innervation associated with several conditions including neurotrophic keratopathy (NK) and dry eye disease (DED). Currently, Cochet-Bonnet (CB) esthesiometer represents the standard for measuring CS. A novel, single-use corneal esthesiometer (KeraSenseTM) has been developed. The aim of this study is to evaluate the accuracy, reproducibility, and repeatability of the KeraSenseTM in comparison to CB.

Methods: 26 healthy subjects (60±13 years of age) and 41 patients (60±17 years of age) with NK (N=16), diabetes (N=14) and dry eye (N=11) were included. CS was assessed in all subjects with KeraSenseTM (Dompé Farmaceutici SPA, Milan, Italy) and CB. KeraSenseTM assesses CS by disposable devices of fixed nylon thread lengths: 15, 35 and 55 mm. Repeatability and reproducibility of KeraSenseTM were assessed by comparing results of 3 different measurements by the same masked investigator and by two different physicians, respectively. Sensibility, specificity, and accuracy for the diagnosis of NK have also been evaluated.

Results: CB evaluation showed that patients with NK had significant ($P<0.001$) decrease of CS (30±23 mm) when compared with healthy subjects (59±1 mm), and with patients with DM (57±5 mm) and dry eye (58±2 mm). KeraSenseTM showed repeatability and reproducibility, respectively with 100% agreement between different measurements and 99.6% concordance between different operators (Kappa index interrater agreement $P<0.001$). Corneal sensitivity values assessed by KeraSenseTM were significantly associated with CB values (ANOVA $P<0.001$). A 55mm KeraSenseTM value was adequate to exclude an NK diagnosis, while all patients with a KeraSenseTM value of 0 or 15mm had NK. KeraSenseTM response at 35mm showed good sensitivity and specificity to discriminate the presence of NK.

Conclusions: KeraSenseTM showed significant association with CB assessment and represents an expeditious and accurate device to assess CS without need of calibration, and being single-use, ensuring better safety also in the context of SARS-Cov2 outbreak.

CONTROL ID: 3534837

SUBMITTER (NAME ONLY): Zia Chaudhuri

TITLE: Age-related connective tissue degeneration in Indian eyes: A high-resolution magnetic resonance imaging (MRI) study

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Chaudhuri, Department of Ophthalmology, Lady Hardinge Medical College, New Delhi, Delhi, INDIA|Z. Chaudhuri, Department of Ophthalmology and Vision Research Lab, Dr Ram Manohar Lohia Hospital and Post Graduate Institute of Medical Education and Research, New Delhi, Delhi, INDIA|P. Kataria, Vision Research Lab, Dr Ram Manohar Lohia Hospital and Post Graduate Institute of Medical Education and Research, New Delhi, Delhi, INDIA|U.C. Garga, Department of Radio-Diagnosis, Dr Ram Manohar Lohia Hospital and Post Graduate Institute of Medical Education and Research, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: Cross-sectional assessment of connective tissue changes by high-resolution surface coil orbital MRI was performed in Indian subjects to establish age specific normative data in this group and aid trans-ethnic comparison with Caucasian subjects, where these changes have now been found to be causal for the genesis of the “sagging eye syndrome” (SES), a small-angle mechanical strabismus associated with symptomatic diplopia.

Methods: 52 orbits of 27 adult non-strabismic subjects in the age group between 18-40 years (Group A, n=18 subjects (36 orbits), average age=25±5.6 years, M:F::10:8), 41-60 years (Group B, n=05 subjects (10 orbits), average age=46.4±4.7 years, M:F::2:3) and >60 years (Group C, n=04 subjects (08 orbits), average age=74±6.3 years, M:F::3:1) were imaged by high-resolution fast spin echo T2 weighted (T2FSE) surface coil MRI sequences with the subject fixating at a central target (1.5T, Siemens Symphony). 2 mm thick quasi-coronal image planes perpendicular to the orbital axis were analysed for extra-ocular muscle (EOM) pulley locations, EOM cross-sections and LR-SR band length while quasi-sagittal and axial planes were used to analyse rectus EOM length, all by Image J software as per published norms.

Results: The average LR-SR band length was 8.6±2.2 mm in Group A, 10.5±2.7 mm in Group B and 15.5±2.4 mm in Group C. The inter-group differences were significant at p≤0.05 with the Group A versus Group B difference being 0.03, Group B versus Group C difference being 0.001 and the Group C versus Group A being 2.65785E-09 (Figure 1).

Conclusions: Age-related connective tissue changes in non-strabismic Indian subjects were similar to those observed in Caucasian subjects. This may translate as the basis of strabismus due to SES in this ethnic group.

CONTROL ID: 3534838

SUBMITTER (NAME ONLY): Uri Soiberman

TITLE: Reduced WNT10A in keratoconus corneal epithelium and Bowman's layer and upregulation of collagen I suggest Wnt signaling as a therapeutic target

SESSION TITLE: Keratoconus and Corneal Biomechanics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Soiberman, J.W. Foster, M. Lu, A.S. Jun, C. Eberhart, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|S. Chakravarti, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The hallmark of keratoconus (KC) is biomechanical failure of the cornea, with fragmentation of Bowman's layer (BL) contributing to reduced corneal strength. Proteomic studies of collagen I in the KC corneal epithelium have shown underexpression of this major structural component of the extracellular matrix. Collagen I spatially localizes to BL and is produced in part by corneal epithelium. Wnt signaling, which regulates extracellular matrix production, has been shown to be dysregulated in KC, and our transcriptomic study of progressive KC corneal epithelium demonstrates underexpression of WNT10A mRNA. However, it is unclear whether WNT10A regulates collagen I expression in the corneal epithelium.

Methods: RNA-sequencing was performed on corneal epithelium samples of five progressive KC and five myopic control eyes. WNT10A underexpression was validated using TaqMan qPCR on 31 additional independent samples; protein level validation with Western blot analysis. Immunohistochemistry was performed on tissue microarrays containing cores from over 100 KC and control cases. Additionally, WNT10A was overexpressed in vitro in immortalized corneal epithelial cells.

Results: WNT10A was underexpressed in KC corneal epithelium as compared to myopic controls (transcript ratio KC/control=0.59, $p=0.02$ per RNA-sequencing study; transcript ratio=0.66, $p=0.03$ per qPCR; protein ratio=0.07, $p=0.06$ per Western blot). Immunohistochemical analysis demonstrated WNT10A absence or marked decrease in BL of KC corneas ($p<0.0001$). Finally, WNT10A positively regulated COL1A1 expression in corneal epithelial cells (protein ratio=11, $p=0.02$).

Conclusions: Though long suggested historically, our results provide for the first time a potential molecular mechanism supporting the hypothesis that alterations of the epithelium contribute to stromal pathogenesis in KC. Specifically, we find that WNT10A promotes COL1A1 expression, and hypothesize that when WNT10A levels are low, reduced deposition of collagen I in BL may compromise biomechanical strength and potentiate breaks typical of KC. These studies also suggest that the Wnt pathway represents a therapeutic target, as its manipulation in the corneal epithelium may induce collagen I production and increase tensile strength in KC.

CONTROL ID: 3534850

SUBMITTER (NAME ONLY): Kassandra Xanthopoulou

TITLE: Reliability of successive corneal tomography and biomechanical measurements by Pentacam® and Corvis ST® in keratoconus patients without treatment and after corneal crosslinking

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Xanthopoulou, C. Munteanu, B. Seitz, E. Flockerzi, Ophthalmology, Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Homburg/Saar, Saarland, GERMANY|M.W. Belin, Ophthalmology & Vision Science, The University of Arizona James C Wyant College of Optical Sciences, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the reliability of successive measurements of corneal tomography and biomechanics measured by Pentacam® and Corvis ST® (CST, Oculus, Wetzlar, Germany) in keratoconus (KC) patients at least two years after corneal crosslinking (CXL) compared to untreated KC cornea.

Methods: Three successive corneal tomography (n=28 eyes of 21 patients) and biomechanic measurements (n=23 eyes of 16 patients) per eye were performed in the two years after CXL group (CXLG) including mild to advanced KC stages. Two control groups were formed consisting of non-operated and stage-matched KC corneas according to Belin's ABCD classification, the first including KC cornea with three successive Pentacam measurements (n=26 of 24 patients, Pentacam controls, PC) and the second including KC cornea with three successive CST measurements (n=26 of 26 patients, CST controls, CSTC). Main outcome measures included K1, K2, Kmean, astigmatism for anterior and posterior corneal curvature, Kmax, thinnest pachymetry and the KC indices (tomography) and the biomechanical parameters that are included within the Corvis Biomechanical Index (CBI: A1 velocity, DA ratio 2mm, ARTh, integrated radius and SP-A1).

Results: All tomographic parameters in the CXLG and PC group showed excellent reliability (Cronbach's $\alpha > 0.95$) as well as good intra-class correlation coefficients (ICC: CXLG > 0.92 , PC: > 0.709), except for the Index of Height Asymmetry (Cronbach's α : CXLG 0.855, PC: 0.605; ICC: CXLG: > 0.782 , PC: > 0.585). The CST measurements showed better reliability in the CXLG than in the CSTC (Cronbach's α , CXLG|CSTC: A1 velocity: 0.943|0.912, DA ratio 2mm: 0.931|0.906, ARTh: 0.976|0.433, SP-A1: 0.839|0.524). Only the integrated radius showed a better reliability in the CSTC (0.974) than the CXLG (0.857).

Conclusions: Corneal tomography parameters showed excellent reliability independent of preceding CXL with the exception of the KC Index of Height Asymmetry (IHA). The biomechanical parameters turned out to show a better reliability two years or longer after CXL than in untreated cornea with the exception of integrated radius. Despite an overall high reliability of both devices, repeated CST measurements could be useful in the precise evaluation of progression using corneal biomechanics in untreated KC.

CONTROL ID: 3534853

SUBMITTER (NAME ONLY): Mohajeet Bhuckory

TITLE: Retinal integration with a subretinal honeycomb-shaped prosthesis

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In patients with geographic atrophy, subretinal photovoltaic implants with 100µm pixels provided prosthetic acuity of 1.1-1.3 pixels (20/460 – 20/560). Rats with implants of 75 and 55µm pixels also demonstrated grating acuity matching the pixel pitch. However, stimulation threshold increases for smaller pixels in the current design and exceeds the charge injection limit with pixels below 40µm. To decrease the stimulation threshold and decouple it from the pixel width, we added honeycomb-shaped vertical walls surrounding each pixel. This approach relies on migration of the retinal cells into the honeycomb wells. Here, we investigate the structural integration of the inner retinal cells with the wells and its effect on retinal stimulation.

Methods: To evaluate the effect of honeycombs on retinal stimulation, 25µm tall walls were polymerized on flat photovoltaic arrays with 40µm and 20µm pixels. Visually evoked potentials (VEP) were recorded weekly for 9 weeks after implantation of the arrays beneath the degenerate rat retina. Retinal anatomy was examined by confocal imaging of immunolabelled whole mounts.

Results: With both, flat and honeycomb implants, VEP amplitude decreased after the day of implantation and then gradually increased back to the original level during 6-9 weeks post-op. However, stimulation thresholds with honeycombs and flat implants of both pixel sizes remained the same: $0.057 \pm 0.029 \text{ mW/mm}^2$. Majority of cells populating the wells were cone and rod bipolar cells, and much fewer horizontal cells. The macro- and micro-glial response to the honeycomb implants were comparable to that with flat implants and to the degenerate retina controls. The deep capillary plexus (DCP) and amacrine cells, as well as the inner plexiform layer remained entirely above the honeycomb walls.

Conclusions: Retinal migration into the honeycombs does not negatively affect its electrical excitability. Lack of cell death indicates that DCP above the wells provides oxygenation and nutrients to cells within the wells. Comparable glial response to flat implants suggests that migration and separation of the retinal cells by the walls does not cause additional stress. The 25µm deep wells accept majority of the INL, while leaving the tertiary neurons, such as amacrine and ganglion cells, outside. This is important for selective stimulation of the secondary neurons and preservation of the inner retinal signal processing in prosthetic vision.

CONTROL ID: 3534861

SUBMITTER (NAME ONLY): Gurbani Kaur

TITLE: Eye and Orbit Injuries Caused by Electric Scooters and Hoverboards in the United States, 2014-2019

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Electric scooters (e-scooters) and hoverboards are novel personal motorized vehicles. Herein, we comparatively evaluated eye and orbit injuries in non-electric, e-scooter, and hoverboard riders in the United States between 2014-2019.

Methods: We queried the National Electronic Injury Surveillance System (NEISS) for head and neck injuries by body part codes related to non-powered scooters and powered scooters/hoverboards from 2014-2019. We used NEISS complex sampling design to obtain US population projections of injuries and hospital admissions. We queried keywords in case narratives to capture eye and orbit injuries and analyze trends in location, type, and mechanism of ophthalmologic injuries.

Results: A total of 92368 (95% CI, 65633-119107) and 22217 (95% CI, 9761-34673) non-powered and e-scooter injuries occurred. Since its introduction in 2015, 19227 (95% CI, 11308-27148) hoverboard injuries occurred. In contrast to a 24% ($p=0.002$) decrease in non-powered scooters injuries from 2014 to 2019, e-scooter injuries increased 586% ($p=0.01$) and hoverboard injuries increased 866% ($p<0.001$). Increased hospital admissions were associated with non-powered scooters (55.88%, $p=0.03$) and e-scooters (1093%, $p=0.47$). Among all age groups, young adults (18-34) were most injured accounting for 43% of e-scooter injuries in 2019, while specifically experiencing a 5980% ($p=0.002$) uptick in e-scooter injuries. Urban e-scooter cases increased by 830%. (Figure 1)

Descriptive narratives noted eye injuries in 242 unweighted NEISS cases, yet only 30 cases were documented under body part code 77: eyeball. Eye injuries increased 96.9% during the study period ($p=0.23$). The most common ophthalmologic injuries reported included eyebrow (40.9%) and eyelid (11.3%) lacerations, periorbital contusions (18.7%), orbit fractures (6.6%), and corneal abrasions (5.1%). E-scooter riders sustained 5 times more orbit fractures compared to no-powered scooter riders. Ejection and riding while intoxicated increased over the study period as mechanisms of injury with e-scooters (Figure 2).

Conclusions: From 2014-2019, there were significant increases in both head and neck injury cases and hospital admissions related to e-scooters. Eye injuries similarly increased but were under-reported by body part code compared to the injury narratives.

CONTROL ID: 3534869

SUBMITTER (NAME ONLY): Mia Sheindlin

TITLE: Color Contrast Threshold Testing- Novel Method to Evaluate Acquired Color Vision Deficits in Patients with Macular Edema

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.G. Sheindlin, J. Sheindlin, M. Harooni, N. Ragusa, The Bronx Eye Center, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Color contrast threshold testing is not typically explored in the clinical setting to test for worsening visual health. We developed a novel approach to test color contrast threshold testing to evaluate subtle color vision deficits. This feasibility study utilized a retrospective chart review from a clinical retina practice where color contrast threshold testing results from patients with and without macular edema were compared.

Methods: Color contrast threshold testing was performed on all patients. Patients with Snellen visual acuity less than 20/70 were excluded. Patients with retinal vascular disease were divided into two cohorts: patients with macular edema and without macular edema. Macular edema was based on clinical findings including cystic changes on OCT testing and clinical evaluation which was documented on patients' charts from that visit. In this study, macular edema was either from diabetic retinopathy, central retinal vein occlusion, or branch retinal vein occlusion. Additional data collection included age, gender, lens status, OCT central macular thickness (Heidelberg Spectralis), and results were compared to age matched controls. T-tests with bonferroni corrections were used to test for significance in quantitative variables.

Results: 108 eyes from 54 patients were identified and included in this study. 3 eyes from 2 patients were excluded for not meeting visual acuity requirements, and 20 eyes from 10 patients were excluded for having incomplete data sets. Across all colors, average color vision threshold values were significantly greater in patients with macular edema as compared to patients without (1420.60 vs. 669.05) (52.90%). Green showed the highest difference (202 vs. 92) (80.77%), while red showed the least difference (360 vs. 197) (45.28%).

Conclusions: This study showed the feasibility of our diagnostic tool to evaluate worsening acuity in patients with relatively healthy vision measurements and coexisting macular edema. Our examination detected worsening color vision, while Snellen visual acuity and OCT thickness measurements remained relatively equal between the two cohorts. Further work is required to define the application of this new technology across various ophthalmic conditions.

CONTROL ID: 3534920

SUBMITTER (NAME ONLY): Michael Raizman

TITLE: ONSET-2 Phase 3 Study of OC-01 Nasal Spray for the Treatment of Dry Eye Disease

SESSION TITLE: Dry eye clinical treatments

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Raizman, New England Eye Center, Boston, Massachusetts, UNITED STATES|J.

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ABSTRACT BODY:

Purpose: Tear film instability leads to symptoms of ocular discomfort and signs of decreased tear production. OC-01 (varenicline), a novel compound delivered via nasal spray, is a nicotinic acetylcholine receptor agonist that activates the trigeminal parasympathetic pathway to stimulate the lacrimal functional unit to reestablish the natural tear film. This Phase 3 study (ONSET-2) evaluated the efficacy and safety of OC-01 in treating the signs and symptoms of dry eye disease (DED).

Methods: The study randomized 758 subjects at a 1:1:1 ratio to receive 0.6 mg/mL OC-01 nasal spray (N=260), 1.2 mg/mL OC-01 nasal spray (N=246), or placebo (vehicle) nasal spray (N=252) twice daily for 28 days. Outcome measures included anesthetized Schirmer's Test Score (STS) and Eye Dryness Score (EDS, 0-100 scale) at Day 28.

Results: Subjects treated with OC-01 nasal spray showed statistically significant improvement compared with placebo as indicated by a gain in STS of ≥ 10 mm from baseline by Day 28. The percentage of eyes showing improvement in the 0.6 mg/mL, 1.2 mg/mL, and placebo groups were: 47.3% ($p < 0.0001$ compared to placebo), 49.2% ($p < 0.0001$) and 27.8%, respectively. Mean change in STS was 11.3 mm ($p < 0.0001$), 11.5 mm ($p < 0.0001$), and 6.3 mm, respectively (Fig.1). A robust and (nominally) significant reduction in EDS from baseline was demonstrated with 0.6 mg/mL and 1.2 mg/mL compared to placebo at Week 2 of -16.5 mm ($p < 0.05$), -17.9 mm ($p = 0.0078$) and -12.7 mm; and at Week 4 of -19.8 mm ($p < 0.05$), -22.2 mm ($p = 0.0014$), and -15.4 mm, respectively (Fig.2). The improvement in EDS at Day 28 was evident, regardless of baseline EDS categorization, indicating that OC-01 would benefit a broad population of DED patients. The most common adverse event in the 0.6 mg/mL and 1.2 mg/mL groups was sneezing (95.0% and 96.7%, respectively).

Conclusions: Compared to placebo, OC-01 nasal spray demonstrated improvement in both signs and symptoms of DED by Day 28 despite baseline EDS and has an excellent safety and tolerability profile under conditions of the study.

CONTROL ID: 3534923

SUBMITTER (NAME ONLY): Armin Farahvash

TITLE: Understanding the Mechanism of Retinal Displacement Following Surgical Management of Rhegmatogenous Retinal Detachment: A Computer Simulation Model

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Farahvash, R.H. Muni, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|S.B. Marafon, R.H. Muni, Ophthalmology, St Michael's Hospital, Toronto, Ontario, CANADA|A. Ramchandran, Chemical Engineering and Applied Chemistry, University of Toronto Faculty of Applied Science and Engineering, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The management of rhegmatogenous retinal detachment (RRD) involves the use of intraocular tamponades. The most common types of vitreous substitutes include intraocular gas and silicone oil (SO). Retinal displacement, also described as a low integrity retinal attachment (LIRA), is a common complication that occurs after RRD repair, particularly following pars plana vitrectomy (PPV). Here, we developed a theoretical computer model to investigate the physical factors that contribute to retinal displacement.

Methods: We developed a computer simulation model on MATLAB to calculate the contact angle and pressure between the endotamponade and the retina using interfacial tension and the densities of gas, SO, and the vitreous. A second simulation was used to determine the dynamics of fluid motion in the subretinal space and to calculate any deformations of the retina.

Results: We demonstrated that the larger the volume of a gas tamponade, the greater the contact pressure on the retina over a greater area of contact. A gas tamponade that filled 93% of the ocular cavity, as in PPV, exerted a pressure that was four times higher than a tamponade that filled 14% of the ocular cavity, as in pneumatic retinopathy. Moreover, for the same fill ratio, gas had a larger contact angle and contact pressure than SO. At 93% fill, gas exerted a contact pressure of 1.5 mmHg on the retina at a contact angle of 125° , while SO exerted 0.024 mmHg at a contact angle of 100° .

Furthermore, endotamponades stretch the retina by displacing subretinal fluid to non-contact areas, causing retinal displacement. A gas tamponade that filled 14% of the ocular cavity stretched the retina an order of magnitude lower than one that filled 93%, suggesting a greater risk of retinal displacement in PPV. In addition, at the same fill volume, a SO tamponade stretched the retina significantly less than a gas tamponade, indicating that a SO tamponade may confer less risk of retinal displacement.

Conclusions: Our findings suggest that endotamponades stretched the retina by displacing the remaining subretinal fluid after RRD repair. This retinal stretch may be an important mechanism underlying retinal displacement. The degree of gas filling and the type of endotamponade may be modulated to reduce the risk of retinal displacement.

CONTROL ID: 3534931

SUBMITTER (NAME ONLY): Joana Karanxha

TITLE: A Novel Dual-Chamber Vial for Corneal Preservation

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Endothelial cell (EC) loss is the most frequent cause of corneal transplant failure, thus making endothelial preservation critical for good surgical outcomes. Current corneal storage vials (VC) differ greatly from how the cornea exists naturally, where ECs are isolated and physically separated from the epithelium. Our group developed a novel dual-chamber corneal storage vial (DCV) comprised of two compartments that become isolated by the corneal graft and prevent epithelial and endothelial interaction. We hypothesize that the DCV will improve EC viability and better preserve corneal structure during cold storage.

Methods: Donor human cornea pairs (N=9) were recovered by the Florida Lions Eye Bank, with one cornea from each pair stored in the VC and the other in the DCV. All cornea pairs were preserved in Optisol-GS media and stored at 2–8°C for 2 weeks. Corneal thickness and EC density were evaluated at days 1, 7, and 14. Osmolarity was measured in preservation media after 2 weeks. Lactate dehydrogenase and annexin V levels were measured in the media and corneal tissue respectively, to assess for cytotoxicity and apoptosis.

Results: Preliminary results revealed increased corneal thickness in grafts stored in the VC compared to the DCV at days 1, 7, and 14 ($p=0.036$, $p=0.077$, and $p=0.19$, respectively). Osmolarity was significantly increased in both the epithelial ($p=0.0015$) and endothelial ($p=0.0035$) compartments of the DCV compared to the VC, suggesting that smaller volumes in DCV compartments may lead to hyperosmolar conditions that preserve corneal stromal hydration. There was no significant difference in EC density between vials. Despite a small sample size, cytotoxicity was lower in the DCV endothelial media than the VC media in 6 of 8 samples ($p=0.16$), and annexin V concentrations were lower in the DCV endothelium than the VC endothelium in 5 of 6 samples ($p=0.10$).

Conclusions: Use of the DCV decreases corneal swelling, increases osmolarity, and potentially reduces endothelial apoptosis during corneal cold storage by physically separating the corneal epithelium and endothelium. The DCV has the potential to transform the way corneal grafts are preserved and will provide scientists with a platform to develop customized preservation solutions.

CONTROL ID: 3534944

SUBMITTER (NAME ONLY): Yafeng Li

TITLE: Systemic Disease Associations with Angioid Streaks using a U.S. National Healthcare Database

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, J.B. Nadelmann, B. McGeehan, B.L. VanderBeek, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the systemic associations of angioid streaks (AS) using a large U.S. healthcare database.

Methods: This is a retrospective cross-sectional study of all patients diagnosed with AS, identified by ICD9 and ICD10 coding, in a large, national U.S. insurer from 2000 - 2019. All patients were 18 years or older and had at least one active year of enrollment within the plan. Any patient with a diagnosis of choroidal rupture or pathologic myopia were excluded. The literature was reviewed for all published associations with AS, as well as those in the standard mnemonic for AS (PEPSI). The rates of each disease state in those with AS were then calculated.

Results: After applying exclusion criteria, 2,072 patients were eligible for the study. The mean and standard deviation of age for this group is 63.4 (18.5) years, respectively, with 817 (39.4%) males and 1,255 (60.6%) females. The number of patients and rates of association between AS and the well characterized conditions of the PEPSI mnemonic are as follows: Pseudoxanthoma elasticum (PXE) - 258 patients (12.5%), Ehlers-Danlos syndrome - 21 patients (1.0%), Paget's disease - 7 patients (0.3%), hemoglobinopathies (i.e. sickle cell disease) - 33 patients (1.6%), and idiopathic, the largest group -1,756 patients (84.7%). To enumerate the less commonly described but previously reported diseases associated with AS, 514 patients (24.8%) were diagnosed with diabetes, 319 patients (15.4%) familial adenomatous polyposis, 222 patients (10.7%) had lead poisoning, 524 (25.3%) had senile elastosis, and 697 (33.6%) had non-exudative AMD.

Conclusions: AS, pathologically characterized as breaks in Bruch's membrane, has a known significant association with PXE. Concurrently, the association of AS with other less reported diseases lends support to a new mnemonic and new mechanistic understanding of AS formation.

CONTROL ID: 3534961

SUBMITTER (NAME ONLY): Sean Berkowitz

TITLE: Characterization of Ophthalmology Market Saturation and Patient Access

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The national underutilization of eyecare services warrants study of the correlation between geographic market saturation and realized access

Methods: Observational cohort study using datasets from Centers for Medicare & Medicaid Services, U.S. Census Bureau, U.S. Department of Agriculture, and Housing and Urban Development, to calculate county- and state-level ophthalmologic service usage, market saturation, and demographic characteristics. Negative binomial regression models were used to evaluate the association between results and demographic or population-specific variables.

Results: Ophthalmologic service usage ranged from 58.200% to 15.170%, while saturation ranged from 21763.00 to 91.40 FFS beneficiaries per registered ophthalmologist. Usage was statistically significantly associated with several demographic characteristics in each geography: lower proportion of African American ($b = -0.091$, 95% CI: $(-0.159, -0.022)$, $p = 0.009$), Hispanic ($b = -0.226$, 95% CI: $(-0.318, -0.133)$, $p < .001$), and other race beneficiaries ($b = -0.408$, 95% CI: $(-0.520, -0.294)$, $p < .001$), relative to the proportion of white beneficiaries; a higher proportion of female ($b = 2.709$, 95% CI: $(2.347, 3.072)$), $p < .001$ relative to male; a higher proportion of adults having completed an associate degree or some college ($b = 0.255$, 95% CI: $(0.098, 0.412)$), $p = 0.001$, or holding a bachelor's degree or higher ($b = 0.405$, 95% CI: $(0.301, 0.508)$), $p < .001$, relative to the proportion of adults with only a highschool diploma; a lower proportion of adults in each geography experiencing poverty ($b = -0.236$, 95% CI: $(-0.413, -0.060)$, $p = .009$), geographies with lower Multidimensional Deprivation Index ($b = -0.234$, 95% CI: $(-0.358, -0.109)$, $p < .001$); a higher urban-influence code ($b = 0.008$, 95% CI: $(0.006, 0.010)$, $p < .001$).

There was no significant correlation between the usage of ophthalmologic services and the geographic market saturation of ophthalmologists (Spearman's $\rho = -0.030$, $p = 0.227$).

Conclusions: Ophthalmologic service usage is significantly influenced by population demographics and contextual factors. The presence of more ophthalmologists may benefit local population health; however, increased provider density alone appears insufficient to promote the usage of eye care services. As ophthalmologists try to meet the needs of their local population, focus on individual and contextual barriers may help increase realized access and improve population health.

CONTROL ID: 3534993

SUBMITTER (NAME ONLY): Nemanja Milićević

TITLE: Highly-enriched retinal pigment epithelium and photoreceptor genes without circadian variability

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: A number of physiological processes in retinal pigment epithelium (RPE) and photoreceptors (PR) are regulated by the circadian clock. In this study, we tested the hypothesis that circadian clock-regulated genes in RPE and PR overlap with the current lists of known “signature” RPE and PR genes. We defined new lists of highly-enriched RPE and PR genes by using arrhythmic clock gene mutant $Per1^{-/-} Per2^{Brdm1}$ mice.

Methods: We performed RNA-sequencing on laser-capture microdissected (LCM) RPE and PR from WT and $Per1^{-/-} Per2^{Brdm1}$ mouse eyes obtained under constant darkness at 4 time-points over 24h. We compared time-affected genes from WT RPE and PR with current “signature” RPE and PR gene lists. To define the new list of non-rhythmic highly-enriched RPE and PR genes, we first averaged gene expression levels obtained at all time points from RPE and PR genes obtained from $Per1^{-/-} Per2^{Brdm1}$ mice. We ranked the top 10% genes based on expression levels, subtracted overlapping and time-affected genes. Functional annotation was performed using g:Profiler.

Results: RNA sequencing of LCM samples revealed that 594 genes (~3% total) in the RPE and 2,372 genes (~10% total) in PR showed temporal variations in WT mice. In contrast, only 2 genes were time-affected in $Per1^{-/-} Per2^{Brdm1}$ PR and none in RPE. We found that 2 (out of 64) RPE and 12 (out of 65) PR “signature” genes were time-affected. Unexpectedly, we found overlap between “signature” genes of PR and time-affected RPE genes (and vice versa) suggesting that sampling time affected the compiling of current “signature” genes. By using transcriptomes obtained from $Per1^{-/-} Per2^{Brdm1}$ mice, we defined 828 non-rhythmic highly-enriched RPE and 641 PR genes. We found that highly-enriched RPE genes are enriched in MAPK signaling, focal adhesion and oxidative phosphorylation, whereas PR genes are enriched in mTOR signaling and GTPase activity, among others. Finally, we found that 37 RPE and 9 PR genes overlap between “signature” and our new highly-enriched gene lists.

Conclusions: Our findings indicate that sampling time substantially affected the compiling of “signature” RPE and PR genes. Our new lists will be useful in a number of applications such as extrapolating RPE and PR data from whole eye transcriptomics and for assessing the molecular characteristics of stem-cell derived RPE and PR.

CONTROL ID: 3535002

SUBMITTER (NAME ONLY): Chaipayorn Vatanatham

TITLE: Comparison of various statistical methods for calculating laser flare photometry values in patients with uveitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.L. Chen, G.N. Holland, E. Tsui, Ophthalmology, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|C. Vatanatham, G.N. Holland, E. Tsui, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|N.J. Jackson, Division of General Internal Medicine and Health Services Research, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate various statistical methods of calculating laser flare photometry (LFP) values in patients with uveitis. The currently accepted approach to calculating LFP values is to obtain 7 measurements, delete the highest and lowest values, and use the mean of the 5 remaining values to reflect the level of anterior chamber (AC) flare.

Methods: Patients with a history of uveitis were prospectively enrolled and underwent comprehensive eye examinations and grading of AC flare with a modified Standardization of Uveitis Nomenclature (SUN) grading system, which included Grade 0.5+. Seven repeat LFP measurements were obtained on both the Kowa FM-500 (used originally to establish the current approach) and FM-700 laser flare meters during a single visit. Eight statistical methods were utilized to compare LFP measurements, including: 1) comparison of raw data; 2) mean of raw data; 3) mean after removal of highest and lowest values; 4) median of raw data; 5) Median Absolute Deviation (MAD) outlier detection with mean (high threshold of 2.24); 6) MAD outlier detection with mean (low threshold of 1.28); 7) boxplot outlier detection (Carling method) with mean; and 8) boxplot outlier detection (Tukey method) with mean. LFP values were also compared with the SUN grading system. Agreement between the FM-500 and FM-700 was characterized using intraclass correlation coefficients (ICC).

Results: LFP was performed on 126 eyes (64 patients, mean age 42.3±22.7 years, 45/64 [70.3%] female). Distribution of AC flare SUN grades were Grade 0 (n=48 eyes), 0.5+ (6), 1+ (28), 2+ (16), 3+ (6), 4+ (2). Mean LFP values for each grade were: Grade 0 (mean=10.2, range [0, 98]), 0.5+ (19.5, [0, 41.9]), 1+ (16.4, [1.8, 359]), 2+ (24.6, [0, 100.9]), 3+ (135.0, [5.7, 325.5]), 4+ (166.4, [69.3, 377.5]). Mean LFP values (photon units/msec) on the FM-700 across the 8 methods were 23.33, 23.71, 21.08, 22.88, 22.90, 22.81, 22.83, 22.92, respectively. Across all 8 methods, the ICC for LFP values between the two flare meters did not vary substantially, with a range of ICC from 0.81 to 0.84. LFP values correlated with SUN grades (correlation coefficients 0.68-0.72 across all 8 methods, all p<0.001).

Conclusions: All eight statistical methods for calculating LFP values resulted in similar flare values compared to the current standard, suggesting that alternative, simpler methods of calculating LFP values may be suitable.

CONTROL ID: 3535006

SUBMITTER (NAME ONLY): Maria Zaretskaia

TITLE: Ocular pharmacokinetics of a novel class of corticosteroids with ROCK inhibitory activity and potential for reduced steroid-associated risks

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.V. Zaretskaia, K. Carbajal, C.L. Lichorowic, J.M. Sturdivant, M. Germann, C. Romeo, K. Crews, A. Glendenning, M. Weksler, A. McDougal, M.A. deLong, C. Lin, C. Kopczynski, D.A. Hollander, J. White, Research & Development, Aerie Pharmaceuticals Research and Development, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The anti-inflammatory efficacy of corticosteroids in ocular inflammatory conditions is well-established. However, risks of long-term steroid use include steroid-induced ocular glaucoma, which is thought to develop as extracellular matrix proteins accumulate and impair proper function of the trabecular meshwork (TM). Rho kinase inhibition (ROCKi) has been shown to attenuate steroid-induced collagen and fibronectin deposition in cultured TM cells. Furthermore, ROCKi has been shown to lower IOP by increasing aqueous outflow through the TM. Inhibition of ROCK during steroid use for ocular inflammatory conditions may provide a strategy to decrease the risk for steroid-induced glaucoma. Here we demonstrate the in-vitro stability and corneal metabolism of a new class of corticosteroids with ROCKi activity. We also show the ocular tissue distribution of lead candidates, and their metabolites, following topical instillation.

Methods: Multiple compounds were synthesized to contain a steroid covalently linked to the active metabolite of netarsudil, AR-13503. The in vitro stability and ex vivo corneal metabolism of the compounds were determined. Ocular tissue distribution in mice was measured post-tissue harvest by HPLC-mass spectrometry following topical administration of these compounds.

Results: Lead compounds demonstrated good stability profiles in vitro. The corticosteroid and ROCKi metabolites were detected in corneal explants. Following topical dosing with the ROCK-steroids, physiologically relevant levels of both corticosteroid and the ROCKi were found in the cornea, conjunctiva, and meibomian glands of mice.

Conclusions: We have developed a novel corticosteroid with inhibitory activity against ROCK and, thus, strong potential to reduce risks associated with conventional corticosteroids. Our data demonstrate the favorable pharmacokinetic profile of ROCK-steroid compounds for topical anti-inflammatory applications.

CONTROL ID: 3535013

SUBMITTER (NAME ONLY): Runjie Bill Shi

TITLE: Novel Home Monitoring of Visual Fields with the Toronto Portable Perimeter

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.B. Shi, W. Wong, University of Toronto Institute of Biomaterials and Biomedical Engineering, Toronto, Ontario, CANADA|R.B. Shi, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|R. Saha, Y. Buys, G. Trope, M. Eizenman, University of Toronto Department of Ophthalmology and Vision Sciences, Toronto, Ontario, CANADA|Y. Li, W. Wong, University of Toronto The Edward S Rogers Sr Department of Electrical and Computer Engineering, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: To investigate home visual field monitoring with the Toronto Portable Perimeter (TPP) by glaucoma patients in a prospective cohort study.

Methods: Patients with reliable visual fields on the Humphrey Field Analyzer (HFA) were recruited from the Glaucoma Clinic at Toronto Western Hospital. Each participant was instructed in a 20-min session on using the TPP and performed a bilateral TPP-Standard 24-2 protocol. Then, participants were instructed to perform bilateral tests at least twice monthly at home with a personal TPP. Mean deviation (MD), pattern standard deviation (PSD) and test duration of reliable visual fields on the TPP were compared with the most recent reliable HFA SITA-Standard results. A reliable test was defined as: false positive < 20%, false negative < 20%, fixation loss < 33%. Inter-test variability was measured by calculating the root mean squared error (RMSE) of MDs and PSDs in consecutive visual field tests of the same eye.

Results: To date 148 reliable home TPP visual field tests were performed by 8 patients (mean age: 70 years; range: 53 to 81) on 16 eyes (mean HFA MD: -6.05 dB; -13.19 to +0.54). Patients completed home TPP visual field tests at an average rate of 2.8 tests per 30 days (0.9 to 4.3). Compared to HFA there were no significant differences in MD (mean±std: +0.61±1.74 dB, p=0.18); PSD (-0.79±1.43 dB, p=0.04) were significantly lower and test durations (-30.11±46.11 seconds, p=0.02) shorter with TPP. Inter-test variability of MD was similar between the TPP and HFA (1.23 vs. 1.47 dB, p=0.50) while inter-test variability of PSD (0.59 vs. 1.64 dB, p<0.01) was better (lower RMSE) with TPP. In 14 eyes with 5 reliable home tests, the standard error of the mean estimates of MD and PSD in each eye was reduced to 0.32 dB and 0.22 dB, respectively.

Conclusions: Our preliminary results showed that glaucoma patients can perform TPP visual fields reliably at home. Results from the TPP were similar to the HFA. Consecutive tests at home exhibited less variability than consecutive tests on the HFA. Testing on the TPP took less time than HFA (on average 5.6 min on the TPP vs. 6.0 min on the HFA, and no requirement to visit a testing center). Patients also found home tests to be more convenient and relaxing. Frequent testing over short periods of time appears to improve MD and PSD precision and thus may potentially enable earlier detection of change.

CONTROL ID: 3535015

SUBMITTER (NAME ONLY): Glory Mgboji

TITLE: Keratoconus: Trends in Management and Adherence to Preferred Treatment Patterns

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Mgboji, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|V. Varadaraj, U. Soiberman, D. Srikumaran, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The treatment of keratoconus has evolved over the past decades to include advanced contact lenses, intrastromal implants, and corneal crosslinking in addition to keratoplasty— all of which are most appropriate at different stages of disease. We performed a retrospective review to elucidate current trends and identify potential disparities in keratoconus treatment.

Methods: We extracted data from electronic medical records of 1,135 patients with keratoconus seen at the Wilmer Eye Institute from January 2017 to September 2020. We used t-tests and chi square tests to detect associations between patient characteristics and various treatment modalities, including corneal crosslinking and keratoplasty. Logistic regression models adjusted for age, sex, race, insurance, and family history of allergies were constructed to calculate odds ratios (OR) describing these associations.

Results: A total of 1,135 patients with a mean age of 40.5 (SD 16.5), were included, about half of whom were white (51.5%). In unadjusted analysis, patients who were younger (25.0 vs. 42.3 years), male (73.9% vs. 26.1% for females), white (52.3% vs. 25.2% for black patients) and who had private insurance (94.6% vs. 5.4% for government insurance) were significantly ($p < 0.05$ for all) more likely to have had corneal crosslinking. No factor was associated with keratoplasty during this period. In a multivariable logistic regression model, black patients had lower odds of receiving corneal crosslinking compared to white patients (OR 0.58 95% CI 0.34-0.98). Increasing age was also associated with lower odds of corneal crosslinking (OR 0.91 95% CI 0.89-0.93).

Conclusions: This study identifies racial disparities in keratoconus management with corneal crosslinking. These results are of interest as most health care payors have only recently started to endorse CXL as a covered benefit. Further analyses are needed to determine whether these disparities are related to socioeconomic barriers, disease severity, insurance coverage or other factors.

CONTROL ID: 3535016

SUBMITTER (NAME ONLY): Ashley Kras

TITLE: Extending interoperability in ophthalmology through Fast Healthcare Interoperability Resource (FHIR)

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kras, M. Roe, Verana Health, California, UNITED STATES|W. Oliver, Oculo, Victoria, AUSTRALIA|M.C. Gillies, University of Sydney, New South Wales, AUSTRALIA|M. Mair, S. Chu, HL7 Patient Care Workgroup, NEW ZEALAND|N. Morlet, The University of Western Australia, Perth, Western Australia, AUSTRALIA|M. Mbagwu, T. Leng, Stanford University, Stanford University, Stanford, CA, US, academic, California, UNITED STATES|T.S. Hwang, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: The US 21st Century Cures Act promoted Healthcare Level Seven's (HL7's) FHIR API utilization to facilitate real-time health data interoperability. FHIR standards have the potential to mobilize siloed digital clinical data to improve healthcare quality, outcomes and value. Although many FHIR resources have been validated, their applicability to ophthalmology remains limited, presenting challenges to practical specialty adoption and clinical utility.

Methods: To counter this problem, a multidisciplinary collaboration of ophthalmologists, technologists, HL7 representatives, and industry stakeholders compiled an implementation guide (IG) driven by a series of real-world interoperability ophthalmic 'use cases.' FHIR IG development is a semi-structured process defining the technical artifacts and contextual content required to solve such problems.

Manual assembly of FHIR base resources referencing existing terminologies (e.g. SNOMED-CT, LOINC, ICD) has aided the foundational codification of clinical, administrative, and workflow elements. Where resource limitations deemed essential to meet use-case defined requirements were identified, FHIR's flexibility enabled the creation of appropriate extensions, constraints and new value sets. This IG will undergo testing at FHIR connectathons prior to formal submission for H7 international balloting.

Results: We developed 15 use cases to inform IG compilation and published a live, web-accessible IG (based on FHIR v4.0.1), enabling collaborative refinement of FHIR profiles and accompanying content. This provides clinical and implementation guidance, incorporating numerous ophthalmology-specific modifications, such as a uniquely structured laterality definition and novel representations of diagnostic device derivations.

This project has obtained unanimous project support from required HL7 voting procedures, gained formal sponsorship from HL7's Patient Care and EHR Working Groups and approval from the FHIR Management Group, and Clinical Steering Division approval.

Conclusions: Mapping ophthalmology's entire clinical lexicon into FHIR format enables unprecedented healthcare data exchange possibilities. Our framework facilitates iterative IG expansion and validation for clinical accuracy and technical functionality. Drawing broad specialty stakeholder engagement to advance adoption, this serves to improve clinical care quality and patient outcomes.

CONTROL ID: 3535017

SUBMITTER (NAME ONLY): Po Hsiang (Shawn) Yuan

TITLE: Retrospective large-cohort evaluation of trans-epithelial phototherapeutic keratectomy (PTK) for recurrent corneal erosion syndrome (RCES)

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Yuan, G. Ching, M. Bizrah, S. Holland, Department of Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|M. Bizrah, Western Eye Hospital, Imperial College Healthcare NHS Trust, London, London, UNITED KINGDOM|S. Holland, Pacific Laser Eye Center, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: To contribute the largest retrospective study to date on the efficacy of PTK as a treatment for RCES in patients with symptoms refractory to conventional treatments

Methods: A retrospective chart review and telephone survey were conducted in Vancouver, Canada at the Pacific Laser Eye Centre. Inclusion criteria were patients who received PTK for RCES between 2010 and 2020. Exclusion criteria were patients with comorbidities potentially affecting treatment efficacy including band keratopathy, secondary scarring of the cornea from previous ulceration, Salzmann's nodular dystrophy, granular dystrophy, and Reis-Bückler's corneal dystrophy.

555 patients' sex, age, past ocular history, etiology of RCES, symptoms, visual acuity, interventions trialled prior to PTK, need for retreatment, and time to retreatment were collected in a chart review. 112 patients answered the following in a 10-minute telephone survey: symptoms that led them to seek treatment, the presumed cause of their RCES, efficacy of PTK, therapies trialled prior to and following PTK, and overall satisfaction level.

Results: This study included 593 eyes of 555 patients (46.2% male; 50.9 ± 14.2 years old) who underwent PTK for RCES. The leading identified causes of RCES were trauma (45.7%) and anterior basement membrane dystrophy (44.2%). The most common pre-PTK interventions were ocular lubricants (90.9%), hypertonic solutions (77.9%), and bandage contact lenses (50.9%). 36 eyes had undergone surgical interventions such as stromal puncture, epithelial debridement, or diamond burr polishing.

Post-PTK, 78% of patients did not require any subsequent therapies, 20% required ongoing drops and 6 patients (1.1%) reported no symptom improvement. All 6 eyes were successfully retreated with PTK between 11.3 ± 14.9 months from initial PTK. All study patients showed no significant differences in best corrected visual acuity pre- vs. post-operatively.

Conclusions: When compared to other surgical options, PTK is costly but frequently more effective. Most surgical alternatives present cheaper options than PTK for the management of refractive-neutral RCES. Nonetheless, the third-party public health vetted nature of this study, the high patient satisfaction, and the low recurrence rate of RCES suggest that a re-evaluation of the role of PTK as an earlier part of standard management of RCES should be conducted.

CONTROL ID: 3535020

SUBMITTER (NAME ONLY): Dhawal Chobisa

TITLE: Sustained delivery of griseofulvin by polymeric microparticles for neovascular eye disease treatment

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Current treatments for neovascular eye diseases based on anti-vascular endothelial growth factor therapy are ineffective in a significant fraction of patients. In seeking alternative therapeutic targets, ferrochelatase (FECH) has been identified as a promising protein. We set out to develop an injectable, long-acting microparticle (MP) formulation for sustained delivery of griseofulvin (GRF), which is metabolized into a FECH inhibitor.

Methods: GRF was loaded in poly(lactic-co-glycolic acid) (PLGA) MPs by the double emulsion (W1/O/W2) method. GRF and PLGA were added to the organic (O) phase, and magnesium hydroxide ($\text{Mg}(\text{OH})_2$) (0-20 wt%) was added to the internal aqueous (W1) phase. The effects of $\text{Mg}(\text{OH})_2$ content on particle size (laser diffraction), morphology (scanning electron microscopy), and in vitro release were evaluated. The sustained antiproliferative effect of MPs was evaluated on human retinal endothelial cells (HRECs) using an AlamarBlue assay.

Results: The mean particle size (D50) of MPs was measured to be in the range of 15-22 μm (Figure 1a). MPs were spherical with sizes consistent with the laser diffraction measurement. MPs prepared without $\text{Mg}(\text{OH})_2$ had a solid surface, whereas those with $\text{Mg}(\text{OH})_2$ showed porous surfaces. The porosity increased with the amount of $\text{Mg}(\text{OH})_2$ added to the MPs (Figure 1b). MPs without $\text{Mg}(\text{OH})_2$ released ~15% of loaded drug in phosphate-buffered saline (pH 7.4) with 0.2% Tween 80 at 37 °C in 1 day and slowly released the remainder (up to ~80%) in 60 days (Figure 2a). The inclusion of $\text{Mg}(\text{OH})_2$ dramatically changed the GRF release profile. MPs with 20% $\text{Mg}(\text{OH})_2$ showed a high burst release of GRF (~70%), followed by a complete release in 5 days. MPs with 10% and 5% $\text{Mg}(\text{OH})_2$ showed >90% and >75% drug release in 5 days. The MPs containing 2% $\text{Mg}(\text{OH})_2$ showed a minimal burst release (~18% in 1 day) followed by continuous release (~100% in 38 days) and were considered the most suitable for 1 month GRF delivery. GRF released from the MPs throughout the release period remained active and inhibited the proliferation of HRECs (Figure 2b).

Conclusions: GRF-loaded PLGA MP were developed for long-term ocular delivery. The optimized MP formulation provided a sustained release of bioactive GRF over a month and effectively inhibited proliferation of HRECs. These results warrant further evaluation in animal models to test the feasibility of neovascular eye disease treatment.

CONTROL ID: 3535034

SUBMITTER (NAME ONLY): Ke Zeng

TITLE: Effects of lens status on vitreous hemorrhage resolution time

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vitreous hemorrhage is approximated to resolve 1% per day through the trabecular meshwork, but the factors that affect this rate remain unexplored. We performed a retrospective clinical case study to learn how lens status and other factors can affect vitreous hemorrhage (VH) resolution time in proliferative diabetic retinopathy (PDR).

Methods: This is a retrospective analysis of eyes with PDR presenting with acute VH at an academic medical center between May 1, 2015 and December 31, 2019. We gathered information on lens status (phakic and pseudophakic) and other variables including visual acuity, medications, and glaucoma. In the survival analysis, the primary outcome measure was the number of weeks from diagnosis to either 'resolution' or 'progression to surgery', whichever came first. Kaplan-Meier univariate analysis method was used to estimate resolution time, and log-rank test determined significance. Cox proportional hazard regression modeling was used to determine adjusted hazard ratios and predictor variables.

Results: Among 157 total eyes (100 phakic, 57 pseudophakic), the groups were similar in age (57 v. 64 years), visual acuity at presentation (LogMAR 1.33 v. 1.38), past history of VH (41% v. 43%), and progression to surgery (Log-rank=1.422, df=1, p=.23). The mean resolution time was 33.0±4.1 weeks (95%CI: 25.0-41.0) for pseudophakic eyes compared to 63.4±9.1 weeks (95%CI: 45.7-81.2) for phakic ones, with a significant difference in the survival of VH (Log-rank = 7.78, df=1, p=.007). Multivariate cox regression showed pseudophakic eyes were 2.4 times (95%CI: 1.3-4.6, p=.008) more likely to resolve than phakic eyes. Vision at presentation (p=0.51), blood-thinning medication (p=0.63), age (p=0.50), and glaucoma (p=0.28) were not found to be associated with resolution time.

Conclusions: VH secondary to PDR resolves at twice the rate in pseudophakic eyes compared with phakic ones. VH is removed from the eye through the trabecular meshwork, so it is possible that being pseudophakic offers an enhanced pathway around the zonules for red blood cells to travel the posterior segment to the anterior chamber. Being able to account for factors that affect VH resolution better guides patient expectations and decisions on surgery.

CONTROL ID: 3535050

SUBMITTER (NAME ONLY): Mari Ogino

TITLE: New 3D printed Adjustable Eyeglasses to Address the Global Burden of Pediatric Refractive Errors

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ogino, N. Oslie, Medicine, Creighton University, Omaha, Nebraska, UNITED STATES|D. Suh, G. Linke, Ophthalmology, Children's Hospital and Medical Center, Omaha, Nebraska, UNITED STATES|J. Hermesen, none, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Globally, the need for cost-effective delivery of corrective lenses for pediatric refractive error is great. The present study aims to assess the global incidence and financial burden of pediatric refractive error via literature review and to design glasses that provide an accessible and affordable avenue to reduce the burden of refractive errors in pediatric patients.

Methods: The present study involved an investigation into the global need for corrective lenses for astigmatism in resource-poor regions via an extensive literature review. Global prevalence data of refractive error from 1990-2016 WHO regions were extracted and reported as Estimated Pooled Prevalence (EPP). Data on the financial burden of astigmatism was investigated and reported as the United States Dollar (USD) per patient per year. Following the literature review, preliminary designs of cheap, customizable glasses were developed.

Results: In children, the EPP of myopia, hyperopia, and astigmatism was 11.7% (95% CI: 10.5–13.0), 4.6% (95% CI: 3.9–5.2), and 14.9% (95% CI: 12.7–17.1), respectively. (Hashemi 2018) The highest incidence of refractive errors occurs in Southeast Asia and the Americas. The US average financial burden of uncorrected refractive errors (amblyopia, astigmatism) is approximately \$145.92 per patient per year beginning at age 5. Studies have shown that costs tend to increase with time as the severity of the defect increases (Malvankar-Mehta 2018)

The design of the working model is easy to assemble, highly customizable, and affordable. Adjustable straps make the design-friendly to use for those with variable head circumference and anopia. Rotatable lens facilitates adjustment for varied astigmatism axis.

Conclusions: Childhood visual impairment is a global public health problem associated with significant financial strain, especially in low and middle-income countries. Its most common causes are avoidable with comprehensive vision screening and treatment of common refractive errors. The need for a financially feasible and easily accessible solution warrants further research and design of gadgets such as the Adjustable Eyeglasses.

CONTROL ID: 3535051

SUBMITTER (NAME ONLY): ye he

TITLE: Retinal findings on OCT in a convalescent COVID-19 Patient Cohort

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. he, F. Corvi, S.R. Sadda, Retina, Doheny Eye Institute Doheny Image Reading Center, Los Angeles, California, UNITED STATES|Y. he, Retina, Tianjin Medical University Eye Hospital, Tianjin, Tianjin, CHINA|S. Liu, T.L. Yeung, K.K. Li, ophthalmology, United Christian Hospital, Hong Kong, HONG KONG|S. Liu, T.L. Yeung, K.K. Li, ophthalmology, Tseung Kwan O Hospital, Hong Kong, HONG KONG|E.Y. Tso, Medicine and Geriatrics, United Christian Hospital, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Possible retinal involvement by COVID-19 has been a topic of recent debate. We performed a prospective study to determine whether retinal abnormalities can be identified on OCT in convalescent fully recovered patients following COVID-19 infection.

Methods: This is a prospective, case-controlled study that recruited COVID19 patients who were admitted to the United Christian Hospital Hong Kong, China. At 2 months post-recovery, patients' visual acuity, refraction were measured. Spectral-domain OCT of the macula and retinal nerve fiber layer and enhanced depth imaging were performed. Age-matched and refraction-matched healthy individuals that were not infected with COVID-19 were enrolled as controls. Qualitative and quantitative assessment of retinal abnormalities on structural OCT and retinal and choroidal layer thickness are the main outcomes. Principal component analysis (PCA), partial least squares discriminant analysis (PLS-DA), and volcano plot were applied to data analysis.

Results: 20 subjects (40 eyes) with COVID-19 and 25 (50 eyes) age-matched asymptomatic healthy controls were enrolled. Structural OCT abnormalities could be observed in 24% of control eyes and in 25% of COVID-19 subjects. No differences were observed between the post-COVID-19 cohort and the healthy controls for any qualitative retinal abnormalities. PCA and the PLS-DA demonstrated a substantial overlap in the 95% confidence region between the two groups. Further analysis showed there are no significant differences in any quantitative feature including retinal volume, choroidal thickness, retinal layer thicknesses in various macular regions, and peripapillary nerve fiber layer thickness with the exception of the retinal outer temporal quadrant region. However, the impact this quantitative feature has on the dataset is miniscule given that its fold change impact was below 1.0.

Conclusions: Following full recovery from symptomatic COVID 19 infection no significant abnormalities were evident on structural OCT. Although long-term damage to the retina appears to be uncommon after COVID-19 infection, this study provides valuable insight into the recovery process after COVID-19 and provides potential retinal features that should be considered in the larger population to separate between these groups.

CONTROL ID: 3535053

SUBMITTER (NAME ONLY): Bright Ashimatey

TITLE: Regional Capillary Density and Retinal Vascular Reactivity of the Healthy Human Retina

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.S. Ashimatey, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|Z. Chu, X. Zhou, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|A.H. Kashani, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize retinal vascular density and reactivity in the human retina in the macula, temporal macula and peripapillary retina using optical coherence tomography angiography (OCTA).

Methods: OCTA 3*3mm² images were acquired from the macula (M), temporal macula (TM) and peripapillary retina (PP) in 8 healthy subjects. Images from the superficial, deep and choriocapillaris layers of the M and TM were extracted and the vessel skeleton densities (VSD) computed. In addition, the mean flow deficit sizes (MFDS) of the choriocapillaris and mean PP VSD was calculated. Choriocapillaris reactivity (CR) and retinal vascular reactivity (RVR) in each region and layer were assessed under three gas non-rebreathing conditions – room air (RA), 5%CO₂ and 100%O₂. RVR is the percent change in VSD between RA-CO₂ and RA-O₂. CR is computed in a similar manner with MFDS. ANOVA was used to compare the VSD measurements with significance at p=0.05.

Results: Under RA conditions, the mean VSD of the superficial layer was significantly different across regions [M=0.16, TM=0.13, RPV=0.15; F(1,7)=15.6, p=0.006] and a similar trend occurred in the deep layer [M=0.14, TM=0.12; F(1,7)=5.0, p=0.06, Fig 1A]. RVR differed among regions of the superficial layer [M=8%, TM=15%, and PP=7%; F(2,7)=28.22, p<0.001, Fig 1B] and the deep layer [M=19%, TM=37%; F(1,7)=8.7, p=0.02, Fig 1B]. There was a significant heterogeneity in the layer specific vascular reactivities [superficial =12.8%, deep =28.2% and CR =2.8%; F(2,7)=58.03, p<0.001]. However, CR and MFDS did not differ between regions.

Conclusions: There are significant differences in the regional retinal capillary density and vascular reactivity in the macula, temporal macula and peripapillary retina. These regional differences may help explain the spatial distribution of pathology in retinal vascular diseases. Similar regional difference are not present in the choriocapillaris.

CONTROL ID: 3535066

SUBMITTER (NAME ONLY): Anandalakshmi Venkatraman

TITLE: Modulation of In-vitro aggregation properties of TGFB1p peptides by osmolytes and toxicity of disaggregated amyloid fibrils

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Venkatraman, R. Lakshminarayanan, J.S. Mehta, Singapore Eye Research Institute, Singapore, SINGAPORE|J.S. Mehta, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Protein aggregation has been one of the leading triggers of various disease conditions, such as Alzheimer's, Parkinson's and other amyloidosis. TGFB1-associated corneal dystrophies are protein aggregation disorders in which the mutant TGFB1p aggregates and accumulates in the cornea, leading to a reduction in visual acuity and blindness in severe cases. Currently, the only therapy available is invasive and there is a known recurrence after surgery. In this study, we tested the inhibitory and amyloid dissociation properties of four osmolytes in an in-vitro TGFB1p peptide aggregation model. We also tested the toxicity of the disaggregated fibrils on human corneal fibroblasts.

Methods: The 23-amino acid long peptide (TGFB1p 611-633 with the mutation c.623 G>R) from the 4th FAS-1 domain of TGFB1p that rapidly forms amyloid fibrils was used in the study. Several biophysical methods like Thioflavin T (ThT) fluorescence, Circular Dichroism (CD), fluorescence microscopy, and Transmission electron microscopy (TEM) were used to study the inhibitory and amyloid disaggregation properties of four osmolytes (Betaine, Raffinose, Sarcosine, and Taurine). The toxicity of the disaggregated amyloid fibrils on corneal fibroblasts was studied using xCELLigence and Incucyte assays.

Results: The osmolytes were effective in both inhibition and disaggregation amyloid fibrils derived from TGFB1p 611-633 c.623 G>R peptide. The osmolytes did not have an adverse toxic effect on cultured human corneal fibroblast cells and could potentially be a useful therapeutic strategy for patients with TGFB1p corneal dystrophies. The disaggregated amyloid fibrils after treatment with osmolytes did not have any toxic effect on the human corneal fibroblasts.

Conclusions: The osmolytes were not toxic to the human corneal fibroblast cells. The osmolytes were effective to disaggregate the in-vitro amyloid fibrils. The osmolytes were also effective to delay or inhibit amyloid fibril formation in these peptides with G623R mutation. The disaggregated amyloid fibrils after osmolyte treatment added to the human corneal fibroblast cell did not show any toxicity.

CONTROL ID: 3535073

SUBMITTER (NAME ONLY): masahiko tomita

TITLE: Blood flow measurement in retinopathy of prematurity-like fundi induced by vascular endothelial growth factor receptor inhibitors

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. tomita, T. Matsumoto, T. Itokawa, Y. Hori, Department of Ophthalmology, Toho University Omori Medical Center, JAPAN|D. Asano, A. Morita, T. Nakahara, Department of Molecular Pharmacology, Kitasato University School of Pharmaceutical Science, JAPAN|

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor (VEGF) receptor inhibitors can be used to fabricate a rat model that presents with a retinopathy of prematurity (ROP)-like fundus (Nakano et al., 2016). This model of ROP is developed using oxygen-induced retinopathy (OIR). The aim of the present study was to determine the association between the ROP-like fundus and the fundus blood flow.

Methods: This study enrolled a control group of 33 rats and an experimental group of 31 rats, which were subcutaneously administered with a VEGF receptor inhibitor (KRN633; anti-VEGF group) at seven and eight (postnatal) days of age. Subsequently, at two and three weeks of age, the ocular blood flow was measured with Laser Speckle Flowgraphy-Micro and compared between the two groups. After the measurement at three weeks of age, flat-mounted retina specimens were prepared and used to examine the correlations of retinal arterial tortuosity and the avascular region with the blood flow.

Results: At three weeks of age, the mean blur rate (MBR) of the anti-VEGF group was significantly higher than that of the control group ($p = 0.03$). Moreover, the rate of increase in MBR from two to three weeks of age positively correlated with the retinal arterial tortuosity ($r=0.50$ $p=0.0039$).

Conclusions: The MBR of the anti-VEGF group at three weeks of age was significantly higher than that of the control group, identical to a previous experiment that measured the blood flow in OIR. Moreover, higher rates of increase in MBR from two to three weeks of age were associated with greater retinal arterial tortuosity, suggesting that blood flow was higher in the anti-VEGF group than in the control group. Although the reproducibility of this study's results need to be confirmed, they indicate that the pathology of rats with anti-VEGF drug-induced ROP-like fundi correlates with the fundus blood flow. Therefore, in terms of the ocular blood flow, the rat model in the present study can be used as a new model of ROP.

CONTROL ID: 3535074

SUBMITTER (NAME ONLY): Alyssa Lie

TITLE: Age-dependent changes to the free and total water distribution of the in vivo human lens measured by MRI

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.L. Lie, X. Pan, E. Vaghefi, Optometry and Vision Science, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|T.W. White, Physiology and Biophysics, Stony Brook University, Stony Brook, New York, UNITED STATES|P.J. Donaldson, Medical Sciences, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|

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ABSTRACT BODY:

Purpose: To use magnetic resonance imaging (MRI) to noninvasively measure changes in steady-state free and total water gradients in human lenses in vivo with advancing age.

Methods: 57 subjects aged 18 to 86 years were recruited under approval from the University of Auckland Human Subjects Ethics Committee (#017162), fitted with a 32-channel head receiver coil and placed in a 3 Tesla clinical MR scanner. MRI scans of the crystalline lens were obtained using a volumetric interpolated breath-hold examination (VIBE) sequence with dual flip angles, then corrected for field inhomogeneity post-acquisition with a B_1 -map obtained using a TurboFLASH sequence. Corrected lens free water (T_1) and total water (PD) maps were then calculated using an established MRI signal equation (Blüml et al., 1993; Deoni et al., 2003). PD values were normalised to an external water reference included in the scanner. Free and total water profiles along the lens optical axis were extracted using MATLAB custom-written software and the age-dependent changes in parameters determined by linear regression.

Results: No significant changes to either the profile shape or amount of total water in different regions of the lens was observed with age (all $p > 0.05$). Unlike total water, which was linearly distributed across the lens, a gradient in free water that was highest in the periphery and lowest in the central region was observed in all lenses. However, with advancing age, this free water gradient collapsed from an initial parabolic shape in young lenses to one with an enhanced central plateau in older lenses, as indicated by significant increases in the values of the profile shape parameter with age (anterior: 0.067/year, $p = 0.004$; posterior: 0.050/year, $p = 0.020$). Furthermore, with advancing age a significant increase in central free water content was also observed (1.932 ms/year, $p = 0.022$).

Conclusions: MRI can successfully map free and total water distributions of in vivo human lenses. The observation that the steady-state free, but not total, water gradient of the lens collapses with age raises the possibility that age-dependent changes to the way lens proteins bind water is an underlying cause of changes to lens optics and therefore overall vision that is observed as we age.

CONTROL ID: 3535077

SUBMITTER (NAME ONLY): Yuchen Lu

TITLE: Optical coherence tomography imaging-based evaluation of lesion characteristics in a rabbit model of proliferative vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lu, Y. Liu, M. McNally, J. Qian, C. Eberhart, M.S. Singh, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|W. Schubert, K. Nassar, Bayer AG, Leverkusen, Wuppertal, GERMANY|S. Blackshaw, Solomon H. Synder Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|M. Adams, Research Animal Resources, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is an important cause of irreversible vision loss for which no treatment other than surgery is available. Large animal models of induced PVR have been used to study disease mechanisms and to test novel pharmacologic treatments. Photography-based staging scales in these models classify lesion severity by macroscopic features but do not provide data regarding microscopic retinal structure. Here we aimed to study the use of optical coherence tomography (OCT) imaging in characterizing the microscopic in vivo features of retinal lesions in a rabbit model of induced PVR.

Methods: All animal procedures were conducted in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by the Johns Hopkins Animal Care and Use Committee. PVR was induced unilaterally in specific pathogen free Dutch Belted rabbits by vitrectomy, retinotomy, retinal detachment, platelet-rich plasma injection, and cryotherapy. At baseline and different time points after PVR induction, in vivo lesion severity was documented by color fundus photography and staged according to the Fastenberg scale. OCT imaging (EnFocus OCT, Leica Microsystems) was performed at each time point. Qualitative and quantitative features were extracted from OCT images by a masked observer.

Results: The retinas (N=9) of lesioned rabbits were imaged at baseline and at time points ranging from 4 hours to 30 days after PVR induction. PVR lesion severity ranged from Fastenberg stages 3 to 5. Qualitative OCT features that were analyzed included retinal thickening, epiretinal membrane, vitreoretinal traction, media opacity, and retinal detachment. OCT features that could be quantified included retinal thickness and retinal detachment height. Cataract formation impeded OCT imaging in several eyes.

Conclusions: OCT imaging may provide detailed information regarding in vivo retinal structure in rabbit eyes with PVR across the severity spectrum. Qualitative OCT lesion descriptors could reveal abnormalities in the epiretinal, retinal, and subretinal locations. The development of objective and quantifiable OCT-based biomarkers in animal models of PVR might facilitate further preclinical research on developing novel treatment modalities.

CONTROL ID: 3535080

SUBMITTER (NAME ONLY): Fernando Pellerano

TITLE: Population Based Analysis of Neuroradiologic Findings in Idiopathic Intracranial Hypertension - The Bronx Experience

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Various magnetic resonance imaging (MRI) findings have been identified in patients with idiopathic intracranial hypertension (IIH), including optic disc protrusion, globe flattening, empty sella, vertical optic nerve tortuosity, nerve sheath expansion, slit ventricles, transverse venous sinus stenosis, and tonsillar prolapse. We aimed to innumerate these findings in a Bronx cohort and establish clinico-radiological correlations.

Methods: A retrospective chart review of 45 consecutive patients with confirmed IIH and 47 controls who had MRIs for other reasons, was conducted. Demographic, clinical and brain MRI/MRV details were analyzed with Pearson correlation, student's t-test, and Mann Whitney calculations using STATA-14 software. Sensitivity, specificity, positive predictive value (PPV), and likelihood ratios (LR) were calculated, for each MRI sign. Significance was set at $p < 0.05$.

Results: IIH patients were predominately female (91% vs 68%; $p = 0.006$), younger (28.3 vs 45.2yrs; $p < 0.001$) and obese (BMI=34.8 vs 30.7; $p < 0.015$) compared to controls. Mean (SD) number of MRI findings was 2.8(2.1) in IIH and 1.4(1.7) in the controls; ($p < 0.001$). In the IIH group, mean (SD) lumbar puncture opening pressure (LPOP) was 32.2(11.8) cm H₂O. LPOP correlated with the number of MRI/MRV signs ($Rho = 0.31$; $p = 0.04$); BMI had minimal correlation ($Rho = 0.21$; $p = 0.16$). Vertical nerve tortuosity ($p = 0.003$), slit ventricles ($p < 0.001$) and transverse sinus stenosis ($p < 0.001$) occurred more in IIH than controls. Other MRI findings were not significantly different. Optic disc protrusion had low sensitivity, 13.3%; CI 5.9-27.0% but high specificity, 95.7%; CI 84.0-98.9%, PPV, 75.0% and +LR, 3.1 while vertical nerve tortuosity had intermediate sensitivity 52.1%; CI 36.4-65.5% and specificity 78.7%; CI 64.3-88.3% and lower PPV 69.7%, and +LR 2.4. Slit ventricles (sensitivity 53.3%; CI 38.5-67.5%, specificity 93.6%; CI 81.5-97.9%, PPV 88.9%, +LR 8.3), and transverse venous sinus stenosis (sensitivity 40.0%; CI 26.5-55.1%, specificity 93.6%; CI 81.5-97.9%, PPV 85.7%, +LR 6.2) had the highest predictive values.

Conclusions: The results affirm that IIH occurs in young females with high BMI. Opening pressures positively correlated with the number of MRI signs. Ventricular slits and transverse sinus stenosis were the brain MRI/MRV signs that were most predictive of IIH diagnosis.

CONTROL ID: 3535090

SUBMITTER (NAME ONLY): Timothy Lai

TITLE: Association between retinal thickness variability and visual acuity outcome during anti-vascular endothelial therapy for neovascular age-related macular degeneration

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.Y. Lai, Department of Ophthalmology & Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG|T.Y. Lai, R.Y. Lai, 2010 Retina & Macula Centre, Kowloon, HONG KONG|

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ABSTRACT BODY:

Purpose: To evaluate the association between retinal thickness variability and visual outcome at 2 years in eyes receiving anti-vascular endothelial growth factor (anti-VEGF) therapy for neovascular age-related macular degeneration (nAMD).

Methods: Sixty-four eyes receiving anti-VEGF therapy for nAMD were analyzed. Variability in spectral-domain optical coherence tomography central subfield thickness (CST) was calculated from the standard deviation of all visits after 3 loading doses from month 3 to 24. Eyes were divided into quartiles (Q) based on the CST variability values and the visual acuity at 2 years were compared.

Results: The mean \pm standard deviation (SD) age of the patients at the first anti-VEGF injection was 75.3 ± 9.4 years. The mean \pm SD baseline visual acuity and CST were 0.59 ± 0.39 and 364 ± 113 μm respectively. A significant correlation was found between CST variability and visual acuity at 2 years (Spearman's $\rho = 0.54$, $P < 0.0001$), indicating eyes with lower CST variability having better visual acuity at 2 years. Eyes with the lowest CST variability was associated with the best mean visual improvement at 2 years (Q1: +9.7 letters, Q2: +1.1 letters, Q3: -2.5 letters, Q4: -9.5 letters; $P = 0.018$). No significant difference in the number of anti-VEGF injections was found between the 4 groups ($P = 0.21$).

Conclusions: In patients undergoing anti-VEGF therapy for nAMD, eyes with more stable CST were associated with better visual acuity outcome.

CONTROL ID: 3535092

SUBMITTER (NAME ONLY): Signe Jeppesen

TITLE: Predictive value of retinal venous oxygen saturation for the visual prognosis after twelve months in branch retinal vein occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Previous studies have shown that the retinal oxygen saturation at referral has no predictive value for visual outcome after twelve months in patients with central retinal vein occlusion treated with anti-VEGF compound. It is of interest to evaluate whether this conclusion is similar in patients with venous occlusions only involving a part of the retina in whom the epidemiological background, complication pattern and visual prognosis is different.

Methods: The association between oxygen saturation, visual acuity and central retinal thickness was studied at the time of referral and after six and twelve months in 111 patients successively referred to the Department of Ophthalmology, Aarhus University Hospital, between February 2017 and August 2019 with a newly diagnosed venous occlusion affecting branches peripheral from the central retinal venule.

Results: Sixty-seven patients with a visual acuity between 35 and 60 ETDRS letters at referral were treated with intravitreal injection of anti-VEGF compound. The venous oxygen saturation improved in parallel central retinal thickness and visual acuity over twelve months but had no predictive value for visual acuity after twelve months. In twelve untreated patients with better visual acuity, low age and high oxygen saturation at the time of referral were positive predictors for the visual outcome after twelve months.

Conclusions: Oxygen saturation, visual acuity and central retinal thickness improves in parallel during treatment of branch retinal vein occlusion with intravitreal injection of anti-VEGF compound. Retinal oximetry has no value for predicting visual acuity after twelve months in treated patients but may potentially become a tool for predicting the visual prognosis in untreated patients with a high visual acuity at referral.

CONTROL ID: 3535095

SUBMITTER (NAME ONLY): Cord Huchzermeyer

TITLE: Relationship between temporal L-cone flicker sensitivity and established clinical parameters in Stargardt's disease

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.R. Huchzermeyer, J. Fars, J.J. Kremers, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|C.R. Huchzermeyer, J. Fars, J.J. Kremers, Department of Ophthalmology, University Hospital Erlangen, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the relationship between L-cone-specific temporal contrast sensitivity (L-cone tCS) and established functional and structural outcome parameters in Stargardt's disease (STGD).

Methods: Twelve patients (5F, 24±14yrs) with confirmed STGD were included. L-cone-isolating temporal modulation was created in a 12° test field using a four-primary LED stimulator using triple silent substitution. L-cone tCS was defined as 1 / L-cone contrast at threshold. Mean deviation of tCS was calculated by 1) subtracting the logarithm of the observed tCS from age-correlated normal values, 2) converting to decibel and 3) averaging the 12, 16, and 20Hz results.

Clinical parameters were: mean deviation of static white-on-white perimetry in the central 12° (MD12), area of hyporeflexivity (AoH) in infrared scanning-laser-ophthalmoscopy scans, and best corrected visual acuity (logMAR). Principal component analysis (PCA) was performed to identify associations between outcome parameters and to subdivide patients into different clusters. Pearson correlation coefficients were calculated for confirming associations found in PCA.

Results: In the PCA 2D plot, three clinically meaningful clusters were identified: 1) fundus flavimaculatus without central defect (FF; good logMAR, good MD12), 2) bull's-eye maculopathy (BEM; good logMAR and reduced MD12), and 3) central defect and eccentric fixation (CD; both logMAR and MD12 reduced). Interestingly, one patient, who was located between the CD cluster and the BEM clusters, showed signs of BEM in the OCT but seemed to have lost central fixation recently. In our cohort, L-cone tCS deviation was inversely correlated to AoH ($R=-0.63$; $p=0.03$) and positively correlated to MD12deg ($R=0.74$; $p=0.01$).

Conclusions: PCA can be useful to explore phenotypes, when clinical outcomes are intercorrelated. Close association between MD and L-cone tCS is not surprising, because stimulus detection in white-on-white perimetry is also dominated by L-cones. As a consequence, tCS did not provide additional information that might change clustering. However, tCS can be measured faster than perimetric MD and might be used as a surrogate in patients who cannot perform static perimetry.

CONTROL ID: 3535105

SUBMITTER (NAME ONLY): Aditya Venkatesh

TITLE: Antisense oligonucleotide mediated increase in OPA1 improves mitochondrial function in fibroblasts derived from patients with autosomal dominant optic atrophy (ADOA)

SESSION TITLE: Gene therapy in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Venkatesh, S. Ali, R.S. Oh, D. Sonntag, T. McKenty, B.A. Slipp, J. Hoyer, G. Liao, Stoke Therapeutics Inc, Bedford, Massachusetts, UNITED STATES|Z. Li, R.B. Hufnagel, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: ADOA is the most common inherited neuro-ophthalmic disorder which starts in the first decade of life and leads to progressive, irreversible vision loss from degeneration of retinal ganglion cells (RGCs). More than 400 mutations have been reported in ADOA and most patients harbor mutations in the OPA1 gene that lead to haploinsufficiency. Reduced OPA1 levels are associated with impaired mitochondrial function in RGCs leading to apoptosis. Currently, there is no approved disease-modifying treatment for ADOA. Targeted Augmentation of Nuclear Gene Output (TANGO) uses antisense oligonucleotides (ASOs) to reduce inclusion of a non-productive, alternatively spliced exon in OPA1. We previously demonstrated that TANGO ASOs can be utilized to increase OPA1 expression in cultured human cells and in the rabbit retina. In this study, we use fibroblasts from patients with ADOA as an in vitro model to evaluate efficacy of our approach.

Methods: Skin fibroblasts were obtained from 3 unrelated patients with ADOA, each with different heterozygous OPA1 mutations. ASOs were delivered by lipid-based transfection. RNA and protein were isolated to assess changes in OPA1 mRNA splicing and OPA1 protein levels. Mitochondrial respiration was evaluated by measuring the oxygen consumption rate (OCR) using the XFe96 Extracellular Flux Analyzer from Seahorse Biosciences. Flow cytometry with DCFDA dye was used to detect intracellular reactive oxygen species (ROS).

Results: All 3 fibroblast samples showed decreased expression of OPA1 mRNA and OPA1 protein when compared to wild-type fibroblasts. Patient fibroblasts exhibited impairment in mitochondrial respiration as seen by decreased basal OCR, ATP-linked respiration, and spare respiratory capacity. Intracellular ROS levels also increased. TANGO ASOs reduced the non-productive exon inclusion, increased total OPA1 protein levels, and improved mitochondrial function in patient fibroblasts.

Conclusions: We validated the use of patient fibroblasts as an in vitro model of ADOA pathophysiology. Improvement in mitochondrial function suggests that ASO-mediated increase in OPA1 can potentially modify disease progression in ADOA in a mutation-independent manner.

CONTROL ID: 3535131

SUBMITTER (NAME ONLY): Satoko Fujimoto

TITLE: Three-dimensional visualization of intrachoroidal cavitation using the deep learning-based enhancement of optical coherence tomography

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The intrachoroidal cavitation (ICC) is a peripapillary pathological lesion usually associated with high myopia, which may cause serious clinical consequences such as visual field defect. However, due to the challenges in existing imaging devices to visualize three-dimensional (3D) morphology of the ICC, details in structural characteristics and their influence on visual function, remain poorly understood. Using deep learning (DL)-based image enhancement and 3D rendering of volumetric swept-source optical coherence tomography (SSOCT) images, we evaluated the 3D anatomic characteristics of the ICC in comparison with the existing 2D parameters.

Methods: Thirteen eyes of 12 consecutive patients with peripapillary ICC were enrolled (age: 52.5 ± 6.3 years, refractive error: -8.4 ± 3.2 D, and axial length: 27.1 ± 1.4 mm). DL-based image enhancement, automatic segmentation of the ICC, and 3D rendering was applied to parapapillary 6 x 6 mm volumetric SSOCT scans. We evaluated the anatomical relationship between the ICC and the Bruch membrane opening (BMO). The 3D volume, as well as the 2D maximum width and length of the ICC, were calculated as morphologic parameters. Associations between the ICC parameters and visual field mean deviation (VFMD) of standard automated perimetry were investigated.

Results: The ICC was successfully segmented, and 3D visualized in all eyes. The ICC was located inferior to the optic disc in all eyes and observed bilaterally in 1 patient and unilaterally in 11 patients. The ICC was detected with fundus photographs in 12 eyes out of the 13 eyes. VFMD ranged from -11.1 to 0.12 dB (mean -2.61 ± 3.16 dB). All the ICCs showed direct contact with the BMOs and two cases showed the overlap. The ICC volume ranged from 55.3 to $975.4 \times 10^{-3} \text{ mm}^3$ ($358.4 \pm 283.3 \times 10^{-3} \text{ mm}^3$), the ICC width from 118.5 to 512.4 μm ($248.5 \pm 108.9 \mu\text{m}$), and the ICC length from 0.19 to 2.00 mm (1.10 ± 0.47 mm). The ICC volume ($P=0.02$, regression coefficient=-0.007) was significantly associated with VFMD while the ICC width and length were not.

Conclusions: 3D images of the ICC were successfully generated using DL-based enhancement of SSOCT volumetric scans. 3D volume parameter seems to reflect the pathological influence of the ICC on visual function better than the existing 2D metrics, which potentially leads to an improved pathological understanding of the ICC.

CONTROL ID: 3535147

SUBMITTER (NAME ONLY): Marta Gonzalez-Hernandez

TITLE: NEW GIP INDEX FOR PROGRESSION ANALYSIS, USING THE LAGUNA ONhE METHOD FOR THE OPTIC NERVE HEAD HEMOGLOBIN EVALUATION

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Laguna ONhE automatically analyzes hemoglobin distribution in optic disc retinographies (1-9). Its main index, called GDF (Globin Distribution Factor) involves a classifier based on Deep Learning that tends to produce extreme values: (1=normal, 0=glaucoma). The consequence is a good detection performance, outweighed by certain variability in the limit range between normality and glaucoma. Therefore, its influence has been reduced in a new index, called Globin Individual Pointer (GIP). It may be useful in the follow-up of cases.

Methods: Two retinographies of 78 normal eyes and 59 confirmed or suspected glaucomas were obtained using a simple manual fundus camera (DEC-200, MiiS, Taiwan). The reproducibility and diagnostic capability of both indices were compared.

Results: Analyzing the average of both GDF series, a ROC area of 0.937 (CI=0.882-0.971) and a sensitivity of 67.8%% for 99% specificity were obtained. Its intra-class correlation coefficient was 0.970 (CI 0.958-0.978). GIP achieved a smaller ROC area (0.902, CI=0.839-0.946, $p<0.01$), sensitivity of 50.85% for 99% specificity, and a higher intra-class correlation coefficient (0.990, CI=0.985-0.993, $p<0.0001$).

Conclusions: Both indices are complementary: GDF useful for diagnostic classification, especially considering that not all glaucomas were confirmed cases but only with signs of suspicion, and GIP for individual progression assessment.

Figures: Test-retest scatter plots of GDF (Fig1) and GIP (Fig2) indexes. The 0 and -15 value are at 5% and 1% percentile of the normal population.

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CONTROL ID: 3535148

SUBMITTER (NAME ONLY): Simon Kaja

TITLE: Extracellular vesicles (exosomes) derived from primary optic nerve head astrocytes enhance neurite outgrowth.

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Kaja, Ophthalmology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|S. Kaja, W.K. Jones, Molecular Pharmacology and Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|A.K. Ghosh, Graduate Program in Biochemistry and Molecular Biology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|H.N. Hariani, Graduate Program in Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|G. Kalesnykas, Research & Development, Experimentica Ltd., Vilnius, LITHUANIA|

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ABSTRACT BODY:

Purpose: To determine the properties of primary optic nerve head astrocyte (ONHA)-derived extracellular vesicles (exosomes), their uptake into primary neurons, and to identify the functional effects of exosomes on neuronal survival and neurite outgrowth.

Methods: Exosomes were prepared by ultracentrifugation from primary rat ONHAs. To determine the functional effects of lysyl oxidase like-1 (Loxl1) knockdown, we transduced ONHA with lentivirus harboring either control or Loxl1-targeting small hairpin RNA. A stable line with ~50% Loxl1 knockdown was generated. Exosomes were characterized by nanoparticle tracking analysis and immunoblotting. Uptake of exosomes into primary cortical neurons was quantified by quantitative microscopy using RNA-based labeling. Functional effects of exosomes were determined by testing their antioxidative properties in primary cortical neuronal culture. To quantify effects on neuronal differentiation, exosomes were added to neuronal cultures on days 3 and 5 in vitro and neurite outgrowth was quantified on day 7.

Results: Exosomes derived from wildtype, control- and Loxl1 shRNA-transduced ONHAs were of similar size (119.8 ± 4.3 , 121.9 ± 2.8 and 121.1 ± 2.5 nm, respectively, $n=3$, $P=0.89$). ONHA exosomes expressed the prototypical markers Alix and CD63, but were deficient of CD81. Exosomes were taken up by primary neurons, and this uptake was time-dependent and peaked at 4 h after addition ($n=3$, $P<0.05$). Viability of rat primary cortical neuronal cultures in response to oxidative stress insult did not change in the presence of exosomes derived from wild-type, control- or Loxl1 shRNA-transduced ONHA cultures, suggesting lack of antioxidative properties. Wild-type ONHA exosomes increased neurite outgrowth of primary rat cortical neurons by $20.1 \pm 3.3\%$ (from 57.6 ± 4.4 to 77.6 ± 6.5 μm , $n=5$, $P<0.05$); similarly, exosomes from control shRNA-transduced ONHAs increased neurite outgrowth by $18.7 \pm 2.0\%$ (to 76.3 ± 4.6 μm , $n=5$, $P<0.05$). In contrast, exosomes from Loxl1 shRNA-transduced ONHAs prevented any increase in neurite outgrowth ($2.2 \pm 4.0\%$ change; 59.8 ± 3.3 μm , $n=5$, $P=0.98$).

Conclusions: Our data provide evidence that ONHA-derived exosomes can exert functional effects on neurons and identify Loxl1 as a putative mediator of these effects. Altered exosome-mediated neuron-glia signaling in exfoliation

glaucoma, where LOXL1 expression is chronically reduced, may be of pathological importance.

CONTROL ID: 3535157

SUBMITTER (NAME ONLY): Bledi Petriti

TITLE: Preliminary data show Normal Tension Glaucoma patients have lower systemic nicotinamide adenine dinucleotide (NAD⁺) levels and mitochondrial function compared to Controls

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Though raised intraocular pressure (IOP) is the main risk factor, about a third of patients with glaucoma have IOP within the normal range (Normal Tension Glaucoma - NTG). Whilst reducing IOP can slow progression, glaucoma may deteriorate despite IOP lowering, suggesting that other factors confer susceptibility. Mitochondrial dysfunction is an important factor contributing to a number of age-related neurodegenerative diseases and mounting evidence suggests that it contributes to glaucoma pathogenesis. Nicotinamide adenine dinucleotide (NAD⁺) is a central coenzyme involved in mitochondrial function and fundamental biological processes in health, ageing and disease. NAD⁺ depletion has been observed in other neurodegenerations

Methods: NAD⁺ and NADH levels (Promega NAD/NADH-Glo™ Assay; two technical repeats) and mitochondrial function (XFe24 Analyzer), expressed as oxygen consumption rate (OCR) pmol/min, were measured in the same fibroblast lines from 5 NTG patients and 5 non-glaucomatous Controls. NAD⁺ and NADH concentrations were normalised to protein content and expressed as nM/μg. NTG inclusion criteria: minimum 5 years follow up with at least 8 reliable visual fields, IOP ≤ 21mmHg. Controls were age matched with an absence of glaucoma and IOP ≤ 21mmHg. Both groups had absence of active haematological malignancy/recent infection/chemotherapy/radiotherapy or drugs known to affect mitochondrial function

Results: Median (IQR) NAD⁺ (p<0.01) and NADH⁺ (p<0.05) concentrations (average of two runs) were significantly reduced in the NTG group: 374 (372 - 400), 56 (42 - 57), compared to the Control group: 656 (613 - 1164), 121 (80 - 171) respectively (Fig. B, D). Median Basal (p<0.01), ATP-linked (p<0.01), and Maximal Respiration (p<0.05), were significantly lower in the NTG group compared to the Control group (Fig. A, C, D). The estimation of NAD⁺ concentration was relatively imprecise with a mean difference of 29% and SD of differences of 19% between the two runs

Conclusions: Our data show evidence of relative NAD⁺ and NADH depletion in NTG patients, which may contribute to a reduction of various components of systemic mitochondrial function, supporting NAD⁺ levels as a potential therapeutic target

CONTROL ID: 3535176

SUBMITTER (NAME ONLY): Alexis Kassotis

TITLE: Subretinal choroidal neovascularization in central serous chorioretinopathy resistant to mineralocorticoid receptor antagonists

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Choroidal neovascular membranes (CNV) are an infrequently explored complication of central serous chorioretinopathy (CSCR) that can substantially impact recovery. This retrospective case analysis aims to better characterize the role of CNV in patients with CSCR who failed treatment with the mineralocorticoid receptor antagonist eplerenone.

Methods: Those included in this study were diagnosed with CSCR without CNV at presentation in one physician's practice between January 2012 and August 2019. All subjects had imaging with Spectral Domain Optical Coherence Tomography (SD-OCT) and angiography. Chart review was used to extract subjects' age, gender, risk factors, treatment, vision at the time of diagnosis and resolution, and date of resolution if applicable. Central macular thickness (CMT), subfoveal choroidal thickness (SFCT) and choroidal vascularity index (CVI) were determined from SD-OCT images. Binary logistic regression analyses were conducted to identify clinical features associated with CNV development.

Results: This study includes 35 eyes of 31 patients. Twenty-four eyes (68.6%) demonstrated complete resolution of subretinal fluid within 8.5 ± 1.9 months. Eleven eyes (31.4%) developed CNV. CNV incidence doubled after 5 months at which time 50% of the patients had complete resolution of subretinal fluid with eplerenone (Figure 1). Of eyes that did not resolve with eplerenone, a significantly higher proportion had CNV than did not (66.7% vs 20%, $p=0.02$). Binomial regression analyses indicate that the persistence of subretinal fluid (RR 5.99; CI: 1.21-29.41; $p=0.028$) and duration of eplerenone use (RR 1.06; CI: 1.00-1.13; $p=0.042$) were the only clinical features significantly associated with the presence of CNV in CSCR (Figure 2).

Conclusions: Individuals without CNV at presentation who fail to respond to eplerenone treatment within 5 months may have developed an underlying CNV and thus, could benefit from investigatory imaging.

CONTROL ID: 3535191

SUBMITTER (NAME ONLY): Christina Morettin

TITLE: Reducing Adenoviral Patient Infected Days (RAPID) Study: Correlation of adenoviral load with severity of adenoviral conjunctivitis and viral clearance over 21 days

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the correlation of viral load at baseline and over 21 days with severity of signs, symptoms, and viral clearance in participants with adenoviral conjunctivitis.

Methods: Of 212 participants screened for adenoviral conjunctivitis (Ad-Cs), 56 met the following criteria and were randomized: ≥ 18 years of age, symptoms ≤ 4 days, a positive point-of-care immunoassay via AdenoPlusTM (Quidel, San Diego CA). One eye of each participant was randomized to a single, in-office administration of either 5% povidone-iodine (PVP-I) or artificial tears (AT). Examinations at baseline, days 1-2, 4, 7, 14, and 21 included assessment of participant symptoms, clinician graded signs, and conjunctival swabs for qPCR analysis. Repeated measures generalized estimating equations were used for calculating the correlation (r) of viral load with signs and symptoms over 21 days. Severity of signs and symptoms is reported for 3 equal size tertiles of baseline viral load: low ($\log qPCR < 6.13$), middle ($\log qPCR 6.13-6.78$) and high ($\log qPCR > 6.78$).

Results: Twenty-five participants were qPCR positive for adenovirus and had sufficient follow-up visits. Viral load was not correlated with participant symptoms or clinician graded signs at baseline. However, higher viral load over 21 days had correlations with increased severity of participant symptoms of tearing, matting and redness ($r \geq 0.70$; $p < 0.02$) and with clinician graded signs of bulbar redness and serous discharge ($r \geq 0.60$; $p < 0.01$). Higher baseline titers were correlated with longer time to viral clearance ($r = 0.59$, $p = 0.0075$). Days to viral clearance in low, middle and high baseline viral titer tertiles were 10.3 ± 5.6 , 9.5 ± 3.5 , and 19.8 ± 3.8 , respectively. The incidence of subepithelial infiltrates or pseudomembranes was higher in the highest tertile of viral load (75%, 6 of 8) compared to the lowest tertile (40%, 4 of 10, $p = 0.43$).

Conclusions: High correlations were found between viral load with more severe signs and symptoms over 21 days. Higher baseline viral load was associated with longer time to viral clearance.

CONTROL ID: 3535194

SUBMITTER (NAME ONLY): Corinne Gonzalez

TITLE: AMD Drusenoid deposits “L”, Lipid type: Density, Structural, Volume analysis, and their evolution study with Morphology-Structural software. 5 years follow-up

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Gonzalez, SELARL CABINET DR C GONZALEZ, TOULOUSE, FRANCE|

Commercial Relationships Disclosure (Abstract): Corinne Gonzalez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study AMD drusenoid deposits “L”, with regard to their density, structure volume and evolution with morphology-structural software to enhance drusenoid deposits “L” knowledge, evolving potential and etiopathogenesis

Methods: 124 eyes of 64 patients, 22 men, 42 women, with AMD drusenoid deposits “L”, Lipid Type (soft Drusen, Drusenoid PED “L”). Deposits were evaluated by Autofluorescence, IR imaging, OCT, notably OCT en Face (Spectralis HRA-OCT, spectral domain OCT), and Morphology-Structural software (M-S software). ETDRS visual acuity (VA), complete ophthalmic examination with Fundus exam were added. M-S software let analyze drusenoid deposit volume and contours, 3D deposit reconstruction, display in 3D space, let drusenoid deposit contents analyze, discrimination, differentiation, let grading (volume and contours analyze), let measurements: density (grey levels of deposits), structure (structural measures, texture parameters), volume (in μm^3), evaluation and characterization of those “L” type deposits. Evaluation, comparison for each eye, for each patient, between all studied patients, was done every 6 months, so evolution assessment of those drusenoid deposit parameters too. 5 years follow-up.

Results: AMD Drusenoid Deposits “L” are: dark grey, optical empty, fatty, equal and the same in all cross-section (OCT/OCT en face). From M-S software, “L” have rather Low density, each density parameter having not only its own profile, curve modulation and up and down during evolution, but difference in between, and likeness between both eyes. Structural and Volume parameters have also their own profile and similarity between both eyes. Cycle evolution was seen for all parameters curve, specific for each curve, with also similarity between both eyes. So this allow better AMD Drusenoid Deposits “L” knowledge, physiopathology understanding, evolution assessment, evolving potential, particularly to atrophy.

Conclusions: AMD Drusenoid deposits “L”, study and knowledge, especially regarding their contents, in particular through Morphology-Structural Software contribute to and improve AMD physiopathology, etiopathogenesis understanding and hypothesis formulations.

CONTROL ID: 3535202

SUBMITTER (NAME ONLY): Spencer Harris

TITLE: Axial length growth in eyes with childhood cataract does not follow norms

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.J. Harris, S. Ghahghaei, A. Chandna, The Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|S.J. Harris, Ophthalmology, California Pacific Medical Center, San Francisco, California, UNITED STATES|I. Cunningham, A. Chandna, Alder Hey Children's Hospital, Liverpool, Merseyside, UNITED KINGDOM|A. Harb, George Eliot Hospital NHS Trust, Nuneaton, Warwickshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Normal axial length growth (ALG) in infancy is modulated by hyperopic defocus on the retina and accommodation. Childhood cataract (CC) and CC surgery disrupt both mechanisms with potential for altered ALG. We compared axial length (AL) in children with CC before and after surgery to typical children (norms) to determine whether CC and surgery affect ALG.

Methods: 110 eyes of 55 children (age 2 weeks - 7 years) with CC were included: 30 eyes, 15 children with unilateral CC and 80 eyes, 40 children with bilateral CC. Eyes with structural abnormalities were excluded. AL data for cataracts was retrospective. AL norms were derived from a cross-sectional prospective study of 332 typical children (age 8 weeks - 7 years) at the same center. AL was measured pre- and postoperatively. Surgical procedures were performed by a single surgeon (AC). Bilateral CC data was combined, as there was no significant difference between eyes. Preoperative ALG curves were calculated for each population and best described by the function $AL = a + b \cdot \ln(t)$, where t is age in weeks. 95% confidence intervals were calculated via the bootstrap method. We then found the difference in AL between age-matched norms and pre- and postoperative AL 13 months after surgery (range 9-18 months), again via the bootstrap method.

Results: For healthy eyes, a was 16.62 (16.21, 17.01, 95% CI) and b was 1.01 (0.92, 1.09). Between groups, b did not differ significantly. For bilateral CC, a was 15.65 (14.80, 16.48). The trend was towards shorter AL but was not significant. For unilateral CC, the a value for affected eyes was 14.37 (12.33, 16.12) and for fellow eyes 16.47 (15.29, 17.41). The affected eye was significantly shorter than norms. The unaffected eye was no different than controls. 13 months postoperatively, eyes with bilateral CC did not approximate normal ALG; change in difference was only 0.1% (-3.3%, 3.7% 95% CI), but affected eyes of unilateral CC did approximate normal ALG, changing by 5.9% (3.4%, 8.7%) and no longer differing significantly from fellow eyes or norms.

Conclusions: In CC there is altered ALG, and the affected eye(s) at presentation is shorter. This indicates a disease process beyond a structural abnormality alone; the presence of cataract itself is enough to cause a difference in ALG. Additionally, there are likely different mechanisms of visual deprivation between unilateral and bilateral CC and altered ALG mechanisms following surgery.

CONTROL ID: 3535203

SUBMITTER (NAME ONLY): Rachel Fortner

TITLE: Impact of the COVID19 pandemic on glaucoma patients: did delay in elective care lead to progression of disease?

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Fortner, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|J. Lindsey, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|J. Lindsey, Ophthalmology, VA Tennessee Valley Healthcare System, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Rachel Fortner: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Lindsey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The COVID-19 pandemic provided unique insight into delayed glaucoma care, as one of the first events in living memory during which in-person health care services, such as eye care, were abruptly curtailed. In this retrospective cohort study, we tested the hypothesis that among patients with glaucoma, delayed care was associated with increased risk of disease progression necessitating change in clinical management.

Methods: Manual chart review was performed for 172 patients with glaucoma at the Veterans Affairs (VA) Tennessee Valley Healthcare System (TVHS) Eye Clinic. The exposure cohort was a random sample of 78 patients who were already established at the VA and had a scheduled outpatient clinic visit during the closure of the clinic between 3/20/2020 and 6/1/2020. The comparator group involved 94 patients with glaucoma who had at least two appointments before COVID (1/1/2018-2/28/2020). Left eyes were analyzed, and demographics, time between recommended and actual follow-up visits, stage of glaucoma, and change in treatment regimen were compared between the 2 cohorts. Fisher's exact test and Pearson's chi-squared test were used to determine whether there were significant differences in disease progression between the groups.

Results: In the exposure cohort, 56.4% of patients had postponed appointments, 28.2% never returned to clinic, and 15.4% had no delay compared to 13.8%, 0%, and 86.2% respectively in the comparator cohort with a statistically significant difference in all three categories ($p < 0.0001$). In addition, 37.5% of all patients had disease progression during the pandemic compared to 17.0% in pre-pandemic times. There is evidence to suggest that there is a significant difference in disease progression in the exposure group compared to the comparator group ($p < 0.0190$). A larger sample size is needed to determine significance in progression of disease between the cohorts when stratified by delayed/not delayed.

Conclusions: Our results are consistent with our hypothesis that delayed care during the pandemic resulted in a change of clinical management due to an increased risk of disease progression. Moreover, many patients were lost to follow up and did not return for their visit. Further research is needed to determine if disease progression is sustained after multiple appointments.

CONTROL ID: 3535212

SUBMITTER (NAME ONLY): Moustafa Magliyah

TITLE: Giant Retinal Tear Detachments in Nonsyndromic LEPREL1 Mutations Mimicking Ocular Stickler Syndrome

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Magliyah, F. Almarek, S.R. Nowilaty, P. Schatz, S. Alsulaiman, Vitreoretinal Division, King Khaled Eye Specialist Hospital, Riyadh, SAUDI ARABIA|M.S. Magliyah, Ophthalmology Department, Prince Mohammed Medical City, AlJouf, SAUDI ARABIA|F. Almarek, Ophthalmology, Imam Muhammad Ibn Saud Islamic University, Riyadh, SAUDI ARABIA|P. Schatz, Lunds Universitet, Lund, SWEDEN|F. Alkuraya, Department of Genetics, King Faisal Specialist Hospital and Research Center, Riyadh, SAUDI ARABIA|F. Alkuraya, Department of Anatomy and Cell Biology, Alfaisal University, Riyadh, Riyadh Province, SAUDI ARABIA|

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ABSTRACT BODY:

Purpose: To describe the ocular features and characteristics of retinal detachment in high myopia associated with mutations in LEPREL1 gene.

Methods: Retrospective chart review including details of ocular history, ophthalmic examination, multimodal imaging and surgical interventions were obtained during a mean duration of 9.1 ± 4.8 years.

Results: 20 eyes of 10 patients were included. 2 patients were males and 8 patients were females. Mean age of the patients was 18.6 ± 5.5 years followed up for 9.1 ± 4.8 years. Mean axial length was 28.9 ± 1.9 mm and mean refraction was -13.9 ± 2.8 diopters. BCVA on presentation was 0.62 ± 0.65 (Snellen = 20/80) and on last follow up was 0.45 ± 0.69 (Snellen = 20/50). Anterior segment examination revealed posterior subcapsular cataract in 16 eyes (80%) and associated with temporal lens subluxation in 5 eyes (25%). 6 eyes of 5 patients (50%) developed retinal detachments (RD) at age of 11 ± 3.2 years. All eyes (100%) with retinal detachment had giant retinal tears (GRT). Anatomical reattachment was achieved in 5 out of 6 eyes. No significant difference was found in axial length or cycloplegic refraction between eyes with and without RD ($P=0.897$ and 0.861 respectively). Previous lensectomy with PCIOL was not associated with higher risk of RD ($P=0.550$).

Conclusions: LEPREL1-related high myopia confers a high risk of early-onset RD associated with giant retinal tears. Surgical interventions can achieve good anatomical and visual outcomes in these patients. This phenotype mimics the ocular features of Stickler syndrome.

CONTROL ID: 3535214

SUBMITTER (NAME ONLY): Kevin Wang

TITLE: Demographics and Clinical Presentation of Uncorrectable Low Vision Patients, 5-Year Analysis

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Wang, M. DeBenedictis, A. Yuan, A. Rachitskaya, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Determine demographics and clinical characteristics of low vision patients at Cole Eye Institute (Cleveland, Ohio) from 2014-2019.

Methods: This was a single center, retrospective cross-sectional analysis of all adult patients (age>18) seen at Cole Eye Institute between 2014-2019 with best corrected visual acuity (BCVA) of 20/400 or worse in at least one eye. Demographic and clinical data were collected from clinical visits in Oct, 2014-Oct, 2019. One International Classification of Diseases diagnosis code (ICD-9 or ICD-10) was associated to each patient as the most likely cause of low vision. Correctable causes of blindness were excluded.

Results: Out of 500,093 patients seen in 2014-2019, 17,995 eyes from 15,610 patients (3.1%) had vision of 20/400 or worse. Bilateral low vision accounted for 2,384 patients (15.3%). The average age was 69.3 (range: 18-114) with 58.0% being female and 68.4% being Caucasian. The most frequently associated diagnoses in patients with at least one low-vision eye were age-related macular degeneration (AMD, 24.6%), glaucoma (16.9%), retinal detachment (10.6%), and diabetic retinopathy (8.8%). In bilateral low vision, glaucoma (25.9%), retinal detachment (12.1%), and diabetic retinopathy (10.3%) were the most common diagnoses. Glaucoma (34.0%) was more prevalent than AMD (7.4%) in eyes with no light perception (NLP) (Figure 1). Whereas, in eyes with vision between 20/400 and count fingers (CF), AMD and glaucoma accounted for 25.8% and 12.2% of eyes respectively (Figure 1). When stratified by age, the proportion of low-vision patients associated with glaucoma stayed stable at 12-19% whereas low-vision associated with AMD becomes apparent above age 65 accounting for 23% of low-vision patients in age 65-80 and 50% in patients aged >80 (Figure 2).

Conclusions: The most common diagnoses accounting for uncorrectable low vision are AMD and glaucoma. Glaucoma is associated with more profound vision loss, and consistently accounts for 12-19% of low-vision patients irrespective of age. AMD is associated with less profound vision loss compared to glaucoma and is seen in elderly population with 50% of those over 80 having visual acuity of 20/400 or worse in at least one eye.

CONTROL ID: 3535222

SUBMITTER (NAME ONLY): Xinxin Zhang

TITLE: Clinical characteristics, treatments, and outcomes of vitreomacular adhesion and vitreomacular traction

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhang, Y. Zheng, S. Fekrat, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|J. Ma, L. Chew, T. Lee, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uncertainty exists regarding the natural history of vitreomacular adhesion (VMA) and vitreomacular traction (VMT) and patient or ocular characteristics that predispose toward release versus complications. We aim to evaluate the characteristics and outcomes of VMA and VMT at a tertiary care center.

Methods: This retrospective longitudinal cohort study includes eyes from 2008 to 2020 with VMA or VMT with ≥ 6 months of follow-up. Eyes with ocular comorbidities were excluded. The visual acuity (VA), optical coherence tomography characteristics, outcomes and interventions were recorded.

Results: One hundred ten eyes of 93 patients were identified. Of 58 eyes with VMA, 22 were focal ($\leq 1500 \mu\text{m}$ in length) and 36 were broad ($> 1500 \mu\text{m}$). The average age was 63.0 ± 8.6 years. Eighteen (31.0%) spontaneously released, 9 focal and 9 broad. Average time to release was 31.4 ± 27.8 months. A smaller proportion of patients ≥ 65 years old had spontaneous release (4/25) compared to patients < 65 years old (11/25, $p=0.03$). Average VA was 20/23 at presentation, 20/24 at 12 months and 20/24 at release. Six eyes progressed to VMT.

Of 52 eyes with VMT, 45 were focal and 7 were broad. A higher proportion of VMT were focal compared to VMA ($p<0.00001$). The average age was 67.3 ± 10.9 years. Seventeen (32.7%) spontaneously released, similar to proportions of spontaneously released VMA ($p=0.85$). Fifteen were focal and 2 were broad ($p=0.80$). Average time to release was 20.1 ± 19.3 months. The proportion of patients with spontaneous VMT release ≥ 65 years old (5/15) versus < 65 years old (8/28) were similar ($p=0.75$). Average VA was 20/35 at presentation, 20/34 at 12 months and 20/34 at release. Complications include lamellar holes ($n=2$) and full thickness macular hole ($n=1$). Seven eyes were treated. Three eyes received intravitreal ocriplasmin; 2 successfully released and the remaining patient opted for observation thereafter. Four eyes received pars plana vitrectomy. Proportions of patients who were male, pseudophakic or had epiretinal membranes (ERM) were not different between those who had spontaneous release of VMA or VMT versus those who did not.

Conclusions: VMA may spontaneously release after years of observation, particularly in patients < 65 years old. Rates of spontaneous VMA and VMT release are comparable. Sex, lens status, focal versus broad attachment, and presence of ERM do not affect spontaneous release of VMA or VMT.

CONTROL ID: 3535227

SUBMITTER (NAME ONLY): Jinmiao Li

TITLE: Ectoine protects corneal barrier function via promoting IL-37 that suppresses TNF- α -induced Cathepsin S in primary human corneal epithelial cells under hyperosmotic stress

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Li, Y. Zhang, S.C. Pflugfelder, D. Li, Ocular Surface Center, Cullen Eye Institute, Department of Ophthalmology, Baylor College of Medicine, HOUSTON, Texas, UNITED STATES|J. Li, State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, Guangdong, CHINA|Y. Zhang, Zhejiang Eye Hospital, School of Optometry and Ophthalmology, Wenzhou Medical University, Hangzhou, Zhejiang, CHINA|

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ABSTRACT BODY:

Purpose: To explore novel role and molecular mechanism of a natural osmoprotectant ectoine in protecting corneal barrier function through promoting anti-inflammatory cytokine IL-37 in human corneal epithelial cells (HCECs) under hyperosmolarity stress, an in vitro dry eye model.

Methods: Primary HCECs were established from donor limbal tissue. The confluent cultures in iso-osmolar medium were switched to hyperosmotic media (400-500 mOsm), without or with prior incubation of ectoine at different concentrations (1-40 mM) for 2-48 hours. Cell viability and proliferation were evaluated by WST assay. The integrity of apical barrier junction proteins and the expression of cytokines and cathepsin S were evaluated by RT-qPCR, ELISA, immunostaining and confocal microscopy.

Results: HCECs were survived well in 450mOsm but partially damaged in 500mOsm media. Ectoine well protected HCEC survival and proliferation in 450 and 500mOsm media. The integrity of corneal epithelial barrier was largely disrupted in HCECs exposed to 450 mOsm, as shown by 3D confocal images of immunofluorescent staining of tight junction proteins ZO-1 and occludin. Ectoine at 10-20mM well protected the barrier proteins under hyperosmotic stress. The expression of pro-inflammatory cytokines (TNF- α , IL-1 β and IL-6) were dramatically stimulated by hyperosmolarity but significantly suppressed by Ectoine at 5-40 mM as quantified by RT-qPCR and ELISA. The protease cathepsin S, which was stimulated by hyperosmolarity and TNF- α , directly disrupted epithelial barrier while its inhibitor LY3000328 restored the barrier integrity. Interestingly, IL-37 decreased significantly in HCECs by hyperosmolarity, but prior-incubation of ectoine increased IL-37 at mRNA and protein levels, suppressed TNF- α and cathepsin S activity, and protected cells from barrier disruption under hyperosmolarity. Furthermore, rhIL-37 was observed to suppress pro-inflammatory cytokines and TNF- α -induced cathepsin S in HCECs exposed to hyperosmolarity.

Conclusions: Our findings demonstrate that the hyperosmotic stress disrupts corneal epithelial barrier through stimulating pro-inflammatory cytokines and cathepsin S while suppressing IL-37. Ectoine inhibited the pathological course to protect the corneal epithelium. It provides new insight into pathogenesis and therapeutic potential for dry eye disease.

CONTROL ID: 3535231

SUBMITTER (NAME ONLY): Krati Chauhan

TITLE: Age, race and sex influence utilization of care for the inflammatory and infectious eye diseases in the United States

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chauhan, Southern Illinois University- School of Medicine, Springfield, Illinois, UNITED STATES|J.T. Rosenbaum, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|J.T. Rosenbaum, Legacy Health System, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Utilization of the eye care in the United States is influenced by health care disparities, which are defined as care affected by patient's age, race or sex. There is a lack of national level data regarding trend of utilization for inflammatory and infectious eye diseases in the United States, and whether this trend is influenced by health care disparities. We have conducted a retrospective, observational study based on the intelligent research in sight (IRIS) data to study this trend and how this trend is affected by age, race and sex of the patient.

Methods: We have used intelligent research in sight (IRIS) registry data available through National Vision and Eye Health Surveillance System (VEHSS). IRIS, is the United States' first comprehensive eye disease clinical registry. VEHSS uses ICD-10 codes to identify ocular disorders. Each code is categorized in one subgroup and multiple subgroups are combined to form a category. Inflammatory and infectious eye disease category includes subgroups of ocular inflammatory conditions, lacrimal system and orbital inflammation, keratitis, conjunctivitis, eyelid inflammation and infection, and endophthalmitis.

Utilization for the inflammatory and infectious eye disease category is stratified by age, sex and race. We have measured trends of utilization for the years 2016-2018. We have identified the effect of stratification on utilization; by race, sex, age alone; combining race and sex; age and sex; and the combination of race, sex and age.

Results: There is a decrease in utilization for the inflammatory and infectious eye diseases from the years, 2016 to 2018. This trend remains, when utilization is stratified by sex, race and age. Asians and Native American have higher utilization for all the three years for both males and females. (Figure 1). Utilization is low for the younger age groups (0-17, 18-39) and then steadily increases for age > 40 years for 2016-2018 for both males and females and for all the races (Figure 2). Females have higher utilization for all the races from 2016-2018. This remains when utilization is stratified by race; a black female has higher utilization than a black male.

Conclusions: Utilization of care for inflammatory and infectious eye diseases is influenced by age, race and sex. Asian, Native Americans, females and older age groups have higher utilization.

CONTROL ID: 3535248

SUBMITTER (NAME ONLY): Randy Lu

TITLE: Multiplatform Input for Intraocular Lens Implant Calculation after Myopic Corneal Refractive Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lu, J. Ho, H. Jung, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Randy Lu: Commercial Relationship: Code N (No Commercial Relationship) | Joanne Ho: Commercial Relationship: Code N (No Commercial Relationship) | Hoon Jung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Calculating intraocular lens (IOL) power for cataract surgery is more complex in patients with prior corneal refractive surgery. We performed a retrospective, comparative analysis of patients who had surgically treated cataracts with a history of corneal refractive surgery, assessing the accuracy of IOL outcome predictions generated by the ASCRS calculator separately and in conjunction with other devices in multiple combinations.

Methods: The study was performed at a single site. Data from all patients with a history of uncomplicated cataract surgery, prior myopic corneal refractive surgery, and multi-platform analysis was included. Biometric measurements included Zeiss IOLMaster® 700, Zeiss ATLAS® 9000, and Oculus Pentacam®. Eyes with significant additional ophthalmic pathology affecting vision or without one-month post-operative checks were excluded. Outcomes included manifest refraction at post-operative month one, power of implanted IOL, and predicted IOL power from each group. IOL prediction error was found by subtracting the power of implanted IOL from the power of the predicted IOL. A one sample t-test to identify prediction errors significantly different from zero, an ANOVA to determine differences in IOL prediction error between groups, an F test to determine variance of IOL prediction error for each group, and a chi-square test to analyze the difference in percentage of eyes within +0.50D and +1.00D error between groups. A p-value of ≤ 0.05 was considered statistically significant.

Results: Twenty-eight eyes met inclusion criteria. Biometry alone (IOLMaster® 700) predicted significantly higher IOL power as compared to implanted IOL power (mean=0.45D). No significant difference in IOL power prediction performance, variance of IOL prediction error, or percentage of eyes within +0.50D and +1.00D of refractive prediction error was found between groups.

Conclusions: IOLMaster® 700 and Atlas® 9000 group yielded prediction error closest to zero with the highest percentage of eyes within 0.50D and 1.00D, though this result was not statistically significant. Adding parametric data achieved only 36-56% accuracy to within +0.50D.

CONTROL ID: 3535259

SUBMITTER (NAME ONLY): Yingna Liu

TITLE: Diagnostic performance of swept-source anterior segment optical coherence tomography (SS-OCT) in classifying primary angle closure disease

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Previous studies showed that certain quantitative SS-OCT measurements were correlated with increased intraocular pressure, suggesting a possible association between anatomic anterior chamber configurations with glaucomatous changes. This study aims to evaluate the diagnostic performance of SS-OCT in distinguishing primary angle closure disease from control eyes, as well as primary angle closure (PAC) and primary angle closure glaucoma (PACG) from primary angle closure suspect (PACS) eyes.

Methods: In this cross-sectional study, consecutive adult patients who were diagnosed with PACS, PAC or PACG, and control patients who presented to the Zhongshan Ophthalmic Center from June 2018 to June 2019 were enrolled. A total of 385 eligible eyes from 241 participants underwent a complete ocular examination, including Goldmann applanation, gonioscopy, and SS-OCT. Eight SS-OCT images 45 degrees a part, starting from 0° were analyzed per eye. Anterior segment dimension and angle parameters were measured. The probabilities of PACD vs control, and PACS vs PAC/PACG eyes were modeled as functions of patient demographics and SS-OCT parameters using a gradient boosting machine learning approach, either using all measurements across all 8 images or using individual meridional scans only: (0°, 180°), (45°, 225°), (90°, 270°), and (135°, 315°).

Cross-validated area under the receiver operating characteristic curve (cvAUC) of the prediction models were calculated.

Results: SS-OCT showed a strong ability to identify PACD from control subjects with a cvAUC value of 0.94 (0.91, 0.96), with ACD measurement at 180° being the most predictive measurement (Figure 1). Individual meridional scans demonstrated similar diagnostic performance. SS-OCT had a moderate ability in distinguishing PAC and PACG from PACS with a cvAUC value of 0.79 (0.73, 0.85), with lens vault at 270° being the most predictive measurement (Figure 2). The vertical meridional scan (90°-270°) demonstrated the highest cvAUC values of 0.76 (0.70, 0.82).

Conclusions: SS-OCT had excellent diagnostic performance in distinguishing PACD vs control eyes but only moderate performance in distinguishing PAC/PACG eyes vs PACS eyes. As a diagnostic tool, SS-OCT holds potential in associating anterior segment anatomy with its physiologic consequences in understanding the pathway of glaucoma pathogenesis.

CONTROL ID: 3535271

SUBMITTER (NAME ONLY): Claudia Lasalle

TITLE: Telehealth Appointments Increase the Likelihood that Patients with Diabetes and Diabetic Retinopathy Return for Recommended In-person Care

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of this study is to determine whether telehealth (TH) appointments improve the rate of return for in-person diabetic eye exams.

Methods: A retrospective chart review was conducted to determine the rate of return for in-person diabetic eye examinations for patients with diabetes who had been seen in the Department of Ophthalmology at the Lahey Hospital & Medical Center in 2019. Since TH appointments were not initiated at the Lahey Hospital & Medical Center until March 16, 2020 in response to the COVID-19 pandemic, this study looked at only patients who were seen after this date. The main outcome was the number of in-person diabetic eye exams completed by patients who had a prior TH encounter compared with those that did not have a TH encounter. Patient demographic (age, gender, ethnicity, and race) and clinical characteristics (A1c, type of diabetes, and severity of retinopathy) were abstracted from the medical record.

Results: Of the 7,796 patients with a diagnosis of diabetes who were seen in 2019, 1,723 (22.1%) completed TH appointments in 2020. The rate of return for in-person diabetic eye examinations was significantly greater for the cohort of patients who completed a TH appointment compared with those who did not (44.6% compared with 36.5%, OR: 1.71 95% CI: 1.54 - 1.90, $p < 0.0001$). Patients with diabetic retinopathy were more likely to complete a TH visit. Of the 1,202 patients with diabetic retinopathy, 365 patients (30.4%) completed a TH appointment. In contrast, only 1,294 of the 5,999 patients (21.6%) without a history of retinopathy completed a TH appointment ($\chi^2 = 43.693$, $p < 0.0001$). For both groups the likelihood that a patient would subsequently complete an in-person diabetic eye exam increased after the completion of a TH encounter: 74% of patients with diabetic retinopathy completed an in-person visit after a TH appointment, compared with 49.6% of patients who returned for in-person care without a prior TH appointment (OR: 2.89; 95% CI: 2.20 - 3.79, $p < 0.0001$). Similarly, 44.6% of patients without retinopathy who completed a TH visit returned for in-person care, compared with only 36.5% who did not complete a TH visit (OR: 1.40; 95% CI: 1.24 - 1.59, $p < 0.0001$).

Conclusions: TH appointments are an effective method to improve the likelihood that patients with diabetes and diabetic retinopathy will return for recommended in-person care.

CONTROL ID: 3535314

SUBMITTER (NAME ONLY): Andrews Nartey

TITLE: Substrate stiffness modulates gene expression and phagocytosis in segmental human trabecular meshwork cells

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nartey, K. Dhamodaran, V. Raghunathan, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|J. Staverosky, J.A. Vranka, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aqueous humor outflow in the trabecular meshwork (TM) is segmental with regions of high- (HF) or low-flow (LF) that vary in their molecular signature, biomechanics, and response to pressure. Whether these changes are driven by cells or their microenvironment is unclear. Recently, we isolated HF and LF TM cells and found differences in gene expression and extracellular matrix (ECM) stiffness. We hypothesize that cells from these regions are intrinsically different and exhibit phenotypes that vary as a function of substrate stiffness and differ in phagocytic function.

Methods: Using whole human globe perfusion, HF and LF TM were delineated using cell mask orange, a plasma membrane stain. Primary human TM (hTM) cells [n=3 non-glaucomatous donors] were isolated and primary cultures established. Cells were seeded on substrates of relevant stiffness: soft hydrogel (3kPa to mimic normal HF), stiff hydrogel (80kPa to mimic glaucomatous LF) or glass (>1GPa). RT-qPCR was used to determine relative expression levels of COLIV, TIMP1, SPARC, CTGF, and MMP1 genes. HF and LF hTM cells were cultured on these substrates with or without dexamethasone (DEX) for 72 h. Phagocytic ability was measured using quantitative phagocytosis assay.

Results: CTGF mRNA levels were upregulated in HF compared to LF cells (3-fold change) seeded on stiffer substrates. MMP1 and TIMP1 were overexpressed in LF relative to HF cells (1.5-fold change) and expression levels of both were higher on soft substrates. SPARC was upregulated in HF compared to LF cells on soft substrates (2.3-fold change). Phagocytic ability of HF and LF hTM cells was higher on soft substrates and attenuated on stiffer substrates (1.5-2.5-fold change). DEX impaired phagocytosis in both HF and LF cells on soft and stiff substrates (2-fold mean decrease), but not on glass. Following DEX treatment, LF cells seeded on soft and stiff substrates showed a decline in phagocytic uptake by 18-40% compared to their HF counterparts.

Conclusions: Our data demonstrate that HF and LF hTM cells have intrinsic phagocytic differences, a critical property in facilitating aqueous humor outflow and maintaining intraocular pressure homeostasis in TM tissues. That substratum stiffness can differentially mediate phagocytosis and expression of ECM genes in these cells highlights an intricate dynamic relationship between biophysical and biochemical cues in segmental TM cells.

CONTROL ID: 3535329

SUBMITTER (NAME ONLY): Ameay Naravane

TITLE: Short term visual and structural outcomes of anti-VEGF treatment delay during the first COVID-19 wave: a pilot study

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Naravane, R. Munda, Y. Zhou, E.J. Van Kuijk, H. Nazari, J. Yamanu, D. Koozekanani, S.R. Montezuma, Ophthalmology and Visual Neurosciences, University of Minnesota, Minneapolis, Minnesota, UNITED STATES|C. Santilli, University of Minnesota Medical School Twin Cities, Minneapolis, Minnesota, UNITED STATES|G. Emerson, The Retina Center, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-VEGF injections are essential to maintaining and/or improving ocular conditions including neovascular age-related macular degeneration (nAMD) and diabetic retinopathy. This study aims to assess the effect of unintended delays in anti-VEGF treatment during the first wave of the COVID-19 pandemic.

Methods: This retrospective case series identified patients receiving regularly scheduled anti-VEGF injections from two practices in Minnesota. Diagnoses were limited to nAMD, DME, proliferative diabetic retinopathy, and RVO. Patients were grouped based on whether they maintained or delayed their 'post-lockdown follow-up visit' by more than two weeks during the COVID-19 lockdown. The COVID-19 lockdown was declared on March, 28th, 2020 in Minnesota. Visual acuity and structural changes to the retina using ocular coherence tomography (OCT) were assessed to determine whether delayed treatment resulted in worse visual outcomes.

Results: A total of 167 eyes from 117 patients met criteria for inclusion in this study. In the delayed group, the average BCVA at the pre- and post-lockdown visits were 0.614 and 0.715 (logMAR) respectively ($p=0.007$). Treatment intervals were shortened in 21% of patients delayed by 2-4 weeks, 68% of patients delayed by 5-8 weeks, and 42% of patients delayed greater than 9 weeks. Central subfield thickness (CST) increased from 341 to 447 in the DME delayed group ($p=0.03$) and from 301 to 314 ($p=0.4$) in the nAMD delayed group.

Conclusions: These results suggest that treatment delays may negatively impact the visual and anatomic outcomes of patients with nAMD and DME. Further investigation with a larger sample size is ongoing.

CONTROL ID: 3535331

SUBMITTER (NAME ONLY): Tina Felfeli

TITLE: Temporal Trends in Prevalence of Diabetic Retinopathy Screening Amongst Patients with Diabetes in an Urban Setting: A Canadian population-based study over a decade

SESSION TITLE: DR: Epidemiology and service provision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Felfeli, M.H. Brent, D. Wong, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|T. Felfeli, Institute of Health Policy, Management and Evaluation, University of Toronto Dalla Lana School of Public Health, Toronto, Ontario, CANADA|D. Wong, Department of Ophthalmology, Unity Health Toronto, Toronto, Ontario, CANADA|M.H. Brent, Department of Ophthalmology, Toronto Western Hospital, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Early identification of diabetic retinopathy (DR) with screening eye examinations allows for secondary prevention of acquired vision impairment. This study aimed to determine the temporal change in prevalence of DR screening based on patient profiles in a representative Canadian population in an urban setting over ten years.

Methods: This is an analysis of a nationally representative sample of patients with diabetes from the Ontario Diabetes health claims database for 2011-2015 and 2016-2020. The cohort was created using algorithms with ICD diagnosis codes applied to physician billing claims for adults aged 19 years and greater. Prevalence estimates, odds ratio (OR) and 95% confidence intervals (CI) for DR screening based on baseline clinical characteristics and sociodemographic factors were calculated.

Results: Of 1,346,578 patients with diabetes, 455,027 (34%) had not been screened for DR in 2016-2020, which was higher than the number of unscreened patients in 2011-2015 (OR=0.93; 95% CI=0.92-0.93; $p<0.001$). The mean duration of diabetes amongst patients unscreened for DR increased between 2011-2015 to 2016-2020 (9.15 ± 6.80 vs 10.67 ± 7.02 ; $p<0.001$). Although DR screening amongst young adults of 20-39 years old increased from 2011-2015 to 2016-2020 (OR=1.17; 95% CI=1.14-1.20; $p<0.001$), this age group persistently had the highest proportion of unscreened patients than other age groups (58% for 20-39 years old vs 42% for 40-64 years old and 24% for 65 years and older). Immigrants were less likely to have been screened for DR compared to non-immigrants (OR=0.67; 95% CI=0.66-0.68; $p<0.001$). When patients were stratified by access to primary healthcare, those who had a family physician were more likely to be screened for DR (OR=2.31; 95% CI=2.26-2.36; $p<0.001$).

Conclusions: Approximately a third of patients with diabetes in an urban setting in Canada have not been screened for DR. The proportion of unscreened patients has increased over the past decade with the population growth and chronicity of diabetes. Of all patients with diabetes, young adults, immigrants and those not under the care of family physicians are at highest risk of not being screened for DR. These findings guide resource allotment aimed at improving the rates of screening eye examinations for DR.

CONTROL ID: 3535332

SUBMITTER (NAME ONLY): Parth Vaidya

TITLE: Using Intraoperative Triamcinolone Acetonide Irrigation to Reduce Post-Operative Pain from Scleral Buckle Surgery

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Vaidya, V. John, Virginia Tech Carilion School of Medicine, Roanoke, Virginia, UNITED STATES|R. Albuquerque, M. McClintock Jr, V. John, Retina, Vistar Eye Center, Roanoke, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Scleral buckle surgery is a widely used ophthalmic surgery for the correction of rhegmatogenous retinal detachment. Studies suggest that eye pain is a common and underestimated occurrence after scleral buckle surgery, but as of yet, there is no definitive management method for reducing pain following scleral buckle surgery. We aim to control pain following scleral buckle surgery with sub-tenon irrigation with triamcinolone acetonide at the time of surgery. Using a randomized prospective clinical study, we test if this technique will reduce the pain, nausea/vomiting, and analgesic use caused by scleral buckle surgery.

Methods: Forty-eight patients undergoing scleral buckle surgery will be randomized into two groups. The experimental group receives a sub-tenon irrigation of 1 cc 40mg/mL triamcinolone acetonide around the base of the scleral buckle (0.25 cc in each quadrant) at time of operation. The control group does not receive any triamcinolone irrigation. Pain scores are measured 1 day post-operatively via 11-pt numerical rating scale as the primary outcome. The nausea/vomiting score is measured 1 day post-operatively via standard 6-pt scale. Patients track pain medication use via pill count. Values will be measured again at 1-2-week and 6 months post-op.

Results: With 13 patients enrolled, pain was reduced in the experimental group at one day ($x = 2.2$ vs 1.1) and one week post-operatively ($x = 0.8$ vs 0.0), though the difference is not statistically significant ($p = 0.23$ and 0.099 respectively). Acetaminophen use was not significantly different between the groups ($x = 3125, 2750$ mg, $p = 0.85$), nor was ibuprofen use ($x = 600, 683$ mg, $p = 0.9$). The nausea/vomiting score was not significantly different between the groups ($x = 0.2, 0.11$, $p = 0.6$). Not enough patients have reached the 6-month time point for statistical analysis.

Conclusions: Though it is not statistically significant at this time, there is a measurable decrease in median pain score between the control and experimental group at both 1 day and 1 week post-op. We are optimistic this will trend towards significance as we continue to enroll patients. No significant differences or trends could be established with the nausea/vomiting score or analgesic use. This study shows that sub-tenon irrigation of triamcinolone acetonide at the time of scleral buckle surgery may be a promising method for reducing post-operative pain.

CONTROL ID: 3535340

SUBMITTER (NAME ONLY): Paige Richards

TITLE: Factors Predicting Success of Macular Hole Repairs

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Richards, M.M. Altaweel, T. Nork, M. Lasarev, J. Chang, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite growing literature looking at factors that contribute to the closure of full-thickness macular holes, there are still gaps in our knowledge. This study sought to examine the role of preoperative and intraoperative factors in predicting anatomic and visual success of vitrectomy for full-thickness macular holes.

Methods: A retrospective chart review of cases in calendar 2019 was conducted at the University of Wisconsin. Inclusion criteria included vitrectomy for macular hole and pre- and post-operative imaging. Successful closure was defined as the absence of a full-thickness disruption by imaging. Data was summarized using the median and inter quartile range (IQR; span from 25th to 75th percentile capturing central 50% of the sample) for continuous features or with frequencies and percentages for categorical factors. Risk factors associated with hole closure were compared between groups using either rank-sum procedures or Fisher's exact tests. Odds ratios and supporting 95th confidence intervals (CI₉₅) were computed for categorical factors by inverting Fisher's exact test or using logistic regression with Firth's correction in cases where the explanatory factor had more than two levels and data especially sparse. Analyses were performed using R (ver. 4.0.3).

Results: There were 64 subjects who met inclusion criteria and had vitrectomy for macular hole (Table 1). One had a traumatic injury and was especially young (< 15 years old) at the time of repair; all others were between 48.8–87.4 years at time of surgery. Internal limiting membrane was peeled in all cases (1 in a prior surgery). Hole closure was successful for 57 subjects (89%); 55 (86%) had single surgery success. Age, lens status, prior hole repair, and chronicity (present > 1 year) were not associated with the outcome ($p > 0.10$ for each). Pathologic myopia or staphyloma ($n=8$, 12.5%) was associated with lower odds of success (OR=0.14; CI₉₅: 0.02-0.86, $p = 0.036$). Median minimum hole diameter (MHD) was 335.2 μ m. Larger MHD was greater among those who had an unsuccessful repair, but not significantly ($p = 0.071$). Data suggest an estimated 71% (CI₉₅: 42-100%) chance a subject with an unsuccessful outcome would have a larger MHD.

Conclusions: The study suggests that the factors that portend a decreased likelihood of a successful macular hole surgery include pathologic myopia/staphyloma and larger MHD.

CONTROL ID: 3535343

SUBMITTER (NAME ONLY): Cameron Hoerig

TITLE: Relationships between mechanical and microstructural tissue properties in the posterior sclera

SESSION TITLE: Role of choroid and sclera in myopia development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Hoerig, J. Mamou, F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|K. Ito, D. Lee, Q. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS, SINGAPORE|S.A. McFadden, Vision Sciences, Hunter Medical Research Institute and School of Psychology, College of Science, Engineering and Environment, The University of Newcastle, Callaghan, New South Wales, AUSTRALIA|Q. Hoang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Scleral microstructural and mechanical properties can be affected by myopia. Second harmonic generation (SHG) microscopy can glean information about collagen microstructure whereas scanning acoustic microscopy (SAM) is sensitive to bulk mechanical tissue properties. This study used SHG and SAM to investigate the relationship between tissue microstructure and mechanical properties in myopic guinea pig (GP) eyes.

Methods: One week of form-deprivation myopia was induced in the right eyes of four 1-week-old GPs. Left eyes were untreated controls. GPs were euthanized at 14-days of age; both eyes were enucleated, slowly fresh frozen, and stored at -80°C . Whole unfixed globes were vertically cryosectioned every $12\mu\text{m}$. Posterior regions of adjacent tissue sections were scanned with SAM (250-MHz transducer) or SHG (860nm excitation wavelength). Maps of bulk modulus (K), mass density (ρ), sound speed (c), and acoustic attenuation (α) were estimated from SAM data using a Fourier-domain, model-based inverse method. A curvelet-based analysis method operated on SHG images to estimate collagen fiber length (L), straightness (S), orientation (O), and width.

Results: Differences in mean material properties between control and myopic (-5.54 , -3.21 , -9.29 , and -7.13 D) eyes were $\Delta c = -17.55 \pm 5.81$ m/s, $\Delta K = -0.11 \pm 0.2$ GPa, $\Delta \rho = -0.01 \pm 0.002$ g/cm³, and $\Delta \alpha = -0.37 \pm 0.19$ dB/MHz/cm (all $p < 0.05$). Comparing estimated collagen fiber characteristics to material parameters, the standard deviation of O (σ_O) most strongly correlated with ρ and α ($r = 0.79, p < 0.0001$ and $r = -0.75, p < 0.0001$) while S was most strongly correlated with c and K ($r = -0.63, p = 0.001$ and $r = -0.52, p = 0.01$). Associations were weak between control eye L and σ_O with distance from the optic nerve head (ONH, $r = -0.64, p = 0.05$ and $r = -0.43, p = 0.22$) whereas myopic eye L and σ_O were positively correlated with distance ($r = 0.86, p = 0.001$ and $r = 0.83, p = 0.003$). Similarly, K, c, and α did not vary with distance in control eyes (all $p > 0.5$) but increased further from the ONH in myopic eyes ($r = 0.83, 0.9, 0.72, p < 0.001$).

Conclusions: Bulk mechanical parameters measured with SAM correlated with collagen fiber microstructure, particularly fiber orientation. Results of this study demonstrate the effect of myopia on scleral tissue microstructure and subsequent changes in bulk tissue mechanical properties. SAM may be effective for assessing microstructural and mechanical changes associated with myopia.

CONTROL ID: 3535353

SUBMITTER (NAME ONLY): Xiaoying Zhu

TITLE: Vascular Endothelial Growth Factor-A (VEGF-A) and High Myopia in Marmosets

SESSION TITLE: Refractive control: Molecular and Anatomical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Zhu, A. Nour, A. Benavente-Perez, Biological and Vision Sciences, SUNY College of Optometry, New York, New York, UNITED STATES|S. Dellostritto, SUNY College of Optometry, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The exact mechanisms leading to myopic ocular complications are unclear. VEGF has been suggested to play a key role in myopic choroidal neovascularization (CNV), which can lead to irreversible vision loss. VEGF signals endothelial cells to proliferate and migrate causing neovascularization, and is upregulated during ischemia-related myopic axial elongation. This suggests that VEGF may be a direct trigger of myopic CNV. This study investigates the associations between retinal and choroidal VEGF-A concentrations with myopia development and RPE thickness.

Methods: Two-month old marmosets ($n = 10$) wore -5.00 or -10.00 D soft contact lenses for 18 to 38 weeks to induce myopia and axial elongation of various degrees. Refractive error (RE) and axial length (AL) were measured using a Nidek autorefractor and A-scan biometer, respectively, before and after lens treatment. Foveal and parafoveal RPE thickness were measured using optical coherence tomography (OCT) at the end of lens treatment, after which retinal and choroidal VEGF-A concentrations were quantified using ELISA.

Results: Eyes exhibiting myopia had greater axial elongation ($R^2 = 0.50$, $p < 0.001$). The degree of eye growth and myopia developed correlated with retinal VEGF-A concentration, such that larger and more myopic eyes exhibited lower retinal VEGF-A concentrations ($R^2 = 0.27$, $p = 0.037$ and $R^2 = 0.34$, $p = 0.009$, respectively). There was also a trend towards increased choroidal VEGF-A concentrations in myopic eyes that exhibited thicker nasal parafoveal RPE, but it did not reach significance ($R^2 = 0.40$, $p = 0.07$).

Conclusions: VEGF-A concentration changed in marmoset eyes with different degrees of myopia and axial elongation. Low myopic eyes had higher VEGF-A concentrations than high myopic eyes. These differences could be due to a diluting effect caused by increased eye size/volume with a higher turnover rate, or represent an altered physiological production due to sustained RPE cellular stretch.

CONTROL ID: 3535356

SUBMITTER (NAME ONLY): Guangying Ma

TITLE: In vivo optoretinography reveals photoreceptor inner segment ellipsoid as the signal source of the second hyperreflective OCT band of outer retina

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ma, T. Son, T. Kim, X. Yao, Bioengineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|X. Yao, Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study is to verify anatomic and physiological correlates of the second (2^{nd}) hyper-reflective band in optical coherence tomography (OCT) of the outer retina.

Methods: Wild type mice (C57BL/6J) were used for this study. A custom-designed OCT was employed for dynamic near-infrared (NIR) imaging of the retina activated by a visible light flicker stimulation. Stimulus-evoked intrinsic optical signal (IOS) changes at individual retina layers were measured. Spatiotemporal properties of the IOS changes at the photoreceptor outer segment (OS) and inner segment (IS) were investigated. Comparative analysis of structural OCT reflectance and functional IOS change at the photoreceptor intersegment ellipsoid (ISe) was implemented to evaluate the signal source of the 2^{nd} hyper-reflective OCT band of the outer retina.

Results: Rapid IOS change was observed at the OS right away after the stimulation (Fig. 1), and the early OS-IOS was predominantly distributed at the boundaries connected to the IS and RPE. On contrary, the IS-IOS showed a time delay and a relatively slow time course. The IS-IOS distribution perfectly matched the location of the 2^{nd} OCT band of the outer retina. High-speed OCT recording disclosed robust OS-IOS within 2 ms, and the IS-IOS showed a time delay of ~ 12 ms relative to the stimulus onset. The average OCT intensity of IS showed a gradual increase after the retinal stimulation, while the intensity of OS remained the same.

Conclusions: The consistency of the spatial distribution of the stimulus-evoked IS-IOS and the 2^{nd} OCT band supports the ISe, which has abundant mitochondria, as the signal source of the 2^{nd} OCT band of the outer retina.

CONTROL ID: 3535357

SUBMITTER (NAME ONLY): Erika Shaw

TITLE: Optimizing transfection and transduction-based gene delivery in primary and immortalized RPE cells

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shaw, Cell Biology, Neurobiology, Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D.M. Lipinski, Department of Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D.M. Lipinski, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Erika Shaw: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Lipinski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Dry age-related macular degeneration (AMD) is the leading cause of blindness in the elderly and is characterized by the formation of deposits, termed drusen, between the retinal pigment epithelium (RPE) and Bruch's membrane, a selectively permeable barrier that separates the RPE from the choroid. As such, a therapeutic approach capable of breaking down drusen would be beneficial for the treatment of the early stage AMD. A dichotomy exists, however, wherein the delivery of new genetic material to immortalized or primary RPE cells in vitro is highly inefficient, yet the same approaches applied in vivo results in highly efficient gene delivery. As a consequence, the aim of this study is to evaluate methodologies to increase transgene delivery efficiency in vitro using immortalized ARPE19 and primary bovine RPE cells.

Methods: ARPE19 cells (N=5 wells/reagent) were seeded in 6-well plates at passages 23 through 30; primary bovine RPE cells were seeded at 50,000 cells per well without being passaged. At 70% confluency a GFP reporter construct was delivered either by transfection using 1) Lipofectamine, 2) LTX, 3) P3000 or 4) PEI (polyethylenimine) reagents, or through transduction by addition of 1.2×10^{11} vector genomes (vg) of rAAV2/1 directly into media. After 72 hours cells were fixed and gene delivery efficiency quantified by fluorescence microscopy and flow cytometry.

Results: Lipofectamine LTX and P3000 were the most effective transfection reagents with 20.0% transfection and 32.4% transfection at P26, respectively. Transfection efficiency was found to be dependent on cell passage number among all transfection reagents (Figure 1). Specifically, Lipofectamine LTX and P3000 both demonstrated statistically significant decreases in transfection efficiency between passage number P27 and P28, which persisted through P30 ($p < 0.0001$, one way ANOVA with Tukey's multiple comparisons).

Conclusions: Through this study, we identified the most effective method of transfection for transgene delivery into ARPE19 cells in vitro, which we expect to help facilitate the screening of novel therapies to prevent dry AMD.

CONTROL ID: 3535358

SUBMITTER (NAME ONLY): Tova Goldstein

TITLE: Development of Chief Resident Leadership Competencies Following Participation in a Training Program
Housed in the Department of Ophthalmology

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Goldstein, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|T. Goldstein, S. Park, J. Rosenberg, Department of Ophthalmology and Visual Sciences, Montefiore Medical Center, Bronx, New York, UNITED STATES|D. Avendano Morineau, Department of Organization Development and Effectiveness, Montefiore Medical Center, Bronx, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Tova Goldstein: Commercial Relationship: Code N (No Commercial Relationship) | Sunju Park: Commercial Relationship: Code N (No Commercial Relationship) | Diana Avendano Morineau: Commercial Relationship: Code N (No Commercial Relationship) | Jamie B. Rosenberg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Chief residents (CRs) must develop specific leadership competencies. A defined curriculum for this training has not yet been established. We developed an innovative training program for the incoming July 2020 CRs and performed a prospective study to evaluate the effectiveness of the curriculum.

Methods: Twenty incoming 2020-2021 CRs participated in a training program prepared and housed by the Department of Ophthalmology at Montefiore Medical Center (Bronx, NY, USA). Self-assessment surveys were distributed to the participants to evaluate their personal leadership qualities prior to, and six months following their participation in the training program. Additionally, Program Directors (PDs) evaluated the leadership competencies of their 2020-2021 CRs six months following their participation in the program, the results of which were compared to PD evaluations of the prior year's CRs. All surveys were anonymous. Scores ranged from 1 (unsatisfactory) to 5 (mastery), and the statistical difference in average scores was examined using a nonparametric Mann-Whitney U-test.

Results: Participating specialties included Ophthalmology, Anesthesiology, Dermatology, Nuclear Medicine, Obstetrics/Gynecology, Pathology, Physical Medicine and Rehabilitation, Radiation Oncology, and Radiology. CRs felt that the program's stated objectives were met with mean scores of 4.55/5. CR's self-assessment scores showed improvement ($p=.0004$). While no statistically significant improvement was seen in the PD evaluations, the mean scores of several key questions were higher for the 2020-2021 residents than the 2019-2020 residents: addressing conflict diplomatically (4.17 vs. 4.12), maintaining one's emotions (4.25 vs 4), and organizing well (4.42 vs. 4.06).

Conclusions: This study confirms that the training program was beneficial, especially by self-report of the participants. Changes in PD evaluation scores were not statistically significant, but this may be due to the 2020-2021 participants having served six months as CR while the 2019-2020 comparative group was evaluated after a full year. A formal program including multiple specialties allows for ophthalmology CRs to learn from their colleagues and facilitates a more organized approach to the acquisition of leadership qualities.

CONTROL ID: 3535379

SUBMITTER (NAME ONLY): Kristen Kuo

TITLE: Effectiveness of Screening for Diabetic Retinopathy with Teleophthalmology in a Low-Risk Population

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Anjum, S. Roh, J.L. Marx, D.J. Ramsey, Ophthalmology, Lahey Hospital and Medical Center, Burlington, Massachusetts, UNITED STATES|K. Kuo, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection and treatment of diabetic retinopathy (DR) is important for preventing vision loss. We conducted a cross-sectional clinical study to assess the effectiveness of a teleophthalmology screening program that used non-mydriatic fundus photography (nFP) in a low-risk, well-insured suburban population of patients with diabetes.

Methods: 214 patients due for annual diabetic eye screening with no prior history of DR were recruited to undergo nFP through their primary care providers at eight Beth Israel Lahey Health locations. Two 40° color fundus images centered on the disc and macula were obtained of both eyes and transmitted to a retinal specialist for remote review. The characteristics of these patients were compared to those of the total patient population eligible for nFP, as well as a 1:10 age-, sex-, and race-matched cohort. Income was estimated by the average household income based upon patients' zip code. Patients in the teleophthalmology group who were diagnosed with DR through the program were compared with those who screened negative. Chi-square analyses and z-tests were performed for significance and odds ratios were computed for effect size.

Results: The teleophthalmology program enrolled patients of lower income ($p = 0.010$) and with worse diabetes control as measured by HbA1c (7.39 ± 1.65 versus 7.05 ± 1.46 , $p = 0.004$), when compared with the matched cohort. These patients were also less racially diverse, younger, and more likely to be male. Interestingly, these patients had lower blood pressures ($<140/90$ mmHg) and had had more recent eye exams, microalbumin tests, and HbA1c measurements than the matched cohort. A total of six patients (2.8%) were diagnosed with DR as a result of screening by nFP. This rate of new DR was within the expected range in such a low-risk population comprising mainly patients who had recently had a negative eye examination ($\chi^2 = 0.148$, $p = 0.701$; $\chi^2 = 1.678$, $p = 0.195$). Prior diabetic renal disease was predictive of new DR (OR 7.50 95% CI 1.25 – 44.82, $p = 0.010$).

Conclusions: The teleophthalmology program successfully reached a more medically-vulnerable patient population and found a rate of DR consistent with the expected rate of new DR in a low-risk population. Expanding nFP as a component of health maintenance outreach to patients from underserved cohorts will be potentially effective for proactively preventing complications from diabetes.

CONTROL ID: 3535380

SUBMITTER (NAME ONLY): Euido Nishijima

TITLE: Gene Therapy with Mutant TrkB Receptors Protects Retinal Neurons and Promotes Optic Nerve Regeneration without Ligands

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Nishijima, K. Namekata, A. Kimura, Y. Kitamura, S. Miyachi Honda, X. Guo, C. Harada, T. Harada, Vsion research, Koeki Zaidan Hojin Tokyo-to Igaku Sogo Kenkyujo Shikaku Byotai Project, Setagaya-ku, Tokyo, JAPAN|E. Nishijima, T. Nakano, Ophthalmology, Tokyo Jikeikai Ika Daigaku Igakubu Igakuka, Minato-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: TrkB is a receptor for the neurotrophin BDNF and activation of TrkB upon ligand binding exerts neuroprotective effects on retinal ganglion cells (RGCs). In this study, to strengthen the efficiency of gene therapy, we developed a membrane-targeted form of mutant TrkB that contains only the intracellular region of TrkB (iTrkB) as an AAV vector. We then examined the therapeutic effects of AAV-iTrkB on neuroprotection and optic nerve regeneration.

Methods: GLAST KO mice, a mouse model of normal tension glaucoma, and the optic nerve crush (ONC) model were used for examining the effects of AAV-iTrkB. AAV-iTrkB or AAV-control was injected intravitreally into GLAST KO mice (3 weeks old) and WT mice (6 weeks old) for ONC. The number of RGCs was determined by immunostaining of the wholemount retina with an anti-RBPMS antibody and multifocal electroretinogram (mfERG) was measured for assessment of retinal function. ONC was performed 2 weeks after intravitreal administration of AAV-iTrkB or AAV-control. Regenerating axons were detected by injecting Cholera toxin B with alexa 647. Visual function was analyzed electrophysiologically by visual evoked potentials and behaviorally by the optokinetic response test and pupillary light reflex test.

Results: AAV-iTrkB treatment, without BDNF, increased the survival rate of RGCs in GLAST KO mice. Moreover, visual responses measured by mfERG were higher in AAV-iTrkB-treated mice than AAV-control-treated mice. In the ONC model, AAV-iTrkB treatment alone promoted RGC survival and induced robust axon regeneration compared with AAV-control. Regenerated axons reached their brain targets, resulting in partial recovery of visual function and behavior in some mice.

Conclusions: AAV-iTrkB is a potential candidate for treatment of glaucoma and other neurodegenerative diseases.

CONTROL ID: 3535381

SUBMITTER (NAME ONLY): Zer Keen Chia

TITLE: Remote training and administration of a portable virtual reality-based visual field test for home testing during COVID-19

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Chia, M.L. Turner, A.W. Kong, M. Deiner, Y. Ou, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|B.T. Backus, Vivid Vision, Inc., San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To 1) determine the feasibility of remotely administering and training subjects at home on how to use Vivid Vision Perimetry (VVP-10), a portable virtual reality-based visual field test during COVID-19 shelter-in-place; 2) assess the correlation between VVP-10 and standard automated perimetry (SAP) and the test-retest variability of VVP-10.

Methods: Inclusion criteria included subjects 21 or older with glaucomatous visual field defects, and exclusion criteria included those with retinal diseases or significant cataracts. Virtual reality devices were given to subjects during clinic visits or mailed to them. Subjects were remotely trained using training software and coaching via Zoom and proceeded to take 10 tests at home over 14 days. Subject age and sex, test duration, response rate at each of the test points (fraction correct), and SAP results including mean deviation and individual test point sensitivities were recorded. The Pearson correlation coefficients of SAP mean sensitivity versus VVP-10 fraction correct for all eyes together and fraction correct of tests 6-10 versus tests 1-5 for individual eyes were calculated. A bootstrap analysis that resampled eyes with replacement was done to calculate the 95% confidence interval of the Spearman correlation coefficient between SAP sensitivity versus VVP-10 fraction correct for each point of the 54 test locations.

Results: Of the 20 subjects enrolled, 11 (55%) were male and the average (SD) age was 62.9 (10.5) years. Eight (40%) subjects were Asian and 12 (60%) were Caucasian. In total, 37 glaucomatous eyes with an average (SD) mean deviation of -6.1 (6.1) dB were analyzed. The Pearson correlation coefficient of SAP mean sensitivity versus VVP-10 fraction correct for 37 eyes was 0.68. The Pearson correlation coefficient between fraction correct in tests 6-10 versus tests 1-5 for individual eyes ranged from 0.78-0.99 (median = 0.94). Spearman correlation coefficients of SAP sensitivity versus VVP-10 fraction correct at each point ranged from 0.008-0.85 (median = 0.58).

Conclusions: We demonstrate good test-retest variability of VVP-10 and a strong correlation with SAP, both globally and in a pointwise manner. VVP-10 is portable, inexpensive, and can be used entirely remotely while producing results that are similar to the current gold standard for assessing glaucomatous visual fields.

CONTROL ID: 3535384

SUBMITTER (NAME ONLY): Isis Zhang

TITLE: Vision Threatening Disease Triage Using Tele-Ophthalmology during COVID-19 in the Emergency

Department: A Pilot Study

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Zhang, B. Zhou, A.B. Crane, C. Ye, A. Patton, M. Habel, B. Szirth, A.S. Khouri, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Centers for Disease Control reports 28.2% of surveyed US adults had reduced access to medical care (June/August 2020) due to the COVID-19 pandemic, with 8.9% reporting reduced access to vision care. A non-mydratic digital retinal camera was piloted for deployment to the Emergency Department (ED) to help address this gap in vision care. Referrals for clinical follow-up in vision threatening diseases (VTDs) such as age-related macular degeneration, cataracts, diabetic retinopathy (DR), and glaucoma were assessed with human readers. Artificial Intelligence (AI) deep learning software was evaluated in known DR cases.

Methods: 33 patients with known VTDs (48.48% male, avg 59.33 years) and 36 control subjects (41.67% male, avg 31.33 years) were included in tele-ophthalmology screening. A Canon CR-2 Plus AF non-mydratic retinal camera captured 45-degree angle color and auto-fluorescence images of the eyes. Images (136 eyes) were graded by a certified telemedicine reader on site and an off-site clinical ophthalmologist following International Clinical Diabetic Retinopathy Disease Severity Scale (ICDRSS). Intergrader agreement between readers was evaluated with Cohen's kappa. An automated deep learning screening software optimized for DR (SELENA+, EyRIS Pte Ltd, Singapore) performed independent validation of readable color fundus images (17 eyes).

Results: 5.07% of images were deemed unreadable by graders due to poor quality. Intergrader agreement for subject referral was $\kappa = 0.710$ (95% CI 0.545-0.875, $p < .0005$), with the clinical ophthalmologist generating more referrals than the telemedicine reader. Readers had 96.97% sensitivity (95% CI 91.12-1.028) and 72.22% specificity (95% CI 57.59-86.85) in detecting referable disease. Positive predictive value was 76.19% (CI 63.31%- 89.07%) and negative predictive value was 96.30% (CI 89.17%- 1.034%). Of the 10 false positives, 6 were referred for rule out of glaucoma. Four had early stage cataracts that were deemed nonurgent. SELENA+ referred 100% of the known 9 DR patients.

Conclusions: Tele-ophthalmology deployment in the ED helps limit patient and staff exposure to SARS-CoV-2 without sacrificing evaluation for VTDs. Tele-ophthalmology readers err on the side of caution to avoid missing VTD in a given patient. Use of AI can help keep strict adherence to referral guidelines.

CONTROL ID: 3535386

SUBMITTER (NAME ONLY): Kaveri Thakoor

TITLE: A Hybrid Deep Learning System to Distinguish Late Stages of AMD and to Compare Expert vs. Machine AMD Risk Features

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Thakoor, Biomedical Engineering, Columbia University, New York, New York, UNITED STATES|D. Bordbar, O. Moussa, W. Lin, I. Scherbakova, V. Diaconita, R. Chen, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J. Yao, Electrical Engineering, Columbia University, New York, New York, UNITED STATES|P. Sajda, Biomedical Engineering, Radiology (Physics), Electrical Engineering, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To train and characterize the effectiveness of a hybrid deep learning system that combines Optical Coherence Tomography Angiography (OCTA), OCT structural data, and foveal OCT b-scans to distinguish between normal eyes, eyes with non-neovascular age-related macular degeneration (AMD), and eyes with neovascular AMD. To also determine retinal pathology features most predictive of neovascular AMD diagnosis.

Methods: We used 346 retrospective OCTA scans from patients 18 years and older; 97 were diagnosed with no significant vascular pathology (non-AMD), 169 with non-neovascular AMD, and 80 with neovascular AMD with actionable choroidal neovascularization (CNV). For each patient, an OCTA volume and an OCT structural volume were created using deep retinal, avascular, outer retina and choriocapillaris, choriocapillaris, and choroid layers as input for a 3D convolutional neural network (CNN); foveal OCT b-scans were used as input for a 2D CNN. Hybrid CNNs were constructed and trained respectively on: (1) OCTA, (2) OCTA and OCT structure, (3) foveal OCT b-scans, and (4) OCTA, OCT structure, and foveal OCT b-scans combined (Figure [1]). Each CNN's performance was evaluated via accuracy, precision, recall, and F-1 score. In addition, multinomial logistic regression analysis was conducted to determine the predictive importance of 5 retinal features (adjudicated for presence by OCTA experts) for final AMD diagnosis by experts and by CNNs: (1) intra/sub-retinal fluid (IRF/SRF), (2) scarring, (3) geographic atrophy, (4) CNV, and (5) pigment epithelial detachment.

Results: The CNN achieving highest test accuracy of 77.8% for this 3-class detection task combined OCTA and OCT structure. Next came the CNN combining OCTA, OCT structure, and foveal OCT b-scans at 75.2% accuracy. The model combining all 3 modalities had slightly higher precision, recall, and F-1 score for the neovascular AMD class. For CNNs, IRF/SRF was an important predictor for neovascular AMD vs. non-AMD eyes; the CNN was able to predict IRF/SRF presence with up to 82.4% accuracy.

Conclusions: Just as experts rely on both OCTA and OCT structure to diagnose AMD, CNNs also performed best when trained on OCTA and OCT structure combined. IRF/SRF, known to be an important predictor for neovascular AMD diagnosis by experts, was found to be important by CNNs as well and was detected with high accuracy. [1] Thakoor et al., ISBI 2021

CONTROL ID: 3535390

SUBMITTER (NAME ONLY): Zhen Wang

TITLE: Spatially-Resolved Quantitative Proteomic Analysis of Proteins Involved in the Formation of the Lens Extracellular Diffusion Barrier

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Wang, K.L. Schey, Biochemistry, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zhen Wang: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Schey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The presence of a physical barrier to extracellular space molecular diffusion in the lens has been confirmed in multiple species including rat, bovine and human. This extracellular diffusion barrier has been proposed to restrict the movement of solutes into the lens and act to direct nutrients into the lens core via the sutures at both poles. The purpose of this study is to characterize the molecular components that could contribute to the formation of this barrier.

Methods: Three distinct regions of the lens cortex of bovine lenses were captured by laser capture microdissection guided by dye penetration. Mass spectrometry-based quantitative proteomic analysis was performed to determine protein changes. Imaging mass spectrometry was also employed to visualize protein distribution differences in the barrier region. Gene ontology enrichment analysis and protein-protein interaction network analysis were also carried out.

Results: Dye penetration showed that lens fiber cells shrink the extracellular spaces of the broad sides of fiber cells first followed by closing the extracellular spaces at the short sides at normalized lens distance (r/a) of 0.9 in the bovine lens. Accompanying the closing of the extracellular spaces and fiber cell morphologic changes, dramatic proteomic changes were detected. Label free quantification, gene ontology enrichment analysis, and protein-protein interaction network analysis revealed potential proteins that could be involved in formation of the extracellular diffusion barrier include some junction proteins and cytoskeletal proteins. Imaging mass spectrometry also revealed a sharp intermediate filament transition from vimentin to lens-specific beaded filament proteins at this normalized lens distance. AQP0 and its interacting partners, ERM proteins, were among a few proteins that were upregulated in the barrier regions suggesting a particularly important role of the major lens membrane protein AQP0 in controlling the narrowing of the extracellular spaces in lens fiber cells.

Conclusions: The formation of lens extracellular diffusion barrier is accompanied by significant membrane and cytoskeletal protein remodeling.

CONTROL ID: 3535395

SUBMITTER (NAME ONLY): Hesham Gabr

TITLE: Heads-up ocular microsurgery with integrated live volumetric intraoperative optical coherence tomography

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Gabr, W. Zhang, M. Daluvoy, A.N. Kuo, C.A. Toth, L. Vajzovic, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|H. Gabr, Ophthalmology, Ain Shams University Faculty of Medicine, Cairo, EGYPT|C. Viehland, H. Ngo, J. Izatt, C.A. Toth, Biomedical engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To demonstrate the utility of incorporation of intraoperative Swept Source-Microscope Integrated OCT (SS-MIOCT) into the 3D heads-up surgery system (NGENUITY®) during ocular surgery.

Methods: This is a retrospective study on the use of the assimilated NGENUITY® with the SS-MIOCT during anterior and posterior segment surgeries. Eight patients were enrolled. Five patients underwent pars plana vitrectomy for retinal detachment (3 cases), macular hole (1 case) and epiretinal membrane (1 case). The other 3 patients underwent Descemet Stripping Automated Endothelial Keratoplasty (DSAEK).

Images obtained with the NGENUITY® and the SS-MIOCT (B-scan and live 3D OCT images) were displayed concurrently on the same 3D 4K screen. Surgeon feedback was documented intraoperatively. Feedback included comments on image quality, visualization benefits and challenges. Postoperative analysis included evaluation of surgical and OCT image quality and review of intraoperatively documented surgeon's feedback.

Results: The SS-MIOCT was successfully integrated into the NGENUITY® in all 8 cases. The concurrent B-scan and 3D OCT view was useful for detecting residual subretinal fluid, edges of macular holes during ILM peeling, confirming graft attachment in DSAEK (Fig.1) and for live volumetric OCT visualization of instrument-tissue interaction (Fig.2).

Conclusions: The integration of the 3D heads-up surgery with SS-MIOCT could be an ideal interface for both surgical view and OCT view for tissue microanatomy. The display of the OCT data along with the surgical view on the large 4K monitor can provide excellent visualization of OCT images while maintaining the surgeon's attention on the surgical field.

CONTROL ID: 3535397

SUBMITTER (NAME ONLY): Li-Fang Hung

TITLE: Effects of narrowband, short-wavelength ambient lighting on form deprivation myopia in infant rhesus monkeys

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Hung, K.M. Beach, Z. She, L.A. Ostrin, E.L. Smith, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|L. Hung, K.M. Beach, Z. She, E.L. Smith, BHVI, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: We previously reported that rearing infant monkeys under narrowband, long-wavelength lighting (630 nm) prevented the development of form deprivation myopia (FDM). The purpose of this study was to determine the effects of narrowband, short-wavelength lighting on the phenomenon of FDM in infant monkeys.

Methods: Starting at 26.4 ± 2.2 days of age, infant monkeys (*Macaca mulatta*) were reared under short-wavelength blue LED lighting (465 nm; illuminance = 183 ± 28 lux) with a diffuser lens in front of one eye and a plano lens in front of the fellow eye (FD-BL, n = 7). Refractive development, corneal power, and vitreous chamber depth were measured every two weeks by retinoscopy, keratometry, and ultrasonography, respectively. Comparison data were available from previous studies for similar diffuser rearing groups housed under white fluorescent lighting (FD-WL, n = 16) or narrowband, equal-energy, long-wavelength red lighting (630 nm; FD-RL, n = 7).

Results: All seven monkeys in FD-BL group developed at least -0.5 D of relative myopia in the form-deprived eyes during the four month treatment period. At the end of the treatment period, the mean (\pm SD) degree of anisometropia (treated eye refraction – fellow eye refraction) for the FD-BL monkeys was -2.73 ± 3.40 D and comparable to that for the FD-WL monkeys (-4.48 ± 3.73 D; T = 1.06, p = 0.30). Moreover, the developmental time course for the longitudinal interocular differences in refractive error for the FD-BL group was not significantly different from that of the FD-WL monkeys (mixed design, repeated measures ANOVA, F = 1.01, p = 0.36). In contrast, the longitudinal changes in anisometropia for the FD-RL monkeys was statistically different from that of the FD-WL monkeys (F = 4.49, p = 0.03). All the between eye and between group refractive-error differences were correlated with differences in vitreous chamber depth.

Conclusions: Unlike narrowband, long-wavelength red lighting, narrowband blue lighting did not suppress FDM, nor did it enhance the degree of myopia. These results suggest that under open-loop viewing conditions, short-wavelength lighting does not alter the eye's intrinsic axial elongation rate. However, as observed in other species, the effects of quasi-monochromatic ambient lighting on vision-dependent refractive development varies with wavelength.

CONTROL ID: 3535400

SUBMITTER (NAME ONLY): Jessica Wang

TITLE: Changes in Pupillary Light Reflex Metrics in Proliferative Diabetic Retinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Wang, M. Ahn, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A.N. Vu, J.K. To, A.W. Browne, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A.W. Browne, Department of Biomedical Engineering, Institute for Clinical and Translational Science, University of California Irvine, Irvine, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jessica Wang: Commercial Relationship: Code N (No Commercial Relationship) | Minnah Ahn: Commercial Relationship: Code N (No Commercial Relationship) | Anderson Vu: Commercial Relationship: Code N (No Commercial Relationship) | Josiah To: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Browne: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although some investigations have examined the pathologic effects of proliferative diabetic retinopathy (PDR) on the pupillary light reflex (PLR), effects on both the direct and consensual reflex have not been fully explored. This prospective clinical study examines the effects of PDR on the direct and consensual PLR using a clinically marketed objective pupillometer not previously studied in this population. We hypothesize that diabetic retinal changes will decrease constriction amplitude absolute value and change (Ac and Ac%), velocity of constriction (Vc), and velocity of re-dilation (Vr), while prolonging latency of onset of constriction (Loc) and maximal constriction (Lmaxc).

Methods: PLR metrics of 28 right eyes (15 healthy control, 13 with PDR) were measured with the EyeKinetix Objective Pupillometer (Konan Medical, Irvine, California USA) during normal course of care in a retina clinic. Patients diagnosed with PDR were included in the experimental group. Patients with glaucoma or suspect at examination were excluded. Statistical analysis was completed using independent samples t-test.

Results: Ac, Ac%, Vc, and Vr were significantly decreased compared to the control group. Loc and Lmaxc were increased but the change was statistically non-significant.

Conclusions: This data further reinforces that pathologic changes in PDR affect pathways in the PLR. Therefore, complete quantitative characterization of PLR with pupillography metrics may be a valuable biomarker for evaluating ophthalmic disease activity in diabetic patients.

CONTROL ID: 3535401

SUBMITTER (NAME ONLY): Arthur Hu

TITLE:

Efficacy of Hydrogel Carried Drug in Ocular Disease

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hu, The Forsyth Institute, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Arthur Hu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose:

Retinal vascular diseases are the leading cause of blindness, with the most challenging aspect in their treatment being the lack of non-invasive treatment. The purpose of the present study is to investigate the therapeutic potential of a biodegradable hydrogel as a vector in delivering fenofibrate, a clinically proven oral drug, in treating retinal diseases.

Methods:

FB was packaged with PLGA, β CD, and CS - HA. The release kinetics, tissue bioavailability, and stability of each were compared and determined. FB-CS-HA hydrogel was incubated in a solution with various pH to mimic tear conditions nighttime to daytime, respectively. In vitro enzymatic degradation behavior of hydrogel was investigated at 0, 12, 24, 48, 96, 120, and 144 hours, and the bioavailability of FB was measured by HPLC-MS. The anti-inflammatory effect was examined in ARPE 19 cells exposed to LPS in either the presence or absence of FB loading hydrogel. The releasing speed and total releasing amount of FB in ARPE 19 cells were measured by flow cytometry. NF- κ B activation and the levels of inflammatory factors of monocyte chemoattractant protein-1 (MCP-1), intercellular adhesion molecule-1 (ICAM-1), and tumor necrosis factor-alpha (TNF α) were measured.

Results:

FB was released at a therapeutic dose up to 144 hours in all three hydrogels with a 1% (w/v) loading dose. The degradation of hydrogel was slightly faster in an alkaline condition and is likely pH-sensitive. FB was released at a rather stable speed up to 96 hours in the hydrogel. Exposure of ARPE19 cell in the hydrogel to LPS increased the levels of MCP-1, ICAM-1, and TNF α in the absence of FB, whereas their levels decreased in the presence of FB. Exposure of ARPE19 cells to LPS in the hydrogel in the absence of FB elevated NF- κ B phosphorylation and induced NF- κ B nuclear translocation, both of which were inhibited in the presence of FB.

Conclusions: Hydrogel contact lenses are a viable biodegradable and biocompatible tool in the delivery of clinically-proven drugs in the treatment of retinal diseases.

CONTROL ID: 3535408

SUBMITTER (NAME ONLY): Mustafa Jaffry

TITLE: Use of TimololTM and Natural Supplements in the Management of Visual Field Loss in Advanced Optic Nerve Head Drusen

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jaffry, A. Leto, B. Szirth, A.S. Khouri, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mustafa Jaffry: Commercial Relationship: Code N (No Commercial Relationship) | Ashley Leto: Commercial Relationship: Code N (No Commercial Relationship) | Bernard Szirth: Commercial Relationship: Code N (No Commercial Relationship) | Albert Khouri: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optic Nerve Head Drusen (ONHD) are calcified deposits of axonal debris that lie within the optic nerve head. Incidentally found in 2-3% of the population, there are three types of ONHD described: superficial, buried, and pearl. Over time, ONHD progress toward the surface of the optic nerve, causing severe damage and visual field (VF) loss. There are no established treatment modalities for ONHD associated VF defects. We hypothesize that TimololTM and natural supplements may play a role in reducing the development of VF defects.

Methods: Three ONHD patients were evaluated. Visual acuity, non-contact puff tonometry, color and fundus autofluorescence (FAF) photography using a non-mydratic retinal camera were captured. VF was assessed via 60-4 and 10-2 threshold tests on a Zeiss Humphrey Field Analyzer. Ganglion cell complex (GCC) and retinal nerve fiber layer (RNFL) thickness were assessed using Ocular Coherence Tomography (OCT) on an OptoVue RTVue XR Avanti. Subject 1 is a 52 y/o female with long standing OU pearl ONHD. FAF demonstrated hyperfluorescent signals encircling the optic nerve head (Figure 1) and VF testing demonstrated significant peripheral losses OU with visual field index of 8% OD and 21% OS. A daily regimen of 1000mg Citrus Bioflavonoid Complex, AREDS2 supplements and 1053mg turmeric, which have been found to have anti-inflammatory and antioxidant effects on the retina, was started. TimololTM 0.01%, once nightly, was initiated to prevent nocturnal IOP elevation.

Results: After 10 months, IOP decreased from 18mmHg to 14mmHg OU, and VF stabilization was observed. OCT showed a 4.3% increase in RNFL, no change in GCC OS, and a 32% decrease in RNFL with a 14% increase in GCC OD (Figure 2). Subject 2 is a 24 y/o female with pearl ONHD of comparable volume to subject 1 and has no observable VF, RNFL, or GCC changes due to her young age. Subject 3 is a 24 y/o female with buried ONHD OS and peripheral VF loss, RNFL thinning, and GCC loss.

Conclusions: Our findings suggest that early intervention directed at lowering IOP along with neuroprotective supplements may have a role in delaying VF loss, observed through stability on structural testing, albeit over a short period. Lower IOP may slow damage in ONHD patients, especially by preventing nocturnal IOP elevation. These findings suggest that a prospective clinical trial should be considered for patients with advanced ONHD.

CONTROL ID: 3535414

SUBMITTER (NAME ONLY): Richard Polo

TITLE: Utility of Assessment of Suspected Inherited Retinal Dystrophies with a Broad Genetic Screening Panel

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Polo, K. Astafurov, J. Prenner, H. Fine, Department of Ophthalmology, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES|K. Astafurov, J. Prenner, H. Fine, NJRetina, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the spectrum and frequencies of genetic mutations in a cohort of patients with known or suspected retinal dystrophies and correlate them with phenotypical characteristics. Advances in next generation sequencing allow for patients to be tested in a cost-effective and rapid manner with identification of pathogenic mutations becoming more clinically relevant.

Methods: A cohort of 29 patients seen in a general retina clinic with known or suspected retinal dystrophies were evaluated with a broad genetic testing panel comprising at least 248 genes (some patients had an updated panel of 293 genes) associated with the development of retinal dystrophies. Phenotypical characteristics were analyzed and related back to their associated genetic mutations to link disease features with genotypes.

Results: Twenty-seven of 29 patients (93.1%) tested positive for a variant(s) in one or more of the genes tested. Fourteen of these patients (48.3%) tested positive for a pathogenic variant(s) in one or more of the genes tested. Thirteen patients (44.8%) were positive for genetic variants not yet associated with any particular retinal disorder (variants of unknown significance). Both patient groups had similar disease characteristics including reduced visual acuity, legal blindness, and dyschromatopsia. Two patients did not exhibit any specific genetic variants in the genes tested, but one of the two patients was discovered to have Klinefelter Syndrome (XXY).

Mutations were discovered in 69 of the 293 genes with ABCA4 and CA4 the most frequently mutated genes harboring pathogenic variants. GRM6 was the most frequently mutated gene of the variants of unknown significance.

Conclusions: This study supports the utility of genetic testing with a broad screening panel in a cohort of patients who carry a clinical diagnosis of retinal dystrophy. In this cohort, a significant number of patients had a pathogenic genetic mutation or a variant identified.

CONTROL ID: 3535418

SUBMITTER (NAME ONLY): Janice Ong

TITLE: Characterization of Macrophage-Like Cells in Diabetic Retinopathy Using Optical Coherence Tomography Angiography

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.X. Ong, P.L. Nesper, A.A. Fawzi, J.M. Wang, J. Lavine, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantitatively characterize macrophage-like cells (MLC) at the vitreoretinal interface using optical coherence tomography angiography (OCTA) in different severity stages of diabetic retinopathy (DR).

Methods: 72 eyes of 72 subjects (age 46.0 ± 13.6 years)—18 healthy controls, 22 diabetics without DR (DM no DR), 17 with non-proliferative DR (NPDR), and 15 with proliferative DR (PDR)—were included. Repeated (average 6.5; range 3-10) OCTA scans were obtained for each eye. We segmented, registered and averaged the 3- μ m OCT slab above the vitreoretinal interface to visualize MLC distribution, and the OCTA slab of the underlying superficial capillary plexus to compare MLC distribution to vascularity. MLCs were binarized using a semi-automated method and quantified. We compared MLC density in the area overlying blood vessels, within the perivascular 30- μ m watershed region, and within ischemic areas ($> 30 \mu\text{m}$ from nearest vessel).

Results: MLC density was 6.4 ± 7.0 cells/ mm^2 in healthy controls, 7.8 ± 6.5 cells/ mm^2 in DM no DR, 5.8 ± 4.1 cells/ mm^2 in NPDR, and 21.9 ± 19.4 cells/ mm^2 in PDR. MLC density was higher in PDR compared to all other groups (2.8 to 3.8-fold; $p < 0.01$ for all). We next investigated the location of increased MLC density in PDR. MLC density was most increased in perivascular areas (4.9 to 10.2-fold, $p < 0.002$ vs. all groups), up-regulated on blood vessels (3.1 to 3.9-fold, $p < 0.012$ vs. all groups), and marginally elevated in ischemic areas (2.1 to 3.4-fold, $p < 0.033$ vs. all groups).

Conclusions: MLC density is significantly increased in PDR and was more pronounced in the perivascular region and on blood vessels compared to ischemic areas, suggesting a potential role of MLCs in retinal inflammation or damage. As the noninvasive nature of OCT precludes definitive identification of MLCs in this study, further study is needed to confirm their identity and function.

CONTROL ID: 3535426

SUBMITTER (NAME ONLY): Niroj Sahoo

TITLE: Choroidal vascularity map in unilateral central serous chorioretinopathy : A comparison with fellow eyes

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.K. Sahoo, Retina and vitreous, LV Prasad Eye Institute Kode Venkatadri Chowdary Campus, Vijayawada, Andhra Pradesh, INDIA|O. Beale, G. Nkrumah, K.K. Vupparaboina, J. Chhablani, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|S. Singh, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|M.A. Rasheed, University of Waterloo School of Optometry and Vision Sciences, Waterloo, Ontario, CANADA|F. Tatti, C. Iovino, E. Peiretti, University of Cagliari Department of Surgical Sciences Eye clinic, Cagliari, ITALY|K. Chandra, Disha Eye Hospitals Pvt Ltd, 88(63A) Ghosh Para Road, Barrackpore, Kolkata, West Bengal, India, INDIA|

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ABSTRACT BODY:

Purpose: To map the choroidal vascularity index and compare two eyes in patients with unilateral central serous chorioretinopathy (CSCR).

Methods: This was a retrospective, observational study performed in patients with unilateral CSCR. Choroidal thickness (CT) and Choroidal vascularity index (CVI) were measured and mapped in various zones according to the early treatment diabetic retinopathy (ETDRS) grid. The choroidal characteristics in each zone were compared with each other and also with the fellow eyes.

Results: A total of 20 CSCR patients (20 study and 20 fellow eyes) were included in the study. On repeated measures analysis of variance, outer nasal region CT was seen to be significantly lower than central CT ($p=0.042$) and inner nasal CT ($p=0.007$); outer ring CT was significantly less than central ($p=0.04$) and inner ring ($p=0.01$) CT in CSCR eyes. In fellow eyes, outer nasal CT was significantly lower than inner nasal ($p=0.02$), inner temporal ($p=0.02$) and outer temporal CT ($p=0.01$); outer ring CT was found to be significantly lower than inner ring CT; and nasal quadrant CT was significantly lower than superior quadrant CT ($p=0.01$) and temporal quadrant CT ($p=0.02$). CVI values were not significantly different between the different zones (Figure 1). In CSCR eyes, a positive correlation was seen between CT and CVI values ($r=0.58$, $p=0.1$). There was a weak negative correlation between CT and CVI in fellow eyes ($r=-0.183$, $p=0.64$) (Figure 2-A). The correlations were not statistically significant. On plotting all the CVI values against the corresponding CT values, a positive correlation was seen in CSCR eyes ($r=0.54$, $p<0.01$), while it was slightly weaker in fellow eyes ($r=0.3$, $p<0.01$) (Figure 2-B).

Conclusions: Correlation between CVI and CT was altered in CSCR eyes as compared to fellow eyes with increasing CVI towards the center of the macula and superiorly in CSCR eyes. This correlation could be used as a guide to detect sub-clinical activity, although future studies with higher sample size are required to validate the association.

CONTROL ID: 3535428

SUBMITTER (NAME ONLY): Oliver Beale

TITLE: Comparison of choroidal vascular patterns between two eyes in patients with unilateral central serous chorioretinopathy

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Purpose: To compare Haller vessel patterns between two eyes of patients with unilateral central serous chorioretinopathy (CSCR) using enface swept-source OCT scans

Methods: Methods: This was a retrospective, observational study done in patients with unilateral CSCR. We examined reconstructed, pre-treatment en-face SS-OCT images of the patients and compared the frequencies of different Haller vessel patterns between the two eyes. Two masked observers assigned pattern designations with a third observer finalizing designation in non-consensus. Continuous variables were expressed as mean \pm standard deviation. Comparisons were done using Chi-square test.

Results: Results: A total of 202 eyes of 101 patients with unilateral CSCR were included. Of the 101 patients, 29 of them (28%) were female. The mean age was 48 ± 11 years. In study eyes, the reticular was the most common pattern at a prevalence of 46%. In fellow eyes, the herringbone was the most common at 52%. The number of eyes with "herringbone" pattern ($p < 0.001$, $OR = 0.3$) was significantly higher in fellow eyes while "reticular" pattern ($p < 0.001$, $OR = 3$) was significantly higher in CSCR eyes. Other patterns such as branched from below, branched from above, double arcuate and laterally diagonal were not significantly different. A negative trend was observed when comparing herringbone pattern to age, but statistical significance was not reached. Acute CSCR had a larger number (14/49) of herringbone patterns whereas chronic CSCR had the greatest numbers (14/21) of reticular patterns, however, there was no statistically significant difference.

Conclusions: Conclusions: Reticular pattern was more common in CSCR eyes, while herringbone was more in fellow eyes. This is a similar trend to studies comparing CSCR to healthy eyes. Since we are comparing eyes within the same patient, this trend also demonstrates that eyes develop these perturbed vascular patterns in conjunction with disease progression.

CONTROL ID: 3535432

SUBMITTER (NAME ONLY): Andrew Pivovar

TITLE: Characterization of Phospholipid Transfer Protein (PLTP) and Cholesterol Ester Transfer Protein (CETP) expression and activity levels in human Retinal Pigment Epithelium (RPE) cells

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pivovar, L. Ibrahim, A. Yazdanyar, Ophthalmology, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Andrew Pivovar: Commercial Relationship: Code N (No Commercial Relationship) | Leina Ibrahim: Commercial Relationship: Code N (No Commercial Relationship) | Amirfarbod Yazdanyar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Drusen seen in Age Related Macular Degeneration (AMD) are filled with lipid particles. Phospholipid Transfer Protein (PLTP) and Cholesterol Ester Transfer Protein (CETP) are main players of lipid homeostasis systemically, however their role in lipid metabolism and drusen formation remains unknown. In this pilot study, we aim to characterize PLTP and CETP expression and activity levels in human retinal pigment epithelium (RPE) cells.

Methods: Immortalized human ARPE-19 cells were grown at 37°C to 70-80% confluence in Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12 (DMEM:F12) with 5% Fetal Bovine Serum (FBS) and 1% Penicillin/Streptomycin in culture flasks before conducting experiments. PLTP and CETP protein expression levels and activity were measured on RPE cell lysate and media via western blot analysis and activity assay kits. Monolayers of cultured ARPE-19 cells were fixed and immunostained with anti-PLTP and anti-CETP antibodies to examine cellular localization of these proteins.

Results: The presence of PLTP in ARPE-19 cells was confirmed via western blot. PLTP activity in ARPE-19 cell lysate was found to be similar to its activity in WT mouse plasma. Activity assays also detected CETP activity in ARPE-19 cell lysate. Immunohistochemistry (IHC) analysis of PLTP and CETP in ARPE-19 cells was successful in visualizing both proteins but insufficient to determine possible protein localization to a cellular compartment.

Conclusions: Our findings showed that PLTP and CETP are both expressed in RPE cells. PLTP activity is measurable in RPE cells and is comparable to its activity in plasma when adjusted for protein concentration. CETP activity is present but it is low. Our data suggest that RPE cells possess the machinery for lipid production and that the study of these proteins in RPE physiology and their role in AMD pathogenesis is prudent.

CONTROL ID: 3535435

SUBMITTER (NAME ONLY): Evan Chen

TITLE: Gender Differences in Procedural Volume of Retina Specialists in the United States

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Chen, P. Feng, A. Ahluwalia, T.A. Mir, K.H. Nwanyanwu, J. Chow, R. Adelman, Ophthalmology & Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|B.K. Young, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies have found that female ophthalmologist trainees and cataract surgeons perform fewer procedures than their male counterparts even after controlling for clinical productivity and parental leave. However, little is known about gender differences in practice patterns among retina specialists. Thus, we compared procedure volume among practicing male and female retina specialists in the United States.

Methods: We used the Medicare Provider Utilization and Payment Data: Physician and Other Supplier Dataset and the Physician Compare National Downloadable File to identify procedures billed in 2017. Retina specialists were defined as those who performed intravitreal injection or posterior segment photocoagulation while not billing for neodymium-doped yttrium aluminum garnet laser capsulotomy. Common retina procedures were categorized into 3 groups: intravitreal injections, posterior segment laser and surgical retinal detachment repair. We examined associations between gender and procedural volume using linear regression while controlling for providers' clinical volume, years since medical school graduation, and group practice size.

Results: In our cohort, 2,413 (82.4%) male and 516 (17.6%) female retina specialists billed Medicare for a retina procedure in 2017. Female retina specialists billed for significantly fewer clinical visits in 2017 (1,229 vs 1,807 per provider per year; $p < 0.001$) and had significantly more members in their group practice (434 vs 237 per provider; $p < 0.001$) than males. In multiple regression analysis, male gender was associated with greater annual laser volume (β , 12.2; 95% confidence interval [CI], 5.5 to 18.9; $p < 0.001$) as well as surgical retinal detachment repair volume (β , 9.61; 95% CI, 6.5 to 12.7; $p < 0.001$) after controlling for clinical volume, group practice size and years in practice. There was no significant difference in yearly intravitreal injection volume by gender (β , 171.6; 95% confidence interval [CI], -83.5 to 426.6; $p = 0.19$).

Conclusions: Female retina specialists performed fewer clinic visits and procedures than male retina specialists in 2017. After controlling for provider experience, group practice size and clinical volume, male retina specialists performed significantly greater numbers of posterior segment laser and retinal detachment procedures, however, there was a non-significant difference in intravitreal injection volume.

CONTROL ID: 3535449

SUBMITTER (NAME ONLY): Peter Nesper

TITLE: Baseline choriocapillaris flow deficits in treatment-naïve neovascular AMD correlate with number of subsequent anti-VEGF injections

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.L. Nesper, N. Konopek, J.X. Ong, A.A. Fawzi, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using optical coherence tomography angiography (OCTA), we tested the hypothesis that baseline choriocapillaris flow deficits surrounding treatment-naïve choroidal neovascular membranes (CNV) correlate with the number of subsequent anti-vascular endothelial growth factor (VEGF) injections during the course of treatment for age-related macular degeneration (AMD).

Methods: We used a semi-automated method to compensate for focal and global signal attenuation of the treatment-naïve choriocapillaris. We then binarized the choriocapillaris using the local Phansalkar and global MinError(I) methods. We quantified flow deficit density (FDD) in the 200 µm annulus surrounding the dark halo of the CNV and the entire area outside the dark halo of the CNV. We used Pearson r and t-tests to compare FDD at baseline with number of anti-VEGF injections received from 6 to 12 months and 12 to 24 months after starting therapy

Results: Our initial analysis included 9 eyes of 9 patients (6 females; age 69.9 ± 5.7 years). The number of anti-VEGF injections, which ranged from 1 to 6 over the subsequent 6 to 12 months, was significantly correlated with greater baseline FDD in the annulus (Phansalkar, $r=0.797$, $p=0.005$; MinError(I), $r=0.690$, $p=0.020$). When assessing injections received between 6 and 12 months, eyes that received higher number of injections ($n=5$, 4-6 injections) had higher FDD in the annulus and entire area around the dark halo (Phansalkar, $p<0.05$) compared to the low injection group ($n=4$, 1-2 injections). These relationships showed a trend using MinError(I) (both $p>0.05$). No tests were significant for number of injections between 12 and 24 months.

Conclusions: The study highlights the importance of the choriocapillaris during the pathogenesis of neovascular AMD. Our results suggest an early influence for choriocapillaris deficiency on treatment response between 6 and 12 months, but more subjects are needed to confirm these results.

CONTROL ID: 3535466

SUBMITTER (NAME ONLY): Andrea Minella

TITLE: TGM2 inhibition with cysteamine hydrochloride does not impact corneal epithelial and stromal wound healing in vitro and in vivo

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Tissue transglutaminase 2 (TGM2), a protein cross-linker associated with scar tissue development following wound healing, is integral for epithelial cell migration and adhesion and involved in the transformation of keratocytes to fibroblasts and myofibroblasts ("KFM" transformation). We hypothesized that TGM2 inhibition with cysteamine hydrochloride (CH), the active compound in Cystaran[®], would not impair epithelial migration in vitro, would be safe for application to epithelial and stromal wounds, and would result in decreased corneal haze formation following stromal wound healing.

Methods: CH was applied to corneal epithelial cells in vitro and migration assays were performed. 3 New Zealand white rabbits received bilateral corneal epithelial wounds, and 8 rabbits received bilateral stromal wounds by PTK. In each trial, one eye received CH and the contralateral eye received vehicle control, QID (until healed or until euthanasia, respectively). Rabbits received daily ophthalmic examinations, inflammation scoring, and fluorescein photography. SD-OCT was also performed at fixed time-points in the stromal wound trial. Corneas from the stromal trial were collected following euthanasia at day 28 or 42, and H&E, IHC, qPCR, and Western blots were performed to assess healing and KFM transformation.

Results: Epithelial cell migration was unaffected by CH in vitro. Topical application of CH to experimentally wounded rabbit corneas was safe following both epithelial wounding and stromal wounding, with no difference in healing found between treated versus control eyes regardless of depth of wound. There was no difference in KFM transformation in vitro or in stromal haze development in vivo between CH treated and control tissues with comparable haze areas on OCT and α -smooth muscle actin expression in corneal tissue.

Conclusions: Despite previous reports highlighting the importance of TGM2 in epithelial cell processes, no effect on corneal epithelial cell migration or epithelial or stromal wound healing was found in this study. These results support the safe use of this compound in patients, including when corneal wounds are present. There was no effect on corneal scar tissue formation in this study, highlighting the need for future studies investigating additional inhibitors.

CONTROL ID: 3535481

SUBMITTER (NAME ONLY): Muhammad Chauhan

TITLE: Anatomic and Visual Outcomes of patients with Incomplete Closure of Zone 3 Scleral Lacerations

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Prompt repair of post-traumatic scleral lacerations (SLs) is suggested to restore globe integrity. When a zone 3 SL extends posteriorly, repairs can be challenging (Fig. 1). We reviewed the visual outcomes of patients with and without complete repair of zone 3 posterior SLs treated with pars plana vitrectomy (PPV).

Methods: We reviewed 110 patients with ruptured globes who underwent globe exploration and/or repair, followed by PPV for the management of traumatic vitreoretinal sequelae (i.e., non-resolving vitreous hemorrhage, retinal detachment, lens rupture, intraocular foreign body) between 2008 and 2020. Demographic, surgical, perioperative, and visual acuity (VA) data were recorded. Patients whose SL could not be entirely closed, or with signs of posterior globe rupture based on examination, CT, or ultrasonography, were included in the study. At least 6-months follow-up post-PPV was required. Bivariate analysis between the incomplete closure and the complete closure group was used to identify differences between VA. Analysis was reported as mean \pm SD. Two-tailed tests were evaluated with an $\alpha = 0.05$.

Results: Of the 110 patients identified with ruptured globes, 14 had an incompletely repaired zone 3 SL and met our follow-up criteria. The average age of patients with incomplete repair of a zone 3 SL was 43.28 ± 17.83 years. Most of these patients were men (85.71%). The average number of surgical interventions post-initial repair that these patients underwent was 2.92 ± 1.32 . Mean VA at presentation in patients with an incomplete closure was logMAR 2.47 ± 0.28 , compared to 2.36 ± 0.33 in the complete closure group ($n=7$). However, no significant difference in the mean initial VA between these two groups was detected ($p=0.46$). In addition, final VA measured on the most recent follow-up visit showed no significant difference between mean best corrected VA in the incomplete closure (2.03 ± 0.82) and complete closure (2.25 ± 0.32) groups ($p=0.49$). There were no documented cases of endophthalmitis, and one eye was enucleated. The mean final IOP in patients in the incomplete closure group was within normal limits (10.58 ± 5.93 mmHg).

Conclusions: Our study indicates that incomplete closure of posterior SLs can be compatible with good outcomes, provided early vitreoretinal intervention. Therefore, aggressive attempts at closing posterior SLs should be avoided.

CONTROL ID: 3535482

SUBMITTER (NAME ONLY): Yueh-Feng Wu

TITLE: Intravital imaging of the anterior segment by lightsheet microscopy

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Intravital imaging approaches have emerged as a powerful technique to study cellular behaviors in the natural environment. Various intravital microscopy strategies have been used to characterize cell dynamics in live mice; however, an optical modality for large-scale imaging of ophthalmology with the subcellular resolution is still a great challenge. Here, we demonstrate a new lightsheet microscopy that enables live imaging of the anterior segment in fluorescent transgenic mice. Furthermore, we highlight the imaging of the corneal endothelium whose detailed healing process remains unclear.

Methods: The excitation source, equipped with 488, 561, and 640nm lasers, is collimated and expanded to the desired beam diameter at $1/e^2$ width of 3mm. The expanded laser beam uses an acousto-optic tunable filter to control the exposure time and wavelength selection. Two water-immersion objective lenses, 10x NA0.3 and 16x NA0.8, are used for excitation and detection respectively. During imaging, the customized eye holder is designed to stabilize the eyeball as well as minimize motion artifacts. The large-scale 3-dimensional (3D) images can be stitched by 5 sub-stacks of which dimensions are $400 \times 512 \times 250 \mu\text{m}^3$.

Results: Large-scale 3D images of ocular surfaces, including the full thickness of corneas and limbus, and the intraocular lens can be visualized. We create wounds with the precise, controllable size of $50 \mu\text{m} \times 50 \mu\text{m}$ by multiphoton femtosecond laser ablation in corneal endothelium to characterize the 4-dimensional wound healing dynamics. During homeostatic status, corneal endothelial cells were outlined in hexagonal shape without proliferation. After wounding, cells on the wound edge exhibited a latent period for about 9 hours before they started migrating as a sheet toward the wound center. This migratory phase lasted from 10 hours to about 40 hours after wounding and closed the wound. Large-scale imaging showed that endothelial cells across the entire cornea remained arrested in G1-phase during the entire healing process without division. Without replenishment of new cells, the healed wound had reduced cell density with compensatory cell enlargement.

Conclusions: This study not only broadens the application of lightsheet microscopy on intravital imaging in ophthalmology but also provides key insights into the spatiotemporal cell dynamics of corneal endothelium during wound healing.

CONTROL ID: 3535493

SUBMITTER (NAME ONLY): Anat Loewenstein

TITLE: Artificial intelligence algorithm for retinal fluid volume quantification from self-imaging with a Home OCT System

SESSION TITLE: AMD: clinical research - new therapies and technologies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The Notal OCT Analyzer (NOA) is a Deep learning-based algorithm developed for Notal's Home OCT System. This study evaluated the performance of the NOA in segmentation of intraretinal fluid (IRF) and subretinal fluid (SRF) regions, and quantification of fluid volumes, in cube scans from self-imaging of subjects with neovascular age-related macular degeneration at home with the Home OCT System

Methods: The data comprised a total of 2024 B-scans, with 8 eyes contributing 3 volume scans each. Each B-scan was segmented independently by 3 human expert graders to identify and quantify IRF and SRF. Intra-group and inter-group agreement were compared (i.e., agreement between the NOA and human graders, versus within the human graders). The outcome was the Dice coefficient for segmentation comparisons (pixel-wise and compared by Bonferroni-adjusted Kruskal-Wallis test), and the Pearson correlation coefficient and absolute mean difference for volume comparisons.

Results: Of the 2024 B-scans, the number identified with fluid by Grader 1 was 449 (356 with SRF and 96 with IRF). For the segmentation, the Dice coefficient of the NOA was not statistically different from that of the human graders. For the fluid quantification, the correlation coefficient between the NOA and the human graders (mean of three) was . The absolute mean difference between the NOA and the human graders (mean of three) was 1.2 nL. This was lower than the difference between Graders 1 and 2 (1.5 nL) and Graders 1 and 3 (1.8 nL), and similar to the difference between Graders 2 vs 3 (1.2 nL).

Conclusions: The NOA performs robustly in automatically segmenting and quantifying retinal fluid from cube scans acquired by patient self-imaging using the Home OCT System. In sample of eyes, the agreement with human expert grading was very high, and was similar or superior to the level of agreement between different human experts. Automated analysis of OCT images is a prerequisite for efficient remote patient monitoring with a Home OCT System that generates data at scale over time and may be useful for patient care.

CONTROL ID: 3535494

SUBMITTER (NAME ONLY): Elyssa Wong

TITLE: Inter-eye genomic heterogeneity in bilateral retinoblastoma via aqueous humor liquid biopsy

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Children with bilateral retinoblastoma (RB) receive similar treatments for each eye, however, there is often a variable therapeutic response between the eyes. Independent genomic events may occur during tumorigenesis in each eye, but these alterations are not fully understood. In this case report, we use the aqueous humor (AH) liquid biopsy to evaluate the cell-free tumor DNA (ctDNA) from each eye in a single patient with bilateral RB.

Methods: One patient with bilateral RB was included. Multiple samples of AH were obtained from each eye during routine intravitreal melphalan therapy and following enucleation of the left eye. Routine clinical blood testing was performed to determine germline RB1 status. CtDNA was isolated from the AH and sequenced on an Illumina platform to assess genome-wide somatic copy number alterations (SCNAs). The same sequencing libraries were used to identify somatic RB1 pathogenic variants using a custom hybridization and next generation sequencing panel targeting RB1. Tumor fraction (TFx) was estimated using ichorCNA software.

Results: Five AH samples from both eyes (3 from the right eye and 2 from the left eye) were included. Peripheral blood RB1 testing detected germline 13q and 16p deletions. Analysis of AH ctDNA identified a different somatic RB1 mutation and distinct SCNA profiles in each eye. Three SCNAs were consistently identified in all AH samples from the

right eye; two SCNAs were detected in each AH sample derived from the left eye. The right eye was salvaged and TFX values in this eye decreased over the course of treatment. The left eye required enucleation due to tumor recurrence and demonstrated higher TFX values.

Conclusions: We present distinct inter-eye genomic profiles in a case of bilateral RB using the AH liquid biopsy. In addition, the longitudinal alterations in TFX corresponded to therapeutic response in each eye. Identifying inter-eye genomic heterogeneity without the need for enucleated tumor tissue may help direct active management of RB, with particular usefulness in bilateral cases.

CONTROL ID: 3535498

SUBMITTER (NAME ONLY): Rohan Singh

TITLE: Regulatory T cells Modulate Th1 Alloimmune Response by Early Suppression of Graft-site Antigen Presenting Cells via TGF- β 1

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Corneal transplants performed in inflamed high-risk(HR) host beds result in markedly higher immune graft rejection compared to low-risk(LR) setting, primarily due to maturation of host antigen-presenting cells(APCs) & their ability to allosensitize host Thelper1(Th1) cells. We examined the immunomodulatory function of regulatory T-cells(Tregs) in suppressing graft-site APC maturation in the early stages post-transplantation.

Methods: HR & LR allogeneic corneal transplantations were performed with C57BL/6 mice as donors & BALB/c as hosts. On days 3&7, post-transplantation CD4⁺CD25⁺FoxP3⁺ Tregs & phenotypic maturation markers on CD11b⁺MHC-II^{hi} APCs were assessed by flow cytometry in graft recipient mice. Tregs from graft sites were FACS sorted from HR or LR recipient mice & co-cultured to precondition bone marrow GM-CSF-generated CD11b⁺APC(1:20) in the presence of LPS(100ng/ml) & IL-2(10ng/ml) for 48 h. APC maturation markers were evaluated by flow cytometry & proinflammatory cytokine production was assessed by ELISA. Also, sorted Tregs were co-cultured with syngeneic bone marrow GM-CSF-generated CD11b⁺ APC & sonicated allogenic splenocytes(1:20:21) as above in the presence of anti-TGF β 1 blocking Ab. Subsequently, Tregs were removed, CD4⁺CD25⁻ naïve T cells were added for 5 days, IFN γ production was assessed by ELISA.

Results: Tregs frequencies & their functional phenotype (measured by FoxP3 expression) were significantly higher in LR compared to HR(p<0.01). Frequencies of MHC-II^{hi},CD80,CD86,CCR7 in CD11b⁺APC were found significantly lower in LR compared to HR(p<0.001). Expression of MHC-II, CD80, CD86, CCR7, production of IL-1 β ,IL-12 was significantly reduced in LPS-stimulated APC co-cultured with LR Tregs compared to HR (p<0.001). Blocking with TGF- β 1 antibodies abolished the suppressive effect of LR Tregs. IFN- γ production was significantly lower in the supernatant of CD4⁺CD25⁻ naïve T cells co-cultured with LPS-stimulated APC-preconditioned with LR Tregs, this effect was abolished when anti-TGF β 1 Ab was added to the preconditioned media.

Conclusions: These results provide a novel insight into the role of Tregs in suppressing APC maturation at graft-site in the early stages after corneal transplantation and, consequently, suppresses Th1 alloimmunity. These results suggest the therapeutic potential of Tregss in improving graft survival in HR corneal transplantation.

CONTROL ID: 3535513

SUBMITTER (NAME ONLY): Igor Kozak

TITLE: The effect of anti-VEGF injection loading dose in diabetic macular edema as measured by hand-held ERG system

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Kozak, J. Centeno, Moorfields Eye Hospital Abu Dhabi, Abu Dhabi, UNITED ARAB EMIRATES|

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ABSTRACT BODY:

Purpose: Anti-vascular endothelial growth factor (VEGF) is the first line of treatment for diabetic macula edema (DME). Previous retinal function studies using full-field or multifocal electroretinography have investigated late effects of anti-VEGF treatment on retina. The aim of this study is to follow full-field electroretinography (ffERG) changes for the first 6 months of anti-VEGF treatment using portable ffERG system.

Methods: In this prospective pilot study, eyes with diabetic macula edema and either severe NPDR or PDR have been included. Inclusion criteria were treatment naïve patients with no prior ocular surgery willing to participate in study. All patients received 3 injections in the initial loading phase with 3 months follow up and injection if needed. The retinal function has been assessed at baseline and months 1, 2, and at the last follow up - 6 months after the first injection with the full Field Flash ERG (RETeval® ERG). We measured 16Td and 32Td flash stimulus for both a- and b-wave amplitudes and implicit times. Other collected data included best-corrected visual acuity (BCVA) and spectral-domain optical coherence tomography (OCT) at every visit.

Results: Eleven eyes of 7 patients with a mean age of 54 years (range 42-67) have been included in the analysis. Patients have received on average 4 injections in the study period. The mean BCVA improved significantly from 0.41 ± 0.34 to 0.27 ± 0.29 logMar ($p=0.014$). The central retinal thickness improved from 415 ± 151 microns to 333 ± 105 microns, which was not statistically significant ($p=0.1$). The implicit time at 32Td flash intensity significantly prolonged from 32.08 ± 3.68 ms to 33.48 ± 3.05 ms ($p=0.04$) (Figure 1). There was a moderate correlation between the BCVA gain and the implicit time at baseline of $r=0.63$. The amplitudes remained unchanged and stable during the observation. In the majority of patients, the implicit time prolonged after the first injection and then slightly recovered or remained stable at the new level over the course of the following 5 months.

Conclusions: The best corrected visual acuity improved significantly as a result of the anti-VEGF intravitreal treatment. The implicit time significantly prolonged after the first injection followed by stabilization with time. This might be a manifestation of an increased cell stress after the initiation of treatment to which the eye adapts over the course of the treatment.

CONTROL ID: 3535523

SUBMITTER (NAME ONLY): Heijan Ng

TITLE: Retinal damage extends beyond the retinal detachment

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Despite anatomically successful surgery for fovea-on rhegmatogenous retinal detachment (RD), unexplainable loss of vision is regularly observed in these patients. We hypothesize that the retinal function loss induced by the RD extends beyond the detached area, towards the fovea. Thus, the aim of this study is to investigate the retinal sensitivity loss in relation to the distance to the RD border in patients with fovea-on rhegmatogenous RD.

Methods: We prospectively evaluated 15 patients with fovea-on RD and healthy fellow eye. Preoperatively, OCT-scans of the RD border were obtained (Spectralis-OCT2, Heidelberg Engineering). The RD border was located on the B-scans and highlighted on the SLO-image.

Microperimetry (MAIA, Centervue) was performed using a custom grid of 52 points covering the RD border and the retina on both sides. The macular area was investigated using the standard foveal centered grid of 37 points covering a circular area of 10° in diameter (Figure 1). At 6 weeks postoperatively, microperimetry was performed in the fellow eye, covering the same areas as in the study eye.

Microperimetry data was overlaid on the SLO-image and the RD border was indicated; for each sensitivity measurement, the shortest distance to the RD border was calculated. Loss of retinal sensitivity was calculated as the difference in sensitivity between the study and the control eye at each corresponding location (study-control). The relation between retinal sensitivity loss and the distance to the RD border was assessed using a locally weighted scatterplot smoothing (LOWESS) curve.

Results: Retinal sensitivity loss was 22 dB at 3° inside the RD and decreased approximately linearly to 4 dB at 2° outside the RD. The loss further decreased outside the RD until it reached a plateau of 2 dB at 6° (Figure 2).

Conclusions: Retinal sensitivity loss extends beyond the RD border towards the fovea. These results may explain the loss of vision in patients in whom the fovea has not been detached.

CONTROL ID: 3535527

SUBMITTER (NAME ONLY): Roberto dell'Omo

TITLE: Unintentional retinal displacement in eyes treated for rhegmatogenous retinal detachment with pars plana vitrectomy and silicone oil.

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To study the clinical characteristics, outcomes and rate of unintentional displacement in eyes treated for rhegmatogenous retinal detachment (RRD) with pars plana vitrectomy (PPV) and silicone oil (SO).

Methods: This was a retrospective observational study. Overall, 50 eyes of 50 patients who underwent surgical repair by 23-gauge PPV and SO injection for primary RRD complicated by proliferative vitreoretinopathy (PVR) between December 01, 2018 and June 30, 2020, at a single Institutional Center, were followed. One thousand centistokes SO was used in all eyes. The patients postured face-down immediately after surgery. Blue-fundus autofluorescence (B-FAF) pictures were obtained at 1 month after surgical procedures using the Spectralis HRA+OCT (Heidelberg Engineering, Heidelberg, Germany)

Results: Primary success rate was obtained in 44 eyes (88%) on which the final analysis was conducted.

Preoperative PVR was grade A in 7 (15.9%), grade B in 28 (63.6) and grade C in 9 (20.5) eyes. Fovea was off and the detachment involved both the superior and inferior hemispheres of the retina in all cases. Breaks were located in the upper quadrants in 21 (47.7%) eyes, in the lower quadrants in 12 eyes (27.3%), and in both upper and lower quadrants in 11 (25%) eyes. Mean number of breaks was (2.4 ± 1.9) . Intraoperative PFCL was used in 30 (68.2%) eyes. Peeling of epiretinal membrane/internal limiting membrane in the macula area was performed in 13 (29.5%) of eyes during the first operation and carried out in all other eyes in occasion of SO removal. Preoperative BCVA was 2.1 ± 1.0 logMAR and improved to 0.8 ± 0.7 logMAR at the last follow-up ($P < 0.0001$). An upward unintentional retinal displacement was observed in 2 cases (4.5%).

Conclusions: Pars plana vitrectomy and SO tamponade for complicated RRD are associated with good anatomical and functional outcomes and with a very low rate of unintentional retinal displacement. Of the factors potentially implicated in favoring displacement that were studied, none was found significant.

CONTROL ID: 3535540

SUBMITTER (NAME ONLY): Oi Man Mandy Wong

TITLE: Comparison of trabeculectomy and oral valganciclovir in treating cytomegalovirus anterior uveitis(CMV AU) with uncontrolled intraocular pressure(IOP)

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There has been no consensus on the treatment of CMV AU with uncontrolled IOP despite maximal topical medications. This retrospective case series described the efficacy and safety of trabeculectomy with mitomycin-C(MMC) in these patients, and compared it with previously published efficacy data on oral valganciclovir.

Methods: Forty-one eyes of 41 CMV AU patients received either trabeculectomy with MMC(n=30) or a single course(20-148 days) of oral valganciclovir (n=17) for uncontrolled IOP, with 6 in the latter requiring subsequent trabeculectomy. Clinical information, IOP and use of IOP-lowering medication/steroid at baseline and every 3 months over 2 years post intervention were recorded. Survival endpoint was defined as further intervention for uncontrolled IOP(glaucoma surgery or another course of valganciclovir). Treatment success was defined as IOP \leq 21 mmHg with same or less IOP-lowering medications compared to baseline, without systemic acetazolamide or reaching survival endpoint.

Results: For those receiving trabeculectomy, median IOP significantly dropped from 24.1(IQR: 20.5, 32.0)mmHg at baseline to 13.0(10.3, 16.2)mmHg at 24 months, while on 5.0(5.0, 5.0) and 0.0(0.0, 0.8) IOP-lowering medications, respectively, with up to 72.2% IOP reduction(Wilcoxon sign-rank test, $p < 0.01$ at all time points). Treatment success was 80% at 24 months. Those with history of/concomitant intraocular operation had shorter survival(18.8 months versus 23.5 months, log-rank test, $p = 0.041$, Fig.1). 53.5% and 30.0% had hypotony and wound leak, respectively, with no serious sequelae.

In the first interventions for IOP control (n=38, either trabeculectomy or valganciclovir), female, history of endophthalmitis and systemic acetazolamide use at baseline were associated with longer survival compared to their counterparts($p = 0.035$, 0.046 , 0.034 , respectively). After excluding one eye with prolonged valganciclovir use post-trabeculectomy, trabeculectomy group(n=22) had higher chance for treatment success at 24 months than valganciclovir group(n=15)(OR: 6.8, 95% C.I.:1.5 to 30.2), longer survival(21.9 months versus 13.6 months, $p = 0.003$, Fig 2), but less %reduction in steroid use(Fisher's exact test: $p = 0.018$).

Conclusions: Trabeculectomy with MMC is efficacious and safe for IOP control in CMV AU, with higher success than oral valganciclovir but less %reduction in steroid.

CONTROL ID: 3535547

SUBMITTER (NAME ONLY): Mijie Li

TITLE: The association of time outdoors and patterns of light exposure with myopia in children: implications for prevention

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This cross-sectional study evaluates the association of time outdoors and light exposure patterns with myopia in children from the Singapore Growing Up Towards Healthy Outcomes (GUSTO) birth cohort

Methods: We performed cycloplegic spherical equivalent (SE), myopia ($SE \leq -0.5D$) and axial length (AL) measurements in 422 multi-ethnic children (41.2% myopic; 47.6% girls; 59.5% Chinese) who attended the 9-year GUSTO visit and were not on myopia treatment (atropine and orthokeratology). Time outdoors in the past month (physical or leisure activities) was assessed with a questionnaire and outdoor activity types with an activity diary filled over 7 days. Light exposure patterns: light levels (lux), duration, timing (morning: 7-11 AM; afternoon: 11 AM-3 PM; evening: 3-7 PM) and frequency of light exposure (number of outdoor episodes ≥ 1000 lux continuously ≥ 5 mins) were measured with a wrist-worn watch (FitSight) over 14 days. Paired eyes ($n=844$) were analyzed using Generalized Estimating Equations with multivariable linear or logistic regression model

Results: Time outdoors (Mean \pm SD: 1.65 ± 1.42 hours/day) and average light levels (467 ± 231 lux) were low, with 76.0% of the daily duration of light exposure < 5000 lux. Light levels were highest during mid-day, compared to the morning or evening ($P < 0.001$). Children exhibited 1.7 ± 1.0 daily outdoor episodes. Time outdoors, the duration and frequency of light exposure were higher on weekends than weekdays ($P < 0.05$). Boys exhibited higher light levels, duration and frequency of light exposure than girls ($P < 0.05$). While outdoors, children spent the longest duration on walks, neighborhood play and swimming. In multivariable analyses, time outdoors was associated with lower odds of myopia (OR=0.79; 95% confidence interval (CI): 0.67 to 0.93; $P=0.005$) and less myopic SE ($\beta=0.15D$; 95% CI: 0.01 to 0.29; $P=0.034$) but not associated with AL ($P=0.15$). Light levels were not associated with myopia and SE but were marginally associated with AL ($\beta=-0.31mm$; 95%CI: -0.62 to -0.003; $P=0.048$). The duration, timing or frequency of light exposure were not associated with myopia, SE or AL ($P > 0.05$)

Conclusions: Increasing time outdoors was protective against myopia and myopic SE. Light levels or specific outdoor light patterns were not associated with myopia. Longitudinal studies are needed to confirm these findings

CONTROL ID: 3535574

SUBMITTER (NAME ONLY): Ruben Hemelings

TITLE: Convolutional neural network predicts visual field threshold values from optical coherence tomography scans

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Lengthy and unreliable visual field (VF) testing presents a burden to both glaucoma patient and clinician. We retrospectively evaluated the ability to predict VF loss from unsegmented optical coherence tomography (OCT) scans using deep learning (DL) technology.

Methods: Data used in this study consist of 1643 matched OCT-VF pairs encompassing 998 eyes of 542 patients that visited the glaucoma clinic of the University Hospitals Leuven between 2015-2019. Inclusion criteria were defined as having had a SPECTRALIS® OCT scan with the Glaucoma Module Premium Edition (scanning laser ophthalmoscopy (SLO), 24 radial scans and three circumpapillary rings), as well as a reliable Humphrey Field Analyzer (HFA) 3 exam with the strategy 24-2 SITA Standard (52 test points), performed on the same day. Data was split into train/validation/test sets on patient level, following a 60/20/20 key.

The convolutional neural network used across all experiments was an Xception model pretrained on ImageNet. The 52 output nodes feature a linear activation function to allow for regression. The model was trained using mean squared error loss and Adam optimizer. Four models were trained (using the 3.5mm, 4.1mm, 4.7mm circumpapillary scans and SLO images), which were also compared with a combined model. Analysis on the 24 radial scans was beyond the scope of this study. Performance was evaluated using Pearson's r and mean absolute error (MAE). 95% confidence intervals were obtained through bootstrap sampling.

Results: The circumpapillary scan with the largest radius (4.7mm) achieved the best performance among all individual models ($r=0.77$ [0.72-0.82], $MAE=5.08$ [4.68-5.50]). Models trained on circumpapillary OCT scans significantly outperformed the model trained using SLO images ($r=0.65$ [0.58-0.71], $MAE=5.79$ [5.23-6.38]). Model combination resulted in an $r=0.78$ [0.74-0.83] and $MAE=4.86$ [4.43-5.29]. Performance was comparable on the test set ($r=0.79$ [0.75-0.82], $MAE=4.76$ [4.40-5.15]).

Conclusions: This study is the first to report on a DL system that predicts individual VF threshold values from unsegmented OCT scans. The average correlation of 0.79 exceeds the performance of prior work that leveraged retinal layer thickness info using non-DL techniques. Fast, consistent VF prediction from OCT could become an ersatz solution for visual function estimation in patients that are unable to complete HFA exams.

CONTROL ID: 3535586

SUBMITTER (NAME ONLY): Svenja Sonntag

TITLE: Impact of laser-induced damage on the fluorescence lifetimes at the rabbit fundus

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: With the increasing application of funduscopically invisible retinal laser treatments, a sensitive method enabling the detection of small structural and metabolic changes is desired. Aim of this study was to apply the fluorescence lifetime imaging ophthalmoscopy (FLIO) to monitor the sites of laser irradiation to identify its potential in the evaluation of laser-induced tissue changes.

Methods: Seven eyes of Chinchilla bastard rabbits were treated in vivo using a diode laser with a wavelength of 514 nm, spot diameter of 85 µm and single pulses with duration of 5.2 or 50 µs with different power settings. FLIO (excitation at 473 nm, detection with short spectral channel (SSC, 498-560 nm) and long spectral channel (LSC, 560-720 nm) was conducted directly and one week after irradiation. Structural changes were examined by optical coherence tomography (OCT).

Results: Selective damage of retinal pigment epithelium (RPE) was induced with the shorter pulse duration with the power up to 5.6 W, while visible photocoagulation was achieved with the longer pulses and maximum power of 11 W. Directly after irradiation the FLT at laser spots was highly extended (SSC: 1142±109 ps; LSC: 461±47 ps) compared to the one in the non-irradiated periphery (SSC: 705±35 ps; LSC: 211±20, p<0.01). The FLT around photocoagulation was also significantly longer (SSC: 738±45 ps; LSC: 229±22 ps), whereas it was rather shorter at the further surrounding (SSC: 637±55 ps; LSC: 182±28 ps) (p<0.01). At the sites of selective RPE damage, the FLT was slightly longer in the nearby surroundings directly after irradiation, whereas, after one week, shortened over wider region, up to about 1000 µm from the spots. The longer FLT in the nearby surroundings directly after irradiation corresponded to the hypofluorescent area in fundus autofluorescence (FAF), and also to the disruption of ellipsoid zone and external limiting membrane in OCT. These changes in FAF and OCT were no more visible after one week.

Conclusions: Extension of FLT at laser spots is considered due to RPE damage, whereas the longer FLT in their surroundings directly after irradiation might be a result of temporary change of photoreceptor, and the later shortening due to tissue metabolic alterations. FLIO may therefore be a sensitive tool to monitor subtle structural as well as metabolic changes following laser treatment.

CONTROL ID: 3535589

SUBMITTER (NAME ONLY): David McGaughey

TITLE: Million Cell Retina Transcriptome Meta-Atlas for All

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. McGaughey, V. Swamy, T. Fufa, R.B. Hufnagel, OGVFB, National Eye Institute, Bethesda, Maryland, UNITED STATES|Z. Batz, NNRL, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To create an exhaustively optimized single cell retina single cell transcriptome dataset created from all publicly available retina single cell transcriptomes. We use this dataset to provide the basis for a highly responsive reactive web app for querying gene expression across retina cell type, study, species, developmental stage, and other factors. Second, we demonstrate how research groups can project their private single cell experiments onto our reference retina single cell atlas with minimal compute resources.

Methods: We re-quantified over 1 million single cell transcriptomes across three species, 30 studies, and 7 single cell technologies. After quality control we retain over 700,000 high quality transcriptomes. To optimize the batch correction, we tested 12 independent tools methods and benchmarked them with an un-biased algorithm to identify the optimal method and parameters. After batch correction we create a 2 dimensional UMAP projection, run thousands of differential gene expression tests across cell types, and calculate developmental trajectories for the major retinal cell types. We then hand-curated over 300,000 published retina cell type labels to create an xgboost-based machine learning tool to label all cells in our dataset.

Results: After batch correction the 2D UMAP places the retina cell types in distinct spaces with the progenitor populations in the center. The photoreceptor progenitors flow from the center into the differentiated rods and cones. Likewise, the amacrine / horizontal precursors lead into the terminally differentiated amacrine and horizontals. The retinal ganglion and muller glia are also in distinct clusters. Importantly these cell type positions are generally consistent across species and studies. Our differential testing confirms that our machine learning cell type tool correctly labels the cells based on the community knowledge.

Conclusions: Despite a high amount of technical variation between published single cell transcriptome atlases, we confirm that we can create a coherent, high-quality meta-atlas. Furthermore, we demonstrate how our meta-atlas is a community resource by illustrating projection of independent and outside single cell transcriptome data onto our meta-atlas with minimal compute and disk resources. Our dataset is made available for powerful user-led analysis at plae.nei.nih.gov.

CONTROL ID: 3535593

SUBMITTER (NAME ONLY): Abdelhalim Awidi

TITLE: Outcomes of simultaneous Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) and intraocular lens exchange surgery

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Awidi, Y. Daoud, Cornea, Cataract and External Disease, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the outcome of performing simultaneous Descemet Stripping Automated Endothelial Keratoplasty (DSAEK) and Intraocular Lens (IOL) exchange surgery.

Methods: A non-randomized retrospective chart review was conducted on 41 patients. The studied outcomes included status of the intraocular lens, status of the cornea transplant, as well as best corrected distance visual acuity (BCDVA), spherical equivalent (SEQ), and intraocular pressure (IOP) pre-operatively, as well as post-operative 1 day, 1 week, 1 month, 3 months, 6 months, 12 months, and 24 months.

Results: 41 patients, of which, 49% male, and 51% female were included. At the time of pre-operative assessment, 14 patients had an ACIOL implant (34.1%), 11 had a PCIOL implant (26.8%), 8 were aphakic (19.5%), with the 8 remaining patients (19.5%) having either a sulcus or capsular bag IOL implants.

Positioning of the IOL after exchange was 19 iris-sutured (46.3%), 9 scleral-fixated/sutured (22%), 4 ACIOL (9.8%), 4 PCIOL (9.8%), 3 sulcus placements (7.3%), and 2 in the capsular bag (4.9%).

At 1 year follow up, 57% of the patients' corneal grafts were clear, 23% had corneal haze that did not require further surgery, while 23% had either corneal edema, or folds in the Descemet's membrane and stroma, that were managed medically. At the same time period, only one eye had subluxation that necessitated an IOL repositioning surgery.

Mean IOP remained consistent during the follow up periods (14.25 ± 5.85 at baseline and 15.43 ± 7.99 at one year).

Mean BCDVA improved from 1.33 ± 0.66 at baseline to 0.82 ± 0.70 at two years follow up.

Conclusions: Simultaneous DSAEK and IOL exchange surgery may offer a sustained improvement in visual acuity in patients with complex ocular history and may decrease the risk associated with increased trips to the operating room.

CONTROL ID: 3535601

SUBMITTER (NAME ONLY): Karina Esquenazi

TITLE: Evaluation of prevalence and risk factors for vitreoretinal involvement in fungemic patients at a tertiary care hospital

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Esquenazi, C.S. Wilkins, R. Bhuyan, J. Levenson, R.N. Ginsburg, A. Barash, A. Deobhakta, G.M. Lema, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The prevalence of endogenous fungal endophthalmitis varies between studies and the risk factors are poorly defined. This study aims to define prevalence in a large population and identify risk factors warranting ophthalmic evaluation.

Methods: Retrospective review of 291 inpatients with fungemia and a documented ophthalmic evaluation (January 2015-September 2019) was performed. We reviewed the presence of visual complaint, number and duration of positive blood cultures, history of gastrointestinal (GI) surgery in preceding 6 months, solid organ transplant, human immunodeficiency virus (HIV) infection, diabetes mellitus (DM), intravenous (IV) drug use, and central venous access. Student's t-test and chi-squared statistical analysis were performed.

Results: 291 patients were included; 6 had vitreoretinal involvement and 2 required intravitreal antifungal injection. Those with vitreoretinal involvement had an average of 3 positive cultures over 0.69 weeks, while those with normal findings averaged 2.85 positive cultures over 0.59 weeks ($p=0.89$, and 0.80 , respectively). History of GI surgery, organ transplant, immunocompromised state, DM, IV drug use, and central venous catheter were not found to be significant. However, 33.3% of the endophthalmitis group had a visual complaint compared to 4.20% of the non-endophthalmitis group ($p<0.001$). When grouped together, visual complaints, positive blood cultures for 3 or more days, and history of recent GI surgery were significant predictors of ocular involvement. For patients without any of these 3 major risk factors, the negative predictive value was 98.7%.

Conclusions: Patients who have visual complaints at the time of positive fungal blood culture are significantly more likely to have a positive screening examination. No other individual variables were found to be predictive of a positive screening examination. A positive examination is exceedingly rare in patients not meeting risk criteria (major factors) for screening. Serious consideration of replacing the current practice of uniform ophthalmic screening among fungemic patients with examination limited to those meeting major criteria is recommended.

CONTROL ID: 3535603

SUBMITTER (NAME ONLY): Xiaoshuang Jiang

TITLE: Validation of a Novel Automated Algorithm to Measure Drusen Volume and Area using Swept Source Optical Coherence Tomography Angiography

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Jiang, Sichuan University West China Hospital, Chengdu, Sichuan, CHINA|M. Shen, W.J. Feuer, P.J. Rosenfeld, G. Gregori, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|L. De Sisternes, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|L. Wang, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To validate a novel automated swept source optical coherence tomography (SS-OCT) algorithm to measure elevations of the retinal pigment epithelium (RPE) in eyes with non-exudative age-related macular degeneration (neAMD).

Methods: Patients with drusen were enrolled in a prospective OCT study and underwent imaging with both spectral domain OCT (SD-OCT, Cirrus HD-OCT, Carl Zeiss Meditec Inc, Dublin, CA, USA) and SS-OCTA (PLEX Elite, Carl Zeiss Meditec Inc, Dublin, CA, USA) at the same visit using the 6X6mm scan patterns. The RPE elevation measurements (square root area and cube root volume) from the SS-OCTA algorithm were compared with the corresponding measurement produces by the fully automated, validated algorithm on the SD-OCT instrument. Standard deviations of drusen measurements from 4 repeated scans were also calculated to evaluate the reproducibility of the SS-OCTA algorithm.

Results: A total of 53 eyes from 28 patients were scanned on both instruments. A very strong correlation was found between the measurements from the two algorithms (all $r > 0.95$), although the measurements of drusen area and volume were all larger on the SS-OCTA instrument (Figure 1). This systematic increase in area and volume measurements was due to a more accurate segmentation of Bruch's membrane in the SS-OCT algorithm. The reproducibility of the new SS-OCTA algorithm was analyzed using a sample of 66 eyes from 43 patients. The standard deviations were small in comparison to the means over the entire range of measurements. There were no significant correlations between the standard deviations and mean measurements of the square root of area and cube root of volume measurements between repeated scans using the SS-OCTA algorithm (Figure 2). The intraclass correlation coefficient was greater than 99% from different macular regions for both the square root area and cube root volume measurements.

Conclusions: A novel automated SS-OCTA algorithm for the quantitative assessment of drusen was validated against the SD-OCT algorithm and was shown to be highly reproducible.

CONTROL ID: 3535628

SUBMITTER (NAME ONLY): Louis Pasquale

TITLE: An autonomous algorithm shows that African and Hispanic Americans with primary open-angle glaucoma present with severe visual field loss patterns

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.R. Pasquale, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|J.L. Wiggs, M. Wang, T. Elze, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|J.H. Kang, B. Rosner, Epidemiology, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We applied an artificial intelligence algorithm to new-onset visual field (VF) loss encountered in 3 US prospective cohorts followed for primary open-angle glaucoma (POAG). The algorithm objectively quantified VF loss into archetypal patterns. We examined self-reported race in relation to the specific archetypes (ATs) of VF loss.

Methods: Participants aged ≥ 40 years who without glaucoma and reported eye examinations in the Nurses Health Study (NHS) ($n=75,767$; 1980 to 2018), NHS2 ($n=80,857$ women; 1989-2019), and the Health Professionals Follow-up Study ($n=36,838$ men; 1986-2018) were followed. Information on demographics including race, medical conditions and lifestyle were assessed with biennial questionnaires. Incident POAG cases with reproducible VF loss were confirmed by medical record review. The earliest reliable VF for the worse eye was identified, and archetypal analysis was used to identify the optimal number of VF loss patterns. Each case was classified according to the most dominant VF loss archetype. Multivariable-adjusted relative risks (RRs) for each archetype and 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression on pooled data. Major covariates included cohort, age, family history of glaucoma, census-tract based socioeconomic index, number of eye exams during follow-up, and medical history such as diabetes and hypertension. False discovery rate was used to account for multiple comparisons.

Results: Mean age was 57 ± 10 years and 81% were women. Of the 1377 POAG cases, 1301 were Caucasian, 36 were of African descent, 21 were Asian, and 19 were Hispanic white. We observed 14 ATs (see Figure), of which 13 reflected function loss. We observed that having African descent compared to being non-Hispanic White was associated with ATs consistent with advanced glaucomatous loss: AT5 \rightarrow RR=2.84 (95%CI=1.26, 6.41); AT8 \rightarrow RR=5.35 (95%CI=1.79,16.0); AT10 \rightarrow RR=3.80 (95%CI=1.27,11.4); AT11 \rightarrow RR=3.79 (95%CI=1.32,10.9); and AT12 \rightarrow RR=11.43 (95%CI=3.77, 34.6). Being Asian compared to being non-Hispanic White was not significantly associated with any AT. Being Hispanic White compared to being non-Hispanic White was significantly associated with AT10 (RR=4.97; 95%CI=1.48,16.7) and AT11 (RR=6.58; 95%CI=2.56,16.9).

Conclusions: African and Hispanic Americans with POAG were more likely to present with central or advanced VF loss.

CONTROL ID: 3535644

SUBMITTER (NAME ONLY): Deepta Ghat

TITLE: Visual field loss and on-road driving performance in glaucoma

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Ghat, M. Gagrani, D. Anderson, Ophthalmology, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|M. Rizzo, Neurology, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Drivers with glaucomatous field loss are at greater risk for driving errors and motor vehicle crashes compared to age matched controls. This pilot study evaluated relationships between visual field loss and real-world driving in an instrumented vehicle (IV).

Methods: In a prospective pilot study, 11 Glaucoma subjects with visual acuity $\geq 20/40$ in both eyes and 6 controls with normal visual acuity and no history of ocular disease were tested on a standardized drive across commercial, rural, and highway road sections in Omaha NE in the IV, VENUS (Vehicle for Ergonomics, Neuroscience, and Safety). The IV drive video was evaluated by a certified occupational therapist and driving errors were annotated. Drivers in the IV performed a sign identification task (IT) including 73 restaurant and road signs along a 1.4 mile section of the route. Binocular visual field index (OU-VFI) and binocular superior VFI (S-VFI) and binocular inferior VFI (I-VFI) were calculated from monocular Humphrey visual fields (HVF) using previously described techniques. Cognitive ability was assessed using Montreal Cognitive Assessment [MoCA]. Spearman's rank order correlation was used to determine association between variables.

Results: 11 Glaucoma subjects (6 males, age: 57 ± 15 years, MoCA score 26 ± 3) were age matched with 6 controls (4 males, age: 69 ± 5 years, MoCA score 27 ± 2). The mean OU VFI for the glaucoma subjects was $85 \pm 14\%$ (range 61 to 99%). The mean S-VFI was $80 \pm 23\%$ and I-VFI was $89 \pm 11\%$. Driving errors in IV are enumerated in table 1. Glaucoma subjects made more driving errors than controls. Age and MoCA were not significantly associated with driving errors or performance on the LT task.

For the glaucoma subjects, driving errors were associated with OU-VFI ($r = -0.6$, $p = 0.07$). I-VFI correlated better with number of driving errors ($r = -0.7$, $p = 0.03$) than did S-VFI ($r = -0.5$, $p = 0.1$) (Figure 1).

Glaucoma subjects identified fewer street signs than controls (table 1). The percentage of signs identified correlated with worsening OU-VFI ($r = 0.8$, $p = 0.002$), S-VFI ($r = 0.8$, $p = 0.003$) and I-VFI ($r = 0.8$, $p = 0.007$).

Conclusions: Glaucoma subjects make more driving errors, particularly in lane maintenance, and have trouble identifying road signs compared to controls. Inferior field loss has greater influence on driving performance than superior field loss. Glaucoma subjects may benefit from customized driving rehabilitation therapy based on the region of their field loss.

CONTROL ID: 3535651

SUBMITTER (NAME ONLY): Saif Hamdan

TITLE: Predictors of Inadequate Health Literacy Among Comprehensive Ophthalmology Patients

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hamdan, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|E. Brown, Ophthalmology and Visual Sciences, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|S. Gangaputra, Ophthalmology and Visual Sciences, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Health literacy (HL), defined as the ability to get, understand, and use basic health information and services, is essential for effective care delivery. Yet, over quarter of US adults are estimated to have inadequate HL, which is associated with poorer health outcomes and higher health care costs. This study aims to characterize the HL profile among comprehensive ophthalmology patients and to identify the associations with inadequate HL.

Methods: In January 2020, routine HL assessment was integrated into the clinic intake performed by ophthalmic technicians in all comprehensive ophthalmology clinics at an academic eye institute as part of a quality improvement initiative. HL was assessed using the Brief Health Literacy Screening (BHLS), an orally-administered, validated 3-item survey with each question scored on a five-point Likert scale. A retrospective chart review of adult patients seen at all comprehensive ophthalmology clinic sites of an academic eye institute from January 2020 to October 2020 was performed. Information collected included basic demographic factors, education level, neighborhood area deprivation index, HL score, comorbid systemic diseases, and visual acuity. Patients younger than 18 years old or those with a preferred language other than English were excluded.

Results: A total of 5313 patients met the inclusion criteria. The median age was 69 years; the majority of patients were White (85%) and Female (60%) with 51% (2,710) of the study cohort more deprived than the national median. The average best-corrected visual acuity of the best eye was 20/25. Overall, 291 (5.5%) patients had inadequate HL and 313 (5.9%) had not completed high school. Age (both younger and older age), male gender, Black race, higher deprivation index, lower education level, comorbid diabetes, and worse visual acuity were all observed to be associated with a greater likelihood of inadequate HL.

Conclusions: Many comprehensive ophthalmology patients may still have inadequate HL despite generally higher levels of education and socioeconomic status. As many ophthalmic disease processes require chronic management, further studies should review the impact of limited HL and appropriate targeted interventions on visual outcomes.

CONTROL ID: 3535654

SUBMITTER (NAME ONLY): Cary Baxter

TITLE: Comparison of Corneal Culture Techniques Using a Pig Eye Model

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.R. Baxter, B. Tieu, B. Allen, J. Carrere, Ophthalmology, The University of Mississippi Medical Center, Jackson, Mississippi, UNITED STATES|

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ABSTRACT BODY:

Purpose: Calcium alginate (CA) swabs are recommended for culturing corneal ulcers, but cotton tip applicators (CTA) are less expensive and more readily available. Whether one is absolutely better than the other is unknown. We compared the efficacy of each swab in recovering ocular surface bacteria using a novel in vitro model under moistened and dry swabbing conditions.

Methods: Ex vivo pig eyes were de-epithelialized and incubated at room temperature to allow for growth of bacteria on the ocular surface over time. The corneas were swabbed at 4 hour increments from 0 to 24 hours and plated on blood agarose plates. Colonies were counted to create a growth curve. It was determined that swabbing the corneas after six hours of incubation allowed for enough growth of colonies that could be easily counted and was reproducible. Next, 40 pig eyes incubated together were evenly divided into two groups; 20 eyes were swabbed with thioglycolate-moistened or dry CA swabs, and the remaining were swabbed similarly with CTA. The colonies on each blood agarose plate were counted, groups were averaged and a 2-tail T-test was used for statistical analysis.

Results: Overall, there is a statistically significant difference in number of colonies obtained after swabbing the ocular surface with moistened versus dry swabs (51.9 +/- 13.2 vs 28.5 +/- 13.8, respectively; p-value <0.0001). Moreover, swabbing with a moistened CTA yielded more bacteria than dry CTA (56.1 +/- 11.5 vs 29.9 +/- 14.8, respectively; p-value <0.0001); this held true for wet versus dry CA as well (47.6 +/- 13.7 vs 27.2 +/-13.0, respectively; p-value <0.0001). Furthermore, there was a statistically higher number of colonies obtained using moistened CTA over moistened CA (56.1 +/- 11.5 vs. 47.6 +/- 13.7, respectively; p-value 0.0399).

Conclusions: Moistened CTA swabs are superior to moistened CA in isolating bacteria from the ocular surface, but a moistened CA is better than swabbing with a dry CA swab or dry CTA. Regardless of which is used, it is important that all swabs be moistened with a medium such as thioglycolate to increase the recovery of bacteria from the ocular surface.

CONTROL ID: 3535667

SUBMITTER (NAME ONLY): Madeline Curtis

TITLE: Short-term videogaming involving multiple-element tracking enhances attentive motion tracking in the periphery

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Curtis, O. Iteghie, A. Chakraborty, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|A. Chakraborty, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Attentive motion tracking is critical to daily living activities, such as navigation and team sports. Previously, we have used perceptual learning to train attentive motion tracking in the periphery for adults with central vision loss and normal vision. Here we investigated if short-term videogaming on FIFA20 that involves tracking multiple elements (players), enhances peripheral multiple objects tracking (MOT), considered a marker of attentive motion tracking. In addition, we also tested whether performance enhancement from such videogame transfers to two related tasks: global motion perception (GMP) and static numerosity judgment (SNJ, static attention), and one unrelated task: global form perception (GFP). Finally, we used two other video games, Need for Speed (involves fast visual motion) and SIMS 4 (involves feature recognition) were used as control games to test any non-specific effect of videogames.

Methods: 15 adults (26.53 ± 4.5 y) with normal binocular vision played each video game on PlayStation-4 for 30 mins, across separate sessions, with a 5d wash-out period. Psychophysical thresholds were measured for a random hemifield, pre- and post- videogame in each session. Speed threshold of MOT (8 elements, starting speed $4^\circ/\text{s}$), motion coherence threshold (GMP; 2AFC direction discrimination for random-dot-kinematograms [100 dots, 6deg/s speed]), form coherence threshold (GFP; 2AFC Glass pattern discrimination), and presentation time threshold for the SNJ task (static frames from the MOT task with 8 ± 1 element presented temporally in 2AFC) were measured. The participants filled a questionnaire to report their videogaming experience.

Results: Only the FIFA 20 significantly improved performance on MOT ($15 \pm 4.5\%$, $t_{14} = 9.7$, $p = 0.009$) and SNJ ($10.5 \pm 3\%$, $t_{14} = -7.4$, $p = 0.02$) tasks, but not on GMP and GFP. Furthermore, linear regressions were conducted using the percentage change in MOT and SNJ as the dependent variables, and the type of video game, age, gender, and past gaming experience, as predictor variables. Other than FIFA20, no other variable independently predicted task improvement.

Conclusions: Videogaming involving tracking multiple elements significantly improved peripheral attentive motion tracking. Such improvement transferred to one related task. Our results suggest that videogaming could be considered as a medium to train peripheral attention in patients with central vision loss.

CONTROL ID: 3535682

SUBMITTER (NAME ONLY): Johannes Kirchner

TITLE: Eye Tracking based on real-time MRI using a novel, fully-automated segmentation method

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Watson, School of Psychology, Western Sydney University, Penrith South, New South Wales, AUSTRALIA|J. Kirchner, M. Lappe, Institute for Psychology, Westfälische Wilhelms-Universität Münster, Münster, Nordrhein-Westfalen, GERMANY|J. Kirchner, M. Lappe, Otto Creutzfeldt Center for Cognitive and Behavioral Neuroscience, Westfälische Wilhelms-Universität Münster, Münster, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Video-based eye tracking devices cannot measure translational eye motion and require a calibration process that relies on the participant's self-report of accurate fixation. To circumvent these limitations, we developed an eye tracking method based on real-time MRI data. We tested this novel method by measuring the participant's horizontal gaze using real-time MRI and a conventional video-based eye tracker (Eyelink 1000) simultaneously.

Methods: In order to study the human eye in motion we used a balanced steady-state free precession (bSSFP) MRI sequence, collecting data of a single slice with a temporal resolution of 35ms. We start our analysis with a geometric model of the human eyeball, assuming that the sclera, the outer curvature of the cornea and the inner curvature of the lens take the shape of an ellipsoid. The geometric model is fitted to MRI data by matching the normal vectors of the model to the gradient flow field of the MRI data. We used a high-resolution 3D T2-weighted MRI scan to optimise the model for each eye and then collected dynamical single-slice data of the eye in motion for 2 participants. In particular, we collected binocular horizontal eye movements between targets at -7° and 7° and some blink-related eye movements. The eye movement was estimated as the best projection of the 3D model.

Results: A linear regression analysis of the horizontal gaze between Eyelink and MRI yielded highly significant results ($P < 0.001$) for both participants and both eyes. The correlation coefficients were 0.99, 0.97, 0.99 and 0.97. Apart from rotation, we also measured translations of up to 1.7mm during blinks.

Conclusions: We demonstrated a proof of principle that MRI can be used to track the human eye with high temporal resolution using a fully-automated algorithm. We anticipate that our work will lead to a deeper understanding of oculomotor mechanics and will be in particular useful for studying eye movement disorders like nystagmus and strabismus.

CONTROL ID: 3535694

SUBMITTER (NAME ONLY): Cina Karimaghaei

TITLE: Intravitreal injection patterns between retina providers in treating Wet Age-Related Macular Degeneration in a single hospital-based setting

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Anti-VEGF therapy is the gold standard for treatment of wet age-related macular degeneration (wet AMD). Currently, the choice of anti-VEGF drugs, number of injections, and their intervals vary among retina providers. This study investigates the difference in intravitreal injection practice patterns between retina providers in visual outcomes of wet AMD in a single hospital-based setting.

Methods: Data from chart reviews of four retina practitioners between 2010-2020 at the University of Texas Medical Branch hospital were collected. Qualified subjects included a diagnosis of wet AMD (18-100 years) who received Bevacizumab, Ranibizumab, or Aflibercept eye injections. Each eye was counted separately, and eyes that switched providers were excluded. Patient demographics, ophthalmic clinical findings (visual acuity, IOP, macular thickness), and number and intervals of anti-VEGF injections were analyzed using Chi-squared and Kruskal-Wallis tests for quantitative variables.

Results: The study included 182 eyes from 145 patients (80.5 yrs.), predominantly Caucasians (93.1%) and females (66.2%). A significant number of eyes received Bevacizumab (78%) over Ranibizumab (8%), with no significant difference in Aflibercept use ($p=0.77$) amongst all retina providers. Additionally, all providers had statistically significant differences in intravitreal injection regimens with respect to number of injections per eye ($p=0.0001$) and average intervals between injections (min 28 and max 45 days, $p=0.002$). However, there was no statistical difference in the number of injections needed to first achieve 20/30 or better visual acuity ($p=0.80$). Of note, 15.4% patients of Providers 1 & 2, 11% patients of Provider 3, and 7.1% patients of Provider 4 achieved 20/30 after a median number of injections of 9, 6, 2, and 2 at an average interval of 28, 30, 45, and 34 days respectively. Provider 1 had significantly better results compared to others, but when examining the overall effect, the providers were not significantly associated with visual acuity improvement after adjusting for all other clinical variables ($p=0.13$).

Conclusions: Because significantly different intravitreal injection patterns resulted in similar visual outcomes, adopting a "best practice" recommendation may decrease treatment and financial burden in wet AMD patients.

CONTROL ID: 3535716

SUBMITTER (NAME ONLY): Vivian Hawn

TITLE: Expended Effort and Estimated Compensation for Ophthalmological Retinopathy of Prematurity Services at a Single Institution

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.S. Hawn, R. Muhtadi, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|P.D. Suman, U. Mian, Department of Ophthalmology and Visual Sciences, Montefiore Medical Center, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a sight-threatening disease that requires strict, scheduled screening and timely treatment for Type 1 ROP. Examining infants in the neonatal intensive care unit (NICU) confers an added burden for ophthalmologists whose practices are predominantly outpatient. We sought to evaluate the time required to provide ROP services and approximate compensation to better understand incentives for this crucial service.

Methods: The ROP coordinator tracked time ophthalmologists spent providing ROP services at two NICUs (2018-2020). Estimated revenue was calculated using appropriate Current Procedural Terminology (CPT) codes for Medicaid reimbursement (2020 Medicare Physician Fee Schedule; Baltimore, MD; CMS.gov). A level 2 inpatient consultation code was used for examinations. Three pediatric ophthalmologists performed screening only (OS), while four retina specialists screened and treated (ST). Total time comprised examination, photography, and administrative duties; travel time at our institution was estimated as 45 minutes. Extrapolation of the time distributions of various ROP services to 100% estimated the physician reimbursement for a hypothetical full-time ROP service.

Results: The ophthalmologists cumulatively spent an average of 108 hours (h.) yearly providing ROP services (8.24% of an annual practice based on a 47-week schedule of 4 days/week, 7 h./day); this increased to 181 h. yearly (13.76% of annual practice) if travel time was included. Estimated annual Medicaid physician reimbursements for OS and ST were \$14,655 and \$18,182 (\$150/h. and \$168/h.), respectively; with travel time they decreased to \$89/h. and \$100/h., respectively. A hypothetical full-time ROP practice would generate annual physician salaries of \$196,801 for OS and \$220,652 for ST. With travel time, this decreases to \$73,655 and \$82,631, respectively.

Conclusions: At this institution, performing ROP services requires substantial time, especially if travel among facilities is necessary. This highlights the extensive and costly requirements for the critical task of decreasing ROP blindness. As few ophthalmologists prefer to perform ROP services after training, it is important for hospitals to make this highly litigious field more appealing.

CONTROL ID: 3535730

SUBMITTER (NAME ONLY): Rob Chun

TITLE: Investigating Phoria Measures and Visual Discomfort Symptoms of Low Vision Patients Using a Head-Mounted Electronic Low Vision Enhancement System (eLVES)

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Chun, K. Fujiwara, M.R. Gobeille, J. Deremeik, C. Bradley, R.W. Massof, Ophthalmology, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|A. Deemer, Optometry, Southern California College of Optometry, Fullerton, California, UNITED STATES|F.S. Werblin, IrisVision, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limitations in the technical designs of commercially available eLVES may cause some users to experience visual discomfort for a number of reasons including binocular vision and vestibulo-ocular deficits. One possible reason for reported symptoms of visual discomfort using such devices is the decentration of the pupils within the optical viewing systems of these head-mounted displays (HMDs). Thus, we aimed to investigate the impact of pupil decentration (including heterophoria measures) on reported symptoms of visual discomfort in the IrisVision eLVES.

Methods: Fifty low vision patients ($BCVA \leq 20/60$ and at least 70° of visual field) completed phoria testing with Maddox Rod. Interpupillary distances were obtained with a pupillometer and through the IrisVision eLVES in order to derive heterophoria (eso vs exo) measures through the HMD using Prentice's Rule. All subjects took the device home for a 2-4 week trial period. A revised version of the simulator sickness questionnaire (SSQ) was administered twice during the trial period by telephone. Person measures and item measures, for responses to SSQ items relating to visual discomfort, were estimated by Rasch analysis. Deming regression normalized by standard deviation was used to compare 1) distance phoria measurement methods (Maddox Rod vs HMD) 2) phoria vs SSQ person measures (symptoms).

Results: Twenty-one of the 50 subjects were able to complete horizontal phoria testing using the HMD and with the Maddox Rod (mean age = 65.3 years). Deming regression comparing measured Maddox Rod values to predicted HMD phoria values shows the data (prism diopters) are centered around zero (mean = -0.6, stdev = 3.77). When person measures are anchored to item measures, only one participant showed significant symptoms. Pseudo R^2 was 0.490 between SSQ person measure and Maddox Rod phoria, and 0.435 between SSQ person measure and HMD-derived phoria.

Conclusions: To our knowledge, this is the first study to investigate the impact of heterophoria testing and visual discomfort using a head-mounted eLVES among low vision patients. There was no significant correlation to phoria measures on either the HMD test or Maddox Rod to suggest higher simulator sickness symptoms with higher measures of esophoria or exophoria. In addition, predicted phoria measures using the HMD correlates well to Maddox Rod findings.

CONTROL ID: 3535743

SUBMITTER (NAME ONLY): Jace Buxton

TITLE: Fluorescence lifetime imaging ophthalmoscopy (FLIO) follow-up analysis in patients with age-related macular degeneration

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Buxton, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|L. Sauer, A.S. Vitale, N.K. Modersitzki, P.S. Bernstein, John A. Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: In eyes with age-related macular degeneration (AMD), fluorescence lifetime imaging ophthalmoscopy (FLIO) shows a characteristic pattern of prolonged mean autofluorescence lifetimes. This study investigates changes in autofluorescence lifetimes over time in patients with AMD to better understand disease progression.

Methods: 26 patients with AMD (mean age 75 ± 9 years) were followed at the Moran Eye Center with a prototype Heidelberg Engineering FLIO. The mean follow-up time was 16 ± 8 months (range 6 - 34 months). Fundus autofluorescence was excited at 473 nm, and FLIO lifetimes were recorded in short (SSC, 498 - 560 nm) and long (LSC, 560 - 720 nm) spectral channels. Mean autofluorescence lifetimes were investigated.

Results: At baseline, FLIO lifetimes in the outer ring (OR) of a standardized early treatment diabetic retinopathy study (ETDRS) grid were 297 ± 54 ps (SSC) and 405 ± 58 ps (LSC). At follow up, the same area showed FLIO lifetimes of 306 ± 59 ps (SSC) and 411 ± 57 ps (LSC), $p < 0.01$ for both spectral channels. The central area (C) did not show any significant changes ($P = 0.67$ and 0.18). The average 12-months prolongation of FLIO lifetimes in the OR was 7 ± 20 ps (SSC) and 7 ± 13 ps (LSC).

Conclusions: In eyes with AMD, prolonged FLIO lifetimes further increase over time, particularly in the OR of the LSC, as eyes progress to more advanced stages of AMD. The rate of progression is variable amongst patients and even between eyes of the same patient. FLIO may be useful to monitor the progression of AMD.

CONTROL ID: 3535744

SUBMITTER (NAME ONLY): Atul Jaiswal

TITLE: Barriers to health information and health services in COVID-19 for older adults with combined vision and hearing loss

SESSION TITLE: Visual Impairment during a pandemic

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Jaiswal, N.R. Boie, W. Wittich, School of Optometry, Universite de Montreal, Montreal, Quebec, CANADA|M. Savundranayagam, Faculty of Health Sciences, Western University, London, Ontario, CANADA|C. Vincent, Département de réadaptation, Université Laval, Quebec, Quebec, CANADA|E. Kröger, Faculty of Pharmacy, Université Laval, Quebec, Quebec, CANADA|A. Jaiswal, W. Wittich, Centre de recherche interdisciplinaire en réadaptation du Montréal métropolitain (CRIR), Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Older adults with combined vision and hearing loss (dual sensory loss/DSL) are often sidelined in vision and hearing research, and evidence suggests that they are at a high risk of cognitive impairment, functional decline, social isolation, falls, depression, and mortality. These consequences get exacerbated during the COVID-19 pandemic due to physical distancing restrictions on mobility and social interactions. Around one million older adults in Canada experience DSL; yet, there is very limited evidence in the Canadian context that could inform pandemic preparedness for this population. Hence, the present study identifies and describes the barriers to health information and health services access for older adults with DSL during the COVID-19 pandemic.

Methods: We conducted semi-structured qualitative interviews with 11 community-dwelling older adults with DSL (age 62-85 years; 7 female) in Montreal between September and December 2020. Diverse remote communication modes and accessible formats were used to obtain consent and interview participants. Interviews were audio-recorded and transcribed verbatim. Data were managed using NVivo software and analyzed using a thematic analysis approach.

Results: Findings indicate that the central barriers to healthcare information and access are linked to communication breakdown between older adults with DSL and healthcare providers, in addition to the presentation of information through inaccessible formats. Furthermore, healthcare staff rarely have the additional time available that is necessary to interact with the DSL clientele or have the necessary training to accommodate their communication needs. In terms of barriers to accessibility, participants reported that they have difficulty following the 2-meter distance requirements and coloured lines painted on the floor to ensure physical distancing in the healthcare setting.

Conclusions: Our results highlight that the pandemic heightened the risk for older adults with DSL because of the systemic and physical barriers to healthcare access for this population. There is a dire need for training of healthcare professionals to accommodate the communication and accessibility needs of older adults living with DSL. Healthcare administrators and policymakers should consider the distinct accessibility and communication needs of this vulnerable population in order to help them age well.

CONTROL ID: 3535750

SUBMITTER (NAME ONLY): Sophia Zagora

TITLE: Paediatric uveitic cataract and glaucoma in the time of biologic therapy

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Zagora, T. Karaconji, R. Jamieson, P.J. McCluskey, J.R. Grigg, Save Sight Institute, Ophthalmology, The University of Sydney, Sydney, New South Wales, AUSTRALIA|D. Singh-Grewal, J. Chaitow, Paediatric Rheumatology, Children's Hospital at Westmead, Westmead, New South Wales, AUSTRALIA|D. Singh-Grewal, The University of Sydney School of Medicine, Sydney, New South Wales, AUSTRALIA|S.L. Zagora, T. Karaconji, J.R. Grigg, Paediatric Ophthalmology, Children's Hospital at Westmead, Westmead, New South Wales, AUSTRALIA|R. Jamieson, Genetics, Children's Hospital at Westmead, Westmead, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Uveitis is a rare chronic condition, "orphan disease" in the paediatric population. The incidence is 4.3 per 100,000 and prevalence 27.9 per 100,000. It is sight threatening due to disease progression and treatment failure. The mainstay of uveitis treatment is steroids. Steroid induced cataract and glaucoma is well documented and has been found to account for a quarter of all acquired glaucoma in children. Steroid sparing agents and biologic therapy (genetically engineered proteins targeting specific parts of the immune system that cause inflammation) are increasingly being used. The purpose of this study is to investigate rates, timing and visual outcomes of paediatric uveitic cataract and glaucoma surgery in relation to the treatment of the uveitis with biologic therapy and steroid sparing immunosuppression.

Methods: Retrospective chart review of demographic data and treatment outcomes of all paediatric uveitis patients presenting to the Children's Hospital Westmead, Sydney Eye Hospital and Save Sight Institute from 2005- 2020.

Results: Pilot data highlights that there were 115 patients (207 eyes) diagnosed with paediatric uveitis during this period. The majority had bilateral uveitis (n = 100, 80%). 64 patients were female and 51 patients male. The most common aetiological diagnosis was JIA-U (n = 77, 67%), followed by idiopathic uveitis (n = 34, 29.6%). Anatomical diagnosis was 84% anterior uveitis and 16% non-anterior uveitis. Cataract surgery was required in 46 patients / 40% (61 eyes / 29.4%); glaucoma surgery - trabeculectomy or tube surgery in 40 patients / 34.7% (49 eyes / 23.7%). A number of patients underwent multiple surgeries. The mean duration of inflammation prior to commencement of a biological agent was 22.0 months (range: 1-48 months). Baseline age at commencement of biologic therapy was 9.12 years (3.42 SD). Of those patients on biologic therapy, the baseline VA was logMAR 0.24 (0.34 SD) and final VA was logMAR 0.18 (0.28 SD) with a mean change in VA from baseline of logMAR -0.07 (0.23 SD).

Conclusions: Paediatric uveitis is a complex disease. The advent of biologic therapy and other steroid sparing agents, in this real world data, are having beneficial effects on visual outcome, uveitic cataract and glaucoma surgery in these patients.

CONTROL ID: 3535752

SUBMITTER (NAME ONLY): Paul Donaldson

TITLE: Inhibition of water and solute fluxes by oxidative stress in a hyperbaric oxygen (HBO) model of lens ageing

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.J. Donaldson, M. Nye-Wood, Y. Chen, Physiology, School of Medical Sciences, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|P.J. Donaldson, Y. Chen, E. Vaghefi, New Zealand National Eye Centre, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|E. Vaghefi, School of Optometry, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|T. White, Physiology and Biophysics, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|M. Nye-Wood, Edith Cowan University School of Science, Joondalup, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine how water and solute fluxes are affected in a bovine hyperbaric oxygen (HBO) model of lens ageing that has previously been shown to induce an age-dependent hyperopic shift in lens power clinically observed in human lens.

Methods: All experiments were performed on bovine lenses that had been first exposed to either 100% nitrogen (HBN) (pressure control group) or 100% oxygen (HBO) at a pressure of 100atm for 15hr in a Cell Disruption Vessel. A pico-injector/microelectrode based pressure measurement system was utilised to measure the intracellular hydrostatic pressure gradient that drives water efflux. T1 based MRI imaging was used to map free water content and to visualise the delivery of the MRI contrast agent FeraSpin XS to the lens core. Western blotting of dissected lens fractions with Cx46 antibodies was used to assess gap junction protein degradation in the different areas of the lens.

Results: HBO exposure significantly increased the free water content in the inner cortex and core of the bovine lens and this change was associated with an increase in the hydrostatic pressure gradient relative to the HBN control. These effects of HBO were deemed to be associated with an inhibition of microcirculation system as the delivery of the FeraSpin XS to the core of the lens was abolished following HBO exposure but was unaffected by incubation in HBN. HBO also induced the degradation of Cx46 in the outer and inner cortex.

Conclusions: Our results show that acute oxidative damage to the lens gap junctions traps water in the lens core causing an elevation of the hydrostatic pressure gradient and an inhibition of solute delivery to the lens core that is driven by the microcirculation system. We envisage that the age-related accumulation of oxidative damage to gap junctions may trigger similar changes in older human lenses, which may eventually contribute to the onset of lens cataract.

CONTROL ID: 3535754

SUBMITTER (NAME ONLY): Michelle Guo

TITLE: Distribution and density of retinal myeloid cells following elevated intraocular pressure

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Guo, J. Sterling, M.O. Adetunji, J.L. Dunaief, Q.N. Cui, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neuroinflammation is increasingly implicated in glaucoma pathogenesis. We previously showed that decreasing macrophage/microglia activation and astrogliosis rescued retinal ganglion cells (RGCs) following intraocular pressure (IOP) elevation in mice (PMID33147455). Our findings also suggest monocyte infiltration may drive astrogliosis. Using the microbead occlusion model of glaucoma, we examined the association between RGC death and the distribution of retinal myeloid cells following IOP elevation.

Methods: Microbead injections were used to elevate IOP as previously described (PMID32045598). Briefly, 4-month-old C57BL/6J mice received injections of magnetic microbeads in the anterior chamber of one eye while the contralateral eye received sterile balanced salt solution (BSS). Mice were injected on days 0 and 16. IOP was measured immediately prior to the first injection, 4 days post-injection, and then weekly thereafter. After 6 weeks, immunolabeling of retina flat-mounts for RBPMS and Iba1 was used to quantify cellular density [cells per 63x high-power field (HPF)] of RGCs and myeloid cells, respectively, in the central and peripheral retina.

Results: IOP remained elevated for 6 weeks following microbead injections (Mean \pm SEM 15.4 \pm 0.3mmHg vs. BSS 11.9 \pm 0.2, $p<0.0001$). After 6 weeks, RGC density was lower in microbead vs. BSS eyes (107.1 \pm 2.9 vs. 124.3 \pm 2.5, $p<0.05$). In contrast, myeloid cell (Iba1+) density was higher in microbead vs. BSS eyes (4.0 \pm 0.1 vs. 2.8 \pm 0.1, $p<0.001$; Fig. 1). Interestingly, in microbead eyes, higher central myeloid cell density was correlated with lower RGC density, particularly in the periphery ($R=0.14$, $p<0.0001$). The same correlation was not observed in BSS eyes.

Conclusions: Results support increased macrophage/microglia activation in response to ocular hypertension. The correlation between higher central macrophage/microglia density and greater RGC loss suggests that increased central activation and/or monocyte extravasation from the optic nerve are important drivers of RGC death. Examining for evidence of monocyte infiltration immediately after IOP elevation will expand upon this finding.

CONTROL ID: 3535764

SUBMITTER (NAME ONLY): Neal Patel

TITLE: Retrospective Analysis of Retinal Imaging in COVID-19 Positive Patients at a Tertiary Eye Care Center

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.S. Patel, J. Moon, R. Katz, L. Sobrin, D.G. Vavvas, J. Miller, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Since the start of the COVID-19 pandemic, numerous authors have published data demonstrating retinal changes found in patients with COVID-19. These include differences in retinal vascular anatomy, hyper-reflective changes on optical coherence tomography (OCT), and signs of microvascular disease such as cotton wool spots and retinal hemorrhages. However, other authors have debated the validity of these findings and the effects of COVID-19 on the retina remain uncertain. Herein, we aim to retrospectively assess for retinal changes in patients infected by COVID-19 who were seen at a tertiary eye care center.

Methods: A retrospective review of patients who presented to Massachusetts Eye and Ear (Boston, MA, USA) between March 1st and October 31st, 2020 with a history of a positive COVID-19 polymerase chain reaction test was performed. Patients were included if they presented within 90 days of their first positive COVID-19 test and underwent color fundus photography and/or OCT of the macula.

Results: A total of 119 eyes from 61 patients with mean age of 63 years and mean presentation of 60.4 days after first positive COVID-19 test (range 4 to 90 days) were included. Among 83 eyes which underwent OCT of the macula, inner retinal hyper-reflective changes were seen in 16.9% (n=14), outer retinal hyper-reflective changes in 18.1% (n=15), intra-retinal fluid in 28.9% (n=24), and sub-retinal fluid in 14.5% (n=12). Among 48 eyes which underwent color fundus photography, retinal hemorrhage was seen in 27.1% (n=13), optic disc edema in 2.1% (n=1), and cotton wool spots in none of the eyes. Among 109 eyes which underwent a documented exam of the posterior segment, retinal hemorrhage was seen in 23.9% (n=26), optic disc edema in 2.75% (n=3), and cotton wool spots in 3.7% (n=4). Sub-analysis of 70 eyes from 41 patients with no alternative retinal pathology (diabetic retinopathy, retinal vein occlusion, etc.) to potentially cause the above findings revealed that none of the eyes demonstrated any of the above exam findings on OCT macula (n=35), fundus photography (n=28), or documented exam (n=66).

Conclusions: While a number of patients seen after COVID-19 infection demonstrated retinal findings, all could be explained by pre-existing retinal conditions. In a sub-group of eyes without pre-existing retinal disease, we did not identify any retinal findings that could be attributed to COVID-19.

CONTROL ID: 3535770

SUBMITTER (NAME ONLY): Momoko Ponsetto

TITLE: Acute and Chronic Ocular Manifestations of Stevens-Johnson Syndrome in HIV-positive vs. HIV-negative Patients

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Ponsetto, D. Metcalfe, J. Chodosh, H.N. Saeed, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|M.K. Ponsetto, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|D. Metcalfe, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the acute and chronic manifestations of Stevens-Johnson Syndrome(SJS) and Toxic Epidermal Necrolysis (TEN) in an HIV-positive and HIV-negative population of patients.

Methods: This retrospective review evaluated all SJS/TEN patients within the Research Patient Data Registry of the Mass General Brigham healthcare system with and without HIV-infection. Patients were required to have relevant documentation of acute ocular manifestations as well as at least one chronic follow up visit ≥ 3 months post-discharge. Main outcome measures for acute ocular outcomes were acute ocular Sotozono score (AOSS), and for chronic ocular outcomes were severe ocular complications (SOC), chronic ocular Sotozono score (COSS), and best corrected visual acuity (BCVA) as measured using LogMAR VA.

Results: Seventeen patients were reported in the HIV-positive (HIV+) group and 181 patients reported in the HIV-negative (HIV-) group. HIV+ patients had a higher frequency of TEN in comparison to the HIV- patients ($P = 0.003$). However, HIV- patients had a higher AOSS compared to those who were HIV+ ($P = 0.010$). Zero of 17 HIV+ patients required AMT therapy whereas 50 of 181 HIV- patients required AMT therapy ($P = 0.008$). Chronic ocular data was present for only 6 of the 34 eyes of HIV+ patients. Severe ocular complications (SOC) occurred more frequently in the HIV+ group than the HIV- group before and after controlling for AOSS ($P < 0.0001$). LogMAR VA was better in the HIV+ group relative to the HIV- group before controlling for AOSS ($P = 0.004$) and was equivalent after controlling for AOSS ($P = 0.383$). Cornea, conjunctiva, eyelid margin, and total COSS were not significantly different between groups before and after controlling for AOSS.

Conclusions: Despite having more severe systemic presentation of SJS/TEN, HIV-positive patients had less severe acute ocular disease than HIV-negative patients and required less AMT therapy. However, chronic ocular disease was worse in those who were HIV positive. This finding may be due to a different and/or suppressed immune mechanism of disease in those with HIV positivity, or a smoldering and longer acute or subacute disease phase and requires further study. Future studies are indicated to determine the pathophysiology of acute disease in HIV positive SJS/TEN patients and whether there should be a lower threshold to perform AMT.

CONTROL ID: 3535779

SUBMITTER (NAME ONLY): Kennedy Hall

TITLE: Temporary disruption of binocular vision by monocular noise-adaptation induces a naso-temporal asymmetry in global motion perception

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Thompson, A. Chakraborty, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|K. Hall, A. Chakraborty, Chicago College of Optometry, Midwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|B. Thompson, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: A nasalward bias in motion coherence thresholds has been reported in individuals with a history of monocular deprivation. However, the mechanism behind this bias is unclear. Here we investigated whether the locus of such asymmetry lies within the early visual areas, such as V1, or further downstream within the extrastriate cortex.

Methods: In individuals with normal vision ($n = 14$), we measured motion coherence (MT+/V5) and contrast-detection (V1) thresholds for random dot kinematograms (100 dots, 6 deg/sec) in one eye after adaptation of the fellow eye to visual noise. To measure the motion coherence threshold, the contrast of the dots was maintained at 100% and coherence was varied. To measure detection thresholds, coherence was fixed at 100% and contrast was varied. Within separate sessions, thresholds were measured monocularly with and without adaptation of the fellow eye. Adaptation involved 60s viewing a random-dot-kinematogram with an equal number of black and white dots with varying speed and contrast, followed by 15 s periods of top up adaptation after every 10 trials.

Results: Only motion coherence thresholds following noise adaptation exhibited a robust naso-temporal asymmetry in favor of nasalward motion (mean nasal MCT: $8 \pm 2.25\%$ vs mean temporal MCT: $14 \pm 2\%$). When compared to the non-adapted condition, noise-adapted motion coherence thresholds were significantly worse only for temporalward motion post adaptation (noise-adapted $14 \pm 2\%$ vs. non-adapted $8 \pm 1.92\%$). Contrast detection thresholds did not show any naso-temporal asymmetry for any condition.

Conclusions: We were able to simulate the monocular nasal temporal MCT asymmetry we have previously observed in individuals with monocular deprivation using monocular noise adaptation of one eye. The presence of such asymmetry only in the global motion, but not in the contrast-detection task, suggests that MT+/V5 could be a potential site for this asymmetry.

CONTROL ID: 3535784

SUBMITTER (NAME ONLY): Brian Krawitz

TITLE: The effect of trabeculectomy on rates of visual field progression and retinal nerve fiber layer thinning

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Krawitz, G.A. Cioffi, J.M. Liebmann, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|C. De Moraes, C.A. Girkin, M.A. Fazio, The University of Alabama at Birmingham College of Arts and Sciences, Birmingham, Alabama, UNITED STATES|C. Bowd, R.N. Weinreb, L.M. Zangwill, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the effect of trabeculectomy on the rates of functional (visual field, VF) vs. structural (optical coherence tomography, OCT) glaucoma progression.

Methods: Participants were recruited from the African Descent and Glaucoma Evaluation Study (ADAGES). Eyes that underwent trabeculectomy and had at least 3 good quality Humphrey 24-2 VFs and spectral-domain OCT scans of the retinal nerve fiber layer (RNFL) performed before or after surgery were included for analysis. Rates of mean deviation (MD) and global RNFL thickness change were calculated using a linear mixed effects model.

Results: For VF analysis, 86 eyes before trabeculectomy and 134 eyes after trabeculectomy were included. The mean (95% CI) global rate of progression decreased from -0.41 (-0.52 to -0.30) before surgery to -0.25 (-0.33 to -0.17) dB/year after surgery (39% reduction, $p=0.003$). For OCT analysis, 20 eyes before trabeculectomy and 90 eyes after trabeculectomy were included. The mean rate of RNFL thinning decreased from -0.65 (-1.78 to 0.47) before surgery to -0.25 (-0.46 to -0.03) $\mu\text{m}/\text{year}$ after surgery (61% reduction, $p=0.008$).

Conclusions: Trabeculectomy decreases the rate of progression of VF and OCT global parameters. Despite the smaller sample size, the effect was more evident on OCT and may help better understand the effect of IOP reduction on rates of change of structural and functional parameters in glaucoma.

CONTROL ID: 3535786

SUBMITTER (NAME ONLY): Qingnan Liang

TITLE: Integrative analysis of single-cell multi-omics data of the human retina

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The human retina is composed of different neuronal and non-neuronal cell types. Significant cell heterogeneity is observed within many neural retina cell types, with their composition in the tissue ranging anywhere, from 75% to less than 0.05%. However, the number of retinal cell subtypes and their gene expression signature remains largely undiscovered, especially for rarer cell types. Additionally, open chromatin profiles for the human retina at the single-cell level has not yet been reported. Therefore, we are generating the first version of human neural retinal cell atlas reference by characterizing both the transcriptome and open chromatin profile for all cell types in the human retina.

Methods: Single-nuclei RNA-seq and single-nuclei ATAC-seq were carried out to profile well-characterized normal human retina from over twenty donors (average age over 70). Each donor retina was dissected into three geographic regions: the fovea, macula, and peripheral retina and flash-frozen afterward. A fractionation protocol was developed to enrich nuclei from rare neuron cell types, including bipolar cells, amacrine cells, and retinal ganglion cells. Integrative data analysis was performed to identify cell subtypes, marker genes, chromatin signature, and transcription factors and modules. Experimental approaches including immunofluorescence staining and RNA in situ hybridization are performed to validate novel cell populations.

Results: A transcriptome profile was generated for over 250K nuclei, leading to the identification of over 60 cell types in the human retina. Through comparison among the human, and previously reported monkey/mouse datasets, we have identified conserved and primate-specific subtypes. In parallel, single-cell open chromatin profiles were generated using single-nuclei ATAC-seq from 160k nuclei. The integration of the single-nuclei RNA-seq and single-nuclei ATAC-seq data allows us to obtain the open chromatin profiles of each subtype. Key transcription factors and transcription modules were identified at both major- and sub- cell-type levels.

Conclusions: This study represents the most comprehensive single-cell transcriptome and chromatin accessibility profiling for the human neural retina to date. Over 400K single nuclei were profiled for their transcriptome or chromatin accessibility, with over 60 cell types. This well-characterized dataset serves as the first version of a human retina cell atlas reference.

CONTROL ID: 3535788

SUBMITTER (NAME ONLY): Hend Ahmed

TITLE: Usability of AdaptDx for Dark Adaptation Testing in Choroideremia

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.M. Ahmed, Pathology, Mansoura University Faculty of Medicine, Mansoura, EGYPT| H.M. Ahmed, A.M. Dubis, Institute of Ophthalmology, University College London, London, UNITED KINGDOM|L. Da Cruz, A.M. Dubis, R.E. MacLaren, Moorfields Eye Hospital, UNITED KINGDOM|J.K. Jolly, R.E. MacLaren, Oxford University Eye Hospital, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Choroideremia is an X-linked retinal degeneration which causes a circumferentially constricting degeneration of the retinal pigment epithelium and choroid, leading to rod function loss. Current dark adaptation protocols test the full field sensitivity and seek the absolute dark-adapted threshold. Alternatively, single point testing and sub-absolute threshold endpoints may provide the opportunity for quicker, more reliable testing in this disease.

Methods: Choroideremia patients underwent dark adaptation testing using the AdaptDx (Maculogix, Hummelstown, PA, USA) dark adaptometer and autofluorescence imaging. Following 80% rod bleaching, testing was performed at 9-degree superior to fixation. Rod recovery time was defined as the time needed to achieve a sensitivity improvement of 3 AU. The sensitivity at 18min was also recorded. Autofluorescence images were reviewed to assess whether the testing location lay within the preserved retina.

Results: Fifty-six eyes from 28 patients were included in this analysis. Twenty-one eyes had a detectable rod recovery time (mean \pm SD, 15.0 \pm 4.3 minutes), with 3 of them \leq 10 min which was deemed normal. Three patients had a detectable recovery in only 1 eye. At 18 minutes, the average threshold for all eyes was 2.30 \pm 0.82. A strong correlation in 18-minute sensitivity was observed between right and left eyes ($R^2 = 0.70$). Eyes with detectable rod recovery had significantly higher sensitivity (mean \pm SD, 3.12 \pm 0.56) compared with eyes with undetectable recovery (1.81 \pm 0.25, $p < 0.001$). Thirty-two eyes had residual retina at the targeted region. The average threshold at 18 minutes for these eyes was 2.62 \pm 0.77 dB. Of these, only 15 eyes had a detectable rod recovery. Meanwhile, 6 eyes with no remaining retina at the targeted point had a detectable, yet prolonged, rod recovery. Interestingly, no significant association was observed between the undetectable rod recovery and presence/absence of remaining retina the testing location ($p = 0.09$).

Conclusions: The dark adaptation testing maybe useful for assessment of choroideremia. AdaptDX testing provided several key findings. The mean threshold at 18 min was greater for the eyes with detectable rod recovery time. However, the lack of relationship between presence of residual retina and testing threshold suggest eye movement may have played a role and would need to be controlled in future use.

CONTROL ID: 3535797

SUBMITTER (NAME ONLY): Fengting Ji

TITLE: Mechanical properties of scleral collagen fibers obtained using a new fiber-based specimen-specific model of sclera microstructure.

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Ji, I.A. Sigal, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|F. Ji, M. Bansal, Y. Hua, I.A. Sigal, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|B. Wang, Mechanical Engineering, Southwest Jiaotong University, Chengdu, Sichuan, CHINA|

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ABSTRACT BODY:

Purpose: Scleral collagen fiber mechanical properties are central to overall eye mechanics, and thus multiple techniques have been used to determine them using modeling. Most models, however, use continuum approaches that do not consider critical characteristics of the fibers. Our goal was to determine the fiber mechanical properties using a newly developed specimen-specific fiber-based model of sclera.

Methods: Two optic nerve heads (ONHs) were sectioned at 30 μm thickness, one coronally and the other sagittally. The sections were imaged using polarized light microscopy (PLM) to obtain local collagen fiber density and orientations in the section planes. Images of 17 serial coronal sections were registered to form a volume. A square region of sclera was selected and the fibers were traced in all images accordant to local fiber orientations (Fig 1). Fiber overlaps were resolved by an iterative algorithm. The out-of-plane fiber orientations were adjusted to match the sagittal PLM data. The fibers were then embedded in a matrix and the assembly was used in an inverse modeling process to derive fiber mechanical properties by matching published experimental biaxial extension data assuming a hyperelastic Mooney-Rivlin behavior.

Results: A model with 1016 fibers was constructed. Wilcoxon rank sum tests showed that fiber orientations were not significantly different between the model and histology for both coronal ($p>0.7$) and sagittal ($p>0.6$) directions. The estimated fiber stiffness was 1488.7MPa (Fig 2).

Conclusions: Our fiber-based sclera model incorporated detailed specimen-specific architecture, and previously ignored fiber-level mechanics, such as fiber-fiber interactions and long-distance load transfer. Although the model predicts higher fiber stiffness than previous studies (e.g. Grytz et al. 2013), the biomechanical behavior was in excellent agreement with experiments.

CONTROL ID: 3535828

SUBMITTER (NAME ONLY): Saira Khanna

TITLE: Laser Prophylaxis in Stickler Syndrome

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Khanna, S.H. Rodriguez, M. Blair, Ophthalmology and Visual Sciences, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|M.A. Blair, M.J. Shapiro, M. Blair, Retina Consultants, Ltd., Des Plaines, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stickler syndrome (SS) is an inherited, progressive collagenopathy first described in 1965 that is the leading cause of pediatric retinal tears and detachments. Retinal tears or detachments in SS have been shown to occur as early as 8 months, and SS patients require frequent examinations to detect retinal detachments (RD) and prevent development of proliferative vitreoretinopathy which can result in severe vision loss. The purpose of this study is to compare the visual acuity (VA) and odds of RD among patients with SS who received prophylactic laser to those who did not.

Methods: Retrospective chart review included patients with SS at University of Chicago Medical Center or Retina Consultants, Ltd. between 1/1/2006 and 10/6/2020. Patients older than 3 years of age underwent laser indirect ophthalmoscopy and received a pattern of about 10 rows of 360 degrees of laser prophylaxis from the ora serrata to the equator (complete laser). The association between RD and laser was investigated using Pearson chi-square / Fisher's exact test. Frequency weighting to control for 2 eyes of the same patient was used to calculate median logmar visual acuity (VA) and interquartile range (IQR). To compare logmar visual acuity by laser treatment groups, a mixed effects logistic regression controlling for 2 eyes of the same patient; nonverbal patients were excluded from visual acuity regression analysis.

Results: A total of 230 eyes of 124 patients were included. Of those, 90 (39%) eyes had no laser, 7 (3%) received inadequate laser elsewhere, and 133 (58%) received complete laser. Of the eyes who received complete laser, only 5 eyes (4%) had an RD, compared to the 69 eyes (71%) which had inadequate or no laser ($p < 0.001$). Among 204 eyes of 103 patients, patients with complete laser had about 6 lines better vision compared to patients without laser or with inadequate laser (-0.55 logmar, CI -0.79 - -0.30 , $p < 0.001$). The odds of low vision were 2.1 (CI 1.1-3.0, $p < 0.001$) times lower for eyes with complete laser.

Conclusions: Complete laser prophylaxis seems to reduce the chance of retinal detachment and improve visual outcomes in patients with SS. Laser prophylaxis should be considered in all patients with confirmed SS after the age of 3.

CONTROL ID: 3535832

SUBMITTER (NAME ONLY): Samir Patel

TITLE: The influence of universal face mask use on endophthalmitis risk after intravitreal anti-vascular endothelial growth factor injections during the COVID-19 pandemic

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Routine use of face masks for both patients and physicians during intravitreal anti-vascular endothelial growth factor (VEGF) injections has increased with the emergence of the COVID-19 pandemic. This study evaluates the impact of physician, ancillary staff, and patient face mask use on rates and outcomes of post-injection endophthalmitis.

Methods: In this retrospective comparative cohort study, all eye receiving intravitreal anti-VEGF factor injections from 10/1/2019 to 7/31/2020 were included from twelve centers. Cases were divided into a “no face mask” group if no face masks were worn by the physician or patient during intravitreal injections or a “universal face mask” group if face masks were worn by the physician, ancillary staff, and patient during intravitreal injections. The main outcome measures were rate of endophthalmitis, visual acuity, and microbial spectrum.

Results: Of 505,968 intravitreal injections administered, 85 of 294,514 (0.0289%; 1 in 3,464 injections) cases of endophthalmitis occurred in the “no face mask” group, and 45 of 211,454 (0.0213%; 1 in 4,699 injections) cases occurred in the “universal face mask” group (odds ratio, 0.74; 95%CI, 0.51–1.18; p=0.097; Table 1). In the “no face mask” group, there were 27 cases (0.0092%; 1 in 10,908 injections) of culture-positive endophthalmitis compared to 9 cases (0.004%; 1 in 23,494 injections) in the “universal face mask” group (OR, 0.46; 95%CI, 0.22–0.99; p=0.041). Three cases of oral flora-associated endophthalmitis occurred in the “no face mask” group (0.001%; 1 in 98,171 injections) compared to one (0.0005%; 1 in 211,454) in the “universal face mask” group (p=0.645). At endophthalmitis presentation, mean logMAR visual acuity was 2.04 for “no face mask” group compared to 1.65 for the “universal face mask” group (p=0.022), although no difference was observed three months after treatment (p=0.764; Table 2).

Conclusions: Universal face mask use during intravitreal anti-VEGF injections did not show a statistically significant reduction in presumed endophthalmitis, but there was a reduced rate of culture-positive endophthalmitis. Future studies are warranted to assess the role of face mask use to reduce endophthalmitis risk, particularly that due to oral flora.

CONTROL ID: 3535842

SUBMITTER (NAME ONLY): Noreen Shaikh

TITLE: Dark Adaptation Survey as a Screening Tool for Age Related Macular Degeneration

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Nearly 200 million people have age-related macular degeneration (AMD), yet effective screening methods to identify these individuals in the general population are quite limited. Although signs of AMD can readily be identified by means of a comprehensive eye examination or confirmed by special testing, many individuals with AMD remain undiagnosed, representing a significant unmet public health need. The goal of this study is to develop a survey capable of identifying patients with AMD based upon visual symptoms.

Methods: A pilot study was conducted in patients with and without AMD presenting at an eye clinic. Participants were recruited to complete the (DA) Survey instrument at the time of a comprehensive eye evaluation which included optical coherence tomography. Patients were staged according to the Age-Related Eye Disease Study classification system. The 10-item survey utilized asked questions related to DA and night vision using the Likert-type response format (severe, moderate, mild, or no difficulty). Linear regression and multivariate analysis were performed using SPSS® (Version 22.0, IBM Corp.).

Results: A total of 31 patients with AMD and 51 controls were recruited for the pilot study. Cronbach's α showed a high degree of internal consistency reliability ($\alpha = 0.92$). Average DA Survey score in AMD was 3.2 ± 0.8 compared with 2.0 ± 0.9 among controls ($P < 0.001$). For every question, the average response score was significantly higher among patients with AMD compared with controls. Logistic regression analysis was performed to predict AMD among 31 patients with AMD and 51 controls using age, sex, average visual acuity, and DA Survey score. Based on this model, association of AMD with age and DA Survey score was statistically significant ($R^2 = 0.442$, $P < 0.001$), whereas it was not significant for sex or visual acuity.

Conclusions: Night vision problems are common in patients with AMD., and symptom severity correlates with severity of the disease. Screening for DA symptoms may help identify subjects with AMD. Future work will seek to validate the survey in a larger population and determine the extent to which other diseases with and without diminished night vision impact symptom severity. Low-cost and easily administered screening tools such as our DA Survey may aid in identifying individuals in need of referral for evaluation and treatment for undiagnosed eye disease thereby preventing vision loss.

CONTROL ID: 3535868

SUBMITTER (NAME ONLY): Miguel Zapata

TITLE: Validation of an autonomous AI-based diagnostic system for holistic maculopathy screening in a routine occupational health checkup context

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: evaluate the accuracy of an autonomous artificial intelligence (AI) system for holistic maculopathy screening during occupational checkups

Methods: A retrospective study on an unclean and unprepared dataset of 5,918 images from a population of 2,839 people evaluated with non-mydriatic cameras during routine occupational health checkups. The images were obtained by a trained technician using handheld non-mydriatic cameras on the participant's office premises. The camera models employed were Optomed Aurora (field of view (FOV) 50 degrees, 88% of the dataset), Zeiss Visuscout 100 (FOV 40 degrees, 9 % of the dataset), and Optomed SmartScope M5 (FOV 40 degrees, 3% of the dataset). Image acquisition took around two minutes per patient. The ground truth of the dataset was evaluated per eye; 2 retina specialists graded each image; if the grading did not match, a 3rd one reviewed the image to break the tie. The specific pathologies considered for evaluation were diabetic retinopathy (DR) (more than mild DR. Age-related macular degeneration (AMD) (mild or worse, suspected glaucomatous optic neuropathy (GON), and Nevus. Images with possible signs of maculopathy that didn't match the described taxonomy were classified as Other.

Results: the assembly of algorithms for evaluating abnormalities had an area under the curve (AUC) of 0.963 with a sensitivity of 0.929 and a specificity of 0.868. The algorithms individually obtained: AMD: AUC 0.98; Sensitivity 0.938; specificity 0.957. DR AUC 0.95; Sensitivity 0.811; specificity 0.948. GON AUC 0.8892; Sensitivity 0.536 specificity 0.957. Nevus AUC 0.931; Sensitivity 0.867; specificity 0.907.

Conclusions: The holistic IA approach is comparable to human experts at simultaneous detection of DR, AMD, GON, and Nevus. The integration of pathology-specific algorithms allows for obtaining high sensitivities without sacrificing specificity. Deep learning may facilitate wider screenings of eye diseases and become quick and reliable support for ophthalmological experts.

CONTROL ID: 3535872

SUBMITTER (NAME ONLY): Nate Goergen

TITLE: Pragmatic usage of Netarsudil: A retrospective chart review from a tertiary care center

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Netarsudil (NL), a rho kinase inhibitor, lowers intraocular pressure (IOP) by increasing outflow facility. There is limited literature on the efficacy of NL in secondary glaucomas and as combination therapy. This retrospective study aims to evaluate the prescription patterns, compliance, and efficacy of NL in an academic glaucoma clinic.

Methods: A retrospective chart review was conducted at a tertiary glaucoma clinic for patients prescribed NL from 01/17 to 5/20. Patient demographics, diagnosis, medication history were noted. Baseline IOP was defined as mean IOP of all visits before starting NL while on stable medication regimen. IOP lowering efficacy was calculated as the difference between IOP at the first visit after starting NL and baseline IOP.

Results: 133 patients were prescribed NL during the study period with a mean age of 69 ± 20 years. 59% were females and 74% were white. The indications for NL prescription were IOP over target and/or drug regimen simplification. Of the study subjects, 67 had a diagnosis of a primary glaucoma (84%). NL was always used as part of a combination glaucoma medication regimen (average medication usage 3 ± 1). NL prescription was not filled by 17% (n=22) subjects mainly due to cost of medication (n=15). 101 eyes of 76 patients were used for IOP analysis. The mean change in IOP was -1 ± 6 mmHg. IOP decreased in 67% and increased/did not change in 33% patients (Table 1). None of the demographic or ocular factors were statistically associated with the prescription fill status or IOP lowering efficacy. NL was discontinued in 52% (50/96) patients after a mean duration of 78 ± 99 days due to a) surgery due to inability to achieve target IOP (42%) b) allergies or intolerance (30%) c) cost (14%) d) paradoxical rise in IOP (12%).

Conclusions: NL was used as an adjunct 2nd-4th line medication in a tertiary glaucoma practice in Midwestern USA. Of patients prescribed NL, 17% of prescriptions medications went unfilled and NL was discontinued in 52% of patients due to poor efficacy, allergies, and expense. IOP response to NL may be variable in this population with severe complex glaucoma.

CONTROL ID: 3535875

SUBMITTER (NAME ONLY): Mary Ben Apatoff

TITLE: Variability in Schlemm Canal Anatomical Measurements

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Schlemm canal (SC) is characterized by high local variations in morphology. Previously, we reported characteristics of SC using SC area measurements by optical coherence tomography (OCT) in healthy eyes. Herein, we examine the interobserver variability of SC height, width, and area in glaucomatous and healthy eyes.

Methods: The anterior segment of six eyes from three subjects (1 female, 2 male) were imaged using OCT (Cirrus HD-OCT, Zeiss, Dublin, California, USA). A 4x4mm volumetric image of the limbus (depth of 2mm) was acquired with the Anterior Segment Cube scan protocol, comprised of 128 horizontal B-scans composed of 512 A-scans. SC was positioned to the side of the image to maximize visualization of aqueous humor vessel crossings. Scans were processed to maximize visualization of SC; image volumes were averaged (3x3x3 kernel) and contrast was enhanced with the local histogram algorithm using Fiji (version 2.10/1.53c). A cross-sectional B-scan and the two B-scans +/- 5 frames were identified as three reference frames, based on best visualized SC location (Fig. 1). Three independent observers performed manual segmentation to measure SC width, height, and cross-sectional area for these three reference frames per volume. Width was defined as the longest measure of SC and height as perpendicular to the line used for width measurement. The observers performed these measurements on 15 volumes for a total of 45 analyzed frames each. The coefficient of variation was calculated based on standard deviations estimated using hierarchical multi-level random-effects models. Interobserver variability was quantified with a two-way ANOVA to calculate the intraclass correlation coefficient (ICC).

Results: Participants had a mean age of 72.0 ± 7.47 years (range: 66 to 82) and consisted of one healthy subject and two with primary open angle glaucoma. Measurement means and variation are presented in Table 1. The ICCs for interobserver variability are excellent for width measurements and low to moderate for height and area (Table 2).

Conclusions: Excellent ICC for interobserver variability of SC width suggests it is suitable for use in clinical trials.

CONTROL ID: 3535889

SUBMITTER (NAME ONLY): Shikha Gupta

TITLE: Employment profile of adults with seeing disability in Canada: An analysis of the Canadian Survey on Disability 2017

SESSION TITLE: Visual Impairment and Quality of Life

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Several pieces of legislation have been put in place in Canada to ensure employment equity for individuals with disabilities. Yet, there is not much known about the employment experiences of people with seeing disabilities. These estimates are important to ascertain the effectiveness of employment policies for people with sensory disabilities in an equitable way. Our study aimed to provide an employment profile of people with seeing disabilities in Canada.

Methods: We used the 2017 Canadian Survey on Disability (CSD), a national survey of individuals 15 years of age and above with a functional limitation, representing more than 6 million (n = 6,246,640) Canadians. A subset of the larger dataset was created with individuals with seeing disability (25-64 years) and weighted descriptive analyses were performed using SPSS.

Results: Out of the estimated 892,220 adults with seeing disability who were represented on the survey, 54% were employed, 6% were unemployed and 40% were not in the labour force. Of those who reported being employed, 80% were in full-time employment while 20% were in part-time employment; and 85% had a permanent job while 15% reported having a temporary job. The top three employment accommodations that were needed and were made available included: modified work hours (45%); work from home (38.5%) and modified workstation (37%). The top three needed, but least available accommodations were technical aids (14%), communication aids (22%) and computers with specialized software or adaptation (27%). Overall, 26% reported that accommodation was required but was not made available by the employer. While 75% of individuals with seeing disabilities, who were out of the labour force, were so because of their condition, the remaining identified barriers that prevented them from working, which included (top 3): (i) too few jobs available (20%); (ii) inadequate training/experience (19%), (iii) past attempts unsuccessful (19%).

Conclusions: Adults with seeing disability in Canada experience low labour force participation in comparison to general population. Rigorous programs are required that assist them with job search, job retraining and workplace accommodations. Although accessibility legislation has been put in place, programs should be established that provide accessibility solutions to various employers, enabling them to hire individuals with different abilities.

CONTROL ID: 3535901

SUBMITTER (NAME ONLY): Nida Safdar

TITLE: Clinical Practice Patterns of Intravitreal Anti-Vascular Endothelial Growth Factor Injections in Treatment of Patients with Diabetic Macular Edema: A Retrospective Study

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The first line treatment for center-involved diabetic macular edema (CI-DME) utilizes anti-vascular endothelial growth factor (VEGF) drugs. The ophthalmologic community remains disputed regarding an optimized approach as to the choice, number, and frequency intervals of intravitreal injections for best visual outcome. This retrospective study investigates the clinical practice patterns of retinal providers using anti-VEGF therapy on visual outcome in DME patients.

Methods: EPIC EMR was used to identify 185 clinically diagnosed DME eyes of 131 subjects (18-100 years) that were seen between 2010-2020 by any of the four retina specialists practicing in a single hospital-based center at University of Texas Medical Branch. The subjects received either Bevacizumab, Aflibercept, or Ranibizumab for DME treatment. The number, interval, and total length of injection treatment were recorded for each provider. Eyes treated by only the same provider were included. First achieved visual acuity (VA) of 20/30 was used to quantify efficacious treatment, and all data was assessed using Chi-square and Kruskal-Wallis tests.

Results: Identified DME patients (age 61.6 yrs), primarily in Caucasians (67%) with no gender difference, had increased propensity of hyperlipidemia and chronic kidney disease (75% and 51% respectively). Among providers, there was a significant difference in the median number of injections (3-8, $p=0.0002$) and in the time interval between the first and last injections (83-296 days; $p=0.0015$) per eye. However, providers were similar in the average intervals between injections (30-40 days; $p=0.38$). Although VA improved pre- and post-treatment amongst providers, there was no significant difference in improvement when comparing the providers. Bevacizumab was the most common choice of anti-VEGF for all four providers ($p=0.23$) followed by Aflibercept ($p=0.27$). When compared to other anti-VEGF drugs, Aflibercept resulted in significantly better visual outcome ($p=0.001$).

Conclusions: Our results show a consensus of monthly use of injections for improved vision despite differences among providers in the frequency and total length of injections. Aflibercept has better visual outcome among all the providers. Further studies are needed to establish an algorithm to institute a "benchmark" protocol for retina physicians in managing DME.

CONTROL ID: 3535904

SUBMITTER (NAME ONLY): Sanam Mozaffari

TITLE: Actively stabilized AOOCT with independent focus adjustment for optimal AOSLO-based eye tracking

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To demonstrate optimal strategies for structural imaging of the human retina with an adaptive optics optical coherence tomography (AOOCT) system guided with real-time eye tracking signals from an adaptive optics scanning laser ophthalmoscope (AOSLO).

Methods: A 1040 nm swept source OCT system was coaligned with an AOSLO system via a dichroic mirror placed prior the deformable mirror such that the OCT 7.2 mm beam size would benefit from the adaptive optics correction. Independent AOOCT focus-adjustment was implemented with a set of fold mirrors on a motorized stage to adjust the distance between one of the telescopes in the sample arm of the OCT path. A second motorized stage was used in the reference arm to match the path length and maintain the interference signal. Eye position reported from the AOSLO with cellular resolution and at a frequency of 960 Hz was used to drive a 2D scanner in the AOOCT path to compensate for eye motion in real time. The purpose for independent focus control was to allow the AOOCT to be optimally focused on a retinal layer of interest while the AOSLO maintained focus on the photoreceptor layer, which offers rich texture and high signal-to-noise for accurate, high-speed tracking. AOSLO and AOOCT videos were recorded in sync such that each AOSLO frame corresponded to four AOOCT B-scans acquired at 120Hz. Volumes were acquired from two subjects, in which the AOOCT focus was adjusted through the retinal layers.

Results: We successfully implemented actively stabilized AOOCT with independent focus adjustment to image different layers in the retina while maintaining high fidelity active eye motion tracking using the AOSLO locked onto the photoreceptor mosaic. Since the eye motion was corrected in real time using the same spatial reference, the volumes required minimal processing and could be averaged within the entire imaging session over multiple acquisitions with no lateral registration.

Conclusions: We have implemented an AOOCT system with active eye tracking that has full control for focus-optimized targeted imaging in 3 dimensions. The AOOCT offers high throughput as individual volume images require no distortion correction or lateral registration between separate imaging sessions. This is the first step in building a platform technology that will be used for a range of applications including visual psychophysics, clinical applications and measuring the optoretinogram.

CONTROL ID: 3535916

SUBMITTER (NAME ONLY): Chloe Khoo

TITLE: Racial Differences in Outcomes of Full Thickness Macular Hole Repair following Pars Plana Vitrectomy

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To study the racial differences in outcomes of full thickness macular hole (FTMH) repair following pars plana vitrectomy (PPV) between white and black patient population groups.

Methods: A retrospective cohort study was performed using TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple health organizations in the United States. Patients who underwent PPV for FTMH repair were identified and categorized into white and black cohorts. The primary outcomes were retinal tear (RT), retinal detachment (RD) with retinal break, serous RD, epiretinal membrane (ERM), macular hole (MH), macular edema (ME), macular degeneration (MD), glaucoma, cataracts, retinal vein occlusion (RVO), retinal artery occlusion (RAO) and endophthalmitis. Outcomes were compared 90-days postoperative between the groups after propensity score matching using logistic regression and greedy nearest-neighbor matching algorithm.

Results: A total of 2,974 patients were included in the analysis with 1,487 patients in each of the white and black cohorts after propensity matching. At the 90-day postoperative period, black patients had a significantly greater risk of developing macular hole (RR 1.35; 95% CI 1.23,1.49) while white patients had a significantly greater risk of developing RD with retinal break (RR 1.62; 95% CI 1.19,2.21), glaucoma (RR 0.75; 95% CI 0.62,0.9), ERM (RR 2.52; 95% CI 2.07,3.07), ME (RR 2.83; 95% CI 1.79,4.49), and MD (RR 3.30; 95% CI 1.63,6.67). No significant difference was noted in the development of RT, serous RD, cataracts, RVO, RAO and endophthalmitis. The incidence of a second vitrectomy for FTMH repair within the 90-day period was similar in both cohorts (4.8% vs 4.0%).

Conclusions: Racial differences are apparent when evaluating outcomes after FTMH repair. While white patients have a greater risk of post-operative complications when compared to black patients, black patients were noted to have a greater risk of post-operative MH suggesting that the post-operative recovery time period for black patients may be longer compared to white patients.

CONTROL ID: 3535917

SUBMITTER (NAME ONLY): Karan Sethi

TITLE: Modeling the Impact of COVID-19 on Retina Clinic Performance

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: COVID-19, a highly contagious respiratory virus, presents unique challenges to the practice of ophthalmology as a high-volume, office-based specialty. In response to the COVID-19 pandemic, many operational changes were adopted in our ophthalmology clinic to enhance patient and provider safety, while maintaining necessary clinical operations. The aims of this study were two-fold: to evaluate how measures adopted during the pandemic period affected the performance of the retina clinic and patient satisfaction; and to build a model from lessons learned for regulating future clinic operational performance, when the number of patients and providers returns to pre-pandemic levels.

Methods: Timestamps were extracted from the electronic medical records of in-person retina encounters from March 15 to May 15, 2020 and compared with the same period in 2019 to assess patient flow through the clinical encounter. Patient satisfaction was evaluated by Press Ganey patient experience surveys returned by randomly selected outpatients. A discrete-events simulation was designed to model the clinic with COVID-era restrictions to assess operational performance under conditions of increasing patient and provider volumes.

Results: Retina clinic volume declined by 62% during the COVID-19 health emergency. Average check-in-to-technician time declined by 79%, total visit length declined by 46%, and time in the provider phase of care declined by 53%. Interestingly, patient satisfaction with access nearly doubled during the COVID-period compared with the prior year ($p < 0.0001$), while satisfaction with overall care and safety remained high during both periods. A model incorporating COVID-related changes demonstrated that wait time before rooming reached levels similar to the pre-COVID era by 30 patients per provider in a 1-provider model and 25 patients-per-provider in a 2-provider model ($p < 0.001$). Capacity to maintain distancing between patients was exceeded only in the two 2-provider model above 25 patients-per-provider.

Conclusions: Clinic throughput was optimized in response to the COVID-19 health emergency. Modeling these clinic changes can help plan for eventual volume increases in the setting of limits imposed in the COVID- era. The changes implemented enhanced the delivery of eye care and improved patients' sense of wellbeing, thus potentially becoming a new standard of care.

CONTROL ID: 3535928

SUBMITTER (NAME ONLY): Srinivas Sai Kondapalli

TITLE: Effectiveness of a novel eyelid retractor and irrigation device in simulated chemical ocular injury

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kondapalli, Everett and Hurite Ophthalmic Association, Pittsburgh, Pennsylvania, UNITED STATES|W.R. Bloom, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Srinivas Sai Kondapalli: Commercial Relationship(s);Rinsada:Code P (Patent) | William Bloom: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intervention after chemical ocular injury includes prompt irrigation to restore physiologic pH. The purpose of this laboratory study was to assess the effectiveness of a novel eyelid retractor and irrigation device after simulated chemical injury in a porcine model.

Methods: A total of 18 porcine eyes were included in this study. The alkali chemical injury group included eyes receiving 1.0mL of 10.0% sodium hypochlorite solution with a pH of 13.0 (n=10). The acid injury group included eyes receiving 1.0mL of 10.0% acetic acid solution with a pH of 2.5 (n=8). The solution was left in each eye for one minute and the periocular tissue was moved in a blinking motion ten times. To assess standard chemical injury management, eyes in the acid (n=4) and alkali (n=5) injury groups were directly rinsed with saline via 10cc syringe. This process was performed three times total. To assess experimental chemical injury management, eyes in the acid (n=4) and alkali (n=5) injury groups were rinsed with saline using a novel eyelid retractor with irrigation ports connected to a 10cc syringe. Using the device to retract the eyelid, the syringe plunger was depressed to allow simultaneous irrigation. This process was performed three times total. One minute after each rinse, pH was measured using a digital pH meter. Statistical significance of post-rinse mean pH between management conditions was compared using unpaired t-tests ($p < .05$).

Results: A single pH measurement of 7.2 was collected from one porcine eye to establish an approximate physiologic surface pH prior to chemical exposure. In eyes exposed to sodium hypochlorite, there was a significant difference in mean post-rinse pH ($p = .02$) using the novel device (9.0 ± 0.19) compared with using a syringe alone (9.5 ± 0.23). In eyes exposed to acetic acid, there was also a significant difference in mean post-rinse pH ($p < .001$) using the novel device (4.4 ± 0.14) compared with using a syringe alone (3.8 ± 0.10).

Conclusions: A syringe is often the only available frontline irrigation device after chemical exposure and does not facilitate eyelid retraction to irrigate the ocular fornix and palpebral conjunctiva resulting in residual chemicals on the ocular surface. The results of this study suggest use of a modified eyelid retractor and irrigation device more effectively neutralized pH after simulated chemical injuries compared to current irrigation practices.

CONTROL ID: 3535934

SUBMITTER (NAME ONLY): Christopher Mugnaini

TITLE: Predictive Model for Requirement of Future Anti-VEGF Therapy in Diabetic Eye Disease: The Potential Importance of the Leakage Index on Ultra-widefield Fluorescein Angiography

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Mugnaini, D. Sevgi, J. Whitney, A.C. Jiang, S. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|M. Hu, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, UNITED STATES|A.C. Jiang, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify imaging biomarkers and patient characteristics that predict future need for anti-VEGF therapy in diabetic retinopathy (DR) using an integrative machine learning predictive model.

Methods: Retrospective image analysis study of anti-VEGF naive eyes with DR who underwent ultra-widefield fluorescein angiography (UWFA) and optical coherence tomography (OCT). Quantitative UWFA analysis was performed using a custom semi-automated platform for leakage index (LI), ischemic index, microaneurysm (MA) count and vascular density (VD) parameters (skewness, kurtosis, variance, and zero VD index). OCT scans were reviewed for mean central subfield thickness (CST) and the presence of diabetic macular edema (DME). Two random forest classifiers grown with 1000 trees using 3 randomly sampled features as candidates at each split were created to differentiate eyes that required anti-VEGF within 3 months (including on the day of UWFA) and after 3 months of the imaging visit from the eyes that did not require any anti-VEGF during the follow-up period. Features including age, gender, follow-up time, visual acuity (VA), panretinal LI, macular LI, ischemic index MA count, CST, presence of DME and VD parameters were selected for model testing.

Results: Eyes requiring anti-VEGF within 3 months (n=38) of the UWFA imaging session and eyes requiring anti-VEGF after 3 months (n=34) following the imaging visit were compared to the eyes that did not require any anti-VEGF treatment (n=101), independently. The mean follow-up time was 22 (11- 43) months. The area under the curve (AUC) for the anti-VEGF initiation within 3 months model was 0.93 ± 0.03 with the most important features being VA, CST, macular LI, and total LI (importance: 0.211, 0.197, 0.100 and 0.069 respectively). The AUC for differentiating eyes that required anti-VEGF treatment after 3 months vs eyes that did not require any anti-VEGF treatment was 0.77 ± 0.04 with the four most important features being VA, macular leakage index, total leakage index, and follow-up time (importance: 0.112, 0.112, 0.102 and 0.100 respectively).

Conclusions: A ML predictive model was successful identifying eyes requiring immediate and future anti-VEGF therapy. The most important predictive features in both models included VA and macular LI.

CONTROL ID: 3535963

SUBMITTER (NAME ONLY): Mona Camacci

TITLE: Differences in Publication Productivity among Medical and Surgical Retina Specialists at Academic Ophthalmology Departments

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Camacci, M. Chiam, S. Patel, I.U. Scott, E.M. Bowie, S. Pantanelli, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|E. Lehman, I.U. Scott, Public Health Sciences, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retina is the largest subspecialty within academic ophthalmology, comprising 22.0% of all academic ophthalmologists. This study sought to investigate differences in publication productivity between medical and surgical retina specialists.

Methods: The Penn State College of Medicine Institutional Review Board reviewed the study protocol and determined the study was exempt from further review. This was a cross-sectional study of academic retina specialists identified through review of institutional websites of all 113 US ophthalmology residency training programs accredited by the ACGME. Faculty members were categorized as medical or surgical retina specialists based on academic institutional websites regarding the retina fellowship training they completed. Faculty data on residency graduation year were collected between January-March 2019. The h-index measures a published author's publication productivity and citation impact, and was obtained for each retina specialist from the Scopus database. The m-quotient adjusts for career duration and was calculated by dividing the h-index by the total number of years between the author's residency graduation year and 2019. Wilcoxon Rank Sum tests were used to analyze for differences in h-indices and m-quotients between medical and surgical retina specialists.

Results: Among 623 retina specialists identified, 117 (18.8%) were medical specialists and 506 (81.2%) were surgical specialists. Medical and surgical specialists had median career durations of 23.0 (interquartile range (IQR) 20.0) and 19.0 years (IQR 20.0), respectively. Medical specialists had a higher median h-index [14.0 (IQR 28.0) vs. 11.0 (IQR 19.0); $P = 0.023$] and m-quotient [0.83 (IQR 0.90) vs. 0.64 (IQR 0.75); $P = 0.019$] than surgical specialists.

Conclusions: There are fewer medical than surgical retina specialists in academia. Medical retina specialists had a higher median publication productivity than their surgical counterparts, even after accounting for career duration.

CONTROL ID: 3535973

SUBMITTER (NAME ONLY): Sanyam Ratan

TITLE: Gender Gap in the Award Recipients of the Association for Research in Vision and Ophthalmology

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ratan, A. Nguyen, A. Biyani, Y. Sun, S. Saleh, A.Y. Wu, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|X. Trinh, Department of Computer Science, McGill University, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The underrepresentation of women has been observed in several medical societies but has not been examined yet in ophthalmology research.

This retrospective, observational study examined the gender of awardees of the Association for Research in Vision and Ophthalmology (ARVO) over the past 70 years. More specifically, we determined trends in gender distribution of awards by award category (achievement, public service, research) and awardees' individual characteristics (country of affiliated institution, level of education).

Methods: Award data were compiled from lists displayed on the official ARVO society website. Award details were collected, including: name, society, specialty/subspecialty, description, category (designated based on the award name and description), year(s), and demographic type. Professional websites (ex. LinkedIn, Twitter, ResearchGate, university pages, conference pages, private practice pages, newspapers) were searched to extract a gender-specific pronoun and photograph of each awardee.

Results: This study analyzed 13 different awards given to 299 awardees. 43 (14.4%) awardees were women and 254 awardees (85.6%) were men.

Of 248 achievement awards recognizing an individual's overall contribution, 32 (12.9%) awards were given to women and 216 (87.1%) were given to men. Of 43 research awards recognizing scientific advancement, including the best abstract or publication, 11 (25.6%) were given to women and 32 (74.4%) were given to men. Of 8 public service awards, recognizing humanitarianism or volunteer efforts, none were given to women.

In years with relevant sample size ($n > 2$), the smallest gender gap was in 2010 (37.5% women, 62.5% men).

Most awardees were affiliated with a US institution. Amongst 250 domestic awardees, 36 (14.4%) were women. In the case of 49 international awardees, 7 (14.3%) were women.

Awardees with only an MD degree ($n=96$, 32.3% of total) were mostly men (93.8%), as were awardees with only a PhD or equivalent degree ($n=91$, 30.6% of total, 84.6% men). Finally, awardees with both degrees ($n=44$, 14.8% of total) were also often men (86.4%).

Conclusions: Overall, women were underrepresented in awards given ($<50\%$), even when stratified by category ($<25.6\%$ women) or individual characteristics ($<15.4\%$ by degree, $<14.4\%$ by country of affiliated institutions). These findings suggest a need for greater and more conscious representation in ophthalmology.

CONTROL ID: 3535981

SUBMITTER (NAME ONLY): Mark Bui

TITLE: Impact of Baseline Macular Atrophy on Long-Term Outcomes in Neovascular Age-Related Macular Degeneration Patients Treated with anti-VEGF Treatment

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.Q. Bui, G.L. Hom, R.P. Singh, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|A. Iyer, A. Kalur, J. Muste, T.F. Conti, R.P. Singh, K. Talcott, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-vascular endothelial growth factor (anti-VEGF) therapy improves visual acuity (VA) in neovascular age-related macular degeneration (nAMD) patients but the impact of baseline macular atrophy (MA) on long-term visual outcomes is not well understood. This study examines how baseline MA affects long-term visual outcomes in nAMD patients treated with anti-VEGF injections.

Methods: A single eye of patients treated with anti-VEGF injections for nAMD over a 7-year time period at the Cole Eye Institute, Cleveland Clinic were included in this study. Eyes were imaged at baseline using Cirrus SD-OCT and retinal pigment epithelium (RPE) sub-illumination analysis (Cirrus High-Definition Spectral Domain-OCT Review V9.5.1; Carl Zeiss Meditec, Dublin, CA) was used to automate identification of atrophy and measure the total area of RPE sub-illumination within 5mm of the fovea. MA was determined by the presence of atrophy within 5 mm of the fovea. Segmentation errors were manually corrected. Clinical outcomes including VA, number of injections and number of appointments were collected.

Results: 68 patients (60.3% female) with mean age 81.8 ± 9.1 years and baseline VA 68.9 ± 13.7 ETDRS letters were included. 53 eyes (77.9%; mean age 82.1 ± 8.6 years and baseline VA 68.7 ± 15.0 ETDRS letters) had MA at baseline. The mean sub-RPE illumination was $2.9 \pm 2.6 \text{ mm}^2$ in this cohort. 15 eyes did not have MA at baseline had an average age of 80.7 ± 11.1 years and a baseline acuity of 69.7 ± 8.4 ETDRS letters. No differences in baseline characteristics existed between the 2 cohorts (all $p > 0.05$). At 7 years, eyes with baseline MA lost a mean 7.4 ETDRS letters (95% CI, 0.7 to 14.1) from baseline and had received a mean 38.3 ± 16.0 injections over 52.7 ± 16.5 appointments. At 7 years, patients (n=15) without baseline MA lost a mean 10.4 ETDRS letters (95% CI, -2.7 to 23.5) from baseline and had received a mean 40.0 ± 14.4 injections over mean 54.3 ± 11.3 appointments. There were no significant differences in vision loss from baseline, injections, or appointments between the 2 cohorts (all $p > 0.05$).

Conclusions: The results of this study suggest that nAMD eyes with baseline MA treated with anti-VEGF injections were associated with progressive vision loss at 7 years. Further research is needed to examine how the progression of MA affects VA outcomes in nAMD patients treated with anti-VEGF therapy.

CONTROL ID: 3536011

SUBMITTER (NAME ONLY): Bennett Ahearn

TITLE: Intravitreal Dexamethasone Implant for Cystoid Macular Edema

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.E. Ahearn, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|C. Krambeer, Texas Tech University Health Sciences Center, Lubbock, Texas, UNITED STATES|M. Singer, Medical Center Ophthalmology Associates, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal dexamethasone implants (Ozurdex) are not currently indicated for cystoid macular edema (CME), although they are currently being used as therapy for this condition. Additionally, little data exists on the effects of an intravitreal dexamethasone implant as a treatment for CME. We conducted a retrospective chart review to determine changes in visual function and macular thickness following treatment with an intravitreal dexamethasone implant in patients with CME.

Methods: This chart review included 31 eyes in 28 patients who received at least one intravitreal dexamethasone injection for treatment of CME. Visual acuity (VA) and optical coherence tomography central subfield thickness (CST) were compared before and after the first intravitreal dexamethasone implant. P value was calculated from a 2-tailed paired T-test with a statistical significance value of $P < 0.05$.

Results: In 27 out of 31 eyes, after 1 intravitreal dexamethasone implant, there was significant improvement in peak ETDRS VA (mean +15.5 letters, $p = 0.00001$). The peak ETDRS VA change ranged from -12 to +65 letters. There was a significant decrease in CST in 30 out of 31 eyes after 1 intravitreal dexamethasone implant (mean -168.6 μm , $p = 0.0004$). The CST ranged from a peak decrease of 1204 μm to an increase of 22 μm . Intraocular pressure increased in 27 out of 31 eyes. 8 eyes reached an intraocular pressure of ≥ 25 mmHg with 4 of these reaching an intraocular pressure of ≥ 30 mmHg.

Conclusions: Treatment with an intravitreal dexamethasone implant may significantly benefit VA and CST in patients with CME.

CONTROL ID: 3536015

SUBMITTER (NAME ONLY): Ankita Umapathy

TITLE: Spatiotemporal dynamics of photoreceptor outer segment phagosome ingestion by the retinal pigment epithelium

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Umapathy, J. Chung, M. Tomlinson, C. Lim, D.S. Williams, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|D.S. Williams, Neurobiology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) performs several functions crucial to the maintenance of vision, including the daily phagocytosis of the distal tips of the photoreceptor outer segments (OS). Previous visualization of the phagocytic cup formed by the RPE has been limited to electron microscopy. These static images, though informative, do not accurately capture an inherently transient and dynamic process. We used live imaging, for the first time, to visualize the dynamics of OS ingestion and the transient localization of proteins involved in phagocytosis.

Methods: Primary mouse RPE cells were transfected with proteins of interest (Tractin-RFP/GFP, GFP-FBP17, AMPH1-BAR-mCherry, mRFP-RAB5, GFP-RAB7, or LAMP1-YFP), fed labeled isolated OS, and imaged using spinning disk confocal microscopy. Phagosome diameter was measured in cells pre-treated with cytochalasin D (to disrupt actin dynamics) or DMSO vehicle.

Results: Live imaging of RPE cells transfected with Tractin-RFP (actin) and fed labeled OS showed ingestion of OS by apical actin-rich phagocytic cups that bit phagosome-sized pieces. Cytochalasin D pre-treatment provided greater temporal resolution of actin involvement in phagosome scission such as localized increases in actin intensity coinciding with the site and time of scission events, and concentrated bursts of actin polymerization within the cup pushing phagosomes further into the cell. Furthermore, inhibitor-treated cells tended to produce phagosomes with smaller diameters. Membrane curvature-sensing proteins and regulators of actin dynamics, FBP17 and AMPH1-BAR, also localized to the phagocytic cup. Both coincided with highly curved membranes; AMPH1 was found at the rim and base of the cup, and FBP17 was restricted to the rim of the growing (but not regressing) cup. Early and late endosomal markers, RAB5 and RAB7 (but not the lysosomal marker, LAMP1), entered the phagocytic cup, before closure, to interact with incoming phagosomes.

Conclusions: By visualizing actin dynamics during phagocytosis, we show a role for actin in driving phagosome scission, size, and movement into the cell. The spatiotemporal localization of FBP17 and AMPH1-BAR highlight the transient nature of phagocytosis, whereas that of endosomal markers suggests that phagosome maturation may begin earlier than expected. These data provide unprecedented insight into the process of OS phagocytosis.

CONTROL ID: 3536018

SUBMITTER (NAME ONLY): Solin Saleh

TITLE: Outcomes of corneal crosslinking for keratoconus in children and young adults

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Saleh, E.B. Koo, S.R. Lambert, E.E. Manche, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is limited North American data on the efficacy of corneal crosslinking for pediatric keratoconus, which is often severe at diagnosis and progresses rapidly. We performed a retrospective medical record review to assess the effect of corneal crosslinking on vision, keratometry and wavefront aberration in children and young adults with progressive keratoconus.

Methods: We included patients aged ≤ 22 years with keratoconus who underwent corneal crosslinking between January 2013 and November 2019 at Byers Eye Institute at Stanford University. Outcome measures included logMAR corrected distance visual acuity (CDVA), keratometry and total wavefront aberration. Measurements were taken at baseline and 12 and 24 months postoperatively.

Results: A total of 57 eyes of 49 patients aged 12-22 years were included. The mean preoperative CDVA was logMAR 0.38 ± 0.32 (20/48) and postoperative CDVAs were logMAR 0.29 ± 0.31 (20/39) and 0.31 ± 0.31 (20/41) at 12 and 24 months postoperatively. Compared to preoperative mean Kmax, there was an improvement of -0.8 D to a mean postoperative Kmax of 59.1 ± 9.1 D at 12 months and -1.3 D to 59.7 ± 8.8 D at 24 months. Linear mixed modelling showed significant improvements in Kmax at 12 and 24 months ($p=0.013$, $p=0.001$, respectively). In a sub-analysis of available wavefront aberration data, there were no significant changes in root mean square, defocus, astigmatism, coma, trefoil, tetrafoil, spherical aberration or second order astigmatism at 12 months postoperatively.

Conclusions: Corneal crosslinking stabilized, and in some cases improved the visual, topographic and wavefront aberration parameters in pediatric and young adult patients with keratoconus. The procedure may prevent disease progression in this population.

CONTROL ID: 3536028

SUBMITTER (NAME ONLY): Hosein Hoseini-Yazdi

TITLE: Retinal OFF pathway activation leads to greater accommodation-induced choroidal thinning

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Hoseini-Yazdi, S.A. Read, D. Alonso-Caneiro, M.J. Collins, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Both near work and retinal OFF pathway activation have been implicated in the development of myopia. This study examined the interaction between accommodation and retinal ON and OFF pathway activation, and their association with changes in choroidal thickness in healthy young adults.

Methods: Nineteen subjects with a mean age of 25 ± 5 years and refractive error of -1.6 ± 2.2 D (range -5.5 to $+0.75$ D) participated. The left eye's sub-foveal choroidal thickness (SFCT) was assessed with Spectralis optical coherence tomography before and after a series of 30-min long binocular viewing tasks, including reading a passage of bright text on a dark background (ON pathway activation) and dark text on a bright background (OFF activation), and a control condition of viewing a movie with no bias towards ON or OFF pathways. Each task was preceded by a 20-min adaptation period of watching a movie at distance. The tasks were performed with 0 D and 5 D (induced by soft contact lenses) accommodation demands. Repeated measures ANOVA was conducted to examine the change in SFCT associated with contrast polarity (3 levels) and accommodation (2 levels).

Results: Significant main effects of accommodation and polarity were observed (both $p < 0.001$), with the SFCT reducing significantly by $-7 \pm 1 \mu\text{m}$ with 5 D accommodation compared to 0 D accommodation ($-3 \pm 1 \mu\text{m}$, $p < 0.001$), and by $-9 \pm 1 \mu\text{m}$ with OFF pathway compared to ON pathway activation ($-4 \pm 1 \mu\text{m}$, $p = 0.002$) and the control condition ($-2 \pm 1 \mu\text{m}$, $p < 0.001$). The change in SFCT with ON pathway activation was not significantly different from that observed with the control condition, both at 0 D ($-2 \pm 2 \mu\text{m}$ vs $+1 \pm 1 \mu\text{m}$, $p = 0.52$) and 5 D ($-6 \pm 1 \mu\text{m}$ vs $-5 \pm 1 \mu\text{m}$, $p = 0.99$) accommodation. However, selective activation of the retinal OFF pathway resulted in a significantly greater thinning of the choroid compared to the control condition, both at 0 D ($-7 \pm 1 \mu\text{m}$, $p = 0.003$) and 5 D ($-11 \pm 1 \mu\text{m}$, $p = 0.005$) accommodation demands.

Conclusions: The choroidal thinning associated with accommodation was approximately doubled with selective activation of the retinal OFF pathway through reading standard dark on light background text, providing a potential mechanism that involves accommodation and the OFF signalling pathway, linking near work and myopia.

CONTROL ID: 3536055

SUBMITTER (NAME ONLY): Saagar Patel

TITLE: Ophthalmology Resident Surgical Aptitude and Performance of ACGME-Identified Core Oculofacial Procedures

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Patel, I.U. Scott, C. Weller, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|I.U. Scott, Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate qualitative and quantitative measures of ophthalmology resident perceptions and ability to perform ACGME-identified core oculofacial procedures at a single institution.

Methods: Prospective case series. Anonymous questionnaires analyzed residents' perceptions of their knowledge and ability to perform steps of the ACGME-identified oculofacial procedures identified in Table 1. These were graded on a 1 to 5 scale. During an introductory suturing laboratory, an oculoplastics attending evaluated each resident's ability to oppose wounds on a suturing pad with the following surgical knots: simple interrupted, simple running, horizontal mattress, vertical mattress, deep dermal. Scores were based on successful apposition of the wound, appropriate spacing of suture, appropriate knot formation, and efficiency.

Results: Nine residents completed the survey and seven residents completed the introductory suturing lab. The mean score of all residents for the suturing lab was 56.1/100. The mean scores for residents' perceived knowledge and perceived performance of each procedure are listed in Table 1. Scores trended upwards for each postgraduate year (PGY) in both knowledge and performance. No resident felt comfortable with independent performance of the following procedures: levator advancement, ectropion repair, entropion repair. All residents reported that "primary" surgical cases contributed to their skill set and believed that additional "primary" surgical cases and surgical wet labs would improve their surgical skills.

Conclusions: Residents' perceived knowledge correlated with their perceived ability to perform ACGME-identified core oculofacial procedures ($r = 0.96$). Residents believed that additional "primary" surgeries and wet labs would improve their surgical skills. Residents' perceived knowledge and perceived ability to perform the procedures increased with PGY level. Additional objective data via cadaver courses are upcoming.

CONTROL ID: 3536058

SUBMITTER (NAME ONLY): Tzu-Ni Sin

TITLE: Genomic ablation of rhesus macaque VEGFa using CRISPR-Cas9 ribonucleoprotein

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sin, S. Chung, T. Ngo, G. Yiu, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Clustered regularly interspaced short palindromic repeats (CRISPR)-based genome editing technology has significant potential as a novel mode of gene therapy for retinal disorders. We previously identified single guide RNAs (gRNAs) targeting conserved regions in exon 1 of the vascular endothelial growth factor-a (VEGFA) gene in mice, rhesus macaques, and humans, and demonstrated efficient genomic ablation in human cell lines in vitro and mouse eyes in vivo using *S. pyogenes* Cas9 (SpCas9). Here, we evaluate the effectiveness of these gRNAs to target VEGFA in the rhesus macaque genome using SpCas9 ribonucleoproteins (RNPs) in a cell-free system.

Methods: We identified 2 target sequences (V1 and V2) in exon 1 of mouse, rhesus macaque, and human VEGFA gene in silico, then synthesized functional gRNAs by combining these target sequences with trans-activating crisper RNA (tracrRNA) and assembled with SpCas9 protein to generate VEGFA-targeting RNPs. The 1.4kb target VEGFA gene was amplified from rhesus macaque and human genomic DNA separately, then incubated with V1, V2, or both V1+V2 RNPs to compare genome editing efficiency in vitro.

Results: The in silico predictions for on-target activity of V1 and V2 target sequences were 60.5 and 49.5 for rhesus VEGFa, and 60.0 and 54.0 for human VEGFa, respectively. The off-target scores were 43.5 and 45.5 for rhesus VEGFa and 43.0 and 45.0 for human VEGFa. RNPs targeting the V1 and V2 loci of VEGFA demonstrated successful genomic ablation of the target gene sequence of rhesus macaques in vitro, with a genome editing efficiency of 46.39% using V1 gRNAs, 20.95% using V2 gRNAs, and 44.60% using V1+V2 gRNAs. In comparison, genome editing efficiencies using human VEGFA, which has similar on- and off-target scores to those of rhesus macaque, were 84.72% using V1 gRNAs, 37.10% using V2 gRNAs, and 68.54% using V1+V2 gRNAs.

Conclusions: CRISPR-based genomic ablation of the VEGFA gene using SpCas9 RNPs can be achieved with nonhuman primate and human genomes in vitro, although genome editing efficiencies do not reflect in silico predictions. In vitro assays may better indicate in vivo effectiveness of VEGFA ablation than in silico predictions, and may help facilitate clinical translation of CRISPR-based anti-angiogenesis therapies.

CONTROL ID: 3536067

SUBMITTER (NAME ONLY): Yuxi Zheng

TITLE: Vitreomacular separation on OCT in eyes with central retinal vein occlusions

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zheng, X. Zhang, S. Fekrat, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|A. Thomas, Tennessee Retina, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of complete vitreomacular separation on presenting characteristics, treatment patterns, and clinical outcomes of central retinal vein occlusions (CRVO).

Methods: We performed a retrospective longitudinal cohort study of patients seen at our institution for treatment-naïve CRVO between 2009-2017 and who had at least 12 months of follow-up. Presenting OCTs were individually reviewed for vitreomacular status at the presenting visit. Presenting clinical characteristics, treatment patterns, and outcomes were tabulated and analyzed between eyes with complete vitreomacular separation and those without.

Results: Of the 141 treatment-naïve eyes with CRVOs identified, 54 (38.3%) had complete vitreomacular separation on OCT at presentation, while 87 (61.7%) did not. Eyes with vitreomacular separation had baseline central subfield thickness (CST) of $490.0 \pm 296.1 \mu\text{m}$, while those with attached posterior hyaloid (including partially attached) had baseline CST of $548.7 \pm 286.0 \mu\text{m}$ ($p=0.15$). CST on final visit was significantly lower for eyes that presented with vitreomacular separation ($280.5 \pm 139.9 \mu\text{m}$ vs $345.0 \pm 172 \mu\text{m}$, $p=0.02$). 12-month injection burden was lower for eyes that presented with complete vitreomacular separation (3.3 ± 3.6 injections vs 4.8 ± 4.1 injections, $p=0.02$). Presence of cystoid macular edema (CME) at presentation and final visit did not differ between groups. On presentation, 38/54 (70.4%) eyes with vitreomacular separation had CME, while 61/87 (70.4%) of those without had CME ($p=0.97$). At final visit, 15/54 eyes (27.8%) of eyes with vitreomacular separation had CME while 27/87 (31%) did not ($p=0.68$).

Conclusions: Assessment of the vitreomacular relationship on OCT at presentation in eyes with CRVO may serve as a prognostic imaging biomarker. Eyes with complete vitreomacular separation have a significantly lower injection burden and CST at final visit compared to eyes without.

CONTROL ID: 3536075

SUBMITTER (NAME ONLY): Samantha Malka

TITLE: Evaluating the diagnostic yield of whole genome sequencing in genetic eye disease

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Malka, E. Schiff, H. Knight, G. Wright, A. Cordoba Gimenez, M. Michaelides, P. Yu-Wai-Man, O.A. Mahroo, G. Arno, A. Webster, M. Moosajee, Genetics, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|M. Michaelides, O.A. Mahroo, G. Arno, A. Webster, M. Moosajee, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|P. Yu-Wai-Man, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The introduction of whole genome sequencing (WGS) within the UK National Health Service (NHS) represents a global shift from targeted panel testing to genomic analysis. We performed a retrospective analysis of patients with a range of genetic eye disorders who had WGS to evaluate its utility.

Methods: Data was gathered from 1669 families from the ocular genetics service at Moorfields Eye Hospital, who underwent WGS through the UK Genomics England 100,000 Genomes Project. Patients were grouped into 4 categories based on their primary diagnosis: posterior segment disorders (including retinal dystrophies and optic neuropathies); anterior segment abnormalities (including bilateral congenital cataract, primary congenital glaucoma, and corneal dystrophies); ocular malformations (including microphthalmia, anophthalmia and coloboma); and albinism/nystagmus. A targeted virtual gene panel was applied to the WGS data in the first instance, followed by re-analysis incorporating off-panel variant interrogation and expert review with a multidisciplinary team (consisting of bioinformaticians, ophthalmologists specialising in genetic eye disease, clinical geneticist, and genetic counsellors) for unsolved cases.

Results: Overall, WGS yielded a molecular diagnosis in 55.8% of cases (931/1669). Solve rates grouped by diagnosis, family history, ethnicity and prior testing can be found in Table 1.

In 183 families (11.0% of all families; 19.6% of solved families), the genetic diagnosis was missed by initial laboratory analysis, but found through re-analysis by our multidisciplinary team. This was achieved by having expertise in ocular phenotypes, relaxing variant filtering, applying additional gene panels and interrogating copy number variation and non-coding variants.

Conclusions: A multidisciplinary, case-specific approach to genetic testing utilizing unbiased genome sequencing technology has yielded an overall molecular solve rate of 55.8% of patients in this large mixed cohort. It is uniquely possible to further scrutinise WGS data as new discoveries are made enabling additional molecular diagnoses without the need for additional expensive molecular investigations.

CONTROL ID: 3536079

SUBMITTER (NAME ONLY): Kubra Sarici

TITLE: Assessment of retinal pigment epithelial detachment treatment response and impact of size on outcomes in neovascular age-related macular degeneration from the OSPREY study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sarici, T.K. Le, D. Sevgi, J. Reese, J.P. Ehlers, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|L. Lunasco, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|R. Zahid, X. Meng, Novartis Pharmaceuticals Corp, East Hanover, New Jersey, UNITED STATES|S. Srivastava, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate outcomes of eyes with neovascular age-related macular degeneration (nAMD) with moderate to very large retinal pigment epithelial detachments (PEDs) in the OSPREY trial.

Methods: This was a post hoc analysis of the OSPREY phase II, randomized, multicenter, double-masked trial comparing brolucizumab 6mg and aflibercept (AFL) 2mg in nAMD. Treatment-naïve nAMD eyes presenting PEDs were evaluated in the following groups as determined at baseline: (1) all PEDs with a maximum height 150µm (brolucizumab n=20, AFL n=21); (2) very large PEDs with a maximum height 250µm (brolucizumab n=12, AFL n=10). SD-OCT scans were analyzed in a machine-learning enhanced novel software platform for multi-layer volumetric assessment to categorize PED size and provide volumetric measures, including sub-RPE volume and intraretinal fluid (IRF) and subretinal fluid (SRF) volumes. No adjustment was made for multiple comparisons.

Results: A total of 41 eyes were included in this analysis. When considering all PEDs 150µm, the mean change in BCVA was +7.3 letters in the brolucizumab group (p=0.02) and +6.6 letters in the AFL group (p=0.05). In the very large PED cohort, mean change in BCVA was +5.6 letters (p=0.26) and -0.4 letters (p=0.94) in the brolucizumab and AFL groups, respectively. In both cohorts, brolucizumab and AFL demonstrated significant reductions in PED maximum height (p<0.05). In very large PEDs, the mean reduction at Week 4 was -122.7µm with brolucizumab compared to -84.1µm with AFL. At Week 56, the mean reduction was -167.0µm with brolucizumab compared to -153.2µm with AFL. Significant reductions in sub-RPE volume were noted with both treatment regimens across all PED cohorts (p<0.05; all but two time points with AFL). In both cohorts at Week 56, there was a reduction in mean IRF volume (0.11 and 0.12mm³ with brolucizumab, 0.08 and 0.10mm³ with AFL) and SRF volume (0.45 and 0.74mm³ with brolucizumab and 0.40 and 0.78mm³ with AFL).

Conclusions: Both brolucizumab and AFL demonstrated significant improvement in PED features. In very large PEDs, functional response was more limited. Although exploratory in nature, this analysis suggests a possibly more rapid improvement in exudative parameters and possibly greater functional response in the very large PED group with

brolocizumab.

CONTROL ID: 3536088

SUBMITTER (NAME ONLY): Yanan Dong

TITLE: Normative Distribution of Optical Coherence Tomography Retinal Features and Associations with Visual Function in Older Adults (from the Eye Determinants of Cognition Study)

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Dong, R.A. Sharrett, Epidemiology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|X. Guo, L.T. Arsiwala, P.Y. Ramulu, A. Mihailovic, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|A. Abraham, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Structural and angiography measures of retinal optical coherence tomography (OCT) imaging are often employed clinically to evaluate retinal health in individual patients. However, the normative distribution of these measures across older populations has not been well characterized. Here we describe the distribution of retinal features and its associations with visual function in a population-based bi-community sample from the Eye Determinants of Cognition (EyeDOC) study.

Methods: OCT structural and angiographic images were obtained in EyeDOC participants from two communities: Jackson, MS (all Black) and Washington County, MD (all White). Retinal measurements included retinal nerve fiber layer (RNFL) thickness, macular ganglion cell complex (GCC) thickness, macular vessel density (VD, % of area covered by vessels) in the superficial and deep capillary plexus (SCP and DCP), and the area of the foveal avascular zone (FAZ). Aspects of visual function including corrected distance visual acuity (VA) and contrast sensitivity (CS) were assessed. Differences in means for each retinal feature by age and community were tested using t-test and one-way ANOVA. Associations of visual function with retinal features were estimated from adjusted linear regression models.

Results: Retinal measures were available in 759 participants (46% black; 63% female; mean age 80 years[range: 73-94 years]). Mean GCC thickness was lower for Jackson vs. Washington County participants (89.2 μ m, 92.3 μ m, $p < 0.001$). Mean VD in DCP were statistically lower for participants ≤ 80 years old (44.67%, 43.69%, $p < 0.001$). Mean FAZ differed by community (Jackson: 0.36 mm², Washington: 0.26 mm², $p < 0.001$; Table 1). Each 10 μ m increase in RNFL thickness was related to 0.016 logCS better (95% confidence interval[CI]: 0.005-0.027, $p = 0.004$) among all participants and 0.012 logMAR VA better (95% CI: 0.001-0.023, $p = 0.049$) among Jackson participants (Table 2). Each 10 μ m increase in GCC thickness was associated with 0.016 logCS better (95% CI: 0.003-0.029, $p = 0.017$) overall, with a larger effect among Jackson participants ($\beta = 0.022$, 95% CI: 0.006-0.040, $p = 0.009$).

Conclusions: Results from this aging bi-community population suggested that different references should be used for different age and community groups for structural and functional retinal evaluations.

CONTROL ID: 3536089

SUBMITTER (NAME ONLY): Christie Hang I Lam

TITLE: High Glucose Induces Mitochondrial Dysfunction in Photoreceptor cells

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lam, H.H. Chan, D. Tse, School of Optometry, The Hong Kong Polytechnic University, Kowloon, HONG KONG

Commercial Relationships Disclosure (Abstract): Christie Hang I Lam: Commercial Relationship: Code N (No Commercial Relationship) | Henry Chan: Commercial Relationship: Code N (No Commercial Relationship) | Dennis Yan-yin Tse: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Photoreceptors have high metabolic activity, yet limited reserve capacity for mitochondrial oxidative phosphorylation. While mitochondrial dysfunction has been implicated in the cell death of various retinal cell types, including retinal endothelial cells, pericytes, and Müller cells, under simulated hyperglycemic stress, its effect on photoreceptor cells remains unclear. Here we investigated the effects of high glucose on mitochondrial membrane potential ($\Delta\Psi_M$), morphology, bioenergetics, and cell apoptosis of 661w photoreceptor-like cells.

Methods: The effect of high glucose (55mM) on $\Delta\Psi_M$ of 661w cells over time was evaluated with tetramethylrhodamine ethyl ester (TRME) fluorescein intensity level relative to normal glucose condition (5.5mM). Mitochondrial network of 661w cells incubated in these two conditions for 48 hours was identified using MitoTracker Green staining. Mitochondrial images were captured in live cells with confocal microscopy and analyzed for mitochondrial morphology changes based on form factor (FF) and aspect ratio (AR) values. Mitochondrial bioenergetics was assessed by measuring oxygen consumption rate (OCR) using the Seahorse XFe24 Extracellular Flux Analyzer. Cell apoptosis was evaluated by annexin V assay.

Results: 661w cells incubated in high glucose condition exhibited a multiphasic change in $\Delta\Psi_M$ over time (Fig 1). Significant increase in mitochondrial fragmentation was also observed when compared to normal glucose condition (FF= 2.95 ± 0.40 vs 4.82 ± 0.42 , $p<0.01$; AR= 1.96 ± 0.10 vs 2.44 ± 0.08 , $p<0.001$). OCRs were significantly reduced in cells grown in high glucose condition compared to those in normal glucose condition (ATP production: 7.62 ± 0.84 vs 9.86 ± 0.40 ; Maximal respiration: 10.52 ± 0.86 vs 14.33 ± 0.89 , $p<0.05$). Cell apoptosis was also increased by approximately 1.4-fold in high glucose condition compared to normal glucose condition ($p<0.001$).

Conclusions: High glucose affects the mitochondria of 661w cells by disrupting the homeostasis of $\Delta\Psi_M$, changing mitochondrial morphology, and increasing mitochondrial fragmentation. Impaired mitochondrial function and increased cell apoptosis were also observed. The detrimental effects of glucose on mitochondrial function and cellular metabolism may lead to photoreceptor cells apoptosis, contributing to the pathogenesis of diabetic retinopathy.

CONTROL ID: 3536100

SUBMITTER (NAME ONLY): Nkechi Nwabueze

TITLE: Western Blot Total Protein versus a Housekeeping Gene Normalization in the DBA2/J Mouse Retina

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.N. Nwabueze, R. Prasad, K.M. Joos, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma carries a huge disease burden and understanding it is critical. Quantitative Western Blot (WB) analysis requires comparison of the target protein normalized to an internal control. However, the housekeeping proteins can be susceptible to oxidative stress, mechanical changes, and aging in the retina. Normalization to total protein was recently reported. We compared B-actin and total protein as internal controls in mice with increasing age and with elevated intraocular pressure (IOP).

Methods: Mouse tissues were acquired following protocols that were ethically reviewed and approved by the Vanderbilt University Medical Center Institutional Animal Care and Use Committee, and adhered to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. We divided the eyes of 10-month old DBA/2J mice into two groups based upon: 1) normal IOP (NIOP; $<10\text{mmHg}$) and 2) High IOP (HIOP; $>10\text{mmHg}$) measured by tonometer (TONOLAB, Icare). A third group consisted of eyes from 10-week DBA/2J mice. Samples consisted of three retinas. 7 WBs comparing relative quantities among the 3 groups using B-actin, and 7 WBs using total protein levels (REVERT Total Protein Stain, LICOR Biosciences, Lincoln) were run. Comparison of expression among the 3 groups was performed with one-way ANOVA (SigmaPlot 12.5, Systat).

Results: A significant difference in B-actin levels was present among the 3 groups ($P<0.001$) with a significant increase in the HIOP group compared to the other 2 groups (Bonferroni Multiple Comparison, HIOP vs NLIOP $P=0.006$; HIOP vs 10-week old $P<0.001$). No significant difference in total protein staining was present among the 3 groups ($P=0.274$).

Conclusions: Total protein staining may be the superior method for normalization of WB proteins in the mouse retina. There was an increase in B-actin levels in the DBA/2J HIOP retinas compared to B-actin levels in the other groups, suggesting an influence of IOP. Whereas, there was no significant difference in total protein staining among the 3 groups.

CONTROL ID: 3536111

SUBMITTER (NAME ONLY): Taku Yamamoto

TITLE: The close link between hypoxia and autoinduction of placental growth factor in galectin-1 expression in retinal pigment epithelium cells

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yamamoto, A. Kanda, S. Kase, S. Ishida, Laboratory of Ocular Cell Biology and Visual Science, Department of Ophthalmology, Hokkaido University Faculty of Medicine and Graduate School of Medicine, Sapporo, Hokkaido, JAPAN|

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ABSTRACT BODY:

Purpose: Galectin-1/LGALS1, a member of β -galactoside-binding lectin family, contributes to angiogenesis and fibrosis in various ocular diseases. Hypoxia-dependent and -independent pathways increase galectin-1/LGALS1 expression in Müller glial cells. Here, we show new findings on the galectin-1/LGALS1 regulatory system in human retinal pigment epithelium (RPE) cells, the major cellular participant in the pathogenesis of neovascular age-related macular degeneration (nAMD).

Methods: Human RPE cells were used to evaluate changes in gene and protein expression with real-time quantitative PCR and immunoblot analyses, respectively. The promoter and enhancer region of LGALS1 was analyzed by reporter assay and chromatin immunoprecipitation. nAMD patient specimens were examined by immunofluorescence analysis.

Results: Hypoxia induced galectin-1/LGALS1 expression (fold change = 1.7, $p < 0.05$) via binding of hypoxia-inducible factor-1 α to hypoxia-responsive elements in the LGALS1 promoter region. Blockade of vascular endothelial growth factor receptor (VEGFR)1 partially decreased hypoxia-induced galectin-1/LGALS1 expression (fold change = 1.2, $p < 0.01$). Among several VEGFR1 ligands induced by hypoxia, placental growth factor (PIGF)/PGF alone upregulated galectin-1/LGALS1 expression (fold change = 2.2, $p < 0.05$) via phosphorylation of activator protein (AP)-1 subunits following AKT and p38 mitogen-activated protein kinase (MAPK) activation. AP-1 site in the LGALS1 enhancer region was required for PIGF-induced galectin-1/LGALS1 expression in RPE cells. PIGF application upregulated PGF expression (fold change = 1.8, $p < 0.01$) via extracellular signal-regulated kinase 1/2, AKT, and p38 MAPK pathways. nAMD patient specimens demonstrated co-localization of galectin-1 with HIF-1 α , PIGF, and VEGFR1 in RPE cells.

Conclusions: Our present findings implicate the significance of hypoxia as a key inducer of galectin-1/LGALS1 in RPE cells and autoinduction of hypoxia-induced PIGF as a vicious cycle to amplify the pathogenesis of nAMD.

CONTROL ID: 3536124

SUBMITTER (NAME ONLY): Alice Shen

TITLE: Anterior Segment Biometric Measurements Explain Misclassifications by a Deep Learning Classifier for Detecting Gonioscopic Angle Closure

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Shen, M.F. Chiang, A. Pardeshi, R. McKean-Cowdin, B. Xu, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|R. Varma, Southern California Eye Institute, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify biometric parameters that explain misclassifications by a deep learning classifier to detect gonioscopic angle closure based on anterior segment OCT (AS-OCT) images.

Methods: Subjects of the Chinese American Eye Study underwent a complete ocular examination with gonioscopy and AS-OCT imaging of each quadrant of the anterior chamber angle. A previously described deep learning algorithm was applied to one AS-OCT per quadrant to predict a gonioscopy grade based on the modified Shaffer grading scale (grades 0/1 = closed; grades 2/3/4 = open). Median biometric measurements were calculated and compared between prediction classes using the Kruskal-Wallis test due to non-normal distributions. Pairwise comparisons of median biometric measurements between prediction classes were performed using the post-hoc Dunn's test, adjusted for multiple comparisons.

Results: Among 584 total images, 271 images with angle closure (true positive, TP) and 224 images with open angle (true negative, TN) were correctly predicted by the classifier. 77 images with open angle were overcalled as closed (false positive, FP). 12 images with angle closure were undercalled as open (false negative, FN).

There were significant differences ($p < 0.001$) in median parameter measurements between prediction classes among anterior chamber angle (ACA) parameters (angle opening distance, trabecular iris space area, scleral spur angle). The order of median ACA parameter measurements from smallest to largest was: TP, FN, FP, TN.

There were significant differences ($p < 0.036$) in median parameter measurements between prediction classes among anterior segment (AS) parameters. For some AS parameters (iris area, anterior chamber depth), the order of median parameter measurements from smallest to largest differed from the ACA parameters: TP, FP, FN, TN. This order was the same for other AS parameters (iris curvature, lens vault) when median parameter measurements were ordered from largest to smallest.

Conclusions: Overall, there were more FP than FN by the deep learning classifier. Our findings suggest that when there is disagreement between ACA and AS parameters, the classifier preferentially makes predictions based on AS over ACA parameters. A second layer of quantitative analysis may help identify initially misclassified images and improve classifier accuracy in detecting gonioscopic angle closure.

CONTROL ID: 3536126

SUBMITTER (NAME ONLY): Raviv Katz

TITLE: Feasibility of quantitative Visual Acuity analysis for enriching Visual Acuity data collected in retina clinical trials

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Katz, F. Vingopoulos, J.B. Miller, Retina, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|L.A. Lesmes, Adaptive Sensory Technology, California, UNITED STATES|R. Bajaj, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual acuity (VA) remains the primary functional endpoint for quantifying treatment effectiveness. To enrich VA information collected in retina trials, we apply a novel quantitative VA (qVA) framework to estimate VA thresholds from different testing paradigms (1). We propose that novel Bayesian analytics can reduce the uncertainty of VA estimates in patients with retinal disease.

Methods: Prospective, observational study performed at Mass Eye and Ear. We recruited patients with vision ranging from 20/15 to 20/100 during regular retina clinic visits. ETDRS testing, in the right and then left eye, was followed by qVA testing, which consisted of 15 sequential rows of 3 optotypes. Patients were retested in the opposite order after at least 30 minutes. We generate a qVA profile using a Bayesian model of VA that defines the probabilities for correctly reporting the different numbers of optotypes presented in ETDRS/qVA tasks. To quantify the evolution of a qVA profile, we calculate the half-width of 68.2% credible intervals (HWCI) for VA threshold estimates (2), as a function of 1-14 rows completed during ETDRS/qVA testing.

Results: 53 eyes of 31 patients, with mean age of 65.1 ± 13.3 and 21 females (68%) were included in the study. Repeat testing generated a total of 106 ETDRS/qVA tests. Figure 1 presents the Bayesian priors for VA threshold, and final posteriors for two patients. Figure 2a demonstrates the rapid reduction in average HWCI during VA testing. Figure 2b presents HWCIs for an aggregate analysis concatenating two ETDRS/qVA runs for each patient (N=53). Paired t-tests revealed statistically significant HCWI reductions for qVA: 22% for single and 20% for double runs ($p < 10^{-6}$).

Conclusions: We demonstrate that the novel application of a qVA analysis reduces uncertainty in VA estimates from ETDRS/qVA testing. The qVA advantage most likely emerges from its intelligent sampling and fine-grain resolution, relative to coarse, static sampling of ETDRS. These results support the feasibility for qVA testing and analysis to improve the signal-noise features of VA data in clinical trials.

References:

Lesmes & Dorr (2019) https://doi.org/10.475/123_4
Zhao et al (2021) <https://doi.org/10.1167/tvst.10.1.1>

CONTROL ID: 3536131

SUBMITTER (NAME ONLY): Chase Miller

TITLE: Ozurdex Migration to Anterior Chamber in Patients with Sutured Intraocular Lenses

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Miller, A. Miller, C. McCrossin, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Chase Miller: Commercial Relationship: Code N (No Commercial Relationship) | Alex Miller: Commercial Relationship: Code N (No Commercial Relationship) | Christina McCrossin: Commercial Relationship: Code N (No Commercial Relationship) | David Miller: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To review the complication of anterior chamber migration of Ozurdex implant in patients with sutured intraocular lenses (IOL).

Methods: Institutional review board approval was obtained for this retrospective study. The practice management database of a single retinal speciality group was searched by current procedural terminology (CPT) for all patients with sutured IOLs and Ozurdex intravitreal implants over a five year period from 2016 through 2020. Patients matching these parameters had their charts reviewed individually. Data collected includes age, sex, eye, date of sutured IOL, number and dates of intravitreal ozurdex injections, pre and post injection visual acuity, pre and post injection intraocular pressure, occurrence of anterior chamber (AC) migration of ozurdex, further surgical procedures, corneal transplation, and most recent visual acuity and intraocular pressure.

Results: Database search revealed seven patients that fit the criteria of having an Ozurdex implant and sutured IOL. Four of the seven patients experienced AC migration of Ozurdex implant. This resulted in three additional surgical procedures to remove the AC foreign body. One patient was treated with positioning. Three of the four patients who experienced AC migration of the Ozurdex implant required corneal transplant. Of the patients with AC migration, final visual acuity ranged from 20/300 to 20/400. Of the patients without AC migration, final visual acuity values were 20/40, 20/50, and 20/200. There was no significant difference in intraocular pressure in all seven patients.

Conclusions: Patients with Ozurdex implants seem to be at a higher risk of AC chamber migration in sutured IOLs. This appears to lead to corneal failure and poor visual outcomes.

CONTROL ID: 3536132

SUBMITTER (NAME ONLY): Andrew Clark

TITLE: Short term visual outcomes with extended anti-VEGF therapy intervals for macular edema as a result of the COVID-19 pandemic

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Clark, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Andrew Clark: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The COVID-19 pandemic has placed an unprecedented strain on the modern healthcare system with outpatient providers needing to make significant adjustments in practice patterns in response. Ophthalmologists face unique challenges with limited ability to practice remotely, need for close quarters contact to facilitate routine examination and lack of validated personal protection equipment compatible with standard ophthalmic examination equipment. Macular edema is one common retinal condition necessitating frequent examination and in-office intervention. In this single institution retrospective case series, visual outcomes were reviewed for patients with macular edema previously stabilized by regular intravitreal bevacizumab (IVA) injections that were extended as result of limitations imposed by the pandemic.

Methods: Patients with stable macular edema from diabetic disease (DME) or retinal vein occlusion (RVO) were identified. A total of 11 patients (10 DME and 1 RVO, 11 eyes) underwent extended therapeutic interval. Patients were monitored using Snellen visual acuity, clinical examination and macular OCT.

Results: The median injection frequency was increased from 42d (range 28-84d) to 84d (range 42-252d) with an average percentage increase in duration between injections of 45%. The number of treatment cycles under extended therapy was between 1-3 cycles. The length of extension was based on a combination of patient preference, logistical limitations and provider clinical judgment. Only one of eleven patients demonstrated recurrence of center-involving edema with extended injection interval. The visual decline in Snellen visual acuity for the affected patient was one line (20/40 to 20/50) without subjective appreciation of decreased vision. The remaining ten patients demonstrated no visual decline with extended therapy.

Conclusions: These results suggest that temporary extension of IVA treatment interval leads to neither immediate nor significant visual decline in patients with previously well controlled edema. Long term follow-up is necessary to determine if these patients will remain clinically stable with extended therapy or if there is increased risk of recurrent or recalcitrant edema.

CONTROL ID: 3536134

SUBMITTER (NAME ONLY): Fengyang Lei

TITLE: Single-cell RNA-seq reveals a dynamic shift of engrafted peripheral macrophages in the CNS towards a microglia signature.

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Lei, C. Zhou, C.H. Dohlman, J. Chodosh, E.I. Paschalis, Cornea, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|F. Lei, N. Cui, Y. Cai, H. Zhang, D.A. Weitz, Harvard University John A Paulson School of Engineering and Applied Sciences, Cambridge, Massachusetts, UNITED STATES|D.G. Vavvas, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular injuries can result in permanent remodeling of the neuroglia system. This has been associated with increased susceptibility to neuroinflammation and subsequent glaucoma. Here, we employed a high throughput in-drop single-cell RNAseq to assess the dynamic changes in the transcriptional profile of myeloid cells of the retina after ocular injury.

Methods: C57BL/6J mice received corneal alkali burn to induce sterile retinal inflammation. Retinal tissues were collected 1, 4, and 7 days after the injury, CD45⁺CD11b⁺ cells were isolated using FACS sorting and processed for high-throughput microfluidic-based single cell sequencing. Bioinformatic analysis was performed with the Seurat V2 program and key findings were further assessed using a CX3CR1^{+/EGFP} bone marrow chimera model.

Results: One day post injury, we identified two distinct clusters of myeloid cells, representing the resident microglia (Siglec1-) and the peripheral monocytes (Siglec1+) that infiltrate into the parenchyma after injury. Acetylation genes Eif5a, Eif3k, Naa38 were highly upregulated in microglial cells as compared to peripherally engrafted monocytes. However, 4 days post injury, the signatures of the two populations started to overlap, with peripheral monocytes expressing a subset of microglia genes, such as P2ry12, Tmem119, Aif1, Fcrls. At 7 days post injury, the signatures of the two populations appeared to converge further. Further validation in bone marrow chimeras revealed a morphometric convergence between infiltrated and resident CX3CR1⁺ cells, further corroborating the RNAseq findings. The transition of peripheral monocytes to microglia was supported by gradual change from CD45^{hi}CX3CR1^{lo} monocyte to CD45^{lo}CX3CR1^{hi} microglia phenotype. Further, 4 days after injury, P2ry12 was found to be expressed on infiltrated monocytes.

Conclusions: Our results suggested that infiltrated monocytes in the retina undergo in situ phenotypical changes that allow them to adapt to the new environment. This is associated with de novo expression of P2ry12 and Tmem119 "microglia specific genes" and phenotypical changes that promote their long-term engraftment into the tissue.

CONTROL ID: 3536136

SUBMITTER (NAME ONLY): Anindya Samanta

TITLE: Bilateral evolution of OCT biomarkers in dry AMD: long-term follow up study

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Samanta, Department of Ophthalmology & Visual Sciences, Texas Tech University Health Sciences Center, Lubbock, Texas, UNITED STATES|S. Arora, Medical Retina and Vitreoretinal Surgery, Consultant, Division of Ophthalmology, Department of Surgery, Princess Margaret Hospital, Nassau, BAHAMAS|M. Jhingan, S. Singh, Jacobs Retina Center, University of California San Diego Health Sciences, La Jolla, California, UNITED STATES|S. Amarasekera, J. Chhablani, UPMC Eye Center, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|D. Tucci, C. Cagini, M. Lupidi, Department of Biomedical and Surgical Sciences, Section of Ophthalmology, Università degli Studi di Perugia Facoltà di Medicina e Chirurgia, Perugia, Umbria, ITALY|

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ABSTRACT BODY:

Purpose: Age related-macular degeneration (AMD) is a disease that often presents bilaterally, although there have been limited studies in long term progression of Spectral Domain Optical Coherence Tomography (SD-OCT) biomarkers comparing two eyes in the same patient. The aim of the study was to compare progressive OCT changes between two eyes among subjects with dry AMD over a period of 5.7 years.

Methods: We performed a retrospective imaging study on the volumetric SD-OCT of 33 patients (66 eyes) with bilateral dry AMD with a minimum follow-up of at-least 4 years. Yearly OCT scans were evaluated for emergence and progress of four late dry AMD characteristics: iRORA, cRORA, drusen ooze and drusen collapse. Statistical analysis was done using Microsoft Excel. Univariate analysis was done for the various characteristics at baseline.

Results: Patients with a mean age of 77.2 ± 10 years were followed up for a total of 68.7 ± 21.5 months. At baseline, iRORA, cRORA, drusen ooze was present in 12.1%, 15.2% and 21.2% of the patients, respectively. At the final follow up iRORA, cRORA, drusen ooze was present in 27.3%, 48.5% and 57.6% of the patients, respectively. Bilateral drusen ooze was present in 9.1% of the patients at baseline. 15.2% of the patients had bilateral drusen ooze at the final follow up with mean interval of 5.0 ± 1.4 years between the two eyes. Bilateral iRORA was present in none of the patients at baseline. 9.1% of the patients had bilateral iRORA at the final follow up with a mean interval of 4.7 ± 2.1 years between the two eyes. Bilateral cRORA was present in 9.1% of the patients at baseline. 18.2% of the patients had bilateral cRORA at the final follow up with mean interval of 1.7 ± 0.6 years between the two eyes. By the final follow-up 9/33 (27.2%) and 6/33 (18.1%) of the patients had evidence of drusen collapse in unilateral and bilateral eyes, respectively. For patients with observed drusen collapse bilaterally, the mean interval was 2.2 years.

Conclusions: Any single OCT biomarker such as cRORA, iRORA, drusen ooze and drusen collapse is seen bilaterally in a minority (less than 22%) of the patients with dry AMD at presentation. Even over a long-term follow-up, only 36.4% of the patients showed at-least one bilateral biomarker over a period of 5.7 years. In patients with bilateral OCT biomarkers, cRORA had the shortest mean interval in appearance between the two eyes.

CONTROL ID: 3536141

SUBMITTER (NAME ONLY): Nicole Delgado

TITLE: Exploring Determinants of Adherence to Ophthalmology Follow-Up for Diabetes

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.K. Delgado, S. D'Amico, B. Kim, C.J. Brady, Division of Ophthalmology, University of Vermont College of Medicine, Burlington, Vermont, UNITED STATES|

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ABSTRACT BODY:

Purpose: Regular ophthalmology follow-up is essential for patients with diabetic retinopathy (DR), the leading cause of vision loss in working-age people in the US. Research is needed to better understand factors influencing follow-up and to find ways to encourage appropriate attendance. We sought to delineate patient-perceived barriers to ophthalmic follow-up in our mostly rural population. We anticipated patients with poor follow-up would report more barriers, and financial barriers related to transportation, parking, and childcare would be prominent.

Methods: Semi-structured interviews were conducted with adult patients with diabetes mellitus seen at least once in our clinics for diabetic eye care. Participants were randomly selected from a previous retrospective study based on whether they had good (n=10) or poor (n=10) attendance at follow-up appointments. Questions explored factors that supported or prevented their attainment of the prescribed interval, the management and progression of their diabetes, and their knowledge about DR. Results between the two groups were compared with descriptive statistics.

Results: Both groups of patients reported similar barriers to attendance, and 85% of patients reported at least 1 barrier. The most stated barriers for both groups were financial cost, having someone accompany them, and parking. The poor follow-up group also reported taking time off work as a barrier. More patients in the good follow-up group reported regularly checking their blood sugar (90% vs. 70%) and following up with their primary care physician (100% vs. 90%). They also responded more accurately to 3 knowledge questions about DR (77% vs. 57% correct responses).

Conclusions: The interviews challenged the notion that our patients with poor follow-up faced more barriers than those with good follow-up. When patients with good follow-up were asked an open-ended question of what factors allowed them to make it to their appointments, 50% of them responded by describing barriers instead; demonstrating how these patients also overcame challenges. Patients expressed a wide variety of factors that affected their ability to attend appointments, so any specific incentive, such as a parking voucher, ride service, or scheduling assistance may not meet the needs of all patients. It may be more effective to offer a financial incentive to utilize tools of behavioral economics to encourage patients to attend follow-up visits.

CONTROL ID: 3536155

SUBMITTER (NAME ONLY): Muhammad Yasir

TITLE: Antiviral effect of multipurpose contact lens disinfecting solutions against coronavirus

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Yasir, A. Kumar, M. Willcox, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To evaluate the antiviral potential of five multipurpose disinfecting solutions against coronavirus (murine hepatitis virus a surrogate for SARS-CoV-2 human corona virus).

Methods: Murine hepatitis virus ATCC/VR261 stock was prepared prior to testing by growing in A9 ATCC/CCL 1.4 cells in Dulbecco's minimum essential medium (DMEM) containing 5% fetal bovine serum (FBS) and antibiotics (streptomycin sulphate and penicillin G). Test solutions (BioTrue, ReNu Advanced [Bausch and Lomb], ACUVUE RevitaLens [Johnson and Johnson Vision], cleadew [Ophtecs corp.] or AOSept Plus [Alcon]) were mixed with viruses at 10^4 plaque forming units (PFU)/mL as the final concentration and incubated at room temperature for the specified disinfection time as recommended by each manufacturer. Phosphate buffer saline (PBS) was used as a negative control. Surviving virus from each sample was then quantified by standard plaque forming unit assay and the reduction of PFU for each disinfectant was compared to the negative control.

Results: The three multipurpose disinfecting solutions BioTrue (containing PHMB and polyquaternium-1), ReNu Advanced (PHMB, polyquaternium-1 and alexidine) and ACUVUE RevitaLens (polyquaternium-1 and alexidine) did not kill the coronavirus at the manufacturers recommended disinfection time. After treatment, the virus's titer ($3.8 \pm 0.2 \log_{10}$ for BioTrue, $3.7 \pm 0.1 \log_{10}$ for ReNu and $3.7 \pm 0.2 \log_{10}$ for Revitalens) was similar to the negative control ($3.7 \pm 0.1 \log_{10}$). AOSept Plus (hydrogen peroxide) and cleadew (povidone iodine) reduced the numbers of coronaviruses to below the detection limit (i.e. killed $3.7 \pm 0.1 \log_{10}$ viruses compared to control).

Conclusions: This study shows that oxidative contact lens disinfecting solutions (i.e. those containing povidone-iodine or hydrogen peroxide) provide superior antiviral activity against a coronavirus surrogate of SARS-CoV-2.

CONTROL ID: 3536167

SUBMITTER (NAME ONLY): Samuel Law

TITLE: Intraocular pressure and smoking relationship in South Korea

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. Law, M.A. Oh, F. Yu, S.K. Law, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|M.A. Oh, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|F. Yu, Biostatistics, University of California Los Angeles Jonathan and Karin Fielding School of Public Health, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evidence exists that cigarette smoking may be associated with glaucoma; however, the relationship between intraocular pressure (IOP) and smoking is unclear. In this study, relationship between smoking status and IOP in civilian, non-institutionalized participants in the Korea National Health and Nutritional Examination Survey (KNHANES) was investigated.

Methods: Subjects from 2008-2011 KNHANES who were ≥ 40 years of age, who had visual fields and optic disc photographs, and had IOP measured were included. Diagnosis of glaucoma was based on the Rotterdam criteria. Subjects were divided into current smokers, past smokers, and never smoker categories. Mean IOP was compared between the three categories among those with glaucoma and without glaucoma. Multivariate linear regression modeling was used to assess the relationship between IOP and clinical and behavior characteristics.

Results: 14416 subjects in 2008-2011 KNHANES were included. 8510 subjects (59.0%) never smoked, 1733 (12.0%) were past smokers, and 4173 (29.0%) were current smokers.

A greater proportion of male Korean subjects were smokers (84.2% past smokers or current smokers) compared to female subjects (8.1%, $p < 0.0001$).

Past smokers were statistically significantly older than never smokers and current smokers (60.0 ± 11.3 , 57.6 ± 11.3 , 56.7 ± 11.5 years, respectively, $p < 0.0001$).

A greater proportion of current smokers (18.1%) had glaucoma compared to never smokers (11.6%) and past smokers (9.7%, $p < 0.00001$).

The mean IOP of all subjects was 14.0 ± 2.7 mmHg.

Never smokers had statistically significantly lower IOP (13.9 ± 2.7 mmHg) compared to past smokers (14.1 ± 2.7 mmHg, $p = 0.005$) and current smokers (14.0 ± 2.8 mmHg, $p = 0.031$, Tukey post hoc test), while there was no statistically significant difference between past smokers and current smokers ($p = 0.438$).

In multivariable linear regression analysis, IOP did not correlate with smoking status, but varied statistically significantly with age, gender, glaucoma, cataract, and diabetic retinopathy (DR).

Male, glaucoma, cataract and DR were associated with IOP increase of 0.058, 0.068, 0.045, and 0.025 mmHg, respectively ($p < 0.0001$ for male, glaucoma, and cataract, $p = 0.030$ for DR). IOP decreased by 0.087 mmHg per year of age ($p < 0.0001$).

Conclusions: Smoking was more prevalent among Korean males than females. IOP in Koreans was higher with diagnosis of glaucoma, cataract and DR, and lower in female and older subjects.

CONTROL ID: 3536178

SUBMITTER (NAME ONLY): Sai Bo Bo Tun

TITLE: Local dexamethasone treatment to maintain allogeneic islet grafts in the Anterior Chamber of the Eye (ACE)

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tun, P. Berggren, G. Tan, Y. Ali, V.A. Barathi, Singapore Eye Research Institute, Singapore, SINGAPORE|S. Tun, P. Berggren, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|G. Tan, V.A. Barathi, Duke-NUS Medical School, Singapore, SINGAPORE|Y. Ali, Lee Kong Chian School of Medicine, Nanyang Technological University, SINGAPORE|

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ABSTRACT BODY:

Purpose: Pancreatic islet transplantation into the anterior chamber of the eye (ACE) has been shown to improve the glycaemic control and metabolic parameters in both Type-1 and Type-2 diabetic non-human primates (NHPs). This novel transplantation site also allows the delivery of therapeutic agents, such as immunosuppressive drugs, locally to circumvent unwanted systemic side effects.

Methods: Local anti-inflammatory or immunosuppression treatment using micronized dexamethasone (DEX) implant was done intravitreally. Allogeneic transplantation of pancreatic islets was done into the ACEs of non-human primates (allogeneic grafts without immunosuppression, CTL, n=2 eyes; allogeneic grafts with local immunosuppression treatment, DEX, n=8 eyes). Survival of the transplanted islet grafts and DEX concentration in the ACE were assessed in parallel for 24 weeks.

Results: DEX was detected in the aqueous humour of the ACE with a peak at week 8 and started to taper off by week 15. Islet grafts with local DEX treatment showed significantly better survival than the non-treated CTL islets (median survival time- 12 weeks vs 3 weeks, log-rank test $p < 0.0001$). Islet grafts showed a good functional response to high glucose stimulation even though a high dose of DEX showed a transient suppression of islet graft function at week 8 to 12.

Conclusions: The ACE may turn out to be a novel and superior site for pancreatic islet transplantation to treat diabetes and local dexamethasone treatment is a potential therapeutic approach to maintain long-term function and survival of allogeneic islet grafts.

CONTROL ID: 3536196

SUBMITTER (NAME ONLY): Susana Chung

TITLE: Binocular properties of fixational eye movements as assessed using a high-resolution binocular scanning laser ophthalmoscope

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.T. Chung, R.W. Li, M.N. Agaoglu, P.K. Tiruveedhula, A.J. Roorda, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have established that fixational eye movements (FEMs), especially microsaccades and at least the vertical component of slow-drifts, are mostly conjugate in the two eyes. However, specifics of the properties of FEMs during binocular vs. monocular fixation are less well documented. The purpose of this study was to determine how the presence of visual input of a fixation target affects the properties of binocular fixation.

Methods: We used a custom-built, high-resolution two-channel confocal scanning laser ophthalmoscope (bino-TSLO) in this study. The bino-TSLO allows us to deliver visual targets and to record movies of the retina of the two eyes simultaneously and independently. When aligned properly, subjects perceived a single 6°x6° red imaging field. Five adults with normal binocular vision were instructed to fixate at the center of a 1° cross presented at the primary gaze position while we captured videos of the retina of both eyes for trials of 10s each. Three conditions, each with multiple trials, were tested in random order: the cross was presented in both eyes (“both”) or in only one of the two eyes (“left” or “right”). Eye positions were extracted from the videos using a brute-force cross-correlation algorithm at a sampling rate of 540 Hz. Characteristics of FEMs, including (1) fixation stability, (2) rate, amplitude and direction of microsaccades; and (3) direction and amplitude of drifts, were determined for each trial and for each eye.

Results: The two eyes demonstrated a high degree of conjugacy in terms of the occurrence, amplitude and direction of microsaccades, regardless of whether the fixation cross was presented in one or both eyes. Drift direction and amplitude were mostly similar between the two eyes only in the “both” condition; else, the eye that did not receive the cross demonstrated larger drift amplitudes with directions different from that of the fellow eye. Further, for the “left” or “right” conditions, fixation stability of the eye that received the cross was similar to that for the “both” condition; but fixation stability of the fellow eye worsened by ~1.6x.

Conclusions: Despite the high degree of conjugacy of the two eyes during fixation, the lack of visual input to one eye affects the characteristics of drifts and stability in that eye, emphasizing the importance of the presence of visual input in fine oculomotor control.

CONTROL ID: 3536217

SUBMITTER (NAME ONLY): Ojas Srivastava

TITLE: Anti-VEGF switch therapy from bevacizumab to aflibercept in radiation retinopathy secondary to uveal melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Srivastava, University of Alberta Faculty of Medicine & Dentistry, Edmonton, Alberta, CANADA|E. Weis, Ophthalmology, University of Alberta Faculty of Medicine & Dentistry, Edmonton, Alberta, CANADA|

Commercial Relationships Disclosure (Abstract): Ojas Srivastava: Commercial Relationship: Code N (No Commercial Relationship) | Ezekiel Weis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Radiation-induced injury to ocular structures is a common iatrogenic consequence of radiotherapy for uveal melanoma. Radiation retinopathy is a dose-dependent complication of the retina following exposure to ionizing radiation. To the best of our knowledge, this is the first series describing the outcomes of patients treated with monthly aflibercept for radiation maculopathy who have failed monthly bevacizumab. Failure is defined as incomplete resolution of fluid despite monthly injections for 6 months or complete resolution of fluid with monthly injections, but an inability to extend beyond a 1-month interval between treatment. Clinically significant improvement is defined as an improvement of 1 line of visual acuity on an Early Treatment Diabetic Retinopathy Study chart or reduction in sub-retinal fluid of 100 microns. It is hypothesized that a portion of patients who failed bevacizumab will respond with a clinically significant difference with aflibercept.

Methods: A prospective case-series of patients with clinically significant radiation maculopathy were enrolled. The currently utilized clinical treatment algorithm of primary bevacizumab followed by aflibercept for failed cases was employed. Standardized testing, as part of the Alberta Ocular Brachytherapy program, was performed on all patients at two sites in Alberta, Canada. Visual and retinal response to therapy was assessed with regression analyses.

Results: Thirty patients, 17 female and 13 male, with a mean age of 57 years (± 15) underwent the switch from monthly intravitreal bevacizumab treatment to intravitreal aflibercept. The primary endpoints were central foveal thickness (CFT) and visual acuity (VA) at one month, three months, and six months following the switch to aflibercept. Regression analysis showed statistically significant differences between bevacizumab and treatment by aflibercept at one month ($P=0.003$, $P=0.02$), three months ($P=0.004$, $P=0.004$), and six months ($P=0.003$, $P=0.013$) in both CFT and BCVA, respectively. Fourteen patients showed a clinically significant improvement in CFT and seven patients showed a clinically significant VA improvement following six months of aflibercept.

Conclusions: This pilot study suggests that a portion of patients who have failed monthly bevacizumab may respond to aflibercept. A larger series would be beneficial in quantifying this response.

CONTROL ID: 3536219

SUBMITTER (NAME ONLY): Marko Oydanich

TITLE: Assessing the Risk of Vitreous Hemorrhage Following Mechanical Vitrectomy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A broad range of complications may present following mechanical vitrectomy (MV), including vitreous hemorrhage (VH), cataract formation, and endophthalmitis. Using a large sample population database, we investigated the impact of MV along with other clinical and non-clinical factors on the risk of developing VH.

Methods: Cases of MV were obtained from the National Inpatient Sample (NIS) database between 2002 and 2013 using ICD-9 codes. Associated morbidities and procedures were assessed in cases labelled with a principal procedure of MV and a non-primary diagnosis of VH. Perioperative complications occurring during the same operative admission were abstracted using secondary ICD-9 diagnosis codes. Univariate and multivariate logistic regression analyses were carried out in MV cases to determine risk factors for the development of VH. The data was weighted using the NIS-provided discharge-level weights in order to generate nationally representative estimates. The Bonferroni correction method was applied to decrease risk of type II errors.

Results: There were 3,927 MV cases identified in the dataset. These were divided into vitreous hemorrhage (n=610, median age = 55, 52% male) and non-vitreous hemorrhage (n=3,317, median age = 57, 51% male) cohorts. Factors associated with increased risk of vitreous hemorrhage included diabetes with chronic complications (OR=2.02), renal failure (OR=1.60), congestive heart failure (OR=1.56), and obesity (OR=1.58). Demographic factors were analyzed and showed that, relative to white cases, there was an increased risk of VH in Black (OR=1.52), Hispanic (OR=1.43), and Asian (OR=1.80) cases. Confidence intervals can be seen in Figure 1.

Conclusions: Retrospective analysis of a large patient population showed that the risk of VH following MV is increased in cases with complicated diabetes, renal failure, congestive heart failure, and obesity. Black, Hispanic, and Asian cases were also independently associated with an increased risk of VH. Limitations of this study include its inability to demonstrate temporal relationships due to its retrospective nature, a database that records cases rather than individual patients, and the limited cases of MV that occur in inpatient settings.

CONTROL ID: 3536233

SUBMITTER (NAME ONLY): William Gange

TITLE: Perifoveal Chorioretinal Atrophy Following Subretinal Injection of Voretigene Neparvovec-rzyl for RPE65-mediated Leber Congenital Amaurosis

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report a phenomenon observed in a series of patients who underwent subretinal injection of voretigene neparvovec-rzyl (VN) for RPE65-mediated Leber congenital amaurosis.

Methods: Multi-center retrospective chart review of patients who underwent subretinal VN injection at four participating institutions. Patients were identified as having perifoveal chorioretinal atrophy if: i) the areas of atrophy were not directly related to the touch-down site of the subretinal cannula; and ii) the areas of atrophy enlarged over time. Demographic data, visual acuity, refractive error, fundus photos, optical coherence tomography, visual fields, and full-field stimulus threshold (FST) were analyzed.

Results: 18 eyes of 10 patients who underwent subretinal injection of VN developed perifoveal chorioretinal atrophy. 8/10 patients (80%) had bilateral atrophy. Mean age was 11.6 years (range: 5-19), and 6 patients (60%) were male. Baseline mean logMAR visual acuity and FST were 0.82 (standard deviation (SD): 0.51) and -1.3 log cd.s/m² (SD: 0.44), respectively. The mean spherical equivalent was -5.7 diopters (range: -11.50 to +1.75). Atrophy was identifiable at an average of 4.7 months (SD: 4.3) following surgery, and progressively enlarged in all cases up to a mean follow-up period of 11.3 months (range: 4-18). The atrophy developed within and outside the area of the subretinal bleb in 10 (55.5%) eyes, exclusively within the area of the bleb in 7 (38.9%) eyes, and exclusively outside the bleb in 1 (5.5%) eye. There was no significant change in visual acuity (p=0.45). There was a consistent improvement in FST with a mean improvement of -3.21 log cd.s/m² (p<0.0001). Additionally, all 13 eyes with reliable pre- and post-operative visual fields demonstrated improvement (expansion or gain of isopters) following surgery, but 3 (23.1%) eyes demonstrated paracentral scotomas related to the atrophy.

Conclusions: A subset of patients undergoing subretinal VN injection developed progressive perifoveal chorioretinal atrophy following surgery. Further study is necessary to determine what ocular, surgical delivery, and vector-related factors predispose to this complication.

CONTROL ID: 3536242

SUBMITTER (NAME ONLY): Stephanie Jinno

TITLE: Clinical characteristics and treatment for dupilumab-related ocular complications in atopic dermatitis patients

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ocular adverse events have been reported in association with dupilumab, a monoclonal antibody therapy to treat allergic diseases including atopic dermatitis (AD). We sought to describe clinical findings and treatment for dupilumab-related ocular complications.

Methods: Retrospective case series of 20 dupilumab-treated AD patients seen for a new ocular complaint in an academic ophthalmology practice. Primary outcomes were specific ocular exam findings (conjunctival injection, eyelid dermatitis, corneal fluorescein staining, blepharitis, or meibomian gland dysfunction (MGD)) and treatments prescribed at the initial visit and follow-up visits.

Results: A total of 20 dupilumab-treated AD patients were included. The mean age was 47 years (range 18-73), with over half being women (55%) and the majority Caucasian (70%). Symptom onset occurred at a mean of 101 days (SD=109, 95% CI: 49.91 to 151.79) from the first dupilumab dose. The most common ocular findings were conjunctival injection (75%) and corneal staining (60%). Blepharitis was seen in about a third (30%) of patients and 25% had MGD. After the initial visit, 10% were observed without treatment, while 15% patients were treated with artificial tears (AT) alone. Other treatments included antihistamine drops (20%) and steroid drops alone (15%). In 40% of patients, a combination of steroids and various other topical eye drops were prescribed. Out of the 20 patients, 17 were seen in follow-up. Steroid drops were required at follow-up in 3 out of 4 patients initially treated with antihistamines alone and in two-thirds of patients initially treated with AT only. Mean follow-up period was 89 days (range 5-369). Dupilumab was discontinued in 7 out of 20 patients; of those who discontinued, 3 were able to restart it later.

Conclusions: Conjunctival injection was the most frequent dupilumab-related ocular complication observed followed by corneal staining. The majority of patients initially treated with antihistamines or AT alone subsequently required steroid drops to control symptoms. Some patients who discontinued dupilumab were able to restart the medication after achieving adequate control of their ocular symptoms. Future larger studies are needed to confirm the incidence of dupilumab-related ocular complications, identify risk factors, and compare treatment outcomes.

CONTROL ID: 3536244

SUBMITTER (NAME ONLY): Rachel Israilevich

TITLE: Good Visual Acuity Outcomes Following Retinectomy During Repair of Retinal Detachment with Proliferative Vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Israilevich, V. Swaminathan, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|M. Starr, M. Salabati, R. Mahmoudzadeh, M. Ammar, L. Patel, J. Hsu, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate pre- and intra-operative metrics associated with good visual acuity (VA) following retinal detachment (RD) repair for proliferative vitreoretinopathy (PVR) that included relaxing retinectomy at time of surgery.

Methods: This was a single-institution, retrospective study evaluating all patients (pts) undergoing retinectomy during repair of RD with PVR from 1/1/2015-12/31/2019 with a final VA of 20/70 or better.

Results: Of 3,789 pts undergoing RD surgery during the study period, only 57 underwent retinectomy at time of RD surgery and had a final VA of 20/70 or better. 16 pts were female (28%) and the mean age was 61.8 ± 10.5 years. The mean time from diagnosis to initial surgery was 2.1 ± 1.1 days. The mean initial RD size was 160 ± 60 degrees. 22 eyes (39%) were macula on at time of initial diagnosis. Only 7 eyes' (12%) macula never detached during the study period. The mean pre- and post-operative logMAR VA was 0.93 ± 0.85 and 0.33 ± 0.16 respectively. The mean number of surgeries was 2.4 ± 0.9 . The average retinectomy size was 151 ± 12.1 degrees. 14 eyes (25%) had a scleral buckle (SB) placed at initial surgery (Table 1). There was no difference in mean number of surgeries in eyes with a SB placed at initial surgery compared to those that did not (2.1 ± 0.6 vs 2.4 ± 1.0 , $p = 0.28$), or in mean final VA (0.28 ± 0.16 vs 0.34 ± 0.17 , $p = 0.20$). 16 eyes (28%) had primary PVR, of which 7 eyes (44%) had primary retinectomy (Table 2). Significantly fewer surgeries were required in these 7 eyes compared to the 9 eyes not undergoing primary retinectomy for initial RD with baseline PVR (1 ± 0.0 vs 2.3 ± 0.7 , $p = 0.0002$), but no difference in final VA was seen (0.33 ± 0.16 vs 0.39 ± 0.11 , $p = 0.52$). The mean time from recurrent RD diagnosis to surgery was 2.5 ± 1.2 days, with no difference in time to surgery for recurrent RDs in eyes with macula on versus off RDs (3.1 ± 2.4 vs 2.3 ± 1.4 days, $p=0.12$, Table 2). 2 eyes (3.5%) had silicone oil tamponade at the final visit.

Conclusions: Eyes undergoing primary or secondary retinectomy during repair of RD with PVR can still achieve good VA. Macula status and time to surgery may be important factors in determining visual outcomes.

CONTROL ID: 3536254

SUBMITTER (NAME ONLY): Ying Zhu

TITLE: Single cell RNA sequencing of retinal ganglion cells with enhanced perinuclear cAMP signaling after optic nerve crush injury

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhu, B. Tanasa, M. Nahmou, J.L. Goldberg, M. Kapiloff, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Enhanced cyclic-AMP (cAMP) signaling promotes neuronal survival after injury. cAMP signaling is highly compartmentalized in cells, and distinct compartments regulate different cellular processes. We recently showed that elevation of cAMP in a perinuclear compartment organized by the scaffold protein muscle A-kinase anchoring protein α (mAKAP α) is sufficient to protect retinal ganglion cells (RGCs) in the mouse optic nerve crush model. However, the underlying mechanisms remain unclear. In this study, we aim to identify neuroprotective gene expression regulated by perinuclear cAMP in RGCs.

Methods: We intravitreally injected 4-week-old C57BL/6J mice with the adeno-associated virus gene therapy vector AAV2.4D3(E)-mCherry to express in RGCs the type 4D3 phosphodiesterase anchoring disruptor peptide 4D3(E)-mCherry, which displaces PDE4D3 from mAKAP α signalosomes in neurons and elevates cAMP in that compartment. Control mice were injected with AAV2.mCherry. Two weeks later the mice were subjected to right-sided optic nerve crush. RGCs pooled from 8 eyes for each cohort were isolated by immunopanning with Thy-1 antibody one day after crush. Cell suspensions were submitted to the Stanford Genome Sequencing Service Center (GSSC) for 10X Chromium Single Cell 3' library preparation and HiSeq 4000 sequencing. scRNA-seq analysis was carried out with Seurat using R.

Results: 3800-6000 cells were sequenced for each condition, among which 15%-25% expressed RBPMS and were identified as RGCs. About half of the RGCs in each group expressed the mCherry reporter gene. Analysis of differentially expressed genes showed that expression of the 4D3-mCherry anchoring disruptor reversed many of the changes in gene expression induced by crush injury ($p=1e-16$). In particular, Npy, Mmp12, Ucn and Timp2 were differentially regulated by elevation of cAMP in the perinuclear compartment.

Conclusions: Our study shows that elevation of perinuclear cAMP can reverse changes in gene expression following acute optic nerve crush injury, providing an explanation for the pro-survival effects of PDE4D3 anchoring disruption. In addition, our results provide candidate therapeutic targets for subsequent testing. In the future, we will apply this approach to derive further insight into the diversity of gene expression programs relevant to RGC neuroprotection and axon regeneration therapies.

CONTROL ID: 3536257

SUBMITTER (NAME ONLY): Minn Oh

TITLE: Cigarette smoking and glaucoma in the United States and in South Korea

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Oh, S.M. Law, F. Yu, S.K. Law, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|M.A. Oh, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|F. Yu, University of California Los Angeles Department of Biostatistics, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The relationship between glaucoma, a leading cause of irreversible blindness globally, and smoking, a major modifiable health hazard, is uncertain. In this cross-sectional study, association between cigarette smoking and glaucoma in the civilian, non-institutional participants of the U.S. National Health and Nutritional Examination Survey (NHANES) and the Korea NHANES (KNHANES) was investigated.

Methods: U.S. participants from 2005-2008 NHANES and Korean participants from 2008-2011 KNHANES who were ≥ 40 years of age and had visual fields and optic disc photographs were included. Participants with non-glaucomatous reason for either abnormal cup/disc ratio or visual fields were excluded. Glaucoma diagnosis was based on the Rotterdam criteria. Logistic regression modeling was performed to assess the association between glaucoma and smoking history, while controlling for age, sex, household income, alcohol consumption, refractive errors, body mass index, diabetes, and hypertension.

Results: Glaucoma prevalence in the US sample was 5.5% (212/3864 subjects) and 7.8% in the Korean sample (1143/14608 subjects). In both populations, subjects with glaucoma compared to those without were older, likely to be male, and to have diabetes and hypertension. Korean subjects with glaucoma were also more likely to have less education, lower income, and greater alcohol consumption.

In the U.S., 54.7% glaucoma subjects were smokers while 50.7% non-glaucoma subjects were smokers ($p=0.25$). In Korea, 51.4% glaucoma subjects were smokers while 45.4% non-glaucoma subjects were smokers ($p<0.001$). Among smokers, 34.2% Korean glaucoma subjects were current smokers while 32.2% non-glaucoma Korean subjects were current smokers ($p<0.001$). In the U.S., 30.2% glaucoma subjects were current smokers and 42.1% non-glaucoma subjects were current smokers ($p=0.01$).

The effect estimations of both non-smoker/smoker and current/ex-smoker comparisons were similar in adjusted models but neither had statistically significant differences.

Among smokers, greater pack/day of smoking history was associated with statistically significantly higher odds of glaucoma in the U.S. population ($OR=1.70$, $95\%CI=1.08-2.67$, $p=0.002$), but not among Koreans.

Conclusions: Smoking habit and exposure differ across populations and cultures. Cigarette smoking may be associated with higher odds of glaucoma in both the U.S. and in South Korea.

CONTROL ID: 3536265

SUBMITTER (NAME ONLY): Kapil Mishra

TITLE: The Impact of the COVID-19 Pandemic on Aflibercept and Ranibizumab Anti-VEGF Injections

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mishra, A. Al Moujahed, S. Sanislo, D.V. Do, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 Pandemic resulted in a substantial decrease in outpatient ophthalmology clinic visits due to stay-at-home orders. Retinal vascular diseases and wet age-related macular degeneration require adherence to treatment regimens with anti-vascular endothelial growth factor (anti-VEGF) injections. The purpose of this study was to assess how the COVID-19 pandemic affected the number of injections compared to pre-pandemic values.

Methods: This retrospective, observational clinical study assessed all anti-VEGF injections of aflibercept and ranibizumab for both 2019 (Jan-Dec) and 2020 (Jan-Nov) at an academic center. The total number of injections for each year was compared, as well as the number of injections for each month in 2020 compared to the average number of monthly injections in 2019. Both 1-sample and 2-sample t-tests were conducted, and a p-value less than 0.05 was considered significant.

Results: The total number of aflibercept and ranibizumab injections in 2019 (Jan-Nov) were 4989 and 522 respectively, compared to 4855 and 515 in 2020 (Jan-Nov). No significant difference in injections was noted between 2019 and 2020 for either aflibercept ($p=0.31$) or ranibizumab ($p=0.80$). When analyzing each month in 2020 compared to the average number of aflibercept injections per month in 2019, there were significantly fewer aflibercept injections administered in February ($p<0.01$), August ($p=0.03$), and November ($p<0.01$), but significantly higher injections administered in July ($p<0.01$) and October ($p<0.01$). For ranibizumab, significantly fewer injections were administered in March ($p=0.02$), April ($p=0.02$), and May ($p<0.01$), but a higher number of injections were administered in September ($p<0.01$) and November ($p<0.01$).

Conclusions: Despite stay-at-home orders, there was no significant decrease in the overall number of aflibercept or ranibizumab injections during the COVID pandemic compared to the prior year. Although further information is needed to determine if these injections represent both new and return patients, these data suggest that in this specific population, patients still returned to their retina specialist for care despite the ongoing pandemic.

CONTROL ID: 3536266

SUBMITTER (NAME ONLY): Yadi Chen

TITLE: Blocking the lens microcirculation system has differential effects on the gradient of refractive index (GRIN) in the bovine lens

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate how inhibition of the lens microcirculation system differentially affects water transport, water content, lens geometry, GRIN, and power of the bovine lens.

Methods: Bovine lenses were incubated in either artificial aqueous humour (AAH), high extracellular K^+ (AAH-High K^+), or ouabain (AAH+ouabain) for 4 hours. A microelectrode/pico-injector based pressure measurement system was utilised to measure the intracellular hydrostatic pressure gradient that drives water efflux. MRI was used to measure free and total water content. A custom-built Laser Ray Tracing (LRT) system that scanned lenses with 151 parallel rays delivered at 4 different angles was used to extract changes in lens geometry, gradient refractive index (GRIN) and power over time. Lens geometry and GRIN were inputted into ZEMAX optical modelling software to assess changes in overall vision quality.

Results: Like smaller rodent lenses, the larger bovine lens exhibited an intracellular hydrostatic pressure gradient that varied from approximately 0 mmHg at the lens surface to 326 mmHg in the core. Inhibiting the microcirculation system by depolarization of the lens membrane potential with AAH-High K^+ , reduced the lens central hydrostatic pressure by 16%, increased the water content across the whole lens, caused a slight rounding of the lens geometry and a decrease in GRIN, which manifested as a slight increase in power in the lens core over time. Inhibiting the microcirculation by blockade of the Na^+/K^+ -ATPase with AAH+ouabain, reduced the lens central hydrostatic pressure by 24%, increased the water content specifically in the lens core, caused a substantial rounding up of the lens geometry, but increased the central GRIN. Taken together these changes induced a significant increase in lens power and resulted in a marked myopic shift in overall vision quality.

Conclusions: While inhibition of the microcirculation system by depolarizing the lens, or blocking the Na^+/K^+ -ATPase both decreased lens pressure, increased lens water content and increased power, ouabain counter-intuitively increased central GRIN. This suggests that blockade of Na^+/K^+ -ATPase has altered the refractive index increment (dn/dc) of crystallins in the lens core, presumably by changing the ionic environment in this lens region.

CONTROL ID: 3536269

SUBMITTER (NAME ONLY): Merry Ruan

TITLE: Retina Vascular Structures Near the Optic Disc and in the Macula in Primary Angle Closure Suspects

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To study the retinal peri-papillary and macular vascular structures in eyes of primary angle closure suspects (PACS)

Methods: Control and PACS subjects were recruited from a community screening. Only one eye per subject was used for analysis. All participants underwent a questionnaire survey, physical and ophthalmic examinations, ocular biometry measurements, and optical coherence tomography angiography (OCTA). We compared basic demographics and vessel structure parameters between control and PACS eyes. Univariate and multivariate linear regression analysis were performed to investigate factors associated with vascular parameters in both groups.

Results: Data from 254 subjects including 155 PACS and 99 controls were analyzed. In the peri-papillary region, PACS eyes showed similar retina nerve fiber layer (RNFL) and vessel densities (VDs) including and excluding large vessels compared to control eyes. Compared to control eyes, all macular OCTA parameters showed significant differences in PACS eyes, including decreased superficial VD (mean=17.23 vs 13.80, $p=0.006$) and deep VD (mean=31.33 vs 27.92, $p=0.004$), larger fovea avascular zone (FAZ) area (mean=0.35 vs 0.39, $p=0.006$) and longer FAZ perimeter (mean=2.29 vs 2.45, $p=0.004$). Gender ($p=0.039$), age ($p<0.001$), and Garway Heath (GH) superior hemisphere RNFL ($p<0.001$) were risk factors influencing optic disc VD excluding large vessels (Table 1). Axial length (AL) was the major factor affecting macula superficial and deep vessel densities ($p=0.004$ and 0.001 respectively), while PACS was independent factors associated with larger FAZ perimeter ($p=0.046$) (Table 2).

Conclusions: While PACS and control eyes have comparable RNFL and vascular structure around the optic nerve head, macular vascular structures are significantly different, which could precede clinical functional and structural abnormalities.

CONTROL ID: 3536271

SUBMITTER (NAME ONLY): Karima Khimani

TITLE: Barriers to low vision care rehabilitation services for visually impaired patients in a multidisciplinary ophthalmology outpatient practice

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Khimani, M. Schmitz-Brown, P. Gupta, Ophthalmology, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|C. Redmon, L. Malaya, A. Zaidi, The University of Texas Medical Branch at Galveston School of Medicine, Galveston, Texas, UNITED STATES|H. Tzeng, School of Nursing, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low vision Rehabilitation (LVR) has a significant benefit in improving the quality of life of visually impaired patients. However, such services are highly underutilized, depriving patients of essential care. This study investigates the barriers to LVR services in a hospital-based setting for patients with impaired vision.

Methods: A retrospective chart review of low vision patients seen at the University of Texas Medical Branch from 2010-2020 identified 487 subjects that were eligible for low vision referral. Low vision was defined as having a best corrected visual acuity of 20/70 or worse in the better eye, or a visual field of less than 20 degrees. The number of patients referred to LVR services were identified from the EPIC EMR database and were interviewed over the phone regarding their referral experience to the LVR services. Another questionnaire was sent to 9 practicing ophthalmologists to capture their referral patterns. Responses were analyzed and tabulated in percentages.

Results: Patients with low vision referrals (n=48) were primarily Caucasians (60%), retired (60%), and females (60.4%), with a mean age of 70.7 years. Only 32 patients utilized LVR services, of which 11 agreed to take the questionnaire. About half of the patients (45.5%) did not know if they had been referred to LVR. Qualitative analysis revealed several barriers to accessing LVR services including: poor physical health (81.8%), denial of need for low vision aid (72.7%), lack of transportation (36.3%), and lack of referrals (33.3%). 88.9% of vision care providers reported referring eligible patients to LVR services in their practices. Common factors for not referring low vision patients included: patient's overall health (66%), older age (33.3%), lack of social support (33.3%), poor cognitive function (33.3%), and less likelihood of following up with LVR services (33.3%). However, all the providers reported familiarity with the available LVR services at the practicing clinic.

Conclusions: This study identified several addressable barriers that can be eliminated to provide LVR services to patients with low vision. Changing the current provider referral pattern and increasing patient awareness of available LVR resources may tremendously improve the quality of life of low vision patients.

CONTROL ID: 3536273

SUBMITTER (NAME ONLY): Meg LaRocca

TITLE: Long-pulsed ultrasound enhances the cytotoxic effect of doxorubicin on cultured human retinal pigment epithelium cells

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. LaRocca, S. Mohammadi, C. Kenney, K. Lin, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze the effects of long-pulsed, 1 MHz ultrasonic application on human retinal pigment epithelium (ARPE-19) cell viability at various doxorubicin concentrations.

Methods: In this in vitro study, ARPE-19 cells were plated in 96-well plates and treated with 360 μ L of solution containing 0.01, 0.1, 1, 10, or 100 μ g/mL of doxorubicin. 5.5 mg of doxorubicin (Fisher Scientific) was first dissolved in 550 μ L of DMSO to form a stock solution. The stock solution was then transferred to 54.45 mL of media and serially diluted to create the various titrated concentrations. Cell plates were sealed with MicroAmpTM Optical Adhesive Film, inverted, and placed in a water bath at room temperature. Cell plates were then treated with 1 MHz of ultrasound (US) at a power of 4.93 W/cm² and pulse repetition frequency (PRF) of 30 Hz for five minutes (Olympus EPOCH 650 Ultrasound). Media were removed from the wells and replaced with 100 μ L of media with the corresponding doxorubicin concentration. The control mimicked all parameters including the 1% DMSO but cells did not receive US application. As an additional control group, US was applied to cells without doxorubicin to analyze the effects of US on cell viability. MTT assays were performed at both 24 and 48 hours to quantify cellular metabolism, which had been used in literature as a marker for cell viability.

Results: At 24 hours after US was applied, there was a significant decrease in viability in cells treated with doxorubicin 0.1 μ g/mL to 100 μ g/mL (Figure 1). The same trend was observed at 48 hours (Figure 2). At both 24 and 48 hours, the untreated group without doxorubicin showed that ultrasound alone did not have a significant effect on cell viability (rightmost two columns in Figures 1 and 2).

Conclusions: US has played a pivotal diagnostic role in ophthalmology, but its therapeutic potential has been largely unexplored. This study demonstrated that long-pulsed US enhanced the cytotoxic effect of doxorubicin at physiologically relevant concentrations. This observation suggests a potential adjunctive role of ultrasound in treating tumors. Further studies using other cell types are underway to further explore the therapeutic role of ultrasound.

CONTROL ID: 3536276

SUBMITTER (NAME ONLY): Christine Kay

TITLE: Qualitative interviews with patients and caregivers regarding visual function impairments and impacts on vision-dependent activities of daily living and health-related quality of life in RPE65-related Retinitis Pigmentosa and Leber Congenital Amaurosis

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Inherited retinal degenerative disorders (IRD) such as Retinitis Pigmentosa (RP) and Leber Congenital Amaurosis (LCA) can be caused by mutations in the RPE65 gene. These mutations cause visual function impairments which have significant impacts on patients' vision-dependent activities of daily living (ADL) and broader health-related quality of life (HRQoL). There is limited evidence on the patient experience of RP more broadly and no known genotype-specific experiences. This study aimed to explore the experience of RPE65-related RP/LCA from patient and caregiver perspectives.

Methods: Semi-structured qualitative concept elicitation interviews were conducted with 11 patients (7 adults, 1 adolescent, 3 children aged 6-11 years) and 5 caregivers of children aged 3-11 years in the US, Germany and France. Patients had a clinical and genetic diagnosis of RPE65-related RP/LCA. Thematic analysis of verbatim interview transcripts was performed.

Results: Night blindness, reduced peripheral vision and problems with color vision were the most frequently reported visual function symptoms of RPE65-related RP/LCA. Proximal vision-dependent impacts included limitations to mobility and ADLs. White cane and low vision assistive devices were visual aids used by adults, adolescents and children. Participants reported impacts on HRQoL domains including emotional well-being, social, financial, and work/school functioning. Severity of limitations varied based on lighting conditions and familiarity of environment. Overall, similar concepts were reported across all participant groups.

Conclusions: These findings provide in-depth insight into the visual function symptoms and impacts on vision-dependent ADLs and broader HRQoL associated with RPE65-related RP/LCA. Findings are largely consistent with evidence generated thus far in other RP genotypes, and suggest that the visual function symptoms and impacts relevant to measure in clinical studies are consistent across RP/LCA genotypes. Interview findings contributed to the

development of patient- and observer-reported outcome measures specific to RP (including RPE65-related RP/LCA) designed for use in clinical trials and to track disease severity in clinical practice.

CONTROL ID: 3536281

SUBMITTER (NAME ONLY): Tyler Dowd-Schoeman

TITLE: Characterizing Intergroup Variation of Fundus Autofluorescence between Multiple Subtypes of Retinitis Pigmentosa

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Dowd-Schoeman, H. Ameri, USC Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There are currently over 90 genes associated with the development of retinitis pigmentosa (RP), an inherited retinal disorder affecting approximately 1 in 3000-5000 people worldwide. Previous research has demonstrated variability in disease severity and rates of disease progression between separate subtypes of RP, but research concerning possible imaging biomarkers that can differentiate between distinct genotypes of RP is limited. Our aim was to use fundus autofluorescence (FAF) imaging in order to examine whether patterns of autofluorescence (AF) differed in a heterogenous group of RP patients.

Methods: We used the NIH EyeGene database to compile FAF images of 31 patients with RP that met our exclusionary criteria. These patients had pathogenic mutations spanning 11 RP-associated genes, including HK1, IMPDH1, KLHL7, NR2E3, PRPF31, RP1, RP2, USH2A, RPGR, RHO, and PRPH2. The FAF images were reviewed for patterns of autofluorescence and qualitative observations were recorded.

Results: Eight patterns of fundus autofluorescence were identified in the RP patients included in the study. Four of these patterns were found within the macula, including a bull's eye pattern of AF, central foveal hyper AF, a perifoveal hyper AF ring, and a macular hyper AF ring. The remaining four patterns were extramacular and included a mid-peripheral hyper AF ring, extramacular spots of hyper AF, patches of hypo AF and diffuse hypo AF in the periphery. A double concentric hyper AF ring was present in 4 of the 11 RP-subtypes studied (RHO, RPGR, USH2A, NR2E3). To our knowledge this is the first report of a double concentric ring of hyper AF in RPGR-linked RP

Conclusions: Of the genes studied, there were no highly-penetrant patterns that were unique to a single subtype of RP, suggesting there may be significant phenotypic overlapping between RP subtypes on FAF imaging. The double concentric hyper AF ring is less specific than previously thought.

CONTROL ID: 3536294

SUBMITTER (NAME ONLY): Abdulrahman Alsaedi

TITLE: The effect of diabetic macular edema treatment on diabetic retinopathy progression: Real-world data from 27 UK hospitals

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Treatment of diabetic macular edema (DME) with anti-vascular endothelial growth factor (Anti-VEGF) injections can improve the severity of diabetic retinopathy (DR). However, little is known about the effect and durability of these agents on DR grading outside of clinical trials. This study aims to explore the development of proliferative DR (PDR) during and after treatment of DME with anti-VEGF injections from a large multi-centre database.

Methods: Data from 27 UK centres using the same electronic medical record system were remotely extracted. The analysis was restricted to eyes that received anti-VEGF agents for DME between February 2013 and December 2018. The primary outcome was the time from first DME treatment (DR grade prior to first treatment) until progression to PDR. Time-to-event analysis was done to demonstrate the rate of progression to PDR stratified by baseline DR grade.

Results: A total of 4 922 patients (58.2% male) were included. Mean age (standard deviation [SD]) was 66.41 (11.90) years and mean(SD) follow-up was 13.07 (15.29) months. On average, each patient received 6.29 (SD 6.3) anti-VEGF injections during this period. More severe DR grades required a higher number of injections; 5.81 injections for grade 1 (Mild non-proliferative DR[NPDR]), 6.56 and 6.84 injections for grade 2 (moderate NPDR) and grade 3 (severe NPDR), respectively. Kaplan-Meier survival curves showed that progression to PDR was strongly influenced by the baseline DR grade (Fig. 1). Controlling for the baseline DR grade, a higher number of injections (>6 compared to 6 injections or less) didn't confer a lower risk of PDR development.

Conclusions: This is the largest cohort of DME patients who received anti-VEGF injections and were evaluated for PDR development. Baseline DR grade is an important influential factor for PDR development during DME treatment. Moreover, DR improvement in clinical trials may not be reproduced in routine care settings where patients receive fewer treatments and could have less rigorous diabetes mellitus control. This will help inform clinicians about the importance of carefully following these patients and adjusting their follow-up intervals accordingly.

CONTROL ID: 3536295

SUBMITTER (NAME ONLY): Michaella Goldstein

TITLE: Fully Integrated Home OCT System – A Longitudinal Pilot StudyFully Integrated Home OCT System – A Longitudinal Pilot Study

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Goldstein, D. Goldberg, D. Zur, A. Loewenstein, T.D. Keenan, Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|D. Goldberg, D. Zur, S. Shulman, Assuta Medical Center, Tel Aviv, Tel Aviv, ISRAEL|A. Loewenstein, Medicine, Tel-Aviv University George S Wise Faculty of Life Sciences, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To demonstrate a fully integrated Home OCT System used by subjects with neovascular age-related macular degeneration and to propose novel reporting parameters of self-imaging performance and retinal fluid volume dynamics.

Methods: Pilot study of 8 eyes from 4 subjects with mean (SD) age of 74 (4) years (mean baseline VA 20/50). Subjects self-imaged at home daily for 1 month. Automatic secure data transmission to the Cloud was followed by volume scan reconstruction and deep learning-based analysis (Notal OCT Analyzer; NOA). Outcomes included subjects' ability to self-image daily, comparison of fluid status with human expert grading, and temporal dynamics of intraretinal (IRF) and subretinal fluid (SRF) volumes

Results: During 232 cumulative study eye-days, the subjects self-imaged 212 times (91%). The mean (SD) self-image acquisition time was 41 (15) seconds. In 100 of the 212 (47%) scans, retinal fluid was identified by the NOA (46% IRF, 46% SRF, 8% both). In 197 of the 212 (93%) scans, there was agreement of fluid status between NOA and human grading. In 5 eyes with a change in fluid status, the mean (maximum) interval between human grading and NOA identifying the change was 1.5 (3) days. In 4 eyes, the change was from fluid absence to presence, and the mean (maximum) fluid volume at detection of recurrence was 1.6 (3) nL. The temporal fluid dynamics over 1 month will be presented, including: identification of fluid status change, interval of fluid increase or decrease in relation to treatment, maximum fluid volume, fluid volume cumulated over time, and spatial distribution of fluid thickness over time.

Conclusions: To the best of our knowledge, this represents the first longitudinal pilot study of a home OCT system. It fulfils the relevant requirements: self-imaging with a device designed for low cost at large quantities, automatic data transmission, volume scan reconstruction, AI-based image analysis, and fluid volume tracking over time. The biomarker of fluid volume, and its related parameters, may present useful information in the management of retinal diseases.

CONTROL ID: 3536299

SUBMITTER (NAME ONLY): Jan Terheyden

TITLE: Psychometric properties of the Vision Impairment in Low Luminance (VILL) questionnaire in age-related macular degeneration in the MACUSTAR study

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Patient-reported difficulties caused by the characteristic functional impact of AMD, in particular in its early and intermediate stages, are only captured in selected patient-reported outcomes (PROs), none of which currently meet the FDA criteria for PRO development. The Vision Impairment in Low Luminance (VILL) questionnaire was designed to meet these criteria as well as to capture the characteristic impact of all AMD stages on patients' lives. Here we report its psychometric functioning and test-retest reliability in the European multi-center study MACUSTAR.

Methods: Using the baseline VILL data from participants of the MACUSTAR study (intermediate, early, late or no AMD) psychometric characteristics including model fit, person reliability (PR), person separation index (PSI), targeting and dimensionality of the existing VILL subscales (reading, VILL-R; mobility, VILL-M; emotional, VILL-E) were investigated using Rasch analysis (Winsteps, Chicago, IL). In a subset with repeated data test-retest reliability was assessed using mean deviation (MD), intra-class correlation coefficients (ICC) and Bland-Altman analysis.

Results: A baseline dataset including 716 participants was available for analysis. The VILL subscales were unidimensional. Dropping five misfitting items in an iterative process (VILL-R, 3 items; VILL-M, 1 item; VILL-E, 1 item) improved model fit. After removal of a total of 39 single misfitting responses from three additional misfitting items, 32 items could be retained and no item showed misfit. PR and PSI were 0.91 and 3.27 (VILL-R), 0.87 and 2.58 (VILL-M) and 0.73 and 1.65 (VILL-E), respectively. The mean person measure-item measure differences were 2.0 (VILL-R), 2.1 (VILL-M) and 1.6 (VILL-E). 289 participants were included in the evaluation of test-retest reliability of the VILL-32. MD and ICC (95% confidence interval) were 0.30 and 0.92 (0.90-0.94, VILL-R), 0.07 and 0.93 (0.91-0.94, VILL-M) and 0.30 and 0.85 (0.81-0.88, VILL-E).

Conclusions: Our results support internal consistency and test-retest reliability of the VILL in AMD in a large sample. The reading and mobility subscales are reliable measures while the emotional subscale is noticeably less precise. Thus, the emotional subscale was dropped, resulting in 29 items overall. The validation process of the instrument using functional data is ongoing.

CONTROL ID: 3536312

SUBMITTER (NAME ONLY): Jacqueline Kajtna

TITLE: Identification of the final time point for a successful therapeutic intervention and arrest of retinal remodeling in a mouse model of retinitis pigmentosa

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Kajtna, S. Koch, Department of Pharmacy, Ludwig-Maximilians-Universität München, München, Bayern, GERMANY|J. Kajtna, S. Koch, Physiological Genomics, Biomedical Center, Ludwig-Maximilians-Universität München, GERMANY|

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ABSTRACT BODY:

Purpose: A typical feature of retinitis pigmentosa (RP) is the initial loss of photoreceptors, followed by remodeling of the inner retina and blood vessels. How these changes may ultimately limit therapy outcome remains unknown. In this study we investigate if gene therapy at different RP disease stages can halt or even reverse retinal remodeling.

Methods: We use a novel genetically engineered RP mouse model ($Pde6b^{STOP/STOP}$, $Pde6g::CreERT2/+$), which carries a floxed STOP cassette on both alleles and expresses a rod specific tamoxifen inducible Cre. Mice were treated at 4, 12, 16 and 24 week of age by tamoxifen-induced Cre activation; at the time point of treatment the outer nuclear layer thickness had decreased by 37%, 67%, 82% and 88%, respectively (relative to the 40 weeks old wild-type). The remodeling and rescue of vision were evaluated by ERG recordings, water maze test and immunohistochemistry. The retinal vasculature was analyzed by immunohistochemistry and trypsin digests stained with H&E.

Results: In our RP mouse model, we observed progressive loss of rod bipolar processes, delocalized rod bipolar cell bodies, and dramatic reductions of horizontal cell neurites. Remodeling of inner retinal cells is halted and the function rescued after treatment at 16 weeks or earlier, but not by treatment at 24 weeks. The successful restoration of vision was preserved at least until age of 40 weeks. The retinal degeneration in our RP model is accompanied by blood vessel remodeling, which can be quantified as the reduced area of the vasculature and increased number of acellular capillaries. Mice treated at 16 weeks of age or earlier had significantly less acellular capillaries at 40 weeks of age than the untreated RP mice.

Conclusions: The results show that inner retinal remodeling can be halted in the long term after treatment at 16 weeks of age or earlier; however, inner retinal plasticity remains limited. In addition, we observed a positive effect of our treatment on the retinal vasculature remodeling.

CONTROL ID: 3536317

SUBMITTER (NAME ONLY): Gilad Fainberg

TITLE: Short Term Visual Related Ocular Side Effects During Treatment with D-MPH for ADHD

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Fainberg, Tel Aviv University, Tel Aviv, ISRAEL|Y. Leitner, Institute of Child Development, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|Y. Leitner, Pediatrics Department, Tel Aviv University, Tel Aviv, ISRAEL|D. Zur, A. Klein, D. Mezaad-Koursh, Ophthalmology Division, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|D. Zur, A. Klein, D. Mezaad-Koursh, Ophthalmology Department, Tel Aviv University, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To evaluate the short-term effect of dexamethylphenidate (D-MPH) on visual acuity, pupil size, anterior chamber depth (ACD), and accommodation-convergence reflex in children treated with D-MPH XR for attention-deficit/hyperactivity disorder (ADHD).

Methods: Prospective cohort study including 15 patients aged 8-16 (11.58 ± 2.39) treated with D-MPH for ADHD. Patients were questioned for subjective complains such as blurred vision and photosensitivity. Ophthalmic evaluation was performed twice; prior to and 1.5 hours following D-MPH administration. The exam included evaluation of best corrected visual acuity at distance and near, accommodation range, convergence range, 3-D vision test and anterior chamber optical coherence tomography (OCT).

Results: A significant association between pupil diameter and D-MPH treatment dose was demonstrated ($p=0.001$). Additionally, a positive correlation between complains about blurred vision and D-MPH daily dosage was found. There were no significant changes in visual acuity, convergence range, stereo vision, accommodation range, or anterior chamber measures.

Conclusions: Our findings provide further support to the effect of stimulants on pupil diameter, as well as on subjective complains about blurred vision in a dose dependent manner. Additionally, future research is required to further investigate a potential role for pupil diameter as a marker of response to D-MPH.

CONTROL ID: 3536323

SUBMITTER (NAME ONLY): Jan Kremers

TITLE: Linking ERG recordings to psychophysical data in human subjects

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The ERG originates in the activity of retinal neurons and therefore can be considered to be an epiphenomenon of the neuronal visual responses. It was found previously that ERG responses to continuous stimulation are correlated with activity of major retinal pathways and with visual perception. In the present study, we tried to find a method to link psychophysical thresholds to ERG recordings.

Methods: Psychophysical flicker detection thresholds were measured foveally (3° diameter) in three normal subjects to luminance stimulation with three temporal profiles: sine-wave, rapid-on sawteeth and rapid-off sawteeth. The temporal frequency was varied between 1 and 39 Hz. We measured full field ERGs to the same waveforms and temporal frequencies at 0, 3, 5, 10, 15 and 20% contrast in four normal subjects (total recording time for each condition: 80 sec). The ERG responses were averaged for all subjects and for a 1 sec episode. Then the ERGs were analyzed with a peak-to-trough detector (PTD) that integrated the ERG responses in two time windows that were shifted in time relative to each other. The two time windows were slid over the whole recording episode and subtracted to obtain the PDT output at each time instant. A root mean square (RMS) calculation was performed on the PTD output for the whole recording period to obtain the cumulative PDT response. Several time windows and shifts (difference between the two time windows) were used.

Results: The response strength of the PTD increased with increasing contrast. Contrasts for a threshold PTD response could be defined. The thresholds strongly depended on the chosen PTD characteristics. With well-chosen PTD characteristics, the PTD thresholds for all stimuli resembled the psychophysical thresholds.

Conclusions: Although the ERG is not the neuronal visual response that is transferred to the brain, it is assumed that it is uniquely related to the neuronal response (if the neuronal response is altered, the ERG is also altered; if the neuronal response is not changed, the ERG is not changed). With the PTD algorithm, the ERG can possibly be used as an objective tool to link retinal activity, elicited by continuous luminance waveforms, with psychophysical data.

CONTROL ID: 3536325

SUBMITTER (NAME ONLY): Donald Tran

TITLE: Behcet's Disease – Clinical Characteristics, Treatment and Ocular Outcomes

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure (Abstract): Donald Tran: Commercial Relationship: Code N (No Commercial Relationship) | Sophie Rogers: Commercial Relationship: Code N (No Commercial Relationship) | Lyndell Lim: Commercial Relationship(s);Allergan:Code F (Financial Support);Allergan:Code C (Consultant);Bayer:Code F (Financial Support);Novartis:Code R (Recipient);Novotech:Code C (Consultant)

ABSTRACT BODY:

Purpose: Behcet's disease (BD) is a chronic, multisystem vasculitis that may result in a blinding uveitis. The introduction of TNF- α inhibitors has substantially changed the treatment of this condition, however there remains a paucity of data regarding long term visual outcomes, particularly compared with conventional immunosuppression, and ocular vs non-ocular manifestations of BD.

Methods: Retrospective case series of patients who met the revised International Criteria for Behcet's Disease (ICBD) and presented between 1990–2018 to the Royal Victorian Eye and Ear Hospital, Melbourne, Australia, were reviewed. Demographic, ophthalmic examination, systemic manifestations, medication use and complications were noted.

Results: Forty-two patients (33 males, median age 30.1 years (IQR 25.7–35.5)) were observed for a median of 6.4 years (IQR 2.8–12.9). At first ocular presentation, 25 patients met the ICBD diagnostic criteria. A further 16 (98%) met the criteria during follow-up. The most common presenting BD manifestations were ocular (N=39), oral ulcers (N=25), genital ulcers (N=8), joint involvement (N=5), skin lesions (N=4) and vascular manifestations (N=1). The majority (N=28) developed ocular disease prior to non-ocular symptoms, with ocular involvement split evenly between unilateral (N=22) vs bilateral disease. Median best corrected logMAR visual acuity at presentation was 0.301 in 54 uveitic eyes; 15 of which were anterior uveitis, 11 intermediate, 2 posterior and 26 were panuveitis. During follow-up, 41 (98%) patients were treated with corticosteroids (CS), 36 (86%) with conventional disease-modifying anti-rheumatic drugs (DMARDs) and 10 (24%) were treated with biologic DMARDs. Despite treatment, visual impairment (logMAR >0.3), legal blindness (logMAR >1) and near total blindness (light or no light perception) persisted in 23, 12 and 5 eyes, respectively. Vision threatening complications included cataract (N=28), hypopyon (N=11), glaucoma (N=7), retinal vasculitis (N=28) and cystoid macula oedema (N=24).

Conclusions: Preliminary data suggests that ocular manifestations typically occur prior to systemic disease in our cohort of patients with BD. As expected, men of working age are most commonly affected, often with sight threatening disease at initial presentation. Despite treatment with CS and CS-sparing agents, including TNF- α inhibitors, visually significant complications with permanent vision loss still occur.

CONTROL ID: 3536337

SUBMITTER (NAME ONLY): Antonio Calcagni

TITLE: A Comparison of Xenon- and LED-based Full-field Electroretinography in Patients with ABCA4-related Macular Dystrophy

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Calcagni, A.G. Robson, Department of Electrophysiology, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|A. Calcagni, S.L. Ginton, P.A. Keane, M. Michaelides, A. Webster, O.A. Mahroo, A.G. Robson, University College London, London, UNITED KINGDOM|S.L. Ginton, P.A. Keane, M. Michaelides, A. Webster, O.A. Mahroo, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The long-established use of xenon flashes in full-field electroretinography (ERG) is being superseded by LED-based stimuli typically involving different recording systems, with potential consequences for studies that involve longitudinal or legacy data. This study compares retrospective recordings from xenon- and LED- based ERG systems in patients with confirmed ABCA4-related macular dystrophy (patients with Stargardt disease and normal full-field ERGs), with the aim of examining potential differences in response components.

Methods: Patients who attended Moorfields Eye Hospital with at least one molecularly confirmed mutation of the ABCA4 gene, a clinical presentation consistent with Stargardt Disease, and with macular dystrophy (full-field ERGs that fall within “normal” reference limits) were ascertained. Full-field ERGs incorporated the International Society for Clinical Electrophysiology of Vision (ISCEV) standard and were elicited using either LED- (Group A; “Diagnosys ColorDome™” system) or xenon-flash (Group B; “CH electronics” system) stimuli, each obtained using a different recording system. The dark-adapted strong flash (DA 10.0) ERG, light-adapted single flash cone (LA 3.0) ERG and 30Hz flicker (LA 30Hz) ERG were compared between the two groups.

Results: A total of 344 patients were analysed. There were 122 subjects in Group A (Mean age 37.5 years, SD: 14.0. Mean pupil size: 8.4; SD: 0.8) and 222 subjects in Group B (Mean age 36.8 years, SD: 14.7. Mean pupil size: 8.2; SD: 1.1). Amplitudes for the DA 10.0, LA 3.0 and LA 30Hz flicker ERGs did not show statistically significant differences (Table 1) between the 2 Groups. Peak times for the three tests showed small but statistically significant differences ($p<0.001$) between Group A and Group B.

Conclusions: The use of xenon- or LED- based flash stimuli and recording methods are important considerations when evaluating ISCEV-standard ERGs in patients with ABCA4-related macular dystrophy. The findings are relevant not only to studies that aim to monitor retinal function longitudinally using different equipment, but also those seeking to establish ERG reference ranges, pool data or interrogate legacy ERG data sets with novel methods, such as artificial intelligence.

CONTROL ID: 3536343

SUBMITTER (NAME ONLY): Meriam Islam

TITLE: Smartphone based Remote Monitoring of Vision in macular disease enables early detection of worsening pathology and need for intravitreal therapy

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the outcomes of home monitoring of distortion caused by macular diseases using a smartphone-based application (app), and to examine them with hospital-based assessments of visual acuity (VA), Optical Coherence Tomography (OCT) derived central macular thickness (CMT) and the requirement of intravitreal injection therapy.

Methods: Participants were trained in the correct use of the app (Alleye, Oculocare Ltd) in person or by using video and telephone consultations. Automated threshold-based alerts were communicated based on a traffic light system. A "threshold alarm" was defined as three consecutive "red" scores, and turned into a "persistent alarm" if present for greater than a 7-day period. Changes of VA and CMT, and the requirement for intravitreal therapy after an alarm were examined. We conducted an observational study with a retrospective analysis of data.

Results: 245 patients performing a total of 11,592 tests (mean 46.9 tests per user) were included and 84 eyes (164 alarms) examined. The mean drop in VA from baseline was -4.23 letters (95%CI: -6.24 to -2.22; $p < 0.001$) and mean increase in CMT was 29.5 μm (95%CI: -0.08-59.13; $p = 0.051$). Sixty-six eyes (78.5%) producing alarms either had a drop in VA, increase in CMT or both and 60.7% received an injection. Eyes with persistent alarms had a greater loss of VA, -4.79 letters (95%CI: -6.73 to -2.85; $p < 0.001$) or greater increase in CMT, +87.8 μm (95%CI: 5.2-170.4; $p = 0.038$).

Conclusions: Smartphone-based self-tests for macular disease may serve as reliable indicators for the worsening of pathology and the need for treatment.

CONTROL ID: 3536348

SUBMITTER (NAME ONLY): Hirotaka Tanabe

TITLE: Comparison of Visual Performance between Bifocal and Rotationally Asymmetric Multifocal with +1.5 Diopters Near Addition Intraocular Lenses

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Tanabe, T. Shoji, T. Yamauchi, K. Takase, H. Tabuchi, Ophthalmology, Tsukazaki Hospital, Himeji, Hyogo, JAPAN|

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ABSTRACT BODY:

Purpose: To compare the visual performance of a bifocal intraocular lens (IOL) (ZMB00) and a rotationally asymmetric multifocal with +1.5 diopters near addition intraocular lens (IOL) (Lentis Comfort LS-313 MF15 [Oculentis GmbH]).

Methods: We evaluated postoperative parameters 10 weeks after the last surgery in cataract patients who underwent bilateral ZMB00 or LS-313 MF15 implantation from August 11, 2011, to March 26, 2020, with the right and left lenses implanted within 3 months of each other.

Results: The study enrolled 1774 eyes of 887 patients. The bifocal group comprised 1326 eyes of 663 patients (67.0 ± 7.8 years; females/males, 518/145), and the rotationally asymmetric multifocal group comprised 448 eyes of 224 patients (73.6 ± 7.0 years; females/males, 125/99). Uncorrected near visual acuity was significantly better and the higher-order aberrations (ocular/internal, scaled to a pupil size of 4 mm)

(WF_4_post_O_TotalHOA/Third/Fourth/Trefoil/Coma/Tetrafoil/Spherical,

WF_4_post_I_TotalHOA/Third/Trefoil/Coma/Tetrafoil/Spherical) were significantly smaller, and distance/near spectacle independence were significantly better in the bifocal group ($p < 0.00068$, Wald test). Contrast sensitivity ($6.3/4.0/2.5/1.6/1.0/0.7$ degrees), and contrast sensitivity with glare ($4.0/2.5/1.6/1.0/0.7$ degrees) were significantly better in the rotationally asymmetric multifocal group ($p < 0.00068$, Wald test).

Conclusions: The two IOL groups had different characteristics in terms of uncorrected near visual acuity, the higher-order aberrations, distance/near spectacle independence, and contrast sensitivity with/without glare.

CONTROL ID: 3536353

SUBMITTER (NAME ONLY): Neha Krishnam

TITLE:

Cardiorespiratory Impact of Handheld Optical Coherence Tomography Compared to Binocular Indirect Ophthalmoscopy in Infants Screened for Retinopathy of Prematurity

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Binocular indirect ophthalmoscopy (BIO) is the gold standard for retinopathy of prematurity (ROP) screening, however associated use of an eyelid speculum and scleral depression results in significant infant stress. Handheld optical coherence tomography (OCT) may identify ROP severity biomarkers and is non-contact. We performed a prospective, observational study to compare vital signs measured during BIO and OCT to identify whether OCT has an advantage in lowering cardiorespiratory impact of screening.

Methods: This study included 16 premature infants screened for ROP, recruited between April 2019 and February 2020. Each infant underwent BIO and OCT (using an investigational handheld swept source OCT) at least 30 minutes apart, alternating the order at each consecutive screening session. Infants who were too unstable were excluded from the study. Vital signs were obtained 1 minute before, 1 and 2 minutes into, and 15 minutes after the examination. Vital sign deviations from baseline were compared for each infant between the two imaging modalities using a paired linear mixed model to adjust for multiple imaging sessions.

Results: This study included 26 examinations among 16 infants (62.5% female, mean gestational age 285.86 ± 2.82 weeks, mean birth weight 1058.25 ± 289.00 grams) with 9 infants at ROP stage 1, 4 at ROP stage 2, and 1 at ROP stage 3. BIO duration was significantly shorter than OCT (4.4 vs. 10.8 minutes, $P < 0.001$). Vital signs increase from baseline were significantly greater for BIO compared to OCT for heart rate at 1 minute (18.81 ± 20.75 vs. 0.00 ± 22.82 beats per minute, $P = 0.04$), diastolic blood pressure at 2 minutes (41.22 ± 31.69 vs. 28.19 ± 25.84 mmHg, $P = 0.04$), mean arterial pressure at 2 minutes (46.83 ± 34.83 vs. 36.99 ± 20.08 mmHg, $P = 0.04$), and systolic blood pressure at 15 minutes (10.85 ± 10.55 vs. -5.12 ± 13.53 mmHg, $P = 0.04$).

Conclusions: OCT resulted in significantly lower impact on heart rate and blood pressure compared to BIO. The ability to screen for ROP using OCT may benefit overall health for these vulnerable premature infants. Further studies should explore the potential utility of OCT as an ROP screening tool.

CONTROL ID: 3536357

SUBMITTER (NAME ONLY): Alfredo Ruggeri

TITLE: Improvement in mixed-type dry eye patients after treatment with the QMR[®]-based electrotherapy device Rexion-Eye[®]

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ruggeri, Resono Ophthalmic, Sandrigo, VI, ITALY|A. Trivli, G. Dalianis, C. Terzidou, Ocular Surface Service, Ophthalmology, Konstantopouleio General Hospital, Athens, GREECE|

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ABSTRACT BODY:

Purpose: We investigated the efficacy of the low-power, high-frequency electrical current treatment administered by Rexion-Eye[®] in a cohort of 18 patients affected by mixed-type dry eye disease (DED) of medium to severe level.

Methods: 18 mixed type DED patients (17 female and 1 male; age range 42-81 years) were randomly recruited and treated. Therapy was administered with the Rexion-Eye[®] device (Resono Ophthalmic, Sandrigo, Italy), which applies, via an electrode mask worn over closed eyes, a weak alternate electrical current with a specific spectrum of frequencies (4-64 MHz, Quantum Molecular Resonance, QMR[®]). The treatment protocol provides for one 20-min session per week, for 4 weeks. Patients were examined at baseline and one month after the last treatment, by measuring: tear meniscus height (TMH), non-invasive tear break-up time (NIBUT), measured with IDRA (SBM Sistemi, Turin, Italy); Meibomian gland number (in lower eyelid) and quality of secretion; Ocular Surface Disease Index (OSDI) score; Schirmer's II test; ocular inflammation, by Oxford staining and by MMP9 (with InflammDry by Quidel, San Diego (CA), USA).

Results: Results are reported in Table 1 and 2. In this cohort of patients, all clinical endpoints markedly improved, with a limited improvement only in the Schirmer's II test. Clinical parameters related to inflammation especially showed a remarkable benefit, as evidenced by the reduction of MMP9 and Oxford staining and normalization of TMH. Subjective benefit (OSDI) was reported by patients and no adverse event was observed in any of them.

Conclusions: In accordance with previous studies, Rexion-Eye[®] proved to be very effective in improving subjective and objective ocular parameters. Of particular interest in this mixed-type DED patients cohort is the capability of Rexion-Eye[®] to normalize the clinical parameters affected by inflammation.

CONTROL ID: 3536358

SUBMITTER (NAME ONLY): Julia Schottenhamml

TITLE: Deep Learning Glaucoma Classification in enface OCTA scans of the human macular region

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Schottenhamml, S.B. Ploner, L. Husvagt, A.K. Maier, Pattern Recognition Lab, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|B. Hohberger, C.Y. Mardin, Department of Ophthalmology, University Erlangen-Nürnberg, Erlangen, GERMANY|S. Mardin, Department of Information Systems and Services, Otto-Friedrich-Universitat Bamberg, Bamberg, Bayern, GERMANY|L. Husvagt, Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is one of the leading causes of irreversible vision loss. Several studies have shown a link between vascular damage and glaucoma on optical coherence tomography angiography (OCTA) images. These studies were mostly conducted in the region of the optic nerve head (ONH) or on larger 6x6 mm macula scans. Moreover, all these studies use handcrafted features for the glaucoma classification. We therefore propose a fully automatic classification algorithm on 3x3 mm macula scans based on convolutional neural networks (CNN) that are able to learn features from the images themselves.

Methods: Whole retina projection OCTA images (Spectralis OCT II, Heidelberg Engineering, Heidelberg) of 75 eyes of 75 healthy persons (h) and 184 eyes of 125 glaucoma patients (g) were retrospectively identified from the Erlangen glaucoma registry. They were divided into training set (h: 45 eyes/45 patients, g: 110 eyes/76 patients), validation set (h: 15 eyes/15 patients, g: 37 eyes/24 patients) and test set (h: 15 eyes/15 patients, g: 37 eyes/25 patients). Eyes of one person only belong to a single set. Different CNNs were trained and the one performing best (according to the AUROC) on the validation set was chosen for evaluation. For comparison, handcrafted features that were compatible with the available data (only a single enface OCTA image available) were selected. We chose the commonly used vessel density (VD) and a combination of global and local features proposed by Ong et al. (Ong). We then trained a support vector machine (SVM) on each of these traditional feature sets and again chose the best performing one on the validation set.

Results: The ROC curves, AUROC values and confusion matrices can be found in Figure 1 and the accuracies in Figure 2 for the different methods on the test set.

Conclusions: We were able to outperform other handcrafted features on 3x3 mm macula scans and achieved results on par with other algorithms proposed for different ocular regions. These other studies often have shown that their features work better on projections of a single vascular plexus than on a whole retina projection. Therefore, the next step would be to apply the deep learning pipeline presented in this paper to the different retinal plexuses separately.

CONTROL ID: 3536369

SUBMITTER (NAME ONLY): Astrid Kindt

TITLE: Increased retinal thickness in patients with ocular sarcoidosis

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Sarcoidosis is a granulomatous inflammatory disease that can affect any organ including the central nervous system (CNS) and the eyes. This cross-sectional study aimed to investigate retinal neural structure in patients with different clinical manifestations of sarcoidosis.

Methods: A total of 200 eyes of 103 biopsy-verified sarcoidosis patients without diabetes mellitus were included and categorized into four groups according to their phenotype: 1) sarcoidosis without ocular or CNS affection (non-ocular/no-CNS), 2) ocular sarcoidosis, 3) CNS sarcoidosis, and 4) combined ocular and CNS sarcoidosis (ocular/CNS).

Best corrected visual acuity (BCVA) was assessed. Swept source optical coherence tomography (SS-OCT) was obtained (Topcon Swept Source DRI OCT Triton), with measurements of central macular thickness (CMT), retinal thickness (RT), retinal nerve fiber layer (RNFL), and ganglion cell layer (GCL) thickness. Differences in retinal neural structures between groups were evaluated by Kruskal-Wallis Test and pairwise by Wilcoxon Rank Sum Test.

Results: The mean age of participants was 50.4 years (SD13.4 years), 52% were males, and 54.5% of patients had a duration of sarcoidosis above five years. Median BCVA was above 80 Early Treatment Diabetic Retinopathy Study letters in all groups.

Eyes of the non-ocular/no-CNS group had a lower CMT and RNFL than the ocular sarcoidosis group ($p=0.003$ and $p=0.011$). Likewise, the RNFL was thinner in non-ocular/no-CNS eyes compared to ocular/CNS ($p=0.002$) and in those with ocular sarcoidosis compared to the CNS group ($p=0.029$).

In subgroup analyses of patients with a duration of sarcoidosis above five years, the CMT in eyes of the non-ocular/no-CNS group was thinner than all other groups: ocular ($p=0.0001$), CNS ($p=0.0002$) and ocular/CNS ($p=0.029$). Moreover, there was a thickening of CMT in the ocular group compared to the CNS group ($p=0.002$). Similarly, RT and RNFL were thinner in the non-ocular/no-CNS group compared to both the ocular ($p<0.0001$ and $p=0.13$) and the ocular/CNS group ($p<0.0001$ and $p=0.03$). Finally, a thickening in those variables was also observed in the ocular compared to CNS group ($p=0.01$ and $p=0.0004$).

Conclusions: In particular for patients with a long duration of sarcoidosis, these results indicate increasing retinal thickening in patients with ocular involvement of sarcoidosis.

CONTROL ID: 3536377

SUBMITTER (NAME ONLY): Julien Fars

TITLE: Psychometric curves in retinitis pigmentosa patients

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fars, C.R. Huchzermeyer, J.J. Kremers, Friedrich-Alexander-Universitat Erlangen-Nurnberg, Erlangen, Bayern, GERMANY|J. Fars, C.R. Huchzermeyer, J.J. Kremers, Department of Ophthalmology, University Hospital Erlangen, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: To study if the contrast range of uncertainty around a flicker detection thresholds was enlarged in patients with retinitis pigmentosa (RP).

Methods: We used a psychophysical procedure based on a temporal contrast sensitivity procedure combined with the silent substitution paradigm in a group of RP patients and in a normal control group. We examined 17 normal subjects (27±8 years, 7 females, 10 males) and 21 RP subjects with different genetic backgrounds (45±15 years, 6 females, 15 males). The subjects had to indicate the presence or absence of perceived flicker. The stimuli were created with a dedicated LED stimulator. Parafoveal L-cone, M-cone, S-cone and Rod-isolating stimuli at different temporal frequencies, between 1 and 4 Hz (low frequencies) and 12 and 20 Hz (high frequencies), were generated using triple silent substitution. Two randomly interleaved staircase procedures were used to determine psychometric curves. The thresholds and slope values of the psychometric curves were extracted. The slope values correspond to the range of uncertainty towards the tested condition. The shallower the slope value (i.e. smaller value), the larger is the range of uncertainty. These slope values were compared between normal subjects and RP patients using Wilcoxon-signed-rank tests.

Results: At high frequencies, the slope values were not significantly different between the two groups and a large slope variability was found especially at high frequencies for M-cone isolating stimuli. At low temporal frequencies, there were significantly shallower slopes for the L-cone, M-cone and for Rod isolating stimuli in RP patients compared to the normal subjects ($p < 0.05$).

Conclusions: RP patients display a larger range of uncertain flicker perception at low temporal frequency for Rod isolating stimuli and at low temporal frequencies for L- and M-cone isolating stimuli where the parvocellular pathway mediates flicker detection. The larger uncertainties in RP patients are possibly related to the area of retinal degeneration and can possibly be used to diagnose and monitor the disease.

CONTROL ID: 3536382

SUBMITTER (NAME ONLY): Alice Motschi

TITLE: Using polarization-sensitive OCT to detect and quantify fibrotic lesions in the human retina

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To facilitate the diagnosis and quantification of fibrotic tissue in the human retina by analyzing polarization-sensitive (PS) OCT data using an automated process.

Methods: 59 eyes of 59 patients (77 ± 6 years) with neovascular age-related macular degeneration (nAMD) were imaged using a custom-built spectral domain PS-OCT system operating at 860nm with an A-scan rate of 70kHz and an integrated retinal tracker. Raster scans consisting of 250 B-scans \times 1024 A-scans were recorded at the macula, covering an area of $8 \times 6 \text{ mm}^2$. After standard SD-OCT data processing, PS data (retardation, optic axis orientation, degree of polarization uniformity) were extracted. The PS data were compensated for the birefringence of cornea and Henle's fiber layer. The double-compensated axis orientation was projected onto an enface map, fibrosis was separated from healthy tissue based on axis uniformity and using a region growing algorithm, and finally the area of the segmented fibrosis was obtained. A sub-set of 16 patients were measured three times to assess the repeatability of the method.

In addition, color fundus photography (CFP) was performed on all eyes.

Results: Fig. 1(a–c) shows an example of measurements in a patient with fibrosis. Patches of well-defined axis orientation (Fig. 1a) are an indicator of fibrosis and are segmented (blue areas in Fig. 1b). The CFP in Fig. 1c shows a yellow-whitish discoloration at the same location, indicating the presence of fibrosis. In 31 of the 59 eyes, fibrosis was diagnosed on CFP. Of the 28 eyes diagnosed as non-fibrotic based on CFP, our algorithm confirmed the absence of fibrosis in 23 cases (82%). Manual inspection of the data of the remaining 5 cases suggests the occurrence of false positives in the PS method. Of the 31 eyes diagnosed with fibrosis based on CFP, our algorithm confirmed fibrosis in 21 cases (68%). After manual inspection of the disagreeing cases, 9 out of 10 cases were assessed to likely be non-fibrotic and the remaining case might have a weak fibrotic lesion.

Fig. 1d shows the results of the repeatability measurements (mean and SD (error bars)). The mean repeatability of the fibrotic lesions $> 0.5 \text{ mm}^2$ was 17%. Patients who have been diagnosed as fibrotic based on CFP are marked with an orange background.

Conclusions: PS-OCT can be used to detect and quantify fibrotic lesions in nAMD with good repeatability. Some discrepancies to CFP require further analysis.

CONTROL ID: 3536383

SUBMITTER (NAME ONLY): Susanne Roosing

TITLE: Long-read technologies unravel hidden inversion-duplication in a family with choroideremia

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The lack of molecular diagnoses in rare genetic diseases can be explained by limitations of current standard genomic technologies. Upcoming long-read (sequencing) techniques have complementary strengths to overcome these limitations. By using optical mapping and long-read sequencing, we aimed to identify the pathogenic variant in a large family with X-linked choroideremia. In this family, aberrant splicing of exon 12 of the choroideremia gene CHM was detected in 2003, but the underlying genomic defect remained elusive.

Methods: We performed optical imaging followed by long-read whole genome sequencing to enable identification of a hidden structural variant in affected cases and carrier females in the studied family. This was followed by Sanger sequencing validation and segregation analysis. In silico analysis was performed to evaluate putative hair-pin formation as an underlying mechanism to exon 12 skipping in the mRNA.

Results: Optical mapping and long-read sequencing approaches now revealed an intragenic 1,752 bp inverted duplication including exon 12 and surrounding regions, located downstream of the wild-type copy of exon 12. Both breakpoint junctions were confirmed with Sanger sequencing, segregate with the X-linked inheritance in the family. The breakpoint junctions displayed sequence microhomology suggestive for an erroneous replication mechanism as the origin of the structural variant. The inverted duplication is predicted to result in hairpin-formation with the wild-type exon 12, which leads to skipping of this exon in the mature mRNA.

Conclusions: The identified inverted duplication is deemed the pathogenic cause of disease in this family. Our study shows that long-read sequencing and optical genome imaging techniques has significant potential for identification of structural variants in genetic diseases.

CONTROL ID: 3536389

SUBMITTER (NAME ONLY): Jian Sun

TITLE: Detecting Severity of Experimental Autoimmune Uveitis in Mice from Retinal Fundus Photographs using Deep Learning

SESSION TITLE: AI in the retina: Algorithms

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To develop a deep learning construct to detect Uveitis from retinal fundus photographs of Experimental Autoimmune Uveitis (EAU) mice and to propose a framework for consistent and reproducible characterization of images related to animal research studies.

Methods: Accuracy, consistency, and reproducibility are critical for animal model characterization. We developed a deep learning model (DLUveitis) based on the VGG16 architecture to grade uveitis from retinal fundus photographs of EAU mice (Fig. 1). We utilized 1800 fundus photographs to train and test the models for detecting five levels of disease severity and used 300 images to independently validate the findings. We further developed a method to calculate the detailed clinical score of EAU and visualize the outcome of different models (Fig. 2)

Results: We analyzed 2100 fundus photographs that corresponded to normal, trace, moderate, advanced and severe stages of the uveitis disease. Three human expert readers annotated the training images based on evaluations from both fundus photographs and optical coherence tomography (OCT) images. Based on the initial dataset of 1800 fundus images, the AUC of the model in distinguishing five levels of severity was 0.98 (95%CI, 0.97-0.99). Based on the additional independent validation subset of 300 images, the AUC of the model in distinguishing five levels of severity was 0.96 (95%CI, 0.93-0.99). Our model outperforms human graders.

Conclusions: Animal models are invaluable tools for studying human diseases and drug testing. The proposed deep learning construct accurately detects uveitis and five severity levels from fundus photographs of EAU mice. In addition, the clinical score generated by DLUveitis provides more details about the disease severity, compared to human experts, thus providing a highly consistent and reproducible pilot model for subsequent animal research studies.

CONTROL ID: 3536392

SUBMITTER (NAME ONLY): James Loughman

TITLE: Macular pigment response to carotenoid supplementation in patients with open angle glaucoma: the ENIGMA trial.

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Loughman, J.S. Butler, I. Flitcroft, E. Loskutova, Centre for Eye Research Ireland, Technological University Dublin, Dublin, Dublin, IRELAND|C.J. O'Brien, Mater Misericordiae University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Recent investigations have demonstrated that macular pigment (MP) is lower in glaucomatous eyes. MP exhibits specific biological qualities which may confer neuro-protective and functional benefits in glaucoma. The European Nutrition In Glaucoma Management (ENIGMA) trial was designed to evaluate, for the first time, the MP response to supplementation in glaucoma.

Methods: ENIGMA (NCT04460365) comprised a randomized, placebo controlled, double masked trial. Individuals with open angle glaucoma, VA < 0.3, no other ocular disease, and no history of dementia were eligible for inclusion. Participants were randomized in a 2:1 ratio to receive a dietary carotenoid supplement [10mg lutein (L), 10mg meso-zeaxanthin (meso-Z) and 2mg zeaxanthin (Z)], or placebo for 18 months. MPOD was measured at baseline, 6, 12 and 18 months by dual-wavelength autofluorescence using Heidelberg Spectralis.

Results: 62 participants were enrolled, 44 assigned to treatment and 18 to placebo. No baseline differences between groups were observed ($P > 0.05$ for all -Table 1). Repeated measures ANOVA showed that sqrt MPOD volume differed significantly for the interaction between treatment and time [$F(3,111) = 31.718690$, $p < 0.001$] with a significant effect of time [$F(3,111) = 71.277135$, $p < 0.001$] and no significant effect of treatment [$F(1,37) = 2.642403$, $p = 0.112$]. Post hoc tests with Bonferroni correction revealed a significant difference between baseline MPOD and MPOD at each timepoint (6, 12 and 18 months) in the treatment group only (Fig 1). There was a significant difference in MPOD volume between the treatment and placebo group at 12 and 18 months.

Conclusions: ENIGMA is the first study to demonstrate that MP levels can be augmented in glaucomatous eyes by carotenoid supplementation, which represents an important pre-cursor to any functional or health-related benefits that may accrue. From a neuro-protective perspective, oxidative stress and chronic inflammation are key pathways of tissue damage involved in glaucoma. As potent antioxidant and anti-inflammatory nutrients, L, Z and meso-Z supplementation to increase MPOD might support retinal ganglion cells and confer protection by preventing the pathophysiological cascades of oxidative stress and inflammation in glaucoma.

CONTROL ID: 3536393

SUBMITTER (NAME ONLY): Amanda Vazquez

TITLE: Tear biomarkers in patients suffering from chronic pain and dry eye disease

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vazquez, M. Blanco-Vázquez, M. Calonge, I. Fernandez, C. García-Vázquez, A. Novo-Diez, E. Martinez-Plaza, E.M. Sobas Abad, M. González-García, A. Enriquez-De-Salamanca, IOBA (Institute of Applied OphthoBiology) - University of Valladolid, Valladolid, SPAIN|M. Calonge, I. Fernandez, M. González-García, A. Enriquez-De-Salamanca, CIBER-BBN (Biomedical Research Networking Center in Bioengineering, Biomaterials and Nanomedicine), SPAIN|

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ABSTRACT BODY:

Purpose: To analyze the concentration of tear cytokines and substance P (SP) in patients suffering from chronic pain and/or dry eye (DE) who either had previous LASIK-type refractive surgery (RS) or did not have it.

Methods: 180 subjects were recruited and divided into 5 groups: 52 patients with pain and/or DE post-RS (P/DE-RS); 31 non-RS patients with pain and DE (P/DE-nonRS); 35 non-RS patients with only DE (DE-nonRS); 30 asymptomatic post-RS control subjects (C-RS); and 32 asymptomatic non-RS control subjects (C-nonRS). Inclusion criteria for DE were: Ocular Surface Disease Index score ≥ 13 and abnormal results in both eyes of at least 2 of the following tests: tear break-up time ≤ 7 sec, Schirmer ≤ 5 mm and corneal or conjunctival staining ≥ 1 (Oxford scale). Chronic ocular pain was considered when lasting ≥ 3 months and the Numerical Rating Scale score was ≥ 2 (range 0-10). Concentration of EGF, fractalkine, IL-1b, IL-1Ra, IL-2, IL-4, IL-6, IL-8, IL-9, IL-10, IL-17A, MCP-1, MCP-3, TNF-a, IFN-g, GRO, MIP-1a, MIP-1b, NGF and RANTES in tear samples was analyzed by multiplex immunobead-based assay and SP concentration by enzyme-linked immunosorbent assay. The relationship between markers and groups were evaluated by ANCOVA using propensity score to control age and sex effect. Molecules with percentage of detection $< 50\%$ (IL-17A, IL-2, IL-9, IFN-g and MIP-1a) were analyzed using contingency tables.

Results: IL-10 tear concentration was significantly higher in the groups who had LASIK RS (P/DE-RS and C-RS) than in DE-nonRS ($p < 0.02$) or C-nonRS ($p < 0.03$). SP was significantly elevated in both LASIK groups (P/DE-RS and C-RS) compared to the two non-RS symptomatic groups (P/DE-nonRS and DE-nonRS) ($p < 0.03$ and $p < 0.02$ respectively). SP concentration was also higher in controls who had RS (C-RS) than in controls who did not have it (C-nonRS) ($p = 0.018$). IL-9 showed the highest percentage of detection in groups with pain (P/DE-RS and P/DE-nonRS) ($p = 0.0001$). LASIK groups followed by P/DE-nonRS group had the highest percentage of detection of MIP-1a ($p = 0.0003$). IL-17A was only detected in the C-RS group.

Conclusions: IL-10, SP, MIP-1a and IL-9 might be involved in the development of chronic pain in patients who had RS and in DE patients. These results add further insight into the molecular mechanisms involved in the development of chronic pain and DE and might be helpful in the design of new therapeutic approaches.

CONTROL ID: 3536396

SUBMITTER (NAME ONLY): Marlies Gijs

TITLE: Prevalence of SARS-CoV-2 viral RNA in conjunctival swabs of symptomatic COVID-19 patients in the Netherlands

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The putative presence of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) in ocular specimen put ophthalmologists and co-workers at risk. So far, few results are available from small sample size studies. The aim of our study is to evaluate the presence of viral RNA of SARS-CoV-2 in conjunctival swabs of a large cohort coronavirus disease 2019 (COVID-19) patients in the Netherlands.

Methods: A total of 243 symptomatic laboratory-confirmed COVID-19 patients were included in this observational multicenter study. Sample collection took place during the 'second wave' of the pandemic (from August to November 2020) in two medical centers in the Netherlands. From a subset of subjects (healthcare workers), consecutive conjunctival samples were available from follow-up visits. Tear/conjunctival samples were obtained by gently sweeping the inferior conjunctival fornices of both eyes with a disposable swab. Samples were analyzed by reverse transcription (RT) PCR for detection of SARS-CoV-2 viral RNA.

Results: Viral RNA was detectable in conjunctival swabs from 17 out of 243 (7.0%) COVID-19 patients. The mean age of those 17 subjects was 46.7 ± 16.2 years (range 26-80 years) and the male-to-female ratio was 4/13. One subject reported increased tearing as ocular symptom. Conjunctival samples were positive for viral RNA as long as 12 days after disease onset. Cycle threshold (Ct) values for conjunctival swabs (mean 34.5 ± 5.1 , range 22.6 – 42.0) were significantly higher than of nasopharyngeal swabs (mean 16.7 ± 3.6 , range 12.1 - 24.3) ($p < 0.0001$). No correlation ($r = -0.10$, $p = 0.70$) between Ct values of conjunctival and nasopharyngeal swabs was observed. The majority of positive conjunctival samples were detected during the first visit, while three subjects became positive during the second visit and one subject during the fourth visit. None of the subjects tested positive in the conjunctival sample more than once.

Conclusions: Ocular transmission of SARS-CoV-2 remains a crucial issue that requires vigilance of protecting the ocular surface by wearing protective equipment. Particularly for ophthalmologists, protective measures are warranted during the ophthalmic examination and ocular surgery.

CONTROL ID: 3536400

SUBMITTER (NAME ONLY): Takashi Itokawa

TITLE: Changes in ocular anterior segment blood flow and temperature after thermal pulsation treatment in patients with meibomian gland dysfunction

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Itokawa, S. Sumazaki, Y. Okajima, K. Kakisu, T. Suzuki, Y. Hori, Ophthalmology, Toho University Omori Medical Center, Tokyo, JAPAN|T. Suzuki, Ishizuchi Eye Clinic, Ehime, JAPAN|

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ABSTRACT BODY:

Purpose: The temperature and blood flow of the ocular surface and peripheral tissue increase when conventional warm compresses are applied. We investigated the effect of thermal pulsation treatment (LipiFlow) on the temperature and blood flow in those areas in patients with meibomian gland dysfunction (MGD).

Methods: We recruited 13 eyes of 13 patients with MGD (mean age, 64.9±18.1 years) and measured the non-invasive tear break-up time (NIBUT), blood flow, and temperature before and 5 minutes after LipiFlow. The blood flow and temperature were measured in the anterior ocular segment, i.e., upper and lower eyelid skin and palpebral and bulbar conjunctiva. The blood flow was measured as the mean blur rate using laser speckle flowgraphy (LSFG-OAS, Soft Care). The temperature was measured using ocular surface thermography (TG-1000, Tomey). The NIBUT was determined using tear film interferometry (DR-1 Alpha, Kowa).

Results: The NIBUT of before and after 5 minutes after LipiFlow was 4.9±2.6 and 7.1±4.8 seconds. The NIBUT was significantly longer 5 minutes after LipiFlow compared to before (paired t-test, P<0.05). The temperature of the upper (34.29±0.52 and 35.49±0.26°C) and lower (33.93±0.60 and 35.13±0.48°C) eyelid skin and palpebral (34.51±0.37 and 35.63±0.41°C) and bulbar (34.61±0.43 and 35.82±0.47°C) conjunctiva increased significantly 5 minutes after LipiFlow compared with before LipiFlow (P<0.01 for both comparisons). The temperature differences of the upper and lower eyelid skin and palpebral and bulbar conjunctiva between before and after LipiFlow were 1.20°C, 1.21°C, 1.13°C, and 1.21°C, respectively. The blood flow in those areas (927.8±354.6 and 1104.8±352.6, 870.6±325.7 and 1273.3±610.9, 1840.7±676.6 and 2424.2±565.7, 287.5±78.1 and 358.9±105.1) also increased significantly 5 minutes after LipiFlow (P<0.05 for all comparisons). The rate changes in those areas between before and after LipiFlow were 124.5%, 144.5%, 188.1%, and 139.5%, respectively.

Conclusions: LipiFlow resulted in significant increases in temperature and blood flow in the ocular anterior segment compared to before its use.

CONTROL ID: 3536403

SUBMITTER (NAME ONLY): Suman Sedai

TITLE: Deep learning-based segmentation uncertainty improves the correlation between RNFL structure and visual function

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The uncertainty quantification of segmentation results is critical for understanding the reliability of the segmentation model. The purpose of this study is to investigate the effect of deep learning-based segmentation with uncertainty measurement in the relationship between RNFL thickness and visual field mean deviation (MD).

Methods: Optical coherence tomography (OCT) scans were acquired from both eyes on 634 glaucoma patients, 404 glaucoma suspects, and 49 healthy controls using commercial OCT device (Cirrus HD-OCT, 200x200 Optic Disc Cubes; Zeiss, Dublin, CA). All subjects had visual field (VF) tests at each visit (Humphrey VF, SITA 24-2 test; Zeiss). A segmentation model was trained using Bayesian deep learning for voxel-wise segmentation of RNFL layer in OCT volume and compute the voxel-wise uncertainty of the segmentation output. The higher uncertainty denotes the unreliability of the segmentation and vice versa and it allows the determination of erroneous segmentation at test time. Uncertainty-guided global mean of the RNFL thickness ($RNFL-U_{mean}$) was then computed by discarding the voxels with erroneous segmentation labels with higher uncertainty during the thickness computation. Also, the global mean of the RNFL thickness ($RNFL_{mean}$) was computed without taking uncertainty into account. Pearson correlation coefficient between $RNFL-U_{mean}$ and MD was computed and compared with the Pearson correlation coefficient between $RNFL_{mean}$ and MD.

Results: The proposed $RNFL-U_{mean}$ gave stronger correlation with MD than $RNFL_{mean}$. The Pearson correlation coefficients were (0.67 ($RNFL-U_{mean}$) vs 0.63 ($RNFL_{mean}$); $p < 0.001$) for glaucoma subjects, (0.56 vs 0.53 ; $p = 0.01$) for glaucoma suspects and (0.08 vs 0.01; $p = 0.21$) for normal subjects.

Conclusions: The proposed uncertainty-guided computation of RNFL thickness showed improved correlation with the visual field MD. This demonstrates that segmentation uncertainty can be used to reduce the effect of inaccurate segmentation in computing the RNFL thickness. This also shows that uncertainty-guided computation of RNFL thickness is a better predictor of visual function than the normal RNFL thickness computed without using uncertainty.

CONTROL ID: 3536407

SUBMITTER (NAME ONLY): Alan Hibbitts

TITLE: A Drug-Eluting Biomaterial Device for Reducing Post-Surgical Inflammation and Fibrosis in Glaucoma Patients

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Hibbitts, M. Lemoine, Z. Demir, F. O'Brien, Dept. of Anatomy and Regenerative Medicine, Royal College of Surgeons in Ireland, Dublin, IRELAND|A. Hibbitts, M. Lemoine, Z. Demir, F. O'Brien, Trinity Centre for Biomedical Engineering, The University of Dublin Trinity College, Dublin, IRELAND|C.J. O'Brien, Dept of Anatomy, University College Dublin, Dublin, IRELAND|C.J. O'Brien, Institute of Ophthalmology, Mater Misericordiae University Hospital Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Drainage tube or trabeculectomy surgeries in late-stage glaucoma remains beset by unacceptably high 1-year failure rates due to post-operative inflammation and fibrosis. Fibrosis is known to follow a two-stage process with inflammation over the first 1-7 days followed by collagen deposition. Current approaches to remedy this rely on administration of anti-metabolites (mitomycin C) and an intensive course of patient-administered corticosteroid drops. These present their own issues, particularly adverse side-effects and poor patient compliance. Therefore, we describe a proteoglycan (PG)-modified hyaluronic acid (HyA) drug-device that aims to address post-surgical inflammation and remove patient compliance issues.

Methods: PG-Hyaluronic acid hydrogels were chemically crosslinked and assessed for percentage crosslinking, swelling, degradation and ease of insertion into cadaveric rabbit eyes. The innate ability of the modified gels to reduce collagen deposition in the absence of drugs was tested using primary human conjunctival fibroblasts stimulated with Transforming Growth Factor-Beta (TGF- β). The device was further enhanced using prednisolone drug loading with release assessed over 28 days in PBS and efficacy evaluated in a chick embryo model.

Results: It was found that HyA hydrogels were capable of rapid swelling in <30 min, stability up to 4 weeks minimum and enzymatic degradation related to cross-linking efficacy. The device was easily implanted using standard surgical tools (Figure 1A). In vitro analysis using drug-free, PG-HyA gels in TGF- β stimulated conjunctival fibroblasts demonstrated a reduction to normal collagen levels at 24 hours (Figure 1 B+C).

Release of prednisolone from gel composites were found to exhibit a biphasic release with an initial burst release over 72 hours and a more gradual release for up to 28 days. Furthermore, this was found to effectively inhibit angiogenesis up to 5 days ex-vivo.

Conclusions: This work demonstrates a strong proof of concept validation for a straightforward solution to a long running issue in glaucoma surgery. Future work now focuses on an in-depth pre-clinical study.

CONTROL ID: 3536409

SUBMITTER (NAME ONLY): Atsuya Miki

TITLE: Three-dimensional morphometry of the lamina cribrosa for glaucoma diagnosis using deep learning-enhanced optical coherence tomography volumetric scans

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deformation of the lamina cribrosa (LC) is a defining characteristic of glaucomatous optic neuropathy and is a potential diagnostic tool. However, due to the limitations in existing imaging modalities, it has not been widely used for glaucoma diagnosis. We propose a new strategy for diagnosing glaucoma by combining multiple LC morphometric parameters obtained from deep learning (DL)-enhanced three dimensional (3D) optical coherence tomography (OCT) imaging.

Methods: Seventy-Four eyes of 74 glaucoma patients and 86 eyes of 86 control subjects without glaucoma who underwent parapapillary swept source OCT were investigated. Mean \pm standard deviation age and axial length in glaucoma and control eyes were 57.7 ± 11.7 and 46.4 ± 8.8 , and 25.7 ± 1.6 and 24.4 ± 1.2 mm, respectively. The 3D OCT images of the LC were obtained through a series of procedures that consists of DL-based noise reduction, projection artifact reduction, adaptive compensation, automatic segmentation, and 3D volume rendering. Multiple morphologic parameters of the LC were measured from 3D images. The performance of the individual LC parameters as well as the extreme gradient boosting (XGBoost) machine learning model integrating multiple parameters for discriminating glaucoma from healthy were assessed by the area under the curve (AUC) values. The performance of retinal nerve fiber layer (RNFL) thickness based on normative database was also evaluated for reference.

Results: The LC was significantly deeper in glaucoma patients (0.53 ± 0.14 mm) than control subjects (0.47 ± 0.09 mm, $P=0.002$). The best performing single LC parameter in discriminating glaucoma from control was the LC depth (AUC 0.64). The optimized XGBoost analyses yielded excellent discriminating performance (AUC 0.90), which was better than the AUC value of the total RNFL thickness (0.85).

Conclusions: Multiple morphologic parameters of the LC were successfully obtained from 3D DL-enhanced OCT images. Integrating multiple LC parameters by machine learning yielded excellent performance that was comparable to existing RNFL parameters. Results of the current study demonstrated the clinical relevance of 3D LC imaging.

CONTROL ID: 3536414

SUBMITTER (NAME ONLY): Mihai State

TITLE: Personalized eye models for negative dysphotopsia assessment

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. State, A. Alarcon, C. Canovas, P. Piers, R&D, Johnson & Johnson Surgical Vision Inc, Groningen, NETHERLANDS|S. Palkovits, O. Findl, Vienna Institute for Research in Ocular Surgery, Hanusch-Krankenhaus, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: With a population incidence varying between 0.20% for severe cases and 25% for mild to moderate ones, negative dysphotopsia (ND) is associated with the perception of dark crescent shadows in the peripheral field of view (PFOV) of pseudophakic patients. As contributing factors, literature reviews enumerate biometry (pupil size in photopic conditions, angle kappa, hyperopia etc) and intraocular lens characteristics (IOL, tilt and decentration, optic body size etc). Building on our previously communicated results, the current study evaluates the predictive ability of personalized theoretical eye models to localize the ND in PFOV.

Methods: In a prospective study conducted at Hanusch Hospital, Vienna, Austria, post-operative biometrical data sets (pupil size, ACD and AL, anterior corneal topography, IOL tilt and decentration and refractive errors) were acquired from six patients implanted with monofocal IOLs and with ND complaints. A Harms tangent screen subjective method was used to localize in PFOV the perceived shadow (HvF). Following a previously presented methodology (M. State et al., IOVS, Vol.60, 3703, 2019), personalized Liou-Brennan (non)-sequential eye models were generated using the acquired biometrical data. Irradiance maps were computed using a polar coordinates detector and compared with the HvF data.

Results: Mean axial length was 22.83 (21.05 – 24.80) mm, mean IOL power 24.4 (20.5 – 30.0) D, mean IOL tilt -1.86 (-6.21 – 2.96) degrees and mean decentration 0.16 (-0.27 – 0.44) mm. Average residual astigmatism difference between theoretical and measured data was 0.49 (0.02 – 0.97) D. Aligned with HvF data, the irradiance maps localized ND in the peripheral visual field up to 85 degrees.

Conclusions: Previously presented theoretical results evidenced that in identical biometrical conditions, IOLs from different manufacturers with similar mechanical platforms but different optic edge designs are characterized by comparable ND profiles with the peripheral location of the shadows between 69 and 76 degrees. Further expanding the utilization of these eye models, the current results demonstrate their clinical relevance in terms of PFOV localization of ND.

CONTROL ID: 3536422

SUBMITTER (NAME ONLY): Christian Mardin

TITLE: 'APSified' Bruch's membrane opening (BMO) based peripapillary OCT-A analysis

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Peripapillary OCT-A scans are a challenge for analysis as VD is dependent on demarcation of the optic disc. Longitudinal VD analysis require that each pixel of the OCT-A scan has to be at the exact same location during follow-up scans in order to see inter-visit differences. Aim of the present study was to investigate BMO-based peripapillary OCT-A analysis with and without implementation of the Anatomical Positioning System (APS; Glaucoma Module Premium Edition [GMPE], Heidelberg Engineering, Germany) compared to manual analysis in healthy eyes.

Methods: Thirty-seven eyes of 37 controls were measured twice by en-face OCT-A (Heidelberg OCT II Spectralis). OCT-A data were analyzed by the Erlangen Angio-Tool (EA-Tool, version 3.0), implementing an APS-based analysis of the peripapillary region in addition to implementation of BMO landmarks. The APS function allows alignment of OCT-A scans according to each individual FoBMOC (Fovea-to-Bruch's Membrane Opening-Center) axis. APS and BMO coordinates were exported by SP-X1902 software (Heidelberg Engineering, Germany). Peripapillary OCT-A scans were analyzed: (I) manually (circle fitted on the shortest distance of the vertical or horizontal diameter of the optic disc), (II) BMO-based, and (III) BMO-based with APS information. II and III allowed an equidistant measurement of VD from BMO. The study was approved by the local ethics committee and was done in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from each participant. Data were presented as mean \pm standard deviation. Coefficients of variation (CV) were calculated. T-tests for paired samples were done.

Results: Peripapillary mean VD was 42.7 ± 16 and 41.1 ± 19 (manually), 50.5 ± 15 and 48.8 ± 16 (BMO-based), and 44.7 ± 11 and 44.4 ± 15 (BMO-based and APSified) for 1st scan and 2nd scan, respectively. Peripapillary mean VD yielded a significant difference between the 1st and 2nd scan for manual ($p=0.02$) and BMO-based ($p=0.04$), yet not for BMO-based and APSified analysis ($p>0.05$). CV were 10.0 (manually), 8.0 (BMO-based), and 8.0 (BMO-based and APSified).

Conclusions: The novel integration of BMO landmarks into the EA-Tool allows a BMO-based peripapillary VD analysis, taking into account individual optic disc anatomy. Additional implementation of APS information increases reproducibility for longterm OCT-A studies of the peripapillary region.

CONTROL ID: 3536423

SUBMITTER (NAME ONLY): Ivan Fernandez-Bueno

TITLE: Retinal cells death rates in in vitro neuroretinal degeneration model: preliminary data

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Fernandez-Bueno, K. Puertas-Neyra, L. Hernández-Rodríguez, N. Galindo-Cabello, J. Pastor, R. Usategui-Martin, IOBA, Universidad de Valladolid, Valladolid, Castilla y León, SPAIN|I. Fernandez-Bueno, J. Pastor, R. Usategui-Martin, Oftared, Red Temática de Investigación Cooperativa en Salud (RETICS), Valladolid, Valladolid, SPAIN|

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ABSTRACT BODY:

Purpose: Neuroretina (NR) cultures are useful tools for cellular and molecular research into neuroretinal degeneration that bridges the gap between cell cultures and in vivo models. Although the degeneration of retinal cells is perfectly described at the micro and ultramicroscopic level in organotypic cultures, cell death rates have not been previously characterized. The purpose of this study was to determine if there are differences in cell apoptosis rates over time in the organotypic culture of pig NR.

Methods: NR explants (n=25) were obtained from porcine eyes (n=5; local slaughterhouse) and cultured over Transwell membranes. Cultures were maintained under standard culture conditions for 1, 3, 6, and 9 days (n=5 each). NR explants were fixed in paraformaldehyde and embedded in Tissue-Tek OCT compound. Furthermore, fresh NR explants (n=5) were processed in parallel before culturing. NR sections were immunostained for TUNEL (In Situ Cell Death Detection Kit, Roche). The apoptosis rate was calculated by counting the number of TUNEL positive elements according to the total number of nuclei (in arbitrary units; AU) and evaluated in the total NR tissue and by layers. Statistical analyses were performed using SPSS software. After confirming homogeneity of variance and normal distribution, ANOVA with Bonferroni adjustment was applied. P-values <0.05 were considered statistically significant.

Results: Total NR apoptosis rate was statistically higher in days 3, 6, and 9 of culture (all $p < 0.001$) in comparison with fresh NR (fresh NR: 0.4 ± 0.6 AU; day 1: 3.9 ± 0.6 AU; day 3: 6.2 ± 0.7 AU; day 6: 12.5 ± 2.0 AU, and day 9: 15.1 ± 1.1 AU). Besides, the apoptosis rate was statistically higher on days 6 and 9 in comparison with days 1 and 3, respectively (all $p < 0.001$). Apoptosis in the NR layers peak at day 6 in the ganglion cells layer (GCL), and day 9 in the outer and inner nuclear layers (ONL and INL), showing significant differences comparing to fresh NR and culture days 1 and 3 (all $p < 0.001$).

Conclusions: Statistically significant differences in apoptosis rates are distinguishable in the organotypic culture of pig NR over time. Early apoptosis in the GCL, in comparison with ONL and INL, could be due to the axotomy produced in this type of culture. These findings enable future research to characterize in-depth the processes of cell death by apoptosis, as well as by autophagy and necroptosis, in NR degeneration in vitro.

CONTROL ID: 3536426

SUBMITTER (NAME ONLY): Marcela Niemczyk

TITLE: The influence of IOP on the correlation of corneal speckle parameters in ex-vivo inflation experiment on porcine eyes

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Niemczyk, M.E. Danielewska, M.A. Kostyszak, D. Iskander, Department of Biomedical Engineering, Wroclaw University of Science and Technology, Wroclaw, Dolnoslaskie, POLAND|

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ABSTRACT BODY:

Purpose: To assess the effects of intraocular pressure (IOP) and duration of the ex-vivo experiment on the correlation between the parameters of the gamma distribution, used to model corneal optical coherence tomography (OCT) speckle, in porcine intact eyes.

Methods: Twenty three eyeballs were subjected to IOP from 10 to 40 mmHg with a step of 5 mmHg (Experiment 1), where a computer-controlled syringe pump allowed maintaining a stable IOP level in the anterior chamber. At each IOP level, horizontal OCT B-scans of the central 5 mm of the cornea were acquired using spectral-domain OCT (SOCT REVO). To evaluate the potential influence of duration of the experiment on the OCT speckle statistics, 10 eyeballs were maintained at the constant IOP of 15 mmHg (Experiment 2) and imaged in the same manner as in Experiment 1, to match the overall duration of the experiments (seven time-points). Spatial maps of the gamma distribution parameters, shape (v) and scale (a), were calculated from OCT scans of size 592x1592 pixels by dividing them into 21x21-pixel segments and assigning the estimated parameters to the segments' central points. For each spatial map, the Pearson's correlation coefficients ($\rho_{v,a}$) were calculated between the gamma parameters, separately for two regions of corneal stroma: central (2 mm) and non-central (the remaining part of the scan).

Results: The group mean values of $\rho_{v,a}$ (see Figure) differed statistically significantly in Experiment 1 (effect of IOP) for both central and non-central regions (rmANOVA, both $p < 0.001$) and in Experiment 2 (effect of duration) for the central region only ($p = 0.034$). Post-hoc analysis with Bonferroni correction in Experiment 2 showed no statistically significant results for any of the time-points.

Conclusions: This study shows that variation in IOP causes significant changes in the correlation between the parameters of the gamma distribution, pointing to the potential of OCT imaging technology for visualising IOP-induced changes in corneal stroma, particularly in its central part.

CONTROL ID: 3536429

SUBMITTER (NAME ONLY): Laura Whelan

TITLE: Sequencing of ABCA4 in a large international Stargardt disease cohort reveals novel pathogenic deep intronic variation and a variant enriched in Ireland.

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Stargardt disease (STGD), the most common form of inherited macular disease, is caused by mutations in the ABCA4 gene. Due to its large size, studies focusing only on exonic regions have resulted in a proportion of genetically unresolved cases. This underscores the necessity for effective sequencing and variant analysis to interrogate the entire 128-kb gene.

Methods: Single-molecule molecular inversion probe (smMIP) based sequencing of the entire ABCA4 gene and 40-kb of flanking sequence was employed for 1054 probands with STGD/STGD-like phenotypes. Most probands (833/1054) were prescreened for exonic variants but remained unresolved. Potentially splice-altering variants were assessed in vitro. 36 Irish probands were included in this cohort, with an additional 126 Irish samples having undergone smMIP sequencing of ABCA4 in a subsequent group. Analysis of the entire recruited Irish STGD cohort was carried out to detect known pathogenic deep intronic variants (DIVs). Detailed clinical examination of all individuals carrying c.4539+2028C>T was performed.

Results: 27 DIVs were identified in 448/1054 probands, 13 of which were novel. Two pathogenic variants were identified in 97/162 Irish cases. 22/97 harboured a pathogenic intronic variant, of which 12/22 carried a DIV. c.4539+2028C>T, resulting in a retina specific pseudoexon inclusion, was detected in 7/12 cases. Analysis of the entire Irish STGD cohort identified 25 individuals who carry this DIV, including two homozygotes who exhibit profound macular hypofluorescence and are the only homozygotes reported to date. In contrast, 15 other heterozygous incidences have been reported globally in STGD patients, indicating significant enrichment in Ireland. One heterozygous incidence has been found in >800 control alleles in Ireland.

Conclusions: The study highlights the importance of interrogating non-coding regions of disease genes. Unique insights into the genetic architecture of STGD in individual populations can be achieved by sequencing large numbers of international cases. Identification of individuals homozygous for intronic variants is paramount in assessing

phenotypic outcome and variant severity. Studies such as this are particularly relevant given recent advances in splice modulating therapeutics, appropriate access to which will only be possible given an accurate genetic diagnosis.

CONTROL ID: 3536431

SUBMITTER (NAME ONLY): Lynn Ebner

TITLE: Transcriptomic Analysis of the Mouse Retina after Acute and Chronic Normobaric and Hypobaric Hypoxia

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.J. Ebner, M. Samardzija, F. Storti, V. Todorova, D. Karademir, J. Behr, C. Grimm, Department of Ophthalmology, Universitat Zurich, Zurich, ZH, SWITZERLAND|F. Simpson, M. Thiersch, Institute of Veterinary Physiology, Vetsuisse Faculty, Universitat Zurich, Zurich, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Oxygen delivery to the outer retina through a continuous choroidal blood flow is crucial for cell metabolism, function, and survival. Mild but chronic conditions of reduced oxygen (hypoxia) can lead to retinal pathologies in patients, and a chronic hypoxic response in rods causes age-dependent retinal degeneration in mice. Apart from a decrease in inspired oxygen (normobaric hypoxia), hypoxia can be caused by exposure to reduced barometric pressure (hypobaric hypoxia). Since the cellular response to such chronic conditions is mostly unknown, we investigated the retinal transcriptome of mice kept for up to 11weeks in normobaric hypoxia and up to 7weeks in hypobaric hypoxia.

Methods: Wild type mice were exposed to normobaric hypoxia in a hypoxic chamber at 400m above sea level (asl) or to hypobaric hypoxia at the high-altitude research station on the Jungfrauoch (3450 masl). Bulk sequencing of retinal RNA was performed for 7 different conditions, ultimately (a) comparing acute and chronic hypoxia to normoxia, (b) investigating the adaptation to hypoxia over a timeframe of 6h, 48h and 11weeks, and (c) identifying differences between hypobaric and normobaric hypoxia. Additionally, length of photoreceptor segments was investigated.

Results: Retinas exposed to acute hypoxic conditions up-regulated gene sets involved in the response to oxygen levels, angiogenesis, ion transport, and programmed cell death. Differentially expressed genes in the hypoxic groups indicated a cellular adaptation process to chronic normobaric hypoxia. Based on their time-dependent response, we identified 23 genes which adapted within 48h and 40 genes which adapted after 11weeks of normobaric hypoxia. 7 genes however, showed an increased foldchange with prolonged exposure, suggesting that they might be key factors for phenotypic changes evoked by chronic hypoxia. A subset of 17 genes was regulated in hypobaric but not normobaric hypoxia. Shorter cone and rod segments were detected in some, but not all, hypoxic conditions.

Conclusions: This study identified differences in the genomic response to different levels and nature of hypoxia and presents data that (I) implies a high adaptability of mouse retina to chronic changes in inspired oxygen, (II) reveals differences in the retinal response to normobaric and hypobaric hypoxia, and (III) suggests that hypoxia may lead to a reduction in the length of photoreceptor segments.

CONTROL ID: 3536433

SUBMITTER (NAME ONLY): Ibraheem Shaikh

TITLE: Assessing the risk of hypopyon formation following mechanical vitrectomy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The formation of a hypopyon, a white blood cell exudate in the anterior chamber of the eye, is a previously reported but uncommon complication of mechanical vitrectomy (MV). Using a large sample population database, we investigated the impact of various clinical and non-clinical factors on the risk of developing hypopyon after MV.

Methods: Cases of MV were obtained from the National Inpatient Sample (NIS) database between 2002 and 2013. ICD-9 diagnosis and procedural codes were used to assess associated morbidities in cases with a principal procedure of MV. Perioperative complications occurring during the same operative admission were abstracted using ICD-9 codes, and secondary diagnoses of hypopyon were identified. Univariate and multivariate logistic regression analyses were carried out in cases that underwent MV to determine risk factors for the development of a hypopyon. The dataset was weighted using the NIS-provided discharge-level weights in order to achieve nationally representative estimates. The Bonferroni correction method was applied.

Results: There were 3,927 MV cases that were grouped into hypopyon (n=50, median age=76, 58% female) and non-hypopyon (n=3,877, median age=61, 49% female) cohorts. Co-morbid factors associated with increased risk of hypopyon formation included retinal vasculitis (OR=18.23), rheumatoid arthritis (OR=4.87), and tobacco use (OR=1.98). Younger age was strongly protective against hypopyon formation in the age groups 0-19 (OR=0.08), 20-39 (OR=0.10), 40-59 (OR=0.34), and 60-79 (OR=0.47) in comparison to the reference group of ≥80 years of age (Figure 1). Race, sex, and insurance status did not show statistically significant associations.

Conclusions: A large patient population was utilized to examine this rare complication following MV. We found an increased risk of hypopyon formation in cases that underwent MV with comorbidities associated with inflammatory states, including retinal vasculitis, rheumatoid arthritis, and tobacco use. Younger age was a protective factor, with an exponential increase in risk of hypopyon development associated with advancing age. Limitations of this study include the limited cases of MV in the inpatient setting, the use of a database that records cases rather than individual patients, and the limited ability to demonstrate casual relationships in a retrospective analysis.

CONTROL ID: 3536434

SUBMITTER (NAME ONLY): Sarah Thiele

TITLE: Natural history of the relative ellipsoid zone reflectivity in eyes with intermediate age-related macular degeneration

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Thiele, B. Isselmann, M. Pfau, Department of Ophthalmology, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M. Pfau, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|R.H. Guymer, C.D. Luu, Center for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|R.H. Guymer, C.D. Luu, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The relative ellipsoid zone reflectivity (rEZR) on spectral-domain optical coherence tomography (SD-OCT) imaging is a potential indicator for photoreceptor's health. The purpose of this study was to investigate the natural history of the rEZR in subjects with intermediate age-related macular degeneration (iAMD) and its association with high-risk factors of disease progression including reticular pseudodrusen (RPD) and pigmentary abnormalities (PA).

Methods: SD-OCT volume scans (49 B-scans, field size 20°x20°, collected every 6 months for 3 years) from an existing natural history cohort of AMD patients with bilateral large drusen (>125 μm) were used in this study. Using an automatic rEZR determination approach, the average rEZR of each raw SD-OCT volume was determined as the mean ratio of the ellipsoid zone (EZ) to the external limiting membrane (ELM) reflectivity (linear range of grey values: 0-1). The change in rEZR over 3 years was determined using linear regression models, adjusting for baseline age and the presence of RPD and PA.

Results: A total of 145 eyes of 145 iAMD patients (mean age: 69.8 ± 8.1 years) were included, with RPD and PA being present in 30 (21%) and 37 (26%) eyes, respectively. At baseline, the average rEZR was lower in eyes with RPD (28.9 ± 15.5, arbitrary units, AU) compared to eyes without RPD (38.7 ± 17.2 AU, p = 0.005), however, there was no significant difference in rEZR between eyes with (33.6 ± 14.2) and without PA (37.8 ± 18.2, p = 0.208). Longitudinal analysis showed that rEZR was associated with age, the presence of RPD and PA. The rEZR linearly decreased over time and that the rate of change was significantly greater in eyes with RPD (-6.66 ± 2.2 AU per 6 months) compared to eyes without RPD (-0.73 ± 0.06 AU per 6 months, p<0.001), adjusted for age and the presence of PA at baseline.

Conclusions: The rEZR decreases over time and the rate of reduction is greater in eyes with RPD, a high-risk phenotype of progression, compared to eyes without. These findings warrant further studies evaluating the rEZR as a prognostic biomarker for progression to advanced AMD.

CONTROL ID: 3536441

SUBMITTER (NAME ONLY): Avinash Gurbaxani

TITLE: The effectiveness of the ILUVIEN[®] (0.2 µg per day of mg fluocinolone acetonide) implant in the treatment of non-infectious posterior uveitis – 12-month outcomes from UAE

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The objective of this study was to evaluate the effectiveness and safety of the ILUVIEN (0.2 µg per day of mg fluocinolone acetonide [FAc]) implant (Alimera Sciences Inc., Georgia, USA) for the treatment of non-infectious posterior uveitis and to focus on the 12-month outcomes in seven patients (10 eyes) in clinical practice in the United Arab Emirates..

Methods: This prospective interventional case review surveyed consecutive patients. Ten eyes from seven patients were treated with the FAc implant for posterior uveitis at the Moorfields Eye Hospital in Abu Dhabi and Dubai, UAE between December 2018 and October 2020 . Patients were monitored for between 3 and 12 months (median, 9.0 months; 25th and 75th quartiles, 6.0 and 12.0) with best-corrected visual acuity (BCVA), central retinal thickness (CRT), vitritis and anterior chamber (AC) cell scores and intraocular pressure (IOP) being recorded.

Results: Diagnoses included panuveitis, retinal vasculitis , vitritis, pseudophakic CME / panuveitis, multifocal choroiditis, vasculitis. Prior treatment with a dexamethasone implant was done in 5 of the 10 eyes (median, 2.0 implants; 25th and 75th quartiles, 1.0 and 2.0 implants). No systemic steroids were being given at the time of FAc therapy or during the 12 months of follow-up. At Month 12, BCVA increased by 16.1±5.5 ETDRS letters (mean±SD) from a baseline of 64.5±15.8 letters (P=0.0029); CRT improved by 79.0±96.0 microns from a baseline of 370.4±101.1 microns (P>0.05); and, mean IOP was unchanged from baseline (P>0.05), remaining below a mean value of 21 mmHg at all time points upto the 12 months. Baseline vitritis score was 1.4±1.2 and improved at months 3 (-0.8±0.8), 6 (-1.0±1.0) and 12 (-2.0±0.7). At Month 12, a vitritis score of zero was observed in four of the five treated eyes. A similar response was also seen for AC cells with the mean baseline value (0.5±0.8) improving at months 3 (-0.4±0.8), 6 (-0.6±0.9) and 12 (-1.0±1.0). Adverse events included posterior capsule opacification in one eye which was managed with YAG laser. Another eye had an epiretinal membrane, but this was not related to treatment.

Conclusions: Results gained from treating patients in clinical practice in the UAE show the FA implant to be effective in the treatment of non-infectious posterior uveitis affecting the posterior segment of the eye.

CONTROL ID: 3536472

SUBMITTER (NAME ONLY): Ebenezer Chan

TITLE: Deep learning for automated quality assessment of optic disc images in neuro-ophthalmic conditions.

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Chan, Duke-NUS Medical School, Singapore, SINGAPORE|E. Chan, Z. Tang, R. Najjar, D. Milea, Singapore Eye Research Institute, Singapore, SINGAPORE|D. Milea, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|V. Biousse, N.J. Newman, Emory Eye Center, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Existing automated retinal image quality assessment (RIQA) models, commonly trained on diabetic retinopathy (DR) images, have limited applicability to neuro-ophthalmic conditions (e.g., papilledema, ischemic optic neuropathy (ION), etc.). Their inconsistent performance is due to the appearance of the abnormal optic disc (swelling, atrophy, etc). Hence, our aim was to develop a new automated RIQA system that can predict, without human intervention, if a fundus image has an acceptable image quality for subsequent evaluation of the optic nerve head (ONH).

Methods: A total of 2,082 fundus images obtained from the EyeQ, a publicly available DR data set, and 5,208 images collected within the Brain and Optic Nerve Study with Artificial Intelligence (BONSAI) Consortium data set (total of 486 ION, 1,644 papilledema, 832 optic atrophy, 559 DR, and 3,769 normal fundoscopic images) were segmented for their ONH region and given quality-labels by a trained human classifier. The data set was divided proportionally into images used for training (80%) or testing (20%). A dedicated deep-learning system (EfficientNet-B5 CNN), was trained to automatically perform a binary quality classification of retinal images (i.e. "Acceptable" or "Rejected"). The classification performance of our RIQA was evaluated by calculating the area under the receiver operating characteristic curve (AUC), accuracy, sensitivity, and specificity.

Results: Using 5-fold cross-validation on the training data set, our model classified ONH segmented fundus images into "Acceptable" vs "Rejected", yielding an average AUC of 0.982, accuracy of 94.2%, sensitivity of 93.3%, and specificity of 94.6%. When tested against the testing data set for external validation, our model achieved an average AUC of 0.982, accuracy of 92.6%, sensitivity of 93.9%, and of specificity 92%.

Conclusions: An automated deep learning system trained on digital color images of normal and abnormal optic discs due to various optic neuropathies can discriminate between acceptable and poor image quality. Further developments will aim to provide instantaneous image quality evaluation coupled to fundus cameras and/or independent deep learning-based diagnostic algorithms.

CONTROL ID: 3536491

SUBMITTER (NAME ONLY): Stefan Ploner

TITLE: Improved OCT motion correction in pathology using advanced eye motion modeling

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Patients of higher age or with reduced acuity exhibit increased involuntary eye motion during fixation. This causes distortion and gaps in optical coherence tomography (OCT) and OCT angiography (OCTA), which can substantially complicate qualitative and quantitative image analysis. We evaluated whether motion correction in late-stage age-related macular degeneration (AMD) can be improved by advanced motion modeling.

While a multitude of correction approaches exist, their accuracy and reliability in pathology is insufficient for the high resolution of OCT due to (1) toleration of implausible displacement estimates that limit distortion correction, (2) independent displacement estimation of A- or B-scans that is unreliable in areas with few features, sequential correction procedures where (3) initial steps lack correction of following ones and require (4) superfluous resamplings that cause interpolation artifacts, and (5) use of inaccurate features.

Methods: Our from-scratch redesigned motion model estimates (1) plausible, (2) closed motion trajectories throughout each volume-scan that map A-scans to their correct position in a single mapping (3, 4) based on the similarity of the OCT data itself (5). 3-D displacements and tilt along the transverse directions were parameterized with a Hermite B-spline along acquisition time. Further key features include regularization for continuity, gradient descent optimization, OCTA white line removal, and preliminary illumination normalization.

Evaluation is ongoing. To date, we evaluated on data of 14 eyes (Table 1) that covers a 3x3 mm (1) or 6x6 mm (13) field around the fovea with a 500x500 orthogonal raster scan (5 B-scan repeats, 3.7 s acquisition) from a prototype 400 kHz swept source OCT device.

Results: Compared to our previous motion correction scheme, inter-scan consistency improved further, and, if present, tilt inaccuracies and motion-induced blurring and double vessels were significantly reduced. However, lack of proper illumination correction compromised the benefits in 2 volumes.

Conclusions: Correct modeling of eye motion can significantly reduce motion-induced artifacts. While broader evaluation is indicated to prove generalization, already using only OCT data improved reliability beyond our combined OCT + OCTA approach based on the previous motion model.

CONTROL ID: 3536492

SUBMITTER (NAME ONLY): Bo Tian

TITLE: Suprachoroidal Injections of AAV for Retinal Gene Delivery in mouse

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tian, J. Xie, W. Su, S. Sun, Q. Su, G. Gao, H. Lin, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|B. Tian, H. Lin, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recombinant Adeno-Associated Virus (AAV) gene therapy has remarkably advanced in the treatment of retinal diseases due to its safety and efficacy. Each of the AAV administration routes of delivery to the retina confers unique advantages and limitations. Intravitreal delivery is hindered by the internal limiting membrane barrier for primates, and induces humoral immune response, while subretinal delivery necessitates invasive surgery and generates retinal detachment. In contrast, suprachoroidal (SC) injection, targeting the space between the sclera and choroid, is emerging as a novel approach to deliver AAV into the posterior segment of the eye with least invasive procedure, but this route has not been fully elucidated in mouse model for different AAV serotypes. Here, we investigated the transduction efficiency, cell tropism and bio-distribution in mouse retina, for three serotypes of AAV via SC administration.

Methods: EGFP reporter gene driven by the ubiquitous promoter CBA was packaged in three conventionally used AAV serotypes. In 12-week old C57BL/6J mice, SC inject 1.0µl Fluorescein Sodium (1.0 x 10E-6 %) or the three scAAVs-CBA-EGFP solution respectively. Retinal structure was imaged pre-, post-injection and 1.5 weeks post-injection by funduscopy and optical coherence tomography (OCT). Transduction efficiency and tropism was assessed 1.5 weeks post injection by funduscopy and histology. Immune response was evaluated by immunostaining for Iba1 macrophages, CD45+ leukocyte and CD3+ T cells.

Results: The retina structure was tracked and shown the successful injection into the suprachoroidal compartment. Transduction of outer retina, and retinal pigment epithelium was observed with these three AAV serotypes by SC delivered, and 3 AAVs displayed varied efficiency and cell specificity. Meanwhile, the activation of inflammatory cells was observed pending on doses adopted. To be noted, retinal detachment was successfully evaded, together with a widespread distribution of the transduction in mouse retina layers.

Conclusions: This study unveils the feasibility of SC injection in mouse, facilitating the proof-of-concept and pre-clinical studies of retinal gene therapy in mouse models. Without the complications of retinal detachment, SC administration is a preferred route to deliver AAV into outer retina layers in comparison with subretinal route. SC injection can serve as an alternative intraocular delivery method of AAV.

CONTROL ID: 3536502

SUBMITTER (NAME ONLY): Camille Guerin

TITLE: Management of oxidative stress and inflammation in dry eye disease patients treated with a preservative free ophthalmic emulsion eye drop combining lipoic acid and sodium hyaluronate

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Guerin, L. Chauchat, M. Sahyoun, M. Claret, Horus Pharma, FRANCE|M. Guillon, OTG, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Recent papers highlight an important role played by oxidation and inflammation in dry eye disease (DED), mainly with over-exposure to screens and air-conditioned environments; but very few DED treatments target both factors. We performed a prospective, non-randomized, investigator masked study to assess the beneficial effect of a preservative free (PF) ophthalmic emulsion eye drop combining lipoic acid (LA), a well-known anti-oxidant agent, with high-molecular weight sodium hyaluronate (HMW HA), in the management of DED with regard to these two stresses.

Methods: 40 symptomatic moderate to severe DED patients were treated with a PF ophthalmic emulsion combining LA and HMW HA (4-6 times/day) for 35 days. Two visits were scheduled (D0&D35) to assess: quality of life (QoL; OSDI score); tears antioxidant levels of superoxide dismutase (SOD); ocular surface inflammation (conjunctival hyperemia); goblet cell (Gc) morphology (conjunctival impression cytology); and conjunctival staining (Oxford score). Subgroup analysis was initially planned considering the different DED etiologies. Statistical analysis was performed (D35 vs D0; paired t-test and Wilcoxon; $p < 0.05$).

Results: At D35, the OSDI score improvement was highly significant for all patients ($p < 0.01$). In the subgroup with deficient levels of antioxidants at D0 ($n=13$), a significant increase in both SOD1 ($p=0.01$) and SOD2 ($p=0.02$) was observed at D35. Total hyperemia decreased significantly in the subgroup of patients with the most severe inflammation at baseline (grade ≥ 2 ; $n=19$; $p=0.04$). For patients whose DED was associated with marked Gc anomaly at D0 ($n=13$), both cell density and thickness were significantly improved at D35 ($p=0.002$ and $p=0.003$, respectively). Oxford score was at the limits of significance in the subgroup of patients with notable anomalies at D0 (grade ≥ 6 ; $n=34$; $p=0.07$).

Conclusions: Regardless of the DED etiology, the use of a PF ophthalmic emulsion combining LA and HMW HA shows a beneficial effect on the ocular surface through the improved QoL score. Noteworthy, in patients presenting high oxidative and inflammatory conditions, significant improvement is highlighted on oxidative stress and inflammation markers; this synergic effect is likely due to the well-known properties of LA and HMW HA, enhancing DED management in environmental stress.

CONTROL ID: 3536503

SUBMITTER (NAME ONLY): Allen Cheong

TITLE: How does lighting and visual task affect gait performance in patients with severe peripheral visual field loss?

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Cheong, H. Lam, V. Suen, C. Tsang, M. Cheung, G. Woo, The Hong Kong Polytechnic University, Kowloon, HONG KONG|J. Cho, Hong Kong Society for the Blind, HONG KONG|J. Kwan, UDA Consultants Ltd, HONG KONG|L.A. Abel, Deakin University, Burwood, Victoria, AUSTRALIA|W. Tsang, The Open University of Hong Kong, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: In our daily life, we might walk under different challenging conditions, such as engaging in visual search or adapting to different lighting levels. These challenges might impose more fall risk to visually-impaired patients. This study was aimed to investigate the possible impact of visual search and lighting on walking in patients with peripheral field loss (PFL).

Methods: Five participants with binocular visual field less than 10° and 5 age-matched healthy controls were recruited. All participants were required to walk a 4-metres obstacle-free pathway at self-pace and step on a force platform at the end of pathway under 3 different lighting levels (100, 520 and 2100 lux). Six monitors were placed at two-metres away from the force platform in an arc-shape to cover ~120° field of view. While walking, they either fixated at a stationary cross or performed a visual search task by identifying a target among 5 distractors shown on the monitors. Inertial measurement unit synchronized with a high-speed camera were used to measure the changes of gait pattern in temporal parameters, including swing phase (%), double support (%), cadence (step/min) and average walking speed (cm/sec).

Results: Visual search task significantly affected the gait pattern, with reduced swing phase (Fix: 36.0%±1.8 vs Search: 35.3%±2.0; $p<0.01$) and increased double support (Fix: 26.7%±3.4 vs Search: 28.2%±3.8; $p=0.01$). It also significantly decreased cadence (Fix: 106±11 vs Search: 103±13 step/min) and average walking speed (Fix: 88.8±12.1 vs Search: 82.2±13.8 cm/s; $p<0.01$). Furthermore, significant interaction effects between group and visual task were found in cadence and average walking speed ($p<0.05$), showing that search task affected the temporal domain of gait in patients with PFL. However, no significant effect of lighting or interaction effect between lighting and group ($p>0.05$).

Conclusions: In this preliminary study, search task caused significant changes in the walking pattern in people with PFL. In contrast, environmental changes due to different lighting conditions did not show significant impact on the gait. Further study is needed to examine the causal relationship between the change of the walking pattern due to search task and the incidence of falls in this population and whether the mobility performance will be further compromised when patients need to negotiate obstacles during walking.

CONTROL ID: 3536505

SUBMITTER (NAME ONLY): An Beckers

TITLE: Intraneuronal energy reshuffling by mitochondrial dynamics drives injury-induced axonal regeneration in adult zebrafish

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Beckers, A. Van Dyck, L. Masin, S. Bergmans, L. Andries, L. De Groef, L.K. Moons, Biology, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|

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ABSTRACT BODY:

Purpose: Neuroregenerative research largely focuses on improving axonal regrowth, leaving dendrites mostly unstudied, despite their importance for neural circuit functioning. We previously determined the dendritic response of retinal ganglion cells (RGCs) during axonal outgrowth after optic nerve crush (ONC) in regeneration-competent adult zebrafish and revealed an antagonistic axon-dendrite interplay, wherein early dendritic retraction boosts axonal regrowth and RGC dendrites only regenerate after target innervation in the brain. One underlying mechanism might be an intraneuronal energy trade-off that prevents simultaneous axonal regrowth and maintenance/regrowth of dendrites. To test this idea, we focused on mitochondria, increasingly recognized to exert a critical role in axonal regeneration.

Methods: The mitochondrial distribution within RGC dendrites, axons and somas was characterized at several time points after ONC, using retinal flat mounts of mitochondrial reporter fish and a Python script. Cryosections were used to localize the mitochondria inside the optic nerve and optic tectum. To study mitochondrial dynamic changes upon injury, IHC and WB for biogenesis, fission, fusion and mitophagy markers were used.

Results: Early after ONC, mitochondrial numbers strongly decreased in the RGC dendrites as well as in their axonal projection areas in the optic tectum, concomitant with dendrite retraction and axonal degeneration in retina and tectum, respectively. Mitochondria re-appeared first in tectal RGC axons at the moment of reinnervation and in the RGC dendrites upon their repair. Regarding mitochondrial dynamics, a biphasic upregulation of biogenesis was found, respectively before the start of axon/dendrite regrowth, suggesting a role of the new mitochondria within these processes. While the level of fusion remained unchanged during the complete regenerative process, fission was strongly increased after ONC during dendritic retraction and axonal regrowth, as well as mitophagy.

Conclusions: The timed dendrite-axon-dendrite mitochondrial translocation after ONC fits the hypothesis that dendritic mitochondria reshuffle energy to the axons to boost repair, and that dendrite regrowth is aided by a return of mitochondria to the retina. Overall, our findings could generate pivotal insights into how re-directing intraneuronal energy channeling may promote neuronal repair in the CNS.

CONTROL ID: 3536508

SUBMITTER (NAME ONLY): Petra Rausch - Koster

TITLE: Prognostic Factors of Vision-related Quality of Life in Patients with Exudative Retinal diseases

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Rausch - Koster, Ophthalmology, Bergman Clinics BV, Naarden, Noord-Holland, NETHERLANDS|P. Rausch - Koster, K. Rennert, R.M. Van Nispen, F.D. Verbraak, G. van Rens, Ophthalmology, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|G. van Rens, Ophthalmology, Elkerliek Hospital, NETHERLANDS|

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ABSTRACT BODY:

Purpose: It is known that clinical factors such as visual acuity do not fully predict vision-related quality of life (VrQoL). Therefore, recognizing patients in need of additional support, e.g. early referral to low vision services, may be challenging for ophthalmologists during busy consultation hours. The aim was to determine which demographic and clinical characteristics are predictive of VrQoL in patients receiving intravitreal anti-vascular endothelial growth factor (VEGF) treatment for macular edema due to exudative retinal diseases.

Methods: Patients (n=712) were recruited from nine different locations of Bergman Clinics in The Netherlands. VrQoL was measured at baseline, 6 and 12 months using a newly developed itembank (EYE-Q) consisting of 47 items measuring VrQoL. The selected demographic characteristics potentially predictive of VrQoL were sex, age, civil status, education, employment status, and presence of non-ocular and ocular comorbidities. Selected clinical characteristics were visual acuity (VA), number of treated eyes, length of intravitreal anti-VEGF treatment, number of intravitreal anti-VEGF injections. Multivariate regression analysis was performed, using a forward selection procedure. The model was internally validated using the heuristic shrinkage factor.

Results: The study population included 344 male participants (48.3%). Mean age was 76.2 years. The majority of participants were diagnosed with exudative age-related macular degeneration (63.3%) and 81.9% received one-sided treatment with anti-VEGF. Most participants (92.4%) had a VA of the better eye equal to or better than 0.5 LogMAR. Factors predictive of a lower VrQoL were a poorer LogMAR VA of the better eye (β 0.97, 95% CI 0.378 to 1.17), female sex (β 0.31, 95% CI 0.18 to 0.45), living alone (β 0.24, 95% CI 0.09 to 0.39), older age (β 0.01, 95% CI 0.00 to 0.02), a longer length of intravitreal anti-VEGF treatment at baseline (β 0.06, 95% CI 0.01 to 0.11), and the presence of non-ocular and ocular comorbidities (β 0.21, 95% CI 0.08 to 0.35 and β 0.13, 95% CI 0.03 to 0.24). The heuristic shrinkage estimate was 0.96.

Conclusions: Visual acuity appeared to be the strongest predictor of VrQoL in patients with macular edema receiving intravitreal anti-VEGF treatment, however other patient characteristics must also be considered for the risk assessment of low VrQoL and may be a reason for referral to low vision services.

CONTROL ID: 3536519

SUBMITTER (NAME ONLY): Vivien Coulson-Thomas

TITLE: Role of Hyaluronan on Aging Meibomian Glands

SESSION TITLE: Lacrimal gland and Meibomian gland

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.J. Coulson-Thomas, M. Sun, I. Moreno, K.N. Mutoji, T.F. Gesteira, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|T.F. Gesteira, Optimvia, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Meibomian gland (MG) produces the lipid layer of the tear film, and changes to the MG that lead to a decrease or alteration in lipid quality/content may lead to MG dysfunction (MGD), a major cause of evaporative dry eye disease with prevalence ranging from 39% to 50%. We have previously shown that hyaluronan (HA) regulates MG morphogenesis and homeostasis. We hereby investigated the role of HA in aging MGs.

Methods: Combined hyaluronan synthase (Has) 1 and 3 null mice, namely Has1^{-/-};Has3^{-/-}, and wild-type mice were used to determine the role of HA in the aging eyelid and MGs. Eyelids were obtained and analyzed at 6 months and 1 year of age. MG morphology, volume, lipid production and HA distribution were analyzed. Susceptibility to developing dry eye disease (DED) was also evaluated.

Results: At 6 months of age, wild-type mice presented a small number of atrophic glands, whereas Has1^{-/-};Has3^{-/-} mice did not present any atrophic glands at this same time point. At 1 year of age, wild-type mice presented ~15 atrophic glands, whereas Has1^{-/-};Has3^{-/-} mice still did not present any atrophic glands at this same time point. Has1^{-/-};Has3^{-/-} mice presented a 5-fold increase in MG volume and a 3-fold increase in lipid production per area at 1 year. Consequently, Has1^{-/-};Has3^{-/-} mice presented resistance to developing DED. Importantly, as previously shown, mice lacking the enzymes Has 1 and 3 up-regulated Has 2, and, consequently, presented an increase in HA throughout the tarsal plate and MGs at both time-points analyzed.

Conclusions: An increase in HA production within the tarsal plate is able to prevent MGD in aging mice, which in turn, makes these mice resistant to DED when compared to aged-matched wild-type mice.

CONTROL ID: 3536542

SUBMITTER (NAME ONLY): Sonisha Neupane

TITLE: Accommodation and vergence conflict in young hyperopes

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Neupane, C. Mestre, K.S. Connolly, D.W. Lyon, T. Candy, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|Y. Wu, V. Sreenivasan, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Young children with hyperopia must accommodate more than a typical adult to achieve focused retinal images and promote typical visual development. In coordinating the coupling between accommodation and vergence they could underaccommodate to the target to maintain alignment, accommodate and converge relatively accurately, or accommodate accurately but over-converge leading to esophoria (with good fusional divergence) or esotropia. This study looked at the accommodation, vergence and fusional abilities of young uncorrected hyperopes.

Methods: A PlusOptix PowerRef3 (Simultaneous Purkinje image eye tracking and eccentric photorefractometry) recorded the alignment and refractive state of 20 hyperopic children (0-10 yrs; Sph. Equiv. refractive error: +2.25 to +6.50D) and 49 control participants (0-10 yrs; Sph. Equiv. refractive error: -0.25 D to +2.00 D) while they viewed cartoon movies at 33cm. Accommodative performance and vergence position were determined in monocular and binocular conditions and prism bars were introduced to drive fusional vergence. Fusional limits were defined as the last prism for which alignment was maintained and, in each case, the role of accommodation was assessed simultaneously.

Results: The median accommodative error was 1.6D lag for hyperopes (range: 0.50D lead to 4.3D lag) and 1.5D lag for the controls (range: 0.80D lead to 3.5D lag) at 33 cm. The median phoria was 1pd exophoria for hyperopes (range: 2pd esophoria to 5pd exophoria) and 3pd exophoria for controls (range: 9pd esophoria to 8pd exophoria). The median fusional vergence ranges in the hyperopic group were 16 pd of divergence (range: 4-32 pd) and 24 pd of convergence (range: 12-40pd) which were similar to the control group (16 pd of divergence, range: 4-24pd & 20pd of convergence, range: 20-40pd). In the hyperopic participants, the median relaxation of accommodation was 1.2D during divergence with a median increase of 1.2D during convergence. The median changes in the control group were 1.7D relaxation of accommodation during divergence and median increase of 1.2D during convergence. These values were less than predicted by a typical AC/A ratio.

Conclusions: Most of the hyperopes had a small exophoria and a typical accommodative lag. Their fusional range and ability to manipulate accommodation to achieve fusion were also clinically similar to the control group. They seemed able to accommodate typically and maintain alignment for this task.

CONTROL ID: 3536546

SUBMITTER (NAME ONLY): Yesa Yang

TITLE: Quantification of color vision impairment in RPGR-associated Retinitis Pigmentosa

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Disease-causing variants in RPGR (retinitis pigmentosa GTPase regulator) account for 70-90% of cases of X-linked Retinitis Pigmentosa (RP) and is currently the subject of multiple ongoing clinical trials. We sought to determine the extent of cone function impairment by assessing color discrimination.

Methods: Twenty four subjects (23 adults, 1 child; aged 14 – 35) with RPGR-associated RP were assessed using the Trivector component of the low vision version of the Cambridge Colour Test (IvCCT). Contrast sensitivity (CS) using the Pelli-Robson chart and best corrected visual acuity (BCVA) were also evaluated. A subset of 15 subjects additionally undertook testing with the Ellipse component of the IvCCT and the American Optical Hardy Rand Rittler (AO-HRR) plates. Tests were performed monocularly in both eyes and repeated three times.

Results: Testing with IvCCT demonstrated a wide range of color discrimination abilities in the study group, from near normal to severe impairment. The median saturation threshold along the protan, deutan and tritan axes, as assessed by the Trivector assessment were: 19.8, 21.4 and 55.7 respectively. The median ellipse area was 2212.7. (For comparison, a normal trichromatic subject has a saturation threshold of less than 10 in all three axes and ellipse area smaller than 340.)

Color discrimination along the tritan axis was the most severely affected, indicated by both IvCCT components used. Out of the three axes, saturation threshold along the tritan axis correlated most strongly with both BCVA [Pearson correlation coefficient (PCC) = -0.69, $p < 0.001$] and CS (PCC = -0.74, $p < 0.001$). PCC for ellipse area with BCVA and with CS was -0.57 ($p = 0.026$) and -0.66 ($p = 0.007$) respectively.

Both Trivector and Ellipse assessments also correlated with performance using AO-HRR plates, indicating consistency across methods [PCC of minimum -0.77 across three axes ($p < 0.001$) and -0.81 ($p < 0.001$)] respectively.

Conclusions: Both the Ellipse and Trivector components of the IvCCT are able to identify mild to severe color vision impairment in a group of genetically confirmed RPGR-associated RP subjects. The preponderance of tritan axis impairment suggests early loss of S-cone function in the disease. The monitoring of color vision with such methods provides information about cone function and disease progression, which may prove useful when assessing the efficacy of novel therapies.

CONTROL ID: 3536551

SUBMITTER (NAME ONLY): Mei ZHAO

TITLE: Peripheral contrast discrimination in high myopia

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Myopic retinal stretching enlarges the space between retinal cells and increases the critical area for spatial summation, potentially leading to a remodeling of neural contact. Thus, this study aimed to investigate the effect of high myopia on contrast discrimination at the fovea and peripheral retina.

Methods: Thirty-six young participants (aged 19 to 41 years), including 17 high myopes (HM, spherical equivalent: -15.00 to -8.88D) and 19 emmetropes (EM, spherical equivalent: -0.63 to 1.00D), were recruited. Monocular threshold versus pedestal contrast (TvC) curves were generated at the fovea, 10° and 20° temporal retina across eight pedestal contrasts (0.1%, 0.32%, 1%, 3.2%, 5.6%, 10%, 17.8%, 32%). The contrast increment threshold at each pedestal level was determined from three-down-one-up staircases in a two-interval-forced-choice paradigm. Vertical Gabor patches (2 cycles per degree) generated by Psykinematix were used as the visual stimuli. Contrast detection thresholds (i.e., 0% pedestal contrast) were also measured for normalizing the TvC curves. The contrast increment and detection thresholds for the fovea and 10° temporal retina were tested at 2 meters and 20° temporal retina at 1 meter. The slopes of the TvC curve from 3.2% to 32% pedestal levels in log-log coordinate and the normalized contrast increment thresholds were compared between the two groups.

Results: The normalized foveal TvC curves of HM and EM were highly overlapped, and both reached their trough at approximately 1% normalized pedestal contrast, i.e., when the tested pedestal contrast was close to the detection threshold. In contrast, the peripheral TvC curves of HM were slightly elevated, especially at 0.1%, 0.32%, and 1% pedestal contrast tested at the 20° temporal retina. The difference in increment threshold at 1% pedestal contrast reached a significant level (median in HM vs. EM, 1.98% vs. 1.24%, $p=0.035$). No significant between-group difference in the slopes of the TvC curve were found at the fovea (median in HM vs. EM, 0.82 vs. 0.81, $p=0.60$), 10° (0.78 vs. 0.71, $p=0.14$), or 20° retina (HM vs. EM, 0.72 vs. 0.72, $p=0.32$).

Conclusions: Opposing to our hypothesis, retinal stretching in HM did not affect the foveal contrast discrimination. However, it appeared to diminish the facilitation effect of the TvC function in the peripheral retina, which might be due to the alteration in spatial pooling at low contrast.

CONTROL ID: 3536556

SUBMITTER (NAME ONLY): Florian Peters

TITLE: Downregulation of ABCA1 in iPSC-derived RPE cells impaired cholesterol efflux leading to intracellular lipid accumulation

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a progressive disease of the macula that at advanced stages leads to blindness in the elderly population. While the neovascular form is characterized by choroidal blood vessels invading the retina, the dry form leads to atrophy of the retinal pigment epithelium (RPE) and degeneration of photoreceptors. Genes involved in lipid metabolism, including ATP-binding cassette transporter A1 (ABCA1) were associated with AMD through genome-wide association studies. ABCA1 is strongly expressed in the RPE and required for lipid metabolism and export. AMD-associated genetic variants near the ABCA1 gene were shown to modulate its expression in patient-derived lymphoblastoid cell lines, suggesting that these variants may lead to disturbed lipid transport in the human RPE.

Methods: Patient induced pluripotent stem cells (iPSC) harboring homozygous ABCA1 genotypes for increased (rs1883025:C and rs2740488:A) or decreased (rs1883025:T and rs2740488:C) risk for AMD were differentiated into RPE. These iPSC-RPE cells were analyzed for ABCA1 gene and protein expression, their ability to phagocytize photoreceptor outer segments (POS) and the efficiency of cholesterol efflux. Experiments were conducted under normoxic and hypoxic (4% O₂) conditions to mimic the physiological conditions in the ageing eye. Furthermore, ABCA1 expression and function was also examined after Liver X receptor (LXR) agonist treatment, a regulator of cholesterol homeostasis.

Results: iPSC-derived RPE cells showed similar gene expression and morphological characteristics of RPE cells in vivo. Interestingly, hypoxia-treated RPE cells exhibited reduced ABCA1 expression and dysregulation of several hypoxia-associated genes (e.g. PDK1 and ADM). Diminished ABCA1 expression was also observed in increased risk genotype-bearing iPSC-RPE cells treated with an LXR agonist compared to iPSC-RPE cells carrying the reduced risk ABCA1 genotype. Subsequently, the lack of ABCA1 expression hampered cholesterol efflux, leading to lipid accumulation in iPSC-RPE cells.

Conclusions: In conclusion, this study points towards a functional effect of AMD-associated genetic variants in ABCA1 on cholesterol efflux in iPSC-RPE cells and suggests that this model system may be used to study the mechanism of altered lipid metabolism in the development of AMD.

CONTROL ID: 3536565

SUBMITTER (NAME ONLY): Taha Soomro

TITLE: Visual acuity and intraocular pressure measurements: Is there a systemic bias in measurement? A UK multicentre study

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Soomro, D. Thomas, R. Schwartz, A. Warwick, A. Olvera-Barrios, G. Gazzard, A. Tufail, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To assess whether there is a bias towards certain visual acuity (VA) values when using an EDTRS logMAR chart and intraocular pressure (IOP) measurement using Goldmann Applanation Tonometry (GAT).

Methods: This study involved VA and IOP data from 27 secondary care providers in the UK using the medisoft electronic medical record (EMR) platform and from the UK BioBank Eye and Vision Consortium (UKBB). Trial data was used from the ABC and LIGHT trial. LogMAR VA values were compared per line, from letter position 1-5 using the remainder modulus (RM) and IOP devices including GAT, iCARE, Tonopen and Airpuff were analysed in the EMR data, as well GAT IOP data from the LIGHT trial and ocular response analyser (ORA) data from the UKBB. Chi-squared tests comparing the frequency of RM 1-5 for LogMAR VA, as well for IOP for all devices was performed for all the data.

Results: There was significantly unequal distribution between the letter positions, which favoured RM 5 in our EMR data ($1=209295$, $2=10368$, $3=113341$, $4=122606$, $5=425664$, $X^2(4,N=974,592)=377889.8$, $p<0.001$). The UKBB also confirmed a significantly unequal distribution of values per RM on the LogMAR chart ($1=8759$, $2=14000$, $3=18014$, $4=11641$, $5=13472$, $X^2(1,N=65,886)=14292$, $p<0.001$). Comparatively the ABC trial did not show any significant difference in the frequency of RM positions ($1=255$, $2=277$, $3=314$, $4=269$, $5=285$, $X^2(4,N=1400)=6.941$, $p=0.141$). EMR data showed a significantly unequal distribution in even vs. odd IOP values for GAT compared to other IOP measuring devices (even/odd, GAT $83129/489324$, iCARE $307929/288118$, Tonopen $262890/255362$, Airpuff $8776/66882$, $X^2(3,N=2,510,935)=96863.010$, $p<0.001$). Similarly, the LIGHT trial showed there was significantly unequal distribution for IOP values when using GAT (even/odd, $6433/4642$, $X^2(1,N=718)=292.61$, $p<0.001$). UKBB showed a small but statistically significant unequal distribution between values using ORA (even/odd, $32288/31731$, X

$\chi^2(1, N=64,109)=4.865, p=0.028$).

Conclusions: LogMAR VA had a significantly unequal distribution and GAT IOP values were significantly more likely to be even in our EMR data set. These findings were backed up by UKBB and trial data. This rounding of LogMAR VA and GAT IOP could be due to examiner bias. Outcomes of this study may have consequences in clinical practice and therapeutic trials may require greater scrutiny.

CONTROL ID: 3536569

SUBMITTER (NAME ONLY): Paolo Silva

TITLE: Intergrader Agreement for Diabetic Retinopathy (DR) using Hand-Held Retinal Imaging

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess intergrader agreement when interpreting retinal images acquired with handheld retinal imaging devices for DR screening.

Methods: Mydriatic retinal images acquired using 3 hand-held retinal cameras [Aurora (AU), Smartscope (SS), RV700 (RV)] were compared with Early Treatment Diabetic Retinopathy Study 7-field standard photography (ETDRS photos). All handheld retinal images were independently evaluated by 2 grader-certified nonphysician staff and 1 retina specialist (RPS). The ETDRS photos were evaluated by a senior retina specialist (PSS). All graders had completed a structured certification program in DR assessment. Grading was performed using the International Classification for DR. Agreement was measured using kappa (κ) statistics, multirater κ across graders and sensitivity/specificity was calculated for vision threatening DR [(vtDR): severe NPDR or worse].

Results: Images from 177 eyes of 92 patients with diabetes were evaluated. Severity by ETDRS photos: no DR 40.1%, mild NPDR 19.2%, moderate 14.7%, severe 10.2%, proliferative DR 15.8%. Ungradable rate for DR was AU: 0%; SS: 4.5%; RV: 4.0%; and ETDRS: 0%. Results are presented in table 1. Multirater κ for DR severity (0.58 – 0.65) and vtDR (0.71 – 0.74) was uniform across all devices. Agreement (κ) for DR severity between ETDRS photos and graders was similar across nonphysician graders across devices (0.46 – 0.48) and highest with retina specialist evaluation across devices (0.70-0.78). Sensitivity/specificity for vtDR on ETDRS photo for nonphysician graders was over 0.95 in all devices but specificity was 0.87-0.89. Retina specialist specificity for vtDR was 0.96-0.97.

Conclusions: In assessing DR severity, substantial over-all agreement (0.58-0.74) among all graders was achieved emphasizing the benefit of a structured program of grading certification. Retinal images obtained using all 3 handheld cameras achieved the highest agreement with ETDRS photos (0.70-0.78) when evaluated by a retinal specialist. Among the nonphysician graders for all devices, sensitivity for vtDR was over 90% but specificity remained 87-89%. These findings suggest that in DR screening programs using hand-held retinal imaging, secondary grading of eyes with vtDR by more experienced graders may be necessary to minimize unnecessary referrals that would otherwise decrease the effectiveness of screening programs.

CONTROL ID: 3536577

SUBMITTER (NAME ONLY): Eunice Cheung

TITLE: Intravitreal administration, but not systemic administration, of VEGF Mini-Trap effectively inhibits neovascularization in the Oxygen Induced Retinopathy (OIR) in mice

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Cheung, J. Cao, C. Romano, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vascular Endothelial Growth Factor (VEGF) plays an essential role in normal and pathological angiogenesis. Aflibercept is a potent VEGF inhibitor that binds all isoforms of VEGF-A as well as the VEGFR1 ligands placental growth factor (PlGF) and VEGF-B. When administered systemically (IP) or intravitreally (IVT), VEGF Trap effectively blocks pathological retinal neovascularization in OIR model (IOVS 2006; 47:E-Abstract 1750; IOVS 2011:E-Abstract 3210). In this study, we evaluated the effects of aflibercept (full length) in comparison to VEGF Mini-Trap (REGN7483, Fc cleaved aflibercept) in the murine OIR model.

Methods: C57Bl6 mouse pups were placed in a hyperoxic environment (75% O₂) at postnatal day (P)6 and returned to room air at P11. Study 1 (IVT Screen Study): OIR pups were injected IVT with human Fc 0.25µg, aflibercept 0.125µg, or REGN7483 0.125µg, respectively, at P13 and collected at P16. Study 2 (IVT Dose Response Study): OIR mice were injected IVT with Fc 0.25µg, REGN7483 at 0.025µg, 0.25µg, and 2.5µg, or aflibercept at 0.05µg, 0.5µg, and 5µg at P13 and collected at P16. Study 3 (IP Study): OIR mice were injected IP with Fc 5mg/kg, aflibercept 10mg/kg, or REGN7483 at 5mg/kg, 15mg/kg, and 50mg/kg, respectively, at P12 and collected at P16.

Results: Study 1: Although at equimolar doses IVT Fc, aflibercept, and REGN7483 showed similar avascular areas, aflibercept and REGN7483 notably reduced neovascular tufts compared to Fc. Study 2: IVT aflibercept and REGN7483 reduced tufts in a dose-dependent manner, compared to Fc. There were no differences in abnormal area between aflibercept and REGN7483 at matched molar doses. Study 3: IP aflibercept resulted in a significant tuft reduction, compared to Fc and all REGN7483 groups.

Conclusions: These studies in mice show that VEGF Mini-Trap administered IVT and not systemically demonstrated anti-angiogenic activity. These studies validate that VEGF Mini-Trap dose-dependently inhibits pathological neovascularization. These studies also document the equipotency of intravitreal VEGF Mini-Trap with intravitreal full-length aflibercept. The lack of systemic efficacy of Mini-Trap is likely due to more rapid clearance systemically, although this study did not directly measure PK.

CONTROL ID: 3536588

SUBMITTER (NAME ONLY): Aneesha Kalur

TITLE: Relationships between Intraretinal and Subretinal Fluid in Patients with Diabetic Macular Edema Treated with Anti-Vascular Endothelial Growth Factors

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kalur, A. Iyer, J. Muste, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R.P. Singh, Ophthalmology i-32, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is characterized by an increase in retinal thickness and anti-Vascular Endothelial Growth Factor (VEGF) injections decrease macular fluid volume to improve outcomes. Improvement in retinal volume by OCT is used both as an indicator of disease control and the variability in treatment response is considered a poor prognosis for visual acuity (VA). The purpose of this study was to track retinal fluid volume fluctuation and discern prognostic patterns to indicate positive and negative treatment outcomes.

Methods: This was a retrospective cohort study of 147 DME eyes from patients seen at the Cole Eye Institute Cleveland Clinic from January 1st, 2012 to October 1st, 2019. Patients with visits and spectral domain optical coherence tomography (OCT) scans at 0, 3, 6, and 12 months were selected. Total retinal fluid (TRF), IRF (Intra-retinal fluid), and SRF (Subretinal Fluid) volumes were quantified using the Notal OCT Analyzer (NOA) algorithm. Demographic data and injection status were also collected at each timepoint from electronic medical records. A linear mixed-effects regression (LMER) model was used to calculate the relationship between TRF, IRF, SRF, and VA by quartiles.

Results: The mean total anti-VEGF injections given was 8.57 ± 2.43 . Mean VA at baseline and 12 months was 65.03 ± 13.03 and 70.43 ± 11.68 (p<0.001) ETDRS letters respectively. The mean total retinal fluid (TRF) at baseline and 12 months was 1.06 ± 1.14 mm³ (mean + SD) and 0.51 ± 0.67 mm³. The mean IRF at baseline and 12 months was 10.25 ± 11.16 mm³ and 5.01 ± 6.58 mm³ respectively. Baseline VA was a significant predictor of final VA (p<0.001) in the LMER. The LMER analysis also showed that patients in the 3rd Quartile had -4.39 ETDRS letter gain (p=0.048) and those in the 4th Quartile had -7.09 ETDRS letter gain (p=0.002) at 12 months compared to those in the 1st Quartile. SRF changes were not significantly correlated to final VA (p=0.381).

Conclusions: Patients with higher levels of IRF were associated with decreased VA gain from baseline to 12 months. Further testing in treatment-naïve patients could identify a specific threshold at which IRF contributes to more or less VA gain. Clinicians can apply these findings to patient care and personalize treatment plans for each visit based on retinal fluid levels and VA.

CONTROL ID: 3536596

SUBMITTER (NAME ONLY): Ellen Elsmann

TITLE: Quality of life and participation in children with visual impairment: comparisons to reference groups

SESSION TITLE: Visual Impairment and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Elsmann, M. Koel, R. Van Nispen, G. van Rens, Ophthalmology, Amsterdam UMC
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Commercial Relationships Disclosure (Abstract): Ellen Elsmann: Commercial Relationship: Code N (No Commercial Relationship) | Mitchel Koel: Commercial Relationship: Code N (No Commercial Relationship) | Ruth Van Nispen: Commercial Relationship(s);MeiraGTx UK II Ltd:Code C (Consultant) | Ger H.M.B. van Rens: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate quality of life and participation in children aged 3-17 years with visual impairment (VI) compared to reference groups and between subgroups with increasing severity levels of VI.

Methods: Participants were recruited from Dutch nationwide low vision services. Parents of children aged 3-17 years (n=502) and children aged 13-17 years (n=74) completed the Child and Adolescent Scale of Participation (CASP). Both children aged 7-17 years and their parents (n=268) completed the Kidscreen-27. CASP scores of children aged 3-11 years and Kidscreen scores were compared to age and/or gender appropriate population-based samples and effect sizes (ES) were calculated. Because of lacking population-based samples for older children, CASP scores of children aged 12-17 years were compared to children with chronic conditions or disabilities. In addition, the association between severity of VI and quality of life or participation was analysed with linear regression models within the VI sample.

Results: Children performed significantly worse on Physical Wellbeing (ES: 0.18) and Social Support & Peers (ES: 0.23), but better on the School Environment (ES: -0.36) Kidscreen subscales compared to reference groups. Similar results were found for parents (ES: 0.35, 0.13, -0.14, respectively), and they also reported worse scores on the Parents & Autonomy subscale (ES: 0.18). Children's participation was significantly worse compared to a population-based sample (ES: 1.58), but significantly better compared to children with various chronic conditions and disabilities, both reported by parents and children themselves (ES: -1.90 and -3.06, respectively). After correcting for potential confounders, having moderate or severe VI/blindness was significantly associated with worse participation as reported by parents relative to those with no VI.

Conclusions: Quality of life of children with VI is affected especially regarding Physical Wellbeing and Social Support & Peers when compared to a reference population and their participation is considerably worse. Participation was more affected in children with more severe VI. These results contribute to the understanding of the impact of VI and interventions targeting physical health, social skills and participation are warranted.

CONTROL ID: 3536637

SUBMITTER (NAME ONLY): ashok jha

TITLE: To determine the relationship between corneal endothelial parameters with diabetes mellitus and diabetic retinopathy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To analyze the central corneal thickness, corneal endothelial cell density, and morphology in patients with type 2 diabetes mellitus (DM)

Methods: In this prospective study, corneal endothelial parameters including central corneal thickness (CCT), endothelial cell density (ECD), coefficient of variation in cell size (CV), and hexagonality (Hex) were assessed by specular microscopy (EM 3000 Tomey Nishi-Ku, Nagoya, Aichi, Japan) in patients with type 2 DM and compared with age-matched control group. Further analysis was done to assess the influence of diabetic retinopathy severity, duration of DM, and level of glycosylated hemoglobin (HbA1c) on the corneal endothelium

Results: The study cohort included 592 eyes of 592 diabetic patients and 596 eyes of 596 control subjects. On comparing the two groups, a significant difference was found in CCT ($522.1 \pm 36.6 \mu\text{m}$ in DM, $514.9 \pm 37.1 \mu\text{m}$ in controls; $P=0.001$), ECD ($2484.5 \pm 299.5 \text{ cells/mm}^2$ in DM, $2555.9 \pm 258.2 \text{ cells/mm}^2$ in controls; $P = 0.017$), CV (40.3 ± 6.1 in DM, 37.2 ± 6.1 in controls; $P<0.001$) and Hex (39.9 ± 5.2 in DM, 44.6 ± 6.0 in controls; $P<0.001$). The longer duration of DM (>10 years) and poor glycemic control ($\text{HbA1c} > 7.5\%$) were associated with similar results. A significantly reduced ECD ($P<0.001$) and Hex ($P<0.001$) and higher CV ($P = 0.007$) and CCT ($P = 0.01$) was noted when assessed against various stages of DR. Spearman correlation between duration, HbA1C, and DR status and the corneal parameters showed a significant negative correlation for ECD and Hex, and a significant positive correlation for CCT and CV respectively. Multivariate regression analysis showed that increasing age was significantly associated with lower ECD ($P<0.001$), Hex ($P<0.001$), and CCT ($P=0.004$); and a higher CV ($P<0.001$). Also, increasing HbA1c was associated with significantly lower ECD ($P<0.001$) and a higher CV ($P=0.002$)

Conclusions: Diabetes mellitus, especially if long-standing or poorly controlled, has deleterious effects on corneal endothelium and thickness. The presence of diabetic retinopathy may further warrant a thorough corneal evaluation, especially when planning intraocular surgery

CONTROL ID: 3536649

SUBMITTER (NAME ONLY): Rushil Brahmabhatt

TITLE: A Functional and Histological Analysis of Oxygen Sensitivity during the Critical Period of Retinal Development

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Brahmabhatt, J. Bernstein, C. Suter, E. Tsai, P. Lecker, J. Kim, M. Villegas, E. Gdovin, N. Morrison, G. Gorski, M. George-Weinstein, A. Bravo Nuevo, Division of Research, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|Z. Antonello, Department of Surgery, Rowan University Cooper Medical School, Camden, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The critical period (CP) is a post-natal time in which neuronal cell death occurs in development of the mouse retina. In the case of photoreceptors (PRs), the CP is important for creating a balance between the number of PRs and the metabolic resources. In rodent models, many PR-related abnormalities commence during the CP. It has been established in previous studies that a hyperoxic environment is effective in limiting PR death, but no functional studies have been performed to see whether it is translated to vision. The experiments were conducted to test the hypothesis that hyperoxia would ameliorate stress and cell death during the CP and improve retinal function and morphology in both C57 (wild type) and C3H mice, a rapidly progressing degenerative model for retinitis pigmentosa (RP).

Methods: Both C57 and C3H mice were exposed to normoxia (21% oxygen, control), hyperoxia (75% oxygen), or hypoxia (12% oxygen) from post-natal days (P) 7-20. Slides double-labelled for G8 and TUNEL (markers for stress and cell death, respectively) were used to obtain cell counts at P: 10, 12, 16, and 28. Optical coherence tomography (OCT) and scotopic Electroretinograms (ERG) were used to assess the effect of oxygen levels on retina morphology and function, respectively. The OCTs were only conducted on C57 mice, while the ERGs were executed on both C57 and C3H mice.

Results: The OCT revealed that the outer nuclear layer (ONL) was thicker in C57 mice exposed to hyperoxia than control animals. Treatment with hyperoxia resulted in a significant increase in the mean ERG A-and B-wave amplitudes in both C57 and C3H mice. The cell count data indicated that hypoxia decreased while hyperoxia increased the number of PR cells during the CP.

Conclusions: These findings indicate that hyperoxia reduces PR cell death and improves function during the CP in the normal neonatal mouse retina and the C3H model of RP. Further studies are warranted to examine whether the beneficial effects of hyperoxia on slowing degeneration in C3H mice are more pronounced in less aggressive models of RP that resemble disease progression in humans.

CONTROL ID: 3536666

SUBMITTER (NAME ONLY): Sukhumal Thanapaisal

TITLE: Does Tube-Iris Touch Cause Anterior Chamber Inflammation in Patients with Ahmed Valve Implantation?

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Thanapaisal, Q. Zhang, J.A. Gonzales, J. Wu, T.C. Porco, J. Oatts, Y. Han, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|S. Thanapaisal, Ophthalmology, Khon Kaen University, Khon Kaen, THAILAND|S. Shao, University of California San Francisco School of Medicine, San Francisco, California, UNITED STATES|Y. Yu, G. Ying, Center for Preventive Ophthalmology and Biostatistics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate whether significant anterior chamber inflammation and/or cystoid macular edema (CME) occurs in patients with tube-iris touch after Ahmed glaucoma valve (AGV) implantation.

Methods: This is a cross-sectional study. Patients aged ≥ 18 years old who underwent AGV implantation at least 3 months prior to the study were included. Patients with any uveitis, corneal haze, prior macular diseases or prior intraocular surgery (with the exception of cataract surgery) were excluded. Tube-iris touch was identified by slit lamp examination and confirmed with anterior segment optical coherence tomography. Anterior chamber (AC) inflammation was graded using Standardization of Uveitis Nomenclature classification. CME was evaluated using spectral domain OCT to measure central foveal thickness (CFT).

Results: 103 eyes (84 patients) were included. The tube was inserted into the anterior chamber in 33 eyes (32%) and the sulcus in 70 eyes (68%). Tube-iris touch was identified in 47 eyes: 10 shunts (21.3%) had anterior chamber placement and 37 (78.7%) had sulcus placement. Pigmented and inflammatory cells in the AC were found in 5 of 47 eyes (10.6%) with tube-iris touch and 3 of 56 eyes (5.4%) without tube-iris touch ($P=0.34$), presenting a non-significant difference in AC inflammation between the two groups. Mean CFT was 245 and 250 microns for the tube-iris touch and no tube-iris touch groups, respectively ($P=0.60$).

Conclusions: Tube-iris touch following AGV implantation is not associated with increased post-operative AC inflammation or cystoid macular edema regardless of whether the tube is placed in the anterior chamber or ciliary sulcus.

CONTROL ID: 3536671

SUBMITTER (NAME ONLY): Ruth Van Nispen

TITLE: Quality of life outcomes and prognostic factors one year after corneal transplantation: a nationwide cohort study

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose was to investigate predictors of vision and health-related quality of life (QOL) one year after corneal transplantation.

Methods: Patients (N=233, mean age 68) were recruited from eleven hospitals across the Netherlands. In this longitudinal prospective cohort study, patients were assessed 1 month before and 3, 6 and 12 months after corneal transplantation using the Low Vision QOL questionnaire (LVQOL) and the EuroQOL 5 Dimensions questionnaire (EQ-5D). Demographic and clinical characteristics were considered as potential predictors. Linear mixed models were used to analyse the LVQOL, and generalized estimating equations for dichotomized EQ-5D scores due to skewed data.

Results: LVQOL-scores improved over time ($b=13.4$; 95%CI 9.0 to 17.8 at 12 months). Worse baseline logMAR visual acuity of the best eye predicted worse LVQOL-scores ($b=-13.8$; 95%CI -19.1 to -8.5). Worse baseline scores on the Eye Complaint Questionnaire and the Dry Eye Questionnaire (DEQ) predicted worse LVQOL-scores (respectively $b=-0.9$; 95%CI -1.1 to -0.7; $b=-1.2$; 95%CI -1.2 to -0.7). The odds of having a perfect EQ-5D score did not change over time, however, the odds of having a perfect score were lower when having comorbidity (odds ratio, OR 0.41; 95%CI 0.3 to 0.6) or at higher age (OR 0.97; 95%CI 0.94 to 0.99 at 12 months). Patients with worse DEQ-scores had a lower odds of having a perfect EQ-5D over time (ORs between 0.95 and 0.97 and 95%CI between 0.91 and 1.0). Finally, people eligible for lamellar keratoplasty had a higher odds of having a perfect score compared to penetrating keratoplasty (OR 2.6; 95%CI 1.5 to 4.4).

Conclusions: Vision-related QOL improved considerably over time with a linear upward trend, which means that the corneal transplantation seems to be very effective and has an important positive impact on daily life. Low visual acuity and eye complaints related to corneal disease were important predictors of vision-related QOL. Long term follow-up data will show whether this upward trend will continue. Although there were some significant predictors, effects of transplantation for health-related QOL were less outspoken. However, many patients had a (near) perfect score at baseline, hence no room for improvement. The results of this study may contribute to realistic communications about expectations of corneal transplantation and to recommendations for patient-centered care.

CONTROL ID: 3536681

SUBMITTER (NAME ONLY): Jessica Cooke Bailey

TITLE: POAG genetic risk score performs worse in African-descent than European-descent samples, highlighting need for expanded genetic studies in diverse populations

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Genetic risk scores (GRS), sums of additive genetic risk, have strong potential for application in clinical risk stratification and early disease diagnosis in primary open-angle glaucoma (POAG). Recent studies in primarily European-descent population samples suggest that GRS associate with POAG case status, diagnosis age, and disease-specific outcomes. Further study in diverse populations is necessary to ensure generalizability of GRS in POAG, particularly as POAG is generally worse in people of African descent (earlier onset, higher prevalence and likelihood of vision loss/blindness). We investigated a POAG-specific GRS of published risk variants and apply it to the diverse Million Veteran Program (MVP), an ongoing observational cohort study and mega-biobank with >825K Veterans.

Methods: GRS summing 83 POAG-associated risk alleles in MVP samples with POAG phenotype, imputed genetic data, and harmonized ancestry and race/ethnicity (HARE) data. Association analyses of unweighted and effect estimate-weighted GRS and binary POAG phenotype were performed via logistic regression in European-descent (3382 cases, 58,829 controls) and African-descent (2448 cases, 5665 controls) samples. Unadjusted models and models adjusting for age, sex, age*sex interaction, and 10 sample-specific principal components were evaluated. GRS score deciles and quartiles were tested for association with POAG phenotype via logistic regression. Receiver operating characteristic (ROC) curves were composed and statistically compared.

Results: GRS was significantly associated with POAG in unadjusted and adjusted models ($P < 5E-05$). While odds ratio estimates generally increased across deciles, the trend was stronger in the European-descent sample than in the African-descent sample; this was consistently supported by ROC plots and statistical hypothesis testing. GRS identified European-descent cases more consistently than African-descent cases (top quartiles: 37%, 29%, respectively). Unweighted GRS outperformed the weighted GRS in all models.

Conclusions: The ability of known POAG-associated variants to differentiate POAG cases from controls was dampened in African-descent population sample compared to European-descent. These outcomes drive the necessity of further diverse POAG genomic studies.

CONTROL ID: 3536689

SUBMITTER (NAME ONLY): Russell Quinn

TITLE: M1 and M2 Macrophage contributions towards RPE health and development

SESSION TITLE: Microglia and other Macrophages in Health and Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Utilizing a 3D Bioprinted tissue system consisting of vascularized choroidal tissues co-cultured with confluent RPE monolayers, we aim to model the developmental processes of the Outer Blood Retinal Barrier (OBRB). Recently, we included mature macrophages in this system, which become polarized into M1 and M2 macrophages by environmental cues inside tissues likely to fulfil specialized functions. As macrophages are integral to maintaining choroidal function, this study aims to investigate the role of polarized pro-inflammatory (M1) and pro-angiogenic (M2) macrophages, in both the early development and degeneration of the Retinal Pigment Epithelium (RPE) in the 3D-OBRB.

Methods: Endothelial cells, choroidal fibroblasts, and ocular pericytes were encapsulated in a collagen-derived gel and 3D-printed on a degradable scaffold with hydrogels to facilitate microvascular networks. iPSC-RPEs were seeded on the apical side of the scaffold 7 days after bioprinting. Finally, primary activated M1 (pro-inflammatory), M2(pro-angiogenic), and M1+M2 polarized macrophages were added to the tissue at the time of printing (at varying concentrations and ratios), as well as at 28 days post printing. Confocal microscopy, quantitative cytokine analysis, trans-epithelial electrical resistance measurements (TEER), were used to analyze RPE health and components.

Results: When M1 and M2 macrophages were added separately on the day of printing or at day 28 post printing, we observed minor changes in TEER. However, these single macrophage populations were able to strongly influence RPE cytokine secretions; with both M1 and M2 separately increasing wet-AMD associated apical secretions. When M1 and M2 macrophages were combined on the day of printing however, TEER of the RPE monolayers degraded after 5 weeks, with increasing TEER decrease associated with increasing M2 content.

Conclusions: The addition of macrophages in this model system influence the growth/survival of our 3D cultured tissues. This 3D-in vitro model may enable investigations into immune mechanisms influencing OBRB development in humans, maximizing ease of access without heavily sacrificing physiological relevance.

CONTROL ID: 3536691

SUBMITTER (NAME ONLY): Farzan Abdolahi

TITLE: Assessment of Physiological Changes in Retinal Capillary Blood Flow in the Healthy Human Retina Using OCTA

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To compare optical coherence tomography angiography (OCTA) derived flux with conventional OCTA measures of retinal vascular density

Methods: 3 x 3 mm² fovea-centered images were acquired from healthy human subjects using a commercially available swept-source OCTA (SS-OCTA). Imaging was performed while subjects were breathing either room air (RA), 100% O₂, or 5% CO₂. Retinal perfusion was quantified in each condition using previously described measures of vessel area density (VAD) and vessel skeleton density (VSD) derived from binarized OCTA images. Vessel area flux (VAF) and vessel skeleton flux (VSF) are two novel measures of retinal perfusion based on non-binarized intensities from raw OCTA images. Flux approximates the number of red blood cells moving through a vessel segment per unit time and more accurately reflects small changes in blood flow. Retinal vascular reactivity (RVR) is reported as the percentage change in each OCTA measure between gas conditions (O₂-RA and CO₂-RA). Analyses were performed for all-vessel (including arterioles and venules) as well as capillary-only OCTA images. Statistical significance was determined using paired t-tests and a linear mixed effects model with a p-value of < 0.05.

Results: 84 OCTA images (one image per gas condition) from 29 subjects were included (mean age 45.9 ± 19.5 years; 48.3% male). Flux measures, VAF and VSF, showed significantly greater relative magnitude of change compared to density measures, VAD and VSD, in all gas conditions. In CO₂ condition, the change was 168% greater in VAF than VAD (p = 0.002), and 124% greater in VSF than VSD (p = 0.004). Similarly, in O₂ condition, the change was 43% greater in VAF than VAD (p = 0.003), and 57% greater in VSF than VSD (p = 0.01), Fig 1. Flux measures also had a significantly greater magnitude of change in capillary-only images compared to all-vessel images. The change in VAF in capillary-only images was 20% greater in CO₂ (p = 0.01), and 25% greater in O₂ (p = 0.001) condition compared to all-vessel images. VSF showed a similarly significant trend.

Conclusions: OCTA-derived flux measures quantify autoregulatory changes in retinal blood flow at the capillary level with a greater effect size than conventional vessel density measures.

CONTROL ID: 3536692

SUBMITTER (NAME ONLY): Brent Siesky

TITLE: Differences in retinal capillary blood flow and visual function in healthy male and female subjects of African and European descent

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate differences between retinal capillary blood flow and visual function in healthy male and female subjects of African (AD) and European (ED) descent.

Methods: A total of 201 healthy subjects (171 ED, 30 AD) were evaluated for: systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), intraocular pressure (IOP) measured via Goldmann applanation tonometry, and calculations of ocular perfusion pressures: (OPP=2/3MAP-IOP), systolic OPP (SOPP=SBP-IOP), diastolic OPP (DOPP=DBP-IOP), and mean OPP (MOPP=MAP-IOP). Retinal blood velocities and the percentage of measured area without active retinal capillary blood flow (estimated as % of retina with no detectable flow) in the superior (SNF) and inferior (INF) superficial retina were assessed with Heidelberg Retinal Flowmetry. Visual function was assessed with both Early Treatment Diabetic Retinopathy Study (ETDRS) and Vector Vision contrast sensitivity (CS) charts. Unpaired t-tests were performed with $p < 0.05$ considered statistically significant.

Results: In all healthy subjects, the percentage non-vascularized retina was significantly higher in females compared to males in both the superior (SNF: 17.6%, vs. 15.5%; $p = 0.009$) and inferior (INF: 18.1% vs. 14.6%; $p = 0.0002$) superficial retina. There were no statistically significant differences in age between groups (female: 44.2 years, male: 43.3 years; $p > 0.05$). The associated blood velocities were also significantly higher in females in both the superior and inferior retina ($p = 0.0003$; $p = 0.0001$, respectively). Healthy subjects of AD had significantly higher systemic blood pressures and all calculations of ocular perfusion pressures compared to those of ED ($p < 0.05$). CS detection was significantly higher in males compared to females (CS Row D: 0.897 vs. 0.727; $p = 0.032$) while ETDRS detection was significantly worse in females compared to males (0.133 vs. 0.084; $p = 0.044$).

Conclusions: In this cohort of healthy subjects, females had a higher percentage of retinal avascular area and associated blood velocities in both the superior and inferior retina compared to males. Visual acuity and contrast sensitivity detection were also worse in females, while healthy subjects of AD had significantly higher blood and perfusion pressures than those of ED.

CONTROL ID: 3536698

SUBMITTER (NAME ONLY): Victoria Tseng

TITLE: Factors Associated with Minimally Invasive Glaucoma Surgery at the time of Phacoemulsification in the California Medicare Population

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To examine factors associated with use of minimally invasive glaucoma surgery (MIGS) at the time of phacoemulsification in patients with primary open angle glaucoma (POAG) in the 2016-2017 California (CA) Medicare Population.

Methods: The study population included all patients with administrative billing codes for POAG and phacoemulsification in the 2016-2017 CA Medicare database. Exposures that were examined included age, gender, race, Charlson Comorbidity Index (CCI) score, age-related macular degeneration (AMD), diabetic retinopathy (DR), and severe cataract. The main outcome measure was use of MIGS at the time of phacoemulsification. This was defined by procedure codes for trabecular micro-bypass stent, goniotomy, canaloplasty, or cyclophotocoagulation. Logistic regression modeling was used to identify multivariable predictors of MIGS use at the time of phacoemulsification separately in 2016 and 2017, with all study covariates included in the statistical model.

Results: In the CA Medicare population, there were 11,003 POAG patients in 2016 and 11,269 in 2017 who underwent phacoemulsification, of whom 3,987 (36.2%) had MIGS in 2016 and 4,331 (38.4%) in 2017. In 2016, multivariable associations with MIGS included age 80-84 (odds ratio [OR]=0.86, 95% confidence interval [CI]=0.75, 0.98), 85-89 (OR=0.80, 95% CI=0.68, 0.94), and 90+ (OR=0.74, 95% CI=0.59, 0.93) versus 65-69, Asian (OR=0.83, 95% CI=0.74, 0.93) and Hispanic (OR=0.88, 95% CI=0.79, 0.99) versus white race, CCI score 1-2 versus 0 (OR=0.91, 95% CI=0.82, 1.00), and DR (OR=0.74, 95% CI=0.63, 0.86). In 2017, multivariable associations with MIGS use included age 85-89 (OR=0.74, 95% CI=0.63, 0.86) and 90+ (OR=0.70, 95% CI=0.56, 0.88) versus 65-69, Asian (OR=0.86, 95% CI=0.77, 0.96) and Hispanic (OR=0.90, 95% CI=0.80, 1.00) versus white race, DR (OR=0.75, 95% CI=0.65, 0.87), CCI 1-2 (OR=1.10, 95% CI=1.00, 1.22) and 3-4 (OR=1.13, 95% CI=1.01, 1.27) versus 0, and severe cataract (OR=1.10, 95% CI=1.02, 1.19).

Conclusions: In California Medicare patients with POAG and phacoemulsification in 2016 and 2017, a higher proportion received phacoemulsification alone compared to phacoemulsification with MIGS. Potential factors associated with decreased MIGS use included older age, Asian and Hispanic race, and diabetic eye disease. Further studies are needed on patient selection for MIGS during phacoemulsification.

CONTROL ID: 3536758

SUBMITTER (NAME ONLY): Qi Wei

TITLE: Biomechanical Modeling of Actively Controlled Rectus Extraocular Muscle (EOM) Pulleys

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

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Commercial Relationships Disclosure (Abstract): Qi Wei: Commercial Relationship: Code N (No Commercial Relationship) | Joseph Demer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Active Pulley Hypothesis posits that Listing's Law (LL) is implemented mechanically by connective tissue pulleys actively positioned by the rectus EOMs (Demer et al., IOVS, 42:1280-1290, 2000). A computational model is needed to clarify this scheme. We developed a new biomechanical model of active horizontal rectus pulleys and examined its behavior.

Methods: A previously developed 3-D neuro-biomechanical model of the orbit (Wei et al., Prog. Biophys. Mol. Biol., 103:2-3:273-283, 2010) was augmented to realistically simulate pulley mechanics. The orbital (OL) and global (GL) layers of the horizontal rectus EOMs were modeled as separate strands. The pulley sleeve was modeled as a tube suspended by elastic strands and receiving the OL insertion. Stiffnesses and orientations of pulley suspensions were determined empirically to limit EOM side-slip while allowing anteroposterior pulley travel. Independent neural drives of the OL greater than GL were assumed. The model was refined in secondary gazes by incremental iterations to implement realistic behavior using the simplest mechanical configuration and neural control strategy.

Results: Quantitatively realistic behavior required both insertion of each OL on its pulley, and differential control of OL and GL tensions. Actively-controlled pulleys stabilized medial (MR) and lateral rectus (LR) paths during vertical ductions. From 30° supra- to 30° infraduction, LR and MR pulleys shifted vertically by less than 1 mm from central position, realistically demonstrating anterior path inflections ~half the gaze angle as necessary for LL. During progressive rotation from 30° add- to 30° abduction, simulated LR and MR insertional forces agreed quantitatively with corresponding empirical measurements (Collins et al., IOVS, 20(5):652-664, 1981). Predicted innervations of horizontal rectus GL and OL, as well as of cyclovertical EOMs, were consistent with previous empirical and computational work.

Conclusions: A novel bilayer biomechanical model realistically implements mechanical behavior of actively-controlled pulleys in secondary gazes that is quantitatively consistent with available EOM force and path data in humans. This simulation, which is consistent with LL, suggests that horizontal rectus pulleys must be under influence of OLs differently innervated from GLs, since physiological behavior could not be implemented without these features.

CONTROL ID: 3536769

SUBMITTER (NAME ONLY): Thuy Le

TITLE: The impact of early central macular total retinal fluid index instability on future exudative volatility in neovascular AMD

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Zahid, Novartis Pharmaceuticals Corp New York, Suffern, New York, UNITED STATES|M. Hu, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|T.K. Le, L. Lunasco, J. Reese, S. Srivastava, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate early total retinal fluid index (TRFI) instability as a potential imaging biomarker for future intolerance of extended anti-VEGF treatment intervals based on recurrence of exudative activity in nAMD.

Methods: This was a post hoc analysis of the phase II OSPREY clinical trial comparing brolucizumab to aflibercept over 56 weeks. Eyes were initially treated with an anti-VEGF agent every 4 weeks for the first 3 months and were then extended to 8-week intervals through week 40 (matched phase). At that time the brolucizumab group was further extended to 12-week intervals. A treatment agnostic approach was used for this analysis. SD-OCT cube scans were imported into a novel machine-learning enabled OCT feature extraction tool, which automatically segmented intraretinal fluid (IRF), subretinal fluid (SRF), and retinal layers including the internal limiting membrane (ILM) and retinal pigment epithelium (RPE). TRFI, defined as the percentage of IRF and SRF between the ILM and RPE, was calculated for the central macula (CM, defined as the central 2-mm zone). Early TRFI instability was defined as an increase in CM-TRFI of $\geq 0.1\%$ from week 4 to 8. High fluid compartment volatility was defined based on eyes in the 75th percentile for fluid volume fluctuation from week 12 to 56. Optimal anatomic response was defined as achieving a dry retina with minimal or no fluid recurrence.

Results: A total of 81 eyes were included in this analysis. Between week 4 and week 8, 9.8% (8/81) of eyes demonstrated a $\geq 0.1\%$ increase in CM-TRFI. Among eyes with early CM-TRFI instability, only 25% achieved optimal anatomic response compared to 78% of all other eyes ($p < 0.01$) during the matched phase. Of eyes with early CM-TRFI instability, 88% had high IRF and/or SRF volatility following treatment interval extension compared to 41% of eyes without early CM-TRFI instability (odds ratio: 10.0; $p = 0.02$).

Conclusions: Eyes with early CM-TRFI instability during the anti-VEGF loading phase demonstrated greater risk of treatment extension intolerance and overall poorer anatomic response to anti-VEGF therapy. CM-TRFI changes during early treatment may provide important insights to eyes at high risk for exudative recurrence with treatment extension.

CONTROL ID: 3536774

SUBMITTER (NAME ONLY): Henry Liu

TITLE: Deep Learning for Detection of Keratoconus and Prediction of Crosslinking Efficacy

SESSION TITLE: Keratoconus and Corneal Biomechanics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Deep learning with convolutional neural networks (CNN), a method of supervised machine learning that uses multiple layers to progressively extract higher level features, is becoming increasingly popular in recent years in the field of ophthalmology. The goal of this study is to implement and test a trained deep learning algorithm using pre-operative corneal topography scans in order to 1) classify between keratoconus and normal corneas 2) stage the disease according to Amsler-Krumeich scale and 3) predict whether a patient will likely to benefit from crosslinking treatment.

Methods: Scans of baseline visits for all patients that had a diagnosis of keratoconus (case group) and those who have been assessed for refractive surgery (control group) between January 2007 and June 2019 were analyzed. A CNN was implemented and trained with our custom dataset of corneal topographies (with 80% and 20% validation). In total, 2410 scans were included (1163 keratoconus and 1247 controls) for stage 1, 985 keratoconus scans were classified according to the Amsler-Krumeich scale for stage 2, and 138 keratoconus scans (69 progressed and 69 stabilized) were labeled for stage 3.

Results: For stage 1, the deep learning model with data including all four pentacam parameters (anterior and posterior corneal elevations, anterior curvature and pachymetry maps) showed a validation accuracy of 0.995 in discriminating between keratoconic and normal corneas. For individual map analysis, corneal pachymetry showed the lowest validation accuracy of 0.771, whereas the other parameters anterior corneal elevation, posterior corneal elevation and anterior curvature maps showed accuracies of 0.987, 0.984 and 0.978 respectively. For stage 2, the algorithm was able to stage the disease with a validation accuracy of 0.735 (excluding manifest refraction as an input parameter) and 0.878 (including manifest refraction as an input parameter). For stage 3, the accuracy in correctly predicting the progression of keratoconus was 0.536.

Conclusions: Deep learning using topography scans obtained from the pentacam effectively differentiates keratoconus versus normal corneas as well as stages the disease according to established criteria. The algorithm was not able to predict the likelihood of disease progression based solely on the pre-operative topography, which may partially be attributed to the reduced sample size given the rarity in disease progression.

CONTROL ID: 3536790

SUBMITTER (NAME ONLY): Alice Chandra Verticchio Vercellin

TITLE: Developing a heterogeneous model of the arteriolar vasculature in the human retina

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Verticchio Vercellin, A. Harris, B.A. Siesky, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|A. Verticchio Vercellin, Universita degli Studi di Pavia, Pavia, Lombardia, ITALY|A. Albright, J. Arciero, Department of Mathematical Sciences, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|B. Fry, Department of Mathematical and Computer Sciences, Metropolitan State University of Denver, Denver, Colorado, UNITED STATES|J.M. Beach, University of Minnesota Center for Drug Design, Minneapolis, Minnesota, UNITED STATES|G. Eckert, Department of Biostatistics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: This work adapts a previous heterogeneous model of the murine retinal vasculature to be relevant to human. Oximetry and structural data are used to translate the mouse model into a human model that can predict blood flow and tissue oxygenation in the retinal arterial architecture.

Methods: A theoretical model of the human retina is extrapolated from a previous mouse model based on confocal microscopy images. The vasculature is represented as a directed graph where each edge corresponds to a blood vessel with a specific diameter and length. Oximetry data from the human retina are used to convert the murine vascular network to a human network by adapting: (i) the number of main arterial branches and the angles between them, (ii) vessel diameters, and (iii) vessel lengths. In the human model, oxygen levels in the retinal arterioles and surrounding tissue are calculated using Green's functions. Blood flow, pressure, and viscosity are also computed.

Results: A scaling factor of 3.6 was used to convert murine diameters to human values based on data averaged from five experimental studies. A mouse-to-man scaling factor of 5.4 for vessel length was obtained based on oximetry images and position of the fovea. Figure 1A shows the predicted values of blood flow along a particular vascular pathway of the human model. Figure 1B depicts the predicted levels of the partial pressure of oxygen (PO_2 , in mmHg) throughout the human arteriolar network. The arteriolar model is not connected to the downstream capillaries and venules, so the figure is a proof of principle but does not give precise levels of PO_2 .

Conclusions: This study provides a mathematical model of the human retinal vasculature that can predict blood flow and oxygen levels within a spatially heterogeneous arteriolar network. The heterogeneous arrangement of arterioles in this model accounts for the complex geometry of blood vessels and diffusion of oxygen from multiple sources into one tissue point; however, it does not account for the oxygen supplied by the capillaries. This heterogeneous model of the retinal arterioles will be connected to a series of compartments representing the capillaries and veins to create a hybrid model description of the retinal microcirculation.

CONTROL ID: 3536795

SUBMITTER (NAME ONLY): John Buch

TITLE: A pilot study on the role of spectral filtering on visual light discomfort

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.R. Buch, D. Nankivil, J. Xu, Research and Development, Johnson and Johnson Vision Care Inc, Jacksonville, Florida, UNITED STATES|A. Gonzalez, V. Graham, C. Rowaan, J. Silgado, G. Amescua, J.A. Parel, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, Miller School of Medicine, University of Miami, Miami, Florida, UNITED STATES|G. Amescua, B.L. Lam, Anne Bates Leach Center, Bascom Palmer Eye Institute, Miller School of Medicine, University of Miami, Miami, Florida, UNITED STATES|B. Hurwitz, Behavioral Medicine Research Center, Miller School of Medicine, University of Miami, Miami, Florida, UNITED STATES|J.A. Parel, Biomedical Engineering, College of Engineering, University of Miami, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to characterize visual light discomfort threshold (VLDT) reliability measured with the ocular photosensitivity analyzer (OPA) and to measure the effect size of differences in VLDT of ultraviolet (UV) and neutral density (ND) control lenses compared with a 476 nm high pass filter (HPF) lens. The OPA generates light stimuli (white LEDs) of varying intensities utilizing unequal ascending and descending steps along with subjective feedback to yield the VLDT.

Methods: This was a 6-visit, single-center, non-dispensing, randomized, single-masked, repeated measures 3×3 crossover study. To determine the optimum rest interval, VLDT was measured across six consecutive trials using 5, 10, and 15 minute intertest periods. Then, using the optimum rest interval, VLDT was measured with the UV filter lens, with the HPF lens, and with the ND filter lens. Skin color, iris color and macular pigment optical density (MPOD) were measured using colorimetry, iris color scale, and heterochromatic flicker photometry, respectively. Of the 11 subjects from the per-protocol population, 3 (27.3%) were female and 8 (72.7%) were male. The average age (±SD) was 24.2 (±3.3) years. VLDT was analyzed using generalized linear mixed models with the lognormal distribution. Type I error was controlled for multiple comparisons.

Results: The intra-class correlation (ICC) was 0.88, 0.92 and 0.87 for the 5, 10, and 15 minute resting intervals, respectively. Within subject variance estimate was 0.26, 0.16, and 0.27 log(lux) for the 5, 10, and 15 minute resting intervals, respectively. The residual variance was not statistically different among resting periods based on the overall homogeneity of variance test (p=0.140). However, the ICC was slightly higher and the residual variance was lower for the 10 minute interval, so the 10 minute interval was used in subsequent experiments. Skin color and MPOD were not statistically significant covariates. VLDT did not vary between the two control lenses. Median VLDT ratio was significantly different than unity for the HPF relative to the both controls. Relative to control, the HPF reduced transmitted source energy by approximately 28% while the VLDT increased by more than 70%.

Conclusions: It is suggested that high energy visible (HEV) light contributes disproportionately to visual light discomfort. Alternatively, an HEV filter is highly efficacious at reducing visual light discomfort.

CONTROL ID: 3536796

SUBMITTER (NAME ONLY): Bettina Hohberger

TITLE: Switch of inhibitory to agonistic autoantibodies directed against the β 2-adrenergic receptor in the pathogenesis of pseudoexfoliation syndrome and glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Hohberger, U. Schlötzer-Schrehardt, C.Y. Mardin, R. Lämmer, Department of Ophthalmology, University of Erlangen-Nürnberg, GERMANY|M. Herrman, Institute of Clinical Immunology and Rheumatology, Department of Internal Clinic III, University of Erlangen-Nürnberg, GERMANY|R. Kunze, Science office, Berlin-Buch, Campus Max Delbrück Center for Molecular Medicine, GERMANY|G. Wallukat, Berlin Cures GmbH, GERMANY|

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ABSTRACT BODY:

Purpose: Pseudoexfoliation syndrome (PEXS) and glaucoma (PEXG) are assumed to be a general elastosis with accumulation of PEX material in ocular and extraocular tissues, yet, the exact pathophysiology is not known. PEXG, the most common type of secondary open-angle glaucoma (OAG), is characterized by large intraocular pressure (IOP) peaks with progressive visual field loss. Recently, agonistic autoantibodies (AAb) against the β 2 adrenergic receptor (AR) were shown to be present in sera of patients with primary and secondary OAG and seemed to be linked to IOP.^{1,2} The present study aimed to investigate the presence of agonistic and inhibitory autoantibodies directed against the β 2-AR in sera of patients with PEXS and PEXG.

Methods: 49 individuals were included: 39 patients (15 PEXG, 9 PEXS, 15 primary OAG) and 10 controls. All patients underwent standard ophthalmological examination with Octopus G1 perimetry. AAbs in serum samples were analyzed by frequency modulation of a specific rat cardiomyocyte bioassay in vitro. Identification of the interacting loop of the β 2-AR and immunoglobulin G analysis were done. The study was approved by the local ethics committee and was done in accordance with the tenets of the Declaration of Helsinki. Informed consent was achieved.

Results: Serum samples of controls were β 2-AAb negative (0.16 ± 0.5 beats/15 sec). No agonistic β 2-AAb (0.24 ± 0.4 beats/15 sec), yet inhibitory β 2-AAb (after additional incubation with $3 \mu\text{M}$ clenbuterol: 5.84 ± 1.7 beats/15 sec), were observed in 80% of PEXS patients, partially blocking the clenbuterol effect (11.10 ± 0.9 beats/15 sec). Loop analysis showed that inhibitory β 2-AAb were directed against the 3rd extracellular loop of β 2-AR. Additionally, they were of IgG3 subtype in PEXS patients. Contrary, PEXG patients showed agonistic β 2-AAb (5.62 ± 0.9 beats/15 sec), yet no inhibitory β 2-AAb. The beating rate was not significantly different between PEXG and POAG patients (3.89 ± 2.8 beats/15 sec; $p > 0.05$). Even synergistic β 2-AAb were observed in sera of 2 PEXG patients (after additional incubation with $1 \mu\text{M}$ clenbuterol: 16.33 ± 0.9 beats/15 sec), overtopping single incubation with $1 \mu\text{M}$ clenbuterol (11.5 ± 0.3 beats/15 sec).

Conclusions: As autoimmune mechanisms were observed to be involved in glaucoma pathogenesis, agonistic and inhibitory β 2-AAb seem to be a part of this multifactorial interplay.

CONTROL ID: 3536799

SUBMITTER (NAME ONLY): Mai Nguyen

TITLE: Generation and characterization of novel Dhdds knock-in mutation mouse models of RP59

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.N. Nguyen, D. Chakraborty, P.I. Cobb, S.J. Pittler, Optometry and Vision Science, Vision Science Research Center, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S.J. Fliesler, Ophthalmology and Biochemistry, SUNY The State University of New York, Buffalo, New York, UNITED STATES|S.J. Fliesler, Research Service, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dehydrodolichyl diphosphate synthase (DHDDS) is ubiquitously expressed and serves an essential function throughout the body, yet certain defects in the gene cause non-syndromic retinitis pigmentosa (RP59). To understand the basis for this retina selectivity, we generated and characterized two novel Dhdds knock-in mouse models: Dhdds^{T206A/T206A} and Dhdds^{T206A/K42E}

Methods: Heterozygous (Dhdds^{T206A/+}) knock-in (KI) mice were generated on a C57Bl/6J background using CRISPR/Cas9 technology (UAB Transgenic & Genetically Engineered Models Core). Dhdds^{T206A/+} littermates were crossed to generate Dhdds^{+/+}, Dhdds^{T206A/+}, and Dhdds^{T206A/T206A} mice, and with Dhdds^{K42E/K42E} to generate Dhdds^{T206A/K42E} mice (to at least 3rd (F3) generation). All mutations were verified by PCR and sequence analysis. Phenotypes were assessed by SD-OCT and electroretinography (ERG). Retinal structure was assessed for Dhdds^{T206A/T206A}, Dhdds^{T206A/+}, Dhdds^{T206A/K42E}, and wild type (WT) mice (N=3-5) at PN 1 and 3 mo., while ERG was performed at PN 3 mo. Statistical analysis: Student t-test, with p<0.05 as significance threshold.

Results: SD-OCT showed no significant differences in retinal morphology, comparing mutant vs. WT mice. Outer nuclear layer (ONL) thickness (μm; mean±S.D.): Dhdds^{T206A/T206A} (55±5); Dhdds^{T206A/+} (54±6); Dhdds^{T206A/K42E} (56±5); vs. WT (55±7). Total retinal thickness (μm): Dhdds^{T206A/T206A} (222±8); Dhdds^{T206A/+} (220±8); Dhdds^{T206A/K42E} (220±9); vs. WT (222±6). Dhdds^{T206A/+} ERG maximum response amplitudes at saturation were not significantly different from WT values under dark-adapted (scotopic) or light-adapted (photopic) conditions. However, photopic ERG amplitude of Dhdds^{T206A/K42E} mice were significantly different from WT values, and trending lower for Dhdds^{T206A/T206A} mice. Additionally, scotopic b-/a-wave ratios (values in parentheses) of Dhdds^{T206A/T206A} (1.2:1) and Dhdds^{T206A/K42E} (1.3:1), vs. WT (2:1) mice were significantly diminished.

Conclusions: Homozygous (T206A/T206A) and compound heterozygous (K42E/T206A) Dhdds knock-in mouse models of RP59 exhibit negative ERGs under light- and dark-adapted conditions, indicative of defective photoreceptor-to-bipolar cell synaptic transmission. There may be common retina-specific target(s) that could explain the lack of systemic effects associated with DHDDS mutations in RP59.

CONTROL ID: 3536820

SUBMITTER (NAME ONLY): Maximilian Pfau

TITLE: Photoreceptor Degeneration beyond Ellipsoid Zone Loss in ABCA4-associated Retinopathy

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pfau, M. Boyle, C. Cukras, L.A. Huryn, W.M. Zein, B.P. Brooks, B.G. Jeffrey, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Pfau, Department of Ophthalmology, Rheinische Friedrich-Wilhelms-Universität Bonn, Bonn, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: To quantify photoreceptor degeneration outside ellipsoid zone (EZ) loss in ABCA4-associated retinopathy, and investigate the association of this photoreceptor degeneration with EZ loss progression.

Methods: As part of a prospective, natural-history study (NCT01736293), patients with a Stargardt disease (STGD1) phenotype and at least one pathogenic ABCA4-mutation underwent spectral-domain optical coherence tomography (SD-OCT) annually. SD-OCT data (37 B-scans, 30°×15°) were segmented using custom deep-learning-based software and standardized (Z-scores) to account for retinal topography and age. Standardized thickness data of the outer nuclear layer (ONL), photoreceptor inner segments (IS) and outer segments (OS) were extracted along evenly spaced contour lines surrounding the EZ loss boundary (spacing of 0.43°). Peri-papillary A-scans (2.5° from disc margin) were excluded. Linear mixed models were used for all analyses considering the hierarchical data structure (visits in eyes in patients). Last, random forest regression was applied to predict EZ loss progression rates.

Results: A total of 95 eyes from 48 patients with a median [IQR] follow-up of 4.19 years [2.88, 5.95] were included. Patients exhibited an average (sqrt transformed) EZ loss progression rate of (estimate [95% CI]) 0.10 mm/y [0.09 – 0.11]. ONL thinning extended well beyond the area of EZ loss; ONL thinning occurred along a steep gradient and the average distance from the EZ loss boundary to normalization of ONL thickness (i.e. within ±2 Z-score units) was 4.36° [4.11 – 4.62]. IS and OS thinning was less pronounced in gradient and extent of change; the average distance from the EZ loss boundary to layer thickness normalization was 0.86° [0.61 – 1.11] for OS and 2.43° [2.17 – 2.68] for IS. ONL, OS and IS thickness outside of EZ loss explained (patient-wise leave-one-out cross-validated R^2) 23.6% of the variability in future sqrt EZ loss progression rates.

Conclusions: Patients with ABCA4-associated retinopathy exhibit significant alterations of photoreceptor laminae outside of EZ loss. This degeneration is prognostic for future EZ loss progression. Deep-learning-based analysis of photoreceptor laminae may help to monitor disease progression beyond mere enlargement of EZ loss.

CONTROL ID: 3536834

SUBMITTER (NAME ONLY): Eleonora Lad

TITLE: The RUSH2A study: Baseline microperimetry and SD-OCT measures

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Lad, G.J. Jaffe, Z. Deng, J. Loo, D. Mukherjee, S. Farsiu, Duke University, Durham, North Carolina, UNITED STATES|W. Liang, Jaeb Centre for Health Research, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To study the natural history of retinal degeneration related to disease-causing sequence variants in the USH2A gene, the Foundation Fighting Blindness Consortium is conducting a 4-year multicenter, international natural history study titled Rate of Progression in USH2A-related Retinal Degeneration (RUSH2A). Herein we evaluate baseline mesopic microperimetry (MP) and spectral domain optical coherence tomography (OCT) metrics and their relationships with other baseline characteristics.

Methods: One eye of each patient had MP with a MAIA system and OCT was tested on both eyes with a Heidelberg Spectralis unit. General linear models were used to assess the association between demographic and clinical characteristics, including gender, race, age, disease duration, smoking, use of dietary supplements, MP mean sensitivity, and OCT ellipsoid zone (EZ) area. The association between MP mean sensitivity and OCT EZ with visual acuity (VA), and central subfield thickness (CST within the center 1mm) was assessed using Spearman correlation coefficients.

Results: All study participants (N=127) had OCT, while MP was obtained at selected sites (N=91). Comparing participants with Usher syndrome type 2 (USH2, N=80) to autosomal recessive non-syndromic RP (ARRP, N=47), the central structural measures of OCT EZ ($3.1 \pm 5.7 \text{ mm}^2$ vs $4.3 \pm 5.6 \text{ mm}^2$, $p=0.26$) and CST ($253.1 \pm 57.5 \text{ }\mu\text{m}$ vs $263.6 \pm 32.9 \text{ }\mu\text{m}$, $p=0.26$) were similar. Longer disease duration was associated with smaller OCT EZ ($p<0.001$) and lower mean sensitivity ($p=0.01$). Comparing MP in USH2 participants (N=55) to those with ARPP (N=36), mean sensitivity was similar by diagnosis ($5.4 \pm 4.9 \text{ dB}$ vs $6.7 \pm 5.1 \text{ dB}$, $p=0.22$). Point-wise sensitivity from repeated MP tests confirmed that central points (within 10-degree) had better sensitivity than peripheral ones (Figure 1). Better VA, larger OCT EZ area, and larger CST were associated with greater MP mean sensitivity ($r>0.3$ and $p<0.01$). Better VA and larger CST were also associated with larger OCT EZ area ($r>0.6$ and $p<0.001$).

Conclusions: The baseline RUSH2A data revealed similar OCT and MP metrics between the USH2 and ARRP participants. Longer disease duration was associated with more severe abnormalities in retinal structure and function. MP and OCT measures may be useful to monitor disease progression in future studies of USH2A-mediated disease.

CONTROL ID: 3536838

SUBMITTER (NAME ONLY): Angela Chang

TITLE: Structural and Functional Progression of Glaucomatous Damage to the Macula with Comorbid Systemic Hypertension

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.Y. Chang, D. Blumberg, G.A. Cioffi, D.C. Hood, J.M. Liebmann, C. De Moraes, Ophthalmology, Columbia University, New York, New York, UNITED STATES|L.A. Al-Aswad, Ophthalmology, NYU Grossman School of Medicine, NYU Langone Health, New York, New York, UNITED STATES|D.C. Hood, Psychology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hypertension (HTN) is a risk factor that may affect glaucoma progression. There is a weak positive correlation between blood pressure (BP) and IOP, and lower ocular perfusion is associated with glaucoma prevalence and progression. Macular damage was once thought to be significant only in late stages of glaucoma, but recent studies have shown it can occur earlier. This study examines glaucomatous structural progression of the global retina nerve fiber layer (RNFL) and the macula ganglion cell layer (GCL+) with optical coherence tomography (OCT) and functional progression with visual fields (VF) and their relationship with hypertension.

Methods: 191 eyes of 119 patients enrolled in a prospective, longitudinal study (Structural and Functional Progression of Glaucomatous Damage to the Macula study) were analyzed. These patients were tested with 10-2 and 24-2 VF and spectral-domain OCT obtained at 4-6 month intervals. 72 eyes (37%) had self-reported diagnosis of HTN. Linear mixed effects regression was used to test the relationship between summary statistics from VF and OCT and HTN diagnosis. The goodness-of-fit of relationships was assessed with Bayesian Information Criterion.

Results: The average (95% CI) 24-2 and 10-2 MD rate of progression was -0.31 dB/year (-0.43 to -0.19) and -0.36 dB/year (-0.48 to -0.24), respectively. The rate of progression for OCT was -1.14 microns/year (-1.53 to -0.75) for global RNFL and -0.89 microns/year (-1.30 to -0.48) for global macula GCL+. There was no significant difference in rate of progression between HTN and non-HTN patients with any OCT or VF parameter. Yet, models with better goodness-of-fit when testing the relationship between HTN and progression had the following OCT parameters: global macula GCL+, inferior macula GCL+, mean GCL+ of macular vulnerability zone (MVZ), and mean macula GCL+ of less vulnerability zone (LVZ), and VF parameters: 10-2 PSD and 10-2 MD.

Conclusions: HTN was not significantly associated with progression using any parameter. However, based on ranked model fits, macular structural and functional parameters had best performance fitting the progression data, suggesting their usefulness as endpoints. Studies defining HTN based on 24-hour BP monitoring and including modalities of treatment may better elucidate whether this prevalent systemic disease is an independent risk factor for glaucoma progression.

CONTROL ID: 3536858

SUBMITTER (NAME ONLY): Thomas Johnson

TITLE: The recipient retinal microenvironment regulates structural engraftment of transplanted human stem cell derived retinal ganglion cells in vivo

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.V. Johnson, K.Y. Zhang, A. Nagalingam, X. Chang, H.A. Quigley, D.J. Zack, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) transplantation holds potential for restoring lost vision in glaucoma and other optic neuropathies, but attempts thus far have been limited by low integration into the recipient retina. In organotypic retinal explants, we recently showed that disruption of the internal limiting membrane (ILM) allows donor RGCs to enter the retina. Here, we assess the effects of proteolytic ILM digestion and traumatic optic nerve injury on retinal localization of RGC somas and neurites following intravitreal transplantation in living mice.

Methods: Human embryonic stem cells expressing tdTomato at the BRN3B locus were differentiated into RGCs using an established protocol. Pronase-E was injected intravitreally into mice at various concentrations and ILM integrity was assessed 2 weeks later using laminin immunofluorescence. Optic nerve crush (ONC) was performed using cross-action forceps for 5 seconds. RGCs (50,000 cells) were transplanted intravitreally 2 weeks after pronase injection or optic nerve crush ($N \geq 13$ per group). Localization of donor RGC somas and neurites was quantified 2 weeks after transplantation using high-resolution 3D reconstructions of confocal microscopy z-stacks.

Results: Intravitreal pronase had a narrow effective concentration window: $<0.06\text{U/mL}$ showed little effect on the ILM, $>0.10\text{U/mL}$ induced frequent intraocular hemorrhage, but 0.08U/mL induced sizeable ILM defects without bleeding. Whereas $>90\%$ of transplanted eyes harbored surviving donor RGCs, $<1\%$ of transplanted cells remained at 2 weeks in control retina. By contrast, ONC and pronase treatment each doubled donor RGC survival ($p < 0.05$). The percentage of surviving donor RGC somas migrating into the host RGC layer ($1.4 \pm 0.7\%$ in control eyes) increased by >4 -fold with ONC ($5.8 \pm 1.5\%$, $p < 0.01$) and >12 -fold with pronase ($18.1 \pm 7.2\%$, $p < 0.001$). Appropriate donor RGC neurite localization to the inner plexiform layer occurred only after pronase treatment.

Conclusions: Both proteolytic ILM digestion and endogenous RGC injury through ONC increased survival and structural migration of transplanted human donor RGCs into the retinal parenchyma. Targeted interventions to promote functional integration of RGCs into the recipient retina, including ILM circumvention, may be required for RGC replacement to restore visual function in human patients with optic neuropathy.

CONTROL ID: 3536879

SUBMITTER (NAME ONLY): Emily Brown

TITLE: NMNAT1-Associated Retinal Degeneration: Consequences of Reduced Nuclear NAD⁺ Production

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: NMNAT1 is expressed ubiquitously, but mutations in this gene lead to retina-specific disease. The molecular mechanisms underlying disease pathogenesis, and why the retina is uniquely affected by mutations in NMNAT1, are poorly understood. We used a mouse model of NMNAT1-mediated disease to address the hypothesis that reduced NMNAT1 enzymatic function results in nuclear NAD⁺ depletion and transcriptional alterations specifically in the retina.

Methods: RNAseq and metabolomic analyses were performed on retina and kidney tissue collected from mice with the p.Val9Met mutation in Nmnat1 (a model of NMNAT1-associated disease) and wild type (WT) littermate controls. Samples were collected at 2 and 3 weeks of age, which is prior to the onset of retinal degeneration that begins at about 4 weeks of age. Western blotting, IHC, and qRT-PCR were performed to further assess the alterations in gene and protein expression identified by RNAseq. All experiments were conducted in compliance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Results: Nmnat1^{V9M/V9M} mice had a retina-specific reduction in the levels of NAD⁺ (P < 0.0001, unpaired t-test) that was not observed in other tissues, including the kidney, brain, skin, and heart. The kidney was used as a control tissue for RNAseq, and there were no differences in gene expression between WT and Nmnat1^{V9M/V9M} kidney samples at 2 or 3 weeks of age. Although no differences in gene expression were detected in the neural retinas of 2-week-old mutant and WT mice, by 3 weeks of age there were over 2,600 differentially expressed genes in the retinas of Nmnat1^{V9M/V9M} mice. These genes were enriched for immune pathways, phototransduction, apoptosis, and variety of other processes. Western blotting, qRT-PCR, and IHC were used to confirm the alteration in expression of several of the most highly significant genes, such as Gfap and Lad1.

Conclusions: These findings suggest that reduced NMNAT1 activity results in a retina-specific reduction in NAD⁺ and retina-specific transcriptional reprogramming prior to retinal degeneration. This includes increased expression of PARPs, the main nuclear consumer of NAD⁺, and other genes associated with DNA damage. Future work aims to further identify how mutations in NMNAT1 lead to this rapid alteration in gene expression and how these alterations contribute to retinal degeneration.

CONTROL ID: 3536882

SUBMITTER (NAME ONLY): Abdullah Abou-Samra

TITLE: Effect of bandpass filtering range on the mfERG parameters in patients undergoing screening for Plaquenil maculopathy

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abou-Samra, Brandon Regional Hospital, Brandon, Florida, UNITED STATES|G. Kiri, S. Bhaleeya, R.T. Tzekov, Ophthalmology, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to examine the effect of digital filtering on multifocal electroretinography (mfERG) parameters of patients sent for Plaquenil maculopathy screening.

Methods: This was a retrospective review of patients' records for patients that underwent HCQ maculopathy screening between December 2014 and October 2019 at USF Eye Institute, Tampa, FL. Only patients who underwent multifocal electroretinography (mfERG) were included. Recording of mfERG was performed binocularly on Espion mfERG system (Diagnosys LLC: Lowell, MA) with DTL electrodes using 61 hexagons stimulus, according to ISCEV mfERG standards. Each recording was subjected to four levels of digital bandpass (FFT/Adaptive) filtering: Level 1 (10-100 Hz), Level 2 (10-90 Hz), Level 3 (10-80 Hz) and Level 4 (10-60 Hz); spatial averaging was tuned off. The effect of filtering was evaluated on grouped ring averages (P1 amplitude) and the results were compared between Level 1 and the other levels of filtering by Dunn's multiple comparisons test.

Results: The retrospective review identified the records of 40 patients (4 males, 36 females), aged 54.7 +/- 14.1 years. Level 4 filtering induced significant decrease in P1 amplitudes compared to Level 1 for all rings ($p > 0.001$); Level 2 filtering did not cause a significant decrease ($p > 0.05$), while Level 3 filtering caused a significant decrease in ring #1 and ring #2 for left eyes ($p < 0.05$), but not in the other rings. Amplitude reduction associated with Level 4 filtering was most pronounced in ring #1 (~10%), while it was less pronounced for the rest of the rings (4.9%-5.7%). When percent difference between P1 amplitude decrease was plotted vs. P1 amplitude values, an interesting pattern emerged: there was a clear negative correlation between amplitude reduction and amplitude for rings #1 to #3 (Level 3 and 4), while it was present only for ring #3 at Level 2. No correlation was observed for rings #4 and #5 at any level of filtering. This result could be clinically important as it indicates that digital filtering has the most pronounced effect at lowest level of amplitudes, where it could be most useful.

Conclusions: The results of this study indicate that careful consideration should be given to digital filtering when evaluating the amplitudes of mfERG recordings for Plaquenil maculopathy screening. Future analysis will expand to effects on timing.

CONTROL ID: 3536891

SUBMITTER (NAME ONLY): Sophia Wang

TITLE: Looking for Low Vision: Deep Learning and Natural Language Processing to Predict Visual Prognosis

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.Y. Wang, B. Tseng, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low vision rehabilitation improves quality-of-life for visually impaired patients, but referral rates fall short of national guidelines. Automatically identifying from electronic health records (EHR) patients with poor visual prognosis could allow targeted referrals to low vision services. Since most clinical information is in free-text progress notes, we hypothesize that using information from notes would improve the ability to predict patients' visual prognosis over using purely structured information such as demographics and billing codes. The purpose of this study was to build deep learning models using natural language processing to integrate EHR data that is both structured and free-text to predict visual prognosis.

Methods: We identified 5612 patients with low vision (best documented visual acuity (VA) <20/40) on ≥ 1 encounter from EHR from 2009-2018, with ≥ 1 year of follow-up from the earliest date of low vision. Patients who did not improve to $> 20/40$ over 1 year were identified. Ophthalmology notes on or prior to the index date were extracted. Structured data available from the EHR included demographics, billing and procedure codes, medications, and exam findings including VA, intraocular pressure, corneal thickness, and refraction. To predict whether low vision patients would still have low vision a year later, we developed and compared deep learning models that used structured inputs to models that used both structured and free-text progress notes, represented by previously developed ophthalmology domain-specific word embeddings. Standard performance metrics including area under the receiver operating curve (AUROC) and F1 score were evaluated on a held-out test set.

Results: Among the 5612 low vision patients in our cohort, 40.5% (N=2278) never improved to better than 20/40 over one year of follow-up. Deep learning models utilizing structured inputs were able to predict low vision prognosis with AUROC of 79.1% and F1 score of 65.7%. Deep learning models further augmented with free-text inputs were able to achieve AUROC of 81.0% and F1 score of 69.0%.

Conclusions: Free text progress notes within the EHR provide valuable information relevant to predicting patients visual prognosis. Deep learning models utilizing data from EHR to predict ophthalmology outcomes should incorporate information from unstructured free-text progress notes where possible.

CONTROL ID: 3536900

SUBMITTER (NAME ONLY): Nan Zhang

TITLE: Electrophysiological and morphological changes in a low dose sodium iodate induced RPE damage model

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Zhang, X. Zhang, P. Girardot, V. Summers, M.A. Chrenek, J.T. Sellers, Y. Li, S. Ferdous, Y. Kim, D. Shelton, J.M. Nickerson, J.H. Boatright, ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|N. Zhang, X. Zhang, ophthalmology, Second Xiangya Hospital, Changsha, Hunan, CHINA|J.H. Boatright, Center of Excellence, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|Y. Kim, ophthalmology, Hallym University Medical Center, Yeongdeongpo-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Sodium iodate (NaIO_3) is selectively toxic to retinal pigment epithelium (RPE), inducing RPE cell death and subsequent photoreceptor degeneration. We explored differences in NaIO_3 -elicited responses of RPE and other retinal cells associated with mouse strains and dosing regimens.

Methods: A single dose of NaIO_3 at 15 mg/kg was injected intravenously into adult male C57BL/6J and 129/SV-E mice while control animals were injected with the vehicle (PBS). Morphological and functional changes were characterized by fundus imaging, spectral domain optical coherence tomography (SD-OCT), ERG, histological, and immunofluorescence techniques.

Results: The 15 mg/kg NaIO_3 dose initially induced a transient increase in scotopic ERG a-, b-wave and c-wave amplitudes in 12 hours post-injection, followed by progressive structural and functional degradation at 3 days in C57BL/6J and at 1 week in 129/SV-E mice, including depression of ERG response, loss of RPE cells, retinal structure disruption, and thinning of retinal thickness. Strain-difference existed in these two strains: 129SV-E mice showed slower photoreceptor degeneration (7 days post-injection) compared with C57BL/6J mice (3 days post-injection), which indicated that C57BL/6J mice are more sensitive to toxicity of NaIO_3 . Immunofluorescence imaging revealed Müller cell activation following NaIO_3 administration. RPE cell death occurred in a large posterior-central lesion, with a ring-like transition zone of highly irregular, abnormally shaped cells that appeared as early as 12 hours after NaIO_3 treatment in both strains. RPE cells in the far periphery survived with generally normal morphology.

Conclusions: The morphological and functional effects of NaIO_3 on RPE and retina were dependent on timing, dosage, and strain of mouse. Transient rise and fall of ERG response were thoroughly characterized in both strains. Far peripheral RPE cells were much more resistant to damage than central RPE. It may be that peripheral vs central RPE cells have fundamentally different properties, or location-specific factors mediate these differences in resiliency.

CONTROL ID: 3536903

SUBMITTER (NAME ONLY): Jimmy Chen

TITLE: Quantifying Oxygen Exposure for Predicting Treatment-Requiring Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Chen, J. Anderson, A.S. Coyner, S. Ostmo, K. Sonmez, J. Campbell, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Singh, J. Kalpathy-Cramer, Radiology, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|D. Erdogmus, Electrical and Computer Engineering, Northeastern University, Boston, Massachusetts, UNITED STATES|C. McEvoy, B. Jordan, D. Dukovny, R. Schelonka, Pediatrics, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|R.V. Chan, Ophthalmology, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxygen exposure and extreme prematurity are among two of the strongest risk factors for severe retinopathy of prematurity (ROP), however current screening criteria focuses on birth weight and gestational age (GA) at birth. Improved risk models may reduce the screening burden for low-risk infants and improve disease detection for infants with the most severe ROP, including aggressive posterior ROP (APROP). The purpose of this study was to evaluate the additive predictive value of quantifying oxygen exposure in early life for detection of treatment-requiring (TR-) ROP and APROP.

Methods: Demographics and oxygen exposure parameters were manually extracted from the electronic health record for each week of life (WOL) for 244 infants, 33 of whom eventually developed TR-ROP and 5 of whom developed APROP. Cumulative minimum, maximum, and total fraction of inspired oxygen (FiO₂) were calculated by summing values per WOL. Using 5-fold cross-validation, models using various combinations of birthweight, GA and FiO₂ were trained using random forest tuned with randomized grid search for prediction of future TR-ROP. Performance was evaluated using mean area under the receiver operating curve (AUROC) and precision-recall curve (AUPRC). To test the predictive value of oxygen exposure for APROP, cumulative minimum FiO₂ exposure was also plotted against eventual ROP outcome (no treatment, TR-ROP without APROP, or APROP) and an AUROC score was generated.

Results: On 5-fold cross-validation, the models trained on GA + cumulative minimum FiO₂ exposure had slightly higher performance than the models trained on GA alone (Figure 1, mean AUROC = 0.93±0.06 vs. 0.91±0.06, AUPRC = 0.76±0.08 vs. 0.74±0.13 respectively) for TR-ROP. For APROP, the AUROC of cumulative minimum FiO₂ exposure was 0.92 with clear dose response between oxygen exposure and level of ROP (Figure 2).

Conclusions: Quantitative oxygen exposure variables can be extracted and used to augment the identification of high-risk infants for developing TR-ROP, including APROP. Future work should focus on prospectively evaluating models that account for oxygen exposure.

CONTROL ID: 3536904

SUBMITTER (NAME ONLY): Nathaniel Mullin

TITLE: Mutational burden of mt3243G in blood correlates with the age of onset of retinal symptoms.

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.K. Mullin, K.R. Anfinson, L.M. Affatigato, J.L. Andorf, M.J. Riker, R.F. Mullins, E.M. Stone, B.A. Tucker, University of Iowa Institute for Vision Research, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The mitochondrial mt3243A>G mutation is a common cause of retinal degeneration in patients with MIDD and MELAS. The relationship between mutational burden in peripheral tissues and severity of retinal disease is not currently well understood. We developed a digital PCR assay to screen blood and skin samples from 8 patients with clinically diagnosed and molecularly confirmed mt3243A>G disease. Using this platform, we correlated onset of visual symptoms with blood and skin mutational burden and explored the relationship between mitochondrial DNA copy number and mt3243A>G.

Methods: DNA was isolated from cultured dermal fibroblasts and peripheral blood mononuclear cells donated by 8 patients (ages 27-64) known to have retinal disease caused by the mt3243A>G mutation. The proportion of mutant (G) to wildtype (A) alleles was measured using digital PCR or TA-cloning with Sanger sequencing of resulting clones. Additionally, the mitochondrial DNA copy number was assessed by digital PCR. Patients were evaluated clinically by a single ophthalmologist. Molecular testing was performed masked to clinical information.

Results: The proportion of mt3243G allele varied greatly both between individuals and between cell type (blood: range 7%-39%, mean 19.13%; skin: 13%-82%, mean 45.63%). However, there was a strong correlation between blood and skin mt3243G proportion within the same individual ($R^2 = 0.606$, P value = 0.023). Additionally, a correlation between mt3243G proportion and mtDNA copy number was observed in cultured skin fibroblasts ($R^2 = 0.626$, P value = 0.019), but not in blood. Finally, we found that age of onset of visual symptoms correlated with proportion of mt3243G in blood ($R^2 = 0.820$, P value = 0.002) but not in skin (Figure 1).

Conclusions: Our results indicate that precise measurement of mt3243G mutational burden in peripheral tissues may be clinically relevant in retinal disease. Higher mutational burden of mt3243G correlated with an earlier onset of visual symptoms. Digital PCR offers a robust method to measure mutational burden in diseases caused by heteroplasmic mutations such as mt3243A>G. Future studies investigating the mechanisms by which mt3243 mutational burden is maintained in various cell types may shed light on the heterogenous phenotypes present in this family of disease.

CONTROL ID: 3536907

SUBMITTER (NAME ONLY): Alexander Miller

TITLE: Analysis of Urgent Follow Up Visits and Complications After Intravitreal Injections: A Retrospective Cohort Study

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the incidence of acute complications following an intravitreal injection.

Methods: A retrospective cohort study was performed at a private retinal practice in Ohio. Using the practice management software database, patients with intravitreal injections over a recent 2 year period were collected. From this group of patients, the search was further refined to include only those with unscheduled or urgent visits within 7 days of an injection. Data collected included: age, gender, eye involved, medication injected, diagnostic reason for injection, reason for urgent follow-up, length between date of injection and urgent follow-up, visual acuity on injection visit and urgent visit, intraocular pressure on day of injection and on date of urgent follow-up, and type of anesthesia during the injection.

Results: A total of 73,286 injections were performed by 15 retinal specialists during the study period, with 441 injections (n=441) resulting in urgent follow-up visits (0.60%). The mean patient age was (72.1 ± 30.4) years, with 187 patients male (42.4%) and 254 female (57.6%).

Medications injected over the 2 years were: Eylea (60.3%), Lucentis (22.4%), Avastin (13.4%), Ozurdex (2%), Triesence (1.6%) Beovu (1.59%), Iluvien (0.2%), and Yutiq (0.03%).

Medications injected in eyes with urgent visits included: Eylea (42.9%), Avastin (37.4%), Lucentis (7.9%), Ozurdex (6.8%), Beovu (2.7%), and Triesence (2.3%).

The length in days between date of injection and urgent follow-up was a mean of 3.96 ± 2.14 days.

Reason for urgent follow-up included: blurred vision in 164 patients (37.2%), seeing flashes or floaters or having posterior vitreous detachment (PVD) in 55 (12.5%), pain in 42 (9.5%), corneal abrasion in 43 (9.8%), subconjunctival hemorrhage in 33 (7.5%), corneal dryness or foreign body sensation in 30 (6.6%), endophthalmitis in 20 (4.5%), vitreous hemorrhage in 18 (4.1%), iritis or uveitis in 11 (2.5%), miscellaneous complications in 9 (2.0%), elevated intraocular pressure in 7 (1.6%), and choroidal neovascular membrane in 4 (0.9%), retinal detachment or tear in 4 (0.9%), and traumatic cataract in 2 (0.45%).

Conclusions: Intravitreal injections resulted in an incidence of 0.60% urgent unscheduled follow-up visits within 7 days of injection in this large retinal specialty practice. Blurred vision and symptoms of PVD were the most common causes of urgent visits.

CONTROL ID: 3536913

SUBMITTER (NAME ONLY): Vittorio Porciatti

TITLE: Progressive shortening of Steady-State Pattern ERG latency with increased LHON severity

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Porciatti, D. Alba, W.J. Feuer, J.L. Davis, B.L. Lam, Bascom Palmer Eye Institute, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the baseline Pattern ERG (PERG) of Leber hereditary optic neuropathy (LHON) patients with different stages of severe visual loss (≤ 35 ETDRS letters) before gene therapy (GT).

Methods: The study was part of a phase I GT trial investigating the safety of a scAAV2 investigational product (IP) containing a wild-type synthetic nuclear encoded ND4 subunit for G11778A LHON. Patients (n=28) were enrolled into groups I (GT I: chronic bilateral), II (GT II: acute bilateral), and III (GT III: unilateral, better eye acuity ≥ 70 letters) and tested with PERG prior to IP injection and compared to PERG measurements of 210 normal control (NC) subjects. Steady-state PERGs (SS-PERG) were recorded simultaneously from both eyes and analyzed in the frequency-domain to retrieve amplitude (nV) and phase (deg), which was converted in latency (ms). The SS-PERG latency corresponds to the time-to-peak of the P50 wave of the standard transient PERG. The 2 baseline measurements of each eye were averaged. Then measurements from the 2 eyes of groups GT I, GT II, and NC were averaged yielding 1 measurement per patient. For group GT III, measurements from asymptomatic (GT III-A) and symptomatic (GT III-S) eyes were analyzed separately. Mean amplitudes and latencies were compared with GEE methods followed by post-hoc least significant difference (LSD) tests to account for inclusion of two measurements of GT III patients.

Results: Ages were similarly distributed in the different subject groups. PERG amplitudes of LHON patients were lower than those of normal controls ($p < 0.001$), but did not differ among patient groups. SS-PERG latencies differed by disease stage (see table) with G III-A shorter than NC ($p = 0.002$) but longer than G III-S ($p = 0.01$). G II (acute bilateral) latencies were further shortened than G III-S ($p = 0.03$). G I latencies were shorter than NC but did not differ from other GT patient groups (all $p > 0.1$).

Conclusions: While the baseline SS-PERG amplitude was much reduced in all LHON groups and did not distinguish between disease stage, SS-PERG latency progressively shortened with increasing disease severity. Latency shortening is consistent with LHON pathophysiology whereby smaller/slower axons are primarily affected resulting in the residual response being dominated by larger/faster axons. These results may inform timing of GT injections for preservation of small axons.

CONTROL ID: 3536917

SUBMITTER (NAME ONLY): Sana alhajri

TITLE: Hypoxic Ischemic Encephalopathy and Visual outcomes: A Single Center Retrospective Study

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Neonatal hypoxic ischemic encephalopathy (HIE) is one of the most common causes of neonatal death and long-term disability. The effect of HIE on visual outcomes, especially the effect of seizure and the correlation of brain MRI finding with visual function abnormalities is not well studied. We aim to study the visual outcomes in infants with HIE.

Methods: We did a retrospective chart review of neonates admitted to University of Illinois, Chicago, with a diagnosis of HIE. We analyzed the visual outcomes of these neonates in their subsequent follow up visits. Univariate and multivariate analysis were performed to determine the predictors of abnormal visual outcomes with a P value less than 0.05, considered significant.

Results: We had 57 neonates (34 Male/23 Female) with a diagnosis of HIE during the study period 2009-2019, which were divided into mild (27) moderate (23) and severe (7) HIE based on SARNAT scoring. Mean birth weight (BW) was 3265 ± 618 grams. 12% had severe HIE, and 11(13%) required inotropic support. 34(59.6%) underwent therapeutic hypothermia (TH), 13 (22.8%) had seizures. 14 of the 48 (29.2%) neonates who underwent MRI of the brain had abnormal imaging findings. 4/14 had lesions of occipital cortex, 7 had optic radiation abnormalities, 10 had DW restrictions, and 4 had geniculate body lesions. 16 (28%) patients had visual assessment on follow up exam, out of which only 2 had visual abnormalities. One of them had reduced visual acuity, and other one had refractory amblyopia. One patient with visual abnormality had a full-term gestation, with an APGAR of 0,0, 2, 4, 7 and a BW of 3420 g, had severe HIE with seizures, had use of inotropes, TH, and seizure medications. Another patient was also a full-term, with an APGAR of 1, 4, 7, BW of 3040 had mild HIE, with no seizures, and no use of TH or inotropes. We didn't find any significant predictors of abnormal visual outcomes. In our cohort, severe HIE was associated with imaging abnormalities ($p=0.003$), inotrope use ($p=0.01$), seizures ($p<0.001$) and use of TH ($p<0.001$).

Conclusions: Severe HIE was found to be associated with imaging abnormalities of visual pathways on brain MRI. However, the sample size was small and had limited follow up to show any significant association between HIE and abnormal visual outcomes. Future research may focus on obtaining larger sample size and better follow up of neonates with HIE, especially with severe HIE.

CONTROL ID: 3536923

SUBMITTER (NAME ONLY): Kyung-Min Roh

TITLE: Remote retinal imaging of patients from the ER using robotically aligned OCT

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Roh, A. Song, E. Choi, S.A. Chandramouli, J. Izatt, R.P. McNabb, A.N. Kuo, Dept of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|P. Ortiz, J. Izatt, A.N. Kuo, Dept of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|A.T. Limkakeng, Div of Emergency Medicine, Dept of Surgery, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Significant percentages of emergency room (ER) patients needing an ocular fundus examination do not always receive one by primary providers in the ER. A key reason is the difficulty in using the standard direct ophthalmoscope available in that setting. We have developed and demonstrated the remote application of a robotically aligned OCT (RAOCT) system capable of self-aligning and acquiring high quality volumetric retinal images of subjects from the ER.

Methods: Patients presenting with eye complaints in the ER with ophthalmology referrals were recruited over 7 nonconsecutive days. Hemodynamically unstable patients were excluded.

5 consented subjects under an IRB approved protocol were imaged by the RAOCT system with the operator either 6 feet behind a Plexiglas barrier (2 subj.) or in a separate room remotely connected to the RAOCT system via the local network (3 subj.). Figure 1 shows the layout of the imaging room and the live information transmitted to the operator including 2-way teleconferencing, OCT acquisition, and face/pupil tracking. The RAOCT system used a swept source retinal OCT system ($\lambda_0=1043\text{nm}$; 100 kHz) to capture 32° FOV retinal images including both the fovea and optic nerve head in single acquisitions. Rectangular volumes (700 A-Scans x 250 B-Scans) and full width repeated B-scans (2000 A-scans x 100 B-scans) were taken. The operator confirmed robot-subject alignment and triggered acquisition via a remote terminal session to the RAOCT computer (or directly when non-remote).

Select volumes were semi-automatically segmented and used for thickness maps. Repeatability was described by the standard deviation of repeated retinal thickness measures in the central 1 mm.

Results: Figure 2 shows thickness maps with representative B-scans for non-remotely (2A) and remotely (2B) imaged subjects. The central zone mean range was 294-300 μm with a mean SD of $\pm 1 \mu\text{m}$ and 260-301 μm with a mean SD of $\pm 2 \mu\text{m}$ for non-remotely and remotely imaged subjects respectively.

Conclusions: We have demonstrated remote imaging of ER patients with RAOCT. RAOCT has the potential to help non-specialist personnel evaluate the eye in non-specialty settings with further potential for telemedicine applications.

CONTROL ID: 3536931

SUBMITTER (NAME ONLY): Emily Chew

TITLE: The Results of the 10 Year Follow-on Study of the Age-Related Eye Disease Study 2 (AREDS2)

SESSION TITLE: Dry AMD therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To assess the long-term effects of adding lutein/zeaxanthin and omega-3 fatty acids to the Age-Related Eye Disease Study (AREDS) supplements on age-related macular degeneration (AMD) progression and adverse side-effects.

Methods: The AREDS2 clinical trial randomly assigned participants with bilateral intermediate AMD or late AMD in one eye to lutein/zeaxanthin and/or omega-3 fatty acids or placebo. Secondary randomization also evaluated varying doses of beta-carotene (0 vs. 15 mg) and zinc (25 vs. 80 mg). At the end of the clinical trial, a follow-up study was conducted with 6-monthly telephone calls to the surviving AREDS2 participants from the central coordinating center to collect outcome data and adverse events for safety monitoring for an additional 5 years. Medical records were obtained from treating physicians to validate any self-reported diagnosis or treatment of late AMD and cataract and side-effects. AREDS2 supplements with lutein/zeaxanthin, vitamin C and E, and zinc plus copper were provided to all participants during this additional follow-up. Repeated measures logistic regression was used in the primary analyses.

Results: 6360 study eyes (3887 participants) were analyzed and 3047 (48%) progressed to late AMD. The main effects of lutein/zeaxanthin vs. no lutein-zeaxanthin and of omega-3 fatty acids vs. no omega-3 fatty acids resulted in hazard ratios of 0.91 (95% CI: 0.89-0.99) ($p=0.03$) and 1.00 (0.92-1.09) ($p=0.91$), respectively. When the lutein/zeaxanthin main effect analysis was restricted to those randomized secondarily to beta-carotene, the HR was 0.80 (0.69-0.92) ($p=0.003$). On direct analysis of lutein/zeaxanthin vs. beta-carotene, the HR was 0.85 (0.74-0.98) ($p=0.026$). For the comparisons of low vs. high zinc and no beta-carotene vs. beta-carotene, the HRs were 1.04 ($p=0.48$) and 1.04 ($p=0.50$), respectively. For those randomized to beta-carotene, the odds ratio (OR) of developing lung cancer was 1.92 (1.11-3.31) ($p=0.02$) while the OR for those randomized to lutein/zeaxanthin was 1.19 (0.82-1.73) ($p=0.35$).:

Conclusions: The 10-year Follow-on study replicated the findings of the randomized clinical trial at 5 years.

Lutein/zeaxanthin, when compared with beta-carotene, had an incremental beneficial effect on progression to late AMD. Beta-carotene doubled the risk of lung cancer, providing support for lutein/zeaxanthin as a replacement of beta-carotene in the AREDS2 supplements

CONTROL ID: 3536942

SUBMITTER (NAME ONLY): Maria Pinazo-Duran

TITLE: Characterization of dolphin tear metabolomics

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dolphin ocular surface (OS) are subjected to continuous adaptation mechanisms between air and aquatic ecosystem. Knowledge on dolphin tears composition may help understanding human OS disorders. We wanted to address tear metabolomic signature in aquarium dolphins

Methods: Tear samples from the external eye canthus were collected from four dolphins (*Tursiops Truncatus*), aged 19-33 years, housed at the Madrid Zoo Aquarium. 40-50 microliters of tears from each dolphin were processed by high-resolution magic angle spinning (HR-MAS) metabolomic platform. HR-MAS spectra were acquired on a Bruker Avance DRX 600 spectrometer, operating at a ¹H of 600.13 MHz frequency. Precise chemical shift region was analysed. Resonances between 0.50-5.26 parts-per-million of spectrometric frequency were considered.

Quantification of signals pertaining to specific regions was done and data analysis routines were performed.

Metabolite assignment was based on academic/proprietary spectral databases and our previous reports. Principal component analysis was applied to the data set to sharpen separation between animals.

Results: Mean age of 1 male and 3 female dolphins was 28 ± 7 years. Dolphins are primarily monocular (with limited capability for binocular vision), similarly in air and water. Neither ocular nor systemic diseases were previously recorded in these cetaceans. Macroscopic appearance of dolphin tears was a greasy gel-like, visco-elastic secretion. 19 metabolites were identified in dolphin tears, being the most abundant: glucose, glycoproteins, fatty acids, and mobile lipids. In the rank of millesimal we found citrulline, lactate, creatine phosphate, carnitine, acetate, and choline. Absence of the lipid/cholesterol fraction was noticed. Study limitations include the small sample size and the necessity of larger metabolomic assays and other indicators, such as tear osmolarity, to complete knowledge on dolphin tear composition

Conclusions: This is the first description of dolphin tear metabolomics. The identified metabolite composition suggests that the circumorbital conjunctival gland may be analogous to the terrestrial lacrimal gland. Dolphin tear metabolites may act by reducing the hydrodynamic resistance on the OS, also protecting the eyes against infectious agents. Our data suggest that dolphin tears is a comprehensive resource to further study OS correlations in humans

CONTROL ID: 3536951

SUBMITTER (NAME ONLY): Liya Xu

TITLE: Establishing Clinical Utility of ctDNA Analysis for Diagnosis, Prognosis, and Treatment Monitoring of Retinoblastoma: the Aqueous Humor Liquid Biopsy

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There are currently no eye-specific molecular biomarkers in clinical practice for retinoblastoma (RB), a rare, pediatric intraocular cancer, because direct tumor biopsy is prohibited. We overcome this problem by using the aqueous humor (AH) as a liquid biopsy source of cell-free tumor DNA (ctDNA). This study aims to detail the first prospective data using the AH liquid biopsy to identify diagnostic and prognostic molecular biomarkers present at diagnosis and discuss the validity and clinical utility of the platform.

Methods: Subjects included 7 eyes of 6 RB patients with at least 12 months of follow-up. The AH liquid biopsy was used at diagnosis and prospectively throughout therapy until the eye was cured or required enucleation due to persistent disease. Cell-free DNA (cfDNA) was isolated and sequenced to assess genome-wide somatic copy number alterations (SCNAs) and mutation in RB1 gene. Results were compared to peripheral blood RB1 testing. Tumor fraction (TFx) was calculated using ichorCNA. Primary clinical endpoint was ocular salvage versus enucleation.

Results: Tumoral genomic information was detected in 100% of diagnostic AH samples. Of the 7 diagnostic AH samples, 5/7 were positive for RB SCNAs. Mutational analysis identified RB1 variants in 5/7 AH samples, including the 2 samples in which no SCNAs were detected. Two eyes failed therapy and required secondary enucleation; both had poor prognostic biomarkers (chromosome 6p gain and MYCN amplification) present in the AH at the time of diagnosis. No patients had any complications from AH sampling or demonstrated extraocular spread of disease.

Conclusions: This initial prognostic study demonstrates feasibility, safety, and utility of an AH liquid biopsy at diagnosis. Molecular profiling of AH provides impactful tumor-derived diagnostic and prognostic information from a single 100 µL AH sample. In the context of previously established pre-analytical, analytical, and clinical validity, this provides evidence for larger, prospective studies to further establish the clinical utility of the AH liquid biopsy and its applications to precision oncology for RB.

CONTROL ID: 3536952

SUBMITTER (NAME ONLY): Devayu Parikh

TITLE: Gonioscopy-assisted transluminal trabeculotomy for the treatment of glaucoma in uveitic eyes

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the outcomes of gonioscopy-assisted transluminal trabeculotomy (GATT) for the management of open-angle glaucoma in the setting of uveitis.

Methods: A retrospective chart review was performed of patients diagnosed with uveitis who underwent GATT between January 1st, 2014 and December 31st, 2019 due to medication-refractory open-angle glaucoma in the setting of uveitis. The primary outcomes analyzed included success rate, defined as IOP reduction >20% from baseline or IOP between 5-21mmHg at the 3-month visits; on a stable number or fewer IOP lowering agents, and no need for additional glaucoma surgery. Additional endpoints include IOP, number of glaucoma medications, and steroid regimen.

Results: 16 eyes from 13 patients were included in the study. The average age was 45.3±12.7 years (56% female). Average follow-up period was 29.5±14.7 months (range of 7.2-48.9 months). The predominant cause of glaucoma was inflammatory in 56%, steroid-induced in 19% and a mixture of both in 25%. At 12 months, the cumulative success rate was 81%. The 19% of eyes that failed required reoperation due to IOP spikes >25 mmHg. Mean IOP was 37.8±13.0 mmHg at baseline and 12.2±3.0 mmHg at 12 months (68% reduction; p<0.0001). The average number of glaucoma medications was 4.6±1.3 at baseline and 2.2±0.7 at 12 months (52% reduction; p<0.0001). At the 12-month visit when compared to the baseline, not only were a greater number of patients on both oral and topical steroid regimens, the mean dose was higher. Transient hyphema was the most common post-operative complication seen in 44% of eyes at 1 week, but all cases self-resolved by 1 month.

Conclusions: This small retrospective study shows that GATT is successful, effective and safe for the management of glaucoma in uveitic adult eyes. As a conjunctival-sparing, minimally-invasive procedure, GATT is promising as an initial treatment for refractory glaucoma in uveitis.

CONTROL ID: 3536953

SUBMITTER (NAME ONLY): Amitha Domalpally

TITLE: Effect of metformin on the development of age-related macular degeneration (AMD) in the Diabetes Prevention Program Outcomes Study (DPPOS)

SESSION TITLE: Dry AMD therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Based on retrospective studies, metformin has been suggested to have a beneficial role in lowering the risk of AMD. The DPPOS is a follow-up phase of a large multicenter randomized clinical trial to investigate the effects of treatment with metformin or an intensive lifestyle modification (lifestyle), compared to placebo on preventing the onset of type 2 diabetes in a population at high-risk of developing diabetes. The DPPOS provides a unique opportunity to study the effects of metformin and lifestyle changes in preventing or delaying the development of AMD.

Methods: Color fundus photographs (FP) and optical coherences tomograms (OCT) were evaluated by the Wisconsin Reading Center in 1592 participants at year 16 of study follow up for presence and severity of diabetic retinopathy and AMD. AMD was classified as early, intermediate, or advanced (neovascular AMD or geographic atrophy) based on FP and OCT. Drusen size was classified as small, intermediate, or large. Differences in the prevalence and severity of AMD across the randomized groups were evaluated using Pearson's Chi² test.

Results: Participants were randomly distributed between three interventional arms; 514 in the lifestyle arm, 549 in metformin, and 529 in the placebo arm. All 3 arms were balanced for baseline characteristics including age, gender, race, smoking habits, body mass index, and education level. AMD was identified in 479 (30.1%) participants; 229 (14.4%) had early, 218 (13.7%) intermediate and 32 (2.0%) had advanced AMD. There was no significant difference in the presence of AMD between the three groups: 29.6% in lifestyle, 30.2% in metformin, and 30.7% in the placebo (p = 0.93). There was also no difference in the distribution of early, intermediate, and advanced AMD between the intervention groups (p = 0.095, Figure).

Conclusions: There was no statistically significant difference in the prevalence and severity of AMD between the three treatment groups after 16 years of follow-up. These data suggest neither metformin nor lifestyle changes for weight loss have a beneficial effect on lowering the risk of AMD. Additional observational analysis with cumulative years of metformin as main exposure is ongoing and may reveal further information.

CONTROL ID: 3536969

SUBMITTER (NAME ONLY): Susan Vitale

TITLE: Does cataract surgery increase the risk of future development of late AMD? A nested case-control study from the AREDS2 and AREDS2 Follow-On studies

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vitale, E. Agron, S. Bhandari, D. Peprah, M.C. Farrell, T.D. Keenan, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|T.E. Clemons, Emmes Corporation, LLC, Rockville, Maryland, UNITED STATES|A. Domalpally, Fundus Photograph Reading Center, University of Wisconsin, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have suggested that cataract surgery may increase the risk of developing late age-related macular degeneration (AMD). The Age-Related Eye Disease Study 2 (AREDS2) and AREDS2 Follow-On (A2FO) studies provided longitudinal information to assess the association between incident cataract surgery (CS) and risk of developing late AMD.

Methods: AREDS2 (2006-2012) was a randomized clinical trial evaluating the potential benefit of a modified nutritional supplement (lutein/zeaxanthin, zinc, and other nutrients) on the development of late AMD; A2FO (2013-2018) provided an additional 5 yrs of follow-up on a subset of AREDS2 participants. AREDS2 assessed CS status and AMD score at annual visits and, every 6-mos between visits, obtained information on CS and late AMD treatment (tx) by telephone. A2FO, initiated after the randomized trial concluded, assessed CS status and information on diagnosis and tx of late AMD at 6-monthly study visits via telephone only. Information regarding CS and tx for late AMD obtained by telephone was confirmed by medical record review. We identified case eyes (incident CS after AREDS2 randomization and no late AMD before or at the time of CS). The study visit when CS was first noted was used as the "baseline" visit for case eyes. We identified potential control eyes (no CS during AREDS2 or A2FO, no late AMD at AREDS2 randomization or before year 1). The year 1 study visit was used as the "baseline" visit for control eyes. We performed 1-1 propensity score matching (SAS 9.4) on age (at "baseline" visit), AMD score at the visit preceding the "baseline" visit, length of follow-up after the "baseline" visit, sex, education level, treatment group, smoking status, diabetes, aspirin use, and statin use. Matched pairs analysis and conditional logistic regression models were used to assess risk of developing late AMD (defined as photographic grading of late AMD or medical record documentation of diagnosis or tx of late AMD).

Results: There were 1201 case eyes and 2645 potential control eyes. Propensity score analysis identified 1081 matched pairs. 412 case eyes (CS) and 433 control eyes (no CS) developed late AMD after the "baseline" visit: matched pairs odds ratio, 0.92, 95% CI, 0.77-1.10, p=0.34.

Conclusions: In the AREDS2 and A2FO studies, cataract surgery did not appear to increase the risk of developing late AMD.

CONTROL ID: 3536977

SUBMITTER (NAME ONLY): Riccardo Cheloni

TITLE: Ability of different enface OCT slab methods to detect RNFL reflectance defects in glaucoma

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Cheloni, J. Denniss, School of Optometry & Vision Science, University of Bradford, Bradford, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Optimal methods to extract enface OCT slab images to detect retinal nerve fibre bundle (RNFB) defects are undetermined. We explored the ability of several methods for slab extraction to objectively assess glaucomatous RNFB reflectance defects in enface OCT images.

Methods: Dense SD-OCT scans were performed in 16 eyes with glaucoma (median age: 70, range 61-77) and 19 age-similar controls. Enface slab images depth-averaging reflectivity below the inner limiting membrane (ILM) were generated with 6 different methods. Five methods considered single slabs of various thickness and depth (Figure 1). One novel method combined seven 16µm thick slabs from 8 to 116µm below the ILM (Figure 2), seeking to explore all depths with potential RNFB presence. In the combined slabs method, defects were defined when occurring in any slab. All methods adjusted for the individual position of the raphe, fovea and optic disc. Superpixels of glaucoma eyes were considered abnormal if reflectivity fell below the kernel density estimated 1st percentile of control data. Ability to detect glaucoma defects was measured by proportion of abnormal superpixels. Proportion of superpixels below the 1st and 5th percentile in controls was used as a surrogate for false positive rate. Differences in performance between slab methods were tested with linear mixed models.

Results: Ability to detect glaucomatous defects varied significantly among slab methods ($\chi^2_{(5)}=119.9$, $p<0.0001$), with the combined slabs method detecting 5-9% more abnormal superpixels than others (all $p<0.0001$). No method found abnormal superpixels at the 1% level in controls. Proportion of abnormal superpixels in controls at the 5% level varied slightly between approaches ($\chi^2_{(5)}=15.5$, $p=0.009$), being similar or slightly larger (1.8-2.2%) for the combined slabs approach.

Conclusions: Slab extraction method affects ability to detect glaucoma abnormalities in enface OCT images. Our novel method evaluates all depths with potential RNFB presence by combining several thin slabs at each location, resulting in greater detection of glaucomatous reflectance abnormalities.

CONTROL ID: 3536987

SUBMITTER (NAME ONLY): Jonathan Lin

TITLE: Anterior segment optical coherence tomography (AS-OCT) for the assessment of corneal alkali injury

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lin, E.R. Kraft, S. Giannos, M. Schmitz-Brown, M. Motamedi, P. Gupta, Ophthalmic and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|J. Luisi, Internal Medicine, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Alkali chemical burns to the cornea can ultimately lead to blindness. Slit lamp exam is traditionally used to assess damage to guide management; however, it is limited by poor depth analysis and obstruction by tissue scarring. Anterior segment optical coherence tomography (AS-OCT) is a non-invasive, high-resolution imaging modality that can potentially be used to overcome these limitations and provide fast, depth-resolved evaluation of corneal wound healing and remodeling.

Methods: Following an IACUC-approved protocol, acute injury model of alkali burn was performed by applying a 2 mm diameter circle of filter paper soaked in 1.0M NaOH to the right eye for 30 seconds, while the left eye was treated with PBS as a control. AS-OCT was performed on the cornea and iris simultaneously, before and after the chemical burn, as well as at 7 and 14 days following the burn. Corneal thickness of each eye was measured at nine points on a central cornea slice in ImageJ and OCT angiography (OCTA) was performed on the images captured by AS-OCT using a custom algorithm.

Results: We determined that alkali burns result in increased corneal thickness immediately post-injury (+70.33%), peaking on day 7 (+105.02%) and regressing slightly on day 14 (+101.95%). AS-OCT observed epithelial bullae and corneal opacity by day 7, and Descemet's membrane detachment by day 14. In addition, beginning on day 7, OCTA showed development of neovascularization from the limbal area towards the center of the cornea. An anterior chamber inflammation was also noted, with hyper- and hypo- reflective stromal cysts, as well as expansive edemas, on day 7.

Conclusions: AS-OCT was able to, with high sensitivity, detect edema/swelling, opacification, and neovascularization resulting from alkali burn. It also provided cross-sectional information for non-invasively exploring angiogenesis and tissue remodeling, as well as 3D visualization of the anterior chamber and corneal layers, regardless of the amount of corneal scarring. AS-OCT can be a valuable adjunct to standard diagnostic tools for the assessment of corneal alkali injury and wound healing.

CONTROL ID: 3537007

SUBMITTER (NAME ONLY): Breyanna Cavanaugh

TITLE: Functional Compensation in a Mouse Model of Inherited Retinal Degeneration Caused by a C-terminal Prph2 Truncation Mutation.

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.L. Cavanaugh, M.L. Milstein, R.C. Boucher, A.F. Goldberg, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: A broad variety of progressive retinal diseases are caused by mutations in PRPH2. This gene encodes peripherin-2/rds (P/rds), an integral membrane protein that shapes rod and cone photoreceptor outer segment (OS) disks. Instances of human pattern dystrophy have been associated with a TYR285stop nonsense mutation predicted to truncate the protein's cytoplasmic C-terminus. To advance understanding of inherited retinal degenerations caused by defects in PRPH2, we have generated and are investigating a TYR285stop gene-edited mouse model.

Methods: TYR285stop mice (Prph2^{Y285x/Y285x} and Prph2^{Y285x/+}) generated via CRISPR/Cas9 gene editing were outcrossed onto the C57BL6/J background until congenic. Prph2^{Y285x/Y285x} and Prph2^{Y285x/+} mutants were compared at postnatal day 21 to WT and to Prph2^{rds/rds} and Prph2^{rds/+} age-matched controls. Phenotyping assays included: western blotting, retinal layer thickness evaluations in paraffin sections, retinal whole mount IHC 3D imaging, full-field electroretinography (ERG), and rod spherule synaptic ribbon counts.

Results: Prph2^{Y285x/Y285x} mice developed significantly reduced (25%) numbers of photoreceptors which were unable to elaborate OSs. In contrast, the Prph2^{Y285x/+} disease model mice developed normal numbers of photoreceptors, which elaborated OSs with abnormal ultrastructure, but a near-normal IS-OS layer thickness. Compared to WT, Prph2^{Y285x/+} retinas expressed less P/rds (49%), rhodopsin (45%), rom1 (49%), and GARPs (66%). Scotopic ERG showed that although rod photoreceptor a-waves were significantly reduced (50%), rod-mediated b-wave amplitudes were maintained at WT levels. Photopic ERG showed that cone-mediated responses (b-wave amplitudes) were also near-normal. No changes were detected in the number of synaptic ribbons present in rod terminals.

Conclusions: The P/rds C-terminus was found to be essential for in vivo protein stability and function for OS morphogenesis and structure. The most striking phenotype observed for the new Prph2^{Y285x/+} disease model was a robust functional compensation, which restored rod-derived signaling, likely lost as a result of OS structural damage. The new findings may reflect an example of homeostatic plasticity at the photoreceptor-bipolar cell synapse, and introduces the possibility this mechanism also applies to instances of human pattern dystrophy associated with the TYR285stop defect.

CONTROL ID: 3537013

SUBMITTER (NAME ONLY): Yueh-Hsun Wu

TITLE: Impact of the COVID-19 Pandemic on Social Isolation in Older Adults with Sensory Loss

SESSION TITLE: Visual Impairment during a pandemic

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Past studies have shown that social isolation and loneliness are risk factors for increasing mortality among older adults. Adults with vision loss and hearing loss are likely to experience greater social isolation and loneliness compared to healthy controls. During the COVID-19 pandemic, in-person interactions were discouraged due to the risk of infection, public-health messaging and governmental stay-at-home orders. This study was designed to understand the impact of the COVID-19 pandemic on the social interactions and emotional wellbeing in adults with sensory loss.

Methods: Three groups of older adults -- vision loss (N = 13, legally blind), hearing loss (N = 24, hearing-aid or cochlear-implant users), and controls (N = 18) -- were recruited from the Twin Cities Minnesota community (mean age = 68.18, range = 57 to 80). Participants were interviewed every 4 to 6 weeks from the end of April to the end of October using the same set of questions. The initial interview at the end of April included retrospective responses to the questions regarding participants' status at the beginning of March, prior to pandemic restrictions, and the beginning of April, after the onset of pandemic restrictions.

The survey questions addressed (1) demographic and health information, (2) average number of in-person and electronic social interactions per week, (3) sense of loneliness, (4) accessibility of daily services such as grocery shopping, (5) mental health, (6) worry levels about COVID infection, and (7) impact on daily activities.

Results: There was a significant decline of in-person social interactions in all three groups after the pandemic started, accompanied by a significant increase of electronic social interaction.

From late April to October, the number of in-person interactions increased in the control and hearing-loss groups but remained depressed in the vision-loss group. The number of electronic social interactions did not change significantly during this time period.

All three groups had worse scores on the patient health questionnaire (PHQ-9) after the start of the pandemic. Participants with vision loss demonstrated higher worry levels about touching things. Participants with hearing loss worried more about understanding speech from people wearing masks.

Conclusions: Our results have shown the widespread impact of the pandemic on social interactions and emotional wellbeing of older adults with sensory loss.

CONTROL ID: 3537017

SUBMITTER (NAME ONLY): Anusha Saga

TITLE: Anterior Segment Ultrasound Biomicroscopy Image Analysis Correlation with Physical Eye Exam Findings

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saga, M.R. Levin, J.L. Alexander, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|C. Martinez, W. Madigan, Children's National Hospital, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal measurements obtained from the physical exam are the gold standard used to monitor the progression of pathological states (for example keratoconus and congenital glaucoma) despite the availability of newer technologies. We tested the hypothesis that structures measured from ultrasound biomicroscopy (UBM) images correlate with related physical exam findings using a prospective comparative clinical study.

Methods: Ultrasound biomicroscopy (UBM) images were obtained from a total of 181 eyes and 53 patients (mean age 6 years, +/- 12 years, median age to years) who were prospectively enrolled after consent in this study at the University of Maryland, Baltimore, Maryland. Ruler and calipers were used to measure external corneal diameter from color photograph (Figure 1a). ImageJ was used to measure angle to angle width of the anterior chamber (Figure 1b). Correlation coefficient and significance testing for eyes with and without glaucoma were performed.

Results: Preliminary data suggests a statistically significant correlation between angle to angle (AA) distance and corneal diameter in glaucoma patients ($r = 0.6$, $p = 0.007$). Correlation for non glaucoma eyes was weak ($r = -0.189$) and not significant ($p = 0.3$) (Figure 2). The linear relationship does not hold for angle to angle distances less than 10mm. Bland Altman plots were constructed to evaluate the agreement between image-based and ruler measurements.

Conclusions: This is the first study identifying relationships between physical exam findings and quantitative features extracted from UBM images in the anterior segment.

CONTROL ID: 3537032

SUBMITTER (NAME ONLY): Daniel Valencia Paredes

TITLE: Morphology of the Normal Conjunctiva Using Optical Coherence Tomography: Normative Database in a Mexican Population

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) allows morphological evaluation in the manner of an invivo biopsy, using properties of coherent light through a spectrophotometry technique. The description of abnormal findings requires a normal informational base from which qualitative and quantitative comparisons can be made. Purpose of the study is to describe the morphology of the conjunctiva of ocularly healthy individuals and to compare the thicknesses of the conjunctiva-tennon complex, by age group in a Mexican population. Therefore, establishing a normative database of morphometry of the conjunctiva by age group.

Methods: Cross-sectional study of 112 non-consecutive cases using a Cirrus 4000 OCT device (ZEISS) in the anterior segment modality of each quadrant. Measurements were done at 3 mm from the limbus of thickness of the epithelium, stroma, and the full-thickness conjunctiva, using the cube acquisition format and high resolution 5-line scan in 90 and 180 degree orientation. SPSS 25 statistical software was used for data analysis, considering significant p-value ≤ 0.05 as statistically.

Results: One hundred and twelve participants between 10 and 90 years of age were included; fourteen individuals from each 10-year cohort, of whom half were male and half were female. The mean thickness of the total superior, inferior, temporal and nasal conjunctiva was $245.30 \pm 27.20 \mu\text{m}$, $237.85 \pm 25.36 \mu\text{m}$, $239.65 \pm 27.39 \mu\text{m}$, $241.04 \pm 28.04 \mu\text{m}$, respectively. The mean upper, lower, temporal and nasal epithelial thickness was $45.28 \pm 10.48 \mu\text{m}$, $47.47 \pm 12.01 \mu\text{m}$, $45.25 \pm 11.07 \mu\text{m}$, $44.86 \pm 11.59 \mu\text{m}$, respectively. The mean superior, inferior, temporal and nasal stromal thickness were $199.5 \pm 24.23 \mu\text{m}$, $193.09 \pm 23.81 \mu\text{m}$, $194.25 \pm 26.28 \mu\text{m}$, $194.52 \pm 27.54 \mu\text{m}$, respectively. When comparing the means by cohort, a incremented thickness was evident at a younger age, presenting a significant inverse correlation between thickness and age in all quadrants (upper $r = -0.455$; lower $r = -0.463$; temporal $r = -0.438$; nasal $r = -0.475$). All such correlation were statistically significant ($p < 0.001$).

Conclusions: The conjunctiva is a surgical target and might be affected by many conditions, knowledge of the morphometry of the healthy conjunctiva allows to have a point of comparison in cases where it is modified, either by pathologies or surgical events. This study provides with a normative database in a Mexican population.

CONTROL ID: 3537042

SUBMITTER (NAME ONLY): Alicia Chacko

TITLE: Voluntary exercise preserves visual function and prevents increased inflammatory cytokine expression in an adult mouse model of autosomal dominant retinitis pigmentosa.

SESSION TITLE: Ocular disease models: molecular mechanisms and therapeutic approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Chacko, A. Karesh, K. Hogan, L. Wood, M.T. Pardue, Coulter Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|K. Bales, J.H. Boatright, M.T. Pardue, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|K. Bales, J.H. Boatright, Department of Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|A. Pybus, L. Wood, Woodruff School of Mechanical Engineering and Petit Institute for Bioengineering and Bioscience, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies support that exercise could potentially be used as a neuroprotective method in patients with retinitis pigmentosa (RP) as well as in animal models of RP. The underlying molecular mechanisms of exercise-induced neuroprotection are elusive. This study investigates the neuroprotective effects of voluntary exercise on retinal structure, function and inflammatory response in an adult mouse model of autosomal dominant retinitis pigmentosa (adRP).

Methods: Adult I307N rhodopsin mice (n=25) were divided into active or inactive groups and received free-spinning or locked running wheels, respectively. After exercising for two weeks, the mice received either a 5-minute period of bright light ("BL"; 6000 lux) or natural light ("dim"; 50 lux). At one and two weeks post-BL, optomotor response (OMR) and electroretinograms (ERG) were measured. After four weeks of exercise, the mice were euthanized and eyes were enucleated for histological and multiplexed cytokine protein expression analysis.

Results: OMR revealed significantly greater spatial frequency and contrast sensitivity thresholds for the active+BL group compared to inactive+BL ($p<0.001$). Histological analysis showed a preservation of the outer nuclear layer between active+BL and inactive+BL ($p=0.007$). ERG a- and b-wave amplitudes in active+BL trended higher compared to inactive+BL, however they did not reach statistical significance ($p>0.05$). Cytokine expression profiles were different for active+BL and inactive+BL animals with trending reductions in interferon gamma-induced protein 10 (IP-10; $p=0.085$) and keratinocyte-derived chemokine (KC; $p=0.093$) in active+BL animals, which are involved in chemotactic signaling of microglia and leukocytes.

Conclusions: Our results show that voluntary exercise is protective against retinal degeneration in an adult mouse model of adRP. Exercise preserved visual function and prevented increased expression of inflammatory cytokine expression. These results suggest that exercise regimens should be assessed as a therapeutic intervention to delay progression of RP in patients.

CONTROL ID: 3537059

SUBMITTER (NAME ONLY): Arijit Chakraborty

TITLE: Naso-temporal asymmetry for global motion perception in children with deprivation amblyopia

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chakraborty, Chicago College of Optometry, Northwestern University - Downers Grove Campus, Downers Grove, Illinois, UNITED STATES|A. Chakraborty, B. Thompson, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|K.R. Kelly, E.E. Birch, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|B. Thompson, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Previous studies have reported a naso-temporal asymmetry for global motion perception, favoring nasalward motion, is present in children and adults with a history of unilateral enucleation. Deprivation amblyopia from unilateral cataract or other forms of unilateral visual impairment results in a less complete form of monocular deprivation. We investigated whether this directional asymmetry is also present in the fellow eye of children with deprivation amblyopia.

Methods: 25 children (10.33 ± 2.44 years) with deprivation amblyopia (VA: 0.5 to 1.6 logMAR) from a history of monocular visual deprivation and 30 age-matched controls (9.85 ± 3.68 years) participated in this study. Global motion perception for horizontal translation motion was measured for the fellow eye in the deprivation amblyopia group and in a random eye of the control group. Motion coherence thresholds (MCT) for nasalward and temporalward random-dot-kinematograms were measured using interleaved 2-down 1-up staircases. LogMAR visual acuity was measured by age-appropriate clinical tests.

Results: Overall, the deprivation amblyopia group exhibited a robust naso-temporal asymmetry in favor of nasalward motion (mean nasal MCT: $10.5 \pm 6\%$ vs mean temporal MCT: $17 \pm 10.5\%$, $t_{24} = 4.39$, $p < 0.001$). No such asymmetry was observed in the control participants (mean nasal MCT: $13.8 \pm 6.8\%$ vs. mean temporal MCT: $13.6 \pm 6.6\%$, $t_{29} = -0.23$, $p = 0.820$). The ratio of temporalward/nasalward MCT asymmetry was significantly higher ($t_{52} = 4.04$, $p < 0.001$) in the deprivation amblyopia group (ratio: 1.86 ± 1.10) compared with the control group (ratio: 0.99 ± 0.34). Furthermore, a linear regression revealed that intervention age, age at testing, and gender did not significantly predict the extent of motion asymmetry in the deprivation amblyopia group.

Conclusions: Naso-temporal asymmetries for global motion perception are present in the fellow eye of children with monocular deprivation. This asymmetry highlights the importance of binocular visual input for the normal development of extrastriate areas such as V5/MT+ that support motion integration. Our results are consistent with the previous reports of similar directional asymmetry in motion perception in monocular enucleation.

CONTROL ID: 3537089

SUBMITTER (NAME ONLY): Matthew Maguire

TITLE: Photopic electroretinograms recorded using a portable device at baseline in patients undergoing treatment for diabetic macular edema

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Maguire, O.A. Mahroo, A. Laidlaw, C.J. Hammond, Guy's and St Thomas' NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Around 25% of patients do not respond to anti-VEGF therapy for diabetic macular edema (DME). Poor response can be determined after 3 months of treatment. Early prediction of poor response might allow the timely choice of alternative treatment strategies. We prospectively recorded and analysed baseline electroretinograms (ERGs) in treatment-naïve patients treated with anti-VEGF for DME to examine for baseline predictors of poor response.

Methods: Patients were prospectively reviewed for the VIDEO trial (ISRCTN59902040). ERGs were performed using a handheld ERG device (RETeval, LKC technologies, MD USA) prior to 1st injection (baseline). Light-adapted flash and flicker stimuli were delivered corresponding to international standard. Waveforms were recorded using skin sensor electrodes affixed beneath the lower eyelid. Patients were classified as poor or good responders after 3 months. Poor response was classified on optical coherence tomography as central 1mm macular subfield thickness greater than 350 microns after 3 injections. Baseline demographics were collected and compared between groups. Only the treated eye was included from each patient.

Results: 23 patients were included for analysis. 14 eyes were classified as responders and 9 as non-responders. Baseline demographics were comparable between groups. Peak times were similar between the two groups. Mean flicker ERG amplitudes and flash a-wave and b-wave amplitudes were greater at baseline in responders, although the differences failed to reach statistical significance. For responders and no-responders respectively, mean flicker ERG amplitudes were 16.1 and 22 microvolts respectively ($p=0.13$); mean flash a-wave amplitudes were 4.9 and 6.1 microvolts respectively ($p=0.34$); mean flash b-wave amplitudes were 19.1 and 24.9 microvolts respectively ($p=0.18$).

Conclusions: Portable photopic ERG recording was rapid and well-tolerated. Eyes that went on to display poorer responses to 3 antiVEGF injections had smaller average ERG amplitudes at baseline than those that responded to treatment, but the difference did not reach statistical significance. A limitation was the small sample size, and larger studies will be able to test this with greater power.

CONTROL ID: 3537101

SUBMITTER (NAME ONLY): Matthew Karl

TITLE: Assessing Outcomes in Pars Plana Vitrectomy for Epiretinal Membrane using Indocyanine Green versus Brilliant Blue

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. Karl, W.R. Bloom, M.P. Ohr, Department of Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Matthew Karl: Commercial Relationship: Code N (No Commercial Relationship) | William Bloom: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Ohr: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The objective of this single institution retrospective chart review study is to assess visual outcomes in patients who underwent pars plana vitrectomy with membrane peel for epiretinal membrane using indocyanine green (ICG) versus brilliant blue (BB) dye.

Methods: A retrospective chart review was performed for patients who underwent pars plana vitrectomy for epiretinal membrane between April 1, 2012 and April 1, 2020. Data collected included de-identified demographics, visual acuity (VA), and optical coherence tomography (OCT) central macular thickness (CMT) through post operative month (POM) three.

Results: 60 eyes of 60 patients were included. 23 eyes received intraoperative BB, 37 received intraoperative ICG. There was no significant difference in baseline VA or CMT. No significant difference in VA or CMT was found in patients receiving intraoperative ICG versus BB during pars plana vitrectomy for epiretinal membrane from baseline to POM three (VA: $-0.15 \pm .25$ with ICG and $-0.16 \pm .23$ with BB, $p = 0.90$; -78.8 ± 87.4 with ICG and -98.7 ± 78.4 with BB, $p = 0.36$). Patients receiving ICG had a greater improvement in VA from baseline to POM one than patients receiving BB (-0.17 ± 0.24 with ICG and -0.03 ± 0.26 with BB, $p = 0.04$), however that difference did not persist through the end of the follow up period. Results are summarized in Table 1.

Conclusions: No significant difference was found between VA or CMT in patients receiving intraoperative ICG versus BB, suggesting both of these vital dyes are safe to use during pars plana vitrectomy for epiretinal membrane removal. This study may be limited by sample size and short follow up.

CONTROL ID: 3537105

SUBMITTER (NAME ONLY): Gustavo Ortiz-Morales

TITLE:

CyberKnife Robot-Assisted Radiosurgery for Ciliochoroidal Melanoma: Early Results in Mexico.

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ortiz-Morales, I.A. Dominguez-Varela, D. Gomez-Elizondo, D. Ancona-Lezama, Institute of Ophthalmology and Visual Sciences, Ocular Oncology Service, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|J.A. Valdez-Balli, E. Perez-Ramos, Institute of Oncology, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose:

To report the initial results of CyberKnife stereotactic body radiotherapy (SBRT) on patients with ciliochoroidal (CBCh) melanoma in our population.

Methods:

Cyberknife SBRT (Accuray, Sunnyvale, CA, USA) was offered as a therapeutic alternative to enucleation and ruthenium-106 brachytherapy. Inclusion criteria included: treatment naïve ciliochoroidal melanoma ≥ 9 mm in initial height and Stage $\geq T3$. Exclusion criteria included ecographic evidence of extrascleral tumoral extension, neovascular glaucoma and systemic metastasis. Ocular akinesia was achieved with 2.5mL of 0.75% bupivacaine retrobulbar block on two surgical times. CT/MRI fusing was performed and target volumes and structures at risks were delineated. Cyberknife radiosurgery was performed delivering a single fraction with a mean dose of 25 Gy to the 70% isodose line. Local tumor control was defined as either shrinking of the tumor or absent progression.

Results: Five patients with CBCh melanoma were treated under this protocol. Mean age was 51.4 years (range 44 - 60 years), 40% were female. Mean tumor height before treatment was 11.07 ± 1.98 mm. Mean follow-up of patients was <12 months. Three patients had serous retinal detachment associated with the tumor at presentation. All of the patients had local tumor control after a single-session radiosurgery within the follow-up period. No acute toxicity was observed, and none of the patients required enucleation during this short follow-up time.

Conclusions:

A multidisciplinary approach with Cyberknife SBRT is an effective and safe therapy for medium to large-sized CBCh melanoma. Further follow-up periods are needed to confirm these findings and to evaluate long-term ophthalmic events.

CONTROL ID: 3537114

SUBMITTER (NAME ONLY): Oswaldo Esteban Duran Carrasco

TITLE: Incidence, severity and identification of risk factors of retinopathy of prematurity in our setting.

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Duran Carrasco, A. Afonso-Rodríguez, M. Alberto-Pestano, N. Pérez-Llombet-Quintana, M. Gil-Hernández, OPHTHALMOLOGY, Hospital Universitario Nuestra Señora de la Candelaria, Santa Cruz de Tenerife, Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) can affect the quality of life in children from early age. We determine the incidence and severity of ROP and identify associated risk factors, in 2015 – 2019 period in our area.

Methods: A descriptive and retrospective study of premature infants examined in our service from January 2015 to December 2019 was carried out. All newborns with a gestational age (GA) less than 32 weeks and / or a birth weight (BW) less than 1500 g were included, as well various risk factors (RF) that may influence the development of ROP were evaluated. Subsequently we realized statistical analysis of the data.

Results: 166 patients were evaluated, with a mean GA of 29.63 weeks and a mean BW of 1260.57 ± 322.85 gr. The incidence of ROP was 10.4% (17 patients), presenting 76.5 % of cases severe stage of ROP. we preformed laser therapy in all these cases and intravitreal ranibizumab as adjuvant treatment in 11.8 % of cases, getting complete regression of retinopathy in all patients.

The frequency of the risk factors was: O₂ therapy in 87.9%, with a mean duration time of 24.72 ± 25.34 weeks. Respiratory distress 83.7%, ductus persistence 52.9%, intracranial hemorrhage 58.8%, sepsis 76.5% and transfusion 70.6%.

The ROP group was compared with a similar newborns group, regarding GA and BW as well the use of O₂, that did not develop ROP. We only find statistically significant difference in the development of ROP comparing frequency of sepsis (OR = 4.28 CI = 1.21-15.13) and transfusions (OR = 6.5 95% CI = 1.12-37.4).

Conclusions: In our hospital, 10.4% of premature infants with risk characteristics developed ROP, 76.5% of these kids showed severe retinopathy, so treatment was applied obtaining complete ROP regression in all patients. Use of O₂ and respiratory distress have been associated RF, however only sepsis and transfusions showed significant differences in our research. According with the expectation of growth in the incidence of this pathology due mainly to the advancement of life support maneuvers employed in modern pediatrics, we must continue to apply these screening criteria in our center, because it has allowed the early detection of all cases of severe ROP in our center.

CONTROL ID: 3537125

SUBMITTER (NAME ONLY): Chulbul Ahmed

TITLE: R9-SOCS1-KIR Peptide Abrogates Lipopolysaccharide Mediated Inflammation: Implications for the Treatment of Endotoxin Induced Uveitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.M. Ahmed, Molecular Genetics and Microbiology, University of Florida, Gainesville, Florida, UNITED STATES|A.P. Patel, Florida State University, Tallahassee, Florida, UNITED STATES|A.S. Lewin, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Suppressor of Cytokines Signaling 1 (SOCS1) is a cytoplasmic protein that limits the extent and duration of inflammatory response. We have shown that a cell penetrating peptide from the kinase inhibitory region (KIR) from SOCS1 (denoted as R9-SOCS1-KIR) can dampen the signaling emanating from JAK/STAT and TLR2/4 pathways. We have examined the ability of this peptide to counteract the inflammation caused by lipopolysaccharide (LPS), which is released during an infection or from leaching of intestinal microbiota.

Methods: R9-SOCS-KIR or its inactive control peptide were tested for anti-inflammatory properties in a mouse macrophage cell line, J774A.1, used as a surrogate for microglia and treated with LPS. Induction of inflammatory markers was tested by ELISA using the supernatants from treated cells, or Western blot analysis of treated cell extracts. Activation of inflammatory transcription factors was analyzed by following their nuclear translocation. ARPE-19 cells that were differentiated by growing for 4 weeks and treated with LPS with or without R9-SOCS1-KIR were used to evaluate the integrity of tight junction protein by immunostaining and by measurement of transepithelial electrical resistance (TEER).

Results: Treatment of J774A.1 cells with LPS resulted in secretion of NO and IL-1b, which was attenuated by R9-SOCS1-KIR. Induction of inflammatory markers, cyclooxygenase 2 (COX2) and iNOS observed in cells treated with LPS was suppressed when R9-SOCS1-KIR was simultaneously present. Treatment with LPS resulted in nuclear translocation of p65, the active subunit of NF-kB and the MAP kinase p38, both of which were prevented in the presence of R9-SOCS1-KIR. Uniform distribution of Zona occludens 1 (ZO-1) along the cell membrane was disrupted and TEER reduced by treatment with LPS, both of which were prevented by R9-SOCS1-KIR.

Conclusions: Protection against inflammatory insults afforded by R9-SOCS1-KIR in a macrophage cell line and a cell line from retinal pigment epithelium suggests that it has therapeutic potential against inflammatory ocular disorders, including infection induced uveitis.

CONTROL ID: 3537131

SUBMITTER (NAME ONLY): Carolina Carvalho Soares Valentim

TITLE: Characterization and Outcomes of Virtual Visit During the COVID-19 Pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Carvalho Soares Valentim, J. Muste, A. Iyer, A. Kalur, R.P. Singh, K. Talcott, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|M.A. Krause, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|S. Gendi, M. Ohlhausen, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Telehealth has a variety of proposed uses in ophthalmology and has become a valuable asset to health care in the COVID-19 pandemic. This retrospective, observational study characterizes the use of virtual visits and compares the outcomes of these visits to in-person visits during the pandemic period at a large academic institution.

Methods: 2,943 virtual and 56,174 in-person visits occurring at Cole Eye Institute, Cleveland Clinic, were identified. A random sample of 3,000 in-person visits was selected for comparison. Canceled, incomplete and duplicated visits, as well as visits for patients aged less than 18 years old were excluded. Pearson's chi-square test of independence and test of proportions were used to assess relationships between categorical variables.

Results: 2,266 virtual visits and 2,590 in-person visits were included. The visits distribution across ophthalmology specialties is summarized in table 1. 72.3% of the virtual visits resulted in a planned follow-up compared to 70.3% following an in-person visit ($p=0.121$). 15.9% of virtual patients were discharged compared to 10.8% of in-person patients ($p<0.001$). 5.6% of virtual patients were referred to a primary care doctor or different ophthalmology subspecialty compared to 6.9% in-person patients ($p=0.081$). 6.0% of the patients had an outpatient surgery scheduled after a virtual visit compared to 4.8% in-person patients ($p=0.08$). 0.2% of the virtual patients had a clinic procedure scheduled compared to 7.2% in-person patients ($p<0.001$). Loss to follow-up occurred due to cancellations (4.6% and 3.5% in the virtual and in-person visits, respectively, $p=0.11$), no shows (2.8% and 2.1%, $p=0.2$) and no schedule (10.4% and 2.3%, $p<0.001$). 84.6% of the completed follow-up visits after virtual visits were in-person and 15.4% were virtual, in comparison to 97.4% and 2.6% after an in-person encounter ($p<0.001$).

Conclusions: The similar number of follow-up, referral and outpatient surgery outcomes across virtual and in-person visits suggests that teleophthalmology is a viable alternative for patient care. Virtual follow-ups occurred more often after a virtual visit. Discharges and unscheduled follow-up visits were also more prevalent in the virtual setting, implying a higher risk of care discontinuation in this group. Further research into the applications of telehealth for ophthalmology may be beneficial.

CONTROL ID: 3537134

SUBMITTER (NAME ONLY): Moaddey ALFARHAN

TITLE: Pharmacological inhibition of spermine oxidase ameliorates neuroinflammation in a model of retinal excitotoxicity

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. ALFARHAN, F. Liu, S. Narayanan, Clinical and Experimental Therapeutics, The University of Georgia, Augusta, Georgia, UNITED STATES|M. ALFARHAN, F. Liu, P. Pichavaram, Augusta VA Medical Center, Augusta, Georgia, UNITED STATES|P. Pichavaram, S. Narayanan, Vision Discovery Institute, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neuroinflammation in the retina is a major cause of vision impairment in blinding diseases such as diabetic retinopathy (DR). Previous studies from our laboratory have shown that inhibition of spermine oxidase (SMOX, a member of polyamine oxidase family) using the pharmacological inhibitor MDL 72527 reduced neurodegeneration in models of retinal excitotoxicity and DR. Utilizing the experimental model of retinal excitotoxicity, the present study was undertaken to determine the impact of SMOX blockade in retinal neuroinflammation.

Methods: Adult mice (8-10 weeks old) were given intravitreal injections (20 nmoles) of NMDA (N-Methyl-D-aspartate) or NMLA (N-Methyl-L-aspartate, control). Intraperitoneal injections of MDL 72527 (40 mg/kg body weight/day) or vehicle (normal saline) were given to NMDA and NMLA treatment groups. Retinal flat mounts or cryostat sections were prepared for immunostaining and fresh frozen retinal samples were used for Western blotting studies. NIH Image J was used for quantitation.

Results: Immunofluorescence staining of retinal flat mounts using Iba1 (Ionized calcium-binding adaptor molecule 1) antibody was utilized to study activation of microglia. An increase in retinal microglia presenting activated morphology was observed in NMDA retinas (7 days post injury) compared to their NMLA controls. Treatment with MDL 72527 reduced this effect in the NMDA retinas. Quantification studies demonstrated that excitotoxicity-induced upregulation of Iba1 positive cells with activated morphology was significantly reduced in response to SMOX blockade (N=5, $p<0.01$). The increased protein levels of Iba1 in NMDA retinas were reduced in response to MDL 72527 treatment ($p<0.01$, N=4). Excitotoxicity-induced upregulation in the number of CD 68 (Cluster of Differentiation 68) positive cells was significantly decreased in response to SMOX inhibition (N=4, $p<0.05$, 3 days post injury). Analysis of molecular pathways revealed a significant increase in NRF2 expression in MDL 72527 treated excitotoxic retinas compared to respective vehicle group ($p<0.05$, N=3, 3 days post injury), suggesting the involvement of antioxidant signaling in response to SMOX blockade.

Conclusions: Our study suggests the critical involvement of SMOX signaling in retinal neuroinflammation thus offering a new therapeutic target for vision disorders.

CONTROL ID: 3537136

SUBMITTER (NAME ONLY): Darren Ting

TITLE: Hybrid Derivative of Cathelicidin (LL-37) and Human Beta-Defensin Against Gram-Positive Bacteria: A Novel Approach for the Treatment of Bacterial Keratitis

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.S. Ting, D. Said, I. Mohammed, H. Dua, Academic Ophthalmology, University of Nottingham, Nottingham, Nottinghamshire, UNITED KINGDOM|D.S. Ting, Ophthalmology, Queen's Medical Centre, Nottingham, Nottingham, UNITED KINGDOM|V.A. Barathi, R. Beuerman, R. Lakshminarayanan, Singapore Eye Research Institute, Singapore, SINGAPORE|M. Nubile, L. Mastropasqua, University of "G d'Annunzio", ITALY|

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ABSTRACT BODY:

Purpose: Bacterial keratitis (BK) represents a leading cause of corneal blindness worldwide. This study aimed to generate potent hybridized human-derived host defense peptides (HDPs) as novel topical antimicrobial therapy for BK.

Methods: Hybrid peptides were rationally designed through combination of functional amino acids in parent HDPs, including human cathelicidin (LL-37) and human beta-defensin (HBD)-1 to -3. Minimal inhibitory concentrations (MICs) were determined using broth microdilution method, and cytotoxicity was evaluated against human corneal epithelial cells (HCE-2) and human erythrocytes. Time- and concentration-dependent antimicrobial activity was examined using time-kill kinetics assay. In vivo safety and efficacy of the most promising peptide was examined using corneal wound healing and Staphylococcus aureus (ATCC SA29213) keratitis murine models, respectively.

Results: A second-generation hybrid peptide (HDP23) demonstrated good efficacy against methicillin-sensitive and methicillin-resistant *S. aureus* (MIC=12.5-25.0µg/ml or 5.2-10.4µM) and *S. epidermidis* (MIC=3.1-12.5µg/ml or 1.3-5.2µM), and moderate efficacy against *P. aeruginosa* (MIC=50µg/ml or 20.9µM). HDP23 (2x MIC) killed all the bacteria within 30 mins, which was 8 times faster than amikacin (20x MIC). At 200µg/ml (16x MIC), HDP23 was shown to be relatively safe against HCE-2 (<30% toxicity) and erythrocytes (<10% toxicity). Pre-clinical murine studies showed that HDP23 0.05% (500µg/ml) achieved a median reduction of *S. aureus* bacterial viability by 94% (or 1.2 log₁₀ CFU/ml) while not impeding corneal healing.

Conclusions: Rational modification of human-derived HDPs, via hybridization of LL-37 and HBD, has led to the generation of an efficacious and safe topical antimicrobial agent that has potential for treatment of Gram-positive BK in humans.

CONTROL ID: 3537156

SUBMITTER (NAME ONLY): Guillaume Albert Mullie

TITLE: Development of a French version of the Visual Function and Corneal Health Status (V-FUCHS) instrument for Fuchs endothelial corneal dystrophy (FECD)

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Mullie, A. Juarez, A. Etcheverry, T. Boutin, J. Choremis, M. Mabon, J.C. Talajic, I. Brunette, Ophthalmology, Université de Montreal, Montreal, Quebec, CANADA|G. Mullie, A. Juarez, A. Etcheverry, N. Taleb, T. Boutin, J. Choremis, M. Mabon, J.C. Talajic, I. Brunette, Ophthalmology, Hopital Maisonneuve-Rosemont, Montreal, Quebec, CANADA|C. Giguère, Institut universitaire en sante mentale de Montreal, Institut universitaire en sante mentale de Montreal, Montreal, QC, CA, academic/hospital, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: To develop a French version of the V-FUCHS instrument and to validate its use among French-speaking patients with FECD before and after DMEK surgery.

Methods: The original V-FUCHS 15-item instrument was designed to assess visual acuity (VA) and glare in FECD patients (Wacker et al. 2018). It was translated from English to French by a professional translator and back translated to English by a second independent translator, followed by the adjustment of minor semantic dissimilarities by an English-speaking ophthalmologist. The French questionnaire was first administered at the HMR Cornea Clinic and best corrected visual acuity (BCVA), modified Krachmer grade, and straylight (C-Quant, Oculus) were measured. Four weeks later, patients received by mail a second copy of the same questionnaire to be completed at the same time as they did the first time. Construct validity, internal consistency, test-retest reliability, and predictive validity were assessed.

Results: A total of 123 French-speaking patients, aged 41 to 86 years, were recruited from July 2019 to October 2020 and classified into five groups: Mild, Moderate, or Severe FECD; Unilateral or Bilateral DMEK for FECD, and Healthy controls (n = 36). Construct validity was confirmed by infit and outfit statistics (range 0.5-1.5) from an Item-response theory model. Cronbach's alpha demonstrated excellent internal consistency for both VA ($\alpha=0.92$; 95% CI 0.9-0.94) and glare ($\alpha=0.9$; 95% CI 0.87-0.94) factors. ICCs showed good test-retest reliability for both VA (raw score: 0.725 [0.634-0.797]; latent score: 0.705 [0.622-0.772]) and glare (raw: 0.820 [0.764-0.863]; latent: 0.816 [0.759-0.860]) factors. A significant correlation was observed between the modified Krachmer grade and both the VA (raw: $r=0.585$, $p<0.001$; latent: $r=0.6232$, $p<0.001$) and glare ($r=0.609$, $p<0.001$; $r=0.605$, $p<0.001$) factors. BCVA was also correlated with both VA ($r=0.316$, $p<0.001$ and $r=0.310$, $p<0.001$) and glare ($r=0.312$, $p<0.001$ and $r=0.303$, $p<0.001$) factors. A weak but significant correlation was found between the glare factor and C-Quant measurements ($r=0.286$, $p<0.01$ and $r=0.254$, $p<0.01$).

Conclusions: The proposed French version of the V-FUCHS instrument provides a valid and reliable tool for the assessment of visual disability in Francophone patients with FECD.

CONTROL ID: 3537157

SUBMITTER (NAME ONLY): Christina Kong

TITLE: Time to Foveal-Distorting Epiretinal Membrane Formation After Laser Therapy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.L. Kong, L. Chen, K. White, D. Banerjee, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A. Alkaliby, M. Doustkhahvajari, M. Han, K. Gustafson, M. Riazzi, A. Browne, B.D. Kuppermann, S. Lu, M. Mehta, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Panretinal photocoagulation (PRP) and laser barricade (LB) are both commonly complicated by epiretinal membrane (ERM) formation but there is little literature on the development of a significant ERM (SERM) that distorts the foveal contour. We performed a retrospective, single-center chart review to better characterize SERM, as seen on macular ocular coherence tomography (OCT).

Methods: Charts of patients with billing codes for retinal laser therapy from 2013 through 2019 at the Gavin Herbert Eye Institute were retrospectively reviewed. Subjects with a history of autoimmune disease, uveitis, immunosuppression during or after treatment, prior laser treatment and pars plana vitrectomy, prior intraocular infection and ocular trauma, existing ERM, and less than 1 year of follow-up and inadequate imaging were excluded. Results between laser treatment groups and by ERM severity were compared using the appropriate statistical tests.

Results: A total of 72 patients and 79 eyes met study criteria with 49 patients (68%; 26 LB and 23 PRP) and 54 eyes (68%; 28 LB and 26 PRP) developing ERM (see Table 1). Median time to ERM formation was 10.5 months overall, including 11.2 months for LB patients and 9.5 months for PRP patients ($p=0.45$). There was a statistically significant difference in median laser energy exposure between the LB and PRP groups (8.3 J to 33.2 J for the PRP group, $p<0.001$). Eleven patients and 12 eyes developed SERM over a median of 30.6 months. A total of 4 eyes with LB compared to 8 eyes with PRP developed SERM ($p=0.029$; see Table 2). Median laser energy was 8.4 J, 19.2 J, and 26.7 J among eyes with no ERM, non-SERM, and SERM, respectively. There was a statistically significant difference in median laser energy between those with no ERM and with non-SERM ($p=0.042$) and between those with no ERM and with SERM ($p=0.03$) but not between those with non-SERM and SERM ($p=0.31$). Median follow-up time was 24.9 months in patients with no ERM and 59.7 months in those with SERM ($p=0.045$).

Conclusions: Compared to eyes treated with LB, eyes with PRP were exposed to statistically significantly more laser energy and a greater proportion of PRP eyes developed SERM. Total laser energy exposure may play a role in the develop of ERM, including membranes that distort the foveal contour. However, the results must be interpreted cautiously given the significantly shorter follow-up time in patients that did not develop ERM.

CONTROL ID: 3537160

SUBMITTER (NAME ONLY): Yan Li

TITLE: Projection-resolved conjunctival and scleral OCT angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, Y. Jia, D. Huang, Casey Eye Institute, Oregon Health and Science University, PORTLAND, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yan Li: Commercial Relationship(s);Optovue, Inc. :Code F (Financial Support);Optovue, Inc.:Code P (Patent) | Yali Jia: Commercial Relationship(s);Optovue, Inc. :Code F (Financial Support);Optovue, Inc. :Code P (Patent) | David Huang: Commercial Relationship(s);Optovue, Inc. :Code F (Financial Support);Optovue, Inc. :Code P (Patent);Optovue, Inc. :Code I (Personal Financial Interest);Optovue, Inc. :Code R (Recipient)

ABSTRACT BODY:

Purpose: To investigate the feasibility of using anterior segment optical coherence tomography (OCT) angiography to evaluate the conjunctival and scleral vasculature.

Methods: The corneoscleral junction of the eye was imaged with a spectral-domain OCT angiography system (AngioVue, Optovue Inc., Fremont CA) operating at 840 nm wavelength and 70,000 axial-scans per second scan speed. An Angio Cornea scan pattern sized at 6 mm x 6 mm was used to image the temporal and nasal limbus of normal volunteers. The participants were instructed to rotate the eye towards the nasal side while the temporal side of the eye was scanned, and vice versa. The split-spectrum amplitude-decorrelation angiography (SSADA) technique were used to detect the blood flow. The flow projection is a prominent artifact in scleral OCT angiography due to high reflectance of the sclera. Custom software was used to resolve flow projection artifact, identify the posterior conjunctival boundary in structural OCT images, and generate the depth-resolved conjunctival and scleral angiograms.

Results: The nasal and temporal limbus of four normal eyes were imaged. Projection-resolved OCT angiography were calculated. En face OCTA of the conjunctival and scleral vascular networks were generated and delineated distinct patterns. OCT angiography of the bulbar conjunctival showed radial loop of vessels that ended at the limbus. OCT angiography of the sclera showed a dense network of no particular orientation. The OCT angiography detected a much denser vascular network including vessels not visible on the slit-lamp photo.

Conclusions: Projection-resolved OCT angiography can visualize the superficial conjunctiva vessels and the deeper episcleral and scleral vasculature separately.

CONTROL ID: 3537171

SUBMITTER (NAME ONLY): Lizzie Anne Aquino

TITLE: Comparison of Nonmydriatic Handheld Retinal Imaging with Early Treatment Diabetic Retinopathy Study (ETDRS) 7-Standard Field Photography for Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rageh, J.K. Sun, L.P. Aiello, P.S. Silva, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|P.S. Silva, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L. Aquino, C. Salva, R.P. Salongcay, A.V. Saunar, G.P. Alog, Philippine Eye Research Institute, University of the Philippines Manila, Manila, Metro Manila, PHILIPPINES|T. Peto, Centre for Public Health, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Lizzie Anne Aquino: Commercial Relationship: Code N (No Commercial Relationship) | Claude Salva: Commercial Relationship: Code N (No Commercial Relationship) | Recivall Salongcay: Commercial Relationship: Code N (No Commercial Relationship) | Aileen Saunar: Commercial Relationship: Code N (No Commercial Relationship) | Glenn Alog: Commercial Relationship: Code N (No Commercial Relationship) | Abdulrahman Rageh: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Sun: Commercial Relationship: Code N (No Commercial Relationship) | Tunde Peto: Commercial Relationship: Code N (No Commercial Relationship) | Lloyd Aiello: Commercial Relationship: Code N (No Commercial Relationship) | Paolo Silva: Commercial Relationship(s);Optomed:Code F (Financial Support);Hill-rom:Code F (Financial Support);Optos plc:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To compare nonmydriatic handheld retinal imaging with ETDRS standard 7-field 30⁰ fundus photographs (ETDRS photos) for assessment of DR and DME severity.

Methods: Following a standard imaging protocol, nonmydriatic retinal images were taken using handheld retinal cameras [Aurora(AU), Smartscope(SS), RV700(RV)] and compared to dilated ETDRS photos. Images were evaluated at a centralized reading center by 4 independent graders (2 certified graders, 1 ophthalmologist, 1 retina specialist) using the International DR/DME classification. A senior retina specialist adjudicated all differences. Kappa statistics [simple (K),weighted (KW)] assessed agreement for DR/DME. Sensitivity and specificity for any DR, referable DR [(refDR) moderate nonproliferative DR (NPDR) or worse, any DME or ungradable images] and vision threatening DR [(vtDR) severe NPDR or worse, clinically significant DME (CSME) or ungradable images] were calculated.

Results: Images from 177 eyes of 92 patients with diabetes were evaluated. Severity by ETDRS photos, DR: no DR 40.1% eyes, mild NPDR 19.2%, moderate 14.7%, severe 10.2%, and proliferative DR 15.8%; DME: No DME 72.9%, DME 6.8%, ciDME 17.0%, 3.4% ungradable. Ungradable rate for DR/DME for AU: 13.0%/15.8%; SS: 15.3%/18.1% and RV: 35.6%/36.7%. Agreement of clinical DR grading between handheld retinal and ETDRS photos are shown in table 1. Among the devices, AU (exact 58.8%; w/in 1-step 83.1%) had the highest agreement with ETDRS photos. These are higher than SS (56.5%; 80.2%) and RV (47.5%; 62.7%). Ungradable images were associated with a higher rate of refDR on corresponding ETDRS photos (AU 4.8x, SS 2.9x, RV 2.1x, p<0.0001). Table 1 shows the sensitivity/specificity for any DR, refDR and vtDR. AU, SS and RV had 71-97% specificity and 82-96% sensitivity for any DR, refDR and vtDR.

Conclusions: Despite a standardized protocol of image capture and evaluation, the ungradable rate of these devices varies from 13%-36%. In this cohort, there was a 2.1 to 4.8-fold increased risk of refDR among ungradable images. Thus, although handheld nonmydriatic retinal devices are able to achieve substantial agreement with DR in some cases, additional methods may be needed to reduce ungradable rates and appropriately triage eyes that require specialized care.

CONTROL ID: 3537174

SUBMITTER (NAME ONLY): Joel Kaluzny

TITLE: Electronic health record medication list accuracy in glaucoma patients

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kaluzny, W. Lin, J.S. Chen, M. Hribar, Oregon Health & Science University, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joel Kaluzny: Commercial Relationship: Code N (No Commercial Relationship) | Wei-Chun Lin: Commercial Relationship: Code N (No Commercial Relationship) | Jimmy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Michael Chiang: Commercial Relationship(s);Novartis:Code C (Consultant);InTelereTina LLC:Code I (Personal Financial Interest);Genentech:Code F (Financial Support);NIH:Code F (Financial Support);National Science Foundation:Code F (Financial Support) | Michelle Hribar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The electronic health record (EHR) is a critical part of patient care. EHR data has potential for use in large-scale research. However, the quality of this research is reliant on accuracy of the data in the EHR. Our aim is to assess the accuracy of the EHR in capturing glaucoma patients' current ophthalmologic medication by comparing their documentation in the medication list and in progress notes.

Methods: Progress notes and medication list data from the EHR were extracted by 3 independent reviewers for encounters containing ICD codes with the word "glaucoma" at the Casey Eye Institute from 1/1/2019 to 12/31/2019. All ophthalmologic medications were included and further stratified according to type: prescription eye drops/ointment, over-the-counter (OTC) eye drops/ointment, and oral medications. For each encounter analyzed, the current medication list was manually abstracted from the progress note text and compared to the EHR medication list at the time of the encounter. A subset of 20 encounters were used to generate an analysis protocol and as cross-validation amongst reviewers (96.4% agreement).

Results: Overall, 9066 encounters met the inclusion criteria. 150 encounters were randomly selected for analysis. Prescription medications were most common (93% of encounters), followed by OTC medications (43%), and oral medications (9%). The average number of ophthalmic medications per encounter was 1.97, while the average number of discrepancies per encounter was 0.55. 57% of encounters contained some discrepancy. Prescription medications were more frequently included in the medication list but left out of the progress notes, whereas, OTC medications were more commonly mentioned in the notes, but left out of the medication lists. Overall, a large portion of encounters (26%) had 2 or more medication list discrepancies.

Conclusions: Medication discrepancies were found to be present in a large percentage of encounters. Approximately 1 in 4 medication entries had a discrepancy between the medication list and the note. These findings demonstrate significant inconsistencies in the EHR medication records, which may affect research that uses this data. There is opportunity for improving the accuracy of medication documentation in the EHR which could have benefits for both research as well as clinical care.

CONTROL ID: 3537220

SUBMITTER (NAME ONLY): Aditya Bansal

TITLE: Real-Time In Vivo Assessment of Retinal Reattachment in Humans using Swept-Source Optical Coherence Tomography

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bansal, W. Lee, T. Felfeli, R.H. Muni, Ophthalmology, St Michael's Hospital, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: To assess the physiology of retinal reattachment in humans using swept-source optical coherence tomography (SS-OCT) in real-time.

Methods: A prospective cohort study of consecutive patients with fovea-involving rhegmatogenous retinal detachment undergoing pneumatic retinopexy (PnR). SS-OCT was performed at presentation and every 2 hours for the first six hours, at day 1, 2, 5, and at week 1, 2, 4, and 6 after PnR. The outcome was defined as the longitudinal assessment of early post-operative SS-OCT findings to determine the stages of retinal reattachment.

Results: Fifteen eyes of 15 consecutive patients were included. All 15 patients (100%) achieved successful retinal reattachment with PnR. Reattachment occurred in five specific reproducible stages based on SS-OCT findings: Stage 1, defined as a redistribution of fluid and approach of the neurosensory retina towards the retinal pigment epithelium (RPE) occurred in 100% (15/15) of patients (Fig 1B, Fig 2B). Stage 2, characterized by a reduction in cystoid macular edema and improvement of outer retinal corrugations was also achieved in 100% (15/15) of patients (Fig 1C&D, Fig 2C). Stage 3, defined by the initial contact of the neurosensory retina to the RPE occurred completely in 66.7% (10/15) and incompletely in 33.3% (5/15) of patients (Fig 1E, Fig 2D). Stage 4, defined as a deturgescence of the inner and outer segments of the photoreceptors occurred completely in 66.7% (10/15) of patients (Fig 1F, Fig 2E). Stage 5, characterized by recovery of photoreceptor integrity occurred in three specific sub-stages, 5A: external limiting membrane (ELM) recovery (10/15, 66.6%) (Fig 2F), 5B: ellipsoid zone (EZ) recovery (7/15, 46.6%) (Fig 2G), 5C: interdigitation zone (IDZ)/foveal bulge recovery (3/15, 20%) (Fig 1G, Fig 2H). 20% (3/15) of patients had delayed progression through Stage 2 which led to the formation of outer retinal folds (Fig 2I). Similarly, 33.3% (5/15) of patients had delayed progression to Stage 3 and developed residual subfoveal fluid blebs (Fig 2J).

Conclusions: This study characterizes the in vivo physiology of retinal reattachment in humans using high-resolution SS-OCT. The reattachment process occurs in five specific and reproducible stages and delayed progression through certain stages can lead to post-operative anatomic abnormalities such as outer retinal folds and residual subfoveal fluid blebs.

CONTROL ID: 3537270

SUBMITTER (NAME ONLY): Seyedeh Zeinab Mirjalili Mohanna

TITLE: Mouse breeding strategies for successful preclinical studies

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mirjalili Mohanna, A.J. Korecki, E.M. Simpson, Centre for Molecular Medicine and Therapeutics at British Columbia Children's Hospital, Vancouver, British Columbia, CANADA|S. Mirjalili Mohanna, E.M. Simpson, Medical Genetics, The University of British Columbia, Vancouver, British Columbia, CANADA|

Commercial Relationships Disclosure (Abstract): Seyedeh Zeinab Mirjalili Mohanna: Commercial Relationship: Code N (No Commercial Relationship) | Andrea Korecki: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Simpson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Well-designed animal studies are critical for establishing the safety and efficacy of ocular gene therapies or drugs prior to clinical trial. Mice have been widely used as a mammalian model in preclinical studies due to their physiological and genetic similarities to humans, relative ease of breeding, and short generation time. Aniridia is a rare congenital blindness with unmet therapeutic needs, which is caused by mutations in the PAX6 gene. Here we will highlight the importance of breeding strategies for successful preclinical studies using cohorts of Pax6 mutant mice as an example.

Methods: First generation hybrid mice are a good choice for therapy development as they are genetically identical, but carry genomic polymorphisms as does the human population. To generate a cohort of age-matched mice with significant statistical power, 8 129S1/SvImJ Pax6 mutant (MMRRC #050624-MU) male studs were chosen based on age (>6 weeks, <8 months) and experienced (5 days of mating with a surplus female followed by 5 days of rest). 8 C57BL/6J ROSA-stop-tdTomato (JAX #007914) females were crowded (group housed in a single cage for 8-10 days prior to mating to suppress estrus cycle). To increase the rate of pregnancy, mice were mated in pairs. After one week, females were removed and singly housed in a fresh cage. Cages were checked (by looking from outside the cage to minimize stress) for births daily 18-27 days after the mating. This breeding strategy was used monthly to generate cohorts. Investigator blinding was not possible during the breeding and treatment due to the phenotype of the Pax6 mutant mice, but it was practiced during assessment of outcome (histological analysis) to minimize bias and maximize result validity.

Results: We have used this breeding strategy 9 times to successfully generate 52 ± 8 (MEAN \pm SD) age-matched (\pm 3.5 days) mice per cohort. The following breeding colony size will help investigators calculate financial costs for generating a single experimental cohort of mice. 8 singly housed studs, and 8 single breeding cages were required to generate the experimental cohorts. With a maximum of 5 adult mice per single cage, 10-12 cages were allocated to weans from each cohort.

Conclusions: We demonstrated the practicality of the suggested breeding strategy by generating age-matched reporter mice in an efficient and timely manner. We have also offered investigators insight on space requirements to generate these mice.

CONTROL ID: 3537285

SUBMITTER (NAME ONLY): Rémy Marcotte-Collard

TITLE: THE EFFECT OF OPTIC ZONE DIAMETER ON CHOROIDAL RESPONSE USING BIFOCAL SOFT MULTIFOCAL CONTACT LENSES

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Marcotte-Collard, P. Simard, L. Michaud, D. Couture, I. Tesevic, J. Hanssens, School of optometry, Universite de Montreal, Montreal, Quebec, CANADA|R. Marcotte-Collard, IRLCM, contact lens department, Universite de Montreal Ecole d'Optometrie, Montreal, Quebec, CANADA|C. Bélanger Nzakimuena, S. Costantino, Biophotonics lab, Hopital Maisonneuve-Rosemont, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The aim of this study is to assess the impact of varying optical zone diameters of multifocal lenses used for myopia management by measuring their effects on the choroidal volume.

Methods: This is a prospective study made on 18 myopes (14 F; 4 M, -2.18D), randomly fitted with customized bifocal contact lenses with different distance zone diameters (L1: 2.3 mm, L2: 4 mm, L3: 7 mm, same peripheral add power of +10D). Visual demand, activities and food intake were controlled. Choroidal thickness was measured using OCT at baseline (no lens) and after 45 minutes of wear. A 15-min washout was observed between measurements. Choroidal volume variation was estimated through computer analysis. (Matlab).

Results: Choroidal volume changes were noticeable with each lens from baseline (L1: +1.25% \pm 7.04 L2: -2.55% \pm 3.98 L3: -7.74% \pm 7.66), with an increase in the choroidal volume only for the smaller distance zone diameter. Significant difference was found between L1 and L3 ($p=0.003$), and between L2 and L3 ($p=0.045$). The choroidal volume response in the central 1X1 mm zone varied for each lense (L1: max= +12.54 mm³ , min= -17.37 mm³ ; L2: max= +11.62 mm³ , min= -15.83 mm³ ; L3: max= +6.95 mm³ , min=-12.46 mm³).

Conclusions: The results of this study indicate that a reduced optical zone diameter is more effective in increasing the choroidal volume. Future work is needed to determine the impact to rely on smaller diameters for myopia control.

CONTROL ID: 3537304

SUBMITTER (NAME ONLY): Jamie Floss

TITLE: Growth characteristics of primary human corneal endothelial cells (HCEnC) at ambient and 2.5% oxygen

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Floss, C.F. Mueller, M. Sousa, S.P. Patel, Ophthalmology, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|M. Sousa, Research Service, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|S.P. Patel, Ophthalmology and Research Service, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The corneal endothelium in vivo is exposed to approximately 2.5% O₂ ([O₂]_{2.5}) while standard culture conditions with ambient air expose HCEnC to ~18% O₂ ([O₂]_A). Oxidative stress is known to contribute to corneal endothelial disease. The purpose of this study was to evaluate the effects of [O₂]_A and [O₂]_{2.5} on the growth of primary HCEnC cultures. We hypothesized the physiologic condition of [O₂]_{2.5} would be more favorable to growth of HCEnC than [O₂]_A.

Methods: Protocols were approved by the Univ at Buffalo and VA IRBs. Human donor eyes were enucleated within 16 hrs of death and used immediately for cultures. Dissociated HCEncs from each cornea were distributed into 96-well format culture plates; one plate at [O₂]_A and another in an environmental chamber at [O₂]_{2.5} (2.5% O₂, 5% CO₂, balance N₂; Billups-Rothenberg, Inc., Del Mar, CA). Following 10-14 days of growth in complete medium, cells were matured for 10-14 days in basal medium. Nuclei were stained with DAPI and digital fluorescence images acquired for cell count analysis (ImageJ, NIH) with conversion to cells/mm² (endothelial cell density; ECD) based upon growth area. Positive cell growth for each well was considered ECD>50 cells/mm². We compared mean ECD under each condition with two tailed Student's t-tests and compared percentage of wells with growth under each analysis condition with two tailed Fisher exact tests with statistical significance at p<0.05.

Results: We analyzed 34 corneas from 20 donors (mean age 72 yrs; range 36-98 yrs; 16 female corneas; 18 pseudophakic corneas). Percentage of wells with growth were greater at [O₂]_{2.5} vs [O₂]_A overall and notably in corneas from pseudophakic eyes but did not reach statistical significance (Table). Of the wells with growth, there were no significant differences in ECD between [O₂]_A and [O₂]_{2.5} overall or when compared by age or lens status.

Conclusions: Our results suggest that [O₂]_{2.5} is more favorable for initiating HCEnC growth than [O₂]_A but does not result in increased ECD. The favorable effects of [O₂]_{2.5} on growth were most apparent with pseudophakic donors which may reflect increased cell stress in these donor corneas, relieved by culture under physiologic O₂ conditions. These findings contribute to our understanding of culture conditions to optimize HCEnC expansion for in vitro study or transplantation.

CONTROL ID: 3537322

SUBMITTER (NAME ONLY): Michelle Hribar

TITLE: Can EHR Data Automatically Calculate Ophthalmic Quality Measures?

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hribar, Medical Informatics & Clinical Epidemiology, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|M. Hribar, J.S. Chen, A. Chen, Ophthalmology, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|M.F. Chiang, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Michelle Hribar: Commercial Relationship: Code N (No Commercial Relationship) | Jimmy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Aiyin Chen: Commercial Relationship: Code N (No Commercial Relationship) | Michael Chiang: Commercial Relationship(s);Genentech:Code F (Financial Support);Novartis:Code C (Consultant);InTeleretina LLC:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Meeting quality measures (QM) is an important for ophthalmic care and reimbursement. QMs use data recorded in the electronic health record (EHR); ideally they are calculated using automated data queries. The quality of EHR data can limit this automatic calculation and require manual chart review for full measure determination. This study examines the ability of EHRs to adequately capture necessary clinical data to calculate QMs.

Methods: Thirty ophthalmic QMs developed by the American Academy of Ophthalmology were assessed for required data elements by reviewing published specifications. The location of each data element was determined in our institution's EHR (Epic, Verona, WI). Challenges for each of the data elements were noted by manually reviewing samples of each data element.

Results: We found 15 categories of data elements in the ophthalmic exam, imaging, visit/procedure, and patient data. Most/all of the QMs used patient age, and procedure & diagnosis codes that were easily extracted. Nevertheless, lack of specificity in diagnosis code data and incomplete problem lists made patient identification for some QMs difficult. Exam data was frequently used; most were stored in free-text fields and needed text processing (e.g. extracting and converting Snellen visual acuity fields to LogMar scale) but non-standard entries were impossible to automatically process (i.e. text instead of numeric data). Two elements were only in notes and required natural language processing (NLP): lid position and marginal reflex distance. Similarly, data from OCT and visual field imaging were in free-text fields and notes; these, too, required additional processing. Finally, patient medications were easily extracted from lists, which were often not complete and required NLP or manual review of notes. In summary, for the study EHR, most measures required text processing or NLP and over half of the measures would require manual review if medication or problem lists were not complete.

Conclusions: The study EHR was unable to capture and report most data elements important for ophthalmic clinical care, quality measure calculation, and research without customization. Generalizability of these results to other EHRs merits studying. Ultimately, tools for automatically extracting this data, as well as improvements and standardization in EHR design and use are required to address this problem.

CONTROL ID: 3537345

SUBMITTER (NAME ONLY): Ying Zhu

TITLE: Intraocular Pressure (IOP) Performance with 27-Gauge Dual-Cutting 20,000cpm Beveled Vitrectomy Probes

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhu, Alcon Laboratories Inc, Lake Forest, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ying Zhu: Commercial Relationship(s);Alcon:Code E (Employment)

ABSTRACT BODY:

Purpose: As IOP maintenance during vitrectomy surgery is a critical parameter, this study aims to 1) understand the IOP performance of 27+® Gauge (Ga) dual-cutting, 20K cuts per minute (cpm) beveled vitrectomy probes under different system settings, and 2) help surgeons to optimize their system settings during surgery.

Methods: 27+® HYPERVIT® beveled 20K cpm vitrectomy probes were driven by a CONSTELLATION® Vision System (Alcon Vision, LLC.) to aspirate sterile irrigating solution (BSS®) in a hollow acrylic eye model. A digital transducer (OMEGA, PX409-001GUSBH) was connected to the bottom of eye model to detect IOP change during aspiration. Six samples were tested under core duty cycle and vacuums of 250mmHg, 450mmHg and 650mmHg. Cut rate ranged from 2500cpm to 20,000cpm. Both system IOP compensation enabled and disabled were used. Average IOP during aspiration was calculated for each test setting and statistical analyses were performed using Kruskal-Wallis test with statistical significance level of $p < 0.05$.

Results: At 450mmHg, without IOP compensation, the IOP ranged from 15.46 ± 0.33 to 15.62 ± 0.33 mmHg when the cut rate changed from 2500cpm to maximum cut rate of 20,000cpm. When IOP compensation was enabled, IOP ranged from 28.21 ± 1.74 to 28.43 ± 1.71 mmHg for cut rate from 2500cpm to 20,000cpm. Statistical analysis indicated that there was no significant difference between results using various cut rate for both IOP compensation enabled and disabled ($p > 0.05$). At the maximum cut rate and without IOP compensation, IOP was 22.81 ± 0.37 mmHg under 250mmHg, 15.62 ± 0.33 mmHg under 450mmHg and 8.33 ± 0.32 mmHg under 650mmHg. Corresponding average flow rate was 3.23 ± 0.1 cc/min under 250mmHg, 5.57 ± 0.17 cc/min under 450mmHg and 7.46 ± 0.27 cc/min under 650mmHg. When IOP compensation was enabled, IOP at maximum cut rate significantly increased to 29.24 ± 0.75 mmHg (28% improvement) for 250mmHg, 28.43 ± 1.71 mmHg (82% improvement) for 450mmHg and 27.42 ± 2.64 mmHg (229% improvement) for 650mmHg compared with result without system's intervention ($p < 0.05$).

Conclusions: 27+® Ga Dual-Cutting 20Kcpm vitrectomy probes have constant IOP performance under different cut rates. IOP ranges during aspiration are improved with IOP compensation enabled. Using 27+® Ga 20K cpm vitrectomy probe and IOP compensation can help surgeons use different operation settings to attain a controllable and efficient process.

CONTROL ID: 3537347

SUBMITTER (NAME ONLY): David Xu

TITLE: Optimal timing for surgical repair of macula-involving rhegmatogenous retinal detachment

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Xu, Midwestern University Arizona College of Osteopathic Medicine, Glendale, Arizona, UNITED STATES|C. Yee, C.J. Flaxel, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K. Traustason, Orion Eye Institute, Redmond, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the effect of time to surgical repair on post-operative visual acuity in order to establish an evidence-based standard of care for the repair of macula-involving rhegmatogenous retinal detachment.

Methods: Retrospective chart review was conducted for patients who underwent surgical repair of a macula-involving rhegmatogenous retinal detachment at two ophthalmology services from 2008 to 2019. Exclusion criteria were post-operative best corrected visual acuity (BCVA) worse than 20/30 before detachment, recurrent detachments, and patients without adequate follow-up. Multivariate linear and logistic regression models were constructed using eyes with a known duration of macular detachment. The primary outcome measure was post-operative BCVA as dependent on duration of macular detachment.

Results:

Three hundred forty eyes from 340 patients met inclusion criteria; 277 eyes had a known duration of macular detachment and were included in linear and logistic regression models. Surgical repair occurred an average of 7.5 ± 8.8 days following macular detachment (range 0 to 76). Mean post-operative BCVA was logMAR 0.15 (95% CI, 0.13 to 0.18) in eyes with 3 or fewer days of macular detachment, and mean post-operative BCVA was logMAR 0.28 in eyes with 4 or more days of macular detachment (95% CI, 0.24 to 0.33; difference, logMAR -0.13 ; $P < 0.001$). Post-operative BCVA increased by 0.007 logMAR units with each additional day of macular detachment ($P < 0.001$). One hundred of 108 eyes (92.6%) that underwent surgical repair within 3 days of macular detachment had post-operative BCVA of logMAR 0.30 or better (Snellen 20/40), compared to 123 of 169 eyes (72.8%) who had surgical repair after 4 or more days of macular detachment (OR 0.21; 95% CI, 0.097 to 0.474; $P < 0.001$). For each additional day of macular detachment, the odds of achieving logMAR 0.30 decreased by a factor of 0.93 (95% CI, 0.89 to 0.96; $P < 0.001$). Pre-operative vision and duration of macular detachment were associated with post-operative BCVA; patient age, surgical eye, and lens status did not significantly affect post-operative BCVA.

Conclusions: Longer duration between macular detachment and repair is associated with a progressive decline of post-operative visual acuity. Surgical repair within 3 days of macular detachment improves visual acuity outcomes and should be the standard of care for macula-involving rhegmatogenous retinal detachments.

CONTROL ID: 3537348

SUBMITTER (NAME ONLY): Ferrin Antony

TITLE: Interleukin (IL)-27 regulates corneal immunopathology and viral clearance during herpes simplex virus-1 (HSV) infection

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Antony, M. Sandey, A. Mishra, A. Suryawanshi, Pathobiology, Auburn University, Auburn, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: HSV induced stromal keratitis (SK) is one of the leading causes of infectious blindness in the world. Although the role of inflammatory cytokines is well defined in SK, the role of a regulatory cytokine IL-27 has not been explored yet. In this study, using murine model of SK, we investigated the role of IL-27 response in cornea after HSV infection. Further, we explored IL-27- mediated regulation of inflammation and antiviral responses during corneal HSV infection.

Methods: IL-27RKO and C57BL/6NJ mice were ocularly infected with HSV. Eye swabs were collected on days 1, 3 and 5 post-infection (pi) for viral titration. The progression of SK lesions were scored on days 8, 11 and 14 pi. Further, the infiltration of neutrophils, macrophages and effector T cells in cornea, lymph node and spleen were analyzed on days 2 and 15 pi. Additionally, bone marrow-derived macrophages from IL-27RKO and C57BL/6NJ mice were cultured ex vivo to investigate IL-27 mediated anti-inflammatory and antiviral responses.

Results: Our data suggested an increased IL-27 production after corneal HSV infection which is mainly produced by dendritic cells and macrophages. In addition, IL-27RKO mice showed significantly increased SK pathology compared to control animals. The increased SK severity in IL-27RKO mice was mainly driven by enhanced migration of neutrophils, macrophages and Th1 cells to cornea. Mechanistically, IL-27 mediated signaling is critical for induction of type-1 interferon (IFN) responses by macrophages after HSV infection. In accordance, we observed significantly higher viral load in the corneas of IL-27RKO mice when compared to the control mice. Further, when stimulated with HSV our data showed reduced IFN- β production and increased viral titers in IL-27RKO macrophages.

Conclusions: Our data indicate that increased IL-27 response is critical for optimum production of IFN- β by macrophages and thus viral clearance. Further IL-27 plays a regulatory role during SK pathology by modulating Th1 cell differentiation and migration. Collectively, our results indicate that modulating IL-27-mediated responses may represent a useful therapeutic approach to control viral replication and inflammation during HSV induced SK pathology.

CONTROL ID: 3537350

SUBMITTER (NAME ONLY): Kristen Nwanyanwu

TITLE: Social Determinants of Health in Diabetic Retinopathy in the US: Evidence from the National Health and Nutrition Examination Survey (2005-2008)

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.H. Nwanyanwu, J. Andoh, E. Chen, Y. Xu, Y. Deng, Yale University, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of preventable blindness. According to Healthy People 2020, five key areas of social determinants of health (SDH) are: social and community context (which includes racial discrimination), education, economic stability, neighborhood and the built environment, and health and healthcare. This study defines a novel set of variables formulated from the National Health and Nutrition Examination Survey (NHANES) and identifies the SDH associated with DR.

Methods: Our NHANES analysis included participants with and without diabetes (HbA1c>6.5% or self-reported), ages 40 years or older with available fundus photography. We compared those with DR to participants with diabetes without DR. We also compared those with DR to the rest of the cohort. Covariates included sociodemographic factors and other SDH variables identified or calculated based on literature review: Depression screening (PHQ-9), Social Support Index, Food Insecurity, and Household crowding. Rao-Scott Chi-Square test was used for categorical variables and t-test was used for continuous variables, with consideration of the survey design.

Results: Among the total 5,399 (weighted 107.6M) participants over age 40 with fundus photography, there were 315 (weighted 4.0M) participants with DR and 692 (weighted 10.3M) participants with diabetes (Table 1). Among those with diabetes, DR was more prevalent in Black, Mexican-American, and Other Hispanic participants ($p=0.0022$). There were no other statistically significant differences in the SDH between those with DR and those with diabetes without DR. When compared to the entire cohort without DR (Table 2), DR was more prevalent in these sociodemographic categories: Black, Mexican-American, and Other Hispanic participants, born in Mexico, less formal education, lower household income (all $p<0.05$). DR was also more prevalent in these other SDH variables: Spanish primary language, food insecurity, no routine place for healthcare, fewer rooms in homes, fewer close friends, and higher depression scores (all $p<0.05$).

Conclusions: Among participants with diabetes, racial discrimination was the only SDH more prevalent DR. SDH variables were more prevalent in participants with DR compared to the overall population. Interventions that include SDH modification may contribute to a decrease in blindness from DR.

CONTROL ID: 3537360

SUBMITTER (NAME ONLY): Shuo Huang

TITLE: RPE-specific knockout of REV-ERB α induces age-dependent RPE degeneration in mice

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) dysfunction and atrophy occur in dry age-related macular degeneration (AMD) and are associated with chronic oxidative stress. Previously, we found that systemic deficiency of nuclear receptor REV-ERB α , a redox-sensitive transcription factor, results in RPE dysfunction and degeneration in mice due to dysregulation of the oxidative stress response in RPE. Here we investigated if RPE-specific knockout of REV-ERB α is sufficient to induce RPE degeneration in mice.

Methods: Mice with RPE-specific deletion of REV-ERB α , BEST1-cre:Rev-erba^{fl/fl} (RPE-KO), was generated by breeding Rev-erba^{flox/flox} (fl/fl) mice with BEST1-cre (cre) mice, with both fl/fl and cre mice as controls. Knockout efficiency and specificity of REV-ERB α in RPE were measured by RT-qPCR, Western blot, and immunostaining of RPE/choroid flat mounts and cross-sections. RPE degeneration of fl/fl (n=4), cre (n=5) and RPE-KO (n=7) mice were monitored by fundus imaging at 3, 6 and 9 months old, and sub-retinal lesions were quantified. RPE atrophy was analyzed by immunostaining of RPE/choroid flat-mounts. RNA and protein expression of REV-ERB α target genes including antioxidant regulators and enzymes was examined in fl/fl and RPE-KO RPE. Oxidative DNA damage was evaluated by immunostaining of 8-hydroxy-2'deoxyguanosine (8-OHdG).

Results: REV-ERB α knockout was specific to RPE cells in RPE-KO mice with up to 80% efficiency in cell counting and mRNA and protein levels. Fundus imaging of RPE-KO mice showed significantly greater number of whitish yellow lesions at both 6- and 9-month-old, compared to both fl/fl and cre controls. In addition, RPE-KO mice showed more severely distorted RPE patches in flat-mounts by immunostaining of β -Catenin, compared with cre controls. Significant downregulation of NRF2 and its target genes Sod1, Sod2 and Catalase was found in RPE-KO vs. fl/fl RPE at both mRNA and protein levels. Furthermore, RPE-KO mice exhibit elevated oxidative stress with 8-OHdG staining, compared to cre RPE at 6 months old.

Conclusions: These findings suggest that RPE specific depletion of REV-ERB α leads to fundus lesions and RPE degeneration similar to those in systemic REV-ERB α knockout mice, demonstrating an RPE cell-autonomous role of REV-ERB α in regulating RPE function and health, potentially through modulating NRF2 transcription and antioxidant self-defense.

CONTROL ID: 3537390

SUBMITTER (NAME ONLY): Jean-Philippe Rozon

TITLE: Fear associated with COVID-19 in neovascular age-related macular degeneration patients

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rozon, Université Laval Faculté de médecine, Québec, Québec, CANADA | M. Hébert, S. Bourgault, M. Caissie, L. Letarte, E. Tourville, A. Dirani, CHU de Québec-Université Laval, Québec, Québec, CANADA |

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ABSTRACT BODY:

Purpose: Since the beginning of the COVID-19 pandemic, news related to the pandemic have created a feeling of fear, particularly among high-risk groups including elderly patients. We performed a prospective, cross-sectional study to assess the fear associated with COVID-19 and the fear of vision decrease related to the delay of treatment in neovascular age related macular degeneration patients (nAMD) during the pandemic.

Methods: 160 actively treated nAMD patients were enrolled between September to November 2020 in a tertiary university hospital in Québec, Canada. Exclusion criteria included: patients with memory disorders and patients with incomplete questionnaire. For each participant, demographic and clinical data were collected. The fear was rated in a questionnaire composed of two sections: the Fear of COVID-19 Scale (FCV-19S) and eight additional questions to assess ophthalmology-related COVID-19 statements. A multivariate linear regression model was built for FCV-19S score and a multivariable ordinal regression model for ophthalmology-related statements.

Results: The mean level of FCV-19S was 17.05 ± 4.38 . In the multivariate analysis, it was significantly higher in women ($p < 0.001$) and patients with elementary school level (compared to high school education level) ($p = 0.009$). In the ophthalmology-related statements, 16% of patients feared vision loss because of difficulties in maintaining regular follow-ups during the pandemic. The female gender was significantly associated with a higher tendency to postpone their appointment ($p = 0.03$) and to prefer "sacrificing" their vision to avoid contracting COVID-19 ($p = 0.05$). No association was found between the patients' underlying nAMD characteristics (visual acuity, bilaterality, duration) and higher fear of vision loss.

Conclusions: Despite the massive impact the pandemic has had on our functioning in most aspects of life, the anxiety related to COVID-19 and delaying ophthalmology treatments remained relatively low in nAMD patients. Greater explanations to address this fear may reduce anxiety level, especially among female patients and those with an elementary school education level.

CONTROL ID: 3537400

SUBMITTER (NAME ONLY): Alexander Laskaris

TITLE: Proteomic Characterization of Extracellular Vesicles in Rabbit Model of Uveal Melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Laskaris, P.R. Bustamante, T. Tsering, C. Mastromonaco, J. Coblenz, J.V. Burnier, McGill University Health Centre, Montreal, Quebec, CANADA]

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ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is often asymptomatic and well controlled; unfortunately 50% of patients develop metastasis plummeting survival to 15%. There is an urgency to identify mechanisms by which these melanocytic tumors are disseminating. Recent studies have focused on extracellular vesicles (EVs); biomolecule containing nanoparticles with propensity to mediate metastasis. We have previously shown UM cell line-derived EVs can induce oncogenic transformation in fibroblasts, resulting in tumor formation in vivo. Further, our group has characterized proteomic profiles of EVs from UM cell lines. The purpose of this study was to characterize EV proteomic profiles in a rabbit model of human UM. In addition, through species classification of EV protein content, to differentiate tumor originating proteins from homeostatic EV proteins.

Methods: Peripheral blood was obtained from 7 rabbits inoculated intraocularly with human UM cells (line 92.1) in a 20-week animal model. EVs were isolated by differential ultracentrifugation from rabbit plasma at week 0 and week following tumor (weeks 10+). Confirmation of EV yield was demonstrated by nanoparticle tracking analysis (NTA). EV proteins were isolated and subjected to mass spectrometry analysis. Raw proteomics data was matched against rabbit and human databases then loaded into Q+ Scaffold_4.4.8 software for visualization, statistical comparison and quantification.

Results: NTA data confirmed presence of EVs ranging in size of 165-210nm. EV protein concentrations showed an increase in protein content correlating with increased tumor size. Statistical analysis in scaffold highlighted significant differences in human and rabbit protein profiles between week 0 and weeks 10+ in all rabbits. Lists of differentially expressed human and rabbit proteins were compiled separately, referenced against literature and loaded into DAVID Bioinformatics database for functional gene ontology analysis. Interestingly, trends seen in human proteins were mirrored by their rabbit homologs.

Conclusions: Here we provided a unique insight into primary UM derived EVs through a rabbit model. Furthermore, the data suggests rabbit host EV compositions may be influenced and adapting to primary UM. This experimental model proves promising for future assessments of primary UM EV contents with hopes to eventually broaden our understanding of metastasis.

CONTROL ID: 3537419

SUBMITTER (NAME ONLY): Terry Lee

TITLE: Characterization of the ocular phenotype in older patients with long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency (LCHADD)

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: LCHADD is an early-onset autosomal recessive fatty acid metabolism disorder due to mutations in HADHA, the LCHAD Trifunctional Multienzyme Complex Alpha Subunit gene, associated with progressive vision loss. Due to high early mortality, previous studies focused mostly on very young patients. Herein, we characterized 4 LCHADD patients in the second to third decade.

Methods: We retrospectively evaluated the records of 4 genetically and biochemically confirmed LCHADD patients (3M/1F; ages 13-21yo) with complete eye exams inclusive of ETDRS acuity, kinetic perimetry, full-field flash (ff)ERGs, multi-focal (mf)ERGs, electrooculograms (EOG), spectral domain (SD)-OCT, wide-field fundus autofluorescence (WF-FAF), fluorescein angiography, and color photography.

Results: According to the classification proposed by Tyni et al. (1998), 1 case was stage 2 OU, 2 cases were stage 3 OU, and 1 case progressed from stage 3 to 4 in OD and stage 2 to 3 in OS over a 7-year period. Mean visual acuity was 20/60 (range 20/20 – 20/400). All cases had central/paracentral scotomas and progressive central choroidal and retinal pigment epithelium (RPE) atrophy. The widespread RPE atrophy presented as nummular, coalescent hypo-autofluorescent patches with peripheral sparing on WF-FAF. SD-OCTs showed ellipsoid zone (EZ) loss with outer retinal tubulations, subretinal hyperreflective material, ectatic lesions, RPE loss with marked hypertransmission defects, and severe choroidal thinning. Consistent with the widespread RPE disease, EOG Arden ratios ranged from borderline low (1.67) with severe light peak delays to markedly reduced (≤ 1.48). ffERGs ranged from normal to moderate reductions and delays in rod and cone responses, with disproportionately reduced a-waves and increased b/a-wave ratios, consistent with prevailing outer retinopathy. mfERGs showed either severe generalized or patchy response density depression, consistent with markedly reduced macular cone function.

Conclusions: LCHADD exhibits choroideremia-like progressive features primarily affecting the RPE, choroid, and photoreceptors, beginning in the posterior pole with eventual foveal and progressive coloboma-like macular lesions and centrifugal involvement. Our report adds new mfERG and EOG data in a series of older patients, improving our understanding of the pathophysiology and characteristics of later-stage LCHADD.

CONTROL ID: 3537464

SUBMITTER (NAME ONLY): Julie Lovell

TITLE: Perceptual Learning of Hue Discrimination in Jewelry Appraisers

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lovell, J.C. Rabin, Rosenberg School of Optometry, University of the Incarnate Word, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Perceptual learning can improve visual acuity, contrast sensitivity, vernier acuity and stereo-acuity in adult amblyopes beyond the critical period for visual development. Latent neural connections and/or development of new connections may underlie these improvements, coupled with the relative balance of excitatory and inhibitory neurotransmitters. Recently we reported superior hue discrimination in largely elderly jewelry appraisers who must discriminate subtle changes in hue to ensure optimal gemstone valuation. We report that the basis for this enhancement depends on M and S cones.

Methods: Jewelry appraisers (n=18, mean 57 ± 12 YO) undergoing color vision certification on the FM 100 hue test in accord with the National Association of Jewelry Appraisers (NAJA) were invited to participate in a study to assess performance on the Ishihara (to rule out hereditary color deficiency), FM-100 Hue (currently used by NAJA), desaturated D15 and the cone contrast test (Innova Systems, Inc) which quantifies L, M and S cone contrast sensitivity (CS). Subjects provided written informed consent for our IRB approved protocol.

Results: All subjects passed the Ishihara and desaturated D15 tests confirming normal color vision. Combined M and S cone CCT scores were predictive of FM 100 Hue total error score (TES; $F = 7.76$, $P < .02$, $r^2 = .45$). 17 of 18 subjects had 100 Hue TES scores which were >2SD below age-matched normal means indicating enhanced hue performance. Partial TES analysis revealed error rates were greatest on the blue-yellow (BY) axis.

Conclusions: Elderly jewelry appraisers show enhanced hue discrimination due to a highly practiced, reward-based repetition—tenets of perceptual learning. Correlation between M and S CCT and FM Hue scores suggests greater importance of M and S cone hue discrimination and CS for accurate gemstone discrimination. This is evident in Fig. 1 which shows perception of a highly valued gemstone (<https://www.thepearlsource.com/blog/most-valuable-gemstones/>) in normal, protan, deutan and tritan views (<https://www.color-blindness.com/coblis-color-blindness-simulator/>). The protan (lacks L cones) and normal views essentially match while deutan (lack M cones) and tritan (lack S) views appear different from the normal, highly valued view, exemplifying M and S cone importance in gemstone hue discrimination.

CONTROL ID: 3537467

SUBMITTER (NAME ONLY): Suzanne Wernimont

TITLE: Applying Normal PedEyeQ Thresholds to Define Reduced Quality of Life in Children with Visual Impairment

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. Wernimont, D.A. Leske, S.R. Hatt, E.D. Bothun, J.M. Holmes, Ophthalmology, Mayo Clinic, Rochester, Minnesota, UNITED STATES|Y.S. Castañeda, C.S. Cheng-Patel, E.E. Birch, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|E.E. Birch, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|J.M. Holmes, Ophthalmology and Vision Science, University of Arizona-Tucson, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Pediatric Eye Questionnaire (PedEyeQ) assesses eye-related quality of life (ER-QOL) and functional vision in children with any eye condition. Previous studies have compared mean scores in clinical and control populations, but not whether it is meaningful to apply normal thresholds to identify individuals with reduced ER-QOL and functional vision. We evaluated PedEyeQ scores in children with bilateral visual impairment (VI).

Methods: 48 children (22, 0-4 years, 18, 5-11 years and 8, 12-17 years) with bilateral VI (best-eye acuity worse than 20/70) and 310 visually normal controls (104, 0-4 years, 104, 5-11 years and 102, 12-17 years) were prospectively enrolled. Children aged 5-17 years completed the Child PedEyeQ (Functional Vision, Bothered by Eyes/vision, Social, and Frustration/worry domains). Parents completed Proxy PedEyeQ (0-4 years: Functional Vision, Bothered by Eyes/Vision, Social; 5-17 years: same domains plus Frustration/Worry and Eye Care) and Parent PedEyeQ (Impact on Parent and Family, Worry about Child's Eye Condition, Worry about Child's Self-perception/Interactions, Worry about Child's Functional Vision). PedEyeQ domains were Rasch-scored and converted to 0-100. The 5th percentile of scores in the normal cohort defined the "reduced" threshold for each domain in each age group. Proportions with reduced scores were calculated.

Results: Proportions of VI subjects with reduced Child scores ranged from 78% (Functional Vision) to 39% (Frustration/worry) for 5-11 years and from 100% (Functional vision, Frustration/worry) to 88% (Bothered by Eyes/vision, Social) for 12-17 years. Proportions with reduced Proxy scores ranged from 100% (Functional Vision, Bothered by Eyes/Vision) to 55% (Social) for 0-4 years, 94% (Functional Vision) to 61% (Frustration/Worry, Eye Care) for 5-11 years, and 100% (all except Frustration/Worry) to 88% for 12-17 years. Proportions with reduced Parent scores were 95% or 100% for 0-4 years and 83% to 100% for 5-11 years; all domain scores (100%) were reduced for 12-17 years.

Conclusions: A high proportion of visually impaired children and their parents have reduced PedEyeQ domain scores, supporting the application of a normal threshold to identify individuals with reduced ER-QOL and functional vision. Nevertheless, variability of scores by self-report in young children may create challenges for interpreting domain scores in 5- to 11-year-olds.

CONTROL ID: 3537476

SUBMITTER (NAME ONLY): Isabelle Gefke

TITLE: Two Methods for Measuring Cytosolic Alpha Catenin in Individually Segmented Cells of Entire Retinal Pigment Epithelium Flatmounts

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Gefke, V. Summers, K. Donaldson, D. Shelton, J.H. Boatright, J.M. Nickerson, N. Zhang, Emory University, Atlanta, Georgia, UNITED STATES|J.H. Boatright, Veterans Affairs Rehabilitation Research & Development, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cadherins junction protein, alpha-catenin (ACat), is primarily located in the cell membrane of healthy retinal pigment epithelium (RPE) cells, but undergoes a redistribution to the cytosol in cells which exhibit damage-induced changes in morphology. Previously, efforts to quantify the correlation between cytosolic ACat levels and individual cell morphological metrics in situ were limited by small sampling areas, access to prohibitive computational power, and sufficient programming expertise. Here, we introduce two separate analysis protocols allowing for unbiased, computationally minimal, and easy-to-use quantification of ACat cellular distribution using the open-source Cell Profiler application and the commercially available IMARIS software suite.

Methods: Damage to mouse RPE was induced by one of three methods (sub-retinal injection, light induced retinal degeneration, or systemic sodium iodate). Image sets of entire RPE sheets were acquired via confocal microscopy of fluorescently labeled ZO-1, ACat and nuclei. Maximum intensity projection images of each RPE sheet were processed using IMARIS 9.6 (Bitplane, Inc.) where individual cells were segmented, identified, and quantified morphologically. Incorrectly segmented cells and artifacts were manually rejected. ACat cytosolic intensities were derived using ZO-1 defined cell identification. For comparison, the same image sets were then processed using Cell Profiler without manual rejection of segmentation errors.

Results: Entire RPE sheets from both control and damage groups were accurately and successfully segmented using both Cell Profiler and IMARIS analysis protocols on a single lab computer. Segmentation morphometrics of abnormal cells following damage matched previously reported (K. Donaldson, ARVO2017) results showing positive correlations between abnormally sized (area, perimeter) cells and increased ACat cytosolic expression. Once optimized, Cell Profiler and IMARIS protocols were able to be applied uniformly across image sets, enabling unbiased and repeatable segmentation and quantification.

Conclusions: We present both open- and closed-source solutions using Cell Profiler or IMARIS for successful and efficient segmentation of RPE flatmounts. Additionally these protocols allow for simultaneous quantification of cytosolic ACat, a marker for abnormal RPE cells in damage models.

CONTROL ID: 3537513

SUBMITTER (NAME ONLY): David Lutz

TITLE: Duration of Effect of a Single Intravitreal Injection of a Sustained-Release Formulation of Abicipar Pegol Compared to a Bolus Dose of Aflibercept in a Rabbit Model of Persistent Retinal Vascular Leak

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Lutz, M. Tian, L. Hernandez, A. Kulkarni, G. Rodrigues, Research, Non-Clinical and Translational Sciences, AbbVie Inc, Irvine, California, UNITED STATES|H. Shen, H. Rivers, Pharmaceutical Development, AbbVie Inc, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The high treatment burden of frequent intravitreal (IVT) anti-VEGF injections for treatment of nAMD and DME presents an opportunity for sustained release (SR) technologies to increase the interval between injections. To address this unmet need, duration of effect of a single IVT injection of an SR formulation of bioerodible polymer microsphere particles loaded with the DARPin anti-VEGF abicipar pegol (abicipar SR) compared to a bolus dose of aflibercept was evaluated in a rabbit model of persistent retinal vascular leak (PRVL).

Methods: New Zealand Red rabbits previously injected IVT with DL-2-amino adipic acid (0.8 mg; OD) to induce PRVL were injected IVT with 50 µL of either abicipar SR (500 µg drug load; n=8) or aflibercept (700 µg bolus; n=7). Duration of effect was determined by quantitation of retinal leak area compared to pre-treatment leak area using fluorescein angiography bi-weekly for 32 weeks after injection. Retinas were then collected, fixed, and immunofluorescent co-labeling of retinal vasculature with IB4 and CD31 antibody was performed. Confocal images of retinal whole mounts were acquired and the degree of vascular regression in the area of baseline retinal leak was determined by calculating the ratio of CD31/IB4 signal overlap, which inversely correlates with the extent of vascular regression.

Results: A single IVT injection of abicipar SR completely inhibited retinal leak in all eyes for 22 weeks versus 10 weeks with aflibercept treatment. Complete leak suppression persisted in 71, 43, and 17% of abicipar SR-treated eyes at Weeks 24, 26, and 28, respectively. Robust suppression (>90% reduction of baseline leak area) was shown 26 weeks after abicipar SR treatment, which was significantly longer ($P<0.05$) than 12 weeks with aflibercept treatment. IHC analysis of retinal vasculature revealed that abicipar SR and aflibercept induced regression of neovessels within the baseline leak area to a similar extent. Intra-ocular inflammation was not observed in either treatment group.

Conclusions: These data demonstrate that a single IVT injection of abicipar SR was well tolerated in NZW rabbits and suppressed retinal leak for 6 months. Compared to aflibercept, abicipar SR was at least twice as durable with a minimum of 14 additional weeks of activity.

CONTROL ID: 3537519

SUBMITTER (NAME ONLY): Alison Martin

TITLE: Correlation of Intraocular Cytokine Expression with Quantitative Ultra-widefield Fluorescein Angiographic Features in the IMAGINE Retinal Vein Occlusion Study

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Retinal vein occlusions (RVO) result in the overexpression of a variety of intraocular cytokines that contribute to sequelae, such as macular edema. The ability to link imaging biomarkers with specific underlying pathways could enhance therapeutic decision-making. This study correlated cytokine expression with ultra-widefield fluorescein angiography (UWFA) quantitative imaging biomarkers in RVO.

Methods: The IMAGINE RVO study is a post-hoc assessment of the WAVE clinical trial to determine associations between cytokine expression and quantitative imaging features. The WAVE study was a randomized clinical trial that

evaluated the impact of targeted retinal photocoagulation (TRP) on treatment requirement with intravitreal ranibizumab in 30 eyes with RVO. Eyes had aqueous humor samples collected and UWFA performed at baseline. Fifty-four cytokines associated with inflammation and angiogenesis were evaluated using multiplex arrays. Quantitative assessments of ischemia and leakage on UWFA were determined using an automated feature analysis platform with manual validation. Associations between cytokines and quantitative UWFA features were assessed using Spearman's correlation coefficients.

Results: Twenty-seven of the 30 eyes in the WAVE study had sufficient samples for analysis. Increased macular ischemia was associated with ANGPTL4 ($r=0.66$, $p=0.0002$), VEGF ($r=0.52$, $p=0.007$), and MCP-1 ($r=0.40$, $p=0.04$). Increased peripheral ischemia was associated with ANGPTL4 ($r=0.52$, $p=0.007$) and VEGF ($r=0.60$, $p=0.002$), while decreased peripheral ischemia was associated with IL-12p70 ($r=-0.45$, $p=0.02$) and MCP4 ($r=-0.44$, $p=0.02$). Increased macular leakage was associated with ANGPTL4 ($r=0.42$, $p=0.03$) and VEGF ($r=0.63$, $p=0.0008$). Increased peripheral leakage was associated with ANGPTL4 ($r=0.57$, $p=0.002$), VEGF ($r=0.61$, $p=0.001$), and LIF ($r=0.42$, $p=0.03$), while decreased peripheral leakage was associated with FGF-4 ($r=-0.47$, $p=0.02$).

Conclusions: Multiple quantitative UWFA features were associated with intraocular cytokines in eyes with RVO. VEGF and ANGPTL4 correlated with both increased ischemia and increased leakage on UWFA. Further research is needed to evaluate the possibility of using these imaging biomarkers as surrogates for cytokine expression and correlating these features with treatment response.

CONTROL ID: 3537532

SUBMITTER (NAME ONLY): Jana Sellers

TITLE: DMSO Protects Retinal Function in Two Mouse Models

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dimethyl sulfoxide (DMSO) is an FDA-approved treatment for interstitial cystitis. Research shows that DMSO also acts as a neuroprotectant in models of traumatic brain injury, ischemic stroke, and Alzheimer's Disease. We tested the hypothesis that systemic treatment with DMSO would be protective in the light induced retinal damage (LIRD) and the retinitis pigmentosa Pdeb6^{rd10/rd10} (rd10) mouse models.

Methods: 3.5 ml/kg DMSO or Dulbecco's Phosphate Buffered Saline (PBS) vehicle was used for all experiments. Male Balb/c LIRD mice ages 75 to 120 days were intraperitoneally (IP) injected the afternoon before and morning of bright light exposure (5000 lux x 4h). Male and female rd10 pups were injected 8-11 times with DMSO or PBS. Injections between postnatal day 4 (p4) and p12 were subcutaneous, and IP injections were used between p13-p23. Mice in naïve groups received no injections. Retinal function was assessed by electroretinogram (ERG). Retinal preconditioning was assessed by injecting 5, 3, and 1 day prior to bright light. To determine whether DMSO protection is mediated by processes that require significant time, DMSO was injected immediately following bright light and again the next morning. Finally, the effect of DMSO on retinoid cycling was assessed by measuring ERGs following photobleaching (1000 lux x 30 sec). Statistical analysis was 2way ANOVA with Tukey's multiple comparisons test.

Results: LIRD model: a- and b-wave amplitudes at 24.9 cd s/m² decreased 93% and 92% respectively for the vehicle bright group but only 30% and 33% for the DMSO bright group when compared to vehicle dim. DMSO injected 5, 3, or 1 day prior to bright light was not protective, nor was injecting after bright light. DMSO treatment did not slow functional recovery from photobleaching.

rd10 model at p23: scotopic a-wave amplitudes decreased 42% for the vehicle group but increased 107% for the DMSO group when compared to naïve. Photopic a- and b-wave amplitudes decreased 8% and 20% for the vehicle group but increased 65% and 56% respectively for the DMSO group when compared to naïve.

Conclusions: Systemically-delivered DMSO protected retinal function in the LIRD and rd10 models. DMSO did not provide protection by retinal preconditioning or slowing retinoid cycling, nor did it provide protection when given after bright light. DMSO-induced retinal protection may require more time, suggesting gene/protein expression and/or post-translational modification mechanisms.

CONTROL ID: 3537545

SUBMITTER (NAME ONLY): Shaheen Kavoussi

TITLE: Early Switch to the Dexamethasone Implant after Sub-Optimal Response to Anti-VEGF Therapy for Diabetic Macular Edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kavoussi, Ophthalmology, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|S. Kavoussi, Ophthalmology, Houston Methodist, Houston, Texas, UNITED STATES|J. Nezgoda, West Boca Eye Center, Florida, UNITED STATES|J. Chhablani, S. Caplash, J.N. Martel, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|D.F. Kiernan, Ophthalmic Consultants of Long Island, New York, UNITED STATES|S. Hariprasad, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|M. Singer, Medical Center Ophthalmology Associates, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In DRCR Protocol I Early Analysis, 26% of patients were non-responders to anti-vascular endothelial growth factor monotherapy, but visual gains with steroid switch therapy in Protocol U were limited by duration of diabetic macular edema (DME). Study of an earlier multi-factorial approach is indicated. This study assesses treatment for DME with the dexamethasone 0.7 mg implant (DEX) after limited response to 1-3 monthly anti-vascular endothelial growth factor injections (AVF).

Methods: This multi-center, retrospective series included 58 initially treatment-naïve patients with < 200 µm reduction in central retinal thickness (CRT) and/or < 5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters gained after 1-3 intravitreal bevacizumab or aflibercept AVF, who were then switched to DEX with ≥ 6 weeks subsequent follow-up.

Results: Baseline mean ± standard deviation (SD) best-corrected visual acuity (BCVA) was 55 ± 14 letters. CRT was 453 ± 172 microns. After patients received one (26%), two (6%) or three (68%) monthly AVF, mean BCVA was 57 ± 14 letters (p=0.57) and CRT was 412 ± 134 µm (p=0.16). After subsequent DEX, BCVA was 65 ± 13 letters (p=0.0001 compared to baseline and p=0.003 compared to post-AVF) and CRT was 280 ± 57 µm (p<0.0001 compared to both baseline and post-AVF).

Conclusions: In this cohort, patients with DME who had a limited visual and anatomic response to 1-3 monthly doses of either intravitreal bevacizumab or aflibercept demonstrated significant improvements after subsequent treatment with the dexamethasone 0.7 mg implant. Earlier intervention with DEX for treating DME may result in more rapid visual and anatomic gains compared to AVF monotherapy in certain patients.

CONTROL ID: 3537570

SUBMITTER (NAME ONLY): Amy Nau

TITLE: Current Trends in the Holistic, Long-Term Management of Keratoconus

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Studies which examine the degree to which holistic issues related to keratoconus (KC) management are non-existent, but could be an important component to increasing patient satisfaction.

Methods: An internet-based, 22 question, IRB approved RED-Cap survey of providers who managed at least one KC patient per week. Descriptive analyses are presented. Respondents were not required to answer every question, and some questions allowed more than one response.

Results: Of the 296 respondents, 245 providers with an average of 23.1 +12 years in practice met entry criteria. Respondents (n=220) averaged caring for 27.2 +35 KC patients each month. Only 19% of respondents (n=220) administer symptom questionnaires. Of respondents that do (n=42), 28 use them only at the initial visit, 18 use them at every follow up, and 15 do so annually (more than one answer allowed). The majority (98%, n=220) ask about contact lens comfort at every visit. 51% (n=220) of respondents perform dry eye testing as part of follow up examinations. Point of care tests include ((n=299); multiple responses allowed): MMP-9 (n=17), osmolarity (n=23), lipid layer thickness (n= 33), meibography (n=38), KB light test(n=4), break up time (n=108), vital dye staining (n= 78), Schirmer test (n=32), Dry Eye Test 9 (n=19), other (n=19). It is uncommon for patients to be asked about depression related to their condition. Only 4% of providers always ask, 13% most of the time, 45% sometimes, 27% rarely ask and 11% never broach this topic (n=222). Providers rarely refer to support groups or mental health professionals. Only 2% do so all of the time, 6% most of the time, 26% offer sometimes, 43% do so rarely and 23% never refer for such services (n=222). 92.7% of respondents felt that patients were honest about problems related to their disease.

Conclusions: This is the first survey among eye care providers to examine holistic aspects of long-term keratoconus management. Results demonstrate that symptom questionnaires, inquiries about quality-of-life /depression and referrals to mental health professionals are seldom addressed. Dry eye is emerging as a problem for KC patients yet only half of respondents routinely test for this comorbid condition, which can negatively impact contact lens tolerance and overall quality of life. Results of this study identify several high impact, low-cost improvements to current practice patterns.

CONTROL ID: 3537588

SUBMITTER (NAME ONLY): Dillon Brown

TITLE: Oral All-trans Retinoic Acid Treatment Induces Myopia and Alters Scleral Biomechanics in Mice

SESSION TITLE: Refractive control: Molecular and Anatomical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Brown, C.R. Ethier, M.T. Pardue, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|D. Brown, M.T. Pardue, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Both correlational and causal evidence support a connection between increased ocular retinoic acid (RA) concentrations and myopic axial elongation in mammals; however, RA's effects on scleral biomechanics, influential to eye size, are not known. Here, we treated mice with all-trans RA (atRA) to test the hypothesis that exogenous atRA alters scleral biomechanics and causes myopia in mice.

Methods: Male C57BL/6J mice (n=10) were trained to voluntarily ingest sugar pellets and were fed daily (2.5 g pellet/kg) from P29 to P44/45. Pellets dosed with atRA (added at a 1:100 ratio prior to forming pellets) were introduced between P30-31 in a randomly selected subset of animals (n=6 atRA, n=4 control), yielding a daily 25 mg atRA/kg dose. Refractive error (RE) was measured once per week beginning prior to atRA treatment. From a subset of animals (n=8), one eye per animal was randomly selected for biomechanical measurements (n=4 control, n=4 atRA). After sacrifice, sclerae were isolated for biomechanical quantification of tensile stiffness and permeability using unconfined compression and a biphasic material model.

Results: All animals voluntarily ingested the pellets. Oral atRA treatment significantly influenced RE development (interaction: treatment*age, $p < 0.001$), leading to relative myopia at 1 week compared to the control mice (mean \pm STD, 0.3 ± 2.7 vs 4.3 ± 0.4 D, $p = 0.024$), with the difference increasing at 2 weeks (-1.0 ± 2.6 vs 6.3 ± 0.1 D, $p < 0.001$). Changes in RE were accompanied by significantly altered scleral biomechanical properties. Sclerae from atRA fed animals were significantly less stiff compared to control sclerae (95% CI, [83.8, 118] vs [131.6, 186]kPa, $p < 0.001$). Permeability trended towards increasing with atRA treatment but did not reach significance (95% CI, [3.9, 7.4] vs [2.9, 5.5] $\text{m}^2 \cdot 10^{-18}$, $p = 0.18$).

Conclusions: Exogenous atRA is highly myopigenic in mice, a novel result that corroborates previous findings in guinea pigs. Further, we show for the first time that atRA affects scleral biomechanics, indicative of scleral remodeling. The decreased tensile stiffness of the sclera accompanying the atRA-induced myopia is comparable to that measured in mammals experiencing sustained myopigenic visual cues, e.g., form deprivation and lens defocus. This work motivates additional study into the role of RA in the retinoscleral signaling cascade that enables myopigenic visual cues to influence eye size.

CONTROL ID: 3537610

SUBMITTER (NAME ONLY): Hayate Nakagawa

TITLE: The Impact of Donor Diabetes on Corneal Immune Cells and Corneal Transplant Survival

SESSION TITLE: Corneal immunology and neovascularization I

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Nakagawa, T. Blanco, T. Dohlman, S. zhu, H. Alemi, Y. Chen, J. Yin, R. Dana, Ophthalmology, Mass Eye and Ear, Harvard Medical School, Massachusetts, UNITED STATES|B. Gonzalez-Nolasco, Surgery, Center for Transplant Sciences, Massachusetts General Hospital/Harvard Medical School, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is increasing evidence that the diabetic status of tissue donors can adversely impact corneal graft survival. Here, we evaluated the hypothesis that the diabetic state induces an altered corneal microenvironment with increased antigen-presenting cell (APC) maturation that in turn leads to heightened host sensitization and increased graft rejection.

Methods: Type I diabetes mellitus was induced in C57BL/6 mice by injecting 50mg/kg streptozocin (STZ) for 5 days. The altered glycemic state was confirmed by a glucometer. On day 28, mice with blood glucose levels of 300mg/dL were considered diabetic. Corneas were then harvested and either digested for analysis through flow cytometry, or grafted into normal BALB/c recipient mice. Two weeks after transplantation, immune cells from the corneas and draining lymph nodes (DLN) of recipient mice were analyzed by flow cytometry and allospecific cytokine production was evaluated through a mixed lymphocyte reaction.

Results: A significantly higher frequency of CD45⁺ cells (p=0.0009) and higher expression levels of MHC-II by APC (p=0.048) were observed in corneas from diabetic donors compared to normal mice. Allograft survival was decreased in diabetic donors (0%) compared to normal donors (52%, p=0.0002) through eight weeks of follow-up. The frequency of CD45⁺CD11b⁺ APC (p=0.014) as well as their expression of the maturation markers MHC-II (p=0.006), CD80 (p=0.007) and CD86 (p=0.03) was significantly increased in recipients receiving grafts from diabetics as compared to non-diabetic donors.

Conclusions: Our preliminary data suggest that diabetes mellitus leads to increased maturation of resident corneal immune cells and that transplantation of diabetic donor corneas leads to heightened host alloimmunity and increased graft rejection.

CONTROL ID: 3537624

SUBMITTER (NAME ONLY): Azadeh Mobasserian

TITLE: Effect of pupil size on fixed-luminance flicker full-field electroretinogram magnitude

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mobasserian, M. Halim, J.J. Hwang, J. Regenold, A. Akhavanrezayat, H. Ghoraba, W. Matsumiya, N. Yavari, I. Karaca, C. Yasar, S. Lajevardi, B.H. Pham, D.V. Do, Q.D. Nguyen, ophthalmology, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center(OIRRC), Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diopsys® NOVA fixed-luminance flicker full-field electroretinogram (ffERG) is a potential alternative to classic ffERG testing for measuring the electrical activity of cone cells . Pupil size has been shown to effect electrical response. The index study aims to quantify the relationship between pupil size and ffERG magnitude using this device.

Methods: 12 patients (24 eyes) with no known ocular diseases were enrolled in the study. Retinal activity was examined using Diopsys® ffERG before and after dilation. Eyes were initially anesthetized with proparacaine hydrochloride 0.5 % ophthalmic solution and then dilated with tropicamide 1% and phenylephrine 2.5% ophthalmic solutions. Eyes were dilated to a minimum of 5 mm before Diopsys® measurements were made. Paired t-test and robust linear regression were performed on the data set.

Results: Mean age was 34.9 ± 8.4 years and 25% were female. Mean value of pupil diameter and magnitude before and after the dilation was 2.54 ± 0.38 mm/ 7.01 ± 0.90 mm and 10.45 ± 2.92 μ V / 16.56 ± 4.1 μ V , respectively. There was a statistically significant difference in magnitude of response before and after dilation (p : <0.0001). In dilated eyes, linear regression analysis demonstrated an increase in magnitude with each millimeter increase of pupil size (r^2 : 0.44; Coeff.: 2.99; p : <0.0001) (figure1). It also demonstrated a 12% increase in change of magnitude with each millimeter unit increase in pupil size (r^2 : 0.15; Coeff.: 1.12; p : 0.07) (figure2).

Conclusions: Pupil size affects electrophysiologic response of the retina and should be measured and documented. Physicians should take pupil size into consideration when making clinical judgments based on Diopsys® ffERG. The normative values for ffERG devices should include pupil size variability to ensure better clinical judgments.

CONTROL ID: 3537625

SUBMITTER (NAME ONLY): Beatrice Gallo

TITLE: Sick cell retinopathy: is there a role for follow-up?

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Gallo, F.M. D'Alterio, J.S. Talks, Eye Department, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM | M. Hall, Hematology Department, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM |

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ABSTRACT BODY:

Purpose: The role of regular ophthalmic screening in patients with sickle cell retinopathy is controversial and there are no studies guiding the frequency of review, hence the scope of this study.

Methods: Retrospective observational study of 66 eyes of 33 patients (20 females, median age 30 years, age range 17-60 years) with sickle cell disease screened for retinopathy with fundoscopy, ultrawide-field pseudocolour fundus pictures (Optos plc, Dunfermline, UK) and OCT-angiography. Type and progression of retinal findings were recorded at each visit.

Results: 25 patients had SS (sickle cell anemia) and 8 patients had SC (sickle cell/hemoglobin C compound). Ethnicity was African in 21 patients, Caribbean in 8 patients, Asian in 2 patients and Caucasian in 2 patients. 9 patients were on systemic treatment (8 hydroxycarbamide, 1 blood transfusions), 24 were not on treatment (1 received allogeneic transplant), 6 of whom refused treatment. Median follow-up duration was 18 months (range 0-47 months) and median number of visits was 2. Retinopathy was observed in 39 eyes (unilateral in 7 patients and bilateral in 16 patients). Retinal abnormalities included peripheral vascular closure (24 eyes, 15 patients), black sunbursts (17 eyes, 13 patients), sea-fan neovascularization (9 eyes, 5 patients) (Figure 1) and pale retinal patches (5 eyes, 3 patients). At baseline, there was no statistically significant difference in the distribution of the retinal abnormalities according to disease subtype ($p > 0.05$) and according to treatment group. Over the follow-up period, retinopathy progression was observed in 4 eyes from 2 patients (6.3%) affected by SS who refused systemic treatment. Progression consisted in new retinal hemorrhages (1 eye), new sea-fans (1 eye) or fibrosis enlargement (2 eyes), and was not vision threatening. In 4 eyes from 2 SS patients the OCT-A showed foveal avascular zone enlargement and superficial and deep capillary plexus drop-out (Figure 2).

Conclusions: No correlation was found between disease subtype and retinal abnormalities. Progression of retinopathy was detected in a small number of patients refusing systemic treatment that should be considered. Given the low rate of progression, a low frequency in monitoring sickle cell retinopathy would be adequate. Studies on larger cohort of patients are needed to confirm our clinical impression.

CONTROL ID: 3537629

SUBMITTER (NAME ONLY): Praveer Singh

TITLE: External validation of a deep learning algorithm for plus disease classification on a multinational ROP dataset

SESSION TITLE: Retinopathy of prematurity/vein occlusion

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Deep learning (DL) algorithms have been shown to perform well for classifying plus disease in ROP. However it is common for DL algorithms to have reduced performance on external datasets compared to the datasets that they were trained on. In this study, we demonstrate the efficacy of a DL algorithm, trained on a North American population, on two external multinational datasets.

Methods: Retcam images were obtained from India and Thailand through databases hosted by partner institutions, Aravind Eye Hospital (AEH) & Khon Kaen University (KKU) respectively. After filtering out images with inferior quality, Indian dataset consisted of 8811 images captured from 1275 eye-exams, while the Thai dataset had 1299 images from 385 eye-exams all from at risk infants. Both the Indian and Thai datasets were additionally labelled by 2-3 North American experts and gold standards were obtained through mutual consensus among all raters for each dataset. The performance of the iROP-DL model, trained on Retcam images from American population, was evaluated on both the external Retcam datasets after screening out all the non posterior-pole (PP) images.

Results: The two external datasets included many images which were out of distribution compared to the original training and testing iROP population (multiple views of the retina, anterior segment photos, samples with considerable pigmentation), and thus presented challenges for evaluation of the algorithm. The Table shows low performance before PP-filtering (AUC's 0.88 & 0.78 for India and Thai respectively), which improved considerably after PP-filtering (AUC's 0.89 & 0.84) and later by using consensus labels (AUC's 0.97 & 0.95). As shown via UMAPs in Figure, similar to iROP (yellow), AEH (blue) and KKU (red) also have Normal, pre-plus and plus feature points properly aligned in space (resulting in excellent performance), though they are segregated from iROP owing to demographic differences.

Conclusions: Applying DL algorithms on external datasets is prone to challenges due to demographic or phenotypic differences, or differences in acquisition methodology. After PP-filtering, we demonstrate excellent performance for the i-ROP DL system on the international datasets compared to the original test set. UMAP visualization further substantiates our point and highlights segregation of the external datasets owing to remaining ethnic/phenotypic differences.

CONTROL ID: 3537646

SUBMITTER (NAME ONLY): De-Quan Li

TITLE: Single-Cell Transcriptomics Identifies Limbal Stem Cell Population, Differentiation Trajectory and Signature Markers in Human Corneal Limbus

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Human corneal epithelial stem cells or limbal stem cells (LSCs), have been recognized to locate in corneal limbus for three decades. However, the molecular identity and definitive markers of LSCs are still elusive. This study aimed to uncover novel cell types in heterogenous basal limbus of human cornea for identifying LSC population at single cell resolution.

Methods: Single cells of human limbal basal epithelium were isolated from young donor corneas. Single-cell RNA-Sequencing was performed using 10x Genomics platform, followed by clustering cell types through the graph-based visualization method Uniform Manifold Approximation and Projection (UMAP) and unbiased computational informatic analysis. Tissue RNA in situ hybridization with RNAscope, immunofluorescent staining and multiple functional assays were performed using ex vivo donor corneal tissues and in vitro culture models of primary human limbal epithelial cells (HLECs).

Results: Single-cell transcriptomics of 16,360 limbal basal cells revealed 12 cell clusters belonging to three lineages. A smallest cluster (0.4% of total cells) was identified as LSCs based on their quiescent and undifferentiated states with enriched top expressed genes known as markers of putative epithelial stem cells. TSPAN7 and SOX17 are discovered and validated as new LSC markers based on their exclusive expression pattern and spatial localization in limbal basal epithelium by RNAscope and immunofluorescent staining, as well as their functional role in cell growth and tissue regeneration models with RNA interference in cultures. Interestingly, five cell types/states mapping a developmental trajectory of LSC from quiescence to proliferation and differentiation are uncovered by Monocle3 and CytoTRACE pseudotime analysis. The transcription factor networks linking novel signaling pathways are revealed to maintain LSC stemness.

Conclusions: This human corneal single-cell transcriptomics identifies the LSC population and uncovers novel cell types mapping the differentiation trajectory in heterogenous limbal basal epithelium. The findings provide insight into LSC concept and lay the foundation for understanding the corneal homeostasis and diseases.

CONTROL ID: 3537662

SUBMITTER (NAME ONLY): Marcus Turner

TITLE: Remote Longitudinal Monitoring of Glaucoma Using Virtual Reality-Based Oculokinetic Perimetry

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.L. Turner, Z. Chia, A. Nguyen, A.W. Kong, M. Deiner, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|B.T. Backus, Vivid Vision, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Virtual reality-based oculokinetic perimetry (VR-OKP) is a mobile, short, screening visual field test. The purpose of this study is to examine whether VR-OKP could be implemented in a remote fashion and used to assess the stability of the visual field.

Methods: Glaucoma subjects with known glaucomatous defects who had taken an in-person VR-OKP test in 2019 were re-enrolled and underwent the same test remotely in 2020. An exit survey comparing patients' preferences for visual field testing was also conducted remotely. Subjects underwent Humphrey visual field 24-2 (HVF) testing within 3 months of VR-OKP both in 2019 and 2020. For unadjusted comparisons between HVF and VR-OKP, we compared mean sensitivities and fraction of points. A non-parametric bootstrap analysis that resampled eyes with replacement was done to calculate the 95% confidence interval of the Spearman correlation coefficient between HVF sensitivity versus VR-OKP fraction seen at each point of the 54 test locations.

Results: The cohort consisted of 19 eyes of 11 patients (55% female, 73% Caucasian, 27% Asian, mean age 61.4 ± 12.6 yrs) with moderate to advanced glaucoma (2020 average HVF mean deviation $-4.23 \text{ dB} \pm 5.12$). VR-OKP from 2019 to 2020 had a decreased mean percent change of $-6.31\% \pm 17.22$ ($p=0.13$) compared to HVF testing from 2019 to 2020 which had an increased mean change of mean deviation of $+2.41 \text{ dB} \pm 1.35$ ($p<.00005$). The Pearson's Correlation Coefficient between 2019 VR-OKP fraction seen and 2019 HVF mean sensitivity was 0.74, while it was 0.56 in 2020. Spearman correlation coefficients of HVF sensitivity vs VR-OKP fraction seen at each point ranged from -0.01-0.86 (median = 0.33). Subjects found VR-OKP to be as comfortable as HVF ($p=0.8$) and less fatiguing ($p=0.03$).

Conclusions: This study highlights the feasibility of a remote option for visual field assessment. The correlation between VR-OKP and HVF in 2019 was higher than in 2020. One explanation is that the 2019 test was taken with in-person instruction, whereas the 2020 test was administered remotely. While the mean percentage change in VR-OKP was non-significant, the 2019 to 2020 change in HVF was statistically significant and showed improvement, which may be due to long term fluctuation. This short VR-OKP test is less fatiguing to patients, can detect non-progression even when taken at home, and could potentially be deployed to decrease patients' risk of COVID-19.

CONTROL ID: 3537666

SUBMITTER (NAME ONLY): Shayna Sosnowik

TITLE: Morphological Changes to Schlemm's Canal and the Distal Aqueous Outflow Pathway in Monkey Eyes with Laser-Induced Ocular Hypertension

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Sosnowik, D.L. Swain, H. Gong, Department of Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|D.L. Swain, H. Gong, Department of Anatomy and Neurobiology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|S. Fan, C.B. Toris, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although approximately 30-50% of aqueous outflow resistance lies distal to Schlemm's canal (SC), the morphology of the aqueous outflow pathway distal to SC has not been thoroughly examined. This study investigated the morphology of the outflow pathway from SC to the intra-scleral veins (ISVs) in an experimental model of glaucoma in cynomolgus macaques.

Methods: Argon laser photocoagulation was used to create burns to ~270 degrees of the trabecular meshwork (TM) of one eye (n = 6) or both eyes (n = 2) of each monkey until intraocular pressure was consistently elevated. Discrete regions of the TM were left untouched. Contralateral eyes (n = 5) were used as controls. Monkeys were sacrificed at 60 months or more after the last treatment. Eyes were enucleated and perfused at 15 mmHg for 30 min to measure outflow facility, perfusion-fixed with Karnovsky's fixative for 1 hr, and then immersion-fixed overnight. Anterior segments of each eye were cut into 24 to 36 radial wedges and embedded in Epon-Araldite. Semi-thin sections (2 μ m) of select wedges were cut, stained, and imaged. Width, height, and cross-sectional area (CSA) of SC of non-lasered regions of laser-treated eyes and control eyes, as well as number and CSA of ISVs of non-lasered and lasered regions of laser-treated eyes and control eyes were compared. Statistical analyses were conducted using R.

Results: Mean outflow facility was significantly decreased in laser-treated eyes (0.12 μ L/min/mmHg; n = 8) compared to control eyes (0.34 μ L/min/mmHg; n = 5; P = 0.02). Median CSA, width, and height of SC were not different between non-lasered regions of laser-treated eyes and control eyes (P > 0.05). SC was partially or completely obliterated in lasered regions. Median number of ISVs was significantly decreased in lasered regions (1.4 ISVs) compared to non-lasered regions (3.7 ISVs) of laser-treated eyes (P \leq 0.01) and control eyes (6.0 ISVs; P \leq 0.01). Median CSA of ISVs did not differ between groups (P > 0.05). Lasered regions displayed looser, more disorganized scleral stroma in the region surrounding the TM.

Conclusions: Partial or complete obliteration of SC, decreases in ISV number, and changes in scleral composition may account for a portion of the increased outflow resistance in SC and the distal aqueous outflow pathway in monkey eyes with laser-induced OHT.

CONTROL ID: 3537688

SUBMITTER (NAME ONLY): Lin Zhang

TITLE: Transcriptomic and genomic mapping of embryonic development of the human fovea

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Zhang, R. Cai, Y. Peng, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The center region of the human retina undergoes prolonged development to enable foveal formation. Many of these processes, ranging from synaptogenesis to cellular migration, begin at the embryonic stage. This study examines the genetic regulation of cell-type specific processes during embryonic foveal development.

Methods: We combined single-cell RNA-seq and single-cell ATAC-seq to analyze human retinas at fetal weeks (Fwk) 18-19. Foveal center (~1mm in diameter), macula (~2 mm in diameter), and peripheral retina were dissected and dissociated for single-cell transcriptomic and genomic analyses. Single-cell libraries were prepared with 10x Genomics and sequenced with Illumina NovaSeq. Sequencing results were processed using cell ranger and downstream analysis using community single-cell analysis tools and customized scripts.

Results: We obtained ~64,000 cells from scRNAseq and ~24,000 cells from scATACseq. From the scRNAseq dataset, we identified major cell classes of the retina, including progenitor cells, differentiating cells in transition states, photoreceptors (PR), horizontal cells (HC), bipolar cells (BC), amacrine cells (AC), retina ganglion cells (RGC), Müller glia (MG), microglial and others, in all the three regions. Similar to previous studies, we observed asynchronous development between the central and peripheral retinas: Fovea and macula showed earlier differentiation compared to the peripheral retina as determined by percentages of progenitors and transition cells among regions. Interestingly, we found that cones show gradient enrichment along retinal eccentricity as follows: 98.03% of total PRs in the foveal center, 62.28% in the macula, and 13.09% in the peripheral retina. We further identified cell-type- and region-specific gene expression and functional pathways. We integrated the analysis of gene-expression differences with chromatin accessibility results to map genetic regulatory networks of foveal genes.

Conclusions: Our study provides a transcriptomic and genomic landscape of embryonic foveal development.

CONTROL ID: 3537695

SUBMITTER (NAME ONLY): Andrew Boal

TITLE: Astrocyte Gap Junction Protein Cx43 Modulates the Light Response of Mouse Retinal Ganglion Cells

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Boal, Medical Scientist Training Program, Vanderbilt University, Nashville, Tennessee, UNITED STATES|N.R. McGrady, M.L. Risner, D.J. Calkins, Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|A. Boal, J.M. Holden, Neuroscience Graduate Program, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Astrocytes play key supportive roles in neuronal signaling, including providing metabolic support and buffering the extracellular environment. They form broad networks via gap junctions, primarily composed of the protein connexin-43 (Cx43). These networks allow the passage of important biomolecules between cells, connecting distant brain areas. This is a key component for the functioning of various neural circuits, such as in the hippocampus. However, it is less known how astrocyte networks affect retinal circuitry. Here, we evaluate the consequences of Cx43 knockout on the response properties of retinal ganglion cells (RGCs).

Methods: Conditional astrocytic Cx43 knockout (Cx43 ^{-/-}) was induced in GFAP-CreERT2/Cx43(fl/fl) mice by oral tamoxifen gavage. 1 week post-induction, mice were sacrificed and retinas were dissected in a dark room under red light. Retinas were constantly perfused with Ames' medium supplemented with 20mM glucose. Whole-cell current clamp signals were amplified and digitized at a sampling rate of 50kHz. RGCs were classified by light response, dendritic stratification, and soma size. Cx43 ^{-/-} was confirmed by PCR. Recordings were analyzed using the pyABF package and custom python code, and statistical tests were done in GraphPad Prism.

Results: α ON-S cells from Cx43 ^{-/-} mice showed an increased light response latency compared to WT controls ($p = 0.002$), though the rest of the light response was largely unaffected. α OFF-S cells, however, showed significant differences in light response between groups. α OFF-S cells from Cx43 ^{-/-} mice had a significantly lower spike rate ($p = 0.02$) and an increased response latency ($p = 0.02$). The hyperpolarizing response to light was also altered. Cells from Cx43 ^{-/-} mice had a lower mean amplitude of hyperpolarization ($p = 0.04$), although the peak amplitude was unchanged ($p = 0.24$). Cx43 ^{-/-} also affected RGC membrane properties. Cx43 ^{-/-} mice α ON-S cells showed a steeper slope in the firing frequency vs. current relationship ($p = 0.01$) and had a higher overall spontaneous membrane potential variability ($p = 0.01$).

Conclusions: These results suggest that Cx43 ^{-/-} differentially alters the light response and membrane properties of RGCs. Thus, the astrocytic networks formed by Cx43 contribute significantly to RGC encoding of light.

CONTROL ID: 3537720

SUBMITTER (NAME ONLY): Rosica Petrova

TITLE: Alterations to the hydrostatic pressure gradient modulate the subcellular distribution of water channel AQP5 in the rat lens

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To determine whether changes to the lens intracellular hydrostatic pressure gradient that drives water efflux from the lens also alters the subcellular location of AQP5 water channels in the rat lens.

Methods: Enucleated rat eyes were dissected to produce four scleral flaps that exposed the lens but left it attached to the ciliary muscle via the lens zonules. The flaps were pinned to the bottom of a recording chamber and the preparation incubated in AAH in either the absence or presence pilocarpine or tropicamide, to decrease and increase zonular tension, respectively, or different combinations of TRPV1/4 activators and/or inhibitors. The effects of perturbations on hydrostatic pressure and AQP5 membrane localization were monitored by a pico-injector-microelectrode system¹ or immunohistochemistry and confocal microscopy², respectively.

1. Chen et al., IOVS 60:4416-4424, 2019.

2. Petrova et al., IOVS 61:36, 2020.

Results: Tropicamide decreased surface hydrostatic pressure but did not alter the predominately membrane localization of AQP5. In contrast, reducing zonular tension by pilocarpine resulted in a change in AQP5 immunolabeling from membranous to cytoplasmic, which was correlated with a significant and sustained increase in surface hydrostatic pressure. The increase in pressure and the removal of AQP5 from the membrane induced by pilocarpine could also be mimicked by first incubating lenses in the TRPV4 inhibitor HC067047, before then applying the TRPV1 activator capsaicin.

Conclusions: Our pressure measurement results showed that the hydrostatic pressure of the rat lens can be manipulated pharmacologically by changing of the zonular tension or by changing the activity of the TRPV4 and TRPV1 mechanosensors. Our immunolocalization results suggest fiber cells can respond to hydrostatic pressure by shuttling AQP5 out from the cell membrane to dynamically regulate the efflux and influx of water in the rat lens.

CONTROL ID: 3537725

SUBMITTER (NAME ONLY): Kamila Osypiuk

TITLE: Predictors of vocational rehabilitation success among legally blind individuals in Massachusetts

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Osypiuk, A.G. Malkin, C. Idman-Rait, N. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|T. Arango, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|N. Skrocki, Massachusetts Commission for the Blind, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vocational rehabilitation (VR) services aim to help legally blind individuals secure, regain or retain employment following vision loss, as rates of employment among legally blind VR consumers are reportedly low. We evaluated factors contributing to successful VR among individuals receiving services from the Massachusetts Commission for the Blind (MCB) to inform future improvements in services and outreach.

Methods: Using existing data from MCB's central registry of legally blind consumers, logistic regression was used to examine potential predictors of rehabilitation success. Age, gender, race, and diagnosis were explored as possible predictors. Case events between Jan 1, 2018 to Sept 4, 2020 were included in analyses (n=938). Rehabilitation success was a binary outcome defined as maintaining employment for 90 days.

Results: Mean age of consumers was 42 years (SD 17.5); 51% were men, 65% were white. Most common diagnoses included retinal degeneration (13%), glaucoma (8.7%), and diabetic retinopathy (DR) (6.92%). Half of case events had a successful outcome (n=468). Common reasons for unsuccessful outcomes were lack of interest (35%) and being unable to locate the consumer (27%). Those younger than 39 years were 36% less likely to have VR success than those aged 40-44 (OR=0.64; 95% CI= 0.38-1.07; p=0.09). Gender was not a significant predictor of VR success (p=0.30). Those with DR were 45% less likely (OR=0.55; 95% CI= 0.31-0.96; p=0.04) and those with glaucoma were 44% less likely (OR=0.56; 95% CI= 0.33-0.94; p=0.03) to have VR success than those with congenital diagnoses. Asian, black, biracial, and biracial white-latinx consumers were all less likely to be rehabilitated than whites (p's <0.05). There was a significant interaction between race and age among those ≤ 39 years, with those who are biracial being 78% less likely (OR=0.22; 95% CI= 0.06-0.6; p=0.007) and those who are latinx-white being 64% less likely (OR=0.36; 95% CI= 0.18-0.70; p=0.003) to have VR success than whites.

Conclusions: The significant association between age, race, and diagnosis with VR success suggests that these factors should be considered in VR programs. Glaucoma and DR are more prevalent among black and latinx populations, who had lower rates of VR success and are under-represented in VR programs. More targeted outreach and tailored rehabilitation programs may be warranted for these populations.

CONTROL ID: 3537740

SUBMITTER (NAME ONLY): Takako Noguchi

TITLE: Effects of anti-inflammatory eye drops in cultured human corneal epithelial cells

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Noguchi, R. Sella, J. Zhao, R. Lian, A.A. Abbas, E.N. Finburgh, D.F. Hakim, N.A. Afshari, Department of Ophthalmology at the Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|R. Sella, Y. Cohen-Tayar, Department of Ophthalmology, Rabin Medical Center, Petah Tikva, ISRAEL|Y. Cohen-Tayar, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|

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ABSTRACT BODY:

Purpose: To compare the effect of three commonly used anti-inflammatory eye drops containing cyclosporin (0.05%), lifitegrast (5%), and tacrolimus (0.1%) in cell survival.

Methods: Healthy donor corneal transplant tissues were obtained from San Diego Eye Bank. Corneal epithelial cells were scraped from the surface of the corneal rim after 1 h treatment in dispase II. Cells derived from donor tissue were first plated in a well of 12 well plate, passaged to a well of 6 well plate, and finally passaged to a 96 well plate for drug application. Wells were separated into the following five treatment groups: cyclosporine 0.05%; lifitegrast 5%; tacrolimus 0.1% and two controls, a balanced salt solution (BSS) group and a no treatment group. The cells were exposed to medium containing 10% of eye drops (cyclosporine final 0.005%, lifitegrast final 0.5%, and tacrolimus final 0.01%) and eye drop containing medium were washed out after 2 m, 1 h, 2 h, 4 h, and 24 h (N = 6-10 wells for each condition).

Results: The effect of cyclosporine became statistically significant at 24 h compared to control groups [survival rate: 26 +/- 27% (mean +/- SD, N = 6)]. The effect of lifitegrast became statistically significant at 24 h compared to control groups [survival rate: 14 +/- 14% (mean +/- SD, N = 6)]. The effect of tacrolimus became statistically significant at 1, 2, 4 and 24 h [survival rates: 7 +/- 11% at 1 h, 32 +/- 37% at 2 h, 14 +/- 19% at 4 h, and 0 +/- 0% at 24 h (mean +/- SD, N = 10-14)]. BSS application had no effect on cell survival compared to no treatment group. In other words, application of medium containing cyclosporine and lifitegrast had no significant effects up to 4 h, although tacrolimus affected in 1 h.

Conclusions: Epithelial cell culture cytotoxicity was more moderate in cyclosporin and lifitegrast, and more harsh in tacrolimus containing eye drops. These findings may serve as a useful resource to select anti-inflammatory eyedrops in a clinical setting and provide further insights into the study of inflammatory signaling and cell death pathways.

CONTROL ID: 3537744

SUBMITTER (NAME ONLY): Saeideh Ghahghaei

TITLE: The spectrum of reading difficulties in children with Cerebral Visual Impairment (CVI): a qualitative study

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ghahghaei, S. Harris, D. Singh, A. Chandna, The Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reading difficulties are increasingly reported in children with CVI even in the presence of good visual acuity. CVI is now the commonest cause of childhood visual impairment in the western hemisphere and consequent lack of proficiency in reading is likely to have negative consequences for development, academic success and the well-being of the child and society. Oculomotor dysfunction, crowding and delayed comprehension have been suspected but not systematically investigated. We set out to address this gap by documenting the spectrum of reading difficulties.

Methods: We conducted remote, in-depth 40 to 60 minute, semi-structured interviews of parents of children with CVI (and recorded, if permitted). An open statement 'Please tell me about your child's journey in reading' commenced the interview. If needed, interview guides were provided to ensure consistency between participants. Notes were taken, problems were documented Specific questions were reserved for end of interview if not covered by parent's description.

Results: Data from 7 parents (target N = 10) were analyzed by first transcribing then coding interviews . A spectrum of reading difficulties were identified which indicated a range from lower to higher level visual processing. The frequency of reporting each difficulty across participants was calculated. For example, of the 7 parents, 4 reported the need for large fonts (frequently reported in literature) and 2 reported that 'sometimes nothing works' (rarely reported in literature). These documented difficulties indicated the following neurophysiological correlates; in isolation or in combination: (1) acuity and accommodation (2) crowding (3) oculomotor problem (4) restricted visual field (5) spatial attention (6) or central attention.

Conclusions: In-depth interviews with parents reveal multiple reading difficulties in children with CVI presenting in different ways frequently and rarely reported by clinicians. The six areas identified from our study provide a framework for further focused interviews and quantitative research designed specifically to investigate these areas with a potential for targeted (re)habilitation techniques to be assist the child to overcome these difficulties.

CONTROL ID: 3537755

SUBMITTER (NAME ONLY): John O'Fee

TITLE: Factors Associated with Diabetic Macular Edema Development in Patients with Proliferative Diabetic Retinopathy

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. O'Fee, J. Juliano, A.A. Moshfeghi, Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vascular endothelial growth factor is a major mediator of both diabetic macular edema (DME) and proliferative diabetic retinopathy (PDR). In our clinical practice, we have observed a significant number of patients with PDR without any DME. The purpose of our study was to identify demographic, medical, ophthalmologic and OCT image characteristics that significantly affect development of DME and types of DME in patients with PDR.

Methods: Observational, retrospective case series of PDR patients seen in the retina clinics at a single large acute-care teaching hospital in an urban setting between December 2018 to October 2020. IRB approval was obtained. Vitreomacular interface (VMI) status was classified as: vitreomacular adhesion without traction (VMA), vitreomacular traction (VMT), or macular posterior vitreous detachment (PVD). Eyes were excluded if they had received retinal laser or intravitreal injection of a pharmacotherapeutic agent <1 year from OCT date, had any prior intraocular surgery or comorbid ophthalmic disorders associated with DME.

Results: A total of 293 eyes of 210 screened patients with PDR met our inclusion criteria. Of the eyes, 66.2% had DME and 33.8% had no DME. In PDR patients, when comparing those with DME to those without DME, there were significant differences ($p<0.05$) in average visual acuity, retinal thickness, cube volume and dialysis status. There were no significant differences in ERM ($p=.196$) and VMI status ($p=0.340$). In eyes with center-involving (CI)-DME, VMI status was observed as follows: 44.4% with VMA, 7.8% with VMT, and 47.8% with PVD. In eyes with non-center-involving (NCI)-DME, VMI status was observed as follows: 67.3% with VMA, 1% with VMT, and 31.7% with PVD. CI-DME eyes were significantly more likely to have a PVD than NCI-DME eyes ($p=0.001$). There were 90 CI-DME eyes, 82.2% of which had ERMs, and of those with ERM, 66.2% had CI-ERM. There were 104 NCI-DME eyes, 45.2% of which had ERMs, and of those with ERM 44.9% had CI-ERM. CI-DME eyes were significantly more likely to have an ERM ($p=<0.001$) and CI-ERM ($p=0.019$) than NCI-DME eyes.

Conclusions: In this exploratory study evaluating only patients with PDR, we determined that ERM and VMI status did not have a significant association with DME writ large. However, VMI status and the presence of ERM may influence the development of CI-DME more specifically.

CONTROL ID: 3537757

SUBMITTER (NAME ONLY): Vladimir Bantseev

TITLE: Determination of a No Observed Effect Level (NOEL) for Beta Glucans following a Single Intravitreal Administration to Female Dutch Belted Rabbits

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Bantseev, S. Parker, R. Andaya, C. Schuetz, M. Schutten, Genentech Inc, South San Francisco, California, UNITED STATES|B. Christian, Toxicology, Covance Inc, Princeton, New Jersey, UNITED STATES|B. Christian, P.E. Miller, Ocular Services on Demand, Madison, Wisconsin, UNITED STATES|H. Booler, Pathology, Roche Innovation Centre Basel, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Beta glucans are common contaminants in the manufacturing of biopharmaceuticals. The effects of beta glucans on the eye are not well characterized, but the level of beta glucans in intravitreal ophthalmic formulation of biologics are an important consideration in both manufacturing and safety testing. This 8-day study aimed to characterize the in-life and histopathological changes following intravitreal (ITV) administration of beta glucans and determine a no observed effect level in rabbit eyes.

Methods: Female Dutch Belted rabbits were treated with a single ITV beta glucans dose (derived and concentrated from sugars in a vehicle formulation) at nominal concentrations ranging from 10 to 1000 pg/eye. Concentrations of beta glucans dosages were measured pre and post-dosing using a Factor G based assay, and measured actual post dose values were reported as the administered dosage for each portion of the study. A non-terminal, unilateral dose range finding (DRF) portion of this study established 10 to 1000 pg/eye to be well tolerated and provided a range to be confirmed in a larger bilateral definitive study with six treated groups (N=4 animals per group) including a vehicle control. Overall animals were monitored for up to 1-week post-treatment via clinical ophthalmic examination using the modified standardization of uveitis nomenclature (SUN) Working Group Grading Scheme to score aqueous/vitreous cell and flare/haze. At the end of the definitive study animals were necropsied and eyes processed for histopathologic evaluation.

Results: No beta glucan-related findings were identified in treated animals compared to vehicle control. Single dose ITV injection of beta glucan was well tolerated in-life in the DRF portion of the study up to the maximum dose tested of 1,000 pg/eye. Doses up to 800 pg/eye (maximum dose in the definitive part) was well tolerated both in-life and on histopathologic examination. Nominal administered values were up to 1,000 pg/eye for both study portions, however samples used in the definitive study were measured post dose to be 800 pg/eye.

Conclusions: Single dose ITV beta glucans, isolated and concentrated from sugars, in a vehicle formulation did not elicit an inflammatory response or resulted in histopathologic changes. Thus, the no observed effect level (NOEL) over 8-days in rabbits was 800 pg/eye.

CONTROL ID: 3537758

SUBMITTER (NAME ONLY): Vasily SMIRNOV

TITLE: Retinal degeneration in abetalipoproteinemia

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.M. SMIRNOV, I. Audo, Genetics, Institut de la vision, Paris, Île-de-France, FRANCE| V.M. SMIRNOV, Faculté de Médecine, Université de Lille, Lille, Hauts-de-France, FRANCE|F. Mochel, Department of Genetics and Reference Center for Adult Neurometabolic diseases, Institut du Cerveau et de la Moelle Épine, Paris, FRANCE|S. Mohand-Said, J.A. Sahel, Institut de la vision, Paris, Île-de-France, FRANCE|S. Mohand-Said, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|C. Andrieu, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|C. Condroyer, C. Zeitz, Genetics, Institut de la vision, Paris, Île-de-France, FRANCE|J.A. Sahel, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic defects in MTTP are responsible for abetalipoproteinemia, combining spinocerebellar and retinal degeneration. Retinal findings in abetalipoproteinemia are only infrequently reported. We provide a detailed phenotypic description of the retinal degeneration linked with MTTP variants in a cohort of retinitis pigmentosa (RP) patients.

Methods: Patients previously diagnosed with abetalipoproteinemia and patients with gene defects in MTTP identified through next generation sequencing were investigated at the national reference center for rare ocular diseases of Quinze-Vingts hospital. Best corrected visual acuity (BCVA), slit-lamp examination, Goldman perimetry, full field electroretinography (ffERG) and multimodal imaging including color photos, short (SWAF) and near infrared wavelength autofluorescence, optical coherence tomography (OCT) were done for all patients.

Results: Four female patients from four unrelated families were selected. Median BCVA at baseline was 20/40 (range: 20/25 – 20/250). ffERG showed cone-dominated responses. Isopter V4e of Goldman visual field was constricted in all patients. Three patients had fundus findings typical of RP. Two had atrophic patches at the posterior pole. One had angioid streaks and “peau d'orange” aspect. SWAF showed various features. One patient had a ring of increased autofluorescence; another had a water-shed hyperautofluorescent line beneath the macula. One individual had numerous hyperautofluorescent dots scattered over the posterior pole. One patient had confluent hypoautofluorescent patches with scalloped edges. OCT showed a destruction of outer retinal layers outside the macula in all patients. In one individual OCT discovered a type 2 subretinal neovascularization. Two patients had prominent ataxia and peripheral sensitive-motor neuropathy. One patient developed a parietal hemorrhage related with low vitamin K plasmatic level. One patient developed an acute myeloid leukemia. Two patients are free of neurological symptoms to date. All patients descended from inbreed pedigrees. Three individuals harbored known homozygous variants in MTTP. Genetic data were lacking for one patient.

Conclusions: Abetalipoproteinemia represents 0.2% of our RP cohort. Retinal degeneration in abetalipoproteinemia can take various and atypical aspects. It could be the first clinical sign of the disease. On the basis of these findings, we strongly recommend adding MTTP to inherited retinal degeneration gene panels.

CONTROL ID: 3537762

SUBMITTER (NAME ONLY): Zeljka Smit-McBride

TITLE: Altered microRNA expression patterns in the murine retina with diabetic retinopathy following Intravitreal injection of human CD34⁺ stem cells

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Smit-McBride, A. Yazdanyar, S.S. Park, Ophthalmology, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|W. Cary, J. Nolta, Institute for Regenerative Cures, Stem Cell Program, University of California Davis, Sacramento, California, UNITED STATES|A. Yazdanyar, Ophthalmology, SUNY The State University of New York, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In a murine model of diabetic retinopathy (DR), intravitreal injection of human CD34⁺ stem cells from bone marrow(BMSCs) was associated with the preservation of retinal vasculature. Since miRNAs(miRNA) have been implicated to play a role in the pathogenesis of DR, this study tested the hypothesis that intravitreal injection of human CD34⁺ BMSCs alters miRNA expression patterns in the recipient retina in eyes with DR.

Methods: Streptozotocin-induced diabetic mice(C57BL/6J) were used as a model for diabetic retinopathy with chronic systemic immunosuppression using Tacrolimus and Rapamycin to avoid rejection of human cells. Human CD34⁺ BMSCs were harvested from the mononuclear cell fraction of bone marrow from a healthy donor using magnetic beads. The right eye of each mouse received an intravitreal injection of 50,000 healthy CD34⁺ BMSCs or phosphate buffered saline(PBS). After one week time point, the mice were euthanized, and the eyes were removed for microarray analysis of the retina. Ingenuity Pathway Analysis (IPA) was used to identify activated pathways.

Results: Microarray expression analysis showed changes in the expression of 11 miRNAs in the murine retina following CD34⁺ BMSC injection compared to PBS-injected control. Two of these miRNAs are known to be involved in DR pathogenesis: let7c-1 (FC= -1.53, p<0.01) and mir-455 (FC=1.5, p< 0.01). Downregulation of let-7c has been seen in diabetic microvascular complications, while upregulation of miR-455-5p attenuates high glucose-triggered oxidative stress injury. IPA identified that the top canonical activated pathway was "HOTAIR Regulatory Pathways," which can be modulated by let-7c-1. Potential targeting of long non-coding(lnc) RNA HOTAIR by microRNAs is a novel finding for DR – this lncRNA has been implicated in promoting apoptosis, inhibiting cell metastasis, and angiogenesis in cancer, but not yet in diabetic retinopathy.

Conclusions: Gene expression analysis showed that intravitreal injection of CD34⁺ BMSCs harvested from a healthy donor has a robust effect on miRNA expression in the murine retina with DR. Expression of specific miRNAs implicated in the pathogenesis of DR was affected, including let-7 and miR-455. Both miRNAs play important roles in regulating the lncRNA HOTAIR pathway that affects endothelial cell dysfunction and indirectly affects VEGFA transcription.

CONTROL ID: 3537764

SUBMITTER (NAME ONLY): Dibyendu Chakraborty

TITLE: A K42E knockin mouse model of RP59 exhibits a negative ERG and defective postsynaptic signal transmission

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Chakraborty, M.N. Nguyen, P.I. Cobb, S.J. Pittler, Optometry and Vision Science, Vision Science Research Center, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|I. Ignatova, U. Bocchero, J. Pahlberg, Photoreceptor Physiology Group, National Eye Institute, NIH, Bethesda, Maryland, UNITED STATES|S. Ramachandra Rao, S.J. Fliesler, Research Service, VA Western New York Healthcare System, Buffalo, New York, UNITED STATES|S. Ramachandra Rao, S.J. Fliesler, Ophthalmology and Biochemistry, The State University of New York, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously generated a murine Dhdds K42E knockin (KI) mouse model of RP59 that exhibited incipient neuroinflammation and gliosis, but no overt retinal degeneration or cell loss, even by 1 year of age. Here, we further evaluated the phenotype of this animal model.

Methods: K42E homozygous (Dhdds^{K42E/K42E}) KI mice were bred to 4th generation, and compared to age/sex-matched wildtype (WT) mice. Phenotypes were assessed by electroretinography (ERG, n=8-10), whole cell patch-clamp recordings, and fundus imaging (n=3-4) at postnatal 180 days. Immunohistochemistry (IHC) was performed on retinal frozen sections using antibodies to PKC α , synaptotagmin-1, and ribeye.

Results: Scotopic and photopic ERG a-wave responses were comparable in WT and KI mice. These results were confirmed by single cell recordings. By contrast, KI mice exhibited significant reductions in scotopic b-wave (358 ± 34 μ V KI vs. 642 ± 67 μ V WT; p <0.01) and photopic b-wave (178 ± 26 μ V KI vs. 273 ± 32 μ V WT; p <0.05) amplitudes. KI retinas exhibited no overt signs of degeneration or disorganization. IHC did not reveal obvious abnormalities in localization or levels of the markers analyzed, and synaptic ribbons were properly localized and exhibited normal appearance.

Conclusions: This genetic mouse model of RP59 exhibits a negative ERG (reduction in b-wave without a concomitant reduction in a-wave), indicating defective photoreceptor-to-bipolar cell synaptic transmission. The findings suggest that the defect is postsynaptic, involving ON bipolar cells.

CONTROL ID: 3537777

SUBMITTER (NAME ONLY): Samara Hamou

TITLE: A Retrospective Study on the Use of Brolucizumab for the Treatment of NVAMD: A 1-Year Private Practice Experience

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.J. Hamou, C.D. Raimondo, P. Weber, B.C. Woods, Retina, Island Retina, Shirley, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: A retrospective study to investigate our experience with intravitreal injections (IVI) of brolucizumab 6 mg/0.05 ml for the treatment of neovascular age-related macular degeneration (NVAMD) over 1 year.

Methods: A chart review from 11/13/19-11/12/20 was performed on eyes treated with brolucizumab for NVAMD. Our analysis included demographics, ETDRS visual acuity, injection history, adverse events, and medical history. The eyes with intraocular inflammation (IOI) were compared to those without (control). Characteristics of the IOI group were also studied.

Results: Ninety-nine eyes of 88 patients were analyzed. There were 10 treatment-naïve eyes and 89 non-naïve. The average maintenance extension of non-naïve eyes was 3 weeks. However, for eyes with a positive extension on maintenance (58 eyes or 68.2%), the average extension was 9 weeks. Within this group, there were 24 super-responder eyes (defined as injection burden reduction of at least 50%). Of the 99 eyes injected with brolucizumab, 8 eyes experienced IOI. All 8 eyes were diagnosed with vitritis, which persisted for an average of 69 days and was easily managed with topical treatment. Two of the IOI eyes experienced retinal vasculitis: one losing 3 letters and one losing 10 letters of vision. Of the 6 eyes that solely experienced vitritis, the average vision change from IOI to the most recent visit was -2 letters. However, 1 eye lost 10 letters of vision. The average number of days from the first brolucizumab injection to the presentation of IOI was 81 days. Female eyes tended to have a higher incidence of IOI, however, this was not statistically significant. Reactions occurred after 1-2 injections in 7 of the 8 eyes with IOI. Atrial fibrillation (afib) in IOI and control groups was seen respectively: 3 out of 8 (37.5%) and 9 out of 91 (9.9%) eyes ($P<.05$). 30% of naïve eyes had IOI as compared to 5.6% of non-naïve eyes ($P<.01$).

Conclusions: Vitritis was the most common IOI seen with brolucizumab, and had adequate visual recovery with treatment. There was a suggestion that risk factors for IOI include naïve use and afib. Increased maintenance intervals were seen on brolucizumab. There was also a group of super-responders that decreased their injection burden by at least 50%. Our data suggest this drug should not be used as primary treatment but could be considered for patients requiring frequent injections.

CONTROL ID: 3537782

SUBMITTER (NAME ONLY): Abdulrahman Rageh

TITLE: Comparison of 1-Field and 2-Field Mydriatic Handheld Retinal Imaging with Early Treatment Diabetic Retinopathy Study (ETDRS) 7-Standard Field Photography for Diabetic Retinopathy (DR) and diabetic macular edema (DME)

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rageh, C. Jacoba, M.A. Elmasry, J.K. Sun, L.P. Aiello, P.S. Silva, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|R.P. Salongcay, L. Aquino, C. Salva, A.V. Saunar, G.P. Alog, P.S. Silva, Philippine Eye Research Institute, University of the Philippines Manila, Manila, Metro Manila, PHILIPPINES|R.P. Salongcay, T. Peto, Centre for Public Health, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|M.A. Elmasry, J.K. Sun, L.P. Aiello, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine agreement of 1-field (1F, macula centered) and 2-field (2F, disc/macula) mydriatic handheld retinal imaging with standard ETDRS photography for DR/DME.

Methods: Images from 177 eyes of 92 patients with diabetes were evaluated. By ETDRS photos: no DR 40.1% eyes, mild NPDR 19.2%, moderate 14.7%, severe 10.2%, proliferative DR 15.8%; no DME 72.9%, DME 6.8%, CSME 17.0%, ungradable 3.4%. Ungradable rate for DR and a summary of results are shown in Table 1. DME was ungradable in AU:10.2%, SS:13.0%, RV:5.7%. 2F imaging increased exact agreement of DR grading between handheld retinal imaging and ETDRS photos by 8.3% AU, 15.2% SS, 6.3% RV; agreement within 1-step was increased by 6.1% AU, 10.1% SS, 1.3% RV. 2F imaging with AU/SS increased K and K_w although it remained moderate. 2F imaging did not substantially increase sensitivity for any DR, refDR and vtDR across all devices.

Results: Images from 177 eyes of 92 patients with diabetes were evaluated. By ETDRS photos: no DR 40.1% eyes, mild NPDR 19.2%, moderate 14.7%, severe 10.2%, proliferative DR 15.8%; no DME 72.9%, DME 6.8%, CSME 17.0%, ungradable 3.4%. Ungradable rate for DR and a summary of the results is shown in table 1. DME was ungradable in AU:10.2%, SS:13.0%, RV:5.7%. 2F imaging increased exact agreement of DR grading between handheld retinal imaging and ETDRS photos by 8.3% AU, 15.2% SS, 6.3% RV; agreement within 1-step was increased by 6.1% AU, 10.1% SS, 1.3% RV. 2F imaging increased kappa agreement with ETDRS photos for DR by 11.3% AU and 15.6% SS. 2F imaging did not significantly increase sensitivity for any DR, refDR and vtDR across all devices.

Conclusions: Handheld 1F imaging with a field of view less than 60° do not meet established standards for sensitivity (80%) and specificity (90%) in identifying DR and refDR. Ungradable rate was reduced by 36-50% and agreement with ETDRS was increased (6.3-15.2%) with the acquisition of a second field. The benefit of a second field decreased as the field of view of the device increased. For the tested instruments, a minimum handheld 1F 60° or 2F imaging are needed to adequately determine referable DR in DR screening programs.

CONTROL ID: 3537787

SUBMITTER (NAME ONLY): Donald Hood

TITLE: The 24-2 Guided Progression Analysis can miss clear progression of glaucomatous damage identified on a single OCT follow-up test.

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.C. Hood, Psychology and Ophthalmology, Columbia University, New York, New York, UNITED STATES|E. Tsamis, S. La Bruna, J. Grossman, Psychology, Columbia University, New York, New York, UNITED STATES|J.M. Liebmann, C. De Moraes, Ophthalmology, Columbia University, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Donald Hood: Commercial Relationship(s);Topcon, Inc:Code F (Financial Support);Topcon, Inc:Code C (Consultant);Heidelberg Eng, Inc:Code F (Financial Support);Heidelberg Eng, Inc:Code C (Consultant);Novartis:Code F (Financial Support);Novartis:Code C (Consultant) | Emmanouil Tsamis: Commercial Relationship: Code N (No Commercial Relationship) | Sol La Bruna: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Grossman: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Liebmann: Commercial Relationship: Code N (No Commercial Relationship) | C Gustavo De Moraes: Commercial Relationship(s);Heidelberg Engineering:Code R (Recipient);Carl Zeiss Meditec:Code C (Consultant);Novartis:Code C (Consultant);Topcon:Code F (Financial Support);Galimedix:Code C (Consultant);Perfuse Therapeutics:Code C (Consultant)

ABSTRACT BODY:

Purpose: To assess the efficacy of the 24-2 Guided Progression Analysis (GPA) for detecting progression of glaucoma, GPA performance was compared to progression assessed with a single follow-up optical coherence tomography (OCT) test.

Methods: From a prospective study (MAPS) [PI: CGDM], 99 eyes from 99 individuals, including 69 suspect or glaucomatous eyes and 30 healthy controls (HC) had best-corrected visual acuity better than 20/40; an open angle; and a 24-2 mean deviation (MD) better than -6 dB at baseline. All eyes had a recent test at least 12 months after the first of two baseline tests, which were within an average of 5.6 days. In addition, each eye had at least 4 24-2 VF and OCT tests (mean 9.2 tests), with VF and OCT tests obtained on, or close to, the same date. The OCT test consisted of a circle scan of the disc and a cube scan that included the macula. The commercial 24-2 GPA software characterized eyes as “Likely Progressing” (LP), “Probably Progressing” (PP) or “neither” LP or PP. For a post-hoc analysis (E-OCT method), authors familiar with OCT rated the likelihood of progression on a scale from 0-5% (definitely not progressing, OCT-NP) to 95-100% (definitely progressing), OCT-P based upon circumpapillary b-scans, retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) thickness maps, and change/difference plots (see Fig). **Results:** The 24-2 GPA identified 13 eyes as either LP or PP. The E-OCT also classified 13 eyes as P, but 6 (46%) of these 13 OCT-P eyes were “missed” by the 24-2 GPA (red in Table). All 6 GPA misses showed clear progression of glaucoma as indicated by the plots/maps in Fig. Further, 6 of the eyes identified by the GPA as PP or LP (green in Table) were rated as OCT-NP or OCT-neither. These 6 eyes were likely false positives (FP) as: 2 were HC; the post-hoc analysis could not confirm progression in any of these 6; and reasons for a FP were identified on most (e.g., variable VFs, rim artifacts, and/or high local sensitivity at baseline).

Conclusions: The 24-2 GPA missed almost half of the eyes identified as progressing on a single OCT follow-up scan. In addition, FPs occurred. Given the GPA takes a minimum of 4 tests to identify “possible progression”, the results suggest that the testing burden on patients can be reduced with OCT.¹ 1. Hood, Melchior, Tsamis et al., JoG, 2020.

CONTROL ID: 3537791

SUBMITTER (NAME ONLY): Arlene Drack

TITLE: Subretinal gene replacement rescues retinal phenotype in BBS10 mouse

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.V. Drack, A. Mahoney, S. Bhattarai, S. Mayer, J. Thomas, P. Datta, Y. Hsu, J. Garrison, C. Searby, S. Seo, V. Sheffield, Ophthalmology and Visual Sciences, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|E. Heon, The Hospital for Sick Children, Toronto, Ontario, CANADA|A.V. Drack, A. Mahoney, S. Bhattarai, S. Mayer, J. Thomas, P. Datta, Y. Hsu, J. Garrison, C. Searby, S. Seo, V. Sheffield, University of Iowa Institute for Vision Research, Iowa, UNITED STATES|L.H. Vandenberghe, Grousbeck Gene Therapy Institute, Ocular Genomics Institute, Dept. of Ophthalmology, Massachusetts, UNITED STATES|L.H. Vandenberghe, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess toxicity and efficacy of subretinal gene replacement in BBS10 mice. Overexpression toxicity in BBS1 mice occurred with gene therapy;BBS1 is part of the BBSome, while BBS10 is part of the BBS/CCT chaperonin complex.

Methods: A knock out mouse model of Bardet Biedl Syndrome type 10 (BBS10) was developed. AAV2/5-Bbs10FLAG and AAV2/Anc80-Bbs10FLAG vectors were created. Subretinal 2 ul injections of 1E12, 2E12 or 4E12VG/ml were performed in 62 Bbs10^{-/-} and 12 WT mice. Immunoblotting and immunohistochemistry were utilized to assess protein production and restoration of Bbs10 gene function. ERG, OCT, and visually guided swim assay (VGSA) were used to assess efficacy. Due to COVID-19, long term data was collected only for 12 mice treated with 2E9 or 4E9 AAV2/Anc80-Bbs10FLAG and 3 controls.

Results: Neither AAV2/5-Bbs10FLAG nor AAV2/Anc80-Bbs10FLAG were toxic in WT or Bbs10^{-/-}. One month after injection, FLAG was detected in treated, but not untreated Bbs10^{-/-} eyes, documenting presence of BBS10 protein. BBS7, undetectable or barely detectable within photoreceptor cilia in untreated Bbs10^{-/-} eyes, was present in photoreceptor cilia in treated Bbs10^{-/-} eyes. VGSA was partially rescued via either AAV2/5 or AAV2/Anc80 treated at P30-P60 when tested in the dark at age 3.5 months (p= 1.36E-005) and in both light and dark at age 7 months (p= <0.0001 light; p= 0.0094 dark). VGSA improvement endured in AAV2/Anc80 treated mice at 9-12 months old (p=0.0113). Treated eyes had higher amplitude ERG than untreated fellow eyes at 10-11.5 months old (highest p=0.0425). OCT at 11-14 months demonstrated presence of outer nuclear layer in 5/11 treated eyes compared to 0/11 untreated fellow eyes and 0/6 untreated control eyes. 5Hz flicker response was not present at any age in untreated Bbs10^{-/-} (n=18 eyes), but developed in 9 of 12 eyes treated before 4 months old. 4 of 12 treated eyes still had recordable 5 Hz at 11-14 mos, all treated with 4E9. Histology at 11 months demonstrated robust ONL, inner and outer segments with numerous cones, and normal localization of STX3 adjacent to the injection site in 2 treated eyes.

Conclusions: In the Bbs10^{-/-} mouse subretinal gene therapy with AAV2/Anc80-Bbs10FLAG rescues retinal phenotype. Lack of 5 Hz flicker ERG response in untreated eyes was rescued with early high titer gene therapy suggesting that

BBS10 plays an early role in cone development and/or function. Human BBS10 clinical trials are needed.

CONTROL ID: 3537794

SUBMITTER (NAME ONLY): Anastasiya Vinokurtseva

TITLE: Treatment of ocular inflammation: effects of COX-2 acetylating immuno-resolvents (CAIRs) in THP-1-derived macrophages and a rat model of endotoxin-induced uveitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vinokurtseva, J.J. Armstrong, H. Liu, C.M. Hutnik, Ophthalmology, Western University Schulich School of Medicine & Dentistry, London, Ontario, CANADA|J.J. Armstrong, P. Kiser, C.M. Hutnik, Pathology, Western University Schulich School of Medicine & Dentistry, London, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Current treatments for uveitis lack adequate efficacy and impede the body's endogenous inflammation-resolution. Targeted acetylation of cyclooxygenase-2 (COX-2) enzyme redirects its activity from pro-inflammatory to pro-resolving, amplifying resolution of the acute phase of inflammation, and mitigating sequelae of chronic inflammation such as scarring and connective tissue changes. COX-2 acetylating immuno-resolvents (CAIRs) are agents capable of specifically acetylating COX-2 and include locally delivered acetylsalicylic acid (ASA) as well as a more potent derivative compound, o-(acetoxypheyl)hept-2-ynyl sulfide (APHS). We hypothesized that intravitreal injection of CAIRs would reduce histological markers of inflammation in an animal model of uveitis and reduce expression of pro-inflammatory genes in THP-1 macrophages.

Methods: Lipopolysaccharide (LPS) or vehicle was administered subcutaneously to Lewis rats 6 hours prior to intravitreal (IVT) experimental injections. Control animals received vehicle IVT OU while LPS-induced rats received either IVT ASA or APHS OD, with vehicle OS. 25 hours following LPS-induction, both eyes underwent histopathological assessment of the anterior and posterior segments. Effects of experimental treatments on cytokine production were assessed in vitro with phorbol 12-myristate 13-acetate (PMA)-induced THP-1 macrophages. Cells were co-treated for 6 hours with LPS and either ASA or APHS. Total RNA was extracted and expression of pro-inflammatory markers IL-1 β , TNF α and COX-2 was assessed via RT-qPCR.

Results: Eyes of LPS-treated animals, receiving CAIRs IVT showed marked reduction in inflammatory cell infiltration in both anterior and posterior ocular segments, compared to vehicle-treated contralateral eyes of the same animals. In vitro, LPS-treated macrophages demonstrated significant upregulation in inflammatory cytokines IL-1 β , TNF α and COX-2; CAIRs counteracted this effect in a dose-dependent manner.

Conclusions: CAIRs were well-tolerated and efficacious in this rat model of endotoxin-induced uveitis. They also demonstrated significant efficacy in vitro, reducing macrophage pro-inflammatory signaling. These compounds show initial promise as potential novel inflammation-resolving treatments. Next steps are to compare the safety and efficacy of CAIRs to current clinical therapies within this model.

CONTROL ID: 3537797

SUBMITTER (NAME ONLY): Madeeha Afzal

TITLE: Antimicrobial susceptibility of Staphylococcus aureus from different ocular conditions

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Afzal, A. Vijay, F. Stapleton, M. Willcox, School of Optometry and Vision Sciences, University of New South Wales, Sydney, New South Wales, AUSTRALIA]

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ABSTRACT BODY:

Purpose: Staphylococcus aureus is a frequent cause of eye infections, with isolates exhibiting increased antimicrobial resistance to commonly prescribed antibiotics. This study aimed to determine the antimicrobial susceptibility patterns and virulent determinants of S. aureus strains isolated from infectious and non-infectious adverse events from USA and Australia.

Methods: 51 strains of S. aureus from different ocular conditions (11 microbial keratitis [MK], 26 conjunctivitis and 14 from non-infectious contact lens corneal infiltrative events (niCIEs), were analysed for susceptibility to antibiotics commonly used to treat these conditions, using the broth dilution method. The presence of 13 virulence genes was determined by PCR.

Results: All strains were sensitive to vancomycin (100%) and gentamicin (98%). The susceptibility to other antibiotics decreased in the following order: chloramphenicol (80%), oxacillin (70%), ciprofloxacin (45%), ceftazidime (13%), azithromycin (10%) and polymyxin B (2%). All Australian MK strains but only 11% of USA MK strains were susceptible to ciprofloxacin and oxacillin ($p = 0.107$). 75% of Australian conjunctivitis strains from Australia were susceptible to ciprofloxacin compared to 37% of USA conjunctivitis strains ($p=0.278$). Most (90%) Australian niCIEs and USA conjunctivitis (96%) but only 55% of USA MK strains were susceptible to chloramphenicol ($p = 0.0036$). 84% of all strains were multi-drug resistant. All strains possessed Eap which aids in adhesion. Most strains possessed fnbpA, except 2 strains from niCIEs. No MK possessed clfA whereas all strains from niCIEs and 61% of conjunctivitis strains possessed clfA gene. pvl (Panton-Valentine leukocidin), which is associated with community-acquired MRSA, was present in most Australian MK and conjunctivitis strains but not in non-infectious strains ($p = 0.018$). Australian conjunctivitis strains were more likely to possess pvl than USA conjunctivitis strains ($p = 0.031$).

Conclusions: Knowledge of the rates of resistance to antibiotics may be important in decisions on treating these diseases. The differences in possession of virulence genes may be related to the pathogenesis of these conditions.

CONTROL ID: 3537810

SUBMITTER (NAME ONLY): Shih-Chen Chang

TITLE:

Disease Progression and Treatment Patterns in Pediatric and Adult Patients with Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME) in the US, a Commercial Claims-Based Analysis

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chang, A. Abraham, P. Kulkarni, C. Chuo, Genentech Inc, South San Francisco, California, UNITED STATES|B.G. Armendariz, A. Wenzel, Hoffmann-La Roche Limited, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: DR is a common complication of diabetes, and remains a leading cause of vision loss in the US and globally. We aimed to characterize the disease progression and treatment patterns (tx-pats) of DR and DME in children and adults in the US.

Methods: A retrospective cohort study was conducted with the Truven Health Marketscan data from 2011 to 2019. ICD-9 and ICD-10 were used to identify patients (pts) with index diagnoses of diabetes mellitus (DM), DR by severity, and DME. Pts included had ≥ 12 months medical/pharmacy enrollment, DM pts had ≥ 2 diagnoses at least 30 days apart in outpatients or ≥ 1 diagnosis in an inpatient setting. At least one diagnosis was required for DR/DME. For progression and tx-pats analysis, pts were required to have ≥ 180 days of follow-up (F/U) before and after DR/DME index. We excluded pts with prior history of any type of treatments of interest (tx-I; i.e. anti-VEGF, laser, corticosteroid, vitrectomy).

Results:

In total, 253 children and 165,404 adult DR pts were included and examined for progression and tx-pats longitudinally, and 74 children and 63,639 adult DME pts for tx-pats. The prevalence in children with DM is 0.7% and 0.2% for DR and DME, respectively.

The majority (84%) of pediatric DR pts were initially diagnosed with mild Non-Proliferative DR (NPDR), and 2.4% developed DME in a median of 2.1-year F/U. DR progression, and treatments for DR/DME were rarely observed in children.

Among the adult DR pts, 66.9%, 12.3%, 2.2%, and 18.6% had an initial diagnosis of mild, moderate, severe NPDR and Proliferative DR, respectively; 8.5% of them progressed and 15.3% developed DME in a median of 1.9-year F/U. No significant difference was observed between type-1 and type-2 DM pts. In addition, 14.2% of the DR and 52.6% of DME pts received ≥ 1 type of tx-I, the percentage of pts who received treatment increased by DR severity (Table 1). Treatment with Anti-VEGF, laser, and vitrectomy was more frequently observed than corticosteroid.

Conclusions: This work provides a deeper understanding of the DR characteristics in pediatric pts, showing rare DR progression and treatments for DR/DME. The majority of adult DR and half of DME pts did not receive any tx-I. Additional research is warranted to understand the drivers of treatment decisions in pts with DR and DME.

CONTROL ID: 3537827

SUBMITTER (NAME ONLY): Mustafa Ozgul

TITLE: 11-month-old Humanin-G in H₂O High Resolution Mass Spectrometry Analysis

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Katz, Chemistry, University of California Irvine, Irvine, California, UNITED STATES|

M. Ozgul, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: State-of-the-art techniques can be used to identify Humanin-G (HNG) fragments and dimers for possible use in future therapeutic investigation in age-related disease such as age-related macular degeneration, Alzheimer's disease and cancer.

Methods: For long-term stability analyses, HNG solutions were stored for 11 months at 4°C. For High-Resolution Mass Spectrometry (HRMS) studies, samples with a concentration of 30 µM HNG in HPLC water were used to analyze 11-month-old HNG products.

Mass spectrometric analysis was performed using Xevo G2-XS Quadrupole Time-of-Flight (HRMS) mass spectrometer coupled to UPLC. The UPLC method was run on a Water BEH C4 column using a 25 minutes linear gradient at 0.3 mL/min from 97% A to 97% B where A is 0.1% Formic Acid in water and B is 100% Acetonitrile. For HRMS analysis, positive electrospray ionization mode was utilized. A capillary transfer temperature of 300°C and a spray voltage of 3.0 kV were used to accomplish ionization. A resolution of 30,000 Full Width at Half Maximum (FWHM) was used for a full scan experiment within a range of m/z 100–2000 in addition to 15,000 FWHM with an isolation window adjusted to m/z 2.0 for. Leucine Enkephalin was used as a lock mass for nominal mass correction, and a CsNaI ladder was used for detector calibration.

Results: The HRMS spectrum of Humanin-G degraded molecules and humanin-G homodimers are presented in Figure 1A and Table Peptide Sequences (PS). In Humanin-G, disulfide dimerization was observed upon incubation of Humanin-G in HPLC water after 11 months at +4°C constant. Humanin-G homodimers (molecular mass 5312), the main ions were +9, +8, +7, +6, +5, charged states at m/z 532.31, 591.23, 665.01, 759.85, 886.34, 1063.40, (Fig. 2, Table PS). Humanin-G homodimers were detected at the highest intensities. HRMS detected other dimerized Humanin-G fragments (Fig. 1, 2 and Table PS). Dimerized Humanin-G fragments are shown in Figure 3 and Table PS.

Conclusions: For the first time, long-term stability properties of HNG peptide and its degradation products have been analyzed in detail using advanced HRMS technologies. Our data suggest that Humanin-G homodimers represent a more stable form than a single Humanin-G peptide. Our results may help researchers design better in vitro and in vivo experimental parameters to further understand the critical role of HNG in physiological conditions and human diseases.

CONTROL ID: 3537828

SUBMITTER (NAME ONLY): Claudia Farinha

TITLE: Common and rare genetic risk variants for Age-related Macular Degeneration progression in the Coimbra Eye Study.

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Farinha, P. Barreto, R. Coimbra, M. Cachulo, M.H. Madeira, J.G. Cunha-Vaz, R. Silva, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|C. Farinha, M. Cachulo, R. Silva, Ophthalmology, Centro Hospitalar e Universitario de Coimbra EPE, Coimbra, Coimbra, PORTUGAL|J.B. Melo, I.M. Carreira, Cytogenetics and Genomics Laboratory, Clinical Academic Center of Coimbra, Universidade de Coimbra Faculdade de Medicina, Coimbra, Coimbra, PORTUGAL|A.I. Den Hollander, C. Hoyng, Department of Ophthalmology, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To analyze the effect of common and rare genetic risk variants in AMD development in the Epidemiologic Coimbra Eye Study (CES).

Methods: Population-based cohort study. Participants underwent standardized interviews and ophthalmologic examination in the CES for AMD prevalence and incidence in central Portugal(NCT01298674,NCT02748824). Staging at both visits was performed with Rotterdam classification in a centralized reading center. Genomic DNA was isolated from blood samples. The genotyping assay was based on single-molecule molecular inversion probes for target selection and used next-generation sequencing to sequence 87 single nucleotide polymorphisms (SNPs). A total of 792 samples and 69 successfully genotyped SNPs were tested for association under an additive model, using the progression/no progression to AMD as a binary outcome. A logistic regression analysis was performed to assess allelic odds ratio (ORs) at 95% CI for each variant, adjusted for age and sex, significance level was set to 0.05.

Results: We included 142 participants who developed AMD (stages 2,3,4) during the 6.5-year follow-up and 650 controls (no AMD). Both common and rare variants were found to be associated with increased risk of developing AMD: CFH rs35292876 (OR,3.07;95%CI 1.19,7.43;P=0.015); ARMS2 rs10490924 (OR,1.51;95%CI 1.08,2.1;P=0.016); CFHR5 rs10922153 (OR,1.42;95%CI 1.09,1.85;P=0.010); and ARMS2-HTRA1 rs3750846 (OR,1.52;95%CI 1.08,2.12;P=0.015). Protective variants associated to reduced risk of progression to AMD were also identified: CFH rs10922109 (OR,0.68;95%CI 0.51,0.90;P=0.007); CFH rs1410996 (OR,0.66;95%CI 0.49,0.86;P=0.003); CNN2 rs10422209 (OR,0.63;95%CI 0.40,0.95;P=0.035); C2-CFB-SKIV2L rs429608 (OR,0.43;95%CI 0.24,0.71;P=0.002); COL10A1 rs3812111 (OR,0.76;95%CI 0.58,0.99;P=0.045); and SYN3-TIMP3 rs5754227 (OR,0.56;95%CI 0.33,0.91;P=0.026).

Conclusions: Both common and rare variants were found to be associated with the development of AMD in our epidemiological longitudinal study, while others were protective. Genetic characterization is important to pursue in different populations, as the identification of potential genetic therapeutic targets is of major interest. We will also explore the correlation between genetics, clinical and phenotypic features in risk assessment.

CONTROL ID: 3537844

SUBMITTER (NAME ONLY): Su-Yuan Yu

TITLE: Spatial averaging effects on multifocal ERG amplitudes

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yu, G. Kiri, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|S. Bijan, S. Bhaleeya, R.T. Tzekov, Ophthalmology, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the effect of spatial averaging on the multifocal electroretinography (mfERG) averaged ring amplitudes in patients screened for hydroxychloroquine (HCQ) toxicity.

Methods: This was a retrospective review of the records of patients screened for HCQ retinopathy at the USF Eye Institute (University of South Florida) during the period of 2015-2020. Only the records of patients referred internally were used. Patients were tested binocularly with Diagnosys mfERG system (Diagnosys LLC, Lowell, MA) using 61 hexagons grouped in five rings. The effects of the lowest level (level 1, or 4%) of spatial averaging on the mfERG P1 and N2 amplitude ring averaged values were evaluated.

Results: The records of 40 patients (4 males, 36 females) aged 54.4 ± 14.1 yrs. were selected for analysis. The use of spatial averaging had a differential effect on different rings. The effect was most pronounced on ring #1 (central element) amplitudes: for P1 the median change was (right/left eyes) $-2.3/-1.7$ nV/d² (-13.3%/-12.1%); for N2 the median change was $-2.5/-1.8$ nV/d² (-13.6%/-11.9%) and this decrease was significantly different than 0 for all comparisons ($p < 0.001$, one sample Wilcoxon test). In contrast, the effect on the rest of ring amplitudes was small, the median absolute effect was either 0 or 0.1 nV/d² (median % change was $< 2.5\%$), although for ring #4 values this change was significant ($p < 0.02$, one sample Wilcoxon test), except for N2 amplitude left eyes. The analysis of percent change vs. amplitude demonstrated no linear relationship for P1, while there was a negative relationship for N2 (ring #1, #2 and #3 left eyes and ring #1 left eyes), however, the presence of outliers was noted and once these were removed, the relationship remained significant only for ring #1 left eyes ($R^2 = 0.1347$, $p = 0.0198$).

Conclusions: For both P1 and N2 amplitudes spatial averaging has a substantial effect, especially on the amplitude of the central element (ring #1). As this is an mfERG amplitude is an important parameter, which could affect the interpretation of the results, use of spatial averaging should be avoided when analyzing mfERG results for HCQ screening.

CONTROL ID: 3537886

SUBMITTER (NAME ONLY): Cecilia Romero

TITLE: Efficacy of the Treat-and-Extend Regimen in the Management of Neovascular Age-Related Macular Degeneration: 7-Year Results of the RENO Study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Romero, J. Vannavong, A.A. Aziz, A. Wadsworth, A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|J.M. Dang, F. Siddiqui, M. Koci, N. Mojumder, M.M. Hagen, University of Nevada Reno School of Medicine, Reno, Nevada, UNITED STATES|P.E. Shappell, University of Southern California, Los Angeles, California, UNITED STATES|G.M. Gahn, The University of Arizona Department of Ophthalmology and Vision Science, Tucson, Arizona, UNITED STATES|W. Yang, University of Nevada Reno Division of Health Sciences, Reno, Nevada, UNITED STATES|J. Chhablani, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Treat-and Extend (T&E) method is often used by retina specialists in clinical settings in the treatment of neovascular age-related macular degeneration (nAMD). This study evaluated the outcomes of regular intravitreal ranibizumab, aflibercept, bevacizumab, or brolucizumab in patients with nAMD in the United States over the course of seven years.

Methods: This is a retrospective, interventional, consecutive case series. 165 eyes from 137 treatment-naïve patients diagnosed with nAMD after August 2010 were treated at a single site by one physician with ranibizumab, aflibercept, bevacizumab, or brolucizumab for ≥ 1 year using a T&E regimen. Patients needed to receive ≥ 6 injections in the first year and ≥ 3 injections in the following years to be included in this study. Snellen best-corrected visual acuity (BCVA) was converted to ETDRS letters using a standardized formula. The main outcome measures were: BCVA change from baseline to end of patient follow-up, mean number of injections per year, and percentage of eyes losing ≥ 15 letters or gaining ≥ 15 letters.

Results: The average (standard deviation [SD]) baseline patient age was 78 years (8.5); 60% of patients were female. The mean follow-up period was 5 years, with 165, 158, 143, 113, 98, 64 and 32 eyes completing 1, 2, 3, 4, 5, 6, and 7 years of follow up, respectively. The average BCVA at baseline was 53 letters. Mean (SD) changes from baseline in BCVA were 8.2 (21.8) letters, 7.0 (25.0) letters, 4.4 (26.7) letters, 4.2 (27.6) letters, 4.4 (28.7) letters, 4.6 (26.2) letters, and 4.6 (37.0) letters for years 1, 2, 3, 4, 5, 6, and 7 respectively. The mean number of injections received by patients in year 1 was 8. In years 2 through 7, the mean number of injections received by patients was 6. At the final follow-up, 23.4% of male eyes and 25.7% of female eyes had lost ≥ 15 ETDRS letters and 28.1% of male eyes and 27.7% of female eyes had gained ≥ 15 letters.

Conclusions: The Treat-and-Extend regimen was effective in maintaining visual acuity in patients with nAMD treated with ranibizumab, aflibercept, bevacizumab, or brolucizumab for up to 7 years of treatment in patients who received a minimum of 6 injections in the first year and a minimum of 3 injections in follow-up years 2 through 7. To reduce overall treatment burden, the Treat-and-Extend regimen is an effective treatment option for patients.

CONTROL ID: 3537891

SUBMITTER (NAME ONLY): Grant Howell

TITLE: Intraocular Inflammation Associated with Ocular Toxoplasmosis: Relationships Between Episodes of Active Disease

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Host factors, including age, are associated with increased severity of toxoplasmic retinochoroiditis and shorter intervals to recurrence. We have previously shown that more severe inflammation of an episode also predicts shorter intervals to the next recurrence. We sought to determine if severity of an episode predicts other characteristics of recurrences as well.

Methods: We used a dataset of 210 patients with ocular toxoplasmosis from 7 international sites (North/South America, Europe). Longitudinal data for each episode were available for 46 patients with multiple documented recurrences. We compared the following factors at first visits of first-observed episodes to the same factors at first visits in all subsequent episodes: anterior chamber (AC) cell; vitreous haze; and intraocular pressure (IOP). We also compared duration of lesion activity between first-observed episodes and all subsequent episodes.

Results: Of 46 patients, there were 129 episodes (range 1-7 episodes/patient) including 558 visits with active disease. At first visits, AC cell was >1+ in 12 (27.3%) patients during first-observed episodes and in 11 (13.8%) episodes for all subsequent episodes. Median duration of lesion activity was 53 days (interquartile range [IQR] 27-91 days) for first-observed episodes and 45 days (IQR 32-68 days) for subsequent episodes. Those with >1+ AC cell at first-observed episodes more likely had >1+ cell at any subsequent episode (odds ratio [OR] 21.4 [95% CI 3.82-119.7], p=0.0002); agreement between episodes for individual patients was moderate (Kappa coefficient 0.478 [CI 95% 0.222-0.733]); however, >1+ AC cell was not related to elevated IOP (>21mmHg) subsequently (p=0.64). There were no relationships between first-observed episodes and all subsequent episodes for vitreous haze (p=0.18), elevated IOP (p=1.0), and duration of lesion activity (p=1.0).

Conclusions: Severe AC reactions during episodes of toxoplasmic retinochoroiditis predict not only shorter intervals to recurrences, but more intense inflammatory reactions in recurrent episodes. Despite a previously reported relationship between AC cell and elevated IOP at presentation, neither factor predicted elevated IOP at recurrences. Risk factors related to the characteristics of recurrent ocular toxoplasmosis have implications for management decisions, including the need for secondary prophylaxis against recurrence.

CONTROL ID: 3537892

SUBMITTER (NAME ONLY): Atalie Thompson

TITLE: Agreement between trend-based and qualitative analysis of the retinal nerve fiber layer thickness for glaucoma progression on Spectral domain-optical coherence tomography

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Thompson, S. Asrani, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|A. Li, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the agreement between trend-based analysis versus qualitative assessment of the retinal nerve fiber layer (RNFL) thickness for glaucomatous progression on Spectral domain-optical coherence tomography (SDOCT).

Methods: Retrospective cohort of 190 eyes from 103 patients with glaucoma or glaucoma suspect diagnoses who underwent SDOCT imaging during 4 different clinic visits. Trend-based progression was characterized by a significantly negative slope. Progression by qualitative analysis was determined by review of RNFL thickness profiles from automated segmentation and raw B-scan SDOCT images.

Results: The slope was significantly greater in those with progression than without progression for both trend-based and qualitative analysis ($p < 0.001$). However, the qualitative grading classified a significantly greater proportion of eyes as progressing compared to trend-based analysis in both the superotemporal (ST) RNFL (23.2% vs. 10.5%, $p = 0.001$) and inferotemporal (IT) RNFL (27.4% vs 8.4%, $p < 0.001$). The trend-based and qualitative classifications of progression showed poor agreement in both the ST (Kappa 0.0135) and IT RNFL (Kappa 0.1222). The agreement between trend-based and qualitative analysis was lower among eyes with artifacts (ST 58.11%; IT 68.7%) than those without artifacts (ST 80.2%; 74.8% IT). Moreover, among eyes with artifacts, there was no significant difference in slope between those qualitatively categorized as progressing versus not progressing ($p > 0.05$). The figure shows an example of false progression on SDOCT due to vitreomacular traction release.

Conclusions: There is poor agreement between a trend-based definition of glaucoma progression and qualitative analysis of the change in RNFL on SDOCT. Careful qualitative review of SDOCT imaging may identify specific areas of glaucoma progression that are not captured by trend-based methods especially in the presence of artifacts.

CONTROL ID: 3537908

SUBMITTER (NAME ONLY): Gaganashree Shivashankar

TITLE: Pro-inflammatory cytokines prompt metabolic and functional changes in the retina of hyperglycemic mice

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Shivashankar, M.L. Acosta, School of Optometry and Vision Science, The University of Auckland, Auckland, Auckland, NEW ZEALAND|J.C. Lim, Department of Physiology, The University of Auckland, Auckland, Auckland, NEW ZEALAND|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a common complication of diabetes that leads to progressive vision loss. Although hyperglycemia (HG) plays an important role in its pathogenesis, a growing body of evidence suggests that pro-inflammatory conditions in the eye enhance DR development and progression. In this study, we investigated the combined effect of HG and inflammation on the early stages of disease by assessing retinal function and metabolic homeostasis.

Methods: HG was induced in C57Bl/6 mice within one week of administering a single intraperitoneal injection of streptozotocin (150 mg/kg), while control mice received a sham injection. After confirming HG, mice received an intravitreal injection (IVT) of 500 ng/ml of each pro-inflammatory cytokine TNF- α and IL-1 β (HG+cytokines group, n=6) or a sham injection (HG-only group, n=6). Control mice received an IVT of pro-inflammatory cytokines (cytokines-only group, n=6) or a sham injection (control group, n=6). The retinal function (focal electroretinogram on the superior retina) was evaluated two days after IVT and the retina was immediately collected for biochemical analysis to determine retinal glucose, lactate, ATP, glutamate and glutamine levels.

Results: A similar significant decrease in the a-wave amplitude was observed in both HG-only and HG+cytokines groups at higher light intensities 2.6 and 3.2 log cd.s/m² (p<0.01) compared with control. A significant decrease in the b-wave amplitude was observed in the HG-only group at 2.6 log cd.s/m² (p<0.05) and it was significantly further decreased in the HG+cytokines group at the higher light intensities 2, 2.6 and 3.2 log cd.s/m² (p<0.05). While the HG-only group showed elevated glucose levels (p<0.01), the HG+cytokines group showed a significantly higher retinal glucose (p<0.001), lactate (p<0.001), ATP (p<0.001), glutamine (p<0.05) levels, and a significant decrease in glutamate (p<0.05) levels compared with control. The cytokines-only group showed no significant changes compared with control.

Conclusions: The presence of pro-inflammatory cytokines in the eyes of HG mice altered the retinal metabolic homeostasis and retinal function in the photopic range. These findings support the idea that combined presence of HG and inflammation may enhance DR development. Hence, early intervention to prevent inflammation-triggered retinal changes in diabetic patients may improve the disease outcome.

CONTROL ID: 3537923

SUBMITTER (NAME ONLY): Anderson Teixeira

TITLE: To Analyze the dead space syringe for intra-vitreous injections

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Teixeira, I. Silva, A. Pereira, Ophthalmology, Universidade Catolica de Brasilia, Taguatinga, DF, BRAZIL|C. Salaroli, Cornea, Clinica de Olhos Teixeira Pinto, BRAZIL|

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ABSTRACT BODY:

Purpose: We described a novel method to quantify the waste volume left into the plastic syringe after anti-VEGF injection and elected the best plastic syringe to use during intra-vitreous injections.

Methods: We evaluated the amount of fluid retained in eight different types of insulin/tuberculin syringes with permanent needle design and without needle design used to perform intra-vitreous injections commercially available in the Brazilian marketing. Firstly, we divided the syringes types in group of ten samples and they all were weighted using a precise (0.01g) caliper balance.

In a second phase we filled the syringes with water, removed air bubbles and then pushed the syringe piston to the mark of 0,05ml. All the syringes were immediately weighted again. Then, we simulated an intra-vitreous injection pushing the piston to the end (mark 0.00) and we immediately weighted.

Results: All results are described in the table 2 and 3. Mean residual weight into the dead space of syringes with permanent needle design was between 0.002 to 0.006 g and the syringe without needle was 0.032g. No statistic significant was observed in samples of syringe with permanent needle design but comparing all syringes with permanent needle design to the syringe without needle all results were statistically significant ($P < 0.01$). This indicates that a significant amount of volume loss is due to dead space if we use syringe without needle design.

Conclusions: Our study showed if we use a syringe without needle a residual volume of 58 per cent of the total amount injected remains in dead space, which means a despise of one dose treatment (0.05ml) for each two injections . During the years of 2006 to 2015 almost one billion injections were performed in USA. Considering the use of syringe with permanent needle we should save almost half treatment dose per injection and consequently reducing the cost treatment.

In conclusion, we highly incentive physicians to use syringe with permanent needle to perform intra-vitreous injections. New techniques to compounder into multiple doses the anti-VEGF using syringes with permanent needle is necessary to reduce the treatment cost per patient.

CONTROL ID: 3537942

SUBMITTER (NAME ONLY): Urooba Nadeem

TITLE: RNA Sequencing Reveals Changes in Mouse Retinal Transcriptome Caused by High-Fat Diet Induced Gut Dysbiosis

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Nadeem, Pathology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|B. Xie, M.D. Souza, D. sulakhe, Center of Research Informatics, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|A. Movehedan, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|H. Barba, D. Dao, D. Skondra, Ophthalmology, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|E. Xie, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|E. Chang, Department of Medicine, Microbiome Medicine Program, Knapp Center for Biomedical Discovery, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: High-fat diet (HFD) alters the composition of the gut-microbiome-a condition known as gut dysbiosis. Both HFD and gut microbiome are implicated in the pathogenesis of retinal diseases including age-related macular degeneration (AMD) and diabetic retinopathy (DR). However, retinal transcriptome changes secondary to diet-induced gut dysbiosis have not been delineated. Here, we study the effect of HFD-induced gut dysbiosis on retinal gene expression and biologic pathways.

Methods: Fifteen weeks-old male C57BL/6J wild-type mice on normal diet (ND) and 23% HFD for 8 weeks were used (4 mice/group). Bacterial community structure is assessed from fecal DNA using 16S rRNA sequencing done on the Illumina MiSeq DNA platform and analyzed via QIIME software to determine the relative microbiome abundance. Whole retina RNA-sequencing (RNA-seq) was performed on NovaSEQ6000 using the paired-end method. Differentially expressed genes (DEGs) were identified (p-value <0.01); biologic pathways associated with the DEGs were found using the Kyoto Encyclopedia of Genes and Genomes (KEGG). Functional enrichment network and upstream transcription factor analysis were performed using EnrichR.

Results: Mice fed HFD have increased relative abundance of phyla of Firmicutes and Verrucomicrobia and decreased abundance of Bacteroides phylum. RNA seq identified a cohort of 30 DEGs, 14 of which were upregulated, and 16 were downregulated in the HFD group. DEGs included hypermethylated in cancer 1 (HIC1) and heat shock protein family A member 1B (Hspa1b) which are strongly associated with AMD. Pathway analysis revealed that DEGs are involved in purine, pyrimidine, arginine, and glutathione metabolism and mitogen-activated protein kinases (MAPK), cGMP-dependent protein kinase (cGMP-PKG), and phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT) signaling pathways. Transcription factor polymerase 1(PARP1) and forkhead fox M1 (FOXO1) involved in retinal degeneration and epithelial-mesenchymal transformation of retinal pigment epithelium cells, respectively were also affected.

Conclusions: To our knowledge, this is the first study demonstrating that HFD-induced gut-dysbiosis regulates the retinal transcriptome, involving genes known to play a key role in AMD. Altering the gut microbiome via diet may have future implications for treating retinal diseases, especially AMD.

CONTROL ID: 3537948

SUBMITTER (NAME ONLY): Carol Lin

TITLE: Myopia-related changes to retinal astrocytes and associated retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) of juvenile marmosets

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lin, A. Toychiev, A. Nour, R.K. Ablordeppey, M. Srinivas, A. Benavente-Perez, SUNY College of Optometry, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal astrocytes are key elements of neuronal support. We hypothesize that the mechanical elongation of the globe due to myopia progression affects astrocytes and predisposes the myopic eye to ocular complications. In this study, we characterized the effect of lens-induced myopia on retinal astrocyte coverage and distribution in relationship to RNFL and GCL thickness of common marmosets (*Callithrix jacchus*).

Methods: Eight myopic and ten control (myopic average Rx: -5.49 ± 2.48 D, age: 195 ± 16.75 days; controls average Rx: -1.10 ± 0.62 D, age: 293 ± 90.56 days, $p < 0.01$) marmoset retinal whole mounts were labeled with anti-GFAP and anti-Sox9 to visualize astrocytes within the superficial layer. Astrocyte numbers, RNFL and GCL thickness were quantified at the parafoveal, peripapillary, and peripheral retinal regions using confocal microscopy and optical coherence tomography (OCT). Ocular magnification was corrected using Kang's method. Statistical analysis was performed using Mann-Whitney U non-parametric testing at a confidence level of 95%.

Results: Myopes had less astrocytes (controls 248.55 ± 18.55 , myopes 154.96 ± 23.3 , $p < 0.05$), thinner RNFL (controls $33.80 \text{ mm} \pm 12.4$; myopes $24.57 \text{ mm} \pm 3.3$, $p < 0.01$) and thinner GCL (controls $23.38 \text{ mm} \pm 2.9$; myopes 21.52 ± 2.9 , $p = 0.02$) in the parafovea compared to controls. In control eyes, the number of astrocytes increased as the overall GCL ($R^2 = 0.19$, $p < 0.01$) and peripapillary RNFL ($R^2 = 0.81$, $p < 0.04$) thickened; while in myopic eyes, these were not significant. In control eyes, the RNFL thickened as eyes grew normally (superior and nasal peripapillary $R^2 = 0.80$, $p < 0.02$; $R^2 = 0.86$, $p = 0.02$; temporal parafovea $R^2 = 0.79$, $p < 0.05$; temporal periphery $R^2 = 0.97$, $p < 0.02$). In myopic eyes, on the opposite, the GCL thinned as eyes grew larger and developed myopia in the superior periphery ($R^2 = 0.86$, $p < 0.01$).

Conclusions: Untreated marmosets exhibit a thickening of the RNFL as their eyes grew normally and this was accompanied by an increase in the astrocyte bodies observed. Myopic marmosets, however, exhibited lower astrocyte numbers, their RNFL and GCL thinned as eyes grew myopic. These results suggest compromised glial structure and function, leading to inadequate ability to regulate local ions and support neural tissue in eyes with progressing myopia.

CONTROL ID: 3537953

SUBMITTER (NAME ONLY): Abdus Samad Ansari

TITLE: The Dietary Influence of Vitamins, Minerals and Micronutrients on Glaucoma-related Endophenotypes

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Ansari, C.J. Hammond, Section of Academic Ophthalmology, School of Life Course Sciences, FoLSM, King's College London, London, London, UNITED KINGDOM|P. Louca, O.M. Masachs, Department of Twin Research & Genetic Epidemiology, School of Life Course Sciences, FoLSM, King's College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: There is a significant paucity of neuroprotective strategies to reduce the vulnerability to glaucoma-related cellular stressors. Recent work has suggested that patients with glaucoma have reduced plasma levels of nicotinamide adenine dinucleotide (NAD), a precursor for vitamin B3 (niacin). Additionally, mouse models have found a similar age-related decline in NAD with subsequent neuroprotection of retinal ganglion cells with very high-dose oral vitamin B3. We aimed to evaluate whether dietary vitamin B3 and 50 other vitamins, minerals and micronutrients explain variation in glaucoma-related endophenotypes in the general population.

Methods: A population-based cross-sectional study was performed with 1,977 predominantly female participants from the TwinsUK registry. Energy adjusted intakes for 51 nutrients were estimated through a validated food frequency questionnaire. Endophenotypes evaluated included intraocular pressure (IOP), retinal nerve fibre layer (RNFL) thickness and vertical cup to disc ratio (VDCR) adjusted for disc area. Linear mixed models adjusted for age, sex and family structure were used to investigate the associations of individual nutrients and endophenotype. A backwards stepwise regression model was completed for each endophenotype, including all associated nutrients after stratifying intake into quartiles.

Results: Within the study cohort, mean (SD) age was 60.1 (± 14.6) years. Mean endophenotype values measured were IOP: 13.3mmHg (± 2.81), VCDR: 0.4 (± 0.12) and RNFL: 96.1 μ m (± 10.10). Dietary vitamin B3 was not associated with any endophenotypes. Multivariate regression models evaluating lowest versus highest quartiles of dietary intake identified two nutrients associated with RNFL thickness, magnesium ($\beta = -1.83$, $p = 0.04$) and thiamine ($\beta = 2.03$, $p = 0.02$); thiamine intake demonstrated a dose-related association with a thicker RNFL for each quartile. Flavonoids intake was associated with reduced IOP ($\beta = -0.401$, $p = 0.05$), and vitamin E ($\beta = -0.017$, $p = 0.03$) and selenium ($\beta = 0.019$, $p = 0.04$) were associated with VCDR.

Conclusions: Dietary thiamine intake has a dose-response relationship to RNFL thickness, longitudinal studies are required to see if it protects against RNFL loss. In a healthy population dietary vitamin B3 did not appear to be protective for glaucoma-related endophenotypes. Dietary flavonoid intake appears to be associated with lower IOP.

CONTROL ID: 3537982

SUBMITTER (NAME ONLY): Zhijie Charles Chen

TITLE: Optically configurable confinement of electric field with photovoltaic retinal prosthesis

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Prosthetic visual acuity is limited by the pixel size and by crosstalk from the neighboring electrodes. For acuity better than 20/200, pixels should be under 50 μ m, and local returns are required for the crosstalk suppression. However, small bipolar pixels over-constrain the field penetration and thus limit the efficacy of retinal stimulation. Sequential activation of the photodiode pixels transforms active electrodes into transient returns. We explore this approach for dynamic confinement of electric field in the retina by spatiotemporal control of the images projected onto the photovoltaic array.

Methods: The electric field in the retina generated by a photovoltaic subretinal implant with 425 hexagonal monopolar pixels of 40 μ m in pitch was modeled using the finite element method and linear combination of the elementary electric fields emanating from each electrode individually. We quantified the spatial coupling among the pixels and calculated the dynamics of the photodiode circuit in the multidimensional form. Electric fields predicted by the model were compared to the potential mapped by micropipette ex-vivo, as well as that recorded from corneas in implanted rats.

Results: Spatiotemporal modeling shows that the electric field generated by active electrode elevates the local potential on neighboring dark pixels and thereby transiently increases their discharge current by up to 10 fold, effectively transforming them into return electrodes. The distance between the active electrode and the transient return defines the penetration depth of the electric field into tissue. Ex-vivo measurements of the electric potential match the model predictions. Amplitude of the corneal signal in rats increases with the width of the grating projected onto the implants, from 40 to 180 μ m, confirming the configurability of the stimulation depth in-vivo.

Conclusions: Current conducted by photodiodes in an array is affected by other electrodes due to spatial coupling of the electric potential in electrolyte. Therefore, spatiotemporal modulation of light on the array can transform the active electrodes into transient returns. Such optical approach to current steering enables a flexible control of the lateral and axial confinement of electric field, which allows optimization of the stimulation depth and selectivity in every patient, depending on the retinal thickness and its proximity to the electrodes.

CONTROL ID: 3537984

SUBMITTER (NAME ONLY): Amanda Zhou

TITLE: Progression of Retinitis Pigmentosa Associated with Ciliary and Non-Ciliary Genetic Etiologies

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zhou, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|A. Zhou, J. Oh, S.H. Tsang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J. Oh, SUNY Downstate Health Sciences University, New York City, New York, UNITED STATES|S.H. Tsang, Department of Pathology & Cell Biology and Columbia Stem Cell Initiative (CSCI), Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The natural history of retinitis pigmentosa (RP) is known to vary across different inheritance patterns and across genetic etiologies. Two large groups of disease include RP caused by mutations in ciliary genes and RP caused by mutations in non-ciliary genes. This study aims to determine differences in disease progression in patients with mutations in ciliary and non-ciliary genes using spectral-domain optical coherence tomography (SD-OCT) and 30Hz flicker response in full-field electroretinograms. Study of the natural history of disease is critical to improve understanding and may guide clinical therapies by demonstrating which will require more aggressive and earlier intervention.

Methods: Retrospective chart review was performed of patients with genetically confirmed diagnoses of RP. SD-OCT images were obtained from 285 patients, 188 of whom were found to have mutations in ciliary genes. 30Hz flicker amplitudes were obtained from 69 patients with mutations in ciliary genes and 33 patients with mutations in non-ciliary genes. SD-OCT images were evaluated through measurements of ellipsoid zone (EZ) length and central foveal thickness (CFT) using the built-in caliper tool on the Spectralis HRA+OCT. The amplitudes of the 30Hz flicker electroretinograms were collected from a Diagnosys Espion Electrophysiology System.

Results: Longitudinal analysis of SD-OCT images revealed that the EZ deteriorated at a mean rate of 26.4µm/year in the ciliary gene cohort as compared to 15.7µm/year in the non-ciliary gene cohort. Measurement of CFT revealed a mean decrease of 0.7µm/year in the ciliary gene cohort as compared to 1.06µm/year in the non-ciliary gene cohort. 30Hz flicker amplitude decreased at a mean rate of 1.4µV/year in the ciliary gene cohort and 0.8µV/year in the non-ciliary gene cohort. The mean follow-up period for SD-OCT images was 4 years, while the mean follow-up period for 30Hz flicker measurements was 2.2 years.

Conclusions: Our study suggests that on average, RP due to mutations in ciliary genes may progress faster than RP due to mutations in non-ciliary genes as seen by EZ measurements and 30Hz flicker amplitudes. Therefore, patients with ciliary gene mutations may require more aggressive and earlier therapeutic intervention, and EZ line measurements and 30Hz flicker amplitudes may serve as viable outcome measurements for future clinical trials.

CONTROL ID: 3537990

SUBMITTER (NAME ONLY): Charlene Choo

TITLE: Investigation of Oxidative Stress in Ex Vivo Corneal Endothelial Cells During Cell Culture and Expansion

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Choo, D. Chung, A.J. Aldave, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|C. Choo, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ex vivo expansion of corneal endothelial cells (CEnC) has the potential to alleviate the global shortage of donor corneal tissue that limits access to corneal transplantation. However, successful expansion of ex vivo corneal endothelial cells (evCEnC) is limited by early cellular senescence and loss of CEnC-like morphology. To determine whether or not oxidative stress plays a role in the expansion capacity of evCEnC, we cultured evCEnC with and without SkQ1, a mitochondria-targeting antioxidant, and measured the level of intracellular free radical (IFR) levels.

Methods: To determine the optimal SkQ1 dose range that will lead to minimal cell toxicity and maximal oxidative stress protection in CEnC, HCEC-21T, a CEnC line, was cultured in media supplemented with 0nM (untreated), 50nM, 250nM, 500nM or 750nM of SkQ1 for 3-5 days. Then the cells were treated with or without tBH, an oxidative stress inducing agent, and cell viability was assessed by MTT assay.

To determine the impact of SkQ1 treatment on IFR levels, evCEnC were isolated from donor corneas and then split into two culture (SKQ1-treated and untreated), which were each grown to confluence. DCFH-DA assay was performed to measure differences in IFR levels.

Results: When compared to untreated cells, HCEC-21T treated with 50nM or 250nM SkQ1 retained 98.8% and 96.9% cell viability, respectively, while HCEC-21T treated with 500nM or 750nM SkQ1 retained 65.8% and 22.7% cell viability, respectively. Under 100 μ M tBH oxidative stress induction, cell viability protection was observed in a SkQ1 dose-dependent manner with 250nM and 50nM SkQ1 treatment leading to 36.3% and 18.2% cell viability, respectively, while 0nM SkQ1 treatment yielded 14.8% viability.

Compared to their tBH-untreated counterparts, evCEnC treated with 50nM and 250nM SkQ1 demonstrated a ~7.5% and ~22.5% decrease, respectively, in IFR concentrations at passage 0. Additional evCEnC isolations are being assessed in order to perform statistical analyses.

Conclusions: Supplementing culture media with SkQ1 provides a CEnC line with tBH-induced oxidative stress protection and decreases IFR concentrations in cultured evCEnC. The preliminary findings of this study suggest antioxidants, such as SkQ1, may increase the expansion potential of ex vivo CEnC by reducing oxidative stress levels.

CONTROL ID: 3538012

SUBMITTER (NAME ONLY): Jonathan Li

TITLE: Choriocapillaris changes in myopic macular degeneration

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Li, J. Wong, L. Chan, T.C. Porco, J.L. Duncan, D. Schwartz, University of California San Francisco, San Francisco, California, UNITED STATES|H. Zhou, R.K. Wang, Y. Dai, Department of Bioengineering, University of Washington, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myopic macular degeneration (MMD) is rapidly increasing in prevalence worldwide, and severe forms can cause irreversible loss of vision. Recent studies have shown an association between decreased choroidal thickness and increased grade of MMD. Our cross-sectional study aimed to further characterize this choroidal thinning by analyzing choriocapillaris alterations in MMD.

Methods: We recruited controls (n=51 eyes) and high myopes (spherical equivalent ≤ -6 diopters; n=16 eyes) from clinic at the University of California San Francisco. Axial length (AL) from A-scan, best corrected visual acuity (BCVA), fundus photos, and swept-source optical coherence tomography angiography (SS-OCTA) were measured. Fundus photos were graded for stage of MMD by 2 independent ophthalmologists. Inclusion criteria for subjects were those with Grade 2 MMD (diffuse chorioretinal atrophy) and high axial myopia (AL ≥ 26.5 millimeters [mm]). Subjects without MMD, with ages from 19-88 years old (mean=56) and AL from 21.65 to 25.84mm (mean=23.87), were used as controls. Exclusion criterion was BCVA worse than 20/40. 3x3mm SS-OCTA scans were acquired and choriocapillaris (CC) mean thickness was measured by identifying CC peaks in OCTA A-scan intensity profiles. CC flow void percent (CC FV%) was quantified using a fuzzy C-mean thresholding method on enface OCT-A images of an 8-um CC slab below Bruch's membrane. Multivariate regression models were analyzed comparing CC thickness and CC FV% between subjects and controls, with a linear correction for age.

Results: Subjects with diffuse chorioretinal atrophy had both a significantly decreased CC thickness and increased CC FV% compared to controls. CC thickness in subjects with diffuse chorioretinal atrophy measured 5.23 ± 0.68 um (mean \pm standard deviation) versus 15.45 ± 1.82 um in controls ($p < 0.001$). CC FV% in subjects with diffuse MMD measured 26.5 ± 0.04 versus 11.6 ± 0.04 in controls ($p < 0.001$).

Conclusions: Patients with diffuse chorioretinal atrophy and good visual acuity had a 66% reduction in CC thickness and a 230% increase in CC FV% compared to controls. Although these patients have essentially normal BCVA and outer retinal landmarks on optical coherence tomography, they demonstrate significant choriocapillaris alterations that are consistent with reduced perfusion to the outer retina. These results point to a potential vascular etiology for MMD.

CONTROL ID: 3538020

SUBMITTER (NAME ONLY): Benjamin Zhou

TITLE: Comprehensive Tele-Ophthalmology Screening in Vision Threatening Diseases During COVID-19

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Zhou, I. Zhang, A. Patton, C. Ye, N. Bhagat, B. Szirth, A.S. Khouri, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision Threatening Diseases (VTD) (age-related macular degeneration [AMD], cataract, diabetic retinopathy [DR], and glaucoma) account for 37% of all blindness. Screening and follow-up are crucial in preserving vision. During COVID-19, clinics reduced access, using telemedicine for diagnosis and follow-ups. The efficacy of remote screening and triage in the management of single or multiple VTDs was evaluated.

Methods: We screened 41 subjects (19-85 years, 37% male, 17% Caucasian) (20 controls, 21 subjects). Demographics, 45-degree retinal photos, ganglion cell complex (GCC), and optic nerve head (ONH) images were collected using a non-contact puff-tonometer, non-mydratic retinal camera, and an OCTA. Demographics and images were transmitted to two readers (onsite telemedicine screener [TS] and remote ophthalmologist [RO]) for triage. Triage was categorized: immediate referral to specialist, follow-up in person via clinic or telemedicine visit, or no follow-up necessary during COVID.

Results: TS made 19 referrals (46%), 6 in person follow-ups (15%), 15 no follow-ups (37%); RO made 17 referrals (41%), 2 in person follow-ups (5%), 22 no follow-ups (54%). TS identified 12 subjects as possible VTD(s) while RO identified 11 subjects. TS and RO agreed on 8 glaucoma, 7 cataract, 3 DR, and 3 and 2 AMD cases, respectively. Glaucoma was identified using IOPs, retinal funduscopy, and OCT imaging. Mean intraocular pressures were 12.9 and 15.7 (OD, OS) in glaucoma and 14.2 and 14.0 in controls. Funduscopy was used for overall retinal health while OCT images were used to analyze GCC, ONH, nerve fiber layer, cup to disc ratio, and anterior chamber angles. AMD and DR were identified by funduscopy and OCT imaging. 11 of the subjects were known clinic patients; both RO and TS referred all 11 to specialty clinics, matching the in-person clinic management.

Conclusions: During the COVID pandemic, triaging patients can minimize person-to-person contact and help control the spread of the virus. Both readers agreed on the management and triage of a variety of patients with TS and RO differing only on 2 referrals and 4 in person follow-ups. Telemedicine is a promising alternative to in-person patient care for management and triage of vision threatening diseases. Further enrollment and follow-up are needed to increase robustness.

CONTROL ID: 3538032

SUBMITTER (NAME ONLY): Herman Stubeda

TITLE: The agreement of STATPAC and visualFields statistical packages in visual field analyses

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Stubeda, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, CANADA|L. Shuba, M. Nicolela, B.C. Chauhan, J.R. Vianna, Department of Ophthalmology and Visual Sciences, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, CANADA|

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ABSTRACT BODY:

Purpose: STATPAC is a widely used statistical package for visual field analysis, however, its normative dataset and methods are proprietary. The visualFields (vF) statistical package is a tool analogous to STATPAC but with opensource normative dataset and methods, which provides an advantage for collaboration. The purpose of this study was to determine whether vF analyses agree with STATPAC.

Methods: We defined 3 separate statistical environments containing unique normative datasets: STATPAC, vF with its native normative dataset (vF-SUNYIU), and vF with a new normative dataset of healthy fields from previous studies at our centre in Halifax (vF-Halifax). We created a glaucoma dataset using fields from patients in our glaucoma clinic. All data from Halifax were 24-2 SITA Standard, using only one field per subject. The glaucoma fields were analysed with the 3 environments generating 3 sets of total deviation (TD), pattern deviation (PD), global mean deviation (MD), and pattern standard deviation (PSD) values, which were compared with Bland-Altman plots. We also applied five criteria for glaucomatous fields, i.e., Glaucoma Hemifield Test, Hoddap-Anderson-Parrish 2, Foster, United Kingdom Glaucoma Treatment Study, and Low-pressure Glaucoma Treatment Study within each environment and determined agreement in the criteria results with Kappa statistics.

Results: The Halifax normative dataset contained 163 subjects. The glaucoma dataset contained 1848 subjects with mean (standard deviation) age of 67.1 (12.1) years, and mean STATPAC MD of -3.36 (5.25) dB. The agreement in TD and PD values between STATPAC and the two vF environments was high in the -26 to +5 dB range, but there was notable disagreement below -26 dB, in which both vF environments underestimated field loss by on average 1dB (Fig.1 A&B). The agreement in MD and PSD values between STATPAC and the two vF environments demonstrated a trend where vF underestimated field loss by up to 1dB as field loss increased (Fig.1 C&D). In contrast, agreement in values between vF-SUNYIU and vF-Halifax was high and uniform (Fig.1 A-D). The inter-environment agreement of glaucoma criteria exceeded kappa 0.725 in all cases (Fig.2).

Conclusions: Although STATPAC and vF may have differences in computation of TD values for severely damaged locations, our results highlight a robust agreement, which suggests vF is a viable alternative to proprietary statistical packages.

CONTROL ID: 3538036

SUBMITTER (NAME ONLY): Renita Martis

TITLE: Inter-tissue antioxidant exchange between the lens and vitreous: A novel mechanism for maintaining high levels of ascorbate in the vitreous

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Martis, B. Li, P.J. Donaldson, J.C. Lim, Physiology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|R.M. Martis, B. Li, P.J. Donaldson, J.C. Lim, The University of Auckland New Zealand National Eye Centre, Auckland, Auckland, NEW ZEALAND|

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ABSTRACT BODY:

Purpose: Based on our observation that the human lens is able to export glutathione to the vitreous, we have proposed the concept of antioxidant exchange between the lens and the vitreous to ensure oxygen levels at the back of the eye are maintained at low levels. Here we investigate whether ascorbate (AsA) and oxidized AsA (DHA) are exchanged between the lens and the vitreous and determined how these levels are altered as a result of removal of the lens.

Methods: Human lenses of varying ages were cultured in artificial aqueous humour under hypoxic conditions for one hour, and lactate dehydrogenase activity (LDH), AsA and DHA levels measured in the media and lens (n=7). Immunohistochemistry was conducted to localize potential AsA efflux transporters. To determine changes in antioxidant levels in the vitreous, samples were collected from patients (60-86yrs) undergoing vitrectomy with an intact lens or IOLs and antioxidant levels quantified using biochemical assays.

Results: After one hour, minimal LDH activity (<0.5%) was detected in the media for all donor lenses suggesting that membrane integrity was preserved. AsA and DHA were both detected in the media with ~6.9% AsA efflux and ~66.34 % DHA efflux. Immunolabelling revealed connexin 46 to be localized to the membranes of the fibers cells in the anterior and posterior surface of the lens, placing it in an ideal position to mediate AsA or DHA efflux into the vitreous. Measurements of glutathione levels in the vitreous of patients with an intact lens versus an intraocular implant demonstrated that total GSH levels were reduced by ~7-fold indicating that loss of the natural lens may contribute to altered antioxidant levels in the vitreous.

Conclusions: The study demonstrates that the lens is able to export AsA and DHA into the vitreous and that connexin 46 may be involved in mediating this process. In addition, preliminary evidence suggests that removal of the lens results in a decrease in GSH levels in the vitreous. Since it is proposed that the lens exports GSH into the vitreous to maintain high AsA levels, removal of the lens would potentially disrupt antioxidant exchange between the lens and vitreous. These findings highlight the inter-dependence of the lens and vitreous for maintaining antioxidant levels and minimizing oxidative stress in the eye.

CONTROL ID: 3538037

SUBMITTER (NAME ONLY): Nivetha Srinivasan

TITLE: Catching Eyes: An Analysis of Medical Student Publications in the Ophthalmology Match

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Srinivasan, B. Zhou, V. Taruvai, S. Nadkarni, A. Song, A.S. Khouri, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmology is an increasingly competitive specialty with 790 applicants applying to 484 spots in the 2019 Match. Research is an important factor used to evaluate potential applicants. Each year, SF Match releases an ophthalmology match summary report detailing different metrics of applicants. However, this dataset fails to include research output. We aim to analyze the temporal trends in publication volume by medical students who successfully matched into ophthalmology.

Methods: The Doximity Residency Navigator, sorted by reputation, was used to identify the top 30 ophthalmology residency programs in the United States. All residents from the class of 2022 and 2017 were identified from program websites; 158 residents were analyzed from the class of 2022 and 145 residents were analyzed from the class of 2017. Publication volume (first author, second author, ophthalmology journal, and total publications) from before September 15th of the application year for each resident was recorded using PubMed and Google Scholar. Using Welch's t-test, publication volumes were statistically compared against all others.

Results: Total publications (mean \pm SE) for residents were 2.95 \pm 0.33 for the class of 2022 and 1.67 \pm 0.23 for the class of 2017; mean publications in ophthalmology journals were 1.00 \pm 0.18 (2022) and 0.58 \pm 0.13 (2017); mean first author publications were 0.95 \pm 0.12 (2022) and 0.64 \pm 0.11 (2017) and mean second author publications were 0.63 \pm 0.10 (2022) and 0.37 \pm 0.06 (2017) (Table 1). Both total publications and second author publications were significantly higher for the class of 2022 than the class of 2017 ($p<0.01$; $p<0.05$) with observed differences of 55.4% and 52%, respectively. Although there were no significant differences in first author publications ($p=0.069$) or in ophthalmology journals ($p=0.069$), the observed p-values support the trend of increasing research among students.

Conclusions: Overall, the authors found a temporal trend towards increased publications amongst applicants. While this study helps map out a 5-year period, it does not delineate between abstracts, presentations, or publications; further studies are needed to determine the individual value of these subcategories. Nevertheless, this analysis emphasizes both the growing importance of research and can help future applicants navigate the ophthalmology match.

CONTROL ID: 3538053

SUBMITTER (NAME ONLY): DIANA SALAZAR

TITLE: The Michigan Screening and Intervention for Glaucoma and Eye Health through Telemedicine Program (MI-SIGHT): Initial Cohort Characteristics

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. SALAZAR, L.M. Niziol, M.A. Woodward, A. Elam, D. Musch, J. zhang, S. Winter, P. Newman-Casey, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|D. Musch, Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, UNITED STATES|L. Johnson, Hamilton community health network, Flint, Michigan, UNITED STATES|M. Kershaw, hope clinic, Ypsilanti, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The MI-SIGHT program is a telemedicine-based glaucoma and eye health screening program that includes treatment for refractive error, the leading cause of reversible vision loss in the US. Impoverished communities are disproportionately comprised of racial/ethnic minorities who are at higher risk both of glaucoma and visual impairment due to untreated refractive error. We hypothesize that embedding glaucoma screening programs that include treatment for refractive error in trusted community clinics will engage underserved communities in glaucoma screening. We will describe the baseline characteristics and screening outcomes of the initial cohort of participants in the MI-SIGHT Program and how they learned about the program

Methods: Using community-engaged research methods, the MI-SIGHT program was established in a free clinic in Eastern Michigan. Participants completed a baseline survey assessing demographic information and how they learned of the program. Participants underwent refraction, measurement of intraocular pressure and central corneal thickness, external and fundus photos, and retinal nerve fiber layer OCT, which was transmitted to the grading ophthalmologist via the electronic health record. An ophthalmic technician assisted participants in choosing glasses from a low-cost online retailer, and fit the glasses when participants returned to learn about the ophthalmologist's diagnosis and recommendations

Results: Seventy-two participants (65% female; mean \pm SD age 55.2 \pm 16.0 years) were included from 8/1/20-11/20/20. The initial cohort was 43% Black and 15% were of Hispanic ethnicity. 68% of participants did not have insurance and 85% of participants had an annual income < \$30,000. (Table 1) More than half of the participants (58%) learned of the program through the clinic staff and 11% learned of it from flyers in the clinic's dental and food pantry services. Based on the testing, participants presented with: glaucoma or suspected glaucoma (28%), visual impairment (26%), diabetic retinopathy (14%, 45% of those with diabetes), and macular degeneration (6%)

Conclusions: The MI-SIGHT program was set up in a free clinic widely trusted by community members, which enabled engagement of participants from underserved populations who are at high risk of vision impairment and eye disease

CONTROL ID: 3538060

SUBMITTER (NAME ONLY): Di Huang

TITLE: Using induced pluripotent stem cell-derived retinal pigment epithelial cells to model splicing defects of ABCA4 c.5461-10T>C detected in an Australian Stargardt disease cohort

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Huang, M.T. Aung-Htut, A. Adams, S. Fletcher, S. Wilton, Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Perth, Western Australia, AUSTRALIA|S. McLenachan, S. Chen, D. Zhang, R.C. Heath Jeffery, M. Attia, T.L. McLaren, T.M. Lamey, J.N. De Roach, F.K. Chen, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|J.A. Thompson, T.L. McLaren, T.M. Lamey, J.N. De Roach, Australian Inherited Retinal Disease Registry and DNA Bank, Department of Medical Technology and Physics, Sir Charles Gairdner Hospital, Nedlands, Western Australia, AUSTRALIA|S. McLenachan, S. Chen, D. Zhang, R.C. Heath Jeffery, M. Attia, F.K. Chen, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|D. Huang, M.T. Aung-Htut, S. Fletcher, S. Wilton, Centre for Neuromuscular and Neurological Disorders, Perron Institute for Neurological and Translational Science, Perth, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Stargardt disease (STGD1, OMIM: 248200) is mainly caused by missense, frameshifting or nonsense mutations in the ATP-binding cassette transporter gene, ABCA4. However, sequence variants that alter splicing are also pathogenic. Herein, we describe an in vitro investigation of aberrant splicing in ABCA4 variants detected in a STGD1 cohort using patient-derived fibroblast-based assay. In addition, retinal pigment epithelium (RPE) cells differentiated from patient-derived induced pluripotent stem cells (iPSC) were used to further validate such splicing errors.

Methods: A cohort of 68 patients clinically diagnosed with STGD1 were recruited in this study. Genomic DNA obtained from recruited STGD1 patients was analysed by a commercial Stargardt/Macular dystrophy screening panel, targeting all exons of ABCA4 and flanking intronic regions, as well as already-known deep-intronic variants of ABCA4. Fibroblasts were propagated from 68 patients, total RNA was extracted and ABCA4 transcript structure was analysed by RT-PCR. The iPSCs reprogrammed from 2 patients carrying heterozygous c.[5461-10T>C;5603A>T] alleles were differentiated into RPE cells and the ABCA4 transcripts re-examined by RT-PCR.

Results: A total of 73 unique ABCA4 alleles were identified. Biallelic ABCA4 variants were detected in 66 patients (66/68, 97.06%) and 2 patients (2/68, 2.94%) had a single ABCA4 variant detected. Only exons 13-50 of ABCA4 could be readily amplified from fibroblast RNA. In this region, 9 out of 55 (16.36%) variants, carried by 19 patients (28%), resulted in aberrant splicing. The most prevalent splice variant, c.5461-10T>C, is complexed with c.5603A>T and carried heterozygously by 7 patients (10%). This variant results in mature ABCA4 mRNA transcripts missing exon 39, or exons 39 and 40. The splicing defect was also evident in patient-derived iPSC-RPE cells.

Conclusions: Patient-derived fibroblasts are useful for identifying ABCA4 splicing variants affecting exons 13-50. The iPSC-RPE cells provide a feasible platform for further validating retina-specific splice variants of ABCA4 that may be amendable to splice intervention therapies.

CONTROL ID: 3538072

SUBMITTER (NAME ONLY): Fan Yi

TITLE: The impact on short term axial length and vision performance of myopia control optics with coaxial and non-coaxial plus power lenslets

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Yi, B. Davis, M.J. Collins, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|N.A. Brennan, X. Cheng, Johnson and Johnson Vision, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study investigated the changes in short-term axial length (AxL) and vision performance during exposure to simulated optical designs with coaxial and non-coaxial plus power lenslets, induced by adaptive optics (AO).

Methods: An optical design with multiple lenslets of plus power (0.79 mm in diameter at pupil plane) distributed evenly over its optical zone (40% fill factor) was created through a spatial light modulator AO system. Between the plus power lenslets, the remaining optical area (60%) was optimally focussed for distance vision. Two types of plus power zones were tested; (i) coaxial, where lenslets created a single focal point (+10 D) in front of the retina on the optical axis, and (ii) non-coaxial, where lenslets created multiple focal points (+10 D) in front of the retina, with the central ray of each lenslet directed to the fovea. Six healthy young with normal vision subjects participated in the study. Subjects watched a movie through the AO system and AxL was measured with a Lenstar LS-900 biometer before, at 20 mins and after 40 mins exposure to the test designs. VA was tested with high-contrast tumbling E letters displayed on a micro-display in the AO system and contrast sensitivity (CS) was tested with an E letter target (0.5 logMAR) that was controlled by a QUEST algorithm.

Results: At the end of 40 mins, coaxial and non-coaxial designs caused a significant and similar reduction in axial length compared to baseline (-5.7 ± 3.6 vs -8.3 ± 6.2 μm respectively, both $p < 0.05$) (Figure 1). The optical design with coaxial plus power lenslets caused a larger loss of VA of 0.15 ± 0.04 logMAR compared to the design with non-coaxial plus power lenslets with 0.07 ± 0.05 logMAR loss ($t=3.2$, $p < 0.05$) (Figure 2). A greater loss of CS was also found with the coaxial plus power zones causing a loss of 0.08 ± 0.02 of Weber contrast compared to the non-coaxial design, with a CS loss of 0.03 ± 0.02 . ($t=4.8$, $p < 0.005$).

Conclusions: Optical designs utilizing non-coaxial plus power lenslets were found to produce similar shortening effects on short-term axial length, while causing a smaller loss in visual performance than designs using conventional coaxial plus power lenslets.

CONTROL ID: 3538082

SUBMITTER (NAME ONLY): Ziming Luo

TITLE: Rapid protocol for induced retinal ganglion cell differentiation from human stem cells

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Luo, K. Chang, B. Tanasa, J.L. Goldberg, Ophthalmology, Stanford University, Palo Alto, California, UNITED STATES|M. Wernig, Pathology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) replacement therapy could provide an approach to vision restoration in glaucoma and other optic neuropathies. Here we developed a rapid protocol for directly induced RGC differentiation from human stem cells.

Methods: We directly induced RGC-like cells (iRGCs) from hiPSCs and hESCs by overexpression of NGN2. Cells gained their RGC fate in less than two weeks in the full-Sato medium (RGC culture medium) supplied by Notch inhibitor, DAPT. Immunostaining and qRT-PCR were performed to confirm their RGC characteristics. Calcium imaging stimulated by GABA agonist muscimol was used to evaluate their electrophysiologic maturities. Then, we utilized single-cell RNA sequencing (scRNA-seq) to further delineate the iRGC differentiation and compare their transcriptomic profiles to fetal and organoid RGCs. All experiments were conducted at least three times independently. Data were analyzed by ANOVA and post-hoc t-test with Tukey correction, with a P-value of <0.05 considered statistically significant. All use of animals conformed to the ARVO statement for the Use of Animals in Research, and was approved by the IACUC and the Institutional Biosafety Committee of Stanford University.

Results: Within one week of induction, neuronal morphology including neurite growth was observed. Progeny expressed RGC markers, including BRN3a, ISL1, HuD, and NEFL after 8 days of differentiation. qRT-PCR confirmed the reduction of pluripotent genes (POU5F1 and NANOG) and the upregulation of neuronal genes (PAX6, BRN3a, and ISL1). iRGCs demonstrated muscimol-induced calcium influx similar to immature primary mouse RGCs. Unbiased clustering in scRNA-seq data showed that iRGCs distributed closely but not overlapping with day-59 and day-82 fetal human RGCs, indicating high similarity. Compared with day-45 retinal organoid-derived RGCs, iRGCs largely overlapped in most clusters. However, for some marker genes including BRN3a, Brn3b, and NEFL, iRGCs demonstrated expression patterns more similar to fetal RGCs than to retinal organoid RGCs.

Conclusions: In the present study, we describe a new, effective method that generates a homogeneous population of iRGCs after over-expression of a single transcription factor in human stem cells. These iRGCs are highly similar to two-month-old fetal RGCs, although they develop in less than two weeks. The simplicity of this system may benefit the translational studies on human RGCs.

CONTROL ID: 3538096

SUBMITTER (NAME ONLY): Nathan Dhablania

TITLE: Burden and Predictors of Undetected Eye Disease in Adult African Americans: The African American Eye Disease Study (AFEDS)

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Dhablania, M. Torres, B. Burkemper, R. Varma, Southern California Eye Institute, Los Angeles, California, UNITED STATES|B. Burkemper, R. McKean-Cowdin, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To estimate the burden of and to evaluate the factors associated with undetected eye disease (UED) among a population-based sample of African American adults ≥ 40 years of age.

Methods: Data for these analyses were extracted from the African American Eye Disease Study (AFEDS), a population-based study of adult African Americans, aged 40 years and older, residing in and around the city of Inglewood (Los Angeles County, California). All participants underwent a detailed home interview and a comprehensive eye examination, including an assessment of ocular conditions such as age-related macular degeneration (AMD), glaucoma, ocular hypertension, diabetic retinopathy, cataract, and refractive error. Participants with any eye disease ($N = 3500$) were included in these analyses, and the prevalence of UEDs was calculated. Chi-square test analyses were used to evaluate bivariate associations between risk indicators and any UED. The independent association with UED and the predisposing, enabling, need and health behavior characteristics was explored using multiple logistic regression analysis. Standardized β coefficients were used to determine the relative contributory effect of each independent factor on the presence of UED.

Results: Of the 7957 eligible participants in the AFEDS, 6347 (80%) completed both the in-home interview and the clinical examination. Fifty-five percent (3500 of 6347) of the participants had eye disease. Twenty-six percent (914 of 3500) of them had undetected eye disease. The primary undetected eye diseases included diabetic retinopathy (75.1%), cataracts (60.8%), refractive error (55.0%), ocular hypertension (33.3%), open-angle glaucoma (16.5%), and AMD (7.5%). The major risk factors for UED included having diabetes mellitus odds ratio (OR): 4.1, never having had an eye examination (OR: 2.4), having had an eye examination more than 5 years ago (OR: 2.2), lower educational attainment (OR: 2.0), having poor or very poor general vision (OR: 1.7), and trouble getting glasses (OR: 1.6).

Conclusions: These findings provide evidence of the significant burden of UED among African Americans. Interventions that address the modifiable risk factors (e.g., trouble getting glasses, never having had an eye examination) may improve detection of eye disease and decrease the burden of visual impairment in this high-risk minority population.

CONTROL ID: 3538103

SUBMITTER (NAME ONLY): Marwan Abdulaal

TITLE: Subretinal Pneumatic Displacement without Tissue Plasminogen Activator for Submacular Hemorrhage: One-year Outcomes.

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Abdulaal, J.M. Coney, Ophthalmology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|J. Robertson, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|M.T. Moore, University System of Maryland, Adelphi, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the outcome of pneumatic displacement of submacular hemorrhage with Subretinal Air and without tissue plasminogen activator (TPA) for thick submacular hemorrhages (SMH).

Methods: Retrospective analysis of patients with submacular hemorrhage managed surgically via pneumatic displacement without TPA from 2015 and 2020. Surgical intervention across all doctors included subretinal Balanced Saline Solution (BSS) infusion with subretinal sterile air, and intraocular gas tamponade with and without postsurgical anti-vascular endothelial growth factor (VEGF) injection. 24 patients with SMH and at least 8 months of follow up were identified. All medical records and color fundus photographs were reviewed for data collection. The primary outcome measure was best-corrected visual acuity (BCVA) 12 months after treatment. Secondary outcome measures included central retinal thickness (CRT), recurrence rate, and complications.

Results: Patients had a mean age of 81 ± 8.6 years. Wet age-related macular degeneration was the most common etiology associated with thick SMH (92%). Complete blood displacement was observed by final follow up in 92% of the cases and none in 8.0%. Mean logMAR BCVA improved from 1.2 ± 0.27 (20/320 at baseline) to 0.9 ± 0.42 (Snellen 20/160; $p = 0.001$) at final follow-up. 63% of the patients gained at least 2 lines by the 12 months of follow up. Mean central retinal thickness was also improved from $569\mu \pm 220$ at baseline to $252\mu \pm 63$ by 12 months of follow up ($P < 0.001$). Early postoperative complications included vitreous hemorrhage in two cases and retinal detachment in 2 patients. It was noted that 11 patients (46%) developed subretinal fibrosis at 12 months of follow up.

Conclusions: Vitrectomy with subretinal BSS injection and pneumatic displacement without TPA was found to be effective for displacement of thick submacular hemorrhage with improvement in visual acuity

CONTROL ID: 3538104

SUBMITTER (NAME ONLY): Michele Madigan

TITLE: Melanocytes, Inflammation and Responses in the Human Choroidal Microenvironment

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.C. Madigan, C. Wu, Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|M.C. Madigan, R. Conway, Save Sight Institute, The University of Sydney, Sydney, New South Wales, AUSTRALIA|M.J. Jager, Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|R.C. Natoli, V. Cioanca, JCSMR, Australian National University, Canberra, Australian Capital Territory, AUSTRALIA|

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ABSTRACT BODY:

Purpose: In the human choroid, melanocytes (HCMs) contribute functions including melanin-related light absorption and uptake of free radicals, with a potential for immunoregulation via local secretion of chemokines/cytokines and expression of Toll-like receptors (TLRs). The biological responses of HCMs to a proinflammatory stimulus (lipopolysaccharide (LPS) - a TLR4 ligand), related to possible roles in the choroidal stromal microenvironment were studied using transcriptome and pathway analyses, and protein-based methods.

Methods: Primary HCMs isolated from human donor eyes (n=4; <18 hours post-mortem delay; University of Sydney HREC) were established in melanocyte growth medium. RNA from HCMs (P3 to P5: control and LPS-stimulated (1µg/ml, 18 hours) was used to establish cDNA libraries, that were sequenced (Illumina HiSeq 2500) and analysed using bioinformatics (including gene ontology (GO) and gene set enrichment analysis. We confirmed several novel cell-cell adhesion and cell-extracellular matrix (ECM) genes using immunoblotting and immunohistochemistry.

Results: 100 differentially expressed genes were detected (98 genes upregulated, 2 genes downregulated; fold change $\geq \pm 2$, $p < 0.01$) were found for control versus LPS-stimulated HCMs. As expected, a number of most differentially expressed genes included CCL and CXCL cytokines (for example, CCL20, CCL2 and CXCL5; 43 to 316-fold, $p < 0.01$). Genes that can mediate intercellular adhesion and cell-ECM interactions also were highlighted (for example, ITGA1 and 11, CCN3, MMP14, COL7A1 and FN1; 1.4 to 23-fold; $p < 0.01$). We also verified several LPS-induced genes, finding changes in HCM protein expression for CCN3, MMP14, FN1 and ICAM1. We also confirmed in situ immunolabelling in donor human eye choroid sections with confocal microscopy.

Conclusions: Our study confirms a proinflammatory shift in biological processes and genes for LPS-stimulated HCMs. Furthermore, we observed gene and protein expression patterns not previously highlighted, including significant GO terms related to "cellular adhesion" and "cell-matrix adhesion", "cell adhesion mediated by integrins" and "collagen binding involved in cell matrix adhesion". Taken together, these observations suggest HCMs can contribute more to the complex choroidal biology than light-absorption, with roles in maintaining and regulating the local choroidal microenvironment, normally and during inflammatory conditions.

CONTROL ID: 3538107

SUBMITTER (NAME ONLY): Tyler Knight

TITLE: Lensectomy as Treatment for Refractory or Progressive Retinopathy of Prematurity Narrow-Angle Glaucoma

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Knight, D.A. Morrison, K.M. Joos, Ophthalmology, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Tyler Knight: Commercial Relationship: Code N (No Commercial Relationship) | David Morrison: Commercial Relationship(s);Regeneron - unrelated ROP project:Code F (Financial Support) | Karen Joos: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Anatomical narrow angle and glaucoma from increased lens thickness, and/or scarring and forward displacement of the lens-iris-diaphragm can result from threshold retinopathy of prematurity (ROP) treated with laser or cryotherapy. This study investigates the efficacy of lensectomy in treatment of anterior chamber angle narrowing in ROP patients.

Methods: This retrospective study was approved by the Vanderbilt University Medical Center (VUMC) Institutional Review Board and Vanderbilt Institute for Clinical and Translational Research (VICTR). The cohort was identified by querying the VICTR Research Derivative database for clinical data (1995-2020) derived from the VUMC's clinical systems and restructured for research. Patients were identified by ICD-9 or ICD-10 codes for 1) ROP and 2) narrow angle or glaucoma. Patient demographics and clinical course as available in the medical records were recorded in a secure format, including: sex, post-conceptual birth age, treatment of ROP, age at diagnosis of anatomical narrow angle or angle-closure glaucoma, glaucoma medication use, iris procedure performed and outcome, age and angle status at lensectomy, and final outcome. Descriptive statistics were performed.

Results: Initial query yielded 70 patients. 42 patients were excluded for 1) no evidence of narrow angles 2) prematurity without ROP, and 3) limited medical record information/follow up. Of the remaining 28 patients, 48 eyes demonstrated narrow angle or glaucoma: 53.6% were female, mean post-conceptual birth age was 25.1 (23-28) weeks, 90.9% of patients required treatment for ROP. Mean and median age at diagnosis of anatomical narrow angle or angle-closure glaucoma were 9.5, 15 (1-37) years. 66.7% of eyes with narrow/closed angles underwent iridotomy/iridectomy +/- iridoplasty shortly after diagnosis. 57.6% of these eyes subsequently required glaucoma medication. Mean and median age at lensectomy for treatment of narrow angle or angle-closure were 20.3, 17 (2-38) years, with 47.8% occurring during teenage years. Deepening of the anterior chamber occurred in 19/23 eyes after lensectomy.

Conclusions: This case series demonstrated: 1) continued monitoring of patients with history of ROP and narrow angles is crucial into adulthood especially during the teenage years and 2) lensectomy in patients with refractory or progressive narrow angles after iridotomy/iridectomy +/- iridoplasty is efficacious.

CONTROL ID: 3538109

SUBMITTER (NAME ONLY): Supriya Arora

TITLE: One year outcome and predictors of treatment outcome in central serous chorioretinopathy (CSCR): multimodal imaging based analysis

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Arora, T. Arora, Princess Margaret Hospital, Nassau, BAHAMAS|N.K. Sahoo, L V Prasad Eye Institute, Vijaywada, INDIA|D. Parameshwarappa, L V Prasad Eye Institute, Hyderabad, INDIA|D.S. Maltsev, A. Kulikov, Military Medical Academy, St. Petersburg, RUSSIAN FEDERATION|C. Iovino, F. Tatti, E. Peiretti, Department of surgical sciences, University of Cagliari, ITALY|S. Singh, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|R. Gujar, M. Lupidi, Department of biochemical and surgical sciences, University of Perugia, ITALY|J. Chhablani, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|R.S. Venkatesh, N. Reddy, R. Snehith, Narayana Nethralaya, Bangalore, Karnataka, INDIA|

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ABSTRACT BODY:

Purpose: To evaluate treatment outcome of eyes with CSCR based on multimodal imaging based classification over one year of follow up.

Methods: Retrospective data of eyes diagnosed with CSCR and available history, visual acuity (VA) and multimodal imaging at baseline, 3 months, 6 months and 12 months and treatment details were included. Eyes with macular neovascularization, any other disease and inadequate follow up after treatment were excluded. Eyes were classified as per the multimodal imaging based classification of CSCR at baseline and every follow up into i) simple/ complex CSCR ii) primary episode/ recurrence/ resolved CSCR iii) persistent or not iv) outer retinal atrophy (ORA) present or not and v) fovea involved or not.

Results: Ninety-one eyes of 87 patients were classified into 50 eyes with simple CSCR and 41 eyes with complex CSCR. Complex CSCR cases had higher persistence, ORA and recurrent episodes ($p=0.0005, 0.0008, 0.0008$) while simple cases had higher central macular thickness (CMT) ($p=0.02$) at baseline. The most common choice of treatment was observation (58%) in simple CSCR and PDT (36.6%) in complex CSCR ($p=0.02$). In simple CSCR, logarithm of minimum angle of resolution (logMAR) best corrected visual acuity (BCVA), subfoveal choroidal thickness (SCT) and CMT decreased ($p=0.02, 0.02, <0.0001$) while persistence of subretinal fluid (SRF) and ORA increased ($p<0.0001, 0.0002$) over 12 months. In complex CSCR, CMT decreased ($p=0.0009$) and ORA ($p=0.037$) increased over follow up but the decrease in CMT over 12 months was more significant in simple CSCR compared to complex CSCR ($p=0.002$). In multivariate analysis, baseline BCVA ($p<0.0001$) was a significant predictor of final BCVA. Over a mean follow up of 21.7 ± 16.8 months, none of the simple CSCR eyes converted to complex CSCR. Resolution of SRF, occurrence of ORA and recurrence during the follow up period was not significantly different between simple and complex CSCR ($p=0.86, 0.46, 0.73$).

Conclusions: Both visual and anatomical outcomes changed significantly in simplex CSCR group with observation being the most common treatment. PDT in complex CSCR helped to stabilize the vision. Baseline VA was significantly predictive of final visual outcome.

CONTROL ID: 3538123

SUBMITTER (NAME ONLY): Sharon Bentley

TITLE: Concept mapping to develop timed measures of low luminance vision-related ADLs

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Bentley, A.A. Black, G. Hindmarsh, J.M. Wood, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|C. Owsley, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low light levels exacerbate performance deficits and are particularly challenging for adults with vision impairment. This is an important issue in the evaluation and monitoring of changes in performance following novel eye and vision therapies, as existing performance-based measures do not specifically consider low luminance conditions. This study aimed to identify low luminance activities of daily living (ADLs) relevant to adults with vision impairment as the basis for the development of a battery of timed low luminance vision-related performance-based measures.

Methods: 'Group Concept Mapping' (Concept Systems Inc., NY) was used to identify low luminance vision-related ADLs. The process integrates qualitative and quantitative research methods to produce concept maps and data displays, resulting in comprehensive visual representations of key ideas/activities and their interrelationships. In the first 'brainstorming' phase, 24 adults with vision impairment from a range of eye conditions (mean age 73, SD 14 years) and 26 international low vision experts (mean experience 22, SD 11 years) responded to the focus prompt (via mail, phone or a web-based application): "Thinking as broadly as possible, generate a list of statements detailing specific day-to-day activities a person with vision impairment might find challenging under low light conditions, such as in a poorly lit room or outside at dusk." In the second phase, participants rated the importance of each activity generated and sorted activities by their similarity (in a face to face session or a via a web-based application).

Results: 113 potential ideas/activities were generated, rated and sorted. Using multidimensional scaling and hierarchical cluster analysis, concept maps showing clusters of prioritised activities were produced from the data. Eight groups of activities were identified (from highest to lowest importance ratings): mobility hazard detection and safety; navigating outside the house; social communication; selfcare and safety at home; near reading; distance spot reading; home maintenance; and navigating around the house.

Conclusions: The low luminance ADLs identified will be used to develop relevant and sensitive clinical endpoint measures for objectively assessing the efficacy of eye treatments and low vision rehabilitation outcomes in adults with vision impairment.

CONTROL ID: 3538127

SUBMITTER (NAME ONLY): Tony Chen

TITLE: Risk Factors of Ischemic Stroke in Patient Presenting with Amaurosis Fugax

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chen, A. Uppuluri, M.A. Zarbin, N. Bhagat, Rutgers New Jersey Medical School
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ABSTRACT BODY:

Purpose: Amaurosis fugax (AF) is associated with increased cerebrovascular morbidities and mortalities. Better risk stratification of AF is crucial in recognizing those at highest risk of developing ischemic stroke. We performed a retrospective, cross-sectional study using a national database to evaluate the risk factors for ischemic stroke in patients with acute AF.

Methods: The National Inpatient Sample database from 2002–2014 was used. All patients 21 years old and above with a primary admission diagnosis of AF were identified using ICD-9 codes 362.34. Patients were further stratified into two age cohorts: 21-50 years and over 50 years. The primary outcome was to evaluate comorbidities associated with in-hospital ischemic stroke. Chi-square and Firth logistic regression analyses were performed using IBM SPSS 25 and R package version 3.4.3, respectively. $p < 0.05$ was considered significant for Chi-square and univariate analyses, whereas $p < 0.005$ was considered significant for multivariable analysis.

Results: A weighted total of 12,142 patients were identified. The average age of patients was 66 ± 14 years, where 87% of cases were over 50 years of age. Whites accounted for 62.1% of cases. The most common comorbidities included hypertension (66.1%), dyslipidemia (44.7%), tobacco use (23.6%), coronary artery disease (CAD) (23.0%), and diabetes mellitus (19.6%). Tobacco use, alcohol use, and hypercoagulable state were statistically more prevalent in the younger group ($p < 0.001$). Surprisingly, ischemic stroke ($p = 0.033$) and myocardial infarction ($p = 0.008$) were significantly more prevalent in the younger cohort.

Multivariable logistic regression analysis detected the followings comorbidities to be independent risk factors for ischemic stroke: Hypercoagulable state (OR 8.98, $p < 0.001$), systemic vasculitis (OR 4.16, $p = 0.003$), CAD (OR 4.05, $p < 0.001$), and atherosclerosis (OR 3.60, $p < 0.001$). In contrast, dyslipidemia was associated with a decreased risk (OR 0.54, $p = 0.003$). Asian/Pacific Islander ethnicity conferred a 5-fold increased risk in stroke compared to Whites ($p < 0.001$).

Conclusions: In-hospital systemic thrombotic complications occurred in 0.3%-0.9% of acute AF cases (average length of stay was 2.62 ± 2.17 days). Presence of hypercoagulable state, systemic vasculitis, CAD, and atherosclerosis increased the risk of ischemic stroke by over 3-fold. Thus, patients should be closely monitored for stroke within the first week of AF diagnosis.

CONTROL ID: 3538153

SUBMITTER (NAME ONLY): Angela Gauthier

TITLE: Why can't I see 20/20? Factors predictive of suboptimal vision after toric lens implantation

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gauthier, A. Awidi, Y. Daoud, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|P. Noble, University of Iowa, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine patient characteristics and biometry data associated with residual refractive error after toric lens implantation for patients with astigmatism.

Methods: A retrospective case-control chart review of eyes with residual refractive error and eyes that met target refraction at one month and beyond after cataract surgery with toric lens implantation by the same surgeon was conducted. Eyes with residual refractive error were defined as achieving UCVA of 20/40 or worse and BCVA better than 20/40 with a difference in logMAR UCVA and BCVA of 0.3 or more, while eyes that met target refraction achieved an UCVA of better than 20/40 after cataract surgery. All patients were aimed for distance. Pre-operative exam findings, ophthalmologic comorbidities, and intraocular lens measurements were collected.

Results: In total, 30 eyes in 29 patients with residual refractive error and 194 eyes in 167 patients who met target refraction were included. The mean age of patients with residual refractive error was 63.1 years (SD 11.3) vs. 69 years (SD 7.9) for patients who met target refraction ($p=0.009$). Compared to eyes at target refraction, a greater percentage of eyes with residual refractive error had undergone previous LASIK surgery (23.3% vs. 5.7%) and carried a keratoconus diagnosis (6.7% vs. 0.5%). Both groups had a similar prevalence of dry eye (30.0% vs. 30.4%) and ABMD (10.0% vs. 9.3%). A smaller percentage of patients with residual refractive error had Fuch's dystrophy (3.3%) compared to those at target refraction (13.9%). There was no significant difference in axial length between eyes with residual refractive error (24.68 mm, SD 1.84 mm) and those at target (24.60 mm, SD 1.60, $p=0.83$) or anterior chamber depth (3.29 mm, SD 0.52 vs. 3.35 mm, SD 0.42, $p=0.54$). There was a trend toward eyes with residual refractive error having a greater average corneal astigmatism (2.03 D, SD 1.49) compared to eyes at target refraction (1.51 D, SD 0.62, $p=0.076$).

Conclusions: Patients who had residual refractive error after cataract extraction with toric lens implantation on average were younger than those who met target refraction. In addition, a greater proportion of patients who had residual refractive error had previous LASIK and keratoconus compared to those at target refraction. Understanding these factors can help manage visual outcome expectations after toric lens implantation in patients with astigmatism.

CONTROL ID: 3538173

SUBMITTER (NAME ONLY): Christopher Riemann

TITLE: Phase I/IIa Clinical Trial of Transplanted Allogeneic Retinal Pigmented Epithelium (RPE, OpRegen) Cells in Advanced Dry Age-Related Macular Degeneration (AMD): Interim Results

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.D. Riemann, Cincinnati Eye Institute, Cincinnati, Ohio, UNITED STATES|E. Banin, T. Jaouni, Center for Retinal and Macular Degenerations, Department of Ophthalmology, Hadassah-Hebrew University Medical Center, Jerusalem, ISRAEL|A. Barak, Department of Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, ISRAEL|D.S. Boyer, Retina Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|R. Ehrlich, Department of Ophthalmology, Rabin Medical Center, Petah Tikva, ISRAEL|A. Ho, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|R. McDonald, West Coast Retina Group, San Francisco, California, UNITED STATES|D. Telander, Retinal Consultants Medical Group, Sacramento, California, UNITED STATES|J. Mones, Institut de la Màcula, Barcelona, SPAIN|J. Velez, G.S. Hogge, Lineage Cell Therapeutics, Inc., Carlsbad, California, UNITED STATES|B. Reubinoff, Center for Embryonic Stem Cells and the Department of Gynecology and Obstetrics, Hadassah-Hebrew University Medical Center, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: Transplanted healthy RPE cells may benefit AMD patients. We created allogenic RPE cells (OpRegen) using directed differentiation. Safety and tolerability of OpRegen is being evaluated in a Phase I/IIa clinical study in patients with dry AMD and geographic atrophy (GA) (NCT02286089). We report interim safety and imaging data from all patients in the fully enrolled study (N=24).

Methods: Subretinal transplantation of 50-200k OpRegen cells in suspension to the worse vision eye used either pars plana vitrectomy (PPV) and retinotomy or the OrbitTM Subretinal Delivery System (SDS). Short course, perioperative systemic immunosuppression was used. Endpoints include systemic/ocular safety and retinal structure/function.

Results: Patients (VA <20/200) in cohorts 1-3 are in long-term follow-up (10/12; 2-5 years) or withdrawn (2/12). 12 better seeing patients (<20/64) in cohort 4 completed dosing in November 2020 (7 PPV:5 SDS). OpRegen has been well tolerated to date, with no unexpected adverse events (AEs). Using PPV, the most common ocular AEs were epiretinal membranes (ERM), in 15/17 (88%) eyes, mostly mild to moderate; 3 (18%) severe ERM required surgical

peeling. 2 PPV-treated patients (2/17;12%) developed retinal detachments, which were successfully treated. AEs, all mild, in Orbit SDS patients included one asymptomatic extramacular type 2 CNV, successfully treated with a single anti-VEGF injection, and subretinal hemorrhage (3/7;43%), all self-resolved without sequelae. Subretinal delivery of OpRegen was successful in 7/7 patients by 5 different surgeons. Improvement or maintenance of baseline visual acuity has been noted in 11/12 (92%) cohort 4 patients (-9 to +19 letters), which has been maintained from 2 months to >2 years. Treatment effects, including alterations in drusen appearance, subretinal pigmentation and hyper-reflective areas, suggest persistence of transplanted OpRegen. One patient has potential signs of retinal restoration and reduction in GA area based on OCT analyses of the periphery of the GA, which continues to be followed.

Conclusions: Subretinal transplantation of OpRegen cells in patients with dry AMD and GA appears well tolerated. Imaging findings suggest presence of transplanted cells in the subretinal space. Encouraging structural and clinical changes observed in some patients are being followed.

CONTROL ID: 3538222

SUBMITTER (NAME ONLY): Abiramy Logeswaran

TITLE: Responses of conjunctival goblet cells to microbial products promote activation of local antigen presenting cells

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Logeswaran, L. Contreras-Ruiz, S. Masli, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conjunctival goblet cells (GCs) contribute to ocular immune homeostasis via Thrombospondin-1 (TSP-1)-mediated TGF β 2 activation, which in turn modulates dendritic cell (DC) phenotype by decreasing expression of activation markers, including MHC class II. This study determined the location of antigen presenting cells (APCs) in the conjunctiva and tested the hypothesis that microbial product flagellin (FL)-mediated GC responses disrupt homeostasis to promote APC activation that leads to corneal barrier damage.

Methods: Conjunctival explants or frozen sections from WT (C57BL/6) and TSP-1 $-/-$ mice were immunostained for CD11c, MUC5AC, MHC class II or TSP-1 and examined by confocal or fluorescence microscopy. WT mice were treated with FL (10 ng) topically for 7 days. Corneal barrier was monitored for 4 weeks with fluorescein staining. Primary cultured GCs were treated with FL (0-10mg/ml) or heat-killed pathogenic *S. aeruginosa* strain PA14 for 24 hr. Levels of IL-6 and active TGF β were determined in culture supernatants using ELISA and bioassay respectively. Message for TSP-1 was determined by real-time PCR.

Results: In the conjunctiva CD11c $^{+}$ cells were located adjacent to MUC5AC $^{+}$ GCs. Their cell bodies in the stromal layer, immediately below the epithelial layer, extended processes across the epithelium in TSP-1 $-/-$ conjunctiva previously reported to harbor increased microbial frequency. Such processes were not detected in WT tissue. Frequency of CD11c $^{+}$ MHC class II $^{+}$ cells was increased in FL-treated conjunctiva compared to untreated controls. Primary GC cultures responded to PA14 and FL with an increased IL-6 secretion compared to controls (1193 \pm 58.5, 884 \pm 60.6 vs. 5.6 \pm 0.2 respectively, $p < 0.05$). FL-stimulated GCs secreted reduced active TGF β consistent with their reduced expression of TSP-1 message (1715 \pm 40.7 vs. 4459 \pm 75.2, $p < 0.05$) and immunostaining in FL-treated conjunctiva. These changes correlated with an increased fluorescein staining score 4 weeks after FL treatment compared to the baseline (8.3 \pm 0.5 vs. 2.8 \pm 0.6, $p < 0.05$).

Conclusions: Our results demonstrate that DCs in the conjunctiva can extend trans-epithelial processes, presumably to sample microbes at the ocular surface, and support the hypothesis that their activation can be induced by disrupted GC homeostatic responses by microbial stimuli. These findings implicate GC responses in inducing chronic ocular surface damage.

CONTROL ID: 3538291

SUBMITTER (NAME ONLY): Joseph Hakim

TITLE: Longterm outcomes of Ahmed glaucoma valve (AGV) and Baerveldt glaucoma implant (BGI) in patients with Boston Keratoprosthesis type I (K-Pro)

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hakim, M. Harissi-Dagher, Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|D. Geoffrion, Ophthalmology, McGill University, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: To compare the long-term outcomes of glaucoma drainage devices (GDD) in Boston keratoprosthesis type 1 (KPro) patients, specifically those of the Ahmed glaucoma valve (AGV) versus those of the Baerveldt glaucoma implant (BGI).

Methods: Retrospective cohort study of 44 eyes (44 patients) implanted with a KPro between 2008 and 2017. KPro eyes with AGV (n=35) were compared to those with BGI (n=9) in the main cohort. A sub-cohort comparing KPro eyes with AGV installed pre-KPro (n=9) to those with BGI installed pre-KPro (n=7) was further examined. The primary outcome was GDD failure, defined by uncontrolled intra-ocular pressure, additional glaucoma surgery or tube removal. Secondary outcomes included GDD related complications, change in best-corrected visual acuity (BCVA), intraocular pressure (IOP) and number of glaucoma medications.

Differences in outcomes were compared using parametric and non-parametric tests, as well as log-rank test to compare time-to-outcome events.

Results: Mean age was 60.0 ± 15.4 years at KPro surgery and mean follow-up time was 5.4 ± 2.3 years. In the main cohort, KPro eyes with AGV had a higher cumulative failure probability over time compared to that of eyes with BGI (57.1% versus 11.1%; $P=0.039$). More eyes with AGV required additional glaucoma surgery procedures compared to eyes with BGI (37.1% vs. 11.1%; $P=0.135$). The occurrence of GDD-related complications was similar between AGV and BGI (37.1% vs 33.3%, $P=0.832$). Regarding BCVA, there was an improvement in 55.6% of eyes with BGI compared to 42.9% of AGV eyes ($P=0.71$.) Change in IOP and number of topical glaucoma medications was also comparable in both groups ($P>0.05$) over the follow-up period. In the subcohort, outcomes between GDDs implanted before KPro surgery were concordant with those of the main cohort.

Conclusions: Compared to AGV, BGI implanted in KPro eyes was associated with lower GDD failure rates and slightly higher occurrence of improved BCVA while having a comparable occurrence of long-term postoperative complications.

CONTROL ID: 3538304

SUBMITTER (NAME ONLY): Baikai Ma

TITLE: Objective analysis of corneal subbasal nerve tortuosity and its changes in patients with dry eye disease and diabetes

SESSION TITLE: Dry eye and microbiome clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Ma, T. Yang, R. Liu, Y. Liu, T. Sun, H. Qi, Department of Ophthalmology, Peking University Third Hospital, Beijing, CHINA|J. xie, Y. Zhao, Cixi Institute of BioMedical Engineering, Ningbo Institute of Industrial Technology Chinese Academy of Sciences, Ningbo, Zhejiang, CHINA|

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ABSTRACT BODY:

Purpose: To construct an objective analysis system of corneal nerve tortuosity and detect the changes of corneal subbasal nerve tortuosity in patients with dry eye disease (DED) and diabetes.

Methods: Grade I to IV nerve tortuosity were evaluated and 80 photos of each grade were randomly chosen from the in vivo confocal microscopy library. Nerve fibers were extracted, segmented and then analyzed by 6 tortuosity related parameters including L_C, Seg_L_C_mean, Cur_mean, Specific_p, ICM and SCC_mean. After verifying the validity of parameters above, a cross-sectional study was conducted. Subjects were divided into four groups: control group, DED without diabetes group, diabetes without DED group, diabetes with DED group. 23 to 28 persons in each group. Basic and DED information includes sex, age, OSDI, TBUT, SIt and CFS score. FPG and HbA1c were detected in diabetic patients. C-BE was detected to evaluate corneal sensation and 2 corneal subbasal nerve photos of each eye were selected for effective tortuosity and density related parameters analysis. Data was analyzed by SPSS 20.0. This study followed the Declaration of Helsinki and was approved by Ethic Committee of Peking University Third Hospital. Informed consents were obtained.

Results: L_C, Seg_L_C_mean, Cur_mean, Specific_p, ICM and SCC_mean increased as the nerve tortuosity increased from Grade I to Grade IV (Fig. 1A/1B). Among the above 6 parameters, Cur_mean and L_C of any two groups were of significant difference (all at $P < 0.01$). Sex and age were comparable among 4 groups. Diagnostic criteria were met in dry eye disease (DED) and diabetes (Fig. 1C). Corneal sensation (C-BE) decreased in diabetes without DED group and diabetes with DED group compared with control group (all at $^{Adj}P < 0.05$), other than in DED without diabetes group ($^{Adj}P \geq 0.05$). Nerve density of diabetes without DED group and diabetes with DED group was lower compared with control group (all at $P < 0.001$), while no significant difference between DED without diabetes group and control group ($P \geq 0.05$). Among the effective parameters of tortuosity, L_C, Cur_mean, Seg_L_C_mean and SCC_mean of last 3 groups were higher compared with control group (all at $P < 0.05$) (Fig. 1D).

Conclusions: L_C and Cur_mean are most suitable parameters to analyze corneal nerve tortuosity. Compared with volunteers, patients of DED or diabetes showed higher corneal subbasal nerve tortuosity.

CONTROL ID: 3538327

SUBMITTER (NAME ONLY): Yifang Li

TITLE: Topical ocular TRPV1 antagonist SAF312 demonstrated safety, low systemic exposure, and no anesthetic effect in healthy volunteers

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, M. Jain, K. Stasi, Novartis Institute of Biomedical Research, Cambridge, Massachusetts, UNITED STATES|M. Palmer, Novartis Pharmaceuticals Inc, Fort Worth, Texas, UNITED STATES|S. Haque, Novartis Pharma AG, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: SAF312 is a potent inhibitor of the transient receptor potential cation channel subfamily V member 1 (TRPV1). This first-in-human study evaluated the safety, pharmacokinetics (PK), and cornea esthesiometry of topical ocular SAF312 in healthy volunteers.

Methods: This single-center, double-masked, randomized study comprised of three parts: single-ascending dose (SAD), multiple-ascending dose (MAD), and esthesiometry. Each dose cohort (SAF312 0.15%, 1.5%, 2.5%) included 8 healthy volunteers randomized 3:1 to either SAF312 or vehicle, 1 drop once (SAD), or 1 drop 4-times or 8-times (only for 2.5%) daily for 7 days (MAD). Safety and PK were the primary and secondary objectives. Exploratory objectives included tear production (Schirmer test without anesthesia), tear film break-up time (TFBUT), and blink rate in the MAD groups. Esthesiometry included 12 healthy volunteers randomized equally to 4 sequences consisting of a single drop of SAF312 2.5%, tetracaine 0.5% (anesthetic), diclofenac sodium 0.1% (nonsteroidal anti-inflammatory drug), or vehicle, in a Williams square design.

Results: SAF312 was safe and well tolerated at the maximum concentration 2.5%, 1 drop 8-times daily (7.4 mg/day, supratherapeutic dose) in one eye for 7 days. Most of the adverse events (AEs) were mild and similar between SAF312 and vehicle-treated healthy volunteers (54 healthy volunteers exposed to SAF312). No severe AEs, serious AEs, or deaths were reported. SAF312 was rapidly absorbed into systemic circulation with T_{max} ~0.5 h after single or multiple doses. After supratherapeutic dosing for 7 days, mean steady state exposures (C_{max} , 2 ng/mL and AUC_{0-24h} , 45 h*ng/mL) of SAF312 were low and afforded safety margins of >70-fold compared with systemic exposures in preclinical species at no-observed-adverse-event levels following oral dosing. No clinically relevant changes were observed with SAF312 in the blink rate, tear production, and TFBUT. SAF312 showed no anesthetic effect on the cornea, similar to diclofenac and vehicle as opposed to tetracaine (esthesiometry).

Conclusions: Topical ocular SAF312 was well tolerated with no ocular or systemic safety concerns up to a supratherapeutic (8x daily) dose of the maximum concentration (2.5%); it had no anesthetic effect on the cornea and demonstrated a rapid topical absorption with low systemic exposure in healthy volunteers.

CONTROL ID: 3538356

SUBMITTER (NAME ONLY): Anita Chan

TITLE: Plekha7 knock out (KO) rats show an altered ocular barrier function

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Chan, C. Ho, L.M. Naing, V.A. Barathi, E.N. Vithana, T. Aung, Singapore Eye Research Institute, Singapore, SINGAPORE|A.S. Chan, T. Aung, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To characterise the ocular phenotype of Plekha7 knock out (KO) rats. PLEKHA7 is a robust primary angle closure glaucoma (PACG) susceptibility gene reproducibly observed across patient collections of distinct ethnicities.

Methods: Homozygous Plekha7 KO rats were gifted from Geurts Lab (Wisconsin, USA). These rats were created with zinc-finger nuclease technology in the Guerts Lab on an albino Dahl salt sensitive (SS) rat background. Eight age matched KO and SS controls were serially assessed every month from 6 weeks to 12 weeks using tonometry, slitlamp examination, axial length (AC master), anterior segment-ocular coherence tomography (AS-OCT, Visante). Fluorophotometry (FluorotronMaster) was performed with intraperitoneal injection of fluorescein (0.1 mL/100 g body weight). Animals were also sacrificed for immunohistochemistry (IHC) analysis of Plekha7 and barrier proteins (ZO-1 and occludin).

Results: There was no significant difference in baseline parameters between SS control and Plekha7 KO rat eyes ($p > 0.05$). Mean IOP at 12 weeks between the control and Plekha7 KO rats were not statistically significant (11.2 ± 0.8 mmHg SS control vs 10.8 ± 1.1 mmHg Plekha7 KO, $p = 0.150$). Significant anatomical differences at 12 weeks between SS controls and Plekha7 KO were also not detected: axial length ($p = 0.107$), anterior chamber depth ($p = 0.058$), angle in all 4 quadrants (nasal, temporal, superior and inferior, $p > 0.05$). Fluorophotometry readings show higher immediate fluorescein concentration in the vitreous and anterior chamber. Plekha7 IHC expression shows Plekha7 localisation is detected along the intercellular contact between the non-pigmented ciliary epithelium (NPCE) and the pigmented ciliary epithelium, as well as the outer limiting membrane (OLM) of the retina in SS control rats but not the Plekha7 KO eyes (Figure 1). ZO-1 expression is seen in close association with Plekha7 expression in the NPCE and OLM in SS controls.

Conclusions: Plekha7 KO rats show loss of Plekha7 expression in ciliary processes and OLM of the retina. Functionally, these Plekha7 KO rats also show increased fluorescein dye leakage in the vitreous and anterior chamber in comparison to control SS rats. The close association of Plekha7 expression with tight junction protein ZO-1 in the ciliary processes suggests it may contribute to an altered barrier function in PACG pathogenesis.

CONTROL ID: 3538357

SUBMITTER (NAME ONLY): Mark Solinski

TITLE: Standardization of multiplex PCR for detection of viral uveitis causative agents

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Solinski, N. Shah, V.R. Raiji, Ophthalmology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|V.R. Raiji, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|D. Shukla, Microbiology and Immunology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|R. Michael, Ophthalmology, University of Florida College of Medicine, Jacksonville, Florida, UNITED STATES|R.K. Suryawanshi, R. Koganti, D. Shukla, Ophthalmology and Visual Sciences, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|N. Shah, Ophthalmology, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early diagnosis of infectious uveitis may prevent vision loss, but given the small volume, it is notoriously difficult to test ocular fluid for specific viruses in uveitis. Multiplex PCR is an ideal technique to diagnose viral uveitis, however, sensitivity of commercially available kits is an important concern. This study was aimed to optimize primers to increase sensitivity of multiple real time PCR for diagnosis of two viral uveitis causing agents, herpes simplex virus-1 (HSV-1) and human cytomegalovirus (HCMV).

Methods: In the first steps, we performed uniplex PCR to evaluate the sensitivity of at least four different primers designed to detect each HSV-1 (McKrae strain) and HCMV (AD169 strain). During this step, different pathogen loads of virus were used to test the load dependent sensitivity of primers. After optimization of primers with uniplex PCR, the sequences were further validated at least three times each with multiplex PCR. For this purpose, samples containing different concentrations ranging from low (1×10^4) to high (1×10^6) pathogen load mixed in bovine aqueous humor were used. TaqMan probes with intercalated DNA fluorophore (VIC for HSV-1 and FAM for HCMV) primers were used for multiplex PCR validation.

Results: Primer validation resulted in the sequences F: 5'-GCCTTTTGTGTGTGTGTTGG-3', R: 5'-AGGAAAGAGGAAACAGGCCG-3' being sensitive to detect low (1×10^4) and high (1×10^6) pathogen load of HSV-1 glycoprotein B, while F: 5'-CAAGTGACCGAGGATTGCAA-3', R: 5'-CACCATGTCCACTCGAACCTT-3' was sensitive for detecting low (1×10^4) and high (1×10^6) pathogen load of HCMV immediate-early protein 1. The same sequences designed with TaqMan probes with intercalated DNA fluorophore primers showed efficient detection of either HSV-1 or HCMV in standalone or mixture of both viruses at different pathogen loads. The cycle threshold values ranged between 19 to 11 and 22 to 14 for low and high pathogen load of HSV-1 and HCMV respectively.

Conclusions: The primers optimized for multiplex PCR were found to be highly sensitive and specific for HSV-1 and HCMV. The results were reproducible and can be used for simultaneous or independent detection of either of the two viruses with the use of only 5 μ l of aqueous humor. Further studies will be needed to confirm the efficacy of primers in clinical samples.

CONTROL ID: 3538371

SUBMITTER (NAME ONLY): Pavan Verkicharla

TITLE: Impact of short-term exposure to short, middle, and long-wavelength of light and optical defocus on axial elongation in humans

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Verkicharla, S.K. Thakur, Myopia Research Lab, Prof. Brien Holden Eye Research Centre, L V Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Given the potential role of light and its wavelength on ocular growth, this study aimed to investigate the effect of short-term exposure to short, middle, and long-wavelength on axial elongation in presence of ocular defocus.

Methods: A total of 7 young adults (4 emmetropes, 3 myopes) were exposed to long (red-623nm), middle (green-521 nm), and short-wavelength of light (blue-460 nm) for a period of 60 minutes each on 3 separate days (between 9 to 11 am). During the light exposure, monocular (right eye) hyperopic defocus of 3D was induced to the right eye with the fellow eye experience normal view (no defocus). The mean (\pm SD) age of the participants was 23 ± 3 years and spherical equivalent refractive error ranged from -0.50 to $+2.50$ D). Smart LED Bulb ((Wipro Enterprises Ltd., Shezhen, PRC, China) was used in a 3x3x3 meters closed room while the participants were asked to watch the video placed at 3 meters from the eye for the experiment period of 60 minutes. Axial length was recorded pre and post the defocus (in less than a minute) using Lenstar non-contact biometer. Participants were asked to score asthenopic symptoms (headache, eye strain, eye discomfort, eye fatigue, dizziness) after the experiment as none, slight, moderate, severe, intolerable.

Results: There was a small but significant increase in axial length from baseline in the right eye (with defocus) after 1-hour exposure to longer ($13 \pm 4 \mu$, $p = 0.02$) and middle wavelength of light ($16 \pm 5 \mu$, $p = 0.01$), but not with the shorter wavelength ($0 \pm 4 \mu$, $p = 0.49$). Emmetropes showed greater axial elongation compared to myopes in both red and green light conditions. Exposure to middle wavelength alone lead to significant changes in axial length in the left eye ($9 \pm 2 \mu$, $p = 0.01$). None of the participants experienced/complained of any asthenopic symptoms during or after the experiment.

Conclusions: One hour exposure to the shorter wavelength of light did not lead to axial elongation, while the middle and longer wavelengths induced small but significant changes in presence of the hyperopic defocus indicating the potential role of chromatic cues on ocular growth and myopiogenesis. Given that short-term exposure to different wavelengths of light did not induce any asthenopic symptoms, the impact of such specific wavelength exposure on children and its application in myopia control warrants further investigations.

CONTROL ID: 3538378

SUBMITTER (NAME ONLY): Ian Sigal

TITLE: In-vivo evidence of lamina cribrosa deformations induced by chronically elevated IOP in non-human primates

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I.A. Sigal, F. Zhong, Y. Hua, J. Wei, M. Bansal, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|I.A. Sigal, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J. Reynaud, B. Fortune, Devers Eye Institute, Legacy Health System, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure in vivo lamina cribrosa (LC) deformations induced by chronically elevated intraocular pressure (IOP). Specifically, we measure session-to-session (S2S) LC stretch, compression, shear and effective strains.

Methods: The optic nerve heads (ONHs) of both eyes of three monkeys were imaged using optical coherence tomography (OCT, Spectralis) at baseline and longitudinally (S2S interval 7 to 22 days, 7 to 17 sessions) after unilateral laser-induced chronic elevated IOP (experimental glaucoma EG). To remove acute IOP effects and isolate chronic deformations all scans were acquired after IOP was set to 10 mmHg for 30 minutes. Digital volume correlation (DVC) was then employed to determine the local S2S LC deformations. LC deformations were compared longitudinally and between the EG and control eyes of each monkey.

Results: S2S LC changes were much larger in the EG eyes after lasering compared to the baseline sessions and control eyes. As expected, laser-induced IOP increases were highly variable, prompting further treatments. However, the LC changes induced by the transient increases in IOP were not resolved after IOP returned to normal. S2S LC deformations reached low two digits, locally as large as 10% compression and 16% stretch, suggestive of tissue loss. Interestingly, further analysis indicated that in the sessions immediately after lasering, a small anterior-posterior LC stretch was detected, suggesting that the lamina undergoes thickening, not thinning. Later on, the LC exhibited the expected compression consistent with thinning. S2S LC changes were significantly larger in the EG after lasering compared with the baseline sessions and the control eyes ($p < 0.001$).

Conclusions: The monkey LC suffers clearly detectable deformations as a result of chronically elevated IOP. Changes can be detected even after only a few days of elevated IOP, and are not immediately resolved even if IOP comes back to the normal range.

CONTROL ID: 3538391

SUBMITTER (NAME ONLY): Abraham Hang

TITLE: Conjunctival melanomas exhibit decreased 5-hydroxymethylcytosine expression

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Conjunctival melanomas are relatively rare tumors, accounting for a small percentage of ocular melanomas. However, these tumors carry high morbidity and mortality rates, and early diagnosis and treatment are critical. Recent studies have identified 5-hydroxymethylcytosine (5hmC) as a potential diagnostic and prognostic biomarker in cutaneous melanoma. 5hmC is an epigenetic marker, generated from oxidation of 5-methylcytosine (5mC) by TET enzymes. It has been found at high levels in self-renewing and pluripotent stem cells, and has been postulated to regulate gene expression and initiate DNA methylation. We conducted a study to characterize the expression of 5hmC in benign conjunctival nevi, primary acquired melanosis (PAM) with moderate atypia, and conjunctival melanomas to determine whether 5hmC has utility in distinguishing benign from potentially malignant lesions.

Methods: A total of twelve samples were retrieved from archived cases, consisting of histopathologically confirmed benign nevi (n=4), PAM with moderate atypia (n=4), and conjunctival melanoma (n=4). All specimens were fixed in 10% buffered formalin and embedded in paraffin. Sections of 5 µm were cut, stained with hematoxylin and eosin (H&E), and reviewed by light microscopy. Sequential sections were then subjected to immunohistochemical staining with antibody against 5hmC. Negative and positive controls were performed in parallel. Slides were reviewed and graded by an ocular pathologist.

Results: All four nevi samples exhibited positive nuclear staining for 5hmC; in contrast, all four PAM specimens as well as three out of four conjunctival melanomas did not display staining for 5hmC (p=0.03). One melanoma specimen, rated as spindle cell, exhibited rare positive 5hmC staining.

Conclusions: This is the first study to-date which shows that 5hmC expression is significantly decreased in conjunctival melanomas when compared to benign nevi. In addition, specimens confirmed as PAM with moderate atypia exhibited negative staining for 5hmC, which may reflect their potential to progress to malignant melanoma. Future studies are needed to further delineate the level and specificity of 5hmC expression in different conjunctival melanocytic proliferations, as well as its utility as a clinical marker.

CONTROL ID: 3538392

SUBMITTER (NAME ONLY): Farhad Ghaseminejad

TITLE: Developing CRISPR-Based Treatment Strategies for Selective Editing of Mutant Rhodopsin in *Xenopus laevis*

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Ghaseminejad, B.M. Tam, O.L. Moritz, Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Given that mutations in the rhodopsin gene (RHO) are associated with autosomal dominant retinitis pigmentosa (adRP), highly specific gene-editing strategies in RHO may provide effective treatments for this blinding disease. The Moritz lab has previously described CRISPR-based genetically modified *X. laevis* that carry a 12-base pair (bp) deletion in the Rho.L gene, immediately downstream of the start codon. Phenotypically, we observed significantly lower levels of rhodopsin protein as well as substantial retinal degeneration (RD) in these animals. Utilizing this model, we aimed to prevent the detrimental effects of this 12bp deletion by inactivating the dysfunctional gene.

Methods: Methods: Our approaches involved removing the dysfunctional Rho.L start codon by inducing simultaneous double-strand breaks on both sides of the start codon, generating a loss-of-function allele. We designed a single-guide RNA (sgRNA) to target the defective Rho.L gene, but not the other *X. laevis* rhodopsin encoding genes (Rho.2.L and Rho.S) or the wildtype Rho.L allele. A second sgRNA targeted a relatively non-conserved region of the Rho.L promoter which was not specific for the mutant allele. Both sgRNAs were injected alone and in combination into *X. laevis* embryos. Tadpoles from treated and untreated groups were raised to 14 days. One eye from each sacrificed tadpole was solubilized for evaluating rhodopsin levels using a dot-blot assay. The contralateral eye was sectioned, labelled and imaged for assessing histology. Genetic changes were examined by PCR and Sanger sequencing.

Results: Results: Compared to the untreated animals carrying the 12bp deletion, significantly higher levels of rhodopsin were detected in the CRISPR-edited animals. Histologically, considerable RD in the untreated groups was also prevented in animals receiving the sgRNA edit. Treatment with even the single mutation-specific sgRNA dramatically prevented RD, likely due to frameshift mutations similarly causing loss of function. Treatment of wildtype animals with the sgRNAs did not induce any detrimental effects.

Conclusions: Conclusion: We have demonstrated prevention of RD in animals treated with mutation-specific sgRNAs, compared to untreated animals. Both frameshifts and generation of large inactivating deletions dramatically prevented RD, showing that complex approaches may not be necessary for developing effective treatments.

CONTROL ID: 3538424

SUBMITTER (NAME ONLY): Kalliopi Stasi

TITLE: Topical ocular TRPV1 antagonist SAF312 was well tolerated and effectively reduced pain after photorefractive keratectomy (PRK)

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: SAF312 is a potent inhibitor of the transient receptor potential cation channel subfamily V member 1 (TRPV1). This Phase 2a study (NCT02961062) evaluated the safety and efficacy of topical ocular SAF312 in post-PRK ocular pain.

Methods: Patients (pts) aged 18-75 years and eligible for PRK with myopia ≤ -4.00 D sphere, ≤ -4.50 D spherical equivalent, and astigmatism ≤ 3.00 D were allowed in this double-masked, vehicle-controlled, multicenter study. Pts were randomized (1:1) to 2 treatment sequences in a bilateral PRK crossover design (SAF312 2.5% followed by vehicle [or vice versa], 1 drop, 4× daily for 72 h post-PRK; Fig 1). The primary endpoints were visual analog scale (VAS) pain severity scores at 6 h and average VAS scores over 0-12 h postoperatively (postop). Incidence of oral rescue medication (ORM) use, wound healing rate, conjunctival hyperemia, and safety were assessed. $P \leq 0.10$ was deemed statistically significant (per primary endpoint power calculation).

Results: All 40 pts (mean \pm SD age: 34 \pm 9.8 years) completed the study. Both primary endpoints were met; difference between SAF312-treated (n=30) and vehicle-treated (n=29) eyes in mean VAS pain scores at 6 h postop was -11.1 (-25%) (90% CI: -17.54, -4.71; $P=0.005$), and at 0-12 h postop was -8.56 (-22%) (90% CI: -14.29, -2.83; $P=0.017$). The mean VAS pain scores were lower with SAF312 than with vehicle from 1 h postop (-53%) up to 30 h postop ($P \leq 0.10$ in 8/11 timepoints). Less ORM (number of pills) was taken with SAF312 (n=40) vs vehicle (n=40) at 0-6 h postop (-25%, $P=0.10$), and up to 0-72 h postop (-14%, $P=0.07$), with a trend of fewer pts needing any ORM at 0-24 h postop with SAF312 (40%) vs vehicle (30%). No delay in wound healing was noted in SAF312- vs vehicle-treated

eyes. Grade 4 conjunctival hyperemia 24 h postop was significantly lower in SAF312- vs vehicle-treated eyes, especially in the superior conjunctiva associated with most surgical manipulation ($P=0.04$). No deaths or serious adverse events (AEs) were reported. Of the 40 pts in this study, 8 and 5 had AEs while on SAF312 and vehicle, respectively; and all ocular AEs (3 in each group) were mild and transient. No AE was drug-related.

Conclusions: Topical SAF312 was well tolerated and effective in reducing ocular pain in the immediate post-PRK period. SAF312 is currently under evaluation for postop corneal induced chronic pain (NCT04630158).

CONTROL ID: 3538482

SUBMITTER (NAME ONLY): Alexandra Van Brummen

TITLE: Artificial intelligence automation of eyelid and periorbital measurements

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Currently there are no standardized automated tools to assess oculoplastic metrics despite the importance of periorbital measurements in assessing clinical disease and surgical outcomes. To date, only the margin reflex distances (MRD1/MRD2) have been previously automated. To address this, we used a deep learning semantic segmentation network to fully automate 9 periorbital measurements.

Methods: Periorbital photos were collected from routine oculoplastics clinic. In the retrospective phase, photos from 397 patients were collected. Three areas in each photo (eye aperture, iris, and eyebrow) were segmented bilaterally by 3 graders. The segmentations were used to train a deep learning semantic segmentation model consisting of a vanilla PSPNet with a ResNet50 backbone and a U-Net-style upsampling arm. Then, a post-processing algorithm was developed to measure: MRD1, MRD2, medial canthal height (MCH), lateral canthal height (LCH), medial brow height (MBH), lateral brow height (LBH), medial inter-canthal distance (MID), and lateral inter-canthal distance (LID). In the prospective phase, three human graders used Photoshop version 22.0.1 to segment and measure the 9 metrics in photos from 46 participants. The images and grader-derived segmentations and measurements formed the independent test set. The trained network and the post-processing algorithm were used to obtain periorbital measurements for the test-set images (Fig 1).

Results: The mean absolute difference range for MRD1 was 0.43-0.57mm between AI and human graders and 0.24-0.30mm between the 3 human graders. For MRD2 it was 0.38-0.39mm between AI and humans and 0.28-0.35mm between human graders. On average the periorbital measures deviated less than 4.5mm between every pair of raters across all metrics (Fig 2). The 95% confidence intervals are largely overlapping between all pairs of raters indicating the variations between human graders were similar to those between humans and AI.

Conclusions: We present, to the best of our knowledge, the first machine learning automation of 9 different periorbital measurements. This tool has similar variability to human graders and could be clinically useful to objectively track disease progression and surgical outcomes.

CONTROL ID: 3538486

SUBMITTER (NAME ONLY): Hung-Liang Pai

TITLE: Incidence of ocular diseases as related to hyperuricemia and gout based on Taiwan Biobank

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Hyperuricemia has been implicated to be a factor of eye diseases. However, no sufficient evidence in single nucleotide polymorphism (SNP) variations is provided to associate its relation with particular ocular abnormalities. In this study, we investigated this potential relevance based on Taiwan Biobank (TWB).

Methods: A total of 65,076 individuals were enrolled in this study using TWB from 2009-2018, with a mean age of 49.96 (SD=10.91). The TWB is a large-scale national biobank that supplies valuable phenotypic and genetic information to biomedical researchers among Taiwanese population. The study was a case-control study in which the case groups were defined as patients with hyperuricemia (defined as 7 mg or more of uric acid per 100 mL of blood in men and 6.5 mg or more in women before menopause) or self-reported gout, and the control group was age- and gender-matched non-hyperuricemic or non-gouty individuals. The study groups were divided into (1) 55,300 cases with no gout and normal uric acid (2) 7,618 cases with hyperuricemia and no gout (3) 790 cases with gout but normal uric acid (4) 1,368 cases with hyperuricemia and gout. The proportion of variation of groups was compared with that in the control group by GWAS to calculate the relative odds ratio and estimate the significance of each eye disease investigated.

Results: Patients with gout but normal uric acid, compared with those with normal uric acid without gout, had a significantly higher prevalence of eye diseases, including cataract (200/1356 (14.75%) vs 1362/16925 (8.05%)), dry eye (147/1356 (10.84%) vs 1262/16925 (7.46%)), and myodesopsia (212/1356 (15.63%) vs 1722/16925 (10.17%)), after been adjusted for age and gender. Among hyperuricemia-related SNP variants analyzed, rs3741414 and rs1178977 were associated in patients with gout but normal uric acid, concomitant with eye diseases.

Conclusions: The results of this study indicated that gout is a more critical factor in ocular diseases than hyperuricemia, suggesting a potential sub-clinical effect exerted by uric acid or its associated activities in the eye. The two identified SNP variants need further investigation for the underlying mechanism.

CONTROL ID: 3538493

SUBMITTER (NAME ONLY): Clare Fraser

TITLE: Developing a quality assurance framework for neuro-ophthalmology referrals using NODE - the Neuro-ophthalmology database.

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Quality assurance (QA) in neuro-ophthalmology (NOPH) is often lacking. The QA registry, NODE (Neuro-ophthalmology Database), was established and implemented in tertiary NOPH clinics in Australia. We developed a consensus on triage categories according to Australian standardised triage categories; P1 (consult \leq 30 days), P2 (consult \leq 30 to 60 days) and P3 (consult $>$ 60 days). Triage categories and time-to-consult for common NOPH conditions were compared to evaluate quality of referral assessment at a single site.

Methods: We collected data in NODE on 410 patients at Alfred Hospital, Melbourne. We developed a consensus on assignation of NOPH conditions to triage categories using recommendations from a panel of seven experienced neuro-ophthalmologists. Panelists scored conditions and triage categories using a modified Delphi approach (strongly agree, agree, neutral, disagree or strongly disagree). Consensus was considered when $\geq 75\%$ of the panel strongly agreed or agreed. We analysed the mean days from referral to triage, and, from triage to the initial consultation, and compared that to the developed triage category standard.

Results: Most patients presenting to the service were female (n=262, 64%), aged 21 to 30 years. Common diagnoses were Idiopathic Intracranial Hypertension, IIH (24%), Optic Neuropathy, ON (17%), Headaches, (11%) Cranial Nerve Defects, CND (9%) and Eye Movement Disorders, EOMD (9%). Consensus on triage category assignment was reached after 1 round of scoring from expert panel members. The mean time from referral to triage was performed in <2 days for all the common diagnosis at the NOPH clinic. The mean time (days, +-standard deviation (SD)) from P1 category triage to initial consult for IIH was 26 (± 7), ON 27 (± 11), and CND was 17 (± 5). The mean time (days) from P2 triage to initial consultant for Headaches was 27 (± 12), and EOMD was (± 17). The mean time (days) from P3 triage to initial consultant for Myasthenia Gravis was 30 (± 10).

Conclusions: We have established a consensus agreement on triage categories for neuro-ophthalmological conditions. Further validation using a larger panel of experts would be able to refine this further. Data from NODE demonstrated that most conditions are appropriately triaged and seen. We established a QA framework for other NOPH clinics in Australia.

CONTROL ID: 3538526

SUBMITTER (NAME ONLY): Hamed Niyazmand

TITLE: Repeatability of anterior eye surface topography parameters from the Eye Surface Profiler

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Eye Surface Profilometer (ESP) allows measurements of corneal and scleral topography that have provided information about the characteristics of the in-vivo human anterior eye shape and have been used in contact lens fitting and design. This study aimed to examine the intersession and intrasession repeatability of sagittal height and corneal spherocylinder measurements from the ESP.

Methods: Forty-five young healthy adult subjects (mean age 25 ± 5 years) with a range of refractive errors had two sessions of anterior eye surface shape measurements captured with the ESP, separated by 20 minutes. At each session, three consecutive scans were captured by a single operator. Spherocylinder data (M, J0, and J45) from the central cornea and sagittal height data from the central 8 mm of the cornea and the region from 8 to 14 mm of corneal periphery/anterior sclera on the nasal and temporal anterior eye surface were assessed to calculate the measurements' intersession and intrasession co-efficient of repeatability (CR) using Bland-Altman analyses.

Results: The intersession CRs of sagittal height measurements for the nasal (5 μm) and temporal (7 μm) central corneal regions were better than the peripheral nasal (24 μm) and temporal (21 μm) regions (all $p < 0.001$). The sagittal height within-subject standard deviations of the three repeated scans were 3, 3, 10, and 11 μm for central nasal, central temporal, peripheral nasal, and peripheral temporal region, respectively. Figure 1 shows the sagittal height Bland-Altman analysis of the central and peripheral nasal and temporal regions.

Intersession CRs of 0.67, 0.22, and 0.13 D and within-subject standard deviations of the three repeated scans of 0.46, 0.08, and 0.10 D were achieved for measurements of corneal power vectors M, J0, and J45, respectively.

Conclusions: Central corneal sagittal height and spherocylinder measurements provided by the ESP are highly repeatable and comparable with other anterior eye topographers, however, sagittal height repeatability reduces towards the periphery. These outcomes should be considered in the clinical and research applications of anterior eye surface topography results from the ESP.

CONTROL ID: 3538536

SUBMITTER (NAME ONLY): Joanne Wood

TITLE: Visual motion perception predicts postural sway in older adults with and without vision impairment

SESSION TITLE: Visual Impairment - Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.M. Wood, C. Killingly, A.A. Black, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|D. Elliott, University of Bradford, Bradford, West Yorkshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Accurate perception of body position relative to the environment through visual motion cues provides sensory input to control postural sway. Importantly, the role of visual motion information in older adults is not well established. This study evaluated the extent to which visual motion perception affects postural sway in older adults with and without vision impairment and the interaction with physical function.

Methods: Participants included 234 older adults with vision impairment from a range of eye diseases (mean age = 72.6 ± 7.2 years) and 204 with normal vision (71.6 ± 5.7 years). Participants completed a series of vision tests including binocular visual acuity, contrast sensitivity, visual fields and central motion sensitivity, as well as physical function tests to assess aspects of physical frailty and functional mobility, including walking speed, Timed Up and Go Test (TUGT) and grip strength. Postural sway (path length, mm) was measured using an electronic forceplate (HurLabs) on a firm and foam surface with eyes open. Linear regression analysis was used to identify visual predictors of postural sway and moderated linear regression explored whether this relationship was moderated by physical frailty.

Results: Linear regression models indicated that of the vision tests, impairments in motion sensitivity were most strongly associated with increased sway on foam (standardized $\beta = 0.330$; $p < 0.001$), while of the physical function tests, TUGT (standardized $\beta = 0.334$; $p < 0.001$) was most strongly associated with sway on foam, where poorer functional mobility was associated with increased sway. A moderated linear regression demonstrated significant main effects of motion sensitivity and TUGT for sway on foam ($p < 0.001$), as well as a significant interaction effect (standardised $\beta = 0.164$, $p < 0.001$), such that the relationship between motion sensitivity and sway became stronger when TUGT performance was poorer.

Conclusions: A combination of impaired motion perception and reduced physical function negatively impact on postural stability in older adults with and without vision impairment. This finding provides insight into the visual input to postural stability in older adults and its interactions with other sensory and physical impairments and has implications for the assessment of falls risk in older adults.

CONTROL ID: 3538545

SUBMITTER (NAME ONLY): Takafumi Miyatani

TITLE: Morphological change and migration activity of human Müller cells on the amniotic membrane

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Miyatani, H. Tanaka, T. Nakamura, T. Horikiri, M. Kishida, Y. SHINKAI, K. Kojima, C. Sotozono, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: It has recently been reported that amniotic membrane (AM) transplantation is effective for macular hole (MH) closure and improvement of visual function in refractory MH cases. In this study, we investigated the effects of AM on the morphology and migration of cultivated Müller cells (MIO-M1 cells, an immortalized model of Müller glial cells, University College London, London, UK).

Methods: MIO-M1 were cultured using Dulbecco's modified eagle medium with 10% fetal bovine serum in a humidified 5% CO₂ environment at 37°C. AM was then placed in 24-well plates to create an epithelial-side-up group (epithelial group), a chorion-side-up group (chorion group), and a control group on glass slides (n = 10 each). Then, silicon (3mm in diameter) was placed in the center of each. Each group was then seeded with 0.5×10^5 MIO-M1 cells, with the silicon being removed after 24 hours. Next, phase-contrast microscopy images were taken immediately and at 72-hours post removal of the silicon, and actin filaments were visualized with phalloidin staining. Via examination of the obtained images, the cell morphology was analyzed and the migration ability of the cells was evaluated and compared between the three groups by measuring the cell migration area using ImageJ software.

Results: The MIO-M1 cells showed a bipolar morphology with pseudopodia in the epithelial group and control group, and a nearly circular morphology in the chorionic villus group. In the control group, epithelial group, and chorionic group, the cell migration area was $0.34 \pm 0.26 \text{ mm}^2$, $1.14 \pm 0.48 \text{ mm}^2$, and $0.04 \pm 0.03 \text{ mm}^2$ (mean \pm SD), respectively, with the ability of cell migration being significantly higher in the epithelial group ($P < 0.05$).

Conclusions: Human Müller cells on the chorionic side showed a different morphology from the control and epithelial side, and their migration ability was lower than the epithelial-side cells. When performing AM transplantation for the treatment of MH, positioning the epithelial side of the AM toward the vitreous cavity may promote the migration of Müller cells and assist in the closure of the MH.

CONTROL ID: 3538562

SUBMITTER (NAME ONLY): Linjiang Lou

TITLE: Effects of Narrowband Light Rearing on Activity and the Pupil in Infant Rhesus Monkeys

SESSION TITLE: Effects of Light Intensity and Blur on Refractive Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Lou, L. Hung, K.M. Beach, Z. She, E.L. Smith, L.A. Ostrin, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|B. Arumugam, Former employee of College of Optometry, University of Houston, Houston, Texas, UNITED STATES|L. Hung, K.M. Beach, E.L. Smith, BHVI, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Light affects a variety of non-image forming processes, such as circadian rhythm and the pupillary light reflex, which are mediated by intrinsically photosensitive retinal ganglion cells (ipRGCs). ipRGCs are most sensitive to short wavelength light. Thus, the spectral properties of light critically impact melanopsin-mediated ipRGC activity. The purpose of this study was to compare the effects of long- and short-wavelength ambient lighting on activity patterns and pupil responses in rhesus monkeys.

Methods: Infant rhesus monkeys were reared under short wavelength “blue” light ($n=20$; 465 nm; 183 ± 28 lux) on a 12-hour light/dark cycle starting at 24.7 ± 2.8 days of age. Animals wore a Fitbit activity tracking device from 25.4 ± 2.4 days until 148.5 ± 7.7 days of age. Activity was quantified as mean daily “steps” during the lights-on and lights-off periods. At 333 ± 12 days of age, pupil responses to 1 second (s) red (651 nm) and blue (456 nm) stimuli were measured. Pupil metrics included maximum constriction and the 6s post-illumination pupil response (PIPR). Data were compared to age-matched monkeys reared under either broadband “white” light ($n=18$; 480 lux) or long wavelength “red” light ($n=20$; 630 nm; 274 ± 64 lux).

Results: During the lights-on period, daily activity was not significantly different for monkeys reared in blue light (1215 ± 648 steps), red light (877 ± 574 steps), or white light (942 ± 523 steps; $P=0.07$). During the lights-off period, monkeys reared in blue light exhibited significantly greater activity (91 ± 68 steps) compared to those in white light (49 ± 34 steps; $P=0.02$). There was no significant difference in lights-off activity between blue and red light (67 ± 35 steps) reared monkeys ($P=0.08$) or between red and white light reared monkeys ($P=0.24$). Maximum pupil constriction and the 6s PIPR to 1s red and 1s blue stimuli were not significantly different between groups ($P>0.05$ for all).

Conclusions: Rearing monkeys in narrowband blue light resulted in increased nighttime activity, whereas narrowband red light did not significantly impact daytime or nighttime activity patterns. Therefore, exposure to 12-hour narrowband blue light resulted in greater circadian disruption compared to red light, potentially due to increased melanopsin activation in the evenings. However, normal pupil responses later in the rearing period suggests that ipRGCs adapt after long-term exposure to narrowband lighting.

CONTROL ID: 3538564

SUBMITTER (NAME ONLY): Pernilla von Nandelstadh

TITLE: Analyzing the mitochondrial genome of over 2500 patients with retinal disease

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. von Nandelstadh, S. Tuupanen, M. Gandia, S. Vattulainen-Collanus, K. Kampjarvi, J. Kansakoski, K. Merkkiniemi, L. Sarantaus, R. Perez-Carro, J. Tallila, V. Kytola, M. Muona, J. Sistonen, I. Saarinen, J. Koskenvuo, Blueprint Genetics, Espoo, FINLAND|T. Alastalo, Blueprint Genetics, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mitochondrial diseases are a heterogeneous group of disorders that arise as a result of dysfunction of the mitochondrial respiratory chain. The circular 16.5-kb mitochondrial genome (mtDNA) contains 37 genes, which are essential for normal mitochondrial function. Mitochondrial dysfunction caused by pathogenic/likely pathogenic variants in the mtDNA has been associated with retinal disease and vision loss. The goal of the study was to evaluate mtDNA variants in >2500 patients with inherited retinal disease (IRD).

Methods: We developed a highly sensitive and clinically validated mtDNA assay based on hybridization-based capture of mtDNA and next-generation sequencing (NGS) that is able to detect very low heteroplasmy levels of SNVs, INDELs and deletions. The mean read depth for the mtDNA was 18,224x, and 100% of base pairs were covered with a sequencing depth of at least 1000x. Sensitivity to detect SNVs and INDELs with over 10% heteroplasmy was 100%. For SNVs with 5-10% and <5% heteroplasmy levels the sensitivity was 93.3% and 88.9%, respectively. The mtDNA assay was included in diagnostic sequencing of 2597 IRD patients.

Results: A diagnostic (pathogenic/likely pathogenic) mtDNA variant was identified in 22 patients, contributing to a diagnostic yield of 0.85%. The 22 diagnostic variants included one heteroplasmic large deletion (7542bp) and 21 SNVs. Five of the SNVs were homoplasmic and 16 were heteroplasmic (>7%). Homoplasmic variants were associated mainly with Leber hereditary optic neuropathy (LHON). Diagnostic variants were identified in 8 mtDNA genes: MT-ND1, MT-ND4, MT-ND6, MT-ATP6, MT-TN, MT-TH, MT-TL1, and MT-TV. The most common variant was the retinal disease-associated MT-TL1 m.3243A>G, identified in 11 individuals in whom the retinal disease was most often described as macular/ cone dystrophy. Additionally, we reported a mtDNA VUS, likely to contribute to the patient's diagnosis, in 7 cases.

Conclusions: Adding mtDNA analysis to routine genetic diagnostic process of IRD patients can increase the diagnostic yield by >0.85%. Analyzing the full mtDNA is beneficial as several different variants in mtDNA have been associated with both syndromic and non-syndromic IRD.

CONTROL ID: 3538577

SUBMITTER (NAME ONLY): Flavia Chiosi

TITLE: Analysis of Retinal Vessel Density using optical coherence tomography angiography in patients affected by COVID-19.

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Chiosi, G. Manzi, E. Paolillo, E. Minutillo, Ophthalmology, Ospedale Monaldi, Napoli, Campania, ITALY|R. dell'Omo, C. Costagliola, Medicine and Health Sciences, Universita degli Studi del Molise, Campobasso, Molise, ITALY|M. Rinaldi, Ophthalmology, Universita degli Studi della Campania Luigi Vanvitelli, Napoli, Campania, ITALY|

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ABSTRACT BODY:

Purpose: Patients affected by Coronavirus disease 2019 (Covid-19) suffer from a hypercoagulable state that may potentially affect the retinal and choroidal circulation. The aim of this study was to determine whether retinal and choriocapillaris vessel density (VD) as measured by optical coherence tomography angiography (OCTA) resulted abnormal in patients previously affected by Covid-19.

Methods: The right eye of sixty patients who tested positive for Sars-CoV-2 in a reverse transcription PCR assay were examined with structural optical coherence tomography (OCT) and OCTA. A control group of age-matched healthy subjects was selected for statistical comparisons. Raw OCT and OCTA images, acquired with TOPCON DRI OCT Triton, were exported using Topcon IMAGENET 6.0 software. 3D datasets were analysed to determine retinal thickness and VD in the 5 sectors of Early Treatment Diabetic Retinopathy Study (ETDRS).

Results: The images were gradable in 54 eyes (88%) on which the final analysis was conducted. The study and control group did not differ significantly for sex, intraocular pressure (IOP) and refractive error. Vessel density of the superficial capillary plexus did not differ between groups whereas VD of the deep capillary plexus (DCP) and choriocapillaris in the foveal ETDRS sector was significantly lower in the Covid-19 group compared to controls ($P < 0.01$). No significant difference was found in the VD's recorded in any of the other 4 ETDRS sectors between groups. Within the COVID-19 group, subgroups were identified for therapies, underlying diseases and hospitalization. Based on therapies the lowest VD was recorded among patients treated with antiviral therapy compared to antiplatelet therapy ($P < 0.01$). No significant difference was found between patients affected by hypertension, diabetes or thyroid disease. A significantly reduced VD value was registered in patients admitted in ICU compared to asymptomatic ($P < 0.01$).

Conclusions: In patients with previous COVID, the VD of the retinal DCP and choriocapillaris measured with OCTA resulted decreased. The lowest values of VD were recorded in the eyes of patients who had undergone antiviral therapy and ICU-setting. Future studies are needed to further support our preliminary data that individuals with previous COVID might develop abnormalities of the retinal and choriocapillaris vasculature.

CONTROL ID: 3538579

SUBMITTER (NAME ONLY): Todd Appleby

TITLE: Separate pathways for processing local and global motion in the primate retina

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Appleby, F. Rieke, M.B. Manookin, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To successfully guide behavior the visual system must quickly and accurately distinguish between object (local) motion and self (global) motion. Selectivity for local motion has been observed in the superior colliculus of macaque monkeys, but it is not known whether this computation arises earlier in the visual pathway. Further, selectivity for global motion has not been observed in the early visual pathways of primates. Here, we studied local versus global motion processing in several ganglion cell types in the primate retina, including some of the lesser studied types.

Methods: Recordings were performed in an intact, in vitro preparation of the macaque monkey retina. Spike responses or whole-cell synaptic currents in ganglion cells were performed using borosilicate glass electrodes. Several different stimulus classes were used to measure local versus global motion selectivity and also the effects of motion in the receptive-field surround on cellular responsiveness.

Results: We observed a gradient of sensitivity to local versus global motion across ganglion cell types. Local motion selectivity was strongest in broad thorny ganglion cells while global motion selectivity was greatest in On-type smooth monostratified ganglion cells. Other cell types such as parasol and Off-type smooth monostratified cells showed motion selectivities between these two extremes. Further, the degree of local versus global motion selectivity correlated with the effects of the receptive-field surrounds on cellular gain, ranging from strongly suppressive surrounds (local motion) to facilitatory surrounds (global motion).

Conclusions: A set of primate retinal ganglion cells show a range of sensitivity to either local or global motion, bookended by broad thorny and On smooth monostratified cells, respectively. Our results indicate that the encoding of local and global motion arises early in the primate visual stream. Further, the receptive-field surround is critical to the observed motion selectivities with local motion and global motion sensitivities originating from strongly suppressive and facilitatory surrounds, respectively

CONTROL ID: 3538580

SUBMITTER (NAME ONLY): Eun-Ah Lee

TITLE: A Novel Tie2 activating monoclonal antibody ameliorates the lesion of choroidal neovascularization in monkey and mouse

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Lee, B. Park, N. Kang, C. Park, W. Lee, R&D center, PharmAbcine, Daejeon, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Tie2 receptor is mainly expressed in endothelial cells that modulates angiogenesis with angiopoietins (Ang) binding. VEGF neutralizing molecules were approved to treat neovascular ocular diseases but there still is a great need to develop therapeutic agents to treat the patients who do not respond well to anti-VEGF drugs. We recently isolated a Tie2 activating antibody, PMC-403 and are evaluated its potential therapeutic potential to treat neovascular diseases.

Methods: Experimental CNV was induced by laser photocoagulation in C57BL/6 mice and in rhesus monkeys. The animals received IVT administration of aflibercept or PMC-403 and the dose dependent responses were measured in multiple assays: 1) FFA, OCT and ERG were evaluated. 2) The number of leakage spots, the percent changes of leakage area, and the maximum retinal thickness of laser-burned spots were evaluated. 3) In the monkey CNV model, the level of mRNA expression of 10 genes related to angiogenesis and inflammation was measured.

Results: In similar to Ang1, PMC-403 activated Foxo-1 phosphorylation, inhibited VEGFR-2 phosphorylation, and reduced the Survivin expression in HUVEC cells. In a mouse CNV model, PMC-403 reduced the thickness and the leakage of retinal blood vessels comparable to aflibercept in accompanied with improvement of the sensitivity of optic nerves. In a monkey CNV models, PMC-403 improved retina thickness and vessel leakage but the response rate was slower in comparison to aflibercept. Interestingly, PMC-403 showed better responses in sensitivity of optic nerves than aflibercept with decreased level of pro-angiogenesis genes such as Ang2, VEGF, PlGF, and PDGF. In addition, the level of pericyte in retina was dramatically increased by PMC-403 without inflammation.

Conclusions: PMC-403 improved sensitivity of optic neurons in animal CNV models through a normalization of leaky blood vessels. These data strongly support the notion that PMC-403 stabilizes retinal and choroidal blood vessels and it can be developed as an effective therapeutic agent to treat a wide variety of retinal and choroidal vascular disorders.

CONTROL ID: 3538608

SUBMITTER (NAME ONLY): Meng-Tien Hsieh

TITLE: Dose- and time-dependent tear secretion induced by caffeine through dual P1 and P2 purinergic receptors activation in lacrimal gland

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hsieh, T. Lu, C. Hsu, Y. Liu, C. Hsu, D. Lin, Medical Laboratory and Biotechnology, Chung Shan Medical University, Taichung, TAIWAN|H. Chang, Nutrition, Chung Shan Medical University, Taichung, TAIWAN|

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ABSTRACT BODY:

Purpose: Recent studies found that caffeine intake increases tear secretion. However, there is little elucidation on the cascading effects among caffeine, P1 and P2 receptors, and tear secretion. This study investigated the dose- and time-dependent effects of caffeine on tear secretion and whether P1 and P2 purinergic receptors activation may induce changes in external lacrimal gland (ELG) status under the influence of caffeine.

Methods: 5-week and 10-week old ICR female mice (n=3) were orally given caffeine at 17.3 mg/kg in 0.2 ml of 0.9 % NaCl, followed by tear volume (TV) assessments every 10 minutes from 0 to 100 minutes to determine the optimal mouse age for further experiments. After that, 10-week old ICR female mice were randomly divided 3 study groups: (1) Blank (n=3): 0.2 ml of 0.9 % NaCl, (2) 20 mg/kg (n=6): 20 mg/kg caffeine in 0.2 ml of 0.9 % NaCl, and (3) 40 mg/kg (n=6): 40 mg/kg caffeine in 0.2 ml of 0.9 % NaCl. All groups were assessed for tear volume (TV) at 0, 45, and 60 minutes after feeding. The mice were sacrificed after assessments for histopathological, immunohistochemical (IHC), and western blot analysis.

Results: 10-week old mice were more responsive to caffeine induction than 5-week mice. Tear secretion was significantly increased in both 20/45(20 mg/kg caffeine/45 mins) group ($p<0.05$) and 40/45(40 mg/kg caffeine/45 mins) group ($p<0.05$) compared to blank group. The results of IHC and western blot analysis showed that both P1 and P2 purinergic receptors were elevated, most evidently in the 40/45 group.

Conclusions: The results provided some insights in caffeine-induced tear secretion enhancement. First, the ICR female mice external lacrimal gland (ELG) reaches sufficient maturity to respond to caffeine induction at 10-week of age. Second, caffeine enhances tear secretion only within a certain period of time. Third, not only P1 purinergic receptors, but also P2 purinergic receptors are altered in ELG under the influence of caffeine. The interaction of P1 and P2 purinergic receptors and the effects of long-term caffeine intake should be further investigated.

CONTROL ID: 3538614

SUBMITTER (NAME ONLY): Lili Gong

TITLE: Methotrexate attenuates oxidative stress-induced retinal pigment epithelium degeneration and inflammation through promoting heterochromatin-mediated cGAS and STING silencing

SESSION TITLE: Retinal diseases: molecular and biochemical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Gong, M. Zou, R. Qi, Q. Ke, X. Zhu, D. Li, Zhongshan Ophthalmic Center, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Activation of the innate immune cGAS-STING signaling has been detected in retinal pigment epithelium (RPE) of Geographic atrophy (GA) patients, but the regulatory basis is largely unexplored. We have recently shown that transcriptional inert heterochromatin is required for RPE survival. Here, we investigate heterochromatin-mediated regulation of cGAS-STING, and determine the therapeutic potential of methotrexate (MTX), a newly identified heterochromatin-promoting drug and also a commonly used anti-inflammatory agent, in an experimental mouse model of GA.

Methods: In silico analysis was performed to determine the expression of cGAS and STING in dry AMD patients. GA mouse model was established by I.P. injection of sodium iodate. Chaetocin (0.25mg/kg), a heterochromatin inhibitor, or MTX (1mg/kg) was I.P. injected daily for 3 days after SI injection. Fundus photography and immunohistofluorescent analysis determined RPE morphology. Protein cytokine array, western blot and qRT-PCR analysis detected the activation of cGAS-STING pathway. ChIP assay determined the occupancy of heterochromatin on cGAS and STING upon MTX treatment.

Results: cGAS and STING are upregulated in RPE of GA patients and an experimental GA-like mouse model. Disruption of heterochromatin induces cGAS, STING and the downstream proinflammatory factors expression. Systemic application of MTX inhibits inflammatory gene expression in both RPE and retina, attenuates RPE degeneration and immune cell accumulation/activation. MTX promotes heterochromatin formation and thus epigenetically silencing of cGAS and STING.

Conclusions: Together, we demonstrated the anti-inflammatory function of MTX in a GA-like mouse model and revealed a novel mechanism that MTX suppresses cGAS and STING expression through promoting heterochromatin-mediated silencing. This study may provide new treatment strategy for GA.

CONTROL ID: 3538623

SUBMITTER (NAME ONLY): Ygal Rotenstreich

TITLE: Protease-activated receptor 1 is expressed in rods outer segment and nuclei of neuroretina cell

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Protease-activated receptor-1 (PAR1) is activated by the action of serine protease Thrombin. Thrombin plays a role in neurological dysfunction in diabetes. Recent studies have indicated that PAR1 and its activating protease thrombin are expressed in the ocular microenvironment of patients with diabetic retinopathy (DR). The aim of this study is to characterize the distribution of PAR1 in the neuroretina, under physiological conditions, and in diabetes.

Methods: Diabetes was induced in 8 weeks old C57BL/6J male mice by intraperitoneal injection of Streptozotocin (STZ, 150 mg/kg). Five weeks following diabetes induction eyes were removed from diabetic mice (n=12) and healthy C57BL/6J male mice (n=12) and were processed for indirect immunofluorescence analysis. PAR1-/- mice were used as control (n=3). In addition, western blot analysis was performed on mouse neuroretina, optic nerve, brain, and platelets samples.

Results: Significant PAR1 staining was observed in the nuclei of all neuroretinal cell layers (retinal ganglion cells, inner and outer nuclear layers) in diabetic mice (glucose blood > 200mg/dl). Significantly weaker staining was observed in control non-diabetic mice. No staining was observed in PAR1-/- mice. Co-staining of PAR1 with photoreceptor markers demonstrated co-localization of PAR1 and rhodopsin in rod outer and inner segments. By contrast, no PAR1 staining was observed in cone outer segments. The specificity of immunofluorescence staining was confirmed with Western blot analysis.

Conclusions: To the best of our knowledge, this is the first demonstration of PAR1 expression in rod retinal photoreceptors and inner nuclear layer cells. This study suggests that PAR1/thrombin pathway may play a role in the pathophysiology of rods in diabetic retinopathy.

CONTROL ID: 3538632

SUBMITTER (NAME ONLY): Luis Lesmes

TITLE: Hierarchical Bayesian modeling of the contrast sensitivity function

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhao, Z. Lu, Center for Neural Science, New York University, New York, New York, UNITED STATES|Z. Lu, Division of Arts and Sciences, New York University Shanghai, Shanghai, Shanghai, CHINA|M. Dorr, Adaptive Sensory Technology, GERMANY|L.A. Lesmes, Adaptive Sensory Technology, Inc, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The qCSF method applies Bayesian active learning to provide an accurate, precise and efficient assessment of spatial vision (Lesmes et al. 2010). To date, qCSF testing has not been informed by regularities in CSF shape observed when individuals are tested across low, medium, and high luminance conditions. To improve CSF analysis, and leverage information provided by cross-test regularities, we developed a hierarchical Bayesian model (HBM), which infers joint posterior distributions of CSF parameters and hyperparameters from qCSF data obtained from 112 subjects tested in three luminance conditions (Hou et al. 2016).

Methods: The CSF was modeled with a log-parabola with peak gain (PG), peak spatial frequency (PF), and bandwidth at half height (BH). The two-level HBM consisted of multiple 3-dimensional Gaussian distributions of CSF parameters at the population and individual test levels. The 3×3 covariance distributions at two levels quantified cross- and within-test regularities. The means of the parameter distributions at the individual test level were sampled from the hyperparameter distribution at the population level, while all individual tests shared the same 3×3 within-test covariance. We compared the average half-width of the 68.2% credible intervals (HWCIs) of the CSF parameters and area under log CSF (AULCSF) estimates with the qCSF and HBM.

Results: The HBM recovered significant correlations among CSF parameters at the population (Fig. 1; $r(\text{PG}\&\text{PF})=0.441$, $r(\text{PG}\&\text{BH})=0.580$, $r(\text{PF}\&\text{BH})=-0.109$) and individual ($r(\text{PF}\&\text{BH})=-0.719$) test levels. The average HWCI (in log10 units) of the estimated CSF parameters and AULCSF decreased with the number of trials in both the qCSF and HBM analyses (Table 1). Analysis of AULCSF estimates obtained with 50 trials provided HWCI values of 0.040 for qCSF and 0.035 for HBM. Relative to estimates of CSF parameters and AULCSF obtained with the qCSF, the HBM reduced the HWCI by 60-74% and 32% with 15 trials, and 30-55% and 13% for 50 trials. The average absolute difference between qCSF and HBM estimates was not statistically significant.

Conclusions: Incorporating both cross- and within-test regularities, the HBM can further improve the precision of CSF and AULCSF estimates, especially when the number of tested trials is relatively small.

CONTROL ID: 3538634

SUBMITTER (NAME ONLY): Lisa Grönnert

TITLE: Multi-omics based metabolic profiling of the retinal pigment epithelium

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Grönnert, P. Westenskow, Roche Pharma Research and Early Development, Ophthalmology Discovery, Roche Innovation Center Basel, F.Hoffmann-La Roche Ltd, Basel, Basel-Stadt, SWITZERLAND|D. Avila, J. Siebourg-Polster, F. Köchl, M. Tzouros, M. Prasad, J. Gayan, Roche Pharma Research and Early Development, Pharmaceutical Sciences, Roche Innovation Center Basel, F.Hoffmann-La Roche Ltd, Basel, Basel-Stadt, SWITZERLAND|L. Grönnert, Faculty of Science, Universitat Zurich, Zurich, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Photoreceptors rely on continuous nutrient delivery from the choriocapillaris via the retinal pigment epithelium (RPE). With advancing age, choriocapillaris atrophy and reduced choroidal blood flow create a hypoxic environment disturbing metabolism in the RPE that ceases metabolic support for the photoreceptors. Chronic ischemia can induce photoreceptor dysfunction and degeneration, hallmark features of age-related retinal diseases. Learning how hypoxia drives the metabolic stress response in RPE could give insights into hypoxia-induced retinal pathologies and identify strategies to prevent RPE, photoreceptor and vision loss. In this study, we perform proteomic, metabolomic and transcriptomic analyses to characterize the metabolic effects of hypoxia in RPE.

Methods: Primary human retinal pigment epithelial cells were cultured in normoxic (21% O₂) or hypoxic (4% O₂) conditions. After 48 hours, intracellular proteomic and metabolomic profiles were determined using quantitative proteomics and metabolomics (CE-TOF-MS and CE-QqQ-MS). RNA-Seq based transcriptomics was conducted after 4, 8, 12, 24, 48 and 72 hours of hypoxia, respectively. Differential expression and pathway analysis of hypoxia vs normoxia was performed per dataset and timepoint. 48 hour results for all experiments were then assessed jointly.

Results: Hypoxia induced a dependency on anaerobic glycolysis, consistent with increased glucose uptake and lactic acid production. TCA cycle metabolite levels indicate that in hypoxic RPE, reductive carboxylation is favored, whereas oxidative phosphorylation is suppressed. Despite a substantial decrease in ATP, hypoxic RPE maintained an energy status comparable to that of normoxic cells, presumably due to downregulation of anabolic pathways. Reduction in total glutathione and a decreased glutathione redox ratio indicate that hypoxia enhances oxidative stress.

Conclusions: Our study provides a comprehensive metabolic profile of hypoxic RPE that adds to the understanding of hypoxia-induced metabolic reprogramming as a driving force of age-related degenerative diseases in the retina. If confirmed by prospective studies, these findings can be used to develop novel strategies for modifying the metabolic stress response in hypoxic RPE and prevent vision loss.

CONTROL ID: 3538637

SUBMITTER (NAME ONLY): Mengliang Wu

TITLE: The effect of topical decorin on corneal immune cell dynamics after epithelial abrasion

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wu, L.E. Downie, H.R. Chinnery, Optometry and Vision sciences, The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|L.J. Hill, School of Biomedical Sciences, Institute of Clinical Sciences, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Decorin imparts a neuroregenerative effect that is associated with immune cell alterations in injured corneas. This study aims to explore the dynamic changes of corneal immune cell density (dendritic cells, macrophages and neutrophils) after topical application of decorin in a mouse model of sterile epithelial abrasion.

Methods: Bilateral central corneal epithelial abrasions (2-mm, Alger Brush) were performed on young C57BL/6J mice (n = 8). Decorin, or saline, was applied topically on right or left eye respectively, three times per day for one or five days. A control group (n = 8) with application of saline on both eyes was also included. Wholemout immunofluorescence staining and confocal microscopy was used to assess corneal immune cell density (CD45, Iba1, CD11c, NIMP) in the central and peripheral cornea. Cells were counted manually using ImageJ software. Data were analysed by fitting a linear mixed-effects model using restricted maximum likelihood (REML) and Kenward-Roger tests for fixed effects.

Results: At 1 day after injury, compared to the saline-treated control eyes, greater intraepithelial DC recruitment was observed in decorin-treated eyes (central: 13.2 ± 5.7 VS 7.7 ± 4.0 cells/mm², p = 0.010; peripheral: 23.8 ± 6.2 VS 18.2 ± 4.2 cells/mm², p = 0.009) but not contralateral eyes. At 5 days after injury, there was no difference between groups. The density of macrophages was similar in all groups at 1 day, but was significantly lower in the decorin-treated eyes and contralateral eyes at 5 days post-injury (central: 125.1 ± 19.2 [Decorin-treated eyes] and 156.6 ± 25.0 [Contralateral eyes] VS 180.7 ± 28.3 cells/mm² [saline-treated eyes], p < 0.001 and p = 0.041; peripheral: 114.4 ± 16.1 [Decorin-treated eyes] and 133.3 ± 22.9 [Contralateral eyes] VS 159.8 ± 26.8 cells/mm² [saline-treated eyes], p = 0.001 and 0.026). Relative to saline treated eyes, there was a lower density of central corneal neutrophils in decorin-treated eyes at 1 day after injury (155.4 ± 68.2 VS 235.2 ± 82.2 cells/mm², p = 0.041).

Conclusions: Topical decorin treatment was associated with a higher DC density, and less neutrophils during the acute phase after corneal injury, and fewer macrophages after 5 days. The contralateral effect of decorin on macrophage, but not DCs, indicates there may be different mechanisms for decorin-induced immunomodulation during corneal wound healing.

CONTROL ID: 3538642

SUBMITTER (NAME ONLY): Fidan Aghayeva

TITLE: Effect of unilateral trabeculectomy, filtering canaloplasty or PreserfloTM MicroShunt implantation on intraocular pressure in the fellow eye

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.A. Aghayeva, P. Chronopoulos, A.K. Schuster, N. Pfeiffer, E.M. Hoffmann, Johannes Gutenberg Universitat Mainz, Mainz, Rheinland-Pfalz, GERMANY|F.A. Aghayeva, Glaucoma, National Centre of Ophthalmology named after academician Zarifa Aliyeva, Baku, AZERBAIJAN|

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ABSTRACT BODY:

Purpose: This study assesses short-term intraocular pressure (IOP) change in the fellow eye of glaucoma patients after Mitomycin C-augmented trabeculectomy (TE), filtering canaloplasty (FCP) or PreserFloTM microshunt implantation (PMI) in the treated eye.

Methods: Retrospective chart review of 235 patients (235 eyes) with different types of glaucoma was performed. Patients underwent initial TE (187), FCP (25) or PMI (23) in one eye, while the fellow eye was naïve to any previous glaucoma surgery. IOP was evaluated before and on the 1st, 2nd day and at one week after surgery. Study outcomes were IOP change and proportion of clinically significant IOP elevation (postoperative IOP >21 mmHg) in the fellow eye.

Results: The median preoperative and postoperative IOP in the fellow eye on the 1st day and at one week after TE were 17 (14-20) mmHg, 16 (14-21) mmHg and 14 (12-17) mmHg, respectively. The median IOP change in the operated eyes was -12 (-18 to -7) mmHg and in the fellow eyes -3 (-6 to 0) mmHg at one week after TE ($\rho=0.24$, $p=0.001$). The median preoperative and postoperative IOP on the 1st day and at one week after PMI in the fellow eye were 15 (12.5-18) mmHg, 14 (13-16) mmHg and 14 (12-16) mmHg, respectively. The median IOP change in treated eyes at one week after PMI was -9.5 (-14.8 to -6.3) mmHg and -2 (-4 to 1.8) mmHg in fellow eyes ($\rho=0.82$; $p<0.0001$). IOP in the fellow eye at one week after TE was statistically significantly lower than preoperatively ($p<0.0001$), while the IOP did not change significantly in fellow eyes in FCP or PMI groups. The higher the preoperative IOP was in the fellow eye, the larger was the IOP-lowering effect at one week after TE ($\rho=-0.79$, $p<0.0001$) and after PMI ($\rho=-0.6$, $p<0.01$). A clinically significant IOP elevation was noted in 14.2%, 9.5% and 5% of fellow eyes after TE, FCP or PMI, respectively.

Conclusions: This study shows an IOP lowering effect in the fellow eye of glaucoma patients after TE. The higher the preoperative IOP in the fellow eye of TE and PMI patients, the larger the postoperative IOP lowering effect. The one of the possible mechanisms for IOP change could be central nervous system-mediated reflex.

CONTROL ID: 3538643

SUBMITTER (NAME ONLY): Stephanie Watson

TITLE: Acute Adenoviral Conjunctivitis Treatment: A Phase 2 Interim Analysis of OKG-0301

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Watson, Clinical Ophthalmology and Eye Health, Save Sight Institute, The University of Sydney Faculty of Medicine and Health, Sydney, New South Wales, AUSTRALIA|R. Casson, Ophthalmology, Royal Adelaide Hospital, Adelaide, South Australia, AUSTRALIA|M. Tay-Kearney, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|P. Giles, Albury Eye Clinic, Albury, New South Wales, AUSTRALIA|N. Verma, Hobart Eye Surgeon, Hobart, Tasmania, AUSTRALIA|N. Liebenberg, Browns Plains Family Practice, Browns Plains, Queensland, AUSTRALIA|H. Bloom, Vale Medical Practice, Brookvale, New South Wales, AUSTRALIA|M. Daniell, Ophthalmology, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|F. Faigenbaum, Mirrabooka Medical Centre, Mirrabooka, Western Australia, AUSTRALIA|E. Daniels, B. Strem, Okogen Pty Ltd, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Treatment of acute adenoviral conjunctivitis remains an unmet medical need, with no approved therapies available worldwide. OKG-0301 is a topical ophthalmic formulation of ranpirnase, an RNase A family member, with broad-spectrum antiviral properties.

Methods: The RUBY trial is a 219 patient, prospective, multi-center, double-blind, vehicle controlled, Phase 2 trial evaluating the safety, tolerability, and efficacy of OKG-0301 0.03% and OKG-0301 0.012% versus vehicle. Patients within 72 hours of the onset of signs and symptoms of adenoviral conjunctivitis, along with a positive QuickVue (Quidel) adenoviral conjunctivitis test were randomized and dosed in both eyes QID for five days. Four visits at days 1, 4, 7, & 14, each included a clinical assessment and an ocular swab for viral titer determination. The primary outcome was safety and tolerability of OKG-0301 and secondary outcomes included viral titer (Least Square Means [LSMean] comparison) and clinical assessments, including redness and discharge. An interim analysis was performed to evaluate the initial safety and efficacy of OKG-0301.

Results: Fifty-eight subjects were randomized and included in the Intent To Treat (ITT) population. The modified ITT (mITT), defined prospectively as subjects with > 100 viral copies/mL via PCR at visit 1 and who received at least a single dose of investigational product, included 41 patients. In the ITT population, there were no Treatment Emergent Serious Adverse Events and one patient with a Treatment Emergent Adverse Event suspected due to study medication in the vehicle control group. In the mITT evaluation, OKG-0301 had an antiviral effect via reduction of viral titers relative to placebo (day 7 placebo vs OKG-0301 0.012% vs OKG-0301 0.03% (LOG10 transformed, LSEan +/- SE): 1.06 +/- 0.22 vs 0.34 +/- 0.27 vs 0.62 +/-0.27, respectively, p<0.05; Fig 1). There was neither a better nor worse (NS = non-significant) difference in the clinical resolution of redness and discharge in the active vs placebo groups at day 7.

Conclusions: OKG-0301 is a safe and effective antiviral for the treatment of acute adenoviral conjunctivitis. Its main biological activity appears to be limited to acceleration of viral eradication, with no observed effect on redness and discharge. Further formulation and additional clinical evaluation is warranted to develop OKG-0301 as the first approved treatment of acute adenoviral conjunctivitis.

CONTROL ID: 3538653

SUBMITTER (NAME ONLY): Ramin Khoramnia

TITLE: Comparison of real-life treatment of naïve patients with ranibizumab over 24 months for neovascular AMD, diabetic macular edema, retinal vein occlusion and myopic CNV – results of the current interim analysis of the PACIFIC study

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Khoramnia, University Eye Clinic, Ruprecht Karls Universität Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|C. Haritoglou, K. Markova, Augenklinik Herzog Carl Theodor, GERMANY|M. Iwersen, U. Michel, Novartis Pharma GmbH, Nurnberg, Bayern, GERMANY|S. Grisanti, Klinik für Augenheilkunde, Universitätsklinikum Schleswig-Holstein, Campus Lübeck, GERMANY|J. Schrecker, Ophthalmology, Rudolf Virchow Klinikum Glauchau gGmbH, Glauchau, Sachsen, GERMANY|C. Winkler von Mohrenfels, Augenarztpraxis Privatdozent Dr. med. Christoph Winkler von Mohrenfels, GHANA|F. Ziemssen, Ophthalmology, Universitätsklinikum Tübingen, Tübingen, Baden-Württemberg, GERMANY|T. Hammer, Augenzentrum "Frohe Zukunft", GERMANY|

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ABSTRACT BODY:

Purpose: To evaluate real-world health care management of intravitreal ranibizumab 0.5 mg in German treatment-naïve patients within 24 months in the indications documented.

Methods: PACIFIC is a 24-months observational, non-interventional study of 5.014 patients at 186 sites, conducted to evaluate ranibizumab treatment patterns in real-life conditions according to local routine clinical practice in Germany, Switzerland and the Netherlands, respectively.

Results: Upon enrolment, 1572 (45.1%) of 3488 documented German patients were treatment naïve with indication split of neovascular AMD (nAMD (60.8%)), diabetic macular edema (DME (18.5%)), branch retinal vein occlusion (BRVO (10.7%)), central retinal vein occlusion (CRVO (7.7%)) and myopic choroidal neovascularization (mCNV (2.0%)). The mean patient age [years (standard deviation)] was 78.2 (8.5) in nAMD, DME 66.5 (11.8), BRVO 69.3 (11.8), CRVO 71.4 (11.8) and mCNV 58.2 (15.6). The gender distribution female 60.4% (nAMD), 43.3% (DME), 48.2% (BRVO), 47.9% (CRVO) and 58.1% (mCNV) . Visual acuity at baseline [letters (SD)] was for nAMD 52.6 (22.3), DME 62.8 (15.8), BRVO 58.2 (19.1), CRVO 46.9 (26.0) and mCNV 52.7 (23.3). A combination of optic coherence tomography (OCT) and fluorescein angiography (FA) assessment at baseline was performed for nAMD in 56.0%, DME 54.5%, BRVO 59.9%, CRVO 56.8% and mCNV 60.0% of the patients, whereas neither OCT nor FA assessment

at BL was performed for nAMD in 5.4%, DME 6.9%, BRVO 0.6%, CRVO 7.6% and mCNV 10.0% of patients. The average time [days (SD)] from baseline visual acuity to the first injection was for nAMD 8.5 (12.7), in DME 9.9 (14.3), with BRVO 6.2 (8.4), CRVO 7.8 (11.9) and mCNV 10.2 (12.8). The number of injections given within 24 months was in nAMD 10.0 (5.2), DME 9.8 (6.4), BRVO 10.3 (4.1), CRVO 9.6 (5.0) and mCNV 3.0 (2.4). The most common treatment regimen reported at 24 months was “monitor and extend” (nAMD 69.1%, DME 72.5%, BRVO 70.2%, CRVO 79.3% and mCNV 71.0%).

Conclusions: The PACIFIC study provides real-life data on therapy with anti-VEGF ranibizumab and on routine health care structural use. The value of observational insights from routine clinical practice may lead to a better understanding of status quo and challenges in patient health care under real life settings.

CONTROL ID: 3538665

SUBMITTER (NAME ONLY): Rajvi Mehta

TITLE: Effect of Dietary Modification on Incident Open-Angle Glaucoma in a Randomized Trial

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Previous reports have examined the associations between fruit and vegetable intake, dietary fat consumption, and open-angle glaucoma (OAG). Antioxidants were thought to be neuroprotective while a higher ratio of omega-3 to omega-6 fatty acids diet was associated with an increased risk for OAG. We conducted a secondary analysis of a randomized intervention trial to test if dietary modification (DM) altered the risk of OAG.

Methods: Our analyses were based on an intent-to-treat design, with a follow up to the end of continuous coverage in Medicare part B, death, or the last date that Medicare claims data was available (12/31/2018), whichever occurred first. We linked Medicare claims data to 45,203 women in the Women's Health Initiative Dietary Modification Trial, of which 23,776 participants were enrolled in fee-for-service Medicare Part B and had physician claims. Women were randomized to follow either dietary modification (DM) (a diet low in fat, with increased vegetable, fruit, and grain intake) or the usual diet with no modifications. Primary OAG was defined as the first claim with the International Classification of Diseases (ICD)-9 or ICD-10 codes. We used Cox proportional hazards models to calculate hazard ratios (HR) and 95% confidence interval for risk of OAG in intervention and control groups. Subgroup analyses were performed and P-interaction values were evaluated for selected characteristics.

Results: After exclusion of women with Medicare-derived glaucoma prior to randomization, the final analysis included 23,217 women (mean age = 68.5 ± 4.8 years). Baseline characteristics including diabetes, hypertension, BMI ≥ 30 were balanced between the intervention and control groups. The final models were adjusted for age and race/ethnicity. As reported in Table 1, OAG incidence was 12.9% (mean follow-up = 11.6 ± 7.4 years; mean DM duration = 5.2 ± 3.2 years). After adjusting for BMI ≥ 30 , hypertension, diabetes, and statin use, we found no overall benefit of DM in reducing incident OAG (HR = 1.04, 95% CI = 0.96-1.12). Race and participant age did not modify the relation between DM intervention and OAG risk (P interaction 0.25 and 0.44, respectively).

Conclusions: Analysis suggests that DM does not reduce the risk of incident OAG among women regardless of age or race.

CONTROL ID: 3538666

SUBMITTER (NAME ONLY): Massimo Nicolò

TITLE: Real-world use of intravitreal aflibercept (IVT-AFL) in neovascular age-related macular degeneration (nAMD) in Italy: results from PERSEUS-IT at Years 1 and 2

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nicolò, University of Genova, Genova, ITALY|F. Ciucci, San Pietro Fatebenefratelli Hospital, Rome, ITALY|A. Russo, University of Catania, Catania, ITALY|M. Nardi, University of Pisa, Pisa, ITALY|S. Torregrossa, Villa Sofia Cervello Hospital, Palermo, ITALY|A. Scupola, Fondazione Policlinico Universitario "A.Gemelli" IRCCS, Rome, ITALY|M. Vadalà, University of Palermo, Palermo, ITALY|B. Parolini, Clinica Sant'Anna, Brescia, ITALY|

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ABSTRACT BODY:

Purpose: PERSEUS-IT (NCT02289924) was a prospective, observational, 2-year (Y) study to evaluate the effectiveness and safety of IVT-AFL in patients with nAMD in routine clinical practice in Italy.

Methods: Treatment-naïve patients with nAMD for whom the decision was made to treat with IVT-AFL per routine clinical practice and local prescribing information were enrolled. The primary endpoint was mean change in best-corrected visual acuity (BCVA; decimals) from baseline to Y1 and Y2. Outcomes were evaluated (at baseline, Week 4, and every 2 weeks thereafter) for the whole study population and for 2 treatment cohorts: regular (patients receiving 3 initial monthly doses, and a total of ≥ 7 injections in Y1 and ≥ 4 injections in Y2) and irregular (any other pattern).

Results: Of 813 patients enrolled, 709 were included in the full analysis set (FAS); BCVA data were available for 342 patients at Y1 (FAS Y1, 140 regular and 202 irregular) and 233 patients at Y2 (FAS Y2, 37 regular and 196 irregular). Main results are summarized in Table 1. In the FAS, mean BCVA change from baseline was +0.09 decimals at Y1 and +0.02 at Y2.

The percentage of patients who achieved a BCVA ≥ 0.5 decimals (70 Early Treatment Diabetic Retinopathy Study [ETDRS] letters) at Y1 and Y2 was 50.0% and 44.6%, respectively. A repeated measures model considering cohorts, time points and interaction cohort/time point, showed that the difference in mean estimated BCVA between cohorts was statistically significant both in FAS Y1 and FAS Y2, while the interaction cohort/time point was significant only in FAS Y1. Central retinal thickness (CRT) showed a consistent decrease across all analysis sets. Ocular adverse events were reported in 4.1% (n=33/810 [safety set]) of patients; the most common was cataract (0.6%; n=5).

Conclusions: PERSEUS-IT showed that treatment with IVT-AFL resulted in substantial functional and anatomic improvements in patients with nAMD treated in a routine clinical setting. The repeated measures model found the trend of estimated mean BCVA over time was significantly different in the two cohorts (regular and irregular), with BCVA higher at each time point in the regular cohort. The safety profile of IVT-AFL was consistent with prior studies.

CONTROL ID: 3538673

SUBMITTER (NAME ONLY): Claudio Bucolo

TITLE: VITAMIN D3 AND MESO-ZEAXANTHIN COMBINATION PROTECTS HUMAN RETINAL PIGMENTED EPITHELIAL CELLS IN AMD

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bucolo, F. Lazzara, F. Conti, C. Platania, F. Drago, Biomedical and Biotechnological Sciences, University of Catania, Catania, ITALY|C. Bucolo, F. Drago, Center for Research in Ocular Pharmacology - CERFO, University of Catania, Catania, ITALY|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a multifactorial retinal disease. Amyloid- β (A β) deposition has been reported in patients with AMD among the constituents of drusen, which cause inflammation, oxidative stress and retinal pigmented epithelium (RPE) damage. Hereby, we assessed the effect of vitamin D3 and meso-zeaxanthin combination in several in-vitro models of AMD, challenging retinal cells with three different types of damage.

Methods: Human ARPE-19 cells were exposed to three different stimuli (A β , LPS, H₂O₂) in separate set of experiments. For all experiments, the cells were pre-treated for 24 hours with vitamin D3 (50 nM-1 μ M), meso-zeaxanthin (0.1 μ M and 0.5 μ M) or their combination; then, ARPE-19 were exposed to the different insults in separate set of experiments. The damage of A β , LPS, H₂O₂, and the protective effects of molecules were evaluated with MTT, LDH, ROS assay and the modulation of inflammatory mediators (IL-1 β , IL-6, TNF α , MMP-9 and VEGF) was evaluated with RT-PCR.

Results: The combination of vitamin D3 and meso-zeaxanthin significantly protected ARPE-19 against the damage elicited by A β , LPS, and H₂O₂. These three stimuli significantly ($p < 0.05$) reduced cell proliferation, increased LDH and ROS release after different time of treatment. These effects were significantly ($p < 0.05$) counteracted by the combination of vitamin D3 and meso-zeaxanthin treatment. Further, the expression of inflammatory mediators such as IL-1 β , IL-6 and TNF α was significantly ($p < 0.05$) reduced by vitamin D3 and meso-zeaxanthin combination treatment. Finally, a potentiation effect has been demonstrated by vitamin D3/meso-zeaxanthin; the combination was, in fact, able to reduce significantly ($p < 0.05$) the expression of VEGF-A and MMP-9 mRNA, in ARPE-19 challenged with LPS and H₂O₂ in comparison with the single molecules

Conclusions: These findings demonstrated, at least in these in-vitro paradigms, that combination of vitamin D3/meso-zeaxanthin exerts an enhanced protective effect in ARPE-19 cells damaged by amyloid- β , inflammation (LPS) and oxidative stress (H₂O₂) that represent the initiating events leading to AMD.

CONTROL ID: 3538686

SUBMITTER (NAME ONLY): Zou Ming

TITLE: Activation of cGAS-STING signaling in photoreceptors after sodium iodate-induced retinal pigment epithelium injury

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Ming, L. Gong, R. Qi, Q. Ke, D. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA]

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ABSTRACT BODY:

Purpose: Geographic atrophy (GA) is an untreatable form of age-related macular degeneration (AMD) affecting five million individuals worldwide. Dysfunction of innate immunity plays a pivotal role in AMD pathogenesis. However, the cGAS-STING signaling, a key cytosolic DNA sensor system in innate immunity, has not been explored in the retina. In this study, we aimed to investigate the regulation of cGAS-STING signaling in retina of AMD patients and the GA-like mouse model.

Methods: To induce the GA-like mouse model, C57BL/6J mice (5-6 weeks) were intraperitoneally injected with 35 mg/kg of sodium iodate (n=5). The control mice were injected with PBS (n=5). In silico analysis of RNA-seq and ATAC-seq data were performed to evaluate the cGAS and STING genes expression patterns in the retina of AMD patients. Hematoxylin and eosin staining, immunohistochemistry and immunofluorescence were performed to evaluate the cGAS-STING signaling activation and cytosolic DNA accumulation in the mouse retina. Real-time PCR and Western blot assay were used to analyze the expression of cGAS-STING signaling and proinflammatory cytokine in control and SI-exposed mice.

Results: Our in silico analysis shows specifically upregulated STING mRNA level and increased chromatin accessibility around cGAS and STING promoters in macular retinas from dry AMD patients. Further, we found activation of cGAS-STING signaling in retinas after SI injury, which was caused by the releasing of cytosolic double-stranded DNA (dsDNA) in photoreceptors.

Conclusions:

In summary, our study shows that accumulation of cytosolic dsDNA and activation of cGAS-STING signaling in photoreceptors are pivotal innate immunity response after RPE injury. The results suggest that the cGAS-STING signaling may be a potential therapeutic target for photoreceptor degeneration in GA.

CONTROL ID: 3538692

SUBMITTER (NAME ONLY): Onyekachukwu Amiebenomo

TITLE: Effect of viewing distance on fixation characteristics in typical observers

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.M. Amiebenomo, L. Mcllreavy, J.T. Erichsen, J.M. Woodhouse, School of Optometry and Vision Sciences, Cardiff University, Cardiff, Wales, UNITED KINGDOM|O.M. Amiebenomo, Department of Optometry, University of Benin, Benin City, Edo, NIGERIA|

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ABSTRACT BODY:

Purpose: Fixation is the state in which the eyes foveate a target. Previous studies on fixation stability were undertaken at distances of 40cm or greater, and thus have not systematically examined the effect of viewing distance (hence vergence). In some cases of visual impairment, evidence suggests that fixation is more stable while viewing at near. However, the effect of vergence on fixation in typical participants is not known. This study, therefore, explores the stability of fixation with viewing distance, in those without visual impairment.

Methods: Eye position was measured at 1000Hz over 15secs for 10 participants (4 females; mean age, 26.9 years; range, 22–37 years), as they binocularly viewed a 0.5° dot, at 300, 100, 50 and 25cm. Using the last 5secs of data, a bivariate probability density function was used to determine the accuracy and precision with which participants fixated. The isocontour surrounding the gaze positions with the highest 68% probability density were selected for further analysis. Accuracy was computed as the vector from the target position to the centroid of the 68% isocontour, while precision was quantified using the isocontour area and shape, as well as the orientation of its major axis. A repeated measures ANOVA was used to compare the effect of distance. Where Mauchly's test indicated assumption of sphericity was violated, the Greenhouse-Geisser correction was used.

Results: There was no significant main effect of viewing distance on mean accuracy ($F_{1.690, 15.208} = 0.935$, $p = 0.399$, $\eta^2 = 0.047$), contour area ($F_{3, 27} = 0.293$, $p = 0.830$, $\eta^2 = 0.022$) or shape ($F_{3, 27} = 0.641$, $p = 0.595$, $\eta^2 = 0.048$). Between participants, the orientation of the isocontour major axis was similar at all viewing distances (Rayleigh test; $p < 0.05$), except for the left eye at 100cm (mean = 34.66°; 95CI ±55.5°; $p = 0.06$) and at 300cm (mean = -41.23°; 95CI ±72.35°; $p = 0.12$), respectively. Within participants, the orientation of the isocontour major axis was similar at all viewing distances in 7 out of the 10 participants (Rayleigh test; $p < 0.05$).

Conclusions: We found no evidence that distance, and therefore convergence, influences the stability of fixation. We conclude that fixation may not have to be more precise for successful near work. The results suggest that, in a typical classroom for example, where viewing distance varies, the ability of typical students to fixate adequately is unaffected.

CONTROL ID: 3538695

SUBMITTER (NAME ONLY): SARA AISSATI

TITLE: Convolved vs. Optically blurred images-What is the key reason for the observed differences?

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. AISSATI, M. Vinas, C. Benedi-Garcia, S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Image convolutions are often used to simulate the effects of ocular aberrations on image quality. We studied potential discrepancies in the image degradation/visual performance using convolved images (viewed through corrected optics) or the real aberrations, in both monochromatic & white light (WL)

Methods: On bench & visual acuity measurements in patients were obtained using a custom polychromatic Adaptive Optics (AO). The system allows measurement (Hartman-Shack, HASO) & correction/induction (deformable mirror, DM, MIRA, Imagine Eyes) of high order aberrations (HOAs). Stimuli were displayed in a Digital Micro-Mirror Device (DMD), illuminated with 450, 555, 670 nm, & WL. Image convolutions of a stimulus (20/100 black E-letter, 25 cd/m²) were obtained with standard Fourier Optics (Matlab) using subject's HOAs (diffraction limit (DL) control). An artificial eye was used to image the original stimulus through real HOAs (mapped on DM) or the convolved (conv) stimulus (AO). In subjects (4 young cyclopleged) Visual Acuity (VA, tumbling high contrast E-letter, 8 AFC + QUEST) was measured under natural HOAs & with conv images under AO, for the 3λ & WL (6 mm pupil)

Results: Subject's Visual Strehl ranged from 0.17-0.33. On bench, the stimulus contrast through diffracted/aberrated optics & the conv image with a DL/subject PSF differed on avg by 0.40/0.50 (450), 0.34/0.58 (555), 0.30/0.58 (670) & 0.43/0.53 (WL), with conv images overestimating image degradation. Computer simulations revealed that the second-pass (DL/residual aberration) was only responsible of 11/12% loss in contrast. In subjects, logMAR VA was on avg, 0.10 ± 0.01, -0.08 ± 0.03, 0.03 ± 0.02 & -0.03 ± 0.04 with natural aberrations & 0.27 ± 0.03, 0.10 ± 0.05, 0.18 ± 0.02 & 0.14 ± 0.04 (450, 555, 670 & WL) using conv stimulus. Measured VA is correlated with native optical quality in 555 nm with natural optics ($r^2 = 0.98$, $p = 0.01$) but not in WL ($r^2 = 0.45$, $p = 0.30$). Differences (Natural-Conv) ranged btw -0.07 to -0.29 (avg across λ for each subject). There was not a consistent larger difference in monochromatic vs WL

Conclusions: The use of convolved stimuli underestimates the measured VA (comparison with high contrast stimuli & natural optics). Discrepancies must occur in part from optical grounds, as are also found on bench. Although the magnitude of the native optical aberrations & chromatic effects appear to play some role, they do not fully responsible for the effect, likely associated to approximations in the convolution representation of the images

CONTROL ID: 3538696

SUBMITTER (NAME ONLY): Lisa Nivison-Smith

TITLE: Wall-to-Lumen Ratio is altered in Intermediate Age-Related Macular Degeneration but not exacerbated with Hypertension.

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Nivison-Smith, M. Trinh, A. Faiza, T. Roy, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|L. Nivison-Smith, M. Trinh, Centre for Eye Health Ltd, Kensington, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine if wall-to-lumen ratio (WLR) is altered in eyes with age-related macular degeneration (AMD) in individuals with and without systematic hypertension.

Methods: OCT 6 x 6 mm en face retinal images centred on fovea (Zeiss HD-OCT 5000 AngioPlex) were examined for a total of 30 eyes with intermediate age-related macular degeneration, 12 eyes with AMD and hypertension and 43 control eyes. All eyes were from participants aged 50 years or over and did not have diabetes mellitus, hypercholesterolemia or any other systemic vascular disease. Three independent graders were randomly allocated one-third of eyes each to identify the largest arteriole and venule closest to the optic nerve head and within 75 pixels of the image border. Graders then measured the inner and outer diameter in duplicate for all identified vessels in all eyes based on a perpendicular line drawn to a tangent of the vessel. WLR was calculated as the difference between outer and inner vessel diameter divided by inner diameter.

Results: An arteriole and venule that fit the above measurement criteria was identified in 85% and 75% of all study eyes respectively. Sub-group analysis indicated this created no significant difference in age (arteriole: $p = 0.15-0.92$; venule: $p = 0.08-0.76$) or signal strength index (arteriole: $p = 0.16-0.62$; venule: $p = 0.06-0.32$) between all study groups. There was no significant difference in arteriole WLR between control and AMD eyes (1.37 ± 0.41 vs 1.28 ± 0.46 , $p = 0.185$) or control and AMD eyes with hypertension (1.47 ± 0.46 vs 1.21 ± 0.51 , $p = 0.103$). For venules, however there was a significant decrease in WLR between control and AMD eyes (1.47 ± 0.46 vs 1.23 ± 0.36 , $p < 0.001$) and control and AMD eyes with hypertension (1.47 ± 0.46 vs 1.21 ± 0.46 , $p < 0.001$). There was no difference in WLR between AMD eyes with or without hypertension for either vessel type ($p = 0.25 - 0.474$). There was strong agreement within and between graders for all arteriole and venule WLR measurements except for graders 1 and 2 in control eyes ($p < 0.05$).

Conclusions: WLR of venules is significantly decreased in venules in eyes with intermediate AMD but is not necessarily exacerbated in conjunction with hypertension. WLR may be a useful measurement in the assessment of retinal vascular health in intermediate AMD.

CONTROL ID: 3538714

SUBMITTER (NAME ONLY): Hilde van der Aa

TITLE: Economic evaluation of an e-mental health intervention for patients who receive anti-VEGF treatment: outcomes of the E-PsEYE randomized controlled trial

SESSION TITLE: Visual Impairment during a pandemic

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.P. van der Aa, G. van Rens, R.M. Van Nispen, Ophthalmology, Amsterdam UMC Locatie VUmc, Amsterdam, Noord-Holland, NETHERLANDS|M. Koopmanschap, Health Technology Assessment, Erasmus Universiteit Rotterdam, Rotterdam, Zuid-Holland, NETHERLANDS|G. van Rens, Ophthalmology, Elkerliek Ziekenhuis, Helmond, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Patients who receive anti-vascular endothelial growth factor (VEGF) treatment for retinal exudative diseases, often experience mental health problems. To support patients in dealing with these problems, a guided Internet-based self-help course, following the principles of cognitive behavioral therapy (called E-PsEYE), was developed. Our aim was to evaluate whether E-PsEYE was cost-effective in comparison with usual care from a societal perspective.

Methods: A single blinded multicenter randomized controlled trial was performed in two parallel groups with a follow-up of 12 months. In total, 174 patients (58% male, mean age 70 year) who experienced mild to moderate symptoms of depression and/or anxiety and received anti-VEGF treatment participated in our study. Main outcome measures were depression (measured with the Patient Health Questionnaire-9), anxiety (measured with the Hospital Anxiety and Depression Scale – Anxiety), and quality-adjusted life years (QALYs, measured with the EuroQoL-5 Dimensions and the Health Utilities Index-3). Costs were based on direct healthcare costs and indirect non-healthcare costs.

Results: Based on intention to treat, significant intervention effects were found on depression (group difference -0.22, 95% confidence interval (CI) -0.43 to -0.01), but not on anxiety (-0.002, 95%CI -0.18 to 0.17). Non-significant societal cost savings were found (mean difference -1130 Euro; 95%CI -5101 to 2841, which is equivalent to -1387 USD; 95%CI -6263 to 3488), mainly due to less productivity losses in the intervention group. Drop-out (20% in total) was significantly higher in the intervention group. The cost-effectiveness acceptability curve showed that the probability of cost-effectiveness was 72% or more at a willingness-to-pay of €0 per QALY and did not increase at a higher ceiling ratio.

Conclusions: Significant intervention effects on depression and small cost-savings were found, however, the difference with usual care was minimal. Therefore, we cannot state that E-PsEYE is dominant to usual care. Future studies should investigate how the cost-effectiveness of E-PsEYE can be improved.

CONTROL ID: 3538719

SUBMITTER (NAME ONLY): Amy O'Regan

TITLE: The Role of the Lysophosphatidic Acid Axis in the Fibrotic Changes of the Lamina Cribrosa in Glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. O'Regan, S.B. Eivers, C.J. O'Brien, University College Dublin, Dublin, IRELAND|A. O'Regan, S.B. Eivers, C.J. O'Brien, Mater Misericordiae University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Lysophosphatidic acid (LPA) is a bioactive lipid mediator that is essential for a variety of cellular processes including proliferation, differentiation, transcription and survival. LPA signalling is dysregulated in many conditions such as cancer, atherosclerosis, and pulmonary and renal fibrosis. LPA is produced extracellularly by Autotaxin (ATX) and is degraded by three membrane bound lipid phosphate phosphatases (LPP 1-3). It acts via six G-protein coupled receptors on the cell surface (LPA₁₋₆) to activate intracellular pathways. LPA enhances fibroblast proliferation, migration and contraction, and induces expression of pro-fibrotic mediators such as connective tissue growth factor. In glaucoma, there is disturbed extracellular matrix remodelling and fibrosis in the lamina cribrosa of the optic nerve head, and it is within this region that retinal ganglion cell axons degenerate. We wished to assess whether LPA signalling plays a role in mediating fibrosis in the lamina cribrosa in glaucoma.

Methods: We cultured primary human lamina cribrosa cells from age-matched normal and glaucoma patient donors. Quantitative real time PCR was used to assess expression of gene targets within the LPA axis, as well as those involved in fibrosis. These included the LPA₁₋₃ receptors, ATX, the LPPs, Collagen 1a1 (COL1A1), Fibronectin, and Alpha Smooth Muscle Actin (α-SMA).

Results: Genes overexpressed in glaucoma lamina cribrosa cells included ATX, LPP3, LPA₁ and LPA₃ receptors. Expression of the fibrosis genes COL1A1, α-SMA and Fibronectin was also upregulated in glaucoma compared to normal lamina cribrosa cells.

Conclusions: Our results show that the LPA signalling axis is altered in glaucoma. This suggests a role for the LPA axis in the fibrotic changes observed in the lamina cribrosa in glaucoma and may indicate a potential pharmacological target.

CONTROL ID: 3538723

SUBMITTER (NAME ONLY): Joao Furtado

TITLE: Global vision loss due to age-related macular degeneration

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Furtado, Ophthalmology, Universidade de Sao Paulo Faculdade de Medicina de Ribeirao Preto, Ribeirao Preto, São Paulo, BRAZIL|J. Jonas, Department of Ophthalmology, Medical Faculty Mannheim, Heidelberg University, Mannheim, GERMANY|T. Peto, The Queen's University of Belfast, Belfast, UNITED KINGDOM|J.D. Steinmetz, P.S. Briant, T. Vos, Institute for Health Metrics and Evaluation, Seattle, Washington, UNITED STATES|T.Y. Wong, M. He, University of Melbourne, Melbourne, Victoria, AUSTRALIA|A. Bron, Service d'Ophtalmologie CHU Dijon, Dijon, FRANCE|S. Resnikoff, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|J.H. Kempen, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|J.H. Kempen, Harvard University, Cambridge, Massachusetts, UNITED STATES|T. Braithwaite, Medical Eye Unit, St Thomas' Hospital, London, UNITED KINGDOM|R.R. Bourne, Anglia Ruskin University, Cambridge, UNITED KINGDOM|H.R. Taylor, Centre for Eye Research Australia, University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To contribute to the WHO initiative, VISION 2020: The Right to Sight, an assessment of the causes of global vision impairment in 2020 and temporal change is needed. We aimed to extensively update estimates of global vision loss burden due to age-related macular degeneration (AMD), presenting estimates for 2020, temporal change since this initiative commenced, and distribution by sex and region.

Methods: We did a systematic review and meta-analysis of population-based surveys of eye disease from January 1980 to October 2018. The data from these surveys are collated by the Vision Loss Expert Group in the Global Vision Database. We fitted hierarchical models to estimate prevalence (with 95% uncertainty intervals [UIs]) of moderate and severe vision impairment (MSVI; presenting visual acuity from <6/18 to 3/60) and blindness (<3/60 or less than 10° visual field around central fixation) caused by AMD, stratified by age, region, and year. The analysis focused on adults aged 50 years and older.

Results: In 2020, worldwide, an estimated 1.84 million (1.34 to 2.42) people aged 50+ years were blind due to AMD, and a further 6.22 million (5.03-7.57) moderately or severely vision impaired (MSVI). There had been a 42.1% (39.4-43.3) increase in cases of blindness and a 93.7% (92.4-94.2) increase in cases of MSVI since 2000. Over the same period, the age-standardized prevalence of AMD blindness decreased by 22.6% (21.2 to 24.7), and MSVI increased by 8.6% (7.7-9.4). In terms of the age-standardized prevalence of AMD blindness, the ratio of females to males affected was 1.45:1.00 in 2020 and 1.44:1.00 in 2000. Between 2000 and 2020, the age-standardized prevalence of AMD blindness in males and females decreased to a similar extent (22.2% versus 21.7%). Among GBD super-regions, North Africa and Middle East had the highest crude AMD blindness rates in 2020 in adults aged 50+ (0.18%; 0.13-0.25), followed by the High-Income super-region (0.14%, 0.11-0.18). The most profound reduction (>-30%) in age-standardized AMD blindness rates between 2000 and 2020 was in Southeast Asia, East Asia, and Oceania (-34.1%, -32.8 to -36.1).

Conclusions: Despite a decrease in the age-adjusted prevalence of AMD-related blindness, the increase in the age-adjusted prevalence of AMD-related MSVI and the increase and ageing of the population led to a marked increase in

the number of individuals affected by AMD-related blindness and MSVI.

CONTROL ID: 3538741

SUBMITTER (NAME ONLY): Sohaib Rufai

TITLE: Ophthalmologic Detection of Intracranial Hypertension in Surgical Patients with Craniosynostosis: A Diagnostic Accuracy Study

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.R. Rufai, O.R. Marmoy, V. Panteli, K. Schwiebert, D.A. Thompson, R. Bowman, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|S.R. Rufai, F.A. Proudlock, I. Gottlob, Ulverscroft Eye Unit, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|L.S. van de Lande, R.W. Breakey, D.J. Dunaway, R. Hayward, N. Jeelani, Craniofacial Unit, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|C. Bunce, Clinical Trials Unit, Royal Marsden NHS Foundation Trust, London, UNITED KINGDOM|L.S. van de Lande, R.W. Breakey, D.A. Thompson, D.J. Dunaway, R. Hayward, R. Bowman, N. Jeelani, Institute of Child Health, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To assess the diagnostic accuracy of fundoscopy and visual evoked potentials (VEPs) in detecting intracranial hypertension (IH) in patients with syndromic and non-syndromic craniosynostosis undergoing spring-assisted posterior vault expansion (sPVE) surgery; to evaluate visual outcomes.

Methods: Children with craniosynostosis undergoing sPVE and 48-hour intracranial pressure (ICP) monitoring at a quaternary centre were included in this retrospective diagnostic accuracy study. Longitudinal data for ICP, fundoscopy, VEP and best-corrected visual acuity (BCVA) were collected between February 2002 and March 2019. Primary outcome measures were papilloedema on fundoscopy, VEP assessments and IH, defined as mean ICP >20 mmHg. Diagnostic indices were calculated for fundoscopy and VEP against ICH. Secondary outcome measures included final visual outcomes.

Results: Fundoscopic examinations within 6 months of ICP assessments were available for 35 children and isolated VEPs for 29 children, of which 22 children had at least three serial VEPs. Specificity for IH was 100% for all measures. Sensitivity was poor for fundoscopy (32.1%; 95% CI: 15.9-52.4), moderate for isolated VEP (65.2%; 95% CI 44.9-81.2) and good for serial VEP stability (82.4%; 95% CI: 56.6-96.2). Median final BCVA was 0.24 logMAR (n=36; IQR: 0.51; range: -0.06 to 2.7). UK driving standard BCVA was achieved by 26 patients (72.2%), defined as >0.30 logMAR in the better eye.

Conclusions: Papilloedema present on fundoscopy reliably indicated IH, but its absence did not exclude IH. VEP monitoring demonstrated higher sensitivity for detecting IH, with serial testing increasing sensitivity even further. To the best of our knowledge, this represents the largest study of its kind.

CONTROL ID: 3538748

SUBMITTER (NAME ONLY): Clara Benedi-Garcia

TITLE: Gender Identification of faces under manipulated ocular optics

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Benedi-Garcia, S. AISSATI, S. Marcos, Consejo Superior de Investigaciones Cientificas, Madrid, SPAIN|M.P. Eckstein, Vision and Image Understanding Lab, University of California System, Santa Barbara, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Correcting ocular aberrations of the eye improves certain visual tasks such as visual acuity and familiar face recognition. In addition, the eye appears to be adapted to its native optics. We evaluated how manipulated aberrations influence face gender identification (GI) performance

Methods: We used a custom-built Adaptive Optics (AO) system, with a Hartmann-Shack wavefront sensor (32x32 microlenses; HASO, ImagineEyes, 827mm), an electromagnetic deformable mirror (DM, 52 actuators; MIRA0), a motorized Badal system and a psychophysical channel (CRT monitor). Nine subjects participated in the study (sph=-1.6±2.15D, cyl=-0.6±0.6D, age=30.4±9.6yrs). The subjects' ocular aberrations were measured to estimate their Visual Strehl(VS, max 1). Five conditions were evaluated for GI and Visual Acuity (VA): natural aberrations (Nat), AO-correction (AO), 90deg rotated aberrations (Rot), and 2 external patterns, one better (NatB) and worse (NatW). For the GI experiment, we convolved images for each manipulated aberration condition (set of 200male/200female, randomly presented and alternating conditions in blocks of 100 images). Images were presented through the DM correcting subjects' aberrations. VA was measured with conditions mapped in the DM, using tumbling E letters (8 orientations) and QUEST. Learning effects were analyzed with a logistic regression in a binary model

Results: There was no learning effect through the session. GI performance (%GI) was highly correlated with VS ($r=0.90$; $p<0.005$). %GI for the AO vs Nat conditions were highly correlated ($r=0.68$, $p=0.06$) with higher differences %GI AO-Nat in subjects with poorer optical quality ($\geq 8\%$). %GI was higher for Nat than Rot in the less aberrated subjects with a significant %GINat-Rot vs RMS correlation ($r=0.4$; $p=0.33$). Only 29% of the subjects with poorer optics (avg VS=0.2±0.06) obtained a higher %GI with Nat than with either NatB (0%) or NatW (67%). However, 86% of the subjects with better optics (avg VS=0.4±0.2) performed better with Nat than with either NatB (100%) or NatW (75%). %GI and VA correlated across conditions at subject level ($r=0.42$, $p<0.02$)

Conclusions: Both optical aberrations and neural adaptation to native blur (and its orientation) appear to play a significant role in GI, with a potentially larger role of adaptation to native aberrations in subjects with better optics. VA seems to be a good predictor of GI performance

CONTROL ID: 3538751

SUBMITTER (NAME ONLY): Nadiuska Cristine Platero Alvarado

TITLE: Convergence insufficiency in school children in Spain

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Platero Alvarado, J. Oliveros López, R. Garrido Mercado, Departamento de Optometría y visión, Facultad de Óptica y Optometría, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|N.C. Platero Alvarado, Secretaria Nacional de Ciencia Tecnologia e Innovacion, Panama, Panamá, PANAMA|

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ABSTRACT BODY:

Purpose: Convergence insufficiency is the most common binocular vision disorder but there is not much data available on its frequency. We performed a prospective cross-sectional study to determine the prevalence of convergence insufficiency at school age.

Methods: Three schools in the Madrid region of Spain participated in the study. We examined a total of 450 children from October 2019 to February 2020: 151 1st grade (mean age 6.45 ± 0.38), 190 6th grade (mean age 11.55 ± 0.44) and 109 8th grade (mean age 13.61 ± 0.48). 79.9% were males and 20.1% females. The inclusion criteria was of children enrolled in 1st, 6th, and 8th school grades, and the exclusion criteria was having any kind of ocular or systemic pathology that could interfere with ocular function, and mentally handicapped children. 3 children in total were excluded. Clinical evaluation: visual acuity, retinoscopy and binocular vision tests were performed, including near and far cover test (CT), near point of convergence (NPC) and Base In (BI) and Base Out (BO) vergences, measured with prism bar. We defined Convergence Insufficiency (CI) as having: BO break or blur point $\leq 15\Delta$ or failing Sheard's criterion; break point of NPC ≥ 6 cm; and difference between near and far foria $\geq 4\Delta$.

Results: 5 children had strabismus (1.12 %). 4 esotropia and 1 exotropia. The prevalence of CI was 2.0% in 1st grade; 4.80% in 6th grade and 4.60% in 8th grade. The difference of frequency between groups was not significant (χ^2 p= 0.37). There was a 23.10% of 1st grade children with a receded NPC; 40.64 % of 6th grade and 34.26 % of 8th grade. BO vergences ≤ 15 DP was found in 17.68% 1st grade children, in 26.7% of 6th grade and in 24.1% of 8th grade. Difference between near and far foria $\geq 4 \Delta$ was found in 11.60% children of 1st grade, 16.6% of 6th grade and 17.6% 8th grade. Only NPC was found to be significantly different between groups (χ^2 p= 0.003). 50.2% of all children didn't have any of the signs. 32.1% had just one sign, 13.8% had two signs and 3.8% had the three signs.

Conclusions: The convergence insufficiency prevalence found in school children in Spain seems to be of similar extent as in other studies, and did not vary between school grades.

CONTROL ID: 3538772

SUBMITTER (NAME ONLY): Anton Hommer

TITLE: Orally administered dronabinol increases retinal blood flow without altering oxygen extraction in healthy subjects

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We have shown previously that administration of low-dose oral dronabinol, a synthetic tetrahydrocannabinol derivate, increases optic nerve head blood flow in healthy subjects. The aim of the present study was to investigate whether dronabinol also has an effect on retinal blood flow and oxygen extraction.

Methods: A randomized, placebo-controlled, double-masked, two-way crossover study was performed in 24 healthy subjects. Two study days were scheduled for each participant, on which they either received capsules containing 5mg dronabinol or placebo capsules. Total retinal blood flow (TRBF) was measured using a custom-built Doppler Optical Coherence Tomography system. Oxygen saturation of major retinal vessels was measured with a commercially available Dynamic Vessel Analyzer. Based on these parameters, retinal oxygen extraction was calculated. Measurements were performed before and after drug administration on both study days.

Results: Placebo did not alter TRBF, retinal arterial or venous oxygen content and retinal oxygen extraction ($p > 0.1$ each). In contrast, dronabinol induced a significant increase in TRBF from 38.9 ± 6.1 to $40.7 \pm 6.7 \mu\text{l}/\text{min}$ ($p < 0.001$), which was accompanied by a significant increase in retinal venous oxygen content (from 0.129 ± 0.008 to $0.132 \pm 0.009 \text{ ml O}_2/\text{ml}$, $p = 0.02$). As no change in retinal arterial oxygen content occurred ($p = 0.12$), retinal oxygen extraction remained stable (2.2 ± 0.4 vs. $2.2 \pm 0.4 \mu\text{l O}_2/\text{min}$, $p = 0.29$).

Conclusions: These results indicate that orally administered dronabinol increases TRBF in healthy subjects without altering retinal oxygen extraction. The drug may therefore be a candidate for improving perfusion in patients with ocular vascular disease. To confirm this hypothesis, further studies in patients are needed.

CONTROL ID: 3538773

SUBMITTER (NAME ONLY): Miguel Faria-Ribeiro

TITLE: Impact of glare strength on Contrast Sensitivity

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Clinical investigations of intraocular lenses (IOL) are guided by ISO and ANSI standards, which outline parameters for procedures such as contrast sensitivity (CS). The effect of glare on CS is often studied, however, glare strength is not standardized, resulting in varying glare intensities across manufacturers. ISO/ANSI recommend a level of glare that reduces mesopic CS by 0.1 log units at 6 cpd, determined through a pilot study of young, healthy adults, while excluding subjects whose CS increased under glare conditions. Contrary to this, the American Academy of Ophthalmology (AAO) for EDOF IOLs does not specify 6 cpd or the exclusion of subjects. We conducted a pilot study to access how these two criteria might influence the calibration of the glare strength of two commercial systems.

Methods: Adults under 40 years with VA of at least 20/20 and no known ocular abnormalities were enrolled. Mesopic CS at 6 cpd was measured with and without glare in 39 subjects using the Clinical Trial Suite (CTS, M&S Technologies) and in 20 subjects using the CSV-1000 (Vector Vision) at 2.5 meters. Glare strength was set as standard for both devices (150 lux and 12 lux before 1.5 ND filter, for CTS and CSV, resp.). Two attenuated glare levels (69 and 110 lux) were also evaluated with the CTS. Mean delta between CS with and without glare was calculated.

Results: Following ANSI and ISO criteria, mean decrease in CS with glare was 0.16log units for CTS (95% CI 0.05, n=29) and 0.09log units (95% CI 0.08, n=12) for CSV, indicating that standard glare strength was overestimated for the CTS system. Under attenuated glare, decrease in CS on CTS was 0.14 (95% CI 0.06, n=20) and 0.15 (95% CI 0.05, n=24) log units for 69 and 110 lux, respectively, both above 0.1 log unit criteria. Without excluding any subjects (AAO recommendation), mean decrease in CS with standard glare was 0.08 log units (95% CI 0.06) for CTS, while CSV resulted in a mean increase in CS of 0.03 (95% CI 0.09).

Conclusions: Following ANSI and ISO criteria, all glare levels tested on CTS exceeded the requirement of 0.1 log units CS reduction at 6 cpd. Following AAO criteria, the CSV system resulted in a mean increase of CS with the standard settings. These results suggest that different criteria may have been used to calibrate glare strength of both systems, which resulted in ~12 fold difference in strength. Subsequently, clinical data obtained may not be comparable across these systems.

CONTROL ID: 3538780

SUBMITTER (NAME ONLY): Blazaki Styliani

TITLE: Progression of macular atrophy in patients receiving long-term anti-VEGF therapy for age-related macular degeneration; Real Life Data

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Macular atrophy (MA) is found in neovascular AMD, with degeneration of photoreceptors, pigment epithelium and choriocapillaries resulting in significant loss of central vision. The purpose of our study is to evaluate the progression of MA based on optical coherence tomography (OCT) in patients with age-related macular degeneration (AMD) after receiving anti-vascular endothelial growth factor (anti-VEGF) therapy for at least a 6-year period in real life settings.

Methods: This retrospective study included 53 naïve patients (53 eyes) with neovascular AMD from two centers, who were treated with anti-VEGF intravitreal injections and presented without MA at baseline. MA was evaluated in an annual basis using near infrared (IR) and spectral-domain OCT images according to criteria proposed by the Classification of Atrophy Meetings (CAM) group; hyperreflectivity of the choroid, retinal pigment epithelium absence and outer retina atrophy. Incidence and progression of MA were evaluated. Associations with best-corrected visual acuity (BCVA) and total number of injections were also included.

Results: Treatment duration of our patients was 7.34 ± 1.54 years. The mean number of anti-VEGF injections was 24.4 ± 13.6 . BCVA at baseline was 0.38 ± 0.27 logMAR and 0.60 ± 0.35 logMAR at final visit ($p=0.731$). The cumulative incidence of new MA at years 1, 2, 3, 4, 5, and 6 was 2%, 20%, 34%, 42%, 52% and 54% respectively. In patients who developed MA, mean MA area increased from no MA at baseline to $5.66 \pm 67.18 \text{ mm}^2$ at final visit ($p<0.001$). The estimated annual enlargement of MA was 0.86 mm/year based on square root transformation ($1.11 \text{ mm}^2/\text{year}$, untransformed data). Moreover, MA progression doesn't appear to be significantly correlated with age ($R=0.055$, $p=0.784$), gender ($R=0.113$, $p=0.576$), BCVA ($R=0.168$, $p=0.404$) and total number of injections ($R=0.133$, $p=0.255$).

Conclusions: In this real life setting, half of neovascular AMD patients under anti-VEGF treatment without MA at therapy initiation developed MA over a period of at least 6 years. In this study, number of injections did not seem to have a relationship with MA progression.

CONTROL ID: 3538783

SUBMITTER (NAME ONLY): Holly Duncan

TITLE: Real-world outcomes for pro re nata and treat and extend regimens in exudative age-related macular degeneration

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Evidence suggests visual outcomes in exudative age-related macular degeneration (exAMD) are better with treat and extend (TEX) than pro re nata (PRN) protocols. This has not been shown in real-world data and TEX is thought to demand more clinical resources than PRN. This is problematic as the Royal College of Ophthalmologists reports more than 200 vacant UK consultant ophthalmologist posts. We aim to establish if there is value in recommending TEX, to justify stretching resources further.

Methods: Our observational study was performed at a tertiary unit in England. The electronic medical record (EMR) identified patients receiving aflibercept intravitreal injections (IVIs) for exAMD from 2016 with three years of follow up. Visual acuity (VA) was recorded as the best corrected vision in early treatment of diabetic retinopathy (ETDRS) letters. A year of treatment was said to be PRN if 'PRN' was explicitly reported in any visit in that year. Descriptive and comparative statistics were performed with SPSS v.24. Unpaired t-tests were used to compare means between PRN and TEX groups.

Results: 175 eyes (89 left, 87% pseudophakic) from 175 patients (109 female, mean age 79.1 years) were identified with 80 eyes (44.9%) receiving PRN treatment in their second year of treatment and 68 eyes (38.2%) in their third year. PRN eyes had significantly fewer IVIs ($p<0.0001$) than those purely under the TEX regimen in their second (mean IVIs 3.9 (95%CI 3.6,4.2) versus 6.3 (5.9,6.6)) and third years of treatment (mean IVIs 4.5 (4.0,5.0) versus 6.0 (5.7,6.3)). The number of visits to clinic did not differ significantly between the PRN or TEX groups in the second (6.7 (6.3,7.0) and 6.1 (5.6,6.6) mean visits per year respectively ($p=0.077$)) year of treatment, but met an unadjusted threshold for significance in the third year of treatment (7.0 (6.5,7.4) and 6.2 (5.8,6.7) mean visits per year respectively ($p=0.018$)). Change in VA was equivocal between the two treatment groups in the second ($p=0.19$) and third year ($p=0.98$).

Conclusions: These data suggest that a PRN approach offers equivocal visual outcomes to TEX for exAMD patients, whilst imposing significantly fewer IVIs on patients. The burden on clinic appointments between the two regimens is comparable, but PRN's advantages could be realised if disease monitoring was moved to primary care.

CONTROL ID: 3538784

SUBMITTER (NAME ONLY): Giovanni Romano

TITLE: OCULAR SAFETY PROFILE OF A NEW FORMULATION BASED ON HYPOCHLOROUS ACID IN RABBIT EYE

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the ocular safety and tolerability of a new formulation based on hypochlorous acid, well-known for its broad antimicrobial spectrum, in rabbit eye in comparison with two commercially available formulations based on sodium hypochlorite and povidone iodine, respectively.

Methods: New Zealand albino rabbits were used, the animals were handled in accordance to the ARVO statement for the use of animals in ophthalmology and vision research. The animals were divided in three groups and received topical instillation (30 µl) of each formulation BID for 7 days. One separate set of animals was used as control (vehicle-treated) group. The safety profile of the new ocular spray based on hypochlorous acid obtained with Microcyn[®] Technology (Ocudox[™] - marketed in Italy by Alfa Intes) was compared with two commercially available ophthalmic formulations based on sodium hypochlorite (ocular spray) and povidone iodine (eye drops), respectively. Clinical score was assessed by slit-lamp and IOP was measured by TonoPen. At the end of the treatment, tear samples were collected, and MMP-9 were measured by ELISA. Then the animals were sacrificed, and cornea and conjunctiva were collected to perform histological examination.

Results: The results showed a good safety profile of the new formulation based on hypochlorous acid. No changes were observed in terms of clinical score, IOP and tear MMP-9 values compared with control group. Further, the histological examination of cornea and conjunctiva was superimposable to the control group. On the contrary, the eyes treated with the formulations based on sodium hypochlorite and povidone iodine showed a significant ($p < 0.05$) increase of MMP-9 levels in the tears (280 ± 10 pg/ml and 105 ± 10 pg/ml, respectively) in comparison with control (40 ± 8 pg/ml). A slight conjunctival hyperemia was only observed in the group treated with povidone iodine formulation. No change in terms of IOP and ocular tissues morphology was observed in all groups.

Conclusions: All together, these findings showed a very good ocular safety profile of the new ophthalmic formulation based on hypochlorous acid. It is worthy of note, that tear levels of MMP-9, a well-known marker of the inflammatory response, did not change in the eyes treated with Ocudox[™] and they were superimposable to the levels of control group.

CONTROL ID: 3538816

SUBMITTER (NAME ONLY): Stephanie McIlwaine

TITLE: The Belfast Eye and Multiple Sclerosis Study

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Multiple Sclerosis (MS) causes progressive neurodegeneration that is characterised by demyelination of neurons. MS also affects the visual system, including changes in the retina. For this reason, the Belfast Eye and Multiple Sclerosis (BEAMS) study aimed to comprehensively examine whether the retina could become an imaging and functional surrogate for the development and progression of MS.

Methods: Participants are enrolled and were imaged (17 patients with MS and ten controls). A range of retinal imaging methodologies, optical coherence tomography (OCT; Heidelberg Spectralis) and adaptive optics (AO; Image Eyes RTX1), were reported. OCT images were analysed by on-device segmentation software (Heyex) for peripapillary retinal nerve fibre layer (pRNFL), macular ganglion cell layer-inner plexiform layer (GCL-IPL) and outer nuclear layer (ONL) thicknesses. AO images were analysed by the semi-automated cone density detection algorithm (AODetect) on images captured at 2, 4 and 6° eccentricity. Control (ctrl) participants were compared to patients with (MSON) or without optic neuritis (MSnON), and the data obtained were analysed using SPSS and visualised using GraphPad Prism.

Results: The cohorts were statistically balanced for age and gender. Preliminary results suggest significant thinning ($p < 0.0001$) of the pRNFL and macular GCL-IPL in MSON (pRNFL: $81.23 \pm 3.18 \mu\text{m}$; GCL-IPL: $59.73 \pm 2.47 \mu\text{m}$) but no significant changes ($p > 0.05$) were observed in MSnON (pRNFL: $96.78 \pm 2.18 \mu\text{m}$; GCL-IPL: $10.94 \pm 1.8 \mu\text{m}$) compared to ctrl (pRNFL: $97.16 \pm 2.62 \mu\text{m}$; GCL-IPL: $73.50 \pm 3.18 \mu\text{m}$). No change was detected in the ONL thickness between all groups (ctrl 69.20 ± 3.28 vs MSON 68.02 ± 2.29 vs MSnON 68.81 ± 1.76 $p > 0.05$). There was a significant decrease ($p = 0.002$) of cone densities on AO images in patients with both MSON ($21909 \pm 1166/\text{mm}^2$) and MSnON ($22286 \pm 1005/\text{mm}^2$) compared to ctrl ($24355 \pm 1370/\text{mm}^2$).

Conclusions: The preliminary analysis of the images of the BEAMS study replicates the previously reported thinning of the inner retinal layers. Despite no measurable change in photoreceptor layer thickness on OCT images, here we report, the first time, a significant loss of cone numbers in the macula in MS. Whether the loss in cones leads to functional changes is yet to be determined. Our preliminary results suggest a need for a comprehensive analysis of retinal changes to detect and monitor the progression of MS.

CONTROL ID: 3538819

SUBMITTER (NAME ONLY): Ayse Yildiz Tas

TITLE: Automated Diagnosis of Keratoconus from Corneal Topography

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To detect the Keratoconus using machine learning and deep learning algorithms.

Methods: The diagnosis of the Keratoconus is done via investigation of corneal topography image of the cornea. Our dataset consists of 1281 topography images labeled by corneal topography imaging device. In each of these images, 7936 points are selected on patient's eye and sagittal slope, tangential slope, and perpendicular distance from eyeball of both front and back of the corneal surface as well as the corneal thickness are measured. Topography images are classified into five groups: Abnormal or Treated, Keratoconus Compatible, Myopic Post-Operation, Keratoconus Suspected and Normal. We split the dataset into train and validation sets with the fraction of 80% to 20%. To benchmark we trained some machine learning algorithms on the train dataset and measured the accuracy of classification in the validation dataset.

Results: We measured the accuracy of classification in the validation dataset.(Table 1) Our current network model can accurately classify myopic post operated, normal and keratoconus compatible patients. However, it still struggles to classify abnormal or treated and keratoconus suspected patients. The development process for neural network is still ongoing. Our current network has 90% accuracy on the validation set and its' confusion matrix on the validation set. (Table 2)

Conclusions: We will try to optimize neural network to achieve better results especially in the subgroup of the keratokonous suspected and treated patients. Furthermore, we aim to develop an attention layer and obtain the location of the key features that plays crucial role on the classification, so that we can generate a decision and support making system for doctors to report easily.

CONTROL ID: 3538824

SUBMITTER (NAME ONLY): Sarah Hatt

TITLE: Effect of Age on Reduced Child-Reported Eye-Related Quality of Life and Functional Vision in Strabismus

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Previous studies have reported reduced eye-related quality of life (ER-QOL) and functional vision in children with strabismus, using the Pediatric Eye Questionnaire (PedEyeQ), but have not evaluated the effect of age when compared with normals.

Methods: 98 children (70 aged 5-11 years and 28 aged 12-17 years) with horizontal strabismus (allowing coexistent amblyopia, refractive error, dissociated vertical deviation) and 206 visually normal controls (104, 5-11 years and 102, 12-17 years) were prospectively enrolled. Children completed the Child 5-11 or 12-17 year PedEyeQ, consisting of Functional Vision, Bothered by Eyes/Vision, Social, and Frustration/Worry domains. Each PedEyeQ domain was Rasch-scored and then converted to a 0-100 scale. The 5th percentile of scores in the 5- to 11- and 12- to 17-year normal cohorts was used to define the threshold for "reduced," for each domain. We compared the proportions of 5- to 11- and 12- to 17-year-olds who had reduced scores in each domain.

Results: A significantly greater proportion of 12- to 17-year-olds vs 5- to 11-year-olds had reduced scores on each of the four Child PedEyeQ domains: Social 89% vs 19%, (mean difference 71%, 95% CI 56% to 85%; P<0.001), Frustration/Worry 75% vs 21% (mean difference 54%, 95% CI 35% to 72%; P<0.001), Functional Vision 57% vs 34% (mean difference 23%, 95% CI 1% to 44%; P=0.044) and Bothered by Eyes/Vision 57% vs 31% (mean difference 26%, 95% CI 4% to 47%; P=0.02).

Conclusions: A greater proportion of adolescents report reduced (below the 5th percentile threshold) functional vision and reduced ER-QOL domain scores compared with 5- to 11-year-olds, especially on the Social and Frustration/Worry domains. This effect of child age likely reflects, at least in part, a more realistic self-concept in adolescents. Interpretation of individual scores in younger clinical populations is also made challenging by the considerable variability in 5- to 11-year-old normal controls, such that thresholds to define reduced scores are relatively low.

CONTROL ID: 3538825

SUBMITTER (NAME ONLY): Andrew Muthurajah

TITLE: Impact of cataract surgery on donor cornea suitability: an intra-individual retrospective audit

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Pseudophakic donor corneal tissue has been identified as having lower endothelial cell density (ECD) and higher risk of preparation failure compared to donor corneal tissue in eyes without prior cataract surgery. As corneal tissue remains a limited resource, optimal utilisation is essential for all stakeholders. We performed a retrospective, observational audit of donor corneal tissue at a single eye bank to identify the risk factors in pseudophakic eyes that may impact final tissue suitability.

Methods: We reviewed an existing database of donor corneal tissue in NSW Tissue Bank, Australia. Donors who had previously unilateral cataract surgery were identified with the opposite eye serving as an intra-individual control. Demographic data inclusive of age and gender was collated. Corneal assessment data including ECD, biomicroscopy and suitability for both eyes were compared using two sample t-tests.

Results: 191 donors across a 20-year period (1998-2018) were identified as having previously unilateral cataract surgery. The mean age of donors was 73.8 ± 9.2 years with 61.8% donors male. 19.9% of donors had a confirmed history of diabetes. Patient condition at death was rated as good or excellent for 75% of donors. Mean corneal ECD in the pseudophakic eyes was $2798.9 \pm 363.3 \text{ c/mm}^2$ vs. $2952.1 \pm 362.6 \text{ c/mm}^2$ for the phakic counterpart ($p < 0.001$). Biomicroscopy indicated greater incidence of findings in pseudophakic eyes compared to phakic eyes for both suitable and non-suitable eyes (Table 1). Suitability for corneal transplantation was statistically significantly different ($p < 0.001$) with 59% of pseudophakic eyes declared suitable versus 91% of phakic eyes suitable.

Conclusions: Despite mean endothelial cell count in pseudophakic eyes reaching minimum requirements for suitability, the percentage of eyes available for graft surgery was significantly less than the contralateral phakic eye. Increased incidence of corneal endothelial opacities in the pseudophakic eyes was a significant contributing factor in low suitability for eyes with prior cataract surgery.

CONTROL ID: 3538826

SUBMITTER (NAME ONLY): Heather Livengood

TITLE: Preliminary Results of Repetitive Transorbital Alternating Current Stimulation in Optic Neuropathies

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Livengood, G. Wollstein, H. Ishikawa, M. Wu, M. Liu, P. Achanta, L.A. Al-Aswad, J.F. Panarelli, P. Misra, A. Do, J.S. Schuman, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|B. Sabel, Institute of Medical Psychology, Otto von Guericke Universitat Magdeburg, Magdeburg, Sachsen-Anhalt, GERMANY|

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ABSTRACT BODY:

Purpose: Repetitive transorbital alternating current stimulation (rtACS) is an application of weak electric current near the eyes used in vision rehabilitation of optic neuropathies (ON). Conceptually rtACS entrains neuronal oscillations, augmenting neuronal function. In subjects with ON we evaluated whether rtACS influenced visual structure and function.

Methods: 34 subjects with ON enrolled in a prospective trial underwent comprehensive ophthalmic evaluation, visual field (VF) 24-2 and 10-2 tests (Humphrey Field Analyzer) and OCT (Cirrus HD-OCT) retinal nerve fiber layer (RNFL) and ganglion cell inner plexiform layer (GCIPL) thicknesses at baseline and follow-up (FU) visits. Subjects received rtACS 30- to 45-minutes daily for 10 days. Sham subjects (n=4) underwent the same procedures but received no current. Point-by-point analyses of VF total deviation (TD) values were conducted between rtACS and sham groups. Regression analyses determined rate of change for each TD point per eye (significant points with positive rate of change defined as improved, negative rate of change as progressed; insignificant rate of change as no change) and the association between RNFL and GCIPL between groups.

Results: The number of FU visits with VF tests ranged 2 to 7, with no significant differences detected between rtACS vs sham groups' FU duration. No significant differences were detected between groups' baseline VF 24-2 and 10-2 mean deviation (MD) values (Table 1). The average numbers of improved points (VF 10-2) and progressed points (VF 24-2) were greater for rtACS while the average number of no change points was greater for sham (VF 24-2, $p \leq 0.05$, Table 1). Further analysis of FU duration determined a significant interaction with rtACS; number of improved points (VF 10-2) and progressed points (VF 24-2, $p < 0.02$) were not sustained over time. No significant differences were detected in average RNFL and GCIPL thicknesses between groups.

Conclusions: Preliminary analyses of the effect of rtACS in ON indicate initial improvement but not a clear benefit over time. Detection of differences between rtACS vs sham groups may be biased due to the small sham sample and range of FU duration as VF test-to-test variability is known to increase with worsening VF MD. Future analyses will assess interim effect at early vs late FU time points to evaluate the role of rtACS in vision rehabilitation.

CONTROL ID: 3538839

SUBMITTER (NAME ONLY): Duygu Karademir

TITLE: Single-cell RNA sequencing reveals early responses to degeneration in rods and cones of the rd10 retina

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Karademir, V. Todorova, M. Samardzija, L.J. Ebner, C. Grimm, Lab for Retinal Cell Biology, Universitat Zurich, Schlieren, ZH, SWITZERLAND|

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ABSTRACT BODY:

Purpose: In inherited retinal disorders such as retinitis pigmentosa (RP), the initial degeneration of rod photoreceptors is often followed by the secondary death of cones and loss of high-acuity vision. Mechanistic studies of these events are challenging, as cells in different stages of degeneration generally coexist, and the detection of cone responses to rod degeneration is difficult due to the relative paucity of cones in the retina. We utilized droplet-based single-cell RNA sequencing (scRNAseq) to resolve intercellular heterogeneity and elucidate early events in rods and cones during rod photoreceptor degeneration in rd10, an RP mouse model.

Methods: ScRNAseq was performed on rd10 and C57/BL6 wildtype retinas at postnatal day (P) 21 (N=2, 1 male and 1 female per genotype) using the 10X Genomics platform. Data analysis focused on characterizing the transcriptomes of degenerating rods and cones with differential gene expression and trajectory analysis. Transcriptomics data was validated via immunofluorescence in both rd10 retinas and retinas of BALB/c animals damaged by 1 hour of 13'000 lx white light.

Results: Trajectory inference revealed two consecutive phases of rod degeneration at P21. The early phase was distinguished by a marked upregulation of Egr1 (avg. fold change (FC): 4.82 over wildtype rods) and the late phase by Cebpd (FC: 4.55 over Egr1+ rods). Egr1 was also the most highly upregulated transcript in rd10 cones (FC: 5.81 over wildtype cones). Notably, EGR1 was the transcription factor most significantly associated with the promoters of differentially regulated genes in Egr1+ rods in silico. Egr1 upregulation preceded transcriptomic changes related to metabolic dysfunction, synapses, and tubulin remodeling in rods. In cones, it accompanied changes in mitochondrial and signaling pathways, including TNF α and TGF β . Phototransduction genes were downregulated early in both cell types. Immunoreactivity for EGR1 was highly increased in rods and cones of rd10 retinas at P21, with rods losing EGR1 by P28. Cones remained EGR1-positive at least up to P35. EGR1 immunoreactivity also increased 2 hours after light damage, specifically in cones and Müller glia.

Conclusions: Our results identify early cone responses to rod degeneration in the rd10 model and describe various pathways that are initially affected in degenerating rods. Our data suggest EGR1 as a key regulator of these early events.

CONTROL ID: 3538853

SUBMITTER (NAME ONLY): David Leske

TITLE: A New Treatment Questionnaire for Children with Eye Conditions

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Leske, S.R. Hatt, S.M. Wernimont, E.D. Bothun, J.M. Holmes, Ophthalmology, Mayo Clinic, Rochester, Minnesota, UNITED STATES|Y.S. Castañeda, C.S. Cheng-Patel, E.E. Birch, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|E.E. Birch, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|J.M. Holmes, Ophthalmology and Vision Science, University of Arizona-Tucson, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a new pediatric eye treatment questionnaire (PedEyeQ-T), designed to assess the impact of non-surgical eye treatments on function and on eye-related quality of life (ER-QOL) in children under the age of 18 with a variety of eye conditions and eye treatments.

Methods: Child and Proxy master questionnaires were created from specific concerns identified from child and parent interviews. Child master questionnaires (n=34 items), were administered to children (5-17 years old; n=329) currently undergoing any non-surgical eye treatment (glasses, contact lenses, patching, drops, binocular amblyopia treatment, etc.), and Proxy master questionnaires (n= 34 items) were administered to one parent for each child (0-17 years old; n=466). A 3-level frequency rating scale (never, sometimes, always) was used for responses. Exploratory factor analyses were performed to identify domains within function-related items (n=7) and ER-QOL-related items (n=27), labeled based on review of content. Rasch analysis was performed on each domain identified in factor analysis, to reduce items by evaluating differential item functioning (sex, race, age, parent completing), response ordering, local dependence, fit, and targeting.

Results: Factor analysis of Child questionnaires identified 1 domain for function-related items and 2 domains for ER-QOL items. Rasch analysis confirmed unidimensionality of domains and yielded a Child questionnaire with 3 items in a Treatment: Function domain, 10 items in a Treatment: Socioemotional domain, and 6 items in a Treatment: Difficulty domain. For the Proxy questionnaire, Factor analysis identified 1 domain for function-related items and 2 domains for ER-QOL items. Following Rasch analysis the Proxy treatment questionnaire had 3 items in a Treatment: Function domain, 7 items in a Treatment: Socioemotional domain, and 3 items in a Treatment: Difficulty domain.

Conclusions: By following a rigorous process for questionnaire development, we have created the new patient-derived Pediatric Eye Treatment Questionnaire (PedEyeQ-T), for use in children of any age undergoing any non-surgical eye-treatment, with Child and Proxy versions for assessing impact on function and on ER-QOL.

CONTROL ID: 3538855

SUBMITTER (NAME ONLY): Sarah Devaro

TITLE: Outcomes of cataract surgery in pediatric uveitis patients on systemic immunomodulatory therapy

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Compare outcomes of cataract surgery in pediatric uveitis between 3 treatment groups: no systemic treatment, antimetabolites, and biologic response modifiers (BRM) +/- antimetabolites.

Methods: Retrospective chart review of uveitis patients younger than 18 years who underwent cataract surgery at Emory Eye Center in Atlanta, GA 2008-2020. Data collected included demographics, treatment, visual acuity (VA) and postoperative complications, all summarized as frequencies. SPSS software was used for descriptive and inferential statistical analysis. Univariate analyses were performed to compare treatment groups. VA was tested by time and treatment group adjusting for correlation between covariates and eyes over time.

Results: 51 patients were included; 31 (61%) were female. Mean age at surgery was 10.8 years (range 4-17). Anterior uveitis (62%) was most common anatomic location. Of 65 eyes, 20 (31%) were on antimetabolites, most commonly methotrexate (95%); 19 (29%) were on BRM +/- antimetabolites, most commonly infliximab (68%); and 26 (40%) were on no systemic immunomodulation. Of eyes on no treatment, 54% were on oral corticosteroids perioperatively. 14 (74%) patients on BRM also received antimetabolites (mean duration 19.9 months). Mean age at diagnosis was significantly lower in those on BRM ($p=0.009$). Patients with juvenile idiopathic arthritis (JIA) were more frequently on BRM ($p=0.018$). All groups had similar rates of amblyopia, average length of quiescence and number of flares in year prior to surgery. Postoperative complications (prolonged inflammation or development of cystoid macular edema or posterior capsular opacification) approached significance. Intraocular pressure (IOP) increased in all eyes over time ($p=0.0069$) but was significantly higher in BRM compared with anti-metabolites ($p=0.0002$) or all-comers ($p=0.0128$). VA in all eyes improved after surgery, with significantly better VA in BRM compared to the rest of the cohort ($p = 0.002$).

Conclusions: Cataract surgery improved visual outcomes in pediatric uveitis regardless of treatment. Despite younger age of diagnosis, patients on BRM had significantly better long-term vision but also increased IOP. Postoperative complications were similar across groups. This is the first report of outcomes after cataract surgery in pediatric uveitis comparing available treatments.

CONTROL ID: 3538861

SUBMITTER (NAME ONLY): Varsha Pramili

TITLE: A Deep-Learning Based Algorithm for Automated Segmentation of Geographic Atrophy in Swept-Source Optical Coherence Tomography

SESSION TITLE: AI in the retina: Algorithms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Pramili, H. Asad Sheikh, N.K. Waheed, New England Eye Center, Boston, Massachusetts, UNITED STATES|V. Pramili, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|L. De Sisternes, S. Kubach, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|H. Asad Sheikh, University of Massachusetts System, Boston, Massachusetts, UNITED STATES|L. Omlor, Carl Zeiss Meditec Inc, Pleasanton, California, UNITED STATES|W. Lewis, Bayside Photonics, Inc., Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: This work presents the first deep-learning based GA segmentation algorithm for swept-source OCT that provides accurate and reproducible results in GA assessment with high sensitivity to GA changes over time.

Methods: An automated algorithm was trained with 6x6 mm macular SS-OCT scans from 58 GA eyes (38/20 split for training/validation set). It utilizes scan volume data to generate three image inputs characterizing the main OCT features of GA: hyper-illumination in sub RPE slab, regions of RPE loss, and loss of retinal thickness (Figure 1). Advanced data augmentation techniques helped compensate for the small training data size. To evaluate the accuracy of the GA segmentations, 180 SS-OCT macular scans from 30 GA eyes collected from 3 different sites were considered: each eye had 3 repeated scans at baseline and follow-up visits (average of 16.74 months). Area measurements were corrected by their square-root and used to compute enlargement rate per year between the visits. The GA delineations, area measurements and enlargement rates generated by the automated algorithm in addition to algorithm repeatability in repeated scans were compared to the ground-truth manual delineations annotated by two graders.

Results: Figure 2 summarizes the performance of the algorithm. Automated GA delineation accuracy between the algorithm and two graders was measured using the Dice coefficient with average values of 0.88 and 0.87, respectively. GA area measurements produced by the algorithm were comparable and showed no significant difference to those from each grader, with an average absolute difference of 0.19 (p-value 0.73) and 0.19 (p-value 0.77), respectively. GA enlargement rate computed by the algorithm also showed no significant differences to the two graders, with differences of 0.13 (p-value 0.26) and 0.12 (p-value 0.71), respectively. The algorithm also presented a high repeatability for area and enlargement rate measurements, with intra-class repeatability coefficients of 0.997 and 0.947, respectively.

Conclusions: Despite a small training data size, this deep learning based automated GA segmentation algorithm is able to produce accurate and reproducible results in GA assessment with high sensitivity for GA changes over time.

CONTROL ID: 3538869

SUBMITTER (NAME ONLY): Kristen Buehne

TITLE: How Medication Adherence Affects Disease Management in Veterans with Glaucoma

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Without a cure, glaucoma is managed as a chronic disease, most often with eye drops prescribed to reduce intraocular pressure. This implies that poor medication adherence correlates with disease escalation. With a randomized clinical trial, we tested the hypothesis that patients who receive an adherence intervention are more likely to have a stable glaucoma course and will require less intensive treatment over the following 12 months.

Methods: The study population consists of 200 veterans who report less than 100% adherence to their eye drop regimen. The treatment group received a glaucoma education session with drop administration instruction, and virtual reminders from a “smart bottle” of their eye drops. The control group received a general eye health class, and the smart bottle with the reminder function turned off. The bottle reported the date and time it was opened for both groups, supplying objective data for adherence. We previously reported the primary outcome; that the average glaucoma medication adherence was significantly higher for those in the intervention group compared to those in the control group in the 6 months following randomization (0.85 versus 0.62, $p < 0.0001$). For the secondary outcome described here, masked medical chart extraction determined if participants experienced visual field progression, additional glaucoma medications, or a recommendation for surgery due to inadequate IOP control over the 12 months following randomization.

Results: Of the 34 participants with glaucoma medication added, 16 were in the control group and 18 in the intervention group. Of the 17 participants for whom surgery was recommended, 9 were in the control group and 8 were in the intervention group. Of the 37 participants who experienced visual field progression, 16 were in the control group and 21 were in the intervention group. Overall, 66 participants experienced disease escalation in the 12 months following randomization; 31 were in the control group and 35 were in the intervention group.

Conclusions: An intervention that improved glaucoma medication adherence over 6 months did not reduce escalation of glaucoma therapy or reduce glaucomatous visual field loss in the 12 months following the intervention. Further work is needed to determine risk factors for progression despite improved adherence, likely with longer follow-up to measure potential clinical benefit.

CONTROL ID: 3538879

SUBMITTER (NAME ONLY): Aixa Alarcon

TITLE: Optical performance of different refractive technologies that increase the depth of focus

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Alarcon, B. Koopman, M. Faria-Ribeiro, C. Canovas, P. Piers, R&D, Johnson and Johnson Vision, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To compare the optical and predicted clinical performance of a higher-order aspheric IOL design that provides a continuous change in power from the center to the periphery of the lens with a zonal refractive IOL with a distinct add power of 2D in the central zone using optical bench measurements and simulations.

Methods: Binocular visual acuity (sVA) was simulated using the metrics described in Alarcon et al. BOE 2016, calculated from measurements collected in an average corneal eye (ACE) model, in white light, with 3mm pupil and from -2.5D to 0.5D of defocus. Distance image quality was evaluated by the modulation transfer function (MTF) measured in the ACE model, in white light, for 2, 3 and 5mm pupils. Computer simulations in a physiological eye were performed to determine the halo profile for different pupil sizes for the different IOL designs. Measurements of a standard monofocal and a diffractive multifocal IOL of 2.75D add power were included as references.

Results: The higher-order aspheric IOL provides comparable distance sVA to the monofocal IOL and an extended depth of focus in the intermediate range with a monotonical decrease in through-focus sVA. The zonal refractive design provided a decrease of 1 line of sVA at distance and a bifocal defocus curve with a second peak that corresponds to the add power. The design with the central add power showed a lower contrast for all pupil sizes than the higher order aspheric IOL and at the level of the multifocal IOL for 3 and 5mm. For 2mm, the central add power design provided a reduction in contrast with MTF close to zero. Contrary, the higher order aspheric design resulted in consistent distance image quality through different pupil sizes. The pupil dependency of the zonal refractive design was also visible in the halo pictures simulations, with perception of halos and rings especially for the smaller pupils, which are not visible in the higher-order aspheric IOL for any of the pupil sizes evaluated.

Conclusions: The addition of an add power results in a strong pupil dependence and an optical performance that resembles a standard multifocal IOL, with a bifocal defocus curves, a loss in distance image quality and the perception of halos. The higher-order aspheric IOL, that creates a continuous change in power to extend the depth of focus and improve intermediate vision, provides a pupil independent performance and a consistent dysphotopsia profile.

CONTROL ID: 3538905

SUBMITTER (NAME ONLY): Michael Ramos

TITLE: Quantification of ellipsoid zone recovery by optical coherence tomography following intravenous penicillin treatment in syphilitic retinitis patients

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ramos, C. Chen, S. Sharma, K. Baynes, A. Lowe, K. Barekatin, J. Bhangu, P. Le, D. Burton, J.P. Ehlers, S. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Spectral-domain optical coherence tomography (SD-OCT) has proven useful in defining the retinal layer pathology, most notably ellipsoid zone (EZ) disruption, seen in syphilitic retinitis patients; however, a timeline for EZ recovery after intravenous (IV) penicillin treatment in these patients has yet to be established. Here, we report an SD-OCT image analysis study of syphilitic retinitis patients to quantify EZ recovery in a time-dependent manner to determine successful outcomes in this patient population.

Methods: A retrospective chart review of 8 patients diagnosed with syphilitic retinitis was performed. A positive diagnosis included reactive syphilis IgG (>8.0) and rapid plasma reagin (RPR) serological tests and was confirmed by ocular exam. All patients were treated with at least a 14-day course of IV penicillin. Patients had a baseline SD-OCT scan of the diseased eye(s) within 7 days of treatment initiation and at least one scan during the treatment course. All SD-OCT scans up to 45 days post-baseline were analyzed using software that allowed for total EZ volume quantification following retinal layer segmentation. Clinical information, such as disease laterality, HIV status, and visual acuity, were also collected.

Results: Of the 8 patients with confirmed syphilitic retinitis, 4 showed bilateral disease. 7/8 patients had macular EZ disruption, while 1 patient showed peripheral retinal changes consistent with syphilis. 5/8 patients (62.5%) were HIV+ at the time of presentation. In patients with macular involvement, 10/13 eyes were analyzed. Throughout IV treatment, the average change from baseline in total EZ volume was +15.6%; however, this change was variable (range, -20.2% - +48.0%). Patients saw a more consistent improvement once treatment was completed. At a mean follow-up time of 15.7 days after treatment, patients showed an average increase of 73.0% (range, 53.6 - 122.8%) in total EZ volume.

Conclusions: With this study, we have shown that the EZ disruption seen on SD-OCT in syphilitic retinitis patients is a temporary pathological finding and can be resolved with IV penicillin. Furthermore, while EZ recovery begins during a patient's treatment course, most of the recovery is observed in the weeks following the conclusion of intravenous therapy.

CONTROL ID: 3538908

SUBMITTER (NAME ONLY): Jacques Gaudreault

TITLE: Activity and pharmacokinetics of ICON-4, a New Antibody Targeting Tissue Factor

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gaudreault, JJG Pharma Consulting, Basel, BS, SWITZERLAND|G. Burian, GB Biomed Advisors, Oberwil, BL, SWITZERLAND|T. Mlgone, iconic Therapeutics, SSF, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tissue factor (TF) is a 46 kD transmembrane receptor found on vascular endothelial cells (EC). In addition to its role as initiator of coagulation, TF plays an important role in angiogenesis and inflammation. TF is elevated in the retina of Age-related Macular Degeneration (AMD) patients and in the neovascularization (NV). TF inhibition has the potential to affect these processes and modify disease progression by halting formation and growth of macular NV. A clinical proof of concept for the benefit of TF inhibition was achieved in a Phase 2 trial where ICON-1 (an immunoconjugate targeting TF) was given to patients with neovascular AMD. Intravitreal (IVT) ICON-1 administration at 300 ug/eye every month for 6 months, resulted in a decrease in both retinal thickness and NV lesion growth/activity with subsequent decreased need for anti-VEGF therapy. The objective of these studies is to characterize the pharmacology and pharmacokinetics of a new TF inhibitor, ICON-4, with optimized properties for IVT administration.

Methods: ICON-4, a human IgG1, was characterized with a series of in vitro assays. Characterization included affinity measurements (Biacore), ADCC with either a reporter cell line or PBMCs as effector cells, CDC activity, and ADCP. ICON-4 anti-inflammatory effects were characterized using MDA-231 cells to measure the effect on release of GM-CSF and IL-8. ICON-4 effect on coagulation was assessed using Factor X (FX) conversion assay and thrombin generation assays. ICON-4 pharmacokinetics were characterized in NZW rabbits following single IVT administration of 0.6 and 3.6 mg and ocular concentrations quantified by ELISA.

Results: In all in vitro assays, ICON-4 had better activity compared to ICON-1 with improvement in activity ranging from 3 to 20-fold across the different assays. While ICON-4 was more active in all the assays, it still was inert on coagulation, as it did not impact FXa conversion or thrombin generation. Following IVT administration, ICON-4 had a long vitreous $t_{1/2}$ of 6 days, which was about 2X longer than previously observed for ICON-1.

Conclusions: ICON-4 is a potent TF inhibitor with optimized properties well suited and formulated for IVT administration. ICON-4 high affinity is expected to result in more complete TF inhibition with potential for higher efficacy and/or longer duration of action without enhanced risks of bleeding compared to ICON-1.

CONTROL ID: 3538911

SUBMITTER (NAME ONLY): Sandrine Joly

TITLE: Antibody-based Nogo-A neutralization reduces neuroinflammation after retinal injury

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Joly, J.B. Mdzomba, L. Rodriguez, A. Dirani, V. Pernet, Centre de recherche du CHUL, Quebec, Quebec, CANADA|P. Lassiaz, F.F. Behar-Cohen, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|

Commercial Relationships Disclosure (Abstract): Sandrine Joly: Commercial Relationship: Code N (No Commercial Relationship) | Julius Mdzomba: Commercial Relationship: Code N (No Commercial Relationship) | Lea Rodriguez: Commercial Relationship: Code N (No Commercial Relationship) | Ali Dirani: Commercial Relationship: Code N (No Commercial Relationship) | Patricia Lassiaz: Commercial Relationship: Code N (No Commercial Relationship) | Francine Behar-Cohen: Commercial Relationship: Code N (No Commercial Relationship) | Vincent Pernet: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously observed that inactivating Nogo-A, a reticulon protein enriched in Müller glia and in oligodendrocytes, enhanced vascular repair, optic nerve axon regeneration and visual recovery after retinal injury. The mechanisms underlying the effect of Nogo-A in the development of visual defects are not clear. The aim of this study was thus to determine if Nogo-A modulates injury-induced neuroinflammation in the adult mouse retina.

Methods: Excitotoxic injury was induced by intravitreally injecting different concentrations of NMDA (0.5-40 nmol) in adult mouse eyes. Nogo-A level was followed in the vitreous and in the retina of injected animals by Western blotting. Two days after NMDA injection, Nogo-A-blocking antibody (11C7) or a control antibody (IgG) were injected. Quantitative real-time PCR was performed 1 and 7 days after antibody injection to determine gene expression changes for Nogo-A and its receptors, and inflammation and gliosis markers. Microglia was visualized on retinal flatmounts by immunofluorescence. Western blotting and immunofluorescent analyses were also realized on samples from diabetic patients.

Results: Full-length and fragmented Nogo-A proteins were upregulated in the mouse vitreous after NMDA-induced injury. This change was correlated with TNF α trimer release. In injured animals, intravitreal injection of 11C7 significantly improved visual function recovery compared with control IgG delivery. The expression of pro-inflammatory molecules, such as TNF α , was strongly downregulated by 11C7. Immunofluorescent stainings suggested that microglia/macrophages were the main source of TNF α in the damaged retina. TNF α immunofluorescence was markedly reduced in response to 11C7 injection. Further Western blot and histological results suggested that TNF α downregulation may result from cofilin inactivation in microglia/macrophages. In addition, the decrease in Vimentin and Gfap mRNAs in 11C7-treated retinal lysates indicated that 11C7 mitigated gliosis, possibly by downregulating P.Stat3. Increased levels of Nogo-A in the vitreous and in the retina were observed in diabetic donors.

Conclusions: The administration of function-blocking antibody directed against Nogo-A promotes visual recovery after retinal injury. At the same time, the inhibition of neuroinflammation suggests a new function for Nogo-A that could be used to design ophthalmic treatments.

CONTROL ID: 3538912

SUBMITTER (NAME ONLY): Felipe Medeiros

TITLE: Extended duration of IOP lowering with bimatoprost implant in a phase 3 open-label extension study

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.A. Medeiros, Duke Eye Center, North Carolina, UNITED STATES|S. Nagar, M. Bejanian, M.R. Robinson, Allergan, an AbbVie company, California, UNITED STATES|D.L. Wirta, Eye Research Foundation, Newport Beach, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Biodegradable, intracameral bimatoprost implant slowly releases bimatoprost to lower intraocular pressure (IOP). In clinical trials, the implant has provided sustained IOP lowering beyond the period of intraocular drug bioavailability. This analysis evaluated the duration of IOP control provided by the implant in a phase 3 clinical trials study extension.

Methods: A 24-month, open-label, multicenter, long-term safety and efficacy extension study (NCT03891446) enrolled patients with open-angle glaucoma or ocular hypertension after their completion of a bimatoprost implant phase 3 clinical trial. Enrollment was optional; not all eligible patients enrolled. This analysis included patients who had received 10- or 15-µg bimatoprost implant in the study eye on Day 1 and Weeks 16 and 32 in a 20-month, randomized, phase 3 ARTEMIS trial (NCT02247804 or NCT02250651); patients were ineligible to receive implants during the study extension. Rescue with topical drops was allowed if the study eye did not meet/maintain IOP expectations (investigator decision). The analysis evaluated IOP and the number of patients who received no additional (rescue) IOP-lowering treatment in the study eye for ≥ 2 years after the last implant administration during the ARTEMIS trial. The study is ongoing; all data available as of 03 Dec 2020 were analyzed.

Results: Among 181 implant-treated patients who completed ARTEMIS and enrolled in the study extension, 48 had not been rescued at the study extension screening, and 32 did not require rescue for ≥ 2 years after their last implant administration. For these 32 patients (16 treated with 10-µg implant, 16 with 15-µg implant), mean (\pm SD) time without rescue after the last implant administration was 2.6 ± 0.5 years (range, 2.0–4.0), and mean (\pm SD) IOP was 23.4 ± 1.9 mmHg at initial (ARTEMIS study) baseline and 18.1 ± 3.1 mmHg at the last recorded visit (still without rescue). Seven patients remained untreated for ≥ 3 years (range, 3.1–4.0); their mean (\pm SD) IOP was 22.8 ± 1.5 mmHg at baseline and 18.0 ± 4.1 mmHg at the last recorded visit (still without rescue).

Conclusions: Patients treated with the bimatoprost implant can have a sustained IOP lowering and require no IOP-lowering treatment for ≥ 2 years after their last administration in a phase 3 trial. The implant releases drug for 3–4 months and the mechanism of action of the long duration of IOP reduction is under investigation.

CONTROL ID: 3538946

SUBMITTER (NAME ONLY): Naomi Bennett

TITLE: Investigating Sodium Hexametaphosphate as a topical treatment for Band Keratopathy

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Bennett, L.M. Grover, Healthcare Technologies Institute, School of Chemical Engineering, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|L.J. Hill, Institute of Inflammation and Aging, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Naomi Bennett: Commercial Relationship: Code N (No Commercial Relationship) | Lisa Hill: Commercial Relationship: Code N (No Commercial Relationship) | Liam Grover: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate Sodium Hexametaphosphate as a potential non-surgical treatment for corneal mineralization in the form of Band Keratopathy, the demineralization capability under varying conditions, the ocular toxicity and the interaction of the polyphosphate with various polymeric hydrogel materials are assessed with the view of creating a long-lasting, topically applied treatment.

Methods: Demineralisation was assessed by measuring the changes in absorbance of aqueous nanocrystalline hydroxyapatite sol treated with concentrations of sodium hexametaphosphate (HMP) ranging from 0.125 - 1M, versus untreated controls.

Ocular toxicity was investigated through in vitro cellular assays of primary corneal cells, including lactate dehydrogenase production assays and 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assays. The interactions between HMP and chitosan, alginate and gellan hydrogels were investigated using rheometry. Each underwent a series of shear stress ramp assessments from 0-250Pa.

Results: 0.125M, 0.25M, 0.5M and 1M HMP treatments reduced the absorbance of HA sol from 1.000 to a mean (SEM) of 0.419 (0.013), 0.730 (0.028), 0.521 (0.027) and 0.365 (0.017) respectively within 60 minutes. 0.25M, 0.5M and 1M treated samples continue to decrease before stabilising, where as 0.125M treated samples reach a minimum absorbance at 360 mins before then increasing to reach an absorbance of 0.789 (0.034).

The lower concentrations of HMP tested - 0.125M and 0.25M - showed the greatest cytotoxicity at 14.054% and 34.456% after 6 hours of treatment. This corresponds with the lowest formazan production compared to the higher concentration treatment groups, with adjusted absorbance readings of 0.010 and 0.004 respectively.

Chitosan shows increasing viscosity, alginate gradually decreasing viscosity, and gellan an increase followed by a subsequent decrease, with increasing HMP percentage.

Conclusions: The results presented in this study show that Sodium Hexametaphosphate can demineralise hydroxyapatite effectively, can maintain cell viability and can influence the rheological properties of polymeric hydrogels in a concentration dependant manner. A balance should be struck between these behaviours as a topical treatment is developed.

CONTROL ID: 3538953

SUBMITTER (NAME ONLY): Seitaro Komai

TITLE: Prospective evaluation of the safety and efficacy of Cultivated Oral Mucosal Epithelial Transplantation (COMET) for fornix reconstruction in cases of severe ocular surface disease

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Komai, K. Imai, T. Nakamura, T. Inatomi, M. Ueta, C. Sotozono, Ophthalmology, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|T. Inatomi, Kokuritsu Kenkyu Kaihatsu Hojin Kokuritsu Choju Iryo Kenkyu Center, Obu, Aichi, JAPAN|M. Go, Y. Kimura, Translational Research Center for Medical Innovation, JAPAN|M. Fukushima, Medical R&D, Fukushima & Partners, JAPAN|S. Kinoshita, Frontier Medical Science and Technology for Ophthalmology, Kyoto Furitsu Ika Daigaku, Kyoto, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: Since 2002, cultivated oral mucosal epithelial transplantation (COMET) has been used for ocular surface reconstruction in cases of severe ocular surface disease. The purpose of this prospective, interventional clinical study was to examine the safety and efficacy of COMET for fornix reconstruction in cases of severe ocular surface disease.

Methods: This prospective clinical study involved patients with severe ocular surface disease (i.e., Stevens-Johnson syndrome: n = 5 eyes; ocular cicatricial pemphigoid: n =1 eye) with a 50% or greater adhesion of either the upper or lower conjunctival fornix that underwent COMET for fornix reconstruction at the Department of Ophthalmology, Kyoto Prefectural University of Medicine, Kyoto, Japan between January 2014 and February 2017. Surgical outcomes were defined as changes in each score between at pre surgery (baseline) and at 24-weeks postoperative, with the primary outcome being the fornix shortening score. Secondary outcomes were the Ocular Surface Grading Score (OSGS), the best-corrected visual acuity (BCVA), the results of the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25), and adverse events. The changes in each score from at baseline were analyzed using the one-sample t-test.

Results: From baseline to 24-weeks postoperative, the fornix shortening score significantly improved from 4.7 (median: 4.5; range: 3-6) to 1.2 (median: 0; range: 0-3) ($p=0.001$) and the OSGS significantly improved from 15.2 (median: 14.5; range: 11-20) to 6.2 (median: 5.0; range: 2-14) ($p=0.0052$), yet no significant difference in BCVA was observed. In the NEI VFQ-25 findings, 9 of the 12 subscales improved, with significant differences observed in "General vision" and "Ocular pain" ($p=0.0104$, 0.040 , respectively). No complications associated with COMET were observed post surgery.

Conclusions: Our findings clearly demonstrate the safety and efficacy of COMET for fornix reconstruction in cases of severe ocular surface disease.

CONTROL ID: 3538963

SUBMITTER (NAME ONLY): Naomi McLaren

TITLE: Utilization of Confocal Microscopy in the Management of Suspected Microbial Keratitis at a Tertiary Eyecare Center

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. McLaren, D.S. Jacobs, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|D.S. Jacobs, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To better understand the role of confocal microscopy in clinical decision making in the management of suspected microbial keratitis.

Methods: A log of study requisitions was reviewed. The following items were recorded and analyzed: a. Date of confocal imaging, b. Source of request by setting of encounter (Emergency Department [ED], Cornea clinic, community doctor) c. Credential of requesting provider (ED resident, ED attending physician, Cornea Fellow, Cornea attending physician, community doctor), The date of any prior corneal culture(s) was queried from medical record in a pilot study of two seasonal subgroups of consecutive patients (9 winter and 9 summer).

Results: 59 requisitions were logged from Jan 1, 2019 to Nov 30, 2019. 22 (37%) were requested in relation to an Emergency Department encounter (1 by resident, 8 by ED attending, 3 by cornea fellow in conjunction with ED attending, and 10 by cornea fellow), 13 studies (22%) were requested by a cornea fellow in a follow-up clinic, 21 studies (36%) were requested by cornea attending in a scheduled visit, and 3 (5%) studies were requested by a community doctor.

Our pilot sample of winter requisitions showed 3/9 patients were from ED and that 7/9 had culture > 2 days prior, 2/9 had culture 1-2 days prior, and 4/9 had prior confocal imaging or final positive cultures. A sample of summer requisitions found that 5/9 were from the ED and that 1/9 had cultures > 2 days prior, 7/9 had cultures 1-2 days prior, 1/9 was never cultured, and 2/9 had prior confocal imaging or final positive cultures.

Conclusions: Confocal microscopy in the management of suspected microbial keratitis is ordered by a variety of clinicians in a variety of settings at this tertiary care center. Credentials of the requesting physician vary with the season of the initial evaluation, as does the reason for imaging, with surveillance of treated cases being more common in the winter and workup of new infection more common in the summer. The pilot suggests that during summer imaging is requested with no or preliminary culture data. Further review and comparison of confocal and culture results is likely to provide insight into real time utility of this resource in a tertiary care setting.

CONTROL ID: 3538966

SUBMITTER (NAME ONLY): Liqin Jiang

TITLE: Thicker Choroidal Layers are Protective against Myopia Development in both Myopia-Resistant and Spontaneous Myopia Guinea Pig Strains

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Jiang, K.J. Catbagan, J. Fianza Busoy, V.A. Barathi, Singapore Eye Research Institute, Singapore, SINGAPORE|V.A. Barathi, Duke-NUS Medical School, Singapore, SINGAPORE|Q.V. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS, SINGAPORE|Q.V. Hoang, Department of Ophthalmology, Columbia University Medical center, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elm Hill-sourced pigmented guinea pigs (GPs) was previously reported to be resistant to experimentally-induced myopia development, which was presumed to be due to thicker choroidal layer versus other strains. Here we provide further support that choroidal thickness is associated with susceptibility to myopia-inducement.

Methods: Elm Hill-sourced pigmented (n=7 at D13) and albino (n=8 at D7) hyperopic guinea pigs were used to induce unilateral form-deprived myopia (FDM) via facemask. Cycloplegic refraction by retinoscopy and vitreous chamber depth measurement (VCD) via Ascan (Sonomed VuMAX HD Ophthalmic Ultrasound) were obtained in alert animals at baseline (before FDM), and at two weeks FDM and four weeks FDM. At the same time points, fundus and choroidal imaging was obtained by optical coherence tomography (Heidelberg Spectralis OCT) under anaesthesia with ketamine and xylazine (27/0.6 mg/kg body weight).

Results: At baseline, albino GPs had a thinner choroidal layer (mean 49 μ m) with less variation (standard deviation (SD): 9 μ m) than pigmented GPs, which had significantly thicker choroid (mean 119 μ m) but more variation (SD: 42 μ m, p = 0.0009). Thinner choroidal albino GPs developed significant myopia (-4.8 ± 1.7 D after 2 weeks of FD, -5.7 ± 1.5 D after 4 weeks of FD). Among the pigmented GPs, the animal that had a baseline choroid of 56 μ m developed high myopia (-10 D myopia shift with 0.26 mm elongated VCD after 2 weeks of FD and -7 D myopia shift with 0.30 mm elongated VCD after 4 weeks of FD). In contrast, the 6 remaining pigmented GPs with thicker choroidal layers (131 ± 44 μ m) were resistant to FDM.

Conclusions: Our results support the notion that thinner choroidal layers are associated with greater susceptibility to experimental myopia-inducement. This study results also confirms that thicker choroid could protect from, or delay myopia onset, which is a consistent finding in both strains studied.

CONTROL ID: 3538968

SUBMITTER (NAME ONLY): Duriye Damla Sevgi

TITLE: Longitudinal Assessment of Retinal Vascular Changes in Eyes with Diabetic Retinopathy Treated with Intravitreal Aflibercept in the PRIME Trial

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Sevgi, M. O'Connell, J. Hach, S. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|C.C. Wykoff, H. Yu, Retina Consultants of Houston, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the changes in vascular parameters extracted from Ultra-Widefield Fluorescein Angiography (UWFA) of eyes with diabetic retinopathy that received as needed aflibercept injection (IAI) guided by real-time diabetic retinopathy severity scale (DRSS) or panretinal leakage index (PLI) in the PRIME trial.

Methods: The PRIME prospective trial randomized treatment (1:1) to Group 1 (DRSS-guided) and Group 2 (PLI-guided). The centered early-mid phase UWFA frame that captured the maximum vessel area was selected using an automated software for each visit. Selected frames were aligned using Image J and a common region of interest was determined to ensure the same retinal area was analyzed longitudinally. Retinal vasculature was extracted using a machine learning algorithm. Panretinal vessel area and features of panretinal vascular density (mean, median, variance and skewness) were calculated. Longitudinal changes from baseline to week 52 were assessed using paired t-test. Linear regression models adjusting for age, HbA1c and number of IAI were used to identify the factors correlated with the vascular change.

Results: Twenty-six eyes (Group 1 =12, Group 2 = 14) had data available at week 52. Baseline parameters including age (P=0.812), HbA1c (P=0.343) and vascular features (P >0.05) were not significantly different between the two groups except the skewness of vessel density (P=0.032). Group 1 received a mean of 6.7 (range 5-12) IAI and Group 2 received a mean of 7.2 IAI (range 4-9, P=0.591). The mean panretinal vessel area significantly decreased from $79.7 \pm 16.6 \text{ mm}^2$ to $74.62 \pm 14.3 \text{ mm}^2$ (P=0.001). Panretinal mean (P=0.002) and median (P<0.0001) vascular density

significantly decreased, and panretinal skewness of vessel density significantly increased ($P=0.020$). Median vascular density was positively correlated with the change in vessel area ($P=0.024$).

Conclusions: We demonstrated longitudinal progression of panretinal vascular loss in eyes with diabetic retinopathy treated with as needed aflibercept injections. Improved techniques to investigate vascular remodeling and vascular loss independently may provide more insight to ischemia progression in diabetic retinopathy and the impact of anti-VEGF treatment.

CONTROL ID: 3538973

SUBMITTER (NAME ONLY): Arko Ghosh

TITLE: The Effect of Treatment Delay on Exudative Age-Related Macular Degeneration Patients Due to the COVID-19 Pandemic

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ghosh, T. Blahnik, D. Fleischman, A.Y. Zhang, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Arko Ghosh: Commercial Relationship: Code N (No Commercial Relationship) | Tyler Blahnik: Commercial Relationship: Code N (No Commercial Relationship) | David Fleischman: Commercial Relationship: Code N (No Commercial Relationship) | Alice Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Due to the Coronavirus Disease 2019 (COVID-19) pandemic, the AAO announced guidelines which recommended the cessation and postponement of all routine and non-urgent clinic visits and elective surgeries. While this decision was important for the public health effort to mitigate the COVID-19 pandemic, the effect this decision had on patients with exudative age-related macular degeneration (AMD) requiring frequent visits for treatment and monitoring is unknown. This retrospective observational study evaluates the effect that the delay in these visits and treatments had on this patient population.

Methods: This study identified patients with exudative AMD undergoing active treatment who had at least one appointment rescheduled due to the COVID-19 pandemic from March to May 2020 at a single institution. Data was collected from the last appointment prior to March 2020, and the first appointment following delay, and compared to age-matched controls from 2019 with the same diagnosis. Average length of time from postponement to follow-up was calculated. Patient demographics, visual acuity (LogMAR), and central macular thickness (CMT) on spectral-domain optical coherence tomography (OCT) were documented. Statistical analysis was conducted using t-tests with a two-tailed hypothesis.

Results: 69 patients (96 eyes) with exudative AMD met inclusion criteria. The mean (SD) age was 83.7 (8.3) years and 74% of patients were female. The mean (SD) number of days of treatment delay was 45.9 (38.6) days. Mean (SD) increase in CMT was 23.84 (82.71) μ m for the eye that had delayed treatment, which was statistically significant ($t=2.49$, $p=0.01$). Mean (SD) change in visual acuity was +0.11 (0.32) LogMAR, which was significantly worse ($t=3.42$, $p=0.001$).

Conclusions: Central macular thickness and visual acuity of treatment eyes were significantly worse as a result of the delay secondary to the COVID-19 pandemic. Further data collection over time is required to determine whether changes in CMT and VA are reversible over time. Further analyses of sequelae of delayed injections may reveal unique insights into subgroups which may be more tolerant of extended injection schedules.

CONTROL ID: 3538990

SUBMITTER (NAME ONLY): Felix Yemanyi

TITLE: Amino acid transporter SLC38A5 modulates pathological retinal neovascularization in mice

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Yemanyi, Z. Wang, S. Huang, C. Liu, Y. Tomita, A.K. Blomfield, Z. Fu, J. Chen, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pathological ocular neovascularization (NV) frequently results in vision loss and may be influenced by aberrant transport and metabolism of nutrients like amino acids in vascular endothelial cells (EC). Solute carrier (SLC) transporters are responsible for nutrient and metabolic sensing including amino acid transport. Dysregulation of key subfamilies of SLC transporters has been implicated in many metabolic and vascular diseases including neurovascular eye disorders. Here, we determined the specific role of SLC family 38 member 5 (SLC38A5) in pathological retinal NV using a mouse model of oxygen-induced retinopathy (OIR).

Methods: Neonatal C57BL/6J mice were exposed to 75% oxygen from postnatal day (P) 7 to P12 to induce OIR with pathological NV. Slc38a5 mRNA and protein expression levels were determined in OIR or room air control retinas (n=6/group) and laser capture microdissected retinal blood vessels (n=4/group). OIR was induced in Slc38a5 knockout (Slc38a5^{-/-}) and wild type (WT) control mice (n=5/group) and pathological retinal NV and vaso-oblivation (VO) were evaluated at P17. The effect of Slc38a5 deficiency on developmental retinal angiogenesis was analyzed in Slc38a5^{-/-} and WT mice (n=5/group) at P5 and P10. Glutamine uptake and expression of relevant angiogenic regulators were analyzed in human retinal microvascular ECs (HRMECs; n=3) transfected with siRNA targeting SLC38A5 (si-SLC38A5) or control SiRNA (si-Ctrl).

Results: Slc38a5 mRNA or protein levels were substantially upregulated (p<0.01) in P17 OIR whole retinas relative to normoxic control mice, and specifically enriched in pathological NV. Compared with WT controls, genetic deficiency of Slc38a5 significantly attenuated (p<0.01) pathological NV in OIR retinas without markedly affecting VO. Moreover, knockout of Slc38a5 significantly delayed (p<0.01) developmental angiogenesis in P5 and P10 retinas relative to WT. Compared with si-Ctrl, si-SLC38A5 transfected HRMECs exhibited profound decrease in glutamine uptake associated with downregulation of crucial angiogenic factors and their receptors (IGF2, ANG1 and 2, FGF2, VEGFR1 and 2, IGFR, FGFR2 and 3, TIE2).

Conclusions: These data show that SLC38A5 regulates pathological retinal NV potentially via controlling glutamine uptake and angiogenic regulators in vascular ECs. Thus, targeting SLC38A5 may aid the design of novel therapeutics to ameliorate pathological NV in vascular eye diseases.

CONTROL ID: 3538997

SUBMITTER (NAME ONLY): Uwe Oberheide

TITLE: Modeling of intraocular lenses for patients with age-related macular degeneration by ray-tracing

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Oberheide, S. Tölle, Technische Hochschule Köln, Köln, Nordrhein-Westfalen, GERMANY

Commercial Relationships Disclosure (Abstract): Uwe Oberheide: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Tölle: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macula degeneration (AMD) is the most common cause of blindness in people over 65 years in the western world. These people are permanently dependent on special visual aids in order to be able to perform visual tasks with reduced restrictions like magnifying glasses or screen readers. In the case of cataract formation special intraocular lenses dependent on the stage of disease might also help.

Methods: Three different intraocular lenses for patients with AMD were simulated in the Liou-Brennan eye model with a ray-tracing computational software based on literature and patent file data. First, a sulcus based add-on lens with a central add power for magnification in close range. Second, a fresnel prismatic capsular bag intraocular lens, which shifts the central scotoma to peripheral regions and third, a double lens system with a sulcus based lens with high positive dioptric power and a capsular bag lens with high negative dioptric power and slight decentrations to deflect light from the center.

Results: Magnification and beam deflections of the simulated lenses confirm the effect described by the manufacturers. To evaluate the effect for different stages of AMD snellen lines were projected on fictitious retinal defects of different sizes and compared to corresponding visual acuities. The sulcus based add-on lens is suitable for patients with small defects, whereas the two light deflecting lenses can provide a low level of visual acuity even for larger retinal defects. They are mainly limited by maximum angle of deflection and peripheral receptor density.

Conclusions: Dependent on the size of the retinal defect, the simulated lenses offer a possibility to maintain a functional visual acuity in patients with AMD. If the size of retinal disturbance is known the most suitable solution for the patient can be chosen.

CONTROL ID: 3539003

SUBMITTER (NAME ONLY): Meredith Alfred

TITLE: Correlation between the Standard Patient Evaluation of Eye Dryness (SPEED) and Ocular Pain Assessment Survey (OPAS) in Patients with Dry Eye Disease

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Nau, A. McLeod, Korb and Associates, Boston, Massachusetts, UNITED STATES| M. Alfred, A.C. Nau, A. McLeod, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Meredith Alfred: Commercial Relationship: Code N (No Commercial Relationship) | Amy Nau: Commercial Relationship: Code N (No Commercial Relationship) | Andrew McLeod: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Subjective symptoms of dry eye are best monitored clinically with symptom questionnaires. The SPEED is a validated instrument that has been correlated to the severity of meibomian gland dysfunction (MGD). The OPAS is a validated questionnaire designed to measure ocular pain stemming from any origin. Many patients treated for MGD suffer from persistent symptoms, suggesting peripheral or central neuronal sensitization may be present. This study determined whether responses on the SPEED questionnaire were correlated with OPAS responses in a population diagnosed with evaporative dry eye.

Methods: Ninety-one patients (63 females; 27 males, average age 50.36 ± 16.38 years), diagnosed with MGD using standard structural and functional endpoints were enrolled in this IRB approved study at a private practice in Boston, MA, USA. All participants were given both the SPEED and OPAS questionnaires at a single scheduled dry eye follow up visit. Averages, standard deviations, and correlation coefficients were calculated.

Results: The average SPEED score was 11.45 (SD 5.89) out of a possible high score of 28. The average OPAS score was 46.25 (SD 38.88) out of a possible score of 190. SPEED scores were positively correlated to pain intensity over a period of 24 hours prior to the patient's appointment (correlation coefficient = 0.72) as well as over a period of 2 weeks prior to the appointment (correlation coefficient = 0.71). SPEED scores were positively correlated to the impact on the quality of life (correlation coefficient = 0.64) at 24 hours and 2 weeks prior to the appointment. Patients with a high SPEED score were also likely to have a high overall OPAS score at both timepoints (correlation coefficient = 0.76).

Conclusions: Patients with a high SPEED score were likely to have a high OPAS score, indicating that patients with MGD were experiencing pain that may not be accounted for by the SPEED questionnaire. Use of the OPAS as an adjunctive questionnaire could identify patients with either nociceptive or neuropathic corneal abnormalities who may be recalcitrant to treatment. Insights into the severity of affective disorders and issues related to the quality of life uncovered by the OPAS could lead to more personalized and effective treatment plans for evaporative dry eye.

CONTROL ID: 3539016

SUBMITTER (NAME ONLY): Adrian Dockery

TITLE: Genotype-phenotype correlations of known and novel variants in the PRPH2 gene.

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Dockery, L. Whelan, P.F. Kenna, G. Farrar, Genetics, The University of Dublin Trinity College, Dublin, IRELAND|M. Khan, Z. Corradi, F.P. Cremers, Radboud Universiteit, Nijmegen, Gelderland, NETHERLANDS|K.A. Stephenson, J. Zhu, J.J. O'Byrne, J. Turner, D.J. Keegan, Clinical Genetics Centre for Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|C. Kirk, R. Cairns, G. Silvestri, Belfast Health and Social Care Trust, Belfast, Belfast, UNITED KINGDOM|P.F. Kenna, Royal College of Surgeons in Ireland Department of Ophthalmology, Dublin, Dublin, IRELAND|C. Dhaenens, Universite de Lille, Lille, Hauts-de-France, FRANCE|M. Khan, Department of Pathology and Medical Biology, Universitair Medisch Centrum Groningen, Groningen, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Variants in the PRPH2 gene have been previously linked to a plethora of inherited retinal degenerations (IRDs) including retinitis pigmentosa (RP), macular dystrophy (MD), adult vitelliform macular dystrophy, cone-rod dystrophy and many more. This study aimed to correlate known and novel pathogenic variants in PRPH2 with the resulting patient phenotypes.

Methods: Next-generation sequencing of known IRD-associated genes was performed for over 1000 Irish IRD participants with IRD phenotypes. Detailed clinical examinations of all participants carrying a candidate disease-causing variant in PRPH2 were performed to best determine the specific phenotype. The results of these examinations were then compared for differences and consistencies in disease manifestation.

Results: Potentially pathogenic mutations in the PRPH2 gene were established in 18 participants from 15 different families. This accounts for over 2 percent of all resolved genotypes which is consistent with larger studies of a similar nature. 8 out of 18 (44%) of PRPH2 patients presented with a predominantly macular degeneration, while the remaining 10 (56%) patients presented clinically with a RP phenotype. The most prominent variant in this cohort was c.634A>G, p.Ser212Gly. It was present in 8 patients and associated with an autosomal dominant RP (adRP) phenotype. These cases were additional to the previous study of this mutation by the team in a large Irish adRP pedigree. Nine additional PRPH2 variants were observed in the remaining 10 cases, one of which was a novel variant in exon 1 of the gene, c.440dupA, p.Gly148Trpfs*29. These remaining cases presented with a predominately cone-driven degeneration.

Conclusions: Studies such as this are particularly useful for genes associated with multiple phenotypes. The results may help to inform prognoses when dealing with the mutational spectrum of the PRPH2 gene. Although this study was performed on a relatively small subset of IRD participants, we did not observe significant phenotypic variability between patients with the same PRPH2 mutation. Given we are in the era of gene therapy, accurate genetic diagnoses have never been more important to identify needs and enable access to potential future therapeutics.

CONTROL ID: 3539018

SUBMITTER (NAME ONLY): Mayu Nishimura

TITLE: Cluster-Randomized Controlled Trial of School-Based Visual Screening for Kindergarten Children

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Nishimura, A.M. Wong, Ophthalmology & Vision Sciences, The Hospital for Sick Children, Toronto, Ontario, CANADA|M. Nishimura, D. Maurer, Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, Ontario, CANADA|A.M. Wong, Ophthalmology & Vision Science, University of Toronto, Toronto, Ontario, CANADA|D. Maurer, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Some 10% of kindergarten children have undetected refractive errors and 3-5% need treatment to prevent amblyopia. In many jurisdictions, no universal screening program exists to detect these problems. We hypothesized that offering visual screening to children in senior kindergarten (i.e., age 5) would lower the later prevalence of amblyopia and other visual problems.

Methods: 50 high-needs schools in Toronto, Canada were randomly assigned to screening or no screening (i.e., status quo). Children in senior kindergarten (n = 1468) at 25 schools were screened using 3 tests (visual acuity, stereoacuity, photoscreener). 747 children (50.9%) passed screening, 551 children (37.5%) failed screening, 163 children (11.1%) were absent for screening, and 7 children (0.05%) opted out. Children who failed screening or were absent were offered a comprehensive eye exam (with cycloplegia) at school with an optometrist and it was attended by 408 (74%) and 49 (30%), respectively. If glasses were needed, they were dispensed at no cost (n = 225). When the children were in Grade 2 (~1.5 years after screening), visual acuity, stereoacuity, and uncyclopleged refractive errors (with photoscreener) were assessed in all 50 schools (n = 2715 children).

Results: The prevalence of amblyopia in Grade 2 did not differ between screened schools (8.6%) and non-screened schools (7.5%), $p = .10$. There was also no difference in the prevalence of visual problems other than amblyopia (45.1% versus 47.1%, $p = .51$). However, in screened schools more children were wearing glasses (5.0% versus 3.5%, $p = .05$), and more children reported that they had lost or broken their glasses (8.3% versus 4.7%, $p = .01$).

Conclusions: Visual screening is effective in identifying children with previously undiagnosed visual problems. However, the benefits may not translate to better visual outcomes 1.5 years later because of other factors (e.g., delays in seeing an optometrist, no support for buying or replacing glasses, parents' (and teachers') lack of understanding about the importance of treatment, lack of treatment compliance). In addition to visual screening, strategies to mitigate these factors are necessary to improve children's visual health.

CONTROL ID: 3539040

SUBMITTER (NAME ONLY): alice bruscolini

TITLE: The long-term clinical efficacy of recombinant human nerve growth factor in the treatment of neurotrophic keratitis

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. bruscolini, M. Sacchetti, A. Moramarco, G. Albanese, A. Cerini, A. Iambiase, Sense Organs, Universita degli Studi di Roma La Sapienza Facolta di Medicina e Odontoiatria, Roma, Lazio, ITALY

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ABSTRACT BODY:

Purpose: Topical recombinant human nerve growth factor (rhNGF) is FDA-approved to treat patients with neurotrophic keratitis (NK), but current clinical trial data only encompasses 1 year of follow up. We hypothesize that a single course of rhNGF can have a long-term, persistent effect on NK healing and related clinical parameters. Therefore, we evaluated the long-term efficacy of rhNGF in a retrospective, consecutive, observational case series from a single-center setting over a 4-year period.

Methods: A total of 18 patients with stage 2 or 3 NK received rhNGF 20 mcg/ml 6 times a day for 8 weeks. Lesion recurrence during follow-up was evaluated at 12, 24, 36, and 48 months. Clinical efficacy was measured by Cochet-Bonnet aesthesiometer (corneal sensitivity), Schirmer's test (tear production), and Snellen chart [visual acuity (VA)] at baseline, end of treatment (8 weeks), and at 12, 24, 36, and 48 months after treatment was completed.

Results: Four patients experience recurrence during the study; 3 within the first 12 months and 1 within 36 months. Corneal sensitivity was significantly improved by the end of treatment (8 weeks) with improvements persisting throughout 48 months of follow-up ($P < 0.05$). Both tear production and VA were also significantly improved by the end of treatment (8 weeks) and these effects persisted at 12, 24, and 36 months ($P < 0.05$). Improvements in tear production and VA were also seen at 48 months; however, they were not statistically significant.

Conclusions: These results are consistent with our hypothesis that a single, 8-week treatment regimen of rhNGF can have long lasting clinical effects. The long-term clinical utility of rhNGF for the treatment of NK was demonstrated though the low rate of lesion recurrence along with improvements in corneal sensitivity, tear production, and VA over the course of 4 years.

CONTROL ID: 3539050

SUBMITTER (NAME ONLY): Daniel Hill

TITLE: Demonstrating the intranasal route as a viable alternative to intravitreal administration of DARC

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hill, V. Luong, L. Guo, M. Cordeiro, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Cordeiro, Imperial College Healthcare, Western Eye Hospital, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Daniel Hill: Commercial Relationship(s);UCL:Code F (Financial Support) | Vy Luong: Commercial Relationship: Code N (No Commercial Relationship) | Li Guo: Commercial Relationship: Code N (No Commercial Relationship) | M Francesca Cordeiro: Commercial Relationship(s);Santen:Code F (Financial Support);UCL Technology Fund:Code F (Financial Support)

ABSTRACT BODY:

Purpose: DARC (detection of apoptosing retinal cells) is an annexin-based technology that fluorescently marks stressed and dying cells in the retina, allowing in vivo assessment of retinal pathology using a confocal laser scanning ophthalmoscope. As the retina is an integral part of the central nervous system, imaging intravitreally-injected DARC facilitates a unique in vivo assessment of neuronal health which is applicable to a wide range of neurodegenerative animal models. To reduce discomfort associated with intravitreal administration and potential complications, we investigated whether intranasal delivery of fluorescent annexin can be used as an alternative route in DARC treatment.

Methods: 10 female 3xTg transgenic Alzheimer's disease (3xTg-AD) model mice were used as a model of retinal cell death and 10 C57 mice were used as healthy controls (all animals from The Jackson Laboratory). Intranasal administration of DARC involved restraining the animal and carefully administering 5 µL of aqueous-buffered DARC to each nostril, using a p20 pipette. Retinas were imaged at baseline and 2 hours after intranasally administered DARC, in vivo, at the 488 nm wavelength, using a Multiline Spectralis OCT. After in vivo imaging, animals were sacrificed, and the retinas were extracted, fixed, and imaged with fluorescent microscopy. Automated spot counts were collected for both in vivo and ex vivo images.

Results: Administration of DARC via the intranasal route allowed discrimination between healthy and diseased animals both in vivo and ex vivo (significantly higher spot count in disease; $p < .05$) and produced images of similar quality (fluorescence brightness and definition) to those acquired from intravitreally administered DARC retinas. It was found that a higher intranasal DARC dose was required compared to intravitreal administration (approximately 10-fold increase).

Conclusions: The intranasal route has been demonstrated as a viable alternative to intravitreal administration of DARC, thus helping to refine animal procedures to minimise discomfort. Future work should focus on optimising an intranasal buffer to enhance delivery and reduce necessary DARC dose, followed by expansion to rat models. In the long term, standardisation of administration route to intranasal across animal and human applications may help to improve the applicability of DARC-enabled animal experiments to the clinic.

CONTROL ID: 3539061

SUBMITTER (NAME ONLY): Siwei Cai

TITLE: Identification of PGC-1 β as promising therapeutic target of neovascular AMD

SESSION TITLE: Mitochondria in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Cai, D.Y. Shu, H. Philipose, E. Butcher, I. Senthilkumar, S. Frank, M. Saint-Geniez, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|S. Cai, D.Y. Shu, M. Saint-Geniez, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|H. Philipose, Stony Brook University Department of Pharmacological Sciences, Stony Brook, New York, UNITED STATES|E. Butcher, Harvard University, Cambridge, Massachusetts, UNITED STATES|I. Senthilkumar, Northeastern University, Boston, Massachusetts, UNITED STATES|S. Frank, Boston College, Chestnut Hill, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: RPE dysfunction and choroidal neovascularization (CNV) are the major hallmarks of neovascular AMD (nAMD). We previously identified PGC-1 β , a master regulator of mitochondrial function, as a novel stress response gene in RPE positively associated with nAMD. However, the unique pathologic functions of PGC-1 β in RPE during nAMD remained unclear. We hypothesize that PGC-1 β promotes CNV and nAMD by driving RPE toward a pro-angiogenic and pro-inflammatory profile.

Methods: Expression of PGC-1 β in human AMD and age-matched control eyes was analyzed by immunohistochemical staining. Time-course expression of PGC-1 β was measured in murine RPE/choroid in the model of laser-induced CNV. PGC-1 β was overexpressed in RPE of adult WT mice using subretinal injection of pLV-PGC1B. Funduscopy, SD-OCT, TEM, F-actin and IB4 staining of whole mount RPE was performed 4 and 8 weeks after injection. PGC-1 β was induced in matured ARPE-19s using a Tet-responsive adenovirus and doxycycline exposure. Conditioned media collected on PGC-1 β expressing RPE was analyzed using protein arrays.

Results: PGC-1 β was strongly induced in RPE surrounding the fibrovascular lesions in nAMD eyes while no expression could be detected in RPE of both control and atrophic AMD samples. Following laser induction of CNV in mice, PGC-1 β was rapidly induced in the RPE/choroid complex at day 3 (n=6, P<0.05), peaking at day 7 (n=6, P<0.001) post-laser. PGC1B overexpression in the RPE of adult mice led to reduction in total retinal thickness (n=5, P<0.05), pigmentary changes and RPE disorganization characterized by pathological morphology (89% VS 8%, n=4) and larger area (n=4, P<0.05) when compared to pLV-GFP controls. Ultrastructural analysis of PGC-1 β induced RPE showed disordered apical microvilli, shorten basal infoldings, reduced melanosomes and accumulation of undigested outer segments. Vascular leakage and spontaneous CNV were observed in 20% of pLV-PGC-1 β injected eyes (n=15). Analysis of secreted proteins from PGC-1 β expressing RPE revealed the induction of the pro-angiogenic and pro-inflammatory factors AREG (P<0.05), HB-EGF (P<0.05), bFGF (P<0.05), IL8 (P<0.0001) and prolactin (P<0.01) (n=4).

Conclusions: We identify PGC-1 β as a novel biomarker of nAMD. Pathological induction of PGC1B promotes RPE dysfunction and secretion of pro-angiogenic factors, leading to nAMD-like retinal degeneration and CNV in mice.

CONTROL ID: 3539075

SUBMITTER (NAME ONLY): Chee Wai Wong

TITLE: Decreased Macular Sensitivity in Highly Myopic Eyes with Myopic Macular Degeneration is Associated with Reduced Deep Retinal Perfusion Density

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wong, Q. Hoang, Surgical Retina, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|C. Wong, F. Zheng, J. Chua, L. Schmetterer, Q. Hoang, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Reduction in macular sensitivity (MS) has been demonstrated in highly myopic (HM) eyes with myopic macular degeneration (MMD) but the correlation with retinal structural changes is still unclear. We aim to evaluate the MS in eyes with various severities of MMD and its association with anatomical parameters of the retina on optical coherence tomography (OCT) and OCT-angiography (OCTA).

Methods: This is a prospective, observational study that enrolled 138 HM eyes from 82 adult participants from the Singapore National Eye Centre High and Pathologic Myopia clinic. The MS were evaluated using Microperimeter MP-3 comprised of 33 points covering 12° diameter of the macular area. The retinal perfusion density (PD) and retinal thickness (RT) were measured from the 3×3mm² macular scan obtained by the PLEX Elite 9000 swept source OCTA. Pair-wise differences of MS between varying severities of MMD, and the vasculature-function and structure-function relationship were evaluated by the multivariable linear mixed models, with adjustment of age and axial length (AL).

Results: Out of 138 eyes, 53 eyes (38.4%) had tessellated fundus, 26 eyes (18.8%) had peripapillary diffuse chorioretinal atrophy (PDCA), 37 eyes (26.8%) had macular diffuse chorioretinal atrophy (MDCA), and 22 eyes (15.9%) had patchy or macular atrophy. MS significantly correlated with BCVA ($r=0.32$, $P<0.001$). Reduction in MS occurred in MDCA ($P<0.001$), and declined with increasing severity of MMD ($P<0.001$), while changes in BCVA were not significant ($P>0.04$). Older age ($\beta=-0.08$, $P<0.001$), longer AL ($\beta=-0.32$, $P=0.005$), worse MMD ($\beta\leq-2.16$, $P<0.001$), presence of staphyloma involving the macula ($\beta\leq-2.98$, $P<0.001$) and fuch's spot ($\beta=-1.58$, $P<0.04$) were independently associated with declined MS. Decreased deep retinal PD in MMD ($\beta=0.14$, $P=0.004$), but not superficial retinal PD ($P=0.33$) or RT ($P=0.51$), was significantly associated with reduction in MS.

Conclusions: We found a vasculature-function relationship between visual function and deep retinal perfusion density as measured by microperimetry and OCTA respectively. These parameters may serve as early indicators of structural and functional abnormalities in highly myopic eyes with MMD.

CONTROL ID: 3539095

SUBMITTER (NAME ONLY): Joshua Heczko

TITLE: The in vitro Effect of Various Selenium Disulfide Concentrations on Demodex Folliculorum

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Heczko, C. Schell, A. Pansick, M. Vincent, N. Radova, R. Stein, J. Quintero, H. Perry, Ophthalmology, Nassau University Medical Center, East Meadow, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effectiveness of varying concentrations of selenium sulfide in affecting Demodex folliculorum.

Methods: Sixty-five eyelashes with live Demodex from 29 patients seen at the Nassau University Medical Center (17 patients) and Ophthalmic Consultants of Long Island (12 patients) were observed for 90 minutes under 0.1%, 0.5%, 1.0%, and 4.0% selenium sulfide with either carboxymethyl cellulose (CMC) solution or vaseline ointment as excipients. Positive and negative controls were also evaluated as separate solutions of CMC, vaseline, basic saline solution, 50% tea tree oil, and 100% tea tree oil.

Results: Demodex behavior was affected by concentrations as low as 0.1%. Deaths in the selenium sulfide reagents were observed in the the 4.0% selenium sulfide solution with CMC (36.4% kill rate, 4 of 11 Demodex, average time of death 17.5 minutes) and 4.0% selenium sulfide with vaseline ointment (12.5%, 1 of 8 Demodex, time of death 75 min). No Demodex deaths were witnessed in the other treatment groups. However, Demodex mites in concentrations as low as 0.1% were noted to move away from the selenium.

Conclusions: Selenium sulfide has shown efficacy in killing Demodex at a 4% concentration with the CMC solution and mild cidal activity with 4% vaseline. Concentrations as low as 0.1% show avoidance by Demodex folliculorum suggesting that it might function as a natural insect repellent.

CONTROL ID: 3539111

SUBMITTER (NAME ONLY): Fuensanta Vera-Diaz

TITLE: Peripheral blur perception and optical quality in young children

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.A. Vera-Diaz, A. Jnawali, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P. Bex, College of Science, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blur perception is influenced by the eye's optical quality during emmetropization. We measured sensitivity to different types and levels of simulated optical blur and optical quality across the visual field in young children with normal vision.

Methods: Children ($n=27$, 7.86 ± 0.91 yrs) with functional emmetropia ($SE\ OD +0.94\pm0.55D$) participated in 2 tests. (1) Blur discrimination thresholds were measured with an adaptive 4AFC task previously used in adults. Dead leaves stimuli were blurred with different pedestal levels and increments of Defocus (DEF) or Spherical Aberration (SA) kernels beyond 0° , 6° , or 12° eccentricity at 40cm. Participants chose which quadrant appeared blurriest. Blur discrimination thresholds were fit with a 2-parameter (Intrinsic Blur, Blur Criteria) dipper function. (2) Optical quality across the central horizontal $\pm 30^\circ$ was assessed using a scanning aberrometer at 4m and 40cm viewing distances. Strehl ratios, defocus and primary SA were computed for 4mm pupils. Outcomes were analyzed with One-way ANOVAs and correlations with axial length (AXL, 22.78 ± 0.74 mm).

Results: (1) Intrinsic blur showed an overall effect of eccentricity (DEF & SA, $p<0.001$), significantly decreasing for 12° vs. 6° (DEF $p=0.003$, SA $p=0.001$) and 0° (DEF $p<0.001$, SA $p=0.001$), but no differences between 6° and 0° . Blur Criteria showed no general effect of eccentricity. Longer eyes showed lower Intrinsic Blur (DEF $p=0.040$, SA $p=0.014$) and Blur Criteria (SA $p=0.032$). (2) Strehl ratios also showed eccentricity-dependence ($p=0.006$), with better quality in the central 12° ($p=0.014$) and nasal retina ($p=0.004$) that increased with AXL ($p=0.003$). Defocus was more negative (hyperopic) peripherally ($p<0.001$). Primary SA showed no effect of eccentricity but was smaller in longer eyes ($p<0.001$). (3) For 0° ($p=0.009$) and 6° ($p=0.020$), Blur Criteria for DEF was correlated with the eye's defocus. For 12° , Blur Criteria for SA was correlated with the eye's SA ($p=0.050$).

Conclusions: Elevated Intrinsic Blur at 12° but not between 0° and 6° indicate a critical role of the 6- 12° retinal area in blur decoding. A similar pattern was observed of eccentricity dependence for optical quality. These correlations indicate a possible relationship of defocus within the central 12° and SA beyond 12° . Less positive SA was found in longer eyes with less hyperopia, these eyes (at higher risk of developing myopia later) also show lower sensitivity to blur.

CONTROL ID: 3539141

SUBMITTER (NAME ONLY): David Dao

TITLE: High-Fat Diet Alters the Retinal Transcriptome Independently of Gut Microbiome in Germ-Free Mice

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: High-fat diets (HFD) affect the pathophysiology of retinal diseases including, age-related macular degeneration (AMD), diabetic retinopathy and glaucoma by altering the gut microbiome which can directly affect the retinal transcriptome as already shown by our team. However, the effects of diet independent of gut microbiome on the retinal transcriptome are currently unknown. The purpose of this study is to investigate if HFD can have direct effects on retinal gene expression and pathways independently of the gut-microbiome by comparing the retinal transcriptome of germ-free (GF) mice on a normal diet (ND) to GF mice on HFD.

Methods: RNA was extracted from whole retinas (4 per group) from 15-weeks old GF C57BL/6J male mice fed ND and HFD (23% saturated fat for 8 weeks). RNA-seq was performed on NovaSEQ6000 using the paired-end method. Differentially expressed genes (DEGs) were identified (cutoff p-value <0.01) and functional enrichment network analyses (cutoff FDR B&H <0.05) were created for the DEGs using Toppgene.

Results: After correction of the raw data, 20,287 genes were selected for differential gene analysis. In GF-HFD group, a cohort of 1195 DEGs were identified, 801 were upregulated and 394 were downregulated. Key genes involved in oxidative phosphorylation, the citric acid cycle and electron transport chain were affected. Cellular organelle functions affected by HFD included the spliceosomal complex, mitochondrion, endoplasmic reticulum (ER). Enrichment analysis showed that pathways associated with neurodegenerative disorders including Parkinson's disease, Alzheimer's disease, and Huntington's disease were affected by HFD. Notable DEGs include vascular endothelial growth factor receptor 3 (FLT4) and receptor accessory protein 1 (REEP), which play key roles in AMD and retinal degeneration, respectively.

Conclusions: This study demonstrates novel data that diet can directly modulate the retinal transcriptome independently of the gut microbiome. Unbiased analysis of the retinal transcriptome identified genes and pathways involved in retinal metabolism and retinal degenerative disorders affected by HFD alone. Future studies are needed to elucidate the complex relationship between retinal disease, diet and the gut microbiome.

CONTROL ID: 3539150

SUBMITTER (NAME ONLY): Dong Hyun Jo

TITLE: Characterization and adenine base editing of RB1-mutant cells prepared by cytosine base editing: implication in research for retinoblastoma

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Jo, Department of Anatomy and Cell Biology, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|H. Jang, Y. Jung, S. Bae, Department of Chemistry and Research Institute for Convergence of Basic Sciences, Hanyang University, Seoul, KOREA (THE REPUBLIC OF)|J. Kim, Fight against Angiogenesis-Related Blindness (FARB) Laboratory, Biomedical Research Institute, Seoul National University Hospital, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: In this study, we investigated to establish RB1-mutant fibroblast cells by cytosine base editing, characterize them, and treat adenine base editors to correct the mutation.

Methods: Fibroblasts were treated plasmids encoding cytosine base editors, and cells with the intended RB1 mutation (p.R552X) were collected. The following experiments characterized wild-type, heterozygous, and homozygous RB1 mutant cells: 1) quantitative real-time polymerase chain reaction of RB1 mRNA, 2) Western blot, 3) flow cytometry for cell cycle analysis, and 4) cell proliferation assay. Then, each cell was treated with plasmids encoding adenine base editors to investigate the potential of base editing in the context of retinoblastoma.

Results: We successfully established fibroblast cells with heterozygous and homozygous RB1 mutation. Wild-type, heterozygous, and homozygous RB1 mutant cells demonstrated differential characteristics of RB1 mRNA expression, RB1 protein expression, cell cycle distribution, and proliferative potential. We found that adenine base editing of RB1 mutant cells induced the read-through of nonsense mutation.

Conclusions: In conclusion, we suggest that CRISPR-associated base editing might be a tool to mimic the variants in patients with retinoblastoma and correct them for the reversal of disease-related phenotypes.

CONTROL ID: 3539152

SUBMITTER (NAME ONLY): Rachel Cant

TITLE: An investigation of ocular surface intracellular cytokines in asymptomatic versus symptomatic soft contact lens wearers using a novel mass cytometry method.

SESSION TITLE: Cytokines, growth factors, anti-inflammatory

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Cant, Pharmacy and Optometry, The University of Manchester Faculty of Biology Medicine and Health, Manchester, Manchester, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Rachel Cant: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular discomfort is the primary reason for discontinuation from contact lenses. This discomfort may be mediated by ocular surface inflammation, although its precise molecular basis remains unclear. We have developed a novel mass cytometry panel capable of determining surface markers (enabling cell identification) and levels of intracellular cytokines in cells removed from the ocular surface by impression cytology. We sought to identify the biomarkers associated with contact lens discomfort in a group of symptomatic soft contact lens wearers.

Methods: Ten asymptomatic (CLDEQ-8 score ≤ 10) and 10 symptomatic (CLDEQ-8 score ≥ 20) soft contact lens wearers were recruited. Impression cytology samples were taken from the bulbar conjunctiva and central upper eyelid margin using an Eyeprim device (OPIA Technologies, France). Cells were removed from the Eyeprim membrane and stained with a mass cytometry panel targeting 30 cell surface markers or intracellular proteins. This panel allowed the identification of a range of immune cells, epithelial cells, inflammatory proteins and extracellular matrix remodelling proteins. Samples were analysed using mass cytometry and Cytokit was used to assess protein expression levels.

Results: We observed a x2.2 increase in matrix metalloproteinase-9 (MMP-9), x1.1 increase in macrophage- derived chemokine (MDC) and x2.0 increase in interleukin-23 (IL-23) in the eyelid margin epithelial cells of symptomatic compared to asymptomatic lens wearers. A x1.4 increase in MMP-9 was also observed in the conjunctival epithelial cells of symptomatic compared with the asymptomatic wearers. Furthermore, a decrease in the anti-inflammatory cytokine IL-10 was observed in eyelid margin epithelial cells of symptomatic compared with asymptomatic subjects.

Conclusions: Increased levels of MMP-9, MDC, IL-23 and decreased levels of IL-10 were observed in the eyelid margin and conjunctiva of symptomatic compared with lens asymptomatic soft lens wearers. These have potential as biomarkers for contact lens discomfort, and indeed some of these mediators have previously been implicated in the inflammatory events underlying dry eye disease. This methodology enables measurement of precise levels of inflammatory markers inside specific cell types, making it ideal for the investigation of the ocular surface.

CONTROL ID: 3539158

SUBMITTER (NAME ONLY): Sudeshna Sil Kar

TITLE: Computational Imaging Biomarker Correlation with Intraocular Cytokine Expression in Diabetic Macular Edema: Findings from the IMAGINE DME Study

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Various pathways and cytokines are implicated in pathogenesis of diabetic macular edema (DME). Recent work from our group has identified computational imaging biomarkers (CIBs) of vessel tortuosity from quantitative

ultra-widefield angiography (UWFA) and texture patterns from optical coherence tomography (OCT) that are associated with response to anti-VEGF therapy in DME. The goal of this study was to establish the underlying molecular basis of the radiomic features. Hence, we sought to evaluate the association between underlying expression of specific cytokines and CIBs from UWFA and OCT scans.

Methods: The IMAGINE study is post-hoc assessment of aqueous cytokine expression and in-depth assessment of the imaging studies obtained throughout the DAVE DME study. The study included 24 eyes from 20 patients. The concentrations of cytokines including VEGF, ANG2, MCP-1, IL-6, and IL-8 were measured. 598 texture-based radiomic features were extracted from the baseline OCT images for heterogeneity assessment and 156 morphological and vessel tortuosity features were extracted from the baseline UWFA scans. Biclustering allows simultaneous clustering of rows (patients) and columns (features) of a data matrix and was employed on UWFA and OCT features to identify eyes with similar morphological phenotypes. Pearson correlation coefficients (R) assessed the correlation between the OCT and UWFA features that were identified by the most consistent BCs and the cytokines.

Results: Strong correlations were identified between VEGF and 7 morphology-based FA features ($R=0.44-0.51$, $p<0.05$), 1 tortuosity based FA feature ($R=0.45$, $p=0.004$) and 2 OCT-derived intraretinal fluid (IRF) Laws texture features ($R=0.48-0.49$; $p=0.01$). Strong correlation between IRF Laws texture feature and ANGPTL4 ($R=0.52$, $p=0.008$) were identified. Additionally, IRF Laws feature and u-PAR ($R=0.41$, $p=0.04$), HGF ($R=0.47$, $p=0.01$) and TIMP-1 ($R=0.40$, $p=0.004$) were also observed.

Conclusions: This study demonstrates a link between multiple radiomics-based CIBs and pathway-associated cytokine expression in eyes with DME, including a strong link between VEGF levels with retinal leakage morphology and vessel tortuosity.

CONTROL ID: 3539159

SUBMITTER (NAME ONLY): Sujata Rijal

TITLE: Quantification of near word acuity thresholds with and without flankers for individuals with keratoconus

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rijal, D.R. Coates, J.D. Marsack, Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sujata Rijal: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Coates: Commercial Relationship: Code N (No Commercial Relationship) | Jason Marsack: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Residual aberrations are present in the eyes of individuals with keratoconus, even when the eyes are “well corrected” by today’s clinical standards. High contrast visual acuity (VA), the most common method to assess visual performance, does not reflect the full spectrum of challenges that accompany real-world visual tasks. This study aims to move beyond VA and quantify threshold word acuity for “well corrected” individuals with keratoconus.

Methods: To date, 2 typically-sighted individuals (28 and 34 years old) and 1 individual with keratoconus (45 years old) have been recruited. VA was measured at distance with logMAR charts. Residual aberrations were quantified at distance with a wavefront sensor. In addition, subjects were asked to monocularly read words (with and without 4 flanking words) aloud at a 40cm test distance. Ten trials of each condition (5 font sizes and 5 durations at 100% contrast) were randomly presented using Arial font, for a total of 500 trials/eye. Psychometric functions were fitted and thresholds were defined as 80% correct for each font size and duration.

Results: Higher-order root mean square (HORMS) for a 3mm pupil was within normal limits (mean \pm SD = $0.04 \pm 0.02 \mu\text{m}$) for both eyes of the typically-sighted individuals, and elevated for the individual with keratoconus (OD: $0.21 \mu\text{m}$ and OS: $0.14 \mu\text{m}$). All individuals were able to achieve the common clinical standard of 0.00 logMAR (20_{20}) in both eyes. As the word presentation duration was increased to a maximum of 1 second, threshold word acuity decreased with an average slope of -0.17 ± 0.05 (logMAR/log(msec)). There was a moderate correlation between threshold word acuity and HORMS ($r^2 = 0.43$). There was no systematic difference between threshold word acuity with and without flankers for typically-sighted individuals. For the one individual with keratoconus, there was a trend of threshold word acuity being worse in the presence of flankers than without flankers, as HORMS increased.

Conclusions: As stimulus duration is increased, threshold word acuity decreases. In the two eyes with elevated HORMS, threshold word acuity was reduced compared to typical. Flankers impacted threshold levels for the 2 eyes with elevated HORMS. The study is ongoing, and will include more highly aberrated eyes, a range of disease severity and low contrast words.

CONTROL ID: 3539203

SUBMITTER (NAME ONLY): Rachael Allen

TITLE: Retinal and cognitive function deficits in the TgF344-AD rat model of Alzheimer's disease

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Alzheimer's disease is characterized by accumulation of amyloid-beta plaques and neurofibrillary tangles of Tau protein in the brain, associated with neurodegeneration and deficits in memory and cognition. Retinal pathology has been reported with Alzheimer's disease as well. Here, we aimed to determine whether the TgF344-AD transgenic rat model of Alzheimer's disease, which develops progressive brain pathology and cognitive dysfunction similar to patients with Alzheimer's disease, shows retinal changes associated with cognitive deficits.

Methods: Retinal function was assessed in TgF344-AD transgenic rats (n=7) and wild type littermate controls (Fischer 344 background, n=5) using electroretinography (ERG) at 6 and 15 months of age. Spatial cognition (spontaneous alternation) and exploratory behavior (number of entries) were assessed via Y-maze at 6 and 15 months. Spatial memory was assessed via Barnes maze at 15 months. Rats were euthanized at 16 months, and brains, retinas, and serum were analyzed for amyloid precursor protein (APP) as a marker of disease progression.

Results: TgF344-AD rats exhibited significant cognitive deficits at 15 months of age as measured by Barnes maze ($p < 0.01$), but no changes in spontaneous alternation or exploratory behavior in the Y maze. Significant delays in ERG oscillatory potential (OP) implicit times were observed at 6 months with bright flash ($p < 0.001$) and at 15 months with dim and bright flashes ($p < 0.01$ and $p < 0.001$, respectively). A significant delay was also observed for positive scotopic threshold response (STR) at 15 months ($p < 0.01$). Increased levels of APP were observed in both brains and retinas from TgF344-AD rats.

Conclusions: As expected, cognitive decline was observed in the TgF344-AD transgenic rat model of Alzheimer's disease. Notably, retinal function may be useful in predicting and diagnosing changes in the brain with Alzheimer's disease, as we observed deficits in ERG components generated by the inner retina (OPs) and retinal ganglion cells (STR), suggesting these retinal cell types are vulnerable to Alzheimer's pathology. This work provides a basis for pursuing non-invasive retinal analysis, including ERG, as a way to stage Alzheimer's disease.

CONTROL ID: 3539208

SUBMITTER (NAME ONLY): Samuel Whittier

TITLE: Reproducibility of Grading Superficial vs Deep Retinal Hemorrhage in the Study of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2).

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The intraretinal location of hemorrhage in eyes with central retinal vein occlusion (CRVO) may provide important information regarding disease severity and visual acuity outcomes. The purpose of this post-hoc evaluation is to investigate the reproducibility of grading superficial (nerve fiber layer) vs deep retinal hemorrhage on color fundus photographs (CFP) in participants from the Study of COmparative Treatments for REtinal Vein Occlusion 2 (SCORE2).

Methods: Baseline three-field CFP of 54 study eyes in the SCORE2 cohort were evaluated. A grid was developed to differentiate 9 distinct subfields (Figure 1). Expert graders evaluated for percent involvement of superficial hemorrhage in each of the 9 subfields, and evaluated for percent involvement of deep hemorrhage in 8 subfields, excluding the optic disc. Graders also evaluated eyes for optic disc swelling, disc pallor, cotton wool spots, and retinal folds. Reproducibility was measured using predetermined parameters: exact agreement, agreement within 5%, 10% and 20%. Intergrader reproducibility was calculated using kappa statistics.

Results: All 54 study eyes had gradable images. Average intergrader reproducibility among fields with superficial hemorrhage was 36.6% exact agreement, 56.4% within 5%, 67.5% within 10%, and 85% within 20%. Reproducibility among fields with deep hemorrhage was 66.4% exact agreement, 88% within 5%, 93.1% within 10%, and 98.8% within 20%. Across all fields, the weighted kappa score range for grading percent superficial and deep hemorrhage was 0.43 – 0.71 and 0.49 – 0.69, respectively. Kappa scores for the assessments of disc swelling, disc edema, cotton wool spots, and retinal folds were 0.34, 1.0, 0.8, and 0.64, respectively.

Conclusions: In SCORE2, a novel method for grading area of superficial and deep retinal hemorrhage demonstrated agreement within 20% in ≥85% of the eyes. Intergrader reproducibility for both superficial and deep hemorrhage was moderate to substantial, depending on the field graded. Employing this method in a large scale longitudinal analysis will help define the role of retinal hemorrhage location as a predictive biomarker of therapeutic and visual outcome in CRVO.

CONTROL ID: 3539215

SUBMITTER (NAME ONLY): Antony Raharja

TITLE: Photopic negative response in idiopathic intracranial hypertension recorded using a handheld device

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Raharja, I. Chow, M. Indusegaran, C.J. Hammond, S. Wong, Department of Ophthalmology, Guy's and St Thomas' NHS Foundation Trust, London, UNITED KINGDOM|A. Raharja, S. Leo, O. Mahroo, Institute of Ophthalmology, University College London, London, UNITED KINGDOM|S. Leo, O. Mahroo, S. Wong, Moorfields Eye Hospital NHS Foundation Trust, London, UNITED KINGDOM|I. Chow, M. Indusegaran, C.J. Hammond, Section of Ophthalmology, King's College London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The photopic negative response (PhNR) is a late component of the light-adapted electroretinogram (ERG), and derives from retinal ganglion cells. We recorded PhNRs from idiopathic intracranial hypertension (IIH) patients and explored associations with severity.

Methods: ERGs were recorded, following mydriasis and exposure to room light, using conductive fibre electrodes with a portable device (RETeval, LKC technologies, MD USA). Red flashes (1.0 cd.s/m^2) were delivered, at 3.4 Hz, on a 10 cd.s/m^2 blue background (averages from 400 flash presentations). The device software gave PhNR amplitudes (at 72 ms or as a ratio to b-wave). ERGs were assessed for drift, noise and reproducibility. The eye with a better quality trace was chosen for PhNR analysis; if both were equally good, the eye with poorer visual field function was chosen. IIH severity was determined using optical coherence tomography-derived retinal nerve fibre layer (RNFL) thickness and Modified Frisén scale (MFS): mild (MFS1-2), severe (MFS \geq 3, RNFL thickness $>$ 150, or atrophic) or in remission (resolved with no atrophy). Patients without papilloedema deemed not to have IIH or any other eye conditions act as controls. P_{72} and p-ratio were compared in the four groups (Kruskal-Wallis), with each group also compared to control (Mann-Whitney).

Results: Of 99 patients, 86 (7 control, 79 IIH) were included; 13 were excluded (9 poor quality ERG, 4 alternative diagnosis). 91% of IIH patients were female; median (IQR) age was 33 (27-39), BMI 34.8 (30.4-40.0). 86% of controls were female; median (IQR) age was 52 (31-64), BMI 34.5 (32.3-42.2). P_{72} and p-ratio differed significantly across groups with a trend towards smaller PhNR amplitudes in more severe IIH, $p=0.0417$ and $p=0.0389$ respectively. Largest differences were observed between severe IIH and controls (median P_{72} : -3.4 vs. -7.1, $p=0.0096$, and median p-ratio: 0.12 vs. 0.23, $p=0.0073$). Comparing severe and mild IIH groups, p-ratio differed significantly (0.12 vs. 0.17, $p=0.014$), but not P_{72} (-3.4 vs. -6.0, $p=0.064$). Patients in remission and controls exhibited non-significant differences (median P_{72} : -5.0 vs. -7.1, $p=0.19$, and median p-ratio: 0.18 vs. 0.23, $p=0.48$).

Conclusions: We found associations between PhNR parameters and disease severity in a large IIH cohort. The PhNR could potentially provide additional assessment of disease severity in these patients.

CONTROL ID: 3539222

SUBMITTER (NAME ONLY): Gina Wesley

TITLE: Patient-reported symptoms following SYSTANE iLux and LipiFlow treatment: A 12-month, multicenter study

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Wesley, Complete Eye Care of Medina, Hamel, Minnesota, UNITED STATES|K. Bickle, ProCare Vision Centers, Inc., Granville, Ohio, UNITED STATES|J. Echegoyen, Gordon Schanzlin New Vision Institute, A TLC Laser Eye Center, Torrance, California, UNITED STATES|J. Downing, East West Eye Institute, Torrance, California, UNITED STATES|B. Fisher, Eye Center Of North Florida, Panama City, Florida, UNITED STATES|B. Greene, Eye Care Institute, Louisville, Kentucky, UNITED STATES|C. Heinrich, Clarke EyeCare Center, Wichita Falls, Texas, UNITED STATES|D. Kading, Specialty EyeCare Group, Kirkland, Washington, UNITED STATES|P. Majmudar, Chicago Cornea Consultants Ltd, Hoffman Estates, Illinois, UNITED STATES|J. Miller, Insight Research Clinic, LLC, Powell, Ohio, UNITED STATES|S. Modi, Alterman, Modi, and Wolter, Poughkeepsie, New York, UNITED STATES|S. Kannarr, Kannarr Eye Care, LLC, Pittsburg, Kansas, UNITED STATES|J. Lee, Eye Physicians of Long Beach, Long Beach, California, UNITED STATES|D. Ludwick, Ludwig Eye Center, Chambersburg, Pennsylvania, UNITED STATES|J. Tauber, Tauber Eye Center, Kansas City, Missouri, UNITED STATES|S. Srinivasan, Alcon Research, LLC, Duluth, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To demonstrate non-inferiority of iLux when compared to LipiFlow in change from baseline in the Impact of Dry Eye on Everyday Life (IDEEL) questionnaire Symptom Bother (SB) module score at 12 months post-single treatment in Meibomian gland dysfunction (MGD) subjects with evaporative dry eye (EDE).

Methods: This was a prospective, randomized, assessor-masked, parallel-group study comparing iLux to LipiFlow in subjects with EDE. Subjects with IDEEL-SB module scores of >16, non-invasive tear break-up time scores of <10

seconds, and Meibomian gland score ≤ 12 in lower eyelids were randomized for bilateral treatment in a 1:1 ratio to receive a single treatment with either SYSTANE iLux or LipiFlow. Subjects attended a total of 8 visits: Screening/Baseline, Treatment, 2-Week, 1-Month, 3-Month, 6-Month, 9-Month and 12-Month /Exit. At each time point, a paper copy of the IDEEL-SB module was provided to each patient for completion without assistance. Non-inferiority in IDEEL-SB module scores (change from baseline) between iLux compared to LipiFlow was assessed at all time points.

Results: A total of 227 treated (iLux 114; LipiFlow 113) patients completed the 12-month follow-up. Treatment difference (iLux minus LipiFlow) and the corresponding one-sided 95% upper confidence limit (UCL) were computed. Non-inferiority was declared if the UCL was less than 12. Non-inferiority of iLux compared to LipiFlow in change from baseline in IDEEL-SB scores was achieved at 2 weeks (2.56), 1 month (3.00), 3 months (2.21), 6 months (2.23), 9 months (1.92), and 12 months (2.42).

Conclusions: This study demonstrated that SYSTANE iLux MGD Thermal Pulsation System is non-inferior to LipiFlow Thermal Pulsation System in the change in IDEEL-SB scores up to 12 months following a single treatment.

CONTROL ID: 3539234

SUBMITTER (NAME ONLY): David Lally

TITLE: Effect of subretinal fluid (SRF) resolution on visual acuity in patients with neovascular age-related macular degeneration (nAMD)

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.R. Lally, New England Retina Consultants, Springfield, Massachusetts, UNITED STATES|M. Tsuboi, Genentech Inc. (at the time the study was conducted), South San Francisco, California, UNITED STATES|L. Hill, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: This post-hoc analysis of the HARBOR trial in nAMD was conducted to determine if SRF resolution in eyes treated with ranibizumab had a concomitant deleterious effect on best-corrected visual acuity (BCVA).

Methods: Eyes from the pooled arms of the HARBOR trial (NCT00891735) were included in the analysis if SRF, with or without intraretinal fluid (IRF), was present at baseline and fluid resolved during the course of the study, based on spectral-domain optical coherence tomography. Among those eyes that also had IRF present at baseline, IRF must have resolved at least one month prior to SRF resolution. Change in ETDRS BCVA was determined by comparing the BVCA in the month before SRF resolution with BCVA in the month SRF resolution was first detected. Patients who lost vision with SRF resolution, defined as a loss of ≥ 4 ETDRS letters, were compared with those who gained/maintained vision, defined as a loss of < 4 ETDRS letters. Outcomes at M12 and 24 were analyzed in eyes with no SRF recurrence after going dry.

Results: Three hundred and forty-nine eyes met inclusion criteria. Mean time to first detection of SRF resolution was 2.3 months. Between the month prior to dry and the month of SRF resolution, 11% (38/349) lost ≥ 4 ETDRS letters (mean -9.0 letters [-10.9, -7.1]) and 89% (311/349) of eyes gained/maintained BCVA (mean 6.3 letters [5.5, 7.0]; Table 1). Among eyes that had no SRF recurrence after going dry, those that lost ≥ 4 ETDRS letters, compared to those that maintained/gained, at the time of SRF resolution had reduced visual outcome gains from baseline at M12 (1.8 vs 13.1 letters) and M24 (0.5 vs 12.8 letters; Table 2). Once dry, there was little difference between groups in the BCVA gained from the month first dry to M12 or M24 (7.2 vs 4.2 and 5.8 vs 4.0 letters, respectively).

Conclusions: Eleven percent of eyes lost BCVA at the time of SRF resolution, and these eyes had reduced long-term visual outcomes at M12 and M24. Loss of ≥ 4 ETDRS letters at the time of SRF resolution may portend worse long-term visual outcomes. Treating eyes to SRF resolution may be deleterious in some. Further studies are warranted.

CONTROL ID: 3539241

SUBMITTER (NAME ONLY): Yulia Pyatova

TITLE: MAIA microperimeter for central vision loss: Repeatability of short-duration fixation stability measurements

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Pyatova, S. Markowitz, Ophthalmology and Vision Science, University of Toronto, Toronto, Ontario, CANADA|R. Devenyi, Ophthalmology, Toronto Western Hospital, Toronto, Ontario, CANADA|L. Tarita-Nistor, Krembil Research Institute, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Fixation stability has become an important outcome measure for evaluating intervention and/or disease progression in patients with central vision loss. The most common instruments to assess fixation stability in these patients are the Nidek MP (1 and 3) and MAIA microperimeters. Repeatability of short-duration fixation stability has been reported for the MP-1, but not for MAIA. The purpose of this cross-sectional study was to examine the repeatability of fixation stability measured with MAIA microperimeter, for a fixed 20s-duration.

Methods: Fixation stability was evaluated in 32 eyes of 20 patients (8F/12M, mean age 76 ± 8 years) with macular diseases using MAIA and the MP-1 microperimeters, in a random order, twice for each eye and with each instrument. Fixation duration was 20s and all tests were performed in the same day. Based on visual acuity, 17 eyes were identified as the better eye (BE) and 15 as the worse eye (WE). Fixation stability was quantified with the 95% bivariate contour ellipse area (BCEA). The BCEA was recorded from the examination output as well as calculated from the raw data. A log transformation was applied to the BCEA values. Bland-Altman plots were used to determine the bias and the 95% limits of agreement.

Results: For MAIA, the bias and the 95% limits of agreement for the BE, the WE, and the overall sample were 0.1 (-0.56 to 0.76) $\log \text{deg}^2$, 0.0 (-0.72 to 0.72) $\log \text{deg}^2$, and 0.05 (-0.64 to 0.74) $\log \text{deg}^2$, respectively. For the MP-1, these values were 0.06 (-0.46 to 0.58) $\log \text{deg}^2$, 0.03 (-0.33 to 0.38) $\log \text{deg}^2$, and 0.04 (-0.41 to 0.49) $\log \text{deg}^2$. The expected number of raw data points recorded over a 20s interval was 500, but the actual numbers ranged from 241 to 496 for MAIA and from 486 to 512 for the MP-1. Far outliers in the raw data were included in the BCEA values reported in the output for MAIA, but not for the MP-1.

Conclusions: The 95% limits of agreement for 20s-fixation stability are larger for MAIA than for the MP-1. Unlike the MP-1, MAIA includes outliers in the BCEA calculation and, in some instances, fails to record all data points. Repeatability of fixation depends on the instrument used and this should be considered when interpreting changes in fixation stability in patients with central vision loss.

CONTROL ID: 3539247

SUBMITTER (NAME ONLY): Kazuyo Ito

TITLE: Fine Resolution Quantitative Ultrasound Assessment of Posterior Scleral Microstructural Change in Form-Deprived Myopic Guinea Pig Eyes

SESSION TITLE: Role of choroid and sclera in myopia development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Ito, D. Lee, Q.V. Hoang, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS, SINGAPORE|J. Mamou, C. Hoerig, F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|S.A. McFadden, Vision Sciences, Hunter Medical Research Institute and School of Psychology, College of Science, Engineering and Environment, The University of Newcastle, Callaghan, New South Wales, AUSTRALIA|Q.V. Hoang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: As myopia progresses, posterior eye elongation is caused by changes in the microstructural properties of the sclera. High-frequency quantitative ultrasound (QUS) allows non-invasive measures of biomechanical parameters associated with changes in tissue microstructure. This study investigated microstructural changes occurring in the posterior sclera (PS) in myopic guinea pig (GP) eyes by means of QUS with a 20- μ m spatial resolution.

Methods: Form-deprivation myopia was induced in young GPs by diffusers worn over the right eye from 6 days of age for 1, 2 or 3 weeks ($n = 5, 9$ and 4 animals respectively). Untreated paired left eyes were used as controls. On the last day of treatment, cycloplegic spherical equivalent refractive error (SERE) and axial length (AxL) were measured. Following euthanasia, both eyes were enucleated and placed in PBS in its natural in vivo anatomical position and raster-scanned using an 80-MHz transducer (i.e., 20- μ m spatial resolution). The acquired 3D data were processed to yield ten QUS parameters. Parameters are reported as the mean from the entire measured PS, and the means for each of the four quadrants (i.e., nasal, temporal, inferior, superior). After computing interocular differences, Pearson correlations between QUS parameters and SERE or AxL were calculated.

Results: SERE was positively correlated with the PS Homodyned-K QUS parameter k ($r = 0.56, p = 0.01$). k quantifies the ratio of the coherent to diffuse scattering and is hypothesized to be sensitive to the orientation of collagen fibrils; k correlations were the largest in the horizontal quadrants (nasal $r = 0.73, p < 0.01$; temporal $r = 0.51, p = 0.03$). SERE was also positively correlated to scatter size ($r = 0.61, p = 0.01$) and acoustic concentration ($r = -0.51, p = 0.03$), which relate to diameter and scattering power of collagen fibrils respectively. Additionally, AxL correlated positively with the nasal quadrant intercept QUS parameter ($r = 0.65, p < 0.01$), which relates to both the diameter and number density of collagen fibrils.

Conclusions: Several QUS parameters were correlated with eye elongation and myopic refractive changes. Since these parameters are related to collagen fiber size, density and microstructure, QUS approaches have the potential to quantitatively and objectively characterize microstructural changes occurring in the sclera during myopia development.

CONTROL ID: 3539251

SUBMITTER (NAME ONLY): Lakshman Subbaraman

TITLE: Clinical Subjective Performance of Two Daily Disposable Soft Contact Lenses

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.N. Subbaraman, Alcon Research LLC, Johns Creek, Georgia, UNITED STATES|J. Miller, EyeCare Professionals of Powell, Ohio, UNITED STATES|B. Giedd, Maitland Vision Center, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the subjective performance of verofilcon A daily disposable silicone hydrogel contact lenses, which have a core with 51% water content and a surface with >80% water content, with those of etafilcon A hydrogel contact lenses, which have a water content of 58%.

Methods: In this prospective, multicenter, clinical study, successful soft contact lens wearers were randomized to wear verofilcon A or etafilcon A lenses for 8 (-1/+2) days (n=92 completed). After a washout period, subjects were dispensed the alternative lenses. Exploratory endpoints included subjective overall lens preference (5-point scale) and subjective ratings (10 point scale) of end-of-day (EOD) vision, overall handling, insertion comfort, EOD comfort, lens handling at insertion, overall comfort, overall quality of vision, vision throughout the day, and lens handling at removal. Furthermore, Likert questionnaires (5-point scale) were completed at end-of-day during the 1-week follow-up visits conducted after the first and second treatment periods.

Results: Of the study subjects, 68 (73.9%) preferred or strongly preferred verofilcon A lenses, whereas 21 (22.9%) preferred or strongly preferred etafilcon A lenses ($p<0.0001$). Mean \pm SD ratings of EOD vision (8.6 ± 1.5 vs 7.7 ± 1.9), overall handling (8.7 ± 1.5 vs 6.9 ± 2.3), insertion comfort (9.2 ± 1.0 vs 7.7 ± 1.9) and EOD comfort (8.0 ± 1.9 vs 7.0 ± 2.2) were all significantly ($p\leq0.0001$ each) higher for verofilcon A than for etafilcon A lenses. Mean \pm SD ratings of lens handling at insertion (9.0 ± 1.4 vs 6.9 ± 2.5), overall comfort (8.6 ± 1.5 vs 7.4 ± 1.8), overall quality of vision (8.9 ± 1.2 vs 8.2 ± 1.8), vision throughout the day (8.9 ± 1.3 vs 8.1 ± 1.8), and lens handling at removal (8.3 ± 2.1 vs 7.7 ± 2.2) were statistically significantly higher for verofilcon A than for etafilcon A lenses. Compared to etafilcon A, the Likert questionnaires revealed higher percentage of subjects wearing verofilcon A who strongly agreed or agreed for questions about lens freshness, comfort, vision and handling.

Conclusions: These results demonstrate that verofilcon A lenses performed better than etafilcon A lenses with respect to overall preference, and other subjective endpoints evaluated in this study.

CONTROL ID: 3539259

SUBMITTER (NAME ONLY): Hal Heitzmann

TITLE: Human Trabecular Meshwork Cells Appear Healthier & More Viable in Contact with Titanium Stents Than in Contact with Nickel-Titanium Stents

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Ahmed, A. Unser, V. Chari, K.Y. Torrejon, Glauconix Biosciences, Albany, New York, UNITED STATES|B.M. Wirostko, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES| H. Heitzmann, Glaukos Corporation, San Clemente, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Trabecular bypass stents (TBS) are implanted through the human trabecular meshwork (HTM) to improve physiologic outflow and lower intraocular pressure in open-angle glaucoma. Given the widespread use of TBS, improved understanding of their biocompatibility is imperative. Of the two commercially available TBS, one is comprised of titanium & the other of nickel-titanium (nitinol). This study tested the hypothesis that there would be differences in the viability of primary HTM cells in culture when contacted with one versus the other of these devices.

Methods: HTM cells were grown on glass or gelatin-coated glass substrates & then placed into contact with sterile stents. Cell morphology in the vicinity of the stents was monitored every day for 4 days via optical microscopy, and live-dead fluorescence staining was performed to assess cell viability. The corrected total fluorescence of micrographs imaged under identical conditions ($N \geq 21$ per timepoint) was quantitated w/ ImageJ software. Data were analyzed using two-way ANOVA & compared to stent-free samples w/ Tukey's multiple comparison test.

Results: Cells cultured in contact with nitinol stents for 48, 72 & 96 hours demonstrated progressive cell necrosis, clumping, and in some cases, complete cell layer detachment. However, cells in contact with titanium stents remained attached to the substrate & showed little or no necrosis. Dead-cell staining intensity was greater after nitinol vs. titanium stent contact ($p < 0.0001$, $N = 21/\text{stent}$) across all timepoints examined.

Conclusions: HTM cells remained viable & morphologically intact when in contact with titanium stents, whereas contact with nitinol stents led to necrosis & morphological degradation. These differences were statistically significant & visually apparent.

CONTROL ID: 3539267

SUBMITTER (NAME ONLY): Andrew Fausey

TITLE: Interaction between CTRP5 & AdipoR1 and its implication to Late-onset retinal degeneration (L-ORD)

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Fausey, C. Zhang, M. Nimmagadda, K.J. Miyagishima, R. Sharma, K. Bharti, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Late-onset retinal degeneration (L-ORD) is an autosomal dominant disorder in which a missense mutation in the CTRP5 gene leads to retinal pigment epithelium (RPE) atrophy and choroidal neovascularization. CTRP5 is a paralogue of Adiponectin family proteins which regulate cell metabolism. We hypothesize that similar to Adiponectin, CTRP5 acts through Adiponectin Receptor 1 (AdipoR1). In L-ORD RPE cells, mutant CTRP5 forms oligomers with its WT counterpart which is believed to interfere with its apical secretion from RPE and reduce binding affinity toward AdipoR1. While in silico ligand/receptor modeling and immunogold labeling suggest an interaction between CTRP5 and AdipoR1, a direct interaction has yet to be confirmed. Here, we aim to biochemically investigate CTRP5-AdipoR1 protein interactions and provide a mechanism of L-ORD disease progression.

Methods: Induced pluripotent stem cells (iPSCs) were generated from fibroblasts of skin biopsies of four siblings, two clinically and genotypically confirmed L-ORD patients with a pathogenic variant in CTRP5 (p.Ser163Arg), and two unaffected siblings that did not carry the pathogenic variant. Cell membrane preparations from iPSC-derived RPE (iRPE) were prepared using a cellular membrane protein extraction kit and, co-immunoprecipitation was conducted via Dynabead technology using AdipoR1 antibodies as the probe. The components of protein complexes were detected via Western blot.

Results: From AdipoR1 probed protein complexes obtained through co-immunoprecipitation, we detected CTRP5 protein in healthy iRPE. However, in L-ORD-iRPE, we detected lower CTRP5, presumably due to the lower expression and lower AdipoR1 binding affinity of mutant CTRP5. This will be further examined by comparing the binding ability of AdipoR1 to tagged p.Ser163Arg CTRP5 and WT CTRP5.

Conclusions: Compromised AdipoR1 and CTRP5 binding in L-ORD iRPE provides a mechanism for disease pathogenesis. Most notably, the presence of mutant CTRP5 could lead to chronically activated AdipoR1 resulting in sustained AMPK activation and RPE metabolic dysfunction. This data allows potential therapeutic opportunities directly through AdipoR1 and AMPK activity modulation thus circumventing the dominant behavior of the CTRP5 mutation in L-ORD patients.

CONTROL ID: 3539293

SUBMITTER (NAME ONLY): Katie Li

TITLE: Modulation of pyruvate kinase M2 activity as a therapy in a primary RPE cell culture model of proliferative vitreoretinopathy

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.X. Li, M.T. Goswami, Q. Zhang, H.B. Durumutla, S. Chaudhury, C.G. Besirli, J. Miller, T.J. Wubben, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) represents the greatest risk of failure in retinal detachment repair and portends poor visual outcomes. PVR is triggered by fibrovascular proliferation of retinal pigment epithelium (RPE) on the surface of the retina after the RPE undergoes an epithelial-to-mesenchymal transition (EMT). RPE EMT is accompanied by metabolic reprogramming favoring glycolysis. Pyruvate kinase M2 (PKM2) is a key enzyme of glycolysis whose non-enzymatic functions have been implicated in the glycolytic reprogramming and EMT of other cell types. The importance of PKM2 in RPE EMT and PVR is unknown. Here we sought to understand the role of PKM2-driven glycolysis in triggering RPE EMT, and how pharmacologic modulation of PKM2 alters RPE EMT.

Methods: To recapitulate loss of cell contact seen early in the PVR process and induce EMT, primary human fetal RPE (hfRPE) were seeded at 10% density. Immunohistochemistry, western blot, and RT-PCR were utilized to assess the expression of EMT markers and phosphorylation of PKM2 in this in vitro model of PVR. The impact of small molecule (ML-265) pharmacologic modulation of PKM2 on the metabolic profile of hfRPE EMT was evaluated with RT-PCR. The therapeutic potential of ML-265 in attenuating RPE EMT was evaluated in several assays.

Results: HfRPE demonstrated a fibroblastic-like phenotype in this cell culture model of PVR with induction of EMT markers including vimentin, N-cadherin, and TWIST1. PKM2 S37 phosphorylation was increased 7-fold while Y105 phosphorylation was decreased 2.5-fold in the dedifferentiated, fibroblastic-like hfRPE compared to differentiated hfRPE. PKM2 S37 phosphorylation is important for PKM2 dimerization, nuclear translocation, and regulation of glycolytic gene expression via transcriptional co-activation of β -catenin or Hif-1 α . Accordingly, the expression of Hif-1 α , as well as downstream genes of β -catenin and Hif-1 α , such as CCND1, GLUT1, and PDK1, were upregulated in hfRPE EMT. Finally, treatment with ML-265, an allosteric modulator of PKM2 that decreases glycolytic reprogramming, resulted in reduced hfRPE EMT in multiple assays.

Conclusions: This study suggests a critical role of PKM2 in RPE EMT, the triggering event for PVR. Pharmacologic modulation of PKM2 to halt EMT-driven metabolic reprogramming may be an innovative therapeutic strategy in the prevention of PVR.

CONTROL ID: 3539302

SUBMITTER (NAME ONLY): Sara Ramirez

TITLE: Role of NF2 and YAP in regulating RPE fate and proliferation

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ramirez, S. Fuhrmann, Cell and Developmental Biology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|W. Newsome, E. Yu, S. Fuhrmann, Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dysfunction and degeneration of retinal pigment epithelium (RPE) cells leads to detrimental vision diseases such as dry age-related macular degeneration (AMD). One possibility for treating dry AMD is the stimulation of endogenous RPE regeneration, but little is known about the mechanisms that can drive RPE regeneration in vivo. The Hippo signaling pathway regulates cell proliferation and regeneration in many tissues, including during retina regeneration. In the developing RPE, the Hippo pathway is required for proliferation and cell fate decisions. Here, we manipulate the Hippo pathway by inactivating the upstream regulator Neurofibromin 2 (NF2) to investigate whether regeneration in the adult mouse RPE can be achieved after injury.

Methods: We generated Nf2-conditional knockout (CKO) mice using the RPE-specific, doxycycline-inducible tet-on VMD2-Cre. We performed intraperitoneal or retro-orbital injections of sodium iodate (NaIO_3) on 7- to 8-week-old mice to induce oxidative damage mainly to the RPE. Injury and potential regeneration were monitored over the course of 7-11 weeks post injury with electroretinography and optical coherence tomography. Proliferation and extent of regeneration were assessed by EdU incorporation and expression of OTX2 and RPE65 in the presumptive RPE layer 7.5 weeks post injury.

Results: RPE injury reduced ERG A_{max} and B_{max} responses by 80% of baseline at 10 days post-injury. Our preliminary results show that there can be improved tissue integrity and a trend for increased proliferation in adult Nf2-CKOs at 7.5 weeks post-injury. Furthermore, there are more OTX2-positive cells in the presumptive RPE, and several show colocalization with EdU (approx. 4-fold increase compared to damaged controls), suggesting potential de-novo production of RPE cells. We also detect nuclear localization of YAP in Nf2-CKO RPE.

Conclusions: Our results indicate a potential role for Hippo pathway modulation in regenerative proliferation of mature, injured RPE. As mammalian adult RPE cells are post-mitotic, we hypothesize that NF2 normally inhibits regenerative proliferation of mature mammalian RPE through regulation of the Hippo/YAP-TAZ pathway. To investigate a potential mechanism, we are determining whether YAP and the transcription factor TEAD directly regulate RPE-specific gene expression to control RPE specification and maintenance.

CONTROL ID: 3539349

SUBMITTER (NAME ONLY): Hongwei Ma

TITLE: Thyroid Hormone Regulation of Photoreceptor Viability

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Ma, F. Yang, C.M. Primeaux, X. Ding, Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rod and cone photoreceptors play a central role in visual function. Photoreceptors degenerate in inherited retinal degenerative diseases and age-related macular degeneration. Thyroid hormone (TH) signaling regulates cell proliferation, differentiation, and metabolism. Recent studies have shown a link between elevated TH signaling and photoreceptor degeneration. This work investigates the TH regulation of photoreceptor viability using mouse models.

Methods: Treatment with triiodothyronine (T3) was applied to evaluate the effects of excessive TH signaling. C57BL/6, $Thra1^{-/-}$ (deletion of TH receptor $\alpha1$), and $Thrb2^{-/-}$ (deletion of TH receptor $\beta2$) mice at postnatal day 30 received T3 treatment (20 μ g/ml in drinking water) for 30 days. Serum T3 level was analyzed by ELISA. Retinal function was evaluated by electroretinogram (ERG). Cone density/number was evaluated by immunolabeling of peanut agglutinin (PNA) on retinal flatmounts and rod number was assessed by measuring the thickness of outer nuclear layer (ONL). Photoreceptor death and oxidative damage were analyzed by TUNEL and immunofluorescence staining of oxidative damage markers 8-OHdG and p- γ H2AX. The expression of the cellular stress response genes was evaluated by qRT-PCR.

Results: Treatment with T3 increased serum T3 level by 2-3 folds compared to the control level. Rod and cone ERG responses were reduced by about 60% and 30%, respectively, after T3 treatment. ONL thickness and cone density were reduced by about 18% and 50%, respectively, after T3 treatment. Retinal sections prepared from T3-treated mice showed significantly increased number of TUNEL-, p- γ H2AX-, and 8-OHdG-positive cells. Gene expression analysis showed upregulation of the genes involved in oxidative stress, necroptosis, and inflammatory responses after T3 treatment. Deletion of $Thra1$ prevented T3-induced reduction of ONL thickness whereas deletion of $Thrb2$ prevented T3-induced reduction of cone density.

Conclusions: Excessive TH signaling impairs retinal function, induces oxidative stress/damage and apoptosis, and induces rod and cone degeneration. The effects of TH signaling in rods are primarily mediated by $Thra1$ whereas the effects of TH signaling in cones are primarily mediated by $Thrb2$. This work demonstrates that TH signaling regulates rod and cone photoreceptor viability and TH receptors play differential roles in this regulation.

CONTROL ID: 3539364

SUBMITTER (NAME ONLY): Luís Mendes

TITLE: Comparison of different methods for the identification of capillary closure in diabetics retinopathy using OCTA

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mendes, I. Marques, M.H. Madeira, T. Santos, J.G. Cunha-Vaz, AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, PORTUGAL|L. De Sisternes, W. Lewis, M.K. Durbin, Carl Zeiss Meditec, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vessel metrics indicating capillary closure (CC) have shown potential clinical value by identifying eyes at different severity levels and at increased risk for disease progression to more severe stages. We compare the performance of 33 metrics computed based on optical coherence tomography angiography (OCTA) for identification of CC in different ETDRS groups.

Methods: OCTA data from 84 healthy eyes (70 ± 4.8 years) and 78 eyes of diabetic patients (67 ± 7.5 years), ETDRS 10-20 (24 eyes/patients), 35 (31 eyes/patients) and 43-53 (23 eyes/patients), were processed with using different methods: 1) Abnormal intercapillary spaces (AIS) measured using the method proposed by Mendes et al. (2019); 2) Skeletonized vessel density (SVD) and 3) perfusion density (PD), both computed using the Zeiss Meditec Density Exerciser (version 10.0.12787), 4) Entropy, 5) 10 metrics related with the histogram of the slab, 6) Four metrics based on Frangi filter (FF), 7) Coarseness metric of the Tamura filter (CTF) and, 8) 14 features based on Haralick texture features that include the contrast (CT).

The performance of these methods was tested in the superficial capillary plexus (SCP), in the deep capillary plexus (DCP), and in the full retina (FR). Data were acquired using CIRRUS HD-OCT 5000 with AngioPlex® OCTA (ZEISS, Dublin CA) using the acquisition protocol angiography 3x3.

Results: The best separation between the eyes with type 2 diabetics and the control group was obtained in the SCP, with the FR also obtaining a competitive performance. In the SCP the metrics that show better performance were the AIS and the VD (table 1) with a value of AUC equal to 0.89 [CI 95% 0.84-0.94] and 0.85 [CI 95% 0.79-0.91], respectively. The values of these metrics on the ETDRS groups 10-20, 35 and 43-53 show a progressive increase in CC which is correlated with the disease severity (table 2).

Conclusions: On AngioPlex the measurement of CC shows better performance in the SCP using AIS or the SVD. These methods improve the discrimination of eyes with diabetic retinopathy with different degrees of severity (ETDRS groups 10-20, 35 and 43-53).

CONTROL ID: 3539369

SUBMITTER (NAME ONLY): Luca Della Santina

TITLE: Rearrangement of retinal inhibitory and excitatory synapses in experimental glaucoma

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Della Santina, M. Soliño, T. Garcia-Ruiz, A.K. Yu, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|L. Della Santina, Bakar Computational Health Sciences Institute, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is characterized by progressive dysfunction of the retina; animal models shown that synapses between bipolar and ganglion cells are being dismantled early after intraocular pressure (IOP) elevation. We propose to investigate in detail, and on a large-scale, the relative arrangement of excitatory (E) and inhibitory (I) synapses in the inner retina, as well as in specific bipolar cell populations, to understand whether the degenerative process preferentially impacts specific retinal circuits.

Methods: Transient IOP elevation was induced in albino CD1 mice by photocoagulation of the episcleral and limbal vessels. After 14 days, retinal whole mounts were collected and immunolabeled for the excitatory and inhibitory synaptic proteins PSD95, RibeyeA, Gephyrin, and VGAT. Individual bipolar cell types were immunolabeled using PKC-alpha and Synaptotagmin-2 antibodies. Pairwise statistical comparisons use Wilcoxon-Mann-Whitney test.

Results: The average density of inhibitory (I) and excitatory (E) synapses in the inner plexiform layer (IPL) of lasered eyes was reduced compared to control eyes (E: $P=0.1$, I: $P=0.01$), but their loss is non-uniform across the IPL, with a spatial pattern that is sublamina-specific. Axons of rod bipolar cells significantly lose both ribbon and gephyrin density (E: $P=0.04$, I: $P=0.04$), while Type-6 ON cone bipolar axons preserve both (E: $P=0.6$; I: $P=0.6$). In contrast, Type-2 OFF cone bipolar axons preserve their ribbon density (E: $P=0.4$), while significantly increasing inhibitory inputs (I: $P=0.005$).

Conclusions: Excitatory and inhibitory synapses are unevenly disassembled in the inner retina, with more excitatory synapses lost in the OFF sublamina and more inhibitory synapses lost in the central region of the IPL. Within these distributions, specific bipolar cell types are either unaffected, equally affected, or asymmetrically affected in their E/I balance. These findings will help focus the investigation of specific cell types and microcircuits experiencing high synapse loss and ultimately guide the design of stimuli to probe their function in early glaucoma.

CONTROL ID: 3539402

SUBMITTER (NAME ONLY): Ruiyi Ren

TITLE: TSP1 Deficiency Inhibits Steroid-induced IOP Elevation in Mouse Eyes

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Ren, H. Gong, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thrombospondin-1 (TSP1) is a matricellular protein that is expressed in the trabecular meshwork, and its expression increases in glaucoma patients. TSP1-deficient mice were found having lower IOP in a previous study. This study aimed to investigate whether IOP elevation can be inhibited in TSP1-deficient mice using a steroid-induced ocular hypertension (SIOH) mouse model.

Methods: TSP1-deficient mice (N=14) and wild type (WT) mice (N=14), both including equal males and females, were randomly divided into saline-treated and dexamethasone (DEX)-treated groups (4 groups in total, n=7/group). Both eyes of each mouse received 10µl of saline or 0.1% DEX eye drops respectively twice a day for 5 weeks. IOP was measured weekly. IOP data were analyzed with both Student's t-test and Three-way ANOVA with repeated measurements.

Results: TSP1-deficient mice showed a ~2mmHg lower IOP at the baseline ($p<0.001$) when compared to WT mice, and this difference remained consistent between two saline-treated groups for 5 weeks. DEX treatment significantly elevated IOP in week1 ($p<0.001$) and peak IOP occurred at week 4 in WT mouse eyes compared to the saline-treated group. However, in TSP1-deficient mice, DEX did not induce a significant increase in IOP until week2 and the peak of IOP was at week2. The mean DEX-induced elevation in IOP was 3.4mmHg at week1, 5.6mmHg at week2, and 5.9mmHg at week5 in WT mice, while 0.2mmHg at week1, 2.2mmHg at week2, and 1.1mmHg at week5 in TSP1-deficient mice. The mean percentage increase in IOP induced by DEX over saline-treated control was 25% at week1, 41% at week2, and 42% at week5 in WT mice, while 3% at week1, 19% at week2, and 9% at week5. Therefore, DEX-induced increase in IOP was a half in TSP1-deficient mice when compared to WT mice at week2, and about 1/4 at week5. Three-way ANOVA also showed a significant main effect of the genotype ($p<0.0001$) and significant interactions of both genotype X treatment ($p<0.0001$) and genotype X time ($p<0.0001$).

Conclusions: TSP1 deficiency showed significant inhibitory effects on DEX-induced IOP elevation in mouse eyes. These effects included the delayed start-point of IOP elevation, lower peak IOP increase, and unsustainable IOP elevation. Our data suggest that TSP1 may play a role in SIOH. The mechanisms of its inhibition effects and morphological association in the outflow pathway need to be elucidated in further studies.

CONTROL ID: 3539404

SUBMITTER (NAME ONLY): Cristina Campos-Borges

TITLE: Targeting antioxidant strategies for non-proliferative diabetic retinopathy

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Campos-Borges, C. Prudêncio, Department of Chemistry and Biomolecules, Instituto Politecnico do Porto Escola Superior de Saude, Porto, Porto, PORTUGAL|C. Campos-Borges, M.D. Pinazo-Duran, S. Sanz-Gonzalez, M. Valero-Vello, Ophthalmic Research Unit "Santiago Grisolia", Fundacio per al Foment de la Investigacio Sanitaria i Biomedica, Valencia, SPAIN|M.D. Pinazo-Duran, S. Sanz-Gonzalez, V. Zanon-Moreno, M. Valero-Vello, Surgery and Ophthalmology Department, Universitat de Valencia, Valencia, Comunitat Valenciana, SPAIN|J. Garcia-Medina, Hospital General Universitario Jose M Morales Meseguer, Murcia, Murcia, SPAIN|J. Garcia-Medina, Universidad de Murcia, Murcia, Murcia, SPAIN|V. Zanon-Moreno, Universidad Internacional de Valencia, Valencia, Valenciana, SPAIN|J. Salgado-Borges, Clinsborges, Porto, PORTUGAL|J. Salgado-Borges, Ophthalmology, Lenitudes, Santa Maria da Feira, PORTUGAL|L. Duarte, Centro Hospitalar de Entre o Douro e Vouga EPE, Santa Maria da Feira, Aveiro, PORTUGAL|M. López Gálvez, Universidad de Valladolid, Valladolid, Castilla y León, SPAIN|M. López Gálvez, Instituto de Oftalmobiologia Aplicada, Valladolid, Castilla y León, SPAIN|C. Prudêncio, i3S - Health Research and Innovation Institute, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: Overproduction of reactive oxygen species (ROS) and activation of ROS signalling pathways cause damage to the eyes. We studied the oxidative stress (OS) markers and the effects of a daily, core nutritional supplement regimen containing antioxidants and omega 3 fatty acids (A/ω3), in type 2 diabetic (T2DM) eyes.

Methods: A case-control study was carried out in 480 participants, classified into: 1) T2DM patients (n=287) with (+)/without (-) non proliferative diabetic retinopathy (NPDR) and controls (CG; n=194). Participants were randomly assigned to one A/ω3 daily pill. Evaluation through 38 months permitted to outline patient characteristics, NPDR features, and blood classic and emergent parameters, including OS by products and candidate genes. Statistics were performed by the SPSS 24.0 program.

Results: Significantly higher circulating pro-oxidants (p=0.001) and lower antioxidants (p= 0.0001) were detected in the T2DM patients versus the CG. Significantly higher plasma malondialdehyde/thiobarbituric acid reactive substances (MDA/TBARS; p=0.006) and lower antioxidant load, as from the plasma total antioxidant capacity (TAC; p=0.042) and vitamins B₁₂ (p=0.05) and C (p=0.020) levels, were detected in the T2DM+NPDR versus the T2DM-NPDR. Vitamin C is a cofactor for enzymes involved in collagen synthesis. Overexpression of matrix metalloproteinase-9 (MMP-9) gene (a secreted type IV collagenase involved in extracellular matrix remodelling and cell migration) was found in the T2DM+NPDR versus the T2DM-NPDR groups and the CG (p=0.021). Importantly, the A/ω3 regime significantly reduced the pro-oxidants (p<0.05) and increased the antioxidants (p<0.05) in all groups, with special benefit for the diabetic retina.

Conclusions: This follow-up study reinforces the need for new strategies to increase the antioxidant load, as in the case of A/ω3 supplement regimen, that may serve as dietary prophylaxis and adjunctive intervention for better eye care in patients at risk of diabetic blindness.

CONTROL ID: 3539416

SUBMITTER (NAME ONLY): Simrat Sodhi

TITLE: Utilisation of Machine Learning to quantify fluid volume of wet age-related macular degeneration (wARMD) patients based on swept-source optical coherence tomography (SS-OCT) imaging: The ONTARIO Study

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.K. Sodhi, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|J.D. Oakley, D.B. Russakoff, Voxeleron, San Francisco, California, UNITED STATES|N. Choudhry, Department of Ophthalmology & Visual Sciences, University of Toronto, Toronto, Ontario, CANADA|N. Choudhry, Vitreous Retina Macula Specialists of Toronto, Etobicoke, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Evaluate the predictive ability of a deep learning-based, automated, macular fluid segmentation algorithm to determine long-term visual acuity (VA) outcomes in wet age-related macular degeneration (wARMD) patients using baseline swept-source optical coherence tomography (SS-OCT) and OCT-angiography (OCT-A) data.

Methods: Twenty-two SS-OCT volumes of the macula, comprising 5,632 images from 22 wARMD subjects were used to assess retinal layer thicknesses, quantify intraretinal fluid (IRF), subretinal fluid (SRF) and fluid in serous pigment epithelium detachments (PED). Layer thicknesses were manually corrected and fluid segmentation was performed using a novel, deep learning algorithm with results validated relative to two expert graders. OCT-A data was used to manually define the extent of the choroidal neovascularization (CNV) in each scan. Patients received 2 mg of intravitreal aflibercept injections monthly for 3 months, then bimonthly for 12 months. Baseline OCT morphological features and measurements were correlated using the Pearson correlation coefficient (PCC) to changes in VA to determine which features impacted the long-term visual outcomes.

Results: Total fluid volume at baseline and change in LogMar at week 52 relative to baseline had the closest correlation (PCC=0.652, p=0.005). Fluid was subsequently sub-categorized into IRF, SRF and PED, with PED volume having the next highest correlation (PCC=0.648, p=0.005). Average total retinal thickness in isolation gave a lower correlation (PCC=0.334, p=0.189), and mean CNVM size (um²) from 3 mm OCT-A scans was very low (PCC=0.072, p=0.784). When two features were combined and correlated with visual outcomes, the best correlation increased to PCC=0.695 (p=0.002) using mean CNVM size and total fluid volume.

Conclusions: In isolation, total fluid volume best correlates with change in LogMar values between baseline and week 52. In combination with complimentary information from OCT-A, an improvement in the linear correlation score was observed. Average total retinal thickness provided a lower correlation and thus provides a lower predictive outcome than other metrics assessed. Clinically, a machine-learning approach to analyzing fluid metrics combined with lesion size may provide an advantage in personalizing therapy predicting VA outcomes.

CONTROL ID: 3539424

SUBMITTER (NAME ONLY): Michelle Chen

TITLE: A Prospective Longitudinal Four-Year Analysis of Ellipsoid Zone Loss in Stargardt Disease

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Chen, W.M. Zein, L. Huryn, R.B. Hufnagel, A. Turriff, C.A. Cukras, B.P. Brooks, B.G. Jeffrey, National Eye Institute, Bethesda, Maryland, UNITED STATES|M.A. Chen, Howard University College of Medicine, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify the rate of ellipsoid zone (EZ) loss over a four-year period in patients with Stargardt disease

Methods: 16 patients with Stargardt disease with two or more variants in ABCA4 were followed prospectively at baseline, 6, 12, 24, 36, and 48 months with Spectral-domain OCT (SD-OCT) volume scans spanning a $30^{\circ} \times 15^{\circ}$ rectangle centered on the fovea (37 B scans). The length of central discontinuity of the inner segment/outer segment band (EZ band) was measured manually on the Heidelberg for each SD-OCT B-scan and area of EZ band loss (mm^2) was calculated using the Riemann sum. Using a radius linear model, the square-root transformed area of EZ band loss (mm) was calculated.

Results: Twenty-five eyes from sixteen patients were included in this 4-year prospective longitudinal study. The median age of patients at the baseline visit was 34 years (range 12-63) with median best-corrected visual acuity of 20/125 (range 20/32-20/200). The mean (\pm SD) EZ band disruption at the baseline visit was 2.33 ± 0.63 mm. The length of EZ disruption was highly correlated between right and left eyes ($P < 0.0001$; $R = 0.97$) and was correlated with age ($P = 0.025$; $R = 0.56$) but not visual acuity. The median rate of growth in EZ band disruption was 0.061 mm and ranged from minimal change (0.019 mm/yr) to high rates of growth (0.267 mm/yr) but was linear for each eye measured. The rate of growth in EZ band loss was also highly correlated between eyes ($P = 0.0004$; $R = 0.85$) but was not correlated with age, visual acuity or size of EZ band disruption at baseline.

Conclusions: Measuring the rate of EZ disruption provides a direct structural measure that is related to loss of photoreceptors. While the rate of EZ loss varied between patients, all patients demonstrated linear growth over a four-year period. This information is highly relevant to clinical trial planning and sample size calculations. The high correlation in rate of loss EZ band loss between the two eyes suggest that one eye could serve as a control in therapeutic trials aimed at treating a single eye.

CONTROL ID: 3539432

SUBMITTER (NAME ONLY): Catherine Cheng

TITLE: Eph-ephrin signaling plays a role in fiber cell alignment and influences lens shape and resilience

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Cheng, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Catherine Cheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Eph-ephrin bidirectional signaling is essential for lens transparency. Our studies in mouse lenses demonstrate that the ephrin-A5 ligand and the EphA2 receptor are needed for normal lens epithelial cells. Loss of EphA2 leads to disorganized lens fiber cells. We determined whether EphA2 and ephrin-A5 are important for lens biomechanical properties and morphometrics.

Methods: We used tissue mechanical testing and confocal microscopy to examine mouse lenses with genetic disruption of EphA2 or ephrin-A5.

Results: Biomechanical testing revealed no change in the stiffness of EphA2(-/-) and ephrin-A5(-/-) lenses compared to littermate controls. However, knockout lenses were more resilient and recovered almost completely after load removal. Morphometric analysis revealed that while there is no change in the overall lens volume, there is a decrease in lens aspect ratio (equatorial/axial diameter) in both knockout lenses. Confocal microscopy and quantitative image analysis from live lenses before, during and after compression revealed that knockout lenses had misaligned Y-sutures leading to a change in force distribution during compression. Knockout lenses displayed decreased separation of fiber cell tips at high loads and had more complete recovery after load removal, which leads to improved whole-lens resiliency. Further analysis revealed misalignment of the fiber cells tips and the lens suture between each shell of newly added fiber cells.

Conclusions: In summary, disruption of Eph-ephrin signaling in the lens leads to changes in resilience and lens shape. Since EphA2(-/-) lenses with disorganized fiber have no obvious change in lens stiffness, the data suggests that hexagonal fiber cell shape and organized packing are not required for normal lens stiffness. Interestingly, EphA2 and ephrin-A5 are needed for normal patterning of lens fiber cells tips and the formation of a well-aligned Y-suture with fiber tips stacked on top of previous generations of fiber cells. The data suggests that alignment of the Y-suture may affect the overall elasticity and resilience of the lens.

CONTROL ID: 3539438

SUBMITTER (NAME ONLY): Nancy Aguilera

TITLE: Subclinical Retinal Pigment Epithelium Changes Observed in Choroideremia Using Adaptive Optics Enhanced Indocyanine Green Imaging

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Choroideremia (CHM) is an X-linked retinal degeneration that leads to progressive damage to the outer retina. Previous studies on histology and adaptive optics (AO) have reported that the photoreceptors are relatively well-preserved in areas where the RPE is intact. In this study, we investigate RPE structure in CHM using adaptive optics enhanced indocyanine green (AO-ICG) imaging to reveal the extent to which RPE is affected.

Methods: Following comprehensive ophthalmic examination, AO-ICG imaging was performed on two female carriers and two affected male patients (n=8 eyes) with molecularly confirmed CHM. Fluorescent AO images of ICG-labeled RPE cells were acquired across a range of retinal locations in which RPE cells were intact, depending on the locations of discrete RPE atrophy. Following manual identification of RPE cells, measurements of RPE spacing and density in CHM were compared to published normative data.

Results: The late phase AO-ICG fluorescence pattern, corresponding to the RPE layer, was markedly different in both carriers and patients with CHM when compared to the expected pattern observed in healthy subjects. In all eyes, areas of dramatically enlarged RPE cells were observed in areas where fundus autofluorescence and optical coherence tomography confirmed the presence of an intact RPE layer. Measurements of RPE cell spacing and density confirmed that there was lower-than-normal RPE density and higher-than-normal RPE spacing for all eyes when compared to normative data (BOE 8(10):4348-4360, 2017). Based on RPE cell spacing measurements, the affected male patients had a greater degree of RPE enlargement (z-scores: 9 to 74; spacing increased by up to 5.2) compared to female carriers (z-scores: 7 to 44; spacing increased by up to 3) across the range of retinal locations measured (0-4.5 mm).

Conclusions: AO-ICG can be used to detect subclinical changes to the RPE structure and may be useful to monitor the efficacy of future therapies in CHM. The observation of interspersed enlarged RPE cells in female carriers and contiguous enlarged RPE cells in affected males, together with previous studies support the notion that the RPE is a primary site of degeneration in CHM.

CONTROL ID: 3539465

SUBMITTER (NAME ONLY): shuo sun

TITLE: Low-dose mTOR inhibitor alleviates RPE cellular senescence and pro-inflammation induced by accumulation of cytosolic nuclear DNA fragments

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. sun, X. Li, Tianjin Key Laboratory of Retinal Functions and Diseases, Tianjin International Joint Research and Development Centre of Ophthalmology and Vision Science, Eye Institute and School of Optometry, Tianjin Medical University Eye Hospital, Tianjin, Tianjin, CHINA|S. sun, W. Su, H. Lin, B. Tian, Ophthalmology, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|W. Su, Ophthalmology, Tianjin Medical University General Hospital, Tianjin, Tianjin, CHINA|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) dysfunction plays an important role in the progression of age-related macular degeneration (AMD). Our previous studies have showed there is accumulation of damaged nuclear DNA (nDNA) fragments in AMD donor macular RPE cells. This accumulation induced RPE cellular senescence and pro-inflammation via STING pathway. More and more studies found long-term low dose rapamycin treatment, a mTOR inhibitor, reduced inflammation and cellular senescence without side effects. In this study, we explored whether low-dose rapamycin reduces pro-inflammatory factors secretion and cellular senescence induced by accumulation of cytosolic nDNA fragments in RPE cells.

Methods: RPE cell viability was tested by CCK-8 assay. Since lysosomal DNASE2A is essential for damaged nDNA fragments digestion, CRISPR/Cas9 was used to generate DNASE2A^{-/-} RPE cells to produce accumulation of cytosolic nDNA to mimic AMD donor RPE cells. AMD donor RPE cells and DNASE2A^{-/-} RPE cells were treated with 1nM rapamycin for 5 weeks. Cytosolic nDNA, components of mTOR and STING pathway and pro-inflammatory factors were measured by immunostaining, Western blot and ELISA. Cellular senescence was tested by SA-β-galactosidase staining. Autophagy inhibitor was used to explore cytosolic nDNA removal mechanism. nDNA secretion and LC3 conversion was measured.

Results: High-dose rapamycin (≥25μM) significantly decreased ARPE-19 and DNASE2A^{-/-} RPE cell viability while low dosage did not. Long-term low dose rapamycin treatment increased AMD donor macular RPE cells and DNASE2A^{-/-} RPE cells to secrete damaged nDNA fragments via enhancing autophagy. In this way, rapamycin reduced accumulation of cytosolic nDNA fragments in AMD donor macular RPE cells and DNASE2A^{-/-} RPE cells, which led to attenuate mTOR activation and cellular senescence induced by accumulation of cytosolic nDNA fragments in DNASE2A^{-/-} RPE cells. Furthermore, we also found STING and NFκB activation were inhibited by low-dose rapamycin treatment, thereby pro-inflammatory factors secretion (IL-1β, IL-6, IL-8) was reduced in AMD donor macular RPE cells and DNASE2A^{-/-} RPE cells.

Conclusions: Our studies show long-term low dose rapamycin treatment reduces RPE cellular senescence and pro-inflammation induced by accumulation of cytosolic nDNA fragments and has the potential to alleviate progressive RPE dysfunction in AMD.

CONTROL ID: 3539478

SUBMITTER (NAME ONLY): Javier Lozano

TITLE: Corneal sensitivity repeatability with a new non-contact air jet corneal esthesiometer and comparison with Cochet-Bonnet esthesiometer.

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of the study was to assess the safety and repeatability of the measurements taken with a new non-contact esthesiometer -Brill Engines esthesiometer (BEE) and to compare the sensitivity obtained with the Cochet-Bonnet esthesiometer (CBE).

Methods: Young healthy male volunteers were included in the study. Corneal central sensitivity was measured with the new BEE and with the CBE. The procedure was performed three times on the same day and repeated in the same way for 3 days.

Measurement was performed according with the manufacturer instructions. BEE was mounted in the slit lamp and CBE measurement was used manually. A sub-umbral esthesiometry strategy was performed.

To assess whether the data followed a normal distribution, the Shapiro-Wilks test was used. Repeatability was determined by the intraclass correlation coefficient between each day. Likewise, the data obtained with the BEE were compared with those obtained with the CBE. They were also analyzed using the Bland-Altman test. A 95% confidence level was considered statistically significant.

Results: Nineteen consecutive healthy volunteers mean age 23.50 ± 3.62 years underwent and complete the participation in the study. Schirmer test was 7.47 ± 4.12 mm, with a range of 5 to 18 mm and OSDI test was 3.89 ± 3.59 , with a range of 0 to 12.64.

No adverse effected, ocular surface or corneal damage were detected and both test were well tolerated by volunteers. The mean values of corneal sensitivity measured with the BEE was 6.08 ± 0.30 mbar, with a minimum of 5 mbar and for the CBE was 0.61 ± 0.09 g/mm², with a minimum of 0,57 g/mm².

Intraclass correlation coefficient (ICC) of the BEE was 0.764 for a single measurement and 0.907 for the mean of all measurements. Correlation between both esthesiometers ICC was 0.388 and 0.559. Bland Altman plots showed the great majority of data were inside the boundaries (2 SD).

Conclusions: A new non-contact air jet corneal esthesiometer was tested in healthy volunteers with good tolerance, no adverse effects. The BEE showed good repeatability and correlation parameters. Brill Engines esthesiometer could be used as non-invasive alternative of the Cochet Bonnet esthesiometer.

CONTROL ID: 3539532

SUBMITTER (NAME ONLY): Hanmeng Zhang

TITLE: rAAV-mediated ASAH1 overexpression prevents retinal degeneration in Farber disease

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zhang, D.M. Lipinski, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|H. Zhang, D.M. Lipinski, Department of Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|M.S. Nagree, Department of Medical Biophysics, University of Toronto, Toronto, Ontario, CANADA|M.S. Nagree, J.A. Medin, Department of Pediatrics: Section of Hematology/Oncology/BMT, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J.A. Medin, Department of Biochemistry, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Farber disease (FD) is a rare monogenic lysosomal storage disorder caused by mutation of ASAH1, leading to deficiency of acid ceramidase (ACDase) and accumulation of ceramide characterized by retinopathy, macular red spots, corneal opacities, and nystagmus. As gene therapy has been demonstrated to be a promising therapeutic avenue for the treatment of recessive diseases, we evaluated the efficacy of rAAV-mediated hASAH1 over-expression in a mouse model of FD, using in vivo ocular imaging, electroretinography (ERG), post-mortem histology, and mass spectrometry (MS) to assess efficacy.

Methods: Expression and function of ACDase from the rAAV2/2[MAX].hASAH1 vector was assessed by western blot (WB) and activity assay in HEK293T cells. 3-4 week old FD mice (Asah1^{P361R/P361R}) and littermate controls (Asah1^{+/+} and Asah1^{P361R/+}) received a unilateral intravitreal injection of rAAV2/2[MAX].hASAH1 (2×10^{10} vg/eye); the contralateral eye received a sham buffer injection of equal volume (2 μ L). Animals were followed up by confocal scanning laser ophthalmoscopy (cSLO), optical coherence tomography (OCT), and ERG at 5-6 and 8-9 weeks. Eyecups were harvested post-mortem for correlative histology and MS to determine the quantity of each ceramide species.

Results: WB/ceramidase activity assay showed the rAAV2/2[MAX].hASAH1 vector expressed high levels of biologically functional protein. cSLO imaging of untreated Asah1^{P361R/P361R} eyes (N=8) revealed increased hyperreflectivity and autofluorescence surrounding the optic nerve associated with elevated ceramide levels, retinal thickening and decreased ERG amplitudes. rAAV2/2[MAX].hASAH1 treatment (N=8 eyes) significantly reduced central retinal thickening ($P \leq 0.038$), ceramide accumulation ($P = 0.0006$), and limited fundus hyperreflectivity and autofluorescence, but did not lead to functional rescue. Unexpectedly, ACDase over-expression in Asah1^{+/+} and Asah1^{P361R/+} control eyes induced abnormal retinal thickening and ceramide accumulation, similar to FD.

Conclusions: rAAV-mediated over-expression of ACDase effectively prevented the development of anatomical lesions in FD mice, but was not sufficient to rescue function. That over-expression of ACDase in control eyes resulted in increased ceramide accumulation and the development of FD-like lesions indicates that modulating ceramide levels as a therapeutic strategy in diseases other than lysosomal storage disorders may be contraindicated.

CONTROL ID: 3539550

SUBMITTER (NAME ONLY): Haibo Wang

TITLE: Serine Phosphorylation of IQGAP1 Regulates Choroidal Endothelial Activation and Neovascularization

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Wang, E. Kunz, A. Ramshekar, M. Hartnett, John A Moran Eye Center, The University of Utah, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Serine phosphorylation of IQGAP1 regulates signaling leading to neurite cell growth. We previously found that knockout of IQGAP1 inhibited VEGF-mediated choroidal endothelial cell (CEC) activation and migration, a necessary step in the development of choroidal neovascularization (CNV) in neovascular age-related macular degeneration (AMD). We, therefore, tested the hypothesis that IQGAP1 mediates the development of CNV through IQGAP1 serine phosphorylation.

Methods: Serine phosphorylation of IQGAP1 was measured by Co-immunoprecipitation (Co-IP) with anti-IQGAP1 and western blot with anti-phospho-serine antibodies in 1) primary human CECs transfected with plasmid DNA expressing wild type IQGAP1 (IQ-WT) or IQGAP1 with serine mutation into alanine at sites 1441/1443 (IQ-S/A) and treated with control PBS or VEGF (20 ng/ml) for 15 mins, and in 2) retinal pigment epithelium (RPE)/choroid tissues from wild type mice 7 days after laser treatment. Mice with IQGAP1 mutated at serine 1441 (Crispr/IQ) were created by CRISPR-Cas9 edited gene mutation. Seven days post laser, CNV lesion volume was measured in lectin-stained RPE/choroidal flatmounts of Crispr/IQ and littermate controls. IQGAP1 serine phosphorylation was determined in CECs isolated from three different donors and in RPE/choroid tissues from three lasered mice and three non-lasered controls. The volume of CNV lesions were measured in 7 Crispr-IQ mice and 16 littermate wild type controls.

Results: Compared to PBS, VEGF activated serine phosphorylation of IQGAP1 in IQ-WT transfected CECs. VEGF-induced IQGAP1 serine phosphorylation was abolished in CECs transfected with IQ-S/A. In RPE/choroid tissues and compared to non-lasered controls, laser treatment caused a 3-fold increase in IQGAP1 serine phosphorylation. Crispr-IQ mice had a trend toward reduced CNV lesions ($p=0.07$) compared to littermate wild type mice.

Conclusions: VEGF treatment and laser injury activate IQGAP1 by inducing serine phosphorylation. Serine phosphorylation of IQGAP1 mediates experimental CNV in vivo. These data may provide insight into mechanisms underlying neovascular AMD.

CONTROL ID: 3539577

SUBMITTER (NAME ONLY): Allen Ho

TITLE: Suprachoroidal Injections Across Species Analyzed via Multimodal Imaging

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Wan, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|A. Ho, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Potential spaces in anatomy refer to the area between apposed organs or tissues and can represent “druggable” targets, including the epidural space, used to deliver anesthetics, and the suprachoroidal space (SCS), currently undergoing clinical trial with several therapeutics. In clinical trials, optical coherence tomography (OCT) imaging has demonstrated acute and transient opening of the SCS in preclinical and clinical studies. This imaging study characterized the biomechanical response of injection into the SCS in comparison to intravitreal (IVT) injection.

Methods: Suprachoroidal and IVT injections were performed in ex vivo porcine eyes and the biomechanical response was visualized using the imaging modalities: external photography, spread visualization via ultraviolet (UV) with fluorescence, internal endoscopy, and cryo-freeze sectioning under microscopy. Suprachoroidal injections were performed with the SCS Microinjector®. IVT injections were performed with a 1-mL syringe and standard 30-G needle. Tissues change, injectate spread, and globe behavior were analyzed for both therapeutic delivery methods.

Results: Imaging modalities demonstrated differences between suprachoroidal and IVT injection in distribution of injectate, tissue change, and globe behavior. When evaluated under UV light, suprachoroidal injection of fluorescing particles showed spread circumferentially and posteriorly. No injectate spread was visible with IVT injection, as fluorescence is muted by the pigmented choroid and RPE. Cryofreezing and section showed suprachoroidally injected injectate spread posteriorly toward the macula, between sclera and choroidal tissues. IVT injection showed a bolus of injectate located in the vitreous. Endoscopic footage of an ex vivo porcine suprachoroidal injection show a localized depression of the choroidal tissues when the procedure is begun, followed by SCS expansion as fluid is injected. Corresponding imaging during IVT delivery demonstrated differences in spread of injectate within the globe.

Conclusions: In contrast to intravitreal delivery, suprachoroidal drug delivery results in acute opening of the SCS, supporting the potential to target affected tissue layers in chorioretinal disorders.

CONTROL ID: 3539579

SUBMITTER (NAME ONLY): Yixiao Wang

TITLE: Activation of mTORC1 stimulates the ubiquitin-proteasome system in rods

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, K. Lobanova, Department of Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|K. Lobanova, Department of Pharmacology and Therapeutics, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited retinal degenerations are caused by an unusually large number of genetic mutations. Approaches to delay retinal degeneration in a mutation-independent manner would accelerate the delivery of the treatments to the patients. Previous studies demonstrated that activation of the mTORC1 (mammalian Target of Rapamycin Complex 1) pathway had beneficial effects in a broad range of mouse models of retinal degeneration and attributed these observations to the improved glucose metabolism. mTORC1 activation supported the survival of cones in mouse models of rod degeneration, slowed down the early stages of retinal degeneration in PDE6b mutant mice and increased retinal resistance to the RPE injury. Recent studies performed outside of the vision research field suggest that activation of mTORC1 could increase the total proteasomal pool and activity in cell cultures and mouse brains. Therefore, here we investigated the stimulation of mTORC1 also as an approach to delay vision loss caused specifically by proteostatic stressors.

Methods: mTORC1 was stimulated genetically in rods by knocking out its negative regulator Tsc2 (Tuberous Sclerosis Complex 2) in $Tsc2^{flx/flx}$ mice using rod-specific transgenic CRE mouse line. The heterozygote P23H rhodopsin knock-in mouse ($P23H^{+/-}$) was used as a model of retinal degeneration caused by protein misfolding and mice expressing reporter of proteasomal activity (Ub^{G76V} -GFP) were used as a tool to assess the status of ubiquitin-proteasomal system (UPS) in vivo. Proteasomal activity was measured in retinal lysates with fluorogenic substrates. Protein translation and autophagy were probed with puromycin- and chloroquine-based WB methods. Retinal health and function were evaluated with OCT, funduscopy, morphometric studies and ERG.

Results: Genetic activation of mTORC1 delays the late phase of rod photoreceptor loss in $P23H^{+/-}$ mice by approximately 3 months. This improvement is accompanied by stimulation of proteasomal activity and more efficient protein degradation through the UPS as assessed using the Ub^{G76V} -GFP reporter mice. Stimulation of mTORC1 in $P23H^{+/-}$ rods did not result in measurable changes in autophagy and translation.

Conclusions: These findings focus attention on a previously unappreciated ability of the mTORC1 pathway to modulate UPS in degenerating rods and position it as a promising therapeutic target for treating retinal degenerations associated with protein misfolding.

CONTROL ID: 3539584

SUBMITTER (NAME ONLY): Amir Akhavanrezayat

TITLE: Structural and functional changes in non-paraneoplastic autoimmune retinopathy

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Akhavanrezayat, N.L. Onghanseng, M. Halim, G. Uludag, H. Ghoraba, W. Matsumiya, B.H. Pham, A. Mobasserian, J. Regenold, C. Yasar, I. Karaca, V. Bazojo, S. Lajevardi, D.V. Do, Q.D. Nguyen, Byers Eye Institute at Stanford, Palo Alto, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center, Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nonparaneoplastic autoimmune retinopathy (npAIR) is an insidious disease that is difficult to monitor due to often-unremarkable findings in clinical exam; therefore, it might be beneficial to use ancillary imaging/tests to evaluate the disease state. We conducted the index case-series to describe ocular changes in patients with npAIR and to assess the utility of different imaging modalities/tests in monitoring the disease course.

Methods: Eight patients (16 eyes) from a tertiary eye care center, with a verified diagnosis of npAIR using the criteria proposed by Sen (Sen et al., 2014), were recruited. Multimodal testing using functional [Goldmann perimetry (GVF), microperimetry (MP), and electrophysiologic testing (ff-ERG, mf-ERG, VEP)] and structural [wide angle fundus photography (WAFP), wide angle fundus autofluorescence (WFAF), wide angle fluorescein angiography (WFA), spectral domain optical coherence tomography (SD-OCT), and adaptive optics scanning laser ophthalmoscopy (AOSLO)] tests were performed at different time points and results were analyzed.

Results: The median age of patients was 46.0 [15.5-66.7] years and 50% were female. Initial results showed frank abnormalities in both functional (14 of 16 eyes on GVF, 15 of 16 eyes on MP, 11 of 16 eyes on ff-ERG, 12 of 14 eyes on mf-ERG, 14 of 14 eyes on VEP) tests and structural (14 of 16 eyes on WAFP, 14 of 16 eyes on WFAF, 13 of 16 eyes on SD-OCT, 5 of 7 eyes on AOSLO) imaging. WFAF appeared normal except in cases of transient macular edema (3 of 16). Subjects were followed up for the median duration of 11.5 [3.0-18.7] months. Follow up imaging of GVF (8 of 10 eyes), mfERG (4 of 8 eyes), and MP (7 of 16 eyes) demonstrated changes which were not always consistent with each other. Ff ERG (9 of 10 eyes) and VEP (7 of 8 eyes) remained mostly unchanged. No significant changes were noted on WAFP and WFAF. Measurable changes were noted in 4 of 12 eyes on SD-OCT and 6 of 6 eyes on AOSLO. Decrease in retinal sensitivity on MP often preceded subjective symptoms.

Conclusions: Multimodal testing in npAIR patients is crucial to identify and follow changes over time. Deterioration, especially in severe cases, is often subtle, but ongoing as shown by changes in multiple modalities. Most structural modalities might not be able to measure changes once npAIR have become severe. Functional modalities might be able to detect early changes that precede subjective worsening.

CONTROL ID: 3539594

SUBMITTER (NAME ONLY): Dalbert Chen

TITLE: Risk Factors Related with Visual Acuity in Uveitic Patients

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Chen, S.B. Hancock, Z.N. Khademi, A.Z. Chuang, E.L. Crowell, Ophthalmology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveitis is the fourth leading cause of preventable blindness among adults in the United States. We aim to determine risk factors associated with visual acuity outcomes in uveitic patients.

Methods: A retrospective study of patients with ocular inflammation from 01/2011 to 12/2016 at Robert Cizik Eye Clinic was done. Those with inflammation caused by rebound post-surgical inflammation or less than 24 months of follow up were excluded. If both eyes were eligible, both were included. Eyes were classified into anterior, intermediate, posterior, panuveitis, and scleritis. Demographics and baseline medical and ocular characteristics were recorded. Ocular symptoms, best corrected visual acuity (BCVA) and additional procedures were collected at follow-up. Risk factors, including demographics, ocular history, type of uveitis, flare, and additional ocular procedures were identified and estimated using a mixed effect model with a backward selection procedure.

Results: 224 eyes from 166 patients were included. Mean age was 50.9 years (± 19.6 , 3-86) at initial uveitis diagnosis. 103 (62%) were female. 65 (39%) were Black, 60 (36%) White, 12 (14%) Hispanic, 7 (4%) Asian, and 11 (7%) Other. 144 eyes (64%) had anterior uveitis, 13 (6%) had anterior and intermediate uveitis, 17 (8%) had posterior uveitis, 39 (17%) had panuveitis, and 11 (5%) had scleritis. At baseline, BCVA was 0.64 logMAR (± 0.69), 62 eyes (28%) had glaucoma, 40 (18%) had retinal diseases. 77 of 215 eyes reported flare (36%). Panuveitis had the worst BCVA compared to other uveitis types ($P < 0.001$) at months 6, 12 and 24. At month 6, Asian and Black races had worse BCVA by 0.60 logMAR (± 0.23 , $P = 0.012$) and 0.50 (± 0.11 , $P < 0.001$), respectively, compared to White. BCVA was continuously worse in Black race compared to White by 0.37 logMAR (± 0.11 , $P = 0.001$) and 0.40 logMAR (± 0.12 , $P = 0.001$) for month 12 and month 24, respectively. Eyes without retinal disease had better BCVA at month 6 ($P = 0.025$) and month 24 ($P = 0.009$) by 0.28 logMAR (± 0.12) and 0.36 logMAR (± 0.14), respectively. BCVA at 12 months was affected by number of ocular procedures performed (0.13 logMAR (± 0.05) per procedure ($P = 0.012$)).

Conclusions: Panuveitis and eyes with history of retinal disease had worst visual outcomes. Black race, compared to White, Hispanic, and Other is associated with the worst BCVA in all forms of uveitis in 6, 12, and 24 months follow up visits. Flare did not significantly affect BCVA.

CONTROL ID: 3539595

SUBMITTER (NAME ONLY): Nathan Congdon

TITLE: Burden of Global Vision Loss Due to Uncorrected Refractive Error: Temporal and Regional Changes 2000-2020

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To update estimates of the global vision loss burden due to uncorrected refractive error (URE), presenting temporal change since the beginning of Vision 2020 and distribution by sex and region.

Methods: Data gathered from population-based surveys of eye disease from January, 1980, to October, 2018 were collated. We fitted hierarchical models to estimate prevalence (with 95% uncertainty intervals [UIs]) of moderate and severe vision impairment (MSVI; presenting visual acuity from <6/18 to 3/60) and blindness (<3/60) caused by URE, by age, sex, region, and year. Prevalence of near VI from uncorrected presbyopia, defined to avoid double counting individuals with both distance and near VI, was based on 25 studies.

Results: In 2020, 2.29 million (95% UI 1.79 to 2.80) people aged 50+ years were blind due to URE globally, and 86.1 million (74.2-101.0) had MSVI, a 21.8% increase in blindness and 72.0% increase in MSVI since 2000. Age-standardised prevalence of URE blindness and MSVI decreased by 30.5% and 2.4% respectively during this time. The age-standardized ratio of women to men for URE blindness was 1.05:1.00 in 2020 and 1.03:1.00 in 2000. For MSVI, this ratio was 1.08:1.00 in 2020 and 1.06:1.00 in 2000. South Asia had the highest regional 50+ age-standardised URE blindness and MSVI rates in 2020 (blind: 0.33%, 0.26-0.40; MSVI: 10.3%; 8.82-12.1), and also the greatest reductions in age-standardised URE blindness between 2000 and 2020 (46.3%). In 2020, an estimated 419 million (295-562) people 50+ had near VI from uncorrected presbyopia, a 75.3% increase since 2000. Three-quarters of global near VI from presbyopia occurred in Asia (312 million, 217-418).

Conclusions: Raw prevalence of VI from URE grew due to population aging, even as age-standardised prevalence fell since 2000. The striking decline in age-adjusted URE blindness (compared to MSVI) suggests successful targeting of the most severe cases, such as prevention of aphakia with intra-ocular lenses. Further reduction in the burden of VI from URE can be realised by adding refractive services to universal health coverage and otherwise improving access. Focusing on the 50+ population provides an incomplete view of VI due to URE, which frequently affects younger persons. The very large burden of presbyopia and sparsity of available data underscore the need for more research

on this condition.

CONTROL ID: 3539601

SUBMITTER (NAME ONLY): Amanda Henderson

TITLE: Effect of Interleukin-6 Inhibition in a Rodent Model of Non-Arteritic Anterior Ischemic Optic Neuropathy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Henderson, N.R. Miller, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|Y. Guo, Z. Mehrabyan, M.A. Johnson, S.L. Bernstein, Ophthalmology, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic nerve-related cause of vision loss in people over age 50; however, NAION has no proven treatment. Previously, we demonstrated that interleukin-6 (IL-6) is upregulated in an experimental rodent model of NAION (rNAION), based on deep sequencing data from rat optic nerve and retinal tissue. In this experiment, we tested the hypothesis that IL-6 inhibition would decrease inflammatory response and preserve retinal ganglion cells (RGCs) in the rNAION model.

Methods: rNAION was induced in 4 adult male Sprague-Dawley rats. On post-induction day 1, optic nerve edema was assessed by slit lamp and optical coherence tomography (OCT), and animals were paired in terms of similar amounts of edema. One from each pair was treated with subcutaneous sarilumab (human IL-6 inhibitor), whereas the others received vehicle (saline). At 1 week post-induction, rats were euthanized, and eyes and optic nerves were isolated and post-fixed in 4% paraformaldehyde-PBS. Post-fixed retinas were isolated, and RGCs immunostained with Brn3a antibody. Cryopreserved optic nerve laminar sections were immunostained with Iba1 (for microglia), CD68 (for macrophages), and SMI312 (for neurofilaments).

Results: There was no appreciable reduction in resident microglia or extrinsic macrophage recruitment (Figure 1) and no appreciable RGC preservation (Figure 2) in rNAION animals treated with sarilumab compared with controls.

Conclusions: IL-6 inhibition does not appear to reduce inflammatory cell recruitment or to preserve RGCs in rNAION, when administered 1 day after disease-state induction, despite known IL-6 upregulation in this disease model.

Possible explanations for this finding include (1) a narrow time window for therapeutic anti-inflammatory treatment in rNAION, in which case this treatment avenue is not likely to be clinically relevant; (2) the IL-6 response is a nonspecific inflammatory epiphenomenon and may not specifically modulate damage-inducing inflammation in rNAION; or (3) the fully humanized sarilumab antibody is functionally limited in its effects in rat. Further study with a rodentized IL-6 inhibitor may further elucidate the role of IL-6 inhibition in rNAION.

CONTROL ID: 3539639

SUBMITTER (NAME ONLY): Tomás Loureiro

TITLE: Quantitative Optical Coherence Tomography Angiography Biomarkers in a Treat-and-Extend Dosing Regimen in Neovascular Age-Related Macular Degeneration: A 24-Months Follow-up Study

SESSION TITLE: Imaging of posterior segment I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Loureiro, D. Cabral, Centro de Responsabilidade Integrada de Oftalmologia, Hospital Garcia de Orta EPE, Almada, Setúbal, PORTUGAL|D. Cabral, C. Rodrigues, T. Pereira, CEDOC, Universidade Nova de Lisboa Faculdade de Ciencias Medicas, Lisboa, Lisboa, PORTUGAL|C. Rodrigues, Instituto de Oftalmologia Doutor Gama Pinto, Lisboa, Lisboa, PORTUGAL|C. Français, F. Coscas, Centre Ophtalmologique de l'Odéon, Paris, FRANCE|G. Coscas, Ophtalmology, Universite Paris-Est Creteil Val de Marne, Creteil, Île-de-France, FRANCE|M. Falcão, Universidade do Porto Faculdade de Medicina, Porto, Porto, PORTUGAL|F. Coscas, Sorbonne Universite Faculte de Medecine, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The role of optical coherence tomography angiography (OCT-A) in the follow-up of patients with exudative neovascular age-related macular degeneration (enAMD) has not been clearly clarified. Quantitative OCT-A parameters used to describe macular neovascularization (MNV) may be biomarkers that help predict anti-VEGF treatment burden and functional response. We performed an observational and prospective study to evaluate the association between quantitative OCT-A parameters and clinical outcomes over a 24-month follow-up interval.

Methods: Patients with enAMD were treated using a treat-and extend regimen following a loading dose of three anti-VEGF injections (IVI). Swept-source OCT-A was performed at baseline, after the loading dose and at 12 and 24 months. A quantitative analysis was performed for fractal dimension (FD), lacunarity index (LAC), blood flow surface area (SA), and vessel density (VD). Good functional response was defined as a final BCVA superior to/or within 5 letters of the 12th month visit. High treatment burden was defined as having at least 5 IVI in the second 12 months. Associations between quantitative biomarkers, functional outcomes and treatment burden at 24 months of follow-up were assessed. Statistical significance was defined as p-value < 0.05.

Results: Sixty-two eyes of 62 patients with enAMD were enrolled, 50 of whom (81%) completed the 24-month protocol. The median BCVA was 63 ETDR letters (21) at baseline, 74(25) at 12 months and 72 (28) at 24 months. 15 patients (30%) were classified as good functional responders. The median number of injections in the second year was 6 (2), with 40 patients (82%) classified as "high treatment burden". A lower FD at the 12th month-visit was associated with a good functional response (p=0.008, area under the curve (AUC) = 0.74). Low treatment burden was associated with lower SA at the 12-month visit (p=0.013, AUC = 0.76).

Conclusions: FD and SA were two quantitative parameters of MNV blood flow derived from OCT-A that were associated with clinical outcomes whilst LAC and VD were not. The 12-month visit evaluation may give insights regarding the functional outcome and treatment burden for the following year, corroborating the hypothesis that OCT-A may play a role in a comprehensive enAMD follow-up.

CONTROL ID: 3539665

SUBMITTER (NAME ONLY): Lydia Stone

TITLE: Delayed follow up in Wet Macular Degeneration Patients due to COVID-19: Impact on Disease Activity and Visual Acuity

SESSION TITLE: Visual Impairment during a pandemic

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.G. Stone, M. Grinton, J.S. Talks, Ophthalmology, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The coronavirus pandemic has prompted unprecedented delays to treatment with anti-VEGF intra-vitreous injections due to the need to reduce hospital attendances and prioritize the patients at highest risk of vision loss. This study aims to quantify the effect of these delays on visual acuity (VA) outcomes and optical coherence tomography (OCT) features for patients receiving treatment for neovascular age-related macular degeneration (nAMD).

Methods: A retrospective data analysis of an electronic medical record was performed on a random sample of 681 eyes receiving anti-VEGF injections between 1 January and 23 March 2020 for nAMD. Data collected included whether the review was delayed (defined as delayed by 8 weeks or more from planned) and the VA at baseline and follow up. For those eyes not delayed, a VA at 20 weeks was recorded to provide a control group, as this was the mean number of weeks until the delayed group was seen. For the delayed group, the OCT features at follow up were also noted.

Results: The sample of 681 eyes was analysed, of which 194 (28.5%) had been delayed by 8 weeks or more. The mean number of weeks delay was 12.7. Mean change in VA for eyes in the delayed group was significantly worse compared to those not delayed. VA change in the delayed group was 60.1 to 55.2 (-4.9) letters and VA change in the non-delayed group was 61.4 to 59.9 (-1.5) letters ($p = 0.001$). 161 eyes that were delayed had a repeat OCT at their delayed review; mean CMT (μm) had increased from 311 to 342 and 118 eyes (73.3%) showed evidence of intraretinal and/or subretinal fluid. By November 2020, 25.1% of eyes had not returned to within 5 letters of their baseline vision.

Conclusions: Delayed appointments due to COVID-19 affected a significant proportion of nAMD patients receiving intra-vitreous injections. nAMD eyes which were delayed experienced significant visual loss compared to those who were not delayed. This was associated with worsening of disease activity on OCT.

CONTROL ID: 3539667

SUBMITTER (NAME ONLY): Sharnjit Bains

TITLE: Effects of laser iridotomy on anterior segment parameters in primary angle-closure suspects

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bains, P. Moinul, M. Salami, S. Shankar, F. Farrokhyar, E. Sogbesan, McMaster University, Hamilton, Ontario, CANADA|D. Moinul, University of Calgary, Calgary, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: To compare changes in anterior segment optical coherence tomography (AS-OCT) parameters in patients with primary angle closure suspect (PACS) undergoing laser peripheral iridotomy (LPI).

Methods: One-hundred eyes with PACS underwent prophylactic LPI in the temporal iris. Clinical exam including visual acuity, intraocular pressure (IOP) and gonioscopy were assessed. AS-OCT parameters including anterior chamber (AC) depth, lens vault (LV), trabecular iris space area (TISA), angle opening distance (AOD), and nasal and temporal iris thickness were measured at baseline and repeated at 1week, 1 month and 3 months post-laser. Data were analyzed with paired t-test, one-way ANOVA and Wilcoxon test using SPSS V27.

Results: Seventy-six percent of enrolled participants were female (mean age 58.5 ± 11 years). LPI was performed temporally in all eyes at an average 43.4mJ/eye. Clinically on gonioscopy, 82% of angles were deeper at 3-month follow-up ($p=0.000$). The mean visual acuity (logmar 0.12 to logmar 0.08, $p=0.001$) and mean IOP improved from baseline (15.4mmHg) to 3-months (14.9mmHg; $p<0.001$) post-LPI. AOD at 500um and 750um showed significant deepening in the temporal quadrant at 1 week that persisted until 3-months post-LPI ($p=0.001$). Similarly, deepening of the LV, TISA at 500um and 750um from Schwalbe's line and thinning of the temporal iris at 500 um and 750um showed significant improvements at 3-months post-LPI ($p=0.005$, $p=0.001$, $p=0.001$, $p=0.001$, $p=0.001$), respectively. Nasal iris thickness at 500um from the angle was also significantly reduced ($p=0.009$) from baseline, although LPI was performed only in the temporal quadrant. Further, deepening of the ACD ($p=0.001$) was observed at 3-months follow-up.

Conclusions: Deepening of the angle clinically by gonioscopy reflect the long-term changes on AS-OCT parameters demonstrated at 3-months follow-up. AS-OCT showed significant deepening of the angle by reducing lens vault, deepening the TISA, ACD and thinning the temporal and nasal iris. Gonioscopy and AS-OCT are useful tools for screening and assessing patients with PACS. Our results will provide all practicing ophthalmologists with a better understanding of the reliability of AS-OCT in screening and follow-up for patients with PACS to guide further clinical management.

CONTROL ID: 3539681

SUBMITTER (NAME ONLY): Zhiyuan Yu

TITLE: Activation of NFkB and NLRP3 Inflammasome in the corneal epithelium following short-term desiccating stress

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Yu, S.C. Pflugfelder, J. Alam, C.S. De Paiva, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if 24-hour exposure to desiccating stress activates NFkB and NLRP3 inflammasome pathways in the mouse cornea epithelium.

Methods: 6-to-8-week-old C57BL/6J mice were housed under normal humidity (nonstressed) or subjected to desiccating stress from a drafty, low humidity environment combined with SC scopolamine QID for 1 day to suppress tear production (DS1). Eyes were embedded and sectioned for immunofluorescent staining or the corneal epithelium was scraped for immunoassay, caspase-1 assay, western blot or real time PCR. A TransAM kit was used to detect phospho-NFkB p65 in the nuclear fraction. Western blot and real-time PCR were performed to detect NFkB and NLRP3 pathway proteins and gene transcripts, respectively.

Results: There was significantly increased nuclear p-p-65 protein and gene expression of the NFkB inducible cytokine IL-12 (1.9-fold) and its receptors (IL-12Rb1 and IL-12Rb2, 3 and 1.9-fold, respectively) in DS1 compared to nonstressed control. NLRP3 and Caspase 1 proteins (6.4 and 3.1-fold, respectively), RNA transcripts (1.4 and 1.9 fold, respectively), as well caspase 1 enzyme activity (1.5-fold, P=0.006) increased in DS1. IL-18, the inflammasome inducible cytokine protein increased 3.1-fold, while RNA expression of its receptor IL-18Rap increased 1.5-fold (P=0.001). There was no change in IL-1b expression. Immunostaining for NLRP3, Caspase 1 and IL-18 increased in the cornea epithelium at DS1 compared to nonstressed.

Conclusions: These findings indicate that two key innate inflammatory pathways (NFkB and NLRP3 inflammasome) are activated following short term desiccating stress. Cytokines stimulated by these pathways, IL-12 and IL-18, are required for full expression of the dry eye associated cytokine IFN-γ by T and natural killer cells.

CONTROL ID: 3539695

SUBMITTER (NAME ONLY): Monica Melo

TITLE: Association of ABCA1 rs2472493 and GAS7 rs9913911 variants with POAG in a Brazilian population

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.B. Melo, Y.C. Silva, T.R. Rodrigues, F.F. Bajano, Center for Molecular Biology and Genetic Engineering, University of Campinas, Campinas, Sao Paulo, BRAZIL|M.R. Araki, R.B. Schimiti, V.P. Costa, J.C. Vasconcellos, Ophthalmology, University of Campinas, Campinas, Sao Paulo, BRAZIL|R.B. Schimiti, Hoftalon Hospital de Olhos, Londrina, Paraná, BRAZIL|

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ABSTRACT BODY:

Purpose: Genome-wide association studies have identified genetic variants associated with primary open-angle glaucoma (POAG), including ABCA1 gene rs2472493 and GAS7 gene rs9913911. However, no studies have been performed in heterogeneous populations such as Brazilian. Therefore, the aim of this study was to investigate the association of the ABCA1 rs2472493 and GAS7 rs9913911 with the risk of POAG development in a sample of the Brazilian population.

Methods: This was a cross-sectional, candidate gene association study structured as case control. The study was performed with 1036 subjects, encompassing 520 POAG patients and 516 controls. All participants were over 40 years old and underwent a complete ophthalmic evaluation. The genotyping of the variants was performed through Taqman® assays and the results were confirmed by Sanger sequencing in 10% of the samples from each group. The association of the variants was tested by chi-square test and logistic regression analysis.

Results: We identified the association of rs9913911 variant of the GAS7 gene with POAG development in the presence of the A risk allele ($p = 0.0255$; OR = 1.602; CI95% = 1.060-2.421). In the presence of the AA genotype the risk of developing POAG was even higher ($p = 0.0032$; OR = 1.881; CI95% = 1.222-2.896). No significant association was observed for rs2472493 of the ABCA1 gene for alleles or genotypes. However, in the presence of the A risk allele of GAS7 rs9913911 and the G risk allele of ABCA1 rs2472493, an additive effect was observed ($p = 0.0018$; OR = 2.677; CI95% = 1.557-4.602).

Conclusions: Our study confirms the association of the rs9913911 (GAS7 gene) with POAG risk in a sample of the Brazilian population and an additive effect when rs9913911 (GAS7 gene) and rs2472493 (ABCA1 gene) are analyzed simultaneously. This is an important finding for future diagnosis and treatment strategies for the Brazilian population. Further studies are needed to evaluate the frequency of these alleles based on ancestry analyses.

CONTROL ID: 3539722

SUBMITTER (NAME ONLY): Varsha Venkata Srinivasan

TITLE: Head-down tilt reverses neuroretinal rim thinning in healthy eyes

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Venkata Srinivasan, L.P. Pardon, H. Cheng, P. Chetty, N.B. Patel, Optometry, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In healthy eyes, the neuroretinal rim tissue is thickest in the early morning and thins through mid-afternoon. We hypothesize that this change of the neuroretinal rim is a reflection of the translaminal pressure difference as one goes from a supine to sitting or standing position. The purpose of this study was to determine if head-down tilt (HDT) reverses this neuroretinal rim thinning.

Methods: Twenty-six healthy subjects presented to the lab on two separate days at 11 AM. Baseline measures included visual acuity, standard automated perimetry, optic nerve photos, and intraocular pressure (IOP with rebound tonometry), all performed in a seated position. Optic nerve head (ONH) and peripapillary tissue were imaged using radial and circular optical coherence tomography (OCT) scans centered on the ONH, aligned to the fovea-Bruch's membrane opening (BMO) axis. Following 3 hrs in either a seated or 6° HDT, IOP and OCT scans were repeated in that position. OCT data were exported, and programs written in MATLAB were used to quantify global minimum rim width (MRW), peripapillary total retinal thickness (TRT), choroid thickness, retinal nerve fiber layer (RNFL) thickness, BMO area, and BMO position referenced to a 3.5mm plane aligned to the choroid-sclera junction (BMO height). Data are presented as mean ± SEM.

Results: Each of the 26 subjects completed both seated and HDT sessions and one randomized eye from each was used for analysis. Compared to seated baseline measures, IOP decreased by 1.7 ± 0.5 mmHg ($p < 0.01$) in the seated position and increased by 3.1 ± 0.7 mmHg in the HDT position ($p < 0.01$). The average BMO area was 2.1 ± 0.1 mm² and did not change with time or posture ($p > 0.05$). The mean BMO height did not change in the seated condition but was anteriorly displaced in HDT (6.8 ± 3.1 μm, $p = 0.04$). While there was no significant change in MRW in the seated position (0.8 ± 0.8 μm, $p = 0.3$), MRW increased in HDT (4.2 ± 1.7 μm, $p = 0.02$). Similarly, for an annulus of 250 μm from the BMO, TRT in the seated position showed no significant change ($p > 0.05$), but increased in HDT (3.4 ± 1.1 μm, $p < 0.01$).

Conclusions: Thinning of the neuroretinal rim which occurs during waking hours is reversed in HDT. This provides support that changes in the translaminal pressure difference from supine to seated or standing are partly contributory to this diurnal change.

CONTROL ID: 3539759

SUBMITTER (NAME ONLY): Mohammad Shahidullah

TITLE: TRPV1-dependent NKCC1 activation in mouse lens involves integrin and the tubulin cytoskeleton

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shahidullah, A. Mandal, N.A. Delamere, Physiology, The University of Arizona, Tucson, Arizona, UNITED STATES|M. Shahidullah, N.A. Delamere, Ophthalmology and Vision Science, The University of Arizona, Tucson, Arizona, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mohammad Shahidullah: Commercial Relationship: Code N (No Commercial Relationship) | Amritlal Mandal: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Delamere: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In earlier studies we showed the response of the mouse lens to hyperosmotic solution involves TRPV1-dependent ERK1/2 and NKCC1 activation. In studies on different tissues, other investigators have suggested the cytoskeleton plays an important role in responses to osmotic stress. In the present study, we examine whether integrins and tubulins are involved in the activation of NKCC1 in mouse lens epithelium.

Methods: Lenses were obtained from Wild-type (WT) and TRPV1 knockout (KO) mice. Rubidium (Rb) uptake by the intact lens was quantified by atomic absorption spectrophotometry. Previous studies used bumetanide-sensitivity to validate Rb uptake as a measure of lens NKCC activity. ERK1/2 phosphorylation was detected and quantified by Western blot analysis. Cytoplasmic calcium was measured in cultured lens epithelium loaded with Fura-2 using a ratiometric imaging technique.

Results: In WT mice, an integrin agonist leukadherin 1 (LA-1, 25 μ M) increased Rb uptake by intact lenses from a control value of 3.9 ± 0.4 to 5.2 ± 0.4 ($n=7$, $P<0.05$). LA-1 also increased the cytoplasmic calcium concentration in cultured WT lens epithelium from 197 ± 18 to 341 ± 25 nM in ($n=5$, $P<0.001$). In TRPV1 KO lenses, LA-1 failed to produce a significant change of Rb uptake. Moreover, LA-1 failed to increase cytoplasmic calcium concentration in cultured lens epithelium from TRPV1 KO mice. Importantly, the rise of Rb uptake caused by LA-1 in WT lenses was prevented by the putative tubulin stabilizer, paclitaxel (100 nM). The Rb uptake response to LA-1 was abolished by a TRPV1 antagonist, A889425 (1.0 μ M). LA-1 was observed to cause ERK1/2 activation in WT cultured lens epithelium. The TRPV1 agonist capsaicin and hyperosmotic solution (350 mOsm) were shown to cause a similar pattern of ERK1/2 activation in WT cultured lens epithelium. The ERK1/2 responses were transient and displayed a peak at ~5 min. Paclitaxel as well as A889425 markedly reduced the magnitude of the ERK1/2 activation responses to hyperosmotic stress and LA-1.

Conclusions: The findings suggest a functional link between integrins, the tubulin cytoskeleton, and the TRPV1-dependent increase of NKCC1 that occurs when the lens is subjected to hyperosmotic stress. It is noteworthy that the integrin agonist LA-1 as well as hyperosmotic stress both were found to activate ERK1/2, an important step in the signaling associated with activation of NKCC1 in the lens.

CONTROL ID: 3539760

SUBMITTER (NAME ONLY): Raymond Leidich

TITLE: An Aflibercept-derived Mini-VEGF-Trap as a Potential Next-Generation VEGF Inhibitor

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.W. Leidich, K. Patel, A. Rafique, A. Romero Hernandez, M. Franklin, M. Lazo, A. Hermann, G. Sharma, Y. Zhao, H. Chen, N. Liu, M. Rosconi, C. Romano, W. Olson, N. Stahl, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aflibercept (Eylea®) is a VEGF inhibitor indicated for the treatment of patients with Wet AMD, MEfRVO, DME, and DR. Aflibercept is a fusion of the second Ig domain of VEGFR1 with the third Ig domain of VEGFR2 and that fused with to the Fc segment of human IgG, creating a chimeric protein with a very high VEGF binding affinity ($K_D \approx 0.2\text{-}1\text{pM}$). The goal of this study was to characterize a VEGF Mini-Trap generated by removing the Fc portion of the aflibercept, resulting in a smaller protein that could retain the VEGF binding and inhibitory properties of aflibercept and potentially provide higher molar dosing intravitreally. We hypothesize that this higher dosing could result in longer-lived activity.

Methods: We generated REGN7483F (VEGF Mini-Trap) using the IdeS protease derived from *Streptococcus pyogenes*. This enzyme cleaves just below the hinge region of the Fc. Aflibercept was incubated with agarose-immobilized IdeS for 60 mins, then the supernatant was collected and purified by protein A affinity chromatography. REGN7483F and aflibercept were characterized for binding kinetics by BiaCore, potency in a VEGFR1 bioassay, homogeneity by SDS-PAGE, thermal stability, solubility, viscosity, and complex formation with VEGF₁₆₅ by SEC-MALS and negative-stain electron microscopy.

Results: REGN7483F and aflibercept showed similar binding affinity for VEGF₁₆₅ (K_D 1.27 pM and 1.32 pM) and stoichiometric inhibition of VEGF₁₁₀ in the VEGFR1 bioassay. SDS-PAGE showed molecular weights expected for aflibercept (~65 kD) and REGN7483F (~ 32 kD). REGN7483F exhibited a similar degradation pathway as aflibercept under thermal stress analysis. In the base formulation buffer, REGN7483F showed low viscosity (< 14 cP at 120 mg/mL) and high solubility (> 160 mg/mL). SEC-MALS of aflibercept and REGN7483F in complex with VEGF₁₆₅ showed both favored a discrete 1:1 cis-complex containing one VEGF₁₆₅ dimer held between the two arms of REGN7483F or aflibercept.

Conclusions: REGN7483F has comparable binding affinity, bioassay blocking potency, stability and degradation pathway as aflibercept. Each exhibited a discrete 1:1 complex with VEGF₁₆₅. At a concentration of 110 mg/mL (viscosity ~12 centipoise), REGN7483F provides 5.5X molar equivalents of VEGF binding sites as the commercial

aflibercept formulation. Therefore, REGN7483F shows favorable properties as a potential next-generation VEGF inhibitor.

CONTROL ID: 3539767

SUBMITTER (NAME ONLY): Acadia Moeyersoms

TITLE: RNA and proteomic analysis of adenoid cystic carcinoma of the lacrimal gland

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.H. Moeyersoms, M. Zhang, D. Pelaez, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|A.H. Moeyersoms, M. Zhang, Cancer Biology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|V. Stathias, Pharmacology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|D.T. Tse, D. Pelaez, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lacrimal gland adenoid cystic carcinoma is a rare but very lethal cancer originating in the cells of secretory glands. With the 10-year survival rate of 20%, the only life extending technique is to remove the eye and surrounding socket contents entirely. ACC is a very slow growing but aggressive cancer, even with radical treatment, most patients will present with metastatic disease to the brain, lung, liver, or bones several years out from initial diagnosis and before symptoms are noticeable. Due to the rarity of LGACC, it is not well understood which leads to diagnosing, treating and monitoring disease progression difficult. Previously, genome analysis of ACC of the head and neck has uncovered a high mutation rate of MYB and NOTCH in patient samples, yet these two genes remain untreatable as there are no successful therapeutics for these targets. We aim to further understand the molecular drivers of LGACC and discover novel targets for specifically treating LGACC.

Methods: We have RNA sequencing data for 7 primary LGACC tumors, mass spectrometry data for 12 primary tumors and RNA sequencing for 15 cell lines derived from tumors to further understand the molecular signatures of LGACC. We used trimalore and star to prepare and align the RNA sequencing data. We completed extensive statistical analysis using edgeR and limma packages in R for RNA and proteomics, respectively.

Results: The RNA sequencing of the tumor samples revealed the most significantly differentially expressed gene ontology group is the extracellular matrix, including HAPLN1, FABP7, and VCAN. The mass spectrometry data also showed the significant role of extracellular matrix proteins and metabolic regulation. We compared the differentially expressed genes in the mass spectrometry and RNA sequencing data and discovered 194 genes that were differentially expressed in both analysis types. The complete analysis revealed that genes and proteins in the extracellular matrix are significantly differentially expressed between cancer and normal tissue.

Conclusions: With this extensive analysis of the molecular signatures, we now have a deeper understanding of the drivers of this slow growing, lethal cancer. This analysis lays the groundwork for the development of reliable molecular diagnostic, prognostic, and surveillance assays as well as therapies specifically targeting differential expression signatures.

CONTROL ID: 3539768

SUBMITTER (NAME ONLY): Zhengping Hu

TITLE: Specific Role of Endomucin in VEGF-induced VEGF Receptor 2 Internalization and Function

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Hu, I. Cano, M. Saint-Geniez, Y. Ng, P.A. D'Amore, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Z. Hu, I. Cano, M. Saint-Geniez, Y. Ng, P.A. D'Amore, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endomucin (EMCN) is a type I integral membrane glycoprotein selectively expressed by venous and capillary endothelium. Our previous findings showed that EMCN knockdown significantly inhibits VEGF165-induced VEGFR2 internalization and downstream activities. The goal of this study is to further define the specificity of EMCN for VEGF/VEGFR2 system by determining the role of EMCN in VEGF121-induced VEGFR2 activation. We also examined the potential role of EMCN in fibroblast growth factor (FGF) signaling and angiogenesis-related activities in endothelial cells.

Methods: EMCN was knocked down in human retinal endothelial cells (HRECs) using siEMCN, with non-targeting siRNA as a control. Whole cell lysates of HRECs with or without EMCN knockdown, followed by VEGF165 or VEGF121 stimulation at 5, 10, 30 and 60 min, were harvested. Protein levels of total VEGFR2, phospho-VEGFR2 (Y1175), total Akt, phospho-Akt, total Erk, phospho-Erk, total Src and phospho-Src were examined by western blot. A wound-healing assay was used to examine endothelial cells migration.

Results: VEGF165 and VEGF121 stimulation significantly increased HRECs wound closure compared to control (1 ± 0.02 vs. 1.15 ± 0.02 , $p=0.004$; 1 ± 0.02 vs. 1.18 ± 0.03 , $p=0.0001$. $N=3$ for both). SiEMCN treatment led to a significant suppression of EMCN protein levels compared to non-targeting siRNA group by 95% ($P<0.05$). EMCN knockdown prevented HRECs migration induced by VEGF165 (1 ± 0.03 vs. 1.04 ± 0.03 , $p=0.9$, $n=3$) as well as VEGF121 compared to control (1 ± 0.03 vs. 1.07 ± 0.02 , $p=0.5$, $n=3$). The levels of phospho-Src significantly increased following VEGF121 stimulation for 10 min ($n=3$, $p<0.05$); EMCN knockdown inhibited phospho-Src expression compared control ($n=3$, $p<0.05$). No significant differences were detected between EMCN knockdown and control for the expression of phospho-VEGFR2, phospho-Akt and phospho-Erk. FGF stimulation significantly increased HRECs wound-closure ($n=6$, $p<0.0001$), but EMCN knockdown did not significantly affect FGF-induced HRECs migration compared to control ($n=6$, $p<0.001$).

Conclusions: EMCN is essential for VEGF165- and VEGF121-induced endothelial migration and VEGFR2 internalization. However, EMCN does not play a significant role in FGF-induced endothelial cells migration. Our data indicate a specific role for EMCN in the VEGF/VEGFR2 system.

CONTROL ID: 3539791

SUBMITTER (NAME ONLY): Ryan Caezar David

TITLE: Rates of RNFL thinning in distinct glaucomatous optic disc phenotypes in early glaucoma

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.C. David, S. Moghimi, E. Ekici, J.L. Do, H. Hou, J.A. Proudfoot, A. Kamalipour, T. Nishida, R.N. Weinreb, Hamilton Glaucoma Center, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|C.A. Girkin, Department of Ophthalmology and Visual Sciences, UAB Callahan Eye Hospital, Birmingham, Alabama, UNITED STATES|J.M. Liebmann, Bernard and Shirlee Brown Glaucoma Research Laboratory, Department of Ophthalmology, Edward S. Harkness Eye Institute, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare spectral-domain optical coherence tomography (SDOCT) measured circumpapillary retinal nerve fiber layer (cpRNFL) among four glaucomatous optic disc phenotypes in early glaucoma.

Methods: In this longitudinal study, 218 early glaucoma eyes that had at least 3 years of follow-up and a minimum of 4 SDOCT scans were recruited from the Diagnostic Innovations in Glaucoma Study (DIGS) and the African Descent and Glaucoma Evaluation Study (ADAGES). The optic discs were classified into four types based on appearance: generalized cup enlargement (GE), focal ischemic (FI), myopic glaucomatous (MY), and senile sclerotic (SS). A linear mixed-effect model was used to compare the rates of global and regional cpRNFL thinning among optic disc phenotypes.

Results: Of the 218 early glaucoma eyes that were followed for an average of 5.9 years, 76 were classified as generalized cup enlargement (GE), 53 focal ischemic (FI), 22 myopic glaucomatous (MY), and 67 senile sclerotic (SS) discs. After adjusting for confounders, the SS group (mean (95% CI): -1.01 (-1.30, -0.73) $\mu\text{m}/\text{year}$) had the fastest mean rate of global cpRNFL thinning followed by FI (-0.77 (-0.97, -0.57) $\mu\text{m}/\text{year}$), MY (0.59 (-0.81, -0.36) $\mu\text{m}/\text{year}$) and GE (-0.58 (-0.75, -0.40) $\mu\text{m}/\text{year}$) at $p < 0.001$. The inferior temporal sector had the fastest mean rate of cpRNFL thinning among the regional measurements except for the MY group (-0.68 (-1.10, -0.26) $\mu\text{m}/\text{year}$), $p = 0.002$. In the multivariable analysis, higher mean intraocular pressure during follow-up ($p < 0.001$) and optic disc phenotype ($p = 0.014$) were associated with faster cpRNFL thinning. The GE ($p = 0.002$) and MY ($p = 0.010$) phenotypes were associated with significantly slower global rates of cpRNFL thinning when compared to the SS phenotype.

Conclusions: Rates of cpRNFL thinning were different among the four glaucomatous optic disc phenotypes. Those patients with early glaucoma with SS phenotype have the fastest cpRNFL thinning. These patients may benefit from more frequent monitoring and the need to advance therapy if cpRNFL thinning is detected.

CONTROL ID: 3539802

SUBMITTER (NAME ONLY): Dhara Shah

TITLE: Histatin -5 inhibits expression of pro-inflammatory cytokines through TLR- NF-kappa B pathway induced by hyperosmolar conditions in human corneal epithelial cells

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Shah, K. Son, S. Lee, M. Ali, A. Balasubramaniam, V.K. Aakalu, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Toll-like receptors (TLRs) have a key role in triggering the innate immune response. TLR activation causes the production of various pro-inflammatory cytokines, chemokines, and antimicrobial peptides (AMPs) commonly found on the ocular surface. Histatin peptides are potent anti-microbial agents that may have salubrious effects in ocular epithelia. Multiple ocular surface diseases (OSD) including dry eye disease (DED), are driven by inflammation. Here, we investigated how histatin 5 (Hst5) modulates the expression of TLRs in an in vitro experimental model of DED.

Methods: Hyperosmolarity was induced by adding 125 mM NaCl with or without co-treatment with Hst5 in human corneal epithelial (HCE) cells. Cell viability was measured using WST-assay kit following the manufacturer's instruction. The expression of TLRs (TLR2, TLR3, TLR4 and TLR7) and pro-inflammatory cytokines (IL-6, IL-8 and TNF- α) were examined by qPCR. NF- κ B activation was examined by detecting I κ B- α degradation using Western blotting and p65 translocation to nucleus using immunofluorescence staining.

Results: Experimental results showed that Hst5 abrogated cell death induced by hyperosmolar condition in HCE cells. Hyperosmolar conditions significantly induced TLR2 and TLR7 in HCE cells. TLR signaling was inhibited by co-treatment of Hst5. Application of Hst5 reduced the synthesis ocular surface disease relevant pro-inflammatory cytokines significantly. We also found that activation of NF- κ B was reduced in response to Hst5.

Conclusions: Thus, Hst5 application can reduce hyperosmolarity related TLR signaling and innate immune inflammation in the ocular surface.

CONTROL ID: 3539809

SUBMITTER (NAME ONLY): Mercedes Gauthier

TITLE: The brighter the flash, the more synchronized the oscillatory potential response: A Hilbert transform analysis

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gauthier, A. Polosa, P. Lachapelle, Ophthalmology, Research Institute of the McGill University Health Centre, Montreal, Quebec, CANADA|M. Gauthier, J. Lina, Département de Génie Électrique, Ecole de technologie supérieure, Montreal, Quebec, CANADA|A. Polosa, Hopital Maisonneuve-Rosemont Centre Universitaire d'Ophthalmologie, Montreal, Quebec, CANADA|J. Lina, Université de Montreal Centre de Recherches Mathématiques, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Important information can be gathered from non-saturated system responses, such as those obtained from the retina with very dim flashes (i.e., below the rod Vmax) of the scotopic electroretinogram (ERG). This study focuses specifically on the oscillatory potentials (OPs) of these responses to assess how their synchronicity evolves with flash strength, in rats and mice.

Methods: Scotopic ERGs (Intensity: -6.3 to $0.9 \log \text{cd.s.m}^{-2}$; dark-adaptation: 12 h) were performed on 6-8 adult pigmented (C57BL/6; PM) and albino (Balb/c; AM) mice as well as pigmented (Long-Evans; PR) and albino (Sprague-Dawley; AR) rats. ERGs were band-passed filtered (zero-phase FIR filter; order: 150) in 3 frequency bands (65-90 Hz; 90-115 Hz; 115-140 Hz) and a Hilbert transform was performed on each time series leading to a harmonic signal modulated with a time varying envelop. A threshold on the envelopes was set to delimit OP burst segment. The total OP burst duration and mean peak time difference (PTD) between each frequency band envelope were measured.

Results: The OP bursts duration behaved in opposite ways between pigmented and albino animals. In PM and PR the burst duration peaked between -3.9 and $-2.7 \log \text{cd.s.m}^{-2}$, while it was minimal in AM and AR. This difference between pigmented and albino animals was also seen when considering the synchronicity of the OP burst as measured with the PTD. Indeed, at $-3.9 \log \text{cd.s.m}^{-2}$, PM and PR had a large peak of PTD (38.2 ± 11.7 ms and 27.1 ± 13.4 ms, respectively), while AM and AR had very low PTDs, except for the dimmest flashes (Peak PTDs: AM = 21.4 ± 15.2 ms at $-5.1 \log \text{cd.s.m}^{-2}$; AR = 15.6 ± 0 ms at $-6 \log \text{cd.s.m}^{-2}$). Regardless of animal species and pigmentation, all animals had a minimal PTD at the 4 brightest flash intensities (PTD at $0.9 \log \text{cd.s.m}^{-2}$: AM= 3.4 ± 1.6 ms; PM= 3.5 ± 0.8 ms; AR= 4.7 ± 1.4 ms; PR= 5.9 ± 0.8 ms).

Conclusions: Our results suggest a clear distinction between the scotopic OP bursts of pigmented and albino animals. The synchronicity peak found in pigmented animals matched the peak in burst duration, suggesting that longer OP bursts seen at dimmer flashes are more disorganized in their frequency contributions than the shorter bursts seen in albino animals at the same intensities. The increased synchronization observed at the brightest intensities in all animal tested, could suggest an optimization of the retinal (neuronal) response.

CONTROL ID: 3539839

SUBMITTER (NAME ONLY): Paulina Liberman

TITLE: Efficacy of Difluprednate in the Treatment of Scleritis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Liberman, B.M. Burkholder, J.E. Thorne, M. Berkenstock, Uveitis Department, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|P. Liberman, Departamento de Oftalmologia. Escuela de Medicina., Pontificia Universidad Catolica de Chile, Santiago, CHILE|

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ABSTRACT BODY:

Purpose: To present a series of patients where difluprednate was used as a sole topical agent for scleritis treatment. Discuss its effectiveness and side effect profile.

Methods: An observational retrospective study of all patients with scleritis who used difluprednate as a single treatment agent from 1/1/2018 to 1/1/2020. Data collected at each visit was: age, race, sex, anatomic location of scleritis, presence of nodules or necrotizing sclera, changes in scleritis activity, IOP, number of difluprednate drops used, BCVA, and lens status. Exclusion criteria: use of NSAIDs, corticosteroids, and immunosuppressive drugs. Primary outcome was clinical resolution of scleritis. Resolution was defined as no anterior chamber cell, complete blanching of the ocular surface with 10% phenylephrine: no nodules or necrosis. Secondary outcome measures: change in lens status or cataract surgery; IOP elevation defined as IOP ≥ 24 mm Hg.

Results: Twenty-five patients (35 eyes) were analyzed. Median age was 60 years (range 13-78) and 60% were female. Caucasians were the largest group (16; 64%). Forty percent had bilateral disease; 44% of patients had an underlying systemic disease. The majority (86%) had diffuse anterior disease. Eighty percent (28 eyes) achieved quiescence. Nine eyes had IOP elevation; 4 eyes had a decrease in 2 or more lines of vision, of which one required cataract surgery. Overall, 5 eyes underwent cataract surgery. Causes of decreased vision were, dry eye associated with difluprednate (2 eyes), cataract progression (1 eye), and compressive optic neuropathy unrelated with difluprednate use (1 eye).

Conclusions: Difluprednate use alone achieved disease suppression in most eyes treated for anterior scleritis with few having progression of cataracts or IOP elevation. Further studies are needed to assess the efficacy of adjunct difluprednate use in patients refractory to NSAIDs and non-steroidal immunosuppressant treatment alone.

CONTROL ID: 3539843

SUBMITTER (NAME ONLY): Ping Yang

TITLE:

Risuteganib Modulates Multiple Transcription Factors regulated by Hydroquinone in Human RPE Cells

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Yang, N.A. Besley, S.W. Lallier, G.J. Jaffe, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|Z. Shao, J.Y. Park, H. Karageozian, V. Karageozian, Allegro Ophthalmics, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Risuteganib (RSG) is a novel synthetic peptide that regulates integrin functions and has shown promising efficacy in an intermediate dry AMD phase 2 clinical study. We previously reported that RSG protected against retinal pigment epithelial (RPE) cell injury induced by hydroquinone (HQ), a major oxidant in cigarette smoke and atmospheric pollutants, agents implicated in age-related macular degeneration (AMD) pathogenesis. Many transcription factors (TFs) are important regulators of genes that control cellular response to oxidative stress. Herein, we investigate the effect of RSG on expression of several TFs regulated by HQ in human RPE cells.

Methods: Cultured human RPE cells in triplicate wells were treated with HQ at different concentrations in the presence or absence of RSG (400 μ M, Allegro Ophthalmics, LLC) for various treatment times. Expression of TF genes associated with cellular stress response, including activating transcription factor 3 (ATF3), DNA damage-inducible transcript 3 (DDIT3; encodes the multifunctional TF, CHOP), and DNA-binding protein inhibitors (ID-2 and ID-3), were analyzed by qPCR. Expression of ATF3, CHOP, nuclear factor erythroid 2-related factor 2 (NRF2), and X-box binding protein 1s (XBP1) were evaluated by Western blot.

Results: Compared to untreated cells, HQ significantly increased mRNA expression of ATF3, DDIT3, ID2 and ID3 ($P<0.05$). RSG+HQ cotreatment significantly further upregulated HQ-induced ATF3 and DDIT3 ($P<0.05$) and decreased HQ-induced ID2 and ID3 mRNA levels ($P<0.05$). Levels of ATF3, Nrf2, CHOP, XBP1 proteins were significantly upregulated by HQ and further upregulated by RSG+HQ cotreatment ($P<0.05$).

Conclusions: RSG modulated multiple transcription factors involved in oxidant injury pathways, supporting a multifunctional role of RSG on RPE cells against oxidative stress.

CONTROL ID: 3539866

SUBMITTER (NAME ONLY): Alisa Thavikulwat

TITLE: Retinal Photography in a Cohort of Urban Middle-Aged Adults

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.T. Thavikulwat, T.D. Keenan, D. Peprah, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|P.G. Christakis, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|A.B. Zonderman, M.K. Evans, Laboratory of Epidemiology and Population Science, National Institute on Aging, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study is an ongoing prospective cohort study initiated in 2004 to evaluate the influences of socioeconomic status and race on the incidence of age-related diseases in the United States. Participants are urban African American and white adults recruited from 13 neighborhoods in Baltimore City. An ophthalmic component was added in 2017 to evaluate the prevalence and characteristics of eye disease in this population.

Methods: In the HANDLS study, mobile research vehicles are used to evaluate all participants every 4 years. Detailed testing is performed to assess nutrition, cognition, and biologic biomarkers. Participants in wave 5 also underwent color fundus photography (TopCon TRC-NW400 non-mydratic camera) at their study visit. The images were graded by ophthalmologists who were masked to the other clinical data. Presenting visual acuities (VA) were collected beginning in 2019. Data were analyzed using R statistical software.

Results: A total of 965 participants (mean age: 59.3±8.8 years) underwent fundus photography. The participants were 60.8% women (587) and 63.4% African American (612). The image quality was gradable in 1646/1930 (85.3%) of photos.

Roughly half of eyes (1018) were found to have abnormal findings, most commonly glaucoma/glaucoma suspect (295 eyes [15.3%]), hypertensive retinopathy (156 eyes [8.1%]), macular degeneration (100 eyes [5.2%]), and retinal hemorrhage (39 eyes, [2.0%]). Cup-to-disc ratios of the optic nerves were graded as ≥ 0.5 in 434/1761 eyes (24.6%).

Of the 427 participants with VA data, the majority (375; 87.8%) had VA $\geq 20/40$ in at least one eye. Moderate visual impairment was seen in 51 (11.9%) participants who had VA between 20/50 and 20/200 in the better seeing eye.

Conclusions: Fundus photography in this cohort identified potential ocular pathology with recommendation for follow-up with an ophthalmologist in about half of participants. Future work will assess the influences of socioeconomic status and race on eye disease. Analysis of the retinal images will determine their correlations with other medical tests, including cognitive testing, nutrition, and biologic biomarkers.

CONTROL ID: 3539893

SUBMITTER (NAME ONLY): Sanghoon Park

TITLE: Comparison of Octopus perimetry isopter area and Ellipsoid Zone (EZ) width in Retinitis Pigmentosa (RP) patients with and without Cystoid Macular Edema (CME).

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Park, A. Yan, J. Ong, T. Gao, L. Le, E. Bowers, C. Truong, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|B. Usmani, S.A. Shah, Ophthalmology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: CME is a common occurrence in patients with RP. In this study, we have compared isopter area measured by Octopus perimetry and EZ width measured by Spectral domain Optical Coherence Tomography (SD-OCT) in RP patients with or without CME.

Methods: Retrospective chart review of RP patients with Octopus and SD-OCT done on the same day was performed. Patients with visual acuity ≥ 50 letters, and no ocular co-morbidities such as history of retinal detachment and vitreomacular interface abnormality were included. Ellipsoid zone (EZ) width ($^{\circ}$) and foveal thickness (mm) were measured using Heidelberg HEYEX software. A MATLAB program was written to measure the I4e, III4e, and V4e isopter areas ($^{\circ}^2$) from Octopus maps. Mann-Whitney U and two-proportion Z test were performed to compare the CME with the non-CME group.

Results: Forty eyes of 24 patients (9 males, age 22-63 years) qualified based on criteria listed above. Twelve eyes of 7 patients had CME. Peripheral island of III4e was found in 8 non-CME eyes vs. 2 CME eyes ($p=0.49$), and I4e found in 6 non-CME eyes vs. 1 CME eye ($p=0.32$). Table 1 shows the results.

Conclusions: Patients with CME had a statistically significant reduction in all isopter areas, both central and peripheral, as well as a decline in EZ-width when compared to non-CME eyes. This along with the lack of peripheral islands of vision on Octopus perimetry in CME eyes may suggest that CME is more likely to be present in more advanced disease. Further studies are recommended to study the relationship between presence of CME and stage of RP.

CONTROL ID: 3539905

SUBMITTER (NAME ONLY): Gary Hin-Fai Yam

TITLE: Human corneal stromal stem cells express specific microRNAs with anti-inflammatory and anti-fibrotic activities: a novel mechanism to reduce corneal scarring

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Preclinical and clinical studies have shown that human corneal stromal stem cells (CSSC) prevent corneal scarring and regenerate transparent stromal tissue. CSSC treatment blocked neutrophil infiltration into the injured stroma via the paracrine action of extracellular vesicles (EV). This study investigated the mechanisms by which CSSC EV suppress corneal inflammation and fibrosis.

Methods: Conditioned media of primary human CSSC cultures were collected for EV isolation. Total RNA library of EV fractions was analyzed by RNAseq and microRNAs (miRs) specific to CSSC of high regenerative potential were identified. Target gene search and enriched pathway analyses from single or combinations of miR were studied by TargetScan, miRDB, and DAVID bioinformatics. Transfection of miR having statistical significance in association to inflammatory, fibrosis, and immune pathways were examined by (1) mouse macrophage (RAW264.7) for M1/M2 phenotype switch assay; and (2) the fibrosis assay of human corneal stromal fibroblasts after TGFβ1 and ascorbate treatment.

Results: A total of 17 miRs were significantly enriched in EVs of human CSSC having high regenerative potential and scar reduction in mouse corneal wound model. Using target gene search and pathway analyses, 9 miR combinations were predicted to be significantly associated with signaling cascades of tissue inflammatory and fibrosis responses, as well as tissue regeneration ($P < 10^{-6}$). Transfection of miR mimics to RAW cells showed that 4 groups suppressed M1 phenotype (reduced pro-inflammatory iNOS and MCP1 expression) after lipopolysaccharide (50 ng/ml) treatment. Among them, 1 group was shown to revert pre-M1 RAW to M2 phenotype (increased anti-inflammatory Arg1 and Ptgs1 expression), similar to interleukin-4 (20 ng/ml) treatment. These miRs also downregulated the fibrosis gene expression (αSMA and tenascin C) of human CSSC treated by TGFβ1 (10 ng/ml) and ascorbate.

Conclusions: Specific miRs produced by CSSC and delivered via EVs exerted anti-inflammatory and anti-fibrotic activities. Further in vivo study will demonstrate their therapeutic efficiency in preventing corneal scarring and regenerating transparent corneal tissues after injury.

CONTROL ID: 3539918

SUBMITTER (NAME ONLY): Wenqi Su

TITLE: Inhibition of corneal neovascularization with rAAV-anti-VEGF in mouse corneal injury models

SESSION TITLE: Corneal immunology and neovascularization I

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Corneal neovascularization (CoNV) can lead to visual impairment, affecting over 1.4 million people in the United States. It is caused by a variety of pathologies associated with angiogenic stimuli. Several medical and surgical management regimens are currently available, but they are only partially effective. Conbercept (KH902), an anti-vascular endothelial growth factor (VEGF) drug, can successfully inhibit ocular neovascularization, but it requires repeated dosing. In this study, we investigated the long-acting anti-angiogenesis and safety of rAAV-delivered KH902 in mouse corneal injury models.

Methods: We employed two rAAV serotypes with different transduction efficiencies to deliver KH902 gene via single intrastromal or subconjunctival administration. rAAV-mediated eGFP expression was used as a guide to determine transduction efficiency and cell tropism in the cornea. The levels of KH902 mRNA expression mediated by each rAAV serotype were analyzed by Droplet Digital PCR. The potential toxicity was determined through analyzing the central corneal thickness at various timepoints and immune response at two weeks after high- and low-dose rAAV gene delivery. We tracked and quantified the CoNV progression for 12 weeks post-injection of rAAV-KH902 in CoNV models in vivo. The levels of DLL4/Notch signaling and ERK activation, markers for VEGF stimulation, were tested by Western blot.

Results: We found that the two different serotypes when administered by intrastromal injection conferred KH902 expression in corneal keratocytes with different efficiencies, while rAAV rarely transduced cornea tissue via subconjunctival injection. After reaching peak expression at 1-2weeks, KH902 mRNA expression in the cornea gradually decreased but was still detectable at three months following a single intrastromal injection. High doses of rAAV-KH902 induced a strong corneal inflammatory response; while at low doses, inflammation was at a minimum. Furthermore, rAAV-KH902 reduced DLL4/Notch signaling and ERK activation in alkali burn-induced CoNV mouse model. Our data suggest that rAAV-mediated KH902 gene therapy can dramatically inhibit CoNV for an extended period of time in both alkali burn- and suture-induced CoNV mouse models without adverse events.

Conclusions: Our study demonstrates the potential and relative safety of rAAV-based anti-angiogenesis therapy in the treatment of corneal neovascularization progression.

CONTROL ID: 3539944

SUBMITTER (NAME ONLY): Abdallah Abbas

TITLE: Using the What-if Tool to perform nearest counterfactual analysis on an AutoML model that predicts visual acuity outcomes in patients receiving treatment for wet age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Machine Learning (ML) models suffer from a lack of interpretability, particularly in healthcare settings. We used Google Brain's What-if Tool (WIT) in a retrospective cohort study to analyse the decision boundaries of a multi-classification model that predicts visual acuity (VA) outcomes for patients with wet age-related macular degeneration (AMD).

Methods: Our AMD dataset consisted of 3961 eyes from patients who had attended Moorfields Eye Hospital in the UK and were undergoing anti-vascular endothelial growth factor treatment. For each patient, VA was measured at the start of treatment and one year later using Early Treatment Diabetic Retinopathy Study charts. VA after one year of treatment was binned to labels of "Good" for scores of 70+, "Neutral" for scores of 36-69, and "Poor" for scores of 35 or below. A Google Cloud AutoML Tables model was then trained on this data to predict these VA outcome labels based on VA at baseline, age, ethnicity and gender.

We report the AUROC, precision and recall performance of the model. To explore decision boundaries, nearest counterfactual analysis using L1 distance was performed using the WIT – a model-agnostic explainable artificial intelligence tool - as a Jupyter notebook extension.

Results: The trained AutoML model performed with an AUROC of 0.892, a precision of 73.1% and a recall of 71.9%. We present a case study of an 84-year-old British male patient with an initial VA of 70, and his nearest counterfactual, an 84-year-old British female patient, also with an initial VA of 70. The ground truth for both patients was "Good"; this was correctly predicted in the male patient, whilst the model predicted a "Neutral" outcome for the female.

Conclusions: We present a novel way in which clinicians can easily view nearest counterfactuals using the WIT, allowing for a greater understanding into how ML models arrive at their decisions at the level of an individual patient. In our example, there is no clinically strong evidence to support the model's prediction of a "Neutral" outcome in the female patient in comparison to the male patient. Importantly, minimal coding experience is required in both the training of the model on AutoML Tables and the analysis using the WIT. This approach could therefore contribute to the democratisation of ML in healthcare.

CONTROL ID: 3539969

SUBMITTER (NAME ONLY): Bhagwat Alapure

TITLE: Antisense oligonucleotide treatment restores retinal expression of phototransduction proteins in Usher mice

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.V. Alapure, K.N. Robillard, J.J. Lentz, Neuroscience Center of Excellence, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|J. Guidry, Department of Biochemistry and Molecular Biology, Proteomics Core Facility, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|F. Rigo, Ionis Pharmaceuticals, Inc., Carlsbad, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Arrestin and glial fibrillary acidic protein (GFAP) are expressed in photoreceptors and Müller cells, respectively, and play an important role in phototransduction. Harmonin is a scaffolding protein involved in the development and function of ciliated cells including photoreceptors and inner ear hair cells; however, its role in the retina remains unclear. Mutations in harmonin lead to Usher syndrome (Usher), the most common genetic cause of deaf-blindness. Acadian Usher Type 1C is attributed to the USH1C c.216G>A splicing mutation, and knock-in mice display severe hearing impairment, balance disturbances, and visual dysfunction similar to patients. To understand the effects of the 216A mutation on protein expression in the retina, we performed quantitative discovery-based proteomics of retinal extracts from wild type (WT), Usher, and 216A-targeted antisense oligonucleotide (ASO)-treated Usher mice. We hypothesize that Usher retinas have abnormal Arrestin and GFAP protein expression compared with WT controls. Furthermore, we predict that ASO treatment, which improves Ush1c expression and restores visual function in Usher mice, also restores normal Arrestin and GFAP expression in the retina.

Methods: Juvenile Usher mice were treated with 216A-ASOs by intravitreal injection (IVI) and allowed to recover for 2.5 months post-IVI. Visual function was measured in ASO-Usher, Usher, and WT mice at 3 months of age using electroretinogram (ERG) analysis. Retinas were then harvested and processed for proteomic analysis using liquid chromatography and mass spectrometry (LCMS) and confirmed with immunohistochemistry (IHC) and western blot analysis.

Results: ERGs were significantly increased in ASO-Usher mice compared with untreated Usher controls. LCMS identified significantly differentially expressed proteins in WT versus Usher (155/3659) and ASO-Usher versus untreated Usher (124/3663) retinas. Among these, Arrestin levels were significantly decreased and GFAP levels were significantly increased in Usher retinas compared to WT. Expression levels were significantly improved following ASO treatment as measured by LCMS, IHC, and western blot analyses.

Conclusions: These data demonstrate that ASO treatment improves visual function in Usher mice, as well as restores WT Arrestin and GFAP expression levels in the retina, suggesting a new role for harmonin in the healthy retina.

CONTROL ID: 3539979

SUBMITTER (NAME ONLY): Siamak Yousefi

TITLE: Novel Genetic Factors Associated with Primary Open-Angle Glaucoma Identified Using Artificial Intelligence

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the predictive power of an artificial intelligence (AI) construct to predict primary open-angle glaucoma (POAG) from single nucleotide polymorphisms (SNPs) and to identify potentially novel genetic factors associated with glaucoma.

Methods: We included 1012 participants of the Ocular Hypertensive Treatment Study (OHTS) from multiple ancestries. A total of 817 participants remained without evidence of POAG (controls) and 195 participants eventually developed POAG (cases) over ~15 years. We developed a case-control genome-wide association study (GWAS) to identify SNPs that were independently associated with glaucoma and selected top scored SNPs (Fig. 1). We then developed a machine learning model composed of feature subset selection and learning to identify the most promising subset of SNPs that were highly predictive of POAG development. We finally developed an independent machine learning classifier to predict glaucoma from the discovered subset of SNPs (Fig. 1). We evaluated the accuracy of the model using cross-validation of the receiver operating characteristics curves.

Results: The top 1000 highly scored SNPs, out of ~1 million, were selected for the downstream analysis. Machine learning discovered 63 SNPs, out of 1000 (Table 1), that were collectively predictive of glaucoma with an AUC of 0.88 (95% CI: 0.86 – 0.90) without using any additional glaucoma endophenotype features. The AUC of the model using 750 subjects from only (self-reported) European race was 0.93 (95% CI: 0.90 – 0.95). The discovered SNPs were mapped to 45 independent genes, of which eight were previously known to be associated with glaucoma traits and 37 genes remain as potential candidates for development of the POAG.

Conclusions: The combined statistical modelling and machine learning frameworks achieved a high accuracy in predicting glaucoma. Successful development of this learning model may assist clinicians in using DNA testing to identify individuals with ocular hypertension who are at-risk of glaucoma development and future vision loss. Independent datasets are desirable to further validate the findings in this study.

CONTROL ID: 3540010

SUBMITTER (NAME ONLY): William Samuel

TITLE: Long non-coding RNA LINC00276 may encode micropeptides to maintain cellular homeostasis in human retinal pigment epithelial cells

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Emerging evidence indicates that some non-coding RNA molecules may harbor short open reading frames (sORFs) that code for functional micropeptides that may play a major role in regulating many pathophysiological processes. However, the functions of these remain largely unexplored given their small size. sORFs can act independently as ligands or signaling molecules by engaging with and modulating larger regulatory proteins to fine-tune complex biological systems. In this study, we attempt to identify potential protein-coding sORFs from LINC00276, a non-coding RNA identified in differentiated ARPE-19 cells.

Methods: Bioinformatic analyses based on evolutionary conservation were used to identify sORFs with the potential to encode conserved micropeptides. Also, we employed the Coding Potential Calculator version 2 (CPC2) algorithm, a novel discriminative algorithm assessing sequence intrinsic features at the DNA/RNA level, to predict high-quality sORFs. The identified sORFs were then cloned into pEGFP-N1 vector in-frame with C-terminus GFP and 6xHis tag. The expression of these constructs in ARPE-19 cells was analyzed by immunofluorescence and western blotting after transfection.

Results: In a screen of LINC00276 transcripts, we identified an evolutionarily conserved sORF with the potential to encode a highly conserved 19 amino acid (aa) micropeptide located in exon 2, which is common to both LINC00276 transcripts. Using CPC2, we identified another sORF encoding a 74 aa peptide located in exon 4, only present in the second transcript of LINC00276. Expression of these constructs in ARPE-19 cells yielded peptides corresponding to the predicted molecular weight of the fusion peptides, detected by western blot. Both micropeptides, of 19 and 74 aa, showed GFP expression but a distinct GFP expression pattern was observed with the 74 aa micropeptide in ARPE-19 cells.

Conclusions: In this study, we provide evidence for the presence of two putative micropeptides encoded in LINC00276. These may play a role in modulating the expression of genes associated with RPE differentiation. Further studies on the identification and functional characterization of the micropeptides are required to elucidate their biological functions and may provide further insight into the cellular role of LINC00276 in regulating RPE characteristics.

CONTROL ID: 3540011

SUBMITTER (NAME ONLY): Wyndham Batchelor

TITLE: Exploring the Use of Self-Sensing Atomic Force Microscopy Cantilevers for Corneal Biomechanics Studies

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.M. Batchelor, N. Ziebarth, Department of Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|D. Williams, D. Hubbard, Joint Department of Biomedical Engineering, UNC Chapel Hill and NC State University, Chapel Hill, North Carolina, UNITED STATES|O.J. Knight, Department of Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|N. Ziebarth, Department of Physiology and Biophysics, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Atomic Force Microscopy (AFM) has proven to be a useful method for characterizing corneal mechanical properties ex vivo. However, traditional setups are bulky and cannot be used in vivo. Self-sensing cantilevers (SSCs) are an alternative technology that can be used to replace the traditional AFM cantilever and optical lever system to perform biomechanical measurements. In this study, we compared the performance of a SSC system to a traditional AFM optical lever system in measuring the Young's Modulus of elasticity of the full-thickness cornea.

Methods: To avoid variability associated with cadaver tissue, experiments were conducted on a realistic corneal model designed to practice corneal dissection (Cordelia, Bioniko Models). To restore hydration of the corneal model, it was placed in deionized water at room temperature for 30 minutes. After this, it was adhered to a Petri dish and placed in a custom AFM system that has been optimized for biomechanical studies (Ziebarth et al. Mol Vis 2007 Apr; 13:504-510). Traditional AFM cantilevers (1.75N/m, 50mm diameter, sQUBE) were used to measure Young's modulus of the corneal model in 2 different locations on 3 different days, with at least 10 scans recorded in each location each day. A piezoresistive, self-sensing AFM cantilever (Agar Scientific, Ltd., Essex, UK) was then used to measure the mechanical response of the same sample. A total of 14 measurements were performed at 4 different speeds (7.5mm/s, 10mm/s, 15mm/s, and 30mm/s). All data was analyzed using custom software written in MATLAB.

Results: Using the traditional AFM system, Young's modulus of elasticity of the corneal model was 25.8 ± 4.3 kPa. Using the SSC, we were able to record a consistent linear response during indentation of the corneal model. The slope (voltage/displacement) and change in voltage were consistent, independent of speed of indentation or day of measurement. The slope was 0.50 ± 0.06 N/m, and the change in voltage was 7.85 ± 0.81 mV. These values are directly correlated to the Young's modulus of elasticity of the sample.

Conclusions: SSC technology can be used to measure biomechanical properties of the cornea, similar to traditional AFM systems. However, due to its small form factor, it has the capability of being applied in instances of large and geometrically complex samples.

CONTROL ID: 3540025

SUBMITTER (NAME ONLY): Bryon McKay

TITLE: Feasibility of Intravitreal Aqueous Chlorhexidine Gluconate for the Treatment of Bacterial Endophthalmitis

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.R. McKay, B.B. muirhead, F. Lasowski, H. Sheardown, D. Wong, Department of Ophthalmology and Vision Sciences, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Endophthalmitis is a rare but significant vision threatening emergency. The time from symptom onset to treatment is a significant factor in final visual outcome. Standard of care is treatment with fortified broad-spectrum antibiotics that require specialist pharmacy preparation creating a delay in care. Aqueous chlorhexidine gluconate is a readily available, stable antiseptic with broad-spectrum antimicrobial, anti-viral, and anti-fungal action. The purpose of this study is to determine the feasibility of intravitreal injection of aqueous chlorhexidine in terms of retinal toxicity and antimicrobial efficacy in an animal endophthalmitis model.

Methods: Intravitreal injections of aqueous chlorhexidine (0.1%, 0.01%, and 0.001%) were administered to 3-month-old brown Norway rats (n=3 per group). Each group received either 2µL of 0.1%, 0.01% or 0.001% chlorhexidine in one eye (n=3 eyes per group) with the contralateral eye receiving a sham injection of 2µL saline to serve as the control (n=3 eyes per group). The animals were assessed using fundus imaging, optical coherence tomography (OCT), and electroretinography (ERG) at 6h, 24h, 72h, and 1-week post injection. Animals were sacrificed at 1 week and eyes were fixed in 4% paraformaldehyde for histochemical analysis.

Results: 0.1% Chlorhexidine vs. sham: All 3 eyes in the treatment group developed visually significant cataracts by one week. ERG analysis demonstrated severely impaired B-wave in the treatment group at 24h. ERG was normal in the sham group. 0.01% Chlorhexidine vs. Sham: 2 of 3 treatment eyes developed mild cataract by 1 week. Fundus imaging revealed normal retinal morphology in both groups. ERG analysis demonstrated a mild reduction in B-wave amplitude in the 3 treatment eyes compared to the sham eyes. 0.001% chlorhexidine vs. Sham: There were no significant lenticular changes in treatment or sham injected eyes. Fundus imaging demonstrated normal retinal morphological in both groups. ERG amplitudes were similar vs sham eyes.

Conclusions: These data demonstrate concentrations of chlorhexidine above 0.01% injected into the vitreous may have toxic effects on the retina and predispose to cataract formation. This suggests concentrations below 0.01% may be the safe upper limit for intravitreal aqueous chlorhexidine. These data support that aqueous chlorhexidine may be safe for intravitreal use.

CONTROL ID: 3540038

SUBMITTER (NAME ONLY): Myoungsup Sim

TITLE: Primary cilia and the reciprocal activation of AKT and SMAD2/3 regulate stretch-induced autophagy in trabecular meshwork cells

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sim, A. Nettesheim, A. Dixon, P.B. Liton, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported autophagy activation in primary-cultured human trabecular meshwork (TM) cells upon mechanical stress. Here we investigate its mechanosensor and downstream signaling pathway, as well as its role in IOP homeostasis.

Methods: Human TM cells were subjected to cyclic mechanical stretch (CMS, 8% elongation, 1 cycle/sec) for up to 24 h. Autophagy activation was monitored by measuring LC3-II and p62 levels or LC3 puncta formation using western blot or confocal microscopy. Primary cilia (PC) were disrupted by chloral hydrate (CH, 4 mM for 3 day). Ca^{2+} channels were inhibited with 10 μM of amiloride, amlodipine and HC067047. Hedgehog signaling was inhibited by cyclopamine (10 μM). TGF β and AKT signaling were inhibited chemically (10 μM of LY2109761 or SB431542 for TGF β and 4 $\mu\text{g/ml}$ of SC66 for AKT) or genetically (siRNAs targeting SMAD2/3 and AKT1). The effect of deciliation on outflow facility were measured in pig eyes by using iPerfusion system.

Results: Primary cilia disruption with CH abolished autophagy induction, as evaluated by LC3-II and p62 levels (0.23 ± 0.18 and 0.63 ± 0.31 fold, $p < 0.05$, $n = 5$ and 3 , respectively) in CMS cells. Inhibiting Ca^{2+} channels or hedgehog signaling had no effect on it. In contrast, SMAD2/3 knock-down reduced the CMS-induced increase in LC3-II level by approximately 3 folds ($p < 0.01$, $n = 3$). However, similar effect was not observed by the inhibition of TGF β receptors. Intriguingly, AKT inhibition increased LC3-II levels, and the levels were significantly lowered by 1.5~2 folds ($p < 0.01$, $n = 3$) together with SMAD2/3 knock-down in both NS and CMS cells. Furthermore, knock-down of SMAD2/3 or AKT1 reciprocally decreases AKT1 phosphorylation at S473 or SMAD2/3 protein level. In addition, deciliated cells showed higher levels of pAKT1/AKT in both NS (2.36 ± 0.57 folds, $p < 0.01$, $n = 6$) and CMS (3.42 ± 2.14 folds, $p < 0.05$, $n = 6$). Finally, removal of PC disrupted the homeostatic IOP compensatory response and prevented the increase in LC3-II protein levels in response to elevated pressure challenge in pig eye (CNT VS deciliated; 2.55 ± 0.14 VS 1.31 ± 0.44 folds, $p < 0.05$, $n = 3$).

Conclusions: Our results strongly indicate that PC act as a mechanosensor for CMS-induced autophagy, and a novel cross-regulatory talk between AKT1 and SMAD2/3 signaling is critical components for its mechanism of action, which play a role in regulating IOP homeostasis.

CONTROL ID: 3540067

SUBMITTER (NAME ONLY): Omer Trivizki

TITLE: The Impact of Non-Exudative Type I Macular Neovascularization on the Growth of Adjacent Geographic Atrophy

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Trivizki, P. Iyer, G. Gregori, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|E. Moul, F. Fujimoto, Massachusetts Institute of Technology Department of Electrical Engineering and Computer Science, Cambridge, Massachusetts, UNITED STATES|O. Trivizki, Tel Aviv Sourasky Medical Center Ophthalmology Division, Tel Aviv, Tel Aviv, ISRAEL|

Commercial Relationships Disclosure (Abstract): Omer Trivizki: Commercial Relationship: Code N (No Commercial Relationship) | Eric Moul: Commercial Relationship: Code N (No Commercial Relationship) | Prashanth Iyer: Commercial Relationship: Code N (No Commercial Relationship) | Giovanni Gregori: Commercial Relationship(s); Carl Zeiss Meditec: Code P (Patent); Carl Zeiss Meditec: Code F (Financial Support) | Fujimoto Fujimoto: Commercial Relationship(s); Optovue : Code I (Personal Financial Interest); Optovue : Code P (Patent); Topcon: Code F (Financial Support) | Philip Rosenfeld: Commercial Relationship(s); Carl Zeiss Meditec: Code F (Financial Support); Carl Zeiss Meditec: Code C (Consultant)

ABSTRACT BODY:

Purpose: To determine if the growth of geographic atrophy (GA) is influenced by the presence of adjacent non-exudative type I macular neovascularization (MNV), we investigated local GA growth rates along segments of the GA margin at different distances to the adjacent type I MNV. We quantitatively computed the correlations between the local GA growth rates and their positions relative to the MNV lesions in a cohort of eyes having both type I MNV and GA.

Methods: Patients were enrolled into an ongoing institutional review board-approved prospective swept source OCT (SS-OCT) imaging study. Patients selected for this study were diagnosed with non-exudative type I MNV adjacent to an area of GA. Eyes with GA embedded within an area of type I MNV were excluded. The interval between the baseline and follow-up visits was 1 year. SS-OCT angiography (SS-OCTA) 6×6mm scans (PLEX Elite 9000, Carl Zeiss Meditec, Dublin, CA) were acquired centered on the fovea. GA was outlined using hyper-transmission defects identified on an en face structural slab positioned 64-400 µm beneath Bruch's membrane. MNV was outlined using an en face OCTA image from a slab projected between the RPE and Bruch's membrane. Regions of interest were manually traced and confirmed by two independent retina specialists. Pearson correlations were computed between the distance to the adjacent type I MNV versus local growth rates along segments of the GA margin, which were estimated using a biophysical GA growth model (Figure 1). P-values associated with the null hypothesis of no Pearson correlation were estimated using a Monte Carlo permutation scheme that incorporated the effects of spatial autocorrelation.

Results: To date, 9 eyes have been imaged and analyzed. In 7 of the eyes, global growth rates were lower than the average known growth rates for GA (Table 1). In 8 of the eyes there was a positive correlation between distance-to-MNV lesion and local GA growth rates; however, in all but 1 eye, correlations were weak (Table 1; Figure 1).

Conclusions: SS-OCT imaging combined with local GA growth analysis enabled measurement of quantitative associations between MNV position and GA growth direction. Our results are consistent with the possibility that there may be a very weak inhibitory effect of non-exudative MNV on the local growth of GA.

CONTROL ID: 3540073

SUBMITTER (NAME ONLY): Kati Tormanen

TITLE: HSV-1 virus lacking the small non-coding RNA 1 (sncRNA1) region has increased virulence in ocularly infected mice

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Tormanen, S. Wang, U. Jaggi, J. Yu, H. Ghiasi, Surgery, Cedars Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: HSV-1 LAT locus contains several miRNA and two sncRNA sequences. Currently, the function of the two sncRNAs in vivo is largely unknown. LAT is known to play a role in efficient establishment of latency and wild type reactivation, which are in part dependent on the antiapoptotic activity of LAT. Recently, the sncRNA sequences of LAT were shown to promote cell survival in vitro. Therefore, we tested what role, if any, one of these two sncRNAs is playing in vitro and in vivo by constructing a mutant virus (Δ sncRNA1), which lacks the sncRNA1 sequence.

Methods: We constructed an HSV-1 recombinant virus lacking sncRNA1 in McKrae background (i.e., Δ sncRNA1). Replication of the Δ sncRNA1 virus, was measured by plaque assay and LAT stability and expression of ICP0, ICP4 and gB transcripts in infected cells were measured by qRT-PCR. Female C57BL/6 mice were infected ocularly with 2×10^5 PFU/eye of wild type (WT) HSV-1 strain McKrae, LAT-deficient HSV-1 (dLAT2903) or Δ sncRNA1 virus. Virus replication in the eye (days 1-7) and eye disease (day 28) were determined. Level of latency, expression of viral and host transcripts and reactivation from latency were measured on day 28 post infection.

Results: Deletion of the 62 bp sncRNA1 sequence was verified by whole genome sequencing of the mutant virus. Δ sncRNA1 replicated slightly less efficiently in vitro, but similar to dLAT2903 and wt McKrae in vivo. There were no differences in eye disease, latency or reactivation between Δ sncRNA1 and wt McKrae. Interestingly, mouse mortality after ocular infection with Δ sncRNA1 was significantly higher when compared to either dLAT2903 or wt McKrae.

Conclusions: Our results suggest that sncRNA1 sequence of LAT may act to dampen the virulence of HSV-1 during an acute infection. The exact mechanism is currently not known, but likely involves regulating the host immune response to the virus. This hypothesis is currently being tested by Nanostring® assays.

CONTROL ID: 3540076

SUBMITTER (NAME ONLY): Solomon Gibson

TITLE: Serotonin receptor expression and function in mouse retina

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Gibson, B.J. Frankfort, Neuroscience, Baylor College of Medicine, Houston, Texas, UNITED STATES|S.E. Gibson, G. Shen, Y.H. Park, M. Polo-Prieto, B.J. Frankfort, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the retina, serotonin is implicated in neural processing, visual acuity, and neural development. There is some evidence that Selective Serotonin Reuptake Inhibitors (SSRIs), which increase the availability of extracellular serotonin, have a protective association against retinal neurodegenerative diseases such as glaucoma. Despite this potential importance, little is known about the mechanisms by which serotonin functions in the retina. For example, serotonin acts through serotonin receptors (HTRs), but little is known about the cellular distribution of HTRs in the adult retina. As glaucoma is a disease of retinal ganglion cells (RGCs), the purpose of this study is to investigate the expression and function of serotonin receptors in RGCs.

Methods: Adult mouse RGCs were isolated via immunopanning and underwent RNA sequencing as part of a previous study (Park et al., 2019). Sequence data were re-analyzed to determine the relative expression level of all known Htr genes. Immunohistochemistry (IHC) was performed in mouse retinal whole-mounts and 50 µm sections using primary antibodies to HTR1B and HTR1D, and imaged using confocal microscopy. Visual behavior was determined in Htr1b knockout (KO) mice using contrast-dependent optokinetic responses (OKRs) under scotopic and photopic conditions.

Results: Twelve Htr genes were expressed in adult RGCs, with Htr1b and Htr1d at the highest levels. IHC confirmed that HTR1B protein was present diffusely throughout the ganglion cell layer and inner plexiform layer, and that HTR1D protein was present in the ganglion cell layer where it labeled some but not all RGCs. Preliminary OKR analysis of 8-week old Htr1b KO mice (N = 6 eyes) showed reduced scotopic contrast sensitivity compared to heterozygous littermate controls (N = 18 eyes). However, contrast sensitivity did not vary significantly between groups at 20 weeks of age.

Conclusions: HTR1B and HTR1D are both expressed in RGCs, with HTR1B showing a broader pattern. Furthermore, our results suggest that HTR1B may be required for normal scotopic visual function in young adults but not older adults and therefore play a transient role in vision. Further studies will confirm these results and investigate additional roles of key serotonin receptors in RGC biology.

CONTROL ID: 3540110

SUBMITTER (NAME ONLY): Bernard Rosner

TITLE: Tutorial on Biostatistics: Receiver-Operating Characteristic (ROC) Analysis for Correlated Eye Data

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Rosner, R. Glynn, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G. Ying, M.G. Maguire, Penn Medicine, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Bernard Rosner: Commercial Relationship: Code N (No Commercial Relationship) | Gui-Shuang Ying: Commercial Relationship: Code N (No Commercial Relationship) | Maureen Maguire: Commercial Relationship: Code N (No Commercial Relationship) | Robert Glynn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To demonstrate methods for Receiver-Operating Characteristic (ROC) analysis of correlated eye data.

Methods: Using data from the Telemedicine Approaches to Evaluating Acute-Phase Retinopathy of Prematurity Study we previously developed a model for predicting development of treatment-requiring ROP (TR-ROP). The prediction model was based on data from 771 infants with birth weight <1251 grams who completed 1 retinal imaging session by 34 weeks of postmenstrual age and 1 subsequent retinopathy of prematurity (ROP) examination to determine TR-ROP. The factors in the model were: birth weight (BW), gestational age (GA), and findings from the first image session (IM). We calculated the AUC from a prediction model using BW, GA and IM and compared it to the AUC using BW and GA only. We used three methods to estimate the AUC and difference of AUC's for correlated eye data: the Naïve method (NA) treating eyes as independent, the Obuchowski (OB) and Cluster Bootstrap (CB) methods. The OB method empirically estimates the design effect and effective sample size to derive SE's and CI's for AUC estimates and can be used with covariates that are either continuous or ordinal. The CB method selects bootstrap samples (BOOT) by randomly sampling with replacement the same number of subjects as in a given sample and includes all eligible eyes from those subjects. The AUC is computed using BOOT and the process is repeated B times. The 95% CI for AUC is based on the 2.5th and 97.5th percentiles of the ordered distribution of AUC from the B samples.

Results: A comparison of the AUCs from the models predicting TR-ROP using BW and GA only, and using BW, GA and IM are shown in Figure 1 and Table 1. The point estimates of the AUC from the model with BW and GA were identically 0.802 from the NA and OB approaches, and quite similar to the CB approach, but the 95% CIs differed. The NA approach had a narrower width for the 95% CI (0.066) than the OB (0.093) or CB (0.090) approaches. The inclusion of IM findings significantly improved the AUC by 0.076, with narrower 95% CI of Δ AUC from the naive analysis (0.053) than from the OB (0.070) and CB approaches (0.070).

Conclusions: In ROC analysis of correlated eye data, ignoring inter-eye correlation leads to an inappropriately narrower 95% CI, while the OB or CB approaches can properly account for inter-eye correlation.

CONTROL ID: 3540161

SUBMITTER (NAME ONLY): Shigeo Tamiya

TITLE: Rho is involved in regulation of myocardin-related transcription factor and myofibroblast transdifferentiation of RPE cells

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tamiya, G. Jagatheesan, S. Ueda, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|S. Ueda, Tokyo Ika Daigaku Byoin, Shinjuku-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Myocardin-related transcription factor (MRTF) has been implicated as a key signaling molecule involved in transdifferentiation of retinal pigment epithelial (RPE) cells into myofibroblasts, which play a critical role in development of fibrosis. The purpose of this study was to examine the role of Rho signaling in MRTF function and myofibroblast transdifferentiation of RPE cells.

Methods: Transforming growth factor-beta2 (TGF-b2) was used to stimulate primary cultured porcine RPE cells. Confocal microscopy was utilized to examine immunocytochemically stained MRTF-A. Myofibroblast markers, alpha-smooth muscle actin (aSMA) and tropomyosin-1 (TPM1), was examined by western blot analyses. Myofibroblast function was assessed by collagen hydrogel contraction. The following inhibitors were used: CCG-1423, cell permeable C3 transferase, and Y27632 for inhibition of MRTF signaling, Rho and ROCK, respectively.

Results: TGF-b2 stimulation induced MRTF-A nuclear localization and myofibroblast differentiation, characterized by significantly increased myofibroblast marker expression as well as enhanced hydrogel contraction. CCG-1423 prevented induction of these myofibroblastic traits by TGF-b2, confirming the critical role of MRTF in myofibroblast transdifferentiation. Rho inhibitor suppressed MRTF-A nuclear localization, and significantly reduced myofibroblast marker expression as well as hydrogel contraction. In contrast, ROCK inhibition had little effect on TGF-b2 induced MRTF localization or myofibroblast differentiation, and significantly reduced hydrogel contraction only at a higher concentration.

Conclusions: Our data show Rho, but not its downstream effector ROCK, is involved in the regulation of MRTF localization and function. Further understanding of mechanisms involved in Rho activation as well as signaling linking Rho to MRTF nuclear localization may reveal novel targets for therapeutic intervention for fibrotic complications in which RPE cells play a significant role such as proliferative vitreoretinopathy or exudative age-related macular degeneration.

CONTROL ID: 3540176

SUBMITTER (NAME ONLY): Pawan Kumar Singh

TITLE: Resolvin D1 (RvD1) as an Adjunct Anti-inflammatory Therapy to Treat Bacterial Endophthalmitis.

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Singh, S. Singh, A. Kumar, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inflammation is a protective host response evoked during injury or microbial Infection. However, persistent inflammation can cause ocular tissue damage, warranting newer non-immunosuppressive anti-inflammatory therapeutic. In this study, we investigated the anti-inflammatory and adjunct therapeutic role of a bioactive lipid mediator, resolvin D1 (RvD1), in combination with antibiotics and steroids.

Methods: Endophthalmitis was induced in wild type C57BL/6 mice via intravitreal injection of *S. aureus*. Six hours post-infection, eyes were treated with RvD1, sub-MIC levels of vancomycin, and dexamethasone either alone or in various combinations. Untreated eyes and eyes with PBS injection were used as controls. The disease progression was monitored via ophthalmoscopic examination, electroretinography (ERG), histopathological exam, and bacterial burden estimation. The level of intraocular inflammatory cytokines and chemokines was assessed by qPCR and ELISA.

Results: Intravitreal injection of RvD1 either alone or in combination with vancomycin significantly improved the disease outcome as revealed by the drastically reduced bacterial burden, intraocular inflammatory cytokines (IL1 β and IL-6), and chemokines (MIP2 and KC), and preserved ERG 'a' and 'b' wave response. Among the combination therapies, RvD1 + vancomycin exhibited better resolution of inflammation in comparison to the dexamethasone + vancomycin combination. Importantly, RvD1 treatment protected mice even with the sub-MIC levels of vancomycin, whereas dexamethasone failed to exert protection under these conditions. The histopathological analysis also revealed that RvD1 can protect retinal tissue architecture either alone or in combination with vancomycin.

Conclusions: Our study demonstrates that RvD1 could be used as an adjunct therapy in combination with antibiotics to treat bacterial endophthalmitis. RvD1 therapy can also reduce the dosage of the overall antibiotics required to control bacterial proliferation in this devastating ocular complication.

CONTROL ID: 3540185

SUBMITTER (NAME ONLY): YUAN LIU

TITLE: Hematogenous Macrophages Contribute to Fibrotic Scar Formation After Optic Nerve Crush

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. LIU, H. Jin, X. Liu, M. Khodeiry, R.K. Lee, Ophthalmology, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the role of infiltrating hematogenous macrophages in optic nerve fibrotic scar formation and explore the potential effect of macrophage depletion in retinal ganglion cell (RGC) protection and optic nerve regeneration after traumatic injury.

Methods: Col1 α 1-GFP mice and C57BL/6 mice received clodronate encapsulated liposome injection to deplete hematogenous macrophage. Phosphate buffered saline (PBS) liposomes were used as injection vehicle control. Intravenous liposome injection was performed via the retro-orbital sinus 3 days prior to optic nerve crush (ONC) and 1, 4, and 7 after ONC. To further dissect the role of hematogenous and resident macrophages in scar formation, we used Dil liposomes to label hematogenous macrophages. Immunofluorescence staining was used to characterize fibrotic scar after macrophage depletion and differentiate the role of hematogenous macrophage and resident microglia.

Results: Hematogenous macrophages accumulated centrally in the fibrotic scar at the optic nerve crush site, while resident microglia were present at the edge of the scar. Hematogenous macrophage depletion reduced fibrotic scar formation in both Col1 α 1-GFP mice and C57BL/6 mice. The spindle-shaped optic nerve fibrotic scar was not present in the macrophage depleted treated group compared to the control-treated group. Macrophage depletion did not protect RGCs in the retina after traumatic optic nerve injury.

Conclusions: We characterized the fibrotic scar which forms after traumatic optic nerve crush and demonstrates that optic nerve scar formation is dependent on the infiltration of hematogenous macrophages. Depletion of hematogenous macrophages may be the first step towards axonal regeneration and functional recovery by reducing optic nerve scar formation.

CONTROL ID: 3540196

SUBMITTER (NAME ONLY): Jerome Roger

TITLE: CRX gene therapy targeting mouse models of dominant CRX-associated retinopathies.

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Roger, E. Grellier, S. Lourdel, M. Perron, Paris-Saclay Institute of Neuroscience, CERTO-Retina France, CNRS, Université Paris-Saclay, Orsay, FRANCE|

Commercial Relationships Disclosure (Abstract): Jerome Roger: Commercial Relationship(s);Variant:Code F (Financial Support);PCT/EP2020/056199:Code P (Patent);Variant:Code I (Personal Financial Interest) | Elodie-Kim Grellier: Commercial Relationship(s);PCT/EP2020/056199:Code P (Patent) | Sophie Lourdel: Commercial Relationship: Code N (No Commercial Relationship) | Muriel Perron: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Efficacy and safety of gene therapies for recessive retinal diseases (RDs) have been proven with preclinical success translated into clinical effectiveness. However, this approach is rarely chosen for dominant forms. Based on our published work, we decided to focus on dominant-negative mutations in the transcription factor CRX. We developed a mutation-independent AAV vector that could circumvent the clinical and genetic heterogeneity of CRX mutations.

Methods: To express CRX specifically in photoreceptors, the Rhodopsin Kinase 1 promoter and the AAV vector serotype AAV2/5 were chosen (AAV-CRX). To assess the efficacy of AAV-CRX for different CRX-associated diseases, we used $Crx^{Rip/+}$ mice, a model of Leber Congenital Amaurosis and we established a new model for cone dystrophy, $Tg(CRX^{R41W})$ carrying the human CRX^{R41W} mutation driven by Crx promoter. Subretinal injection was done in PN30 animals. Immunohistochemistry, immunoblot, and electroretinogram (ERG) were used for $Tg(CRX^{R41W})$ characterization and gene therapy efficacy assessment.

Results: $Tg(CRX^{R41W})$ characterization revealed a dose-dependent deleterious effect of CRX^{R41W} . Indeed, heterozygous $Tg(CRX^{R41W})$ carrying a single insertion displayed a functional retina while homozygous $Tg(CRX^{R41W})$ exhibited reduced cone function after 3 months. Presence of multiple copies led to rapid and severe photoreceptor degeneration after 2 months. Our results corroborated the relevance of increasing the amount of CRX^{WT} to counteract the dominant-negative effect of mutant CRX. We first verified that AAV-CRX injection led to specific and high expression of CRX in $Crx^{Rip/+}$ immature photoreceptors with no toxicity. In AAV-GFP $Crx^{Rip/+}$ injected retina, photoreceptors still lacked outer segments and visual transduction protein expression. In contrast, 3 months after injection, AAV-CRX led to i) rod and cone opsin expression, ii) outer segment formation, iii) some degree of ERG response whereas it remained flat in controls iv) fully restore behavior response to light stress using a Dark/Light box test. Homozygous $Tg(CRX^{R41W})$ mutant mice are also currently being tested.

Conclusions: Overall, our gene therapy approach shows promising results for treating CRX-associated RDs. It also highlights the potential interest of gene therapy to treat patients with RD carrying dominant-negative mutations.

CONTROL ID: 3540198

SUBMITTER (NAME ONLY): Jessica Morgan

TITLE: Cone mosaic integrity in choroideremia following gene augmentation via subretinal injection of AAV2-hCHM

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.I. Morgan, Y. Jiang, L.W. Serrano, D.J. Pearson, J. Bennett, A.M. Maguire, T.S. Aleman, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|J.I. Morgan, Y. Jiang, D.J. Pearson, J. Bennett, A.M. Maguire, T.S. Aleman, Center for Advanced Retinal and Ocular Therapeutics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jessica Morgan: Commercial Relationship(s);US Patent 8226236 :Code P (Patent);US Patent App. 16/389,942:Code P (Patent);AGTC:Code F (Financial Support) | Yu You Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Leona Serrano: Commercial Relationship: Code N (No Commercial Relationship) | Denise Pearson: Commercial Relationship: Code N (No Commercial Relationship) | Jean Bennett: Commercial Relationship(s);Limelight Bio:Code F (Financial Support) | Albert Maguire: Commercial Relationship(s);Spark Therapeutics:Code F (Financial Support);REGENX:Code F (Financial Support) | Tomas Aleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The subretinal injection used during delivery of gene therapy vectors forces the neural retina to detach from the retinal pigment epithelium posing a risk of photoreceptor damage. Here, we use adaptive optics scanning light ophthalmoscopy (AOSLO) to assess the integrity of the cone mosaic and evaluate cone densities before and one-month after subretinal injections of AAV2-hCHM in subjects with choroideremia (CHM).

Methods: Low dose (up to 5×10^{10} vector genome (vg) per eye, n=5) or high dose (up to 1×10^{11} vg per eye, n=4) AAV2-hCHM was delivered via unocular subfoveal injection in 9 CHM patients, ages 26-57. The macular regions of both eyes were imaged pre- and one-month post-injection using a custom-built, multimodal AOSLO. Images were montaged within each timepoint, then manually aligned across timepoints with cellular accuracy. Cone inner segments were manually identified in pre- and post-injection images at multiple regions of interest (ROIs) in both eyes in all subjects. Bound cone densities were compared between timepoints and between injected and uninjected eyes. AOSLO images were compared with spectral-domain optical coherence tomography (SD-OCT).

Results: AOSLO images showed preservation of the cone inner segment mosaic at one-month post injection in all 9 AAV2-hCHM injected eyes, with the exception of foveal disruption in one patient. Cone-by-cone longitudinal alignment was attained at multiple ROIs in every case. There was no significant difference in cone density across timepoints or between injected and uninjected eyes. Cone densities were the same for injected eyes pre- vs one-month post-injection (mean \pm standard deviation = $22,400 \pm 12,000$ vs $24,000 \pm 11,200$ cones/mm²) and uninjected eyes ($24,500 \pm 11,700$ vs $24,300 \pm 12,100$ cones/mm²). Post-injection SD-OCTs showed retention of the foveal inner segment ellipsoid zone (EZ) in all eyes, but loss of EZ definition and cone outer segment tip signal in the patient with foveal disruption.

Conclusions: Cone mosaic integrity is maintained following subretinal delivery of AAV2-hCHM, providing strong evidence in support of the safety of the surgical injections and short-term exposure to this viral vector. Individual vulnerability to the subfoveal injection may account for the foveal cone loss observed in one patient. Future studies will evaluate the integrity of the cone mosaic following long-term AAV2-hCHM gene augmentation.

CONTROL ID: 3540215

SUBMITTER (NAME ONLY): Jonathan Regenold

TITLE: Evaluation of correlation between Diopsys[®] NOVA fixed-luminance flicker electroretinography and Diagnosys[®] full-field electroretinography

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Regenold, H.L. Doan, A. Akhavanrezayat, M. Halim, A. Mobasserian, J.J. Hwang, N. Yavari, V. Bazojoo, W. Matsumiya, I. Karaca, B. Pham, B.C. Lam, S. Lajevardi, D.V. Do, Q.D. Nguyen, Byers Eye Institute, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center (OIRRC), Sunnyvale, California, UNITED STATES|H. Khojasteh, Farabi Eye Hospital, Tehran, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|H.L. Doan, Truong Dai hoc Y khoa Pham Ngoc Thach, Ho Chi Minh, Ho Chi Minh, VIET NAM|

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ABSTRACT BODY:

Purpose: Diopsys[®] NOVA is a novel full-field electroretinography (ffERG) device with the ability to make rapid measurements of retinal electrophysiologic function. Diagnosys[®] ffERG is a clinical gold-standard ffERG device that can take upwards of four hours to make measurements. The purpose of this study was to investigate whether Diopsys[®] NOVA fixed-luminance flicker ffERG magnitude measurements correlate with amplitude measurements of Diagnosys[®] 30 Hz flicker ffERG.

Methods: Eighteen patients (36 eyes) with a variety of retinal diseases were subjected to conventional 30 Hz flicker ffERG followed by Diopsys[®] NOVA fixed-luminance flicker ffERG. Diopsys[®] magnitude measurements were compared to conventional ffERG amplitude measurements, and a Pearson correlation was used to evaluate any existing correlation. A Bland-Altman plot was also utilized to determine agreement between ffERG modules.

Results: Mean age of patients was 51.3 ± 22.7 years old. 67% of patients were female. The average Diopsys[®] magnitude measurement was 9.79 ± 5.20 μ V while the average Diagnosys[®] amplitude measurement was 56.77 ± 31.85 μ V. A significant, positive correlation ($r=0.936$, $P<0.001$) was observed between magnitude (Diopsys[®]) and amplitude (Diagnosys[®]) measurements. All data points lay within ± 1.96 SD of the mean difference, and a negative bias of -46.98 μ V for the Diopsys[®] NOVA fixed-luminance ffERG flicker measurements. As magnitude and amplitude increased, the difference between these values also increased.

Conclusions: There is a statistically significant positive correlation between values of Diopsys[®] NOVA fixed-luminance flicker ffERG amplitude and Diagnosys[®] 30 Hz flicker ffERG magnitude. Agreement between the two systems of measurement is also demonstrated. Additionally, the Diopsys[®] based measurements have a negative bias compared to those of the conventional, gold-standard ffERG machine. This negative bias can be attributed to the skin electrodes used by the Diopsys[®] NOVA device in lieu of conventional ffERG corneal electrodes. These results suggest that the rapid Diopsys[®] NOVA module can produce accurate information assessing limited retinal function.

CONTROL ID: 3540225

SUBMITTER (NAME ONLY): Sanjay Patel

TITLE: Assessing the Severity of Fuchs Endothelial Corneal Dystrophy by using Scheimpflug Tomography

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.V. Patel, E.J. Treichel, K.H. Baratz, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sanjay Patel: Commercial Relationship(s);GlaxoSmithKline:Code C (Consultant);Senju Pharmaceuticals:Code C (Consultant);Santen Inc.:Code C (Consultant);Emmecell:Code C (Consultant) | Emily Treichel: Commercial Relationship: Code N (No Commercial Relationship) | Keith Baratz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Scheimpflug imaging can be used to predict the prognosis of Fuchs endothelial corneal dystrophy (FECD) by detecting tomographic patterns consistent with the presence of subclinical corneal edema based on posterior elevation and pachymetry maps. In this study, we developed a severity scale for FECD based on these maps, and evaluated intra- and inter-observer variation for assessing severity.

Methods: In a cross-sectional study, eyes with a range of severity of FECD were examined by two cornea specialists and underwent Scheimpflug imaging (Pentacam, Oculus). An ordinal scale was developed to assess the severity of FECD ranging from normal (grade 1) to severe edema (grade 6), based on loss of parallel isopachs, displacement of the thinnest point of the cornea, and posterior surface depression within the central 4 mm of the cornea. Subtle findings suspicious for early tomographic edema were defined as grade 2. Progressive severity of edema was based on the depth of posterior surface depression (mild, moderate, advanced, and severe were grades 3-6, respectively). Masked and randomized images were presented to both cornea specialists without associated clinical information. Intra-observer (1 observer evaluating the same images on 2 occasions separated by 2 weeks) and inter-observer agreement were assessed by using the kappa statistic (κ) with 95% confidence interval (CI), and McNemar's test for significant differences.

Results: Exact agreement between repeated assessments by one observer occurred for 97% (277/286) of eyes ($\kappa=0.96$, CI 0.93 to 0.99, $p=0.88$). All disagreements were by 1 grade only. Exact agreement between assessments by both observers occurred for 85% (244/286) of eyes ($\kappa=0.81$, CI 0.76 to 0.86, $p=0.12$). Disagreements were by 1 grade for 40 eyes and by 2 grades for 2 eyes, and mainly occurred because one observer assigned increased severity relative to the other when determining normal tomography from those with suspicious findings of early edema.

Conclusions: Assessing the severity of FECD from Scheimpflug tomography has excellent intra- and inter-observer agreement based on the proposed severity scale. The lower inter-observer agreement was a result of lack of sufficient standardization between observers rather than limitations of the imaging technology. Further investigation is needed to determine if this severity assessment can detect tomographic and clinical progression.

CONTROL ID: 3540232

SUBMITTER (NAME ONLY): Andrew Bower

TITLE: Direct comparison of photoreceptor reflectivity measurements using simultaneous adaptive optics SLO and OCT

SESSION TITLE: Advanced imaging technologies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate the similarities and differences in reflectivity of individual cone photoreceptors as seen by adaptive optics (AO) scanning light ophthalmoscopy (AO-SLO) in comparison to AO-optical coherence tomography (AO-OCT).

Methods: Simultaneous, co-registered AO-SLO and AO-OCT images unaffected by transverse or longitudinal chromatic aberration were acquired from three subjects at eccentricities from 2.5° to 10° temporal. Images were acquired using a custom multimodal AO ophthalmoscope in which 10% of the 1080 nm light returning from the eye was captured for AO-SLO using a custom-developed avalanche photodiode (Boston Micromachines), with the remaining 90% of 1080 nm light used for AO-OCT. Following manual identification of photoreceptors, the following measurements corresponding to single cones were extracted: (1) AO-SLO intensity, (2) AO-OCT inner segment/outer segment (IS/OS) junction intensity, (3) AO-OCT cone outer segment tip (COST) intensity, and (4) AO-OCT outer segment projection intensity. In addition, outer segment length was measured as the intensity peak-to-peak distance between the IS/OS and COST of each cone.

Results: The variable reflectivity observed in the cone photoreceptor mosaic matched well between the AO-SLO and AO-OCT projection images. AO-SLO intensities of 500 cones identified in the images were significantly correlated with outer segment projection intensity in AO-OCT ($p < 0.01$, F-test on linear regression), with stronger correspondence of the AO-SLO intensity to IS/OS intensity compared to COST intensity. Both the IS/OS and COST layers could be observed in 91% of cones. In the remaining 9% of cones, only a single reflection in the IS/OS was observed with no apparent corresponding COST reflection. When both IS/OS and COST reflections were observed, the IS/OS reflection was brighter for 88% of cones. There was no apparent relationship between AO-SLO reflectivity and outer segment length ($p > 0.01$, F-test on linear regression).

Conclusions: The use of a shared 1080 nm light source for simultaneous acquisition of AO-SLO images and AO-OCT volumes enables direct comparison of cone reflectivity across two inherently co-registered modalities. We show that cone reflectance on AO-SLO images arises more strongly from the IS/OS band, which may have implications for our understanding of cone waveguiding properties and their disc shedding processes.

CONTROL ID: 3540238

SUBMITTER (NAME ONLY): Sang Min Lee

TITLE: Histatin-1 attenuates the production nitric oxide by inhibiting MAPK signaling in LPS-induced RAW264.7 macrophages

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lee, K. Son, D. Shah, M. Ali, A. Balasubramaniam, V.K. Aakalu, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nitric oxide (NO) is a free radical which plays an important role in immune and inflammatory responses as an important intercellular messenger. In addition, NO has an important role in inflammatory responses in the ocular surface. Histatin peptides are well established antimicrobial and wound healing agents. These peptides are important in multiple biological systems, playing roles in responses to the environment and immunomodulation. Given the importance of macrophages in responses to environmental triggers and pathogens, we investigated the effect of histatin-1 (H1) on LPS-induced inflammatory responses and the underlying molecular mechanisms in RAW264.7 macrophages.

Methods: RAW264.7 mouse macrophages were stimulated by adding 10 ng/mL of lipopolysaccharide (LPS) with or without H1, dose-dependently. The production of NO were determined by Griess assay (Sigma, St. Louis, MO) in RAW264.7 seeded in 96-well plates. Expression of inducible nitric oxide synthase (iNOS) was measured by Western blot analysis. Activation of downstream signaling molecules were detected by Western blotting using phosphorylation specific MAPKs antibodies.

Results: Griess assay testing demonstrated that treatment with H1 inhibited significantly the LPS stimulated NO production in RAW264.7 cells, in a dose dependent manner. iNOS expression was detected in LPS treated RAW264.7 cells, and pre-treatment of H1 inhibited activation. Macrophages did not exhibit cytotoxic response to up to 100 μ M of H1 treatment. Phosphorylation of p38 and JNK1/2 MAPKs were inhibited after pre-treatment with H1; however, pro-survival ERK1/2 MAPK protein was not inhibited by H1 in LPS stimulated RAW264.7 cells.

Conclusions: These results demonstrate that H1 can inhibit LPS induced inflammatory mediator production via suppressing activation of MAPK signaling pathways in macrophages.

CONTROL ID: 3540243

SUBMITTER (NAME ONLY): LeAnne Young

TITLE: Automated detection of vascular leakage on fluorescein angiography

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Clinician interpretation of fluorescein angiograms (FA) can be subjective. In a translational study of FA images, we aimed to quantify variability of clinician FA segmentation and hypothesized a deep learning algorithm can segment FAs for vascular leakage and help detect clinically significant change.

Methods: 200 uveitis patient FA images were obtained. As the ground truth, a team of clinicians segmented images for vascular leakage. A deep learning algorithm with a modified U-net architecture was trained to segment leakage. The Dice Similarity Coefficient (DSC) was used to compare the algorithm's segmentation results to the ground truth segmentation (the DSC ranges from 0 to 1, 0 denotes no overlap between 2 segmentations and 1 denotes perfect overlap). For interrater variability, 2 clinicians independently segmented 20 images and the average DSC was calculated. Lastly, 20 pairs of FA images were used to detect clinically significant changes in leakage (the gold standard being an expert clinician's assessment). For each pair, the difference in percentage of the image occupied by the algorithm's leakage segmentation was calculated and used to create a ROC curve and to determine a threshold for clinically significant change.

Results: The 200 images came from 61 uveitis patients (median 2 images/patient, IQR 1-4). Diagnoses by anatomic location included anterior (2), intermediate (24), and posterior/panuveitis (35). The average FA timepoint was 361 seconds (SD 174). The algorithm achieved a best average DSC of 0.572 (Fig 1). Concordance between 2 clinicians was lower, with an average DSC of 0.374 (Fig 2). Lastly, a threshold of >0.8% change in the percent of the retinal area covered by the algorithm's segmentation had a 90% sensitivity and specificity for discerning clinically significant leakage (AUC: 0.95).

Conclusions: A preliminary deep learning algorithm was developed, had initial success in segmenting leakage in uveitis patient FAs, and was used to determine clinically significant change in vascular leakage. Further algorithm development is needed to improve segmentation accuracy. However, this is a first step to more standardized FA interpretation which can be useful as clinical trial outcomes.

CONTROL ID: 3540278

SUBMITTER (NAME ONLY): Xiaoqin Huang

TITLE: Detection of Glaucoma Progression from Retinal Nerve Fiber Layer Thickness Measurements Using Machine Learning

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To develop a machine learning model for detecting glaucoma progression from retinal nerve fiber layer (RNFL) thickness measurements acquired with optical coherence tomography (OCT).

Methods: We developed an unsupervised Gaussian mixture model with an expectation maximization (GEM) framework to identify clusters with similar RNFL thickness patterns in circular OCT scans (768 A-scans) from 691 eyes of 691 patients. We then identified the top prevalent eigenvectors (patterns) of the clusters representing eyes in the mild and advanced stages of glaucoma. We selected the slopes across these eigenvectors such that 95% of 2540 eyes in a separate longitudinal stable dataset (~9 follow-up visits) were not progressing. We used the selected slopes to test the model on a third longitudinal dataset with 254 eyes (~9 visits) and compared the detection rate of the proposed machine learning model with linear regression of RNFL summary parameters.

Results: Machine learning discovered three clusters within 691 RNFL thickness measurements of 691 eyes (Fig. 1). A total of 12 patterns of RNFL loss (eigenvectors) were prevalent and accounted for about 77% of the total variability in the data (Fig. 2). The machine learning model detected glaucoma progression in 38.6% of the eyes tested, while average RNFL in global, superior, and inferior hemifields detected progression in 15.8%, 13.0% and 15.0%, of the eyes, respectively.

Conclusions: The proposed machine learning construct identified a higher proportion of structural progression based on RNFL thickness measurements than linear regression of summary parameters. Additionally, the model identifies the major patterns of RNFL loss, which may aid clinicians in better monitoring of glaucoma subjects.

CONTROL ID: 3540292

SUBMITTER (NAME ONLY): Yang Liu

TITLE: Retinal structural and functional rescue by subretinal delivery of RS1 gene in mouse models of X-linked juvenile retinoschisis

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the retinal structural and functional rescue of gene supplementation therapy by subretinal delivery of human RS1 (hRS1) gene carried by AAV2 7m8 vector in mouse models of X-linked juvenile retinoschisis (XLRS).

Methods: Male pups from three mouse models, a knockout with inserted lacZ reporter gene, a C59S point mutant substitution, and an R141C point mutant substitution, were used for subretinal injection 1uL of AAV2 7m8-Rho-hRS1 at a titer of 3e13vg/mL on postnatal day 21 in the right eyes, and the left eyes were used as no treatment controls. In vivo retinal structural restoration was evaluated with optical coherence tomography (OCT) and functional rescue with electroretinography (ERG) at 2- and 4-months post injection. Ex vivo retinal tissues harvested at 4 months post injection were flat mounted for immunohistochemistry (IHC) using anti-RS1 and anti-arrestin antibodies to assess hRS1 expression and local retinal photoreceptor protection. A subset of retinal tissues from each group were examined using Western Blot (WB) to confirm hRS1 expression.

Results: Retinal structural rescue was observed 2 months through 4 months post subretinal injection in all three Rs1 mutant mouse models, manifested by disappearance of retinoschisis and well-organized retinal layers on OCT imaging, while controls eyes showed worsening retinal splitting and disorganization over time. Dark adapted ERG b wave at 2 months represented 17.2%, 28.2%, and 23.5% functional restoration, respectively compared to their control eyes, which maintained through 4 months post injection. IHC in retinal flat mounts showed the retinal areas covered by RS1 positive signal were 50-70%. WB under reducing condition showed monomeric hRS1 band from retinal samples of the treated eyes. Cone photoreceptor protection was observed locally where there was, or even no RS1 expression, to varying extent, in the treated eyes evidenced by arrestin immunostaining. The local structural protection and cone cell benefit were also observed in the treated eyes without functional rescue.

Conclusions: Subretinal delivery of AAV RS1 is effective in all three Rs1 mutant mouse models, providing partial retinal structural and functional restoration. Gene supplementation shows promise for XLRS gene therapy. Less invasive delivery method and robust photoreceptor promoters for more efficient treatment are being explored.

CONTROL ID: 3540302

SUBMITTER (NAME ONLY): Yangjiani Li

TITLE: Age-controlled correlation between oral glucose tolerance test (OGTT) and thicknesses of ten retinal layers in non-diabetes and prediabetes participants from macular optical coherence tomography (OCT) volume scans

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: People with prediabetes are at higher risk of developing diabetes. We investigate the age-controlled relationship between glucose parameters and ten retinal layer thicknesses in optical coherence tomography (OCT) macular volume scans of non-diabetic and prediabetic participants with/without glaucoma in a large study. The fasting, 30-min, and 2-h plasma glucose (FPG, 30-min PG, and 2-h PG) during an oral glucose tolerance test (OGTT) were employed.

Methods: All eyes of non-diabetic and prediabetic participants with available OGTT and OCT scans from the population-based, sex- and age-stratified LIFE-Adult study (age range: 20-80) were included. Macular volume scans (97 horizontal B-scans with 512 A-scans each) from Spectralis OCT were automatically segmented into ten layers (Figure 1) after exclusion of unreliable B-scans (quality < 20 dB). Pointwise partial Pearson correlation during OGTT adjusted for age was calculated. The analysis was repeated excluding participants with self-reported glaucoma diagnosis or medication.

Results: Figure 2 visualizes the age-controlled correlation of glucose level and A-scans in each layer from 5532 eyes of 2787 participants, including 128 participants with glaucoma. For FPG, a predominantly negative correlation (red) with layer thicknesses of RNFL, ONL, and MZ and a positive correlation (blue) with EZ and OS were observed (Figure 2A). Similar correlation patterns were found for 30-min PG with layer thicknesses of RNFL, MZ, and EZ, with a slightly increasing negative correlation with layer thicknesses of GCL and IPL (Figure 2B). For 2-h PG, there is an apparent negative correlation with layer thicknesses of GCL, IPL, and MZ (Figure 2C). The correlation patterns remained unchanged when participants with glaucoma were excluded.

Conclusions: There were specific correlation patterns between retinal layer thicknesses and measures during OGTT. With the prolongation of the time post-glucose intake, higher glucose level was more clearly related to thinner GCL and IPL and firmly associated with thinner MZ, while the correlation with RNFL, ONL, EZ, and OS became less pronounced. Macular layer thicknesses could be an early indication of the retinal structural change prior to diabetes

and in this cohort did not seem to be impacted by comorbidity of glaucoma.

CONTROL ID: 3540326

SUBMITTER (NAME ONLY): Jasmin Bhangu

TITLE: Imaging Outcomes Using Ultra-Widefield Fluorescein Angiography in Uveitis Patients on Adalimumab

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In this study we investigated whether quantitative analysis of leakage on ultra-widefield fluorescein angiography (UWFA) correlated with disease activity and severity in uveitis patients treated with adalimumab.

Methods: This is a retrospective case series. Patients were included if they were diagnosed with uveitis, were taking adalimumab during the 12-month follow-up period, had follow-up visits, and had UWFA imaging taken. Patients were classified as responsive to adalimumab if they had improvement or stabilization of disease on exam and/or imaging at 12-month follow-up; patients were categorized as non-responders if they had worsening disease at 12 months, stopped treatment, or switched to a different medication. Automated software (Early and Late phase Selection Application) was used to select the highest quality late-frame UWFA image. Leakage as a percent of retinal area was quantified using an automated algorithm (Image-Pro Analyzer 7.0). Leakage area and percent change in leakage over time were compared to LogMAR visual acuity, clinical disease activity, and treatment success or failure using linear regression analysis and two-tailed Student's t-test.

Results: A total of 20 patients (13 female, 7 male) were included in this study. 13 of 20 patients (65%) demonstrated some response to adalimumab, whereas 7 of 20 patients (35%) had no treatment response. At 12 months, treatment-responsive patients had a 62% decrease in leakage area compared to baseline, whereas treatment-failure patients had a 513% increase in leakage compared to baseline ($p = 0.02$). There was a small albeit significant correlation between leakage area and visual acuity ($r^2 = 0.08$, $p < 0.001$).

Conclusions: In this study, we show that leakage correlates with visual acuity and clinical response to adalimumab. Quantitative analysis of leakage on UWFA may be a useful novel biomarker in the evaluation of non-infectious uveitis in the clinical and research settings.

CONTROL ID: 3540334

SUBMITTER (NAME ONLY): Andrew Voigt

TITLE: Single-cell RNA sequencing identifies unique gene expression patterns in the foveal and perifoveal human retina

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.P. Voigt, N.K. Mullin, S.S. Whitmore, T.E. Scheetz, E.M. Stone, B.A. Tucker, R.F. Mullins, The University of Iowa Department of Ophthalmology and Visual Sciences, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: In different retinal diseases, photoreceptors cells at different eccentricities can be selectively damaged or spared. Previous investigations have identified unique foveal features by comparing gene expression between the foveal versus peripheral retina. We refined these preliminary studies by focusing on differences within the macula, comparing the fovea and the directly surrounding perifoveal retina with single-cell RNA sequencing.

Methods: Paired foveal (1 mm) and perifoveal (4 mm) neural retina samples were acquired from four human donor eyes. Retinal tissue was dissociated in papain for one hour and cryopreserved so that cell suspensions could be thawed in parallel for single-cell RNA sequencing. Resulting reads were mapped to the human genome with CellRanger and analyzed with Seurat.

Results: We recovered 5,856 foveal and 28,637 perifoveal cells that corresponded to all major retinal populations (Figure 1A). Next, we compared foveal versus perifoveal gene expression across all retinal populations. Foveal cone photoreceptors demonstrated increased expression of RPGR and RP1L1, which are mutated in cone-rod dystrophy and occult macular dystrophy, respectively. In contrast, perifoveal cone photoreceptors were enriched in COL4A3, a gene with AMD-associated genetic variants. Perifoveal Müller cells showed increased expression of the visual cycle genes RDH10 and RLBP1 as well as the iron-binding protein transferrin (TF). In addition, we compared results from this study to five independent single-cell RNA sequencing investigations comparing central versus peripheral retina (Figure 1B). Foveal enriched genes from our study were increased in the central retina from these datasets. Likewise, perifoveal enriched genes from our study demonstrated increased expression in the peripheral retina of these datasets.

Conclusions: Single-cell RNA sequencing reveals regional patterns of gene expression across many different retinal cell populations. We identified foveal enrichment or depletion of several transcripts involved in inherited retinal disease.

CONTROL ID: 3540358

SUBMITTER (NAME ONLY): Stephen Russell

TITLE: Safety and efficacy of sepfarsen in the second treated eye in a Ph1b/2 extension trial in Leber Congenital Amaurosis type 10 (LCA10)

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: LCA10 is a severe, degenerative inherited retinal disease resulting in childhood blindness, which has no treatment. Sepofarsen is an intravitreal RNA antisense oligonucleotide which showed clinically meaningful results following unilateral injection in a Ph1b/2 trial for LCA10 due to the c.2991+1655A>G mutation in the CEP290 gene. Safety and efficacy of sepfarsen dosed in the second eye was evaluated in the extension trial (Insight; NCT03913130).

Methods: Patients who completed the Ph1b/2 trial, multicenter, open-label, multiple-dose escalation sepfarsen trial were given the opportunity to enroll into the extension trial for continued dosing in their first treated eye as well as initiation of treatment in their second eye with the 160/80µg loading/maintenance dose, using a 6-monthly dosing interval. Nine out of 11 patients from the Ph1b/2 trial enrolled in the extension trial. As main efficacy parameters, change in Best-Corrected Visual Acuity (BCVA) and Full-Field Stimulus Test (FST) were assessed.

Results: At data cut-off in July 2020, 4 patients aged 15–45 years had received 1 intravitreal injection of sepfarsen in their second eye and had completed a 3- or 6-month visit. One patient developed cataract at Month 9 in the second treated eye. No other safety findings were reported. Meaningful BCVA improvements (>-0.8 logMAR) were reported in the second treated eye for 2 of the 4 patients, similar to the improvements observed in their first treated eye. All 4 patients showed a FST improvement ranging from -0.74 to -2.35 log cd/m², generally similar to the FST responses observed in their first treated eyes.

Conclusions: This data analysis strongly corroborates the clinically meaningful vision improvements and safety profile observed in the Ph1b/2 trial. Second eye responses to sepfarsen parallel the first eye treated responses both in visual acuity and retinal sensitivity (FST) improvements. Sepofarsen safety profile for the 160/80µg dose group in this extension trial is consistent with that observed in the Ph1b/2 trial. Further analyses on this ongoing extension trial and

the Ph2/3 trial (Illuminate; NCT03913143) are expected.

CONTROL ID: 3540388

SUBMITTER (NAME ONLY): Naomi Zatarain Barrón

TITLE: Early corneal surface changes after refractive surgery evaluated with an ocular surface analyzer

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Zatarain Barrón, C. Müller-Morales, E.O. Graue-Hernandez, A. Navas, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To evaluate early changes in corneal surface after refractive surgery by LASIK, with an ocular surface analyzer.

Methods: Pre- and 1-week post-operative measurements of OSDI score, Non-Invasive Tear Breakup Time (NIBUT), tear meniscus height (mm), and meibomian gland dropout (%) were made with the ocular surface analyzer LacryDiag (Quantel, Cournon d'Auvergne, France).

Results: 28 eyes of 14 patients were included. Pre- and post-op findings were as following: OSDI score from 8 to 18 ($p= 1.25$); NIBUT from 10.7 seconds to 6.2 seconds OD and 10.9 seconds to 6.3 seconds OI ($p= 1.10$); tear meniscus height from 0.5 mm OU to 0.3 mm OD ($p= 1.64$) and 0.2 mm OI (1.64); and meibomian gland dropout from 21.6 % to 21 % OD and 23.6 % to 23 % OI ($p= 1.50$).

Conclusions: Although statistically significant differences were not found between pre- and post-op measurements, there were clinical and symptomatic differences in patients.

CONTROL ID: 3540415

SUBMITTER (NAME ONLY): Hashem Ghoraba

TITLE: Safety of intravenous high-dose pulse methylprednisolone succinate in the management of pediatric uveitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Ghoraba, A. Akhavanrezayat, W. Matsumiya, B. Pham, C. Yasar, I. Karaca, A. Mobasserian, J. Regenold, B.C. Lam, J.J. Hwang, S. Lajevardi, N. Yavari, M. Halim, Y.J. Sepah, D.V. Do, Q.D. Nguyen, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|M. Halim, Ocular Imaging and Research Center, Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In this case series, we aim to evaluate the safety of intravenous high dose pulse methylprednisolone succinate (IVHDM) in the management of different types of severe or refractory non-infectious uveitis in a pediatric population.

Methods: We reviewed all uveitis patients who were 16 years of age or younger and who received IVHDM with a dose of ≥ 500 mg per day (1 to 3 days a month) for at least 3 months during their management at a tertiary care eye hospital between June 2018 and October 2020. Adverse events (AEs) were recorded up to 6 months after the last infusion.

Results: 20 pediatric patients who received IVHDM of dose of 500 mg or higher per day were identified. 6 patients received IVHDM only once and were excluded. The remaining 14 patients received IVHDM for at least 4 months, 1 or 3 consecutive days per month. Age was 11.9 ± 2.4 years and 5/14 were male. Duration of treatment was 12.1 ± 6.2 months. 13 patients received IVHDM in combination with other immunomodulatory therapy (IMT). IVHDM was given at a dose of 10-20 mg/kg/infusion. Mean cumulative dose per patient was 17.25 gm (Range: 3.5-50). Concomitant IMT was intravenous infliximab (8/13), tocilizumab (3/13) or immunoglobulins (2/13). Indications for IVHDM were panuveitis with retinal vasculitis (9/14), isolated retinal vasculitis (2/14), autoimmune retinopathy (AIR) (2/14) and juvenile idiopathic arthritis (JIA) associated optic neuritis (1/14).

There were three separate major systemic AEs in three separate patients: asymptomatic sinus bradycardia during infusions, pyogenic arthritis in a patient with a preexisting autoimmune arthritis and a single event of fainting and convulsions. The most common minor systemic AEs were derangements in blood count (10/14), mild increase in random blood glucose (10/14) and transient increase in liver enzymes (8/14). Cataract developed/progressed in 4 patients; 2 of them had been on long-term topical steroids.

Number of AEs was strongly correlated with duration of treatment (coef.:0.799; $p<0.001$) and moderately correlated with the cumulative dose (coef.:0.572; $p=0.033$). No statistically significant correlation was found with age of patients.

Conclusions: IVHDM might be a relatively safe therapeutic option for pediatric population with aggressive/refractory posterior or panuveitis. The reported AEs in this series can also be attributed to the concurrent IMT or the underlying disease itself.

CONTROL ID: 3540422

SUBMITTER (NAME ONLY): Alexis Ceecee Zhang

TITLE: Association between the systemic Omega-3 Index and corneal nerve architecture

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zhang, L.E. Downie, Optometry and Vision Sciences, The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA | J.P. Craig, Ophthalmology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND |

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ABSTRACT BODY:

Purpose: The Omega-3 Index is a measure of systemic levels of long-chain omega-3 fatty acids (FAs), eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The aim of this cross-sectional study was to investigate whether an association exists between the Omega-3 Index and corneal nerve structural parameters, in healthy controls and those with diabetes.

Methods: Participants with diabetes and no or mild peripheral neuropathy symptoms (n=26), and age- and sex-matched controls (n=21), underwent systemic FA analysis and comprehensive ocular surface assessments. Corneal sub-basal nerve structure was assessed by in vivo confocal microscopy and quantified with automated software. Corneal sensitivity was measured with non-contact esthesiometry. The relationship between systemic FA levels and corneal nerve parameters was evaluated using multiple linear regression (MLR), adjusted for age, sex, neuropathy symptom score, and the presence of both diabetes and dry eye disease (according to TFOS DEWS II criteria).

Results: The Omega-3 Index was similar in both groups (median [IQR]; control vs diabetes: 5.54% [4.54–6.06] vs 5.00% [4.25–5.68]; p=0.32). Corneal nerve fibre length (CNFL) was higher in the control group than in the diabetes group (mean \pm SD: 14.71 \pm 2.99 mm/mm² vs 12.60 \pm 3.41 mm/mm²; p=0.03). Using MLR modelling, Omega-3 Index (b=0.33; p=0.02), age (b=-0.46; p=0.001) and diabetes (b=-0.30; p=0.03) were significant factors associated with CNFL (R²=0.39, F=4.22; p=0.002). In a separate model, DHA (b=0.32; p=0.027) and age (b=-0.41; p=0.003) were associated with CNFL (R²=0.37, F=3.99; p=0.003). Neither EPA nor omega-6 levels were related to CNFL. There was no association between systemic FA levels and corneal sensitivity in either group.

Conclusions: This study newly describes a relationship between systemic Omega-3 Index and CNFL, the major anatomical feature of the corneal sub-basal nerve plexus.

CONTROL ID: 3540430

SUBMITTER (NAME ONLY): Jaclyn Hwang

TITLE: Altered patient demography and increased complexity of ICD coding in uveitis over 10 years

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Hwang, M. Halim, G. Uludag, C. Yasar, H. Ghoraba, B. Pham, S. Lajevardi, B.C. Lam, J. Regenold, V. Bazojo, I. Karaca, A. Mobasserian, D.V. Do, Y.J. Sepah, Q.D. Nguyen, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center, Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveitis is an inflammatory ocular disease and important cause of visual impairment and blindness. The purpose of this study is to delineate the demography and pattern of clinical coding between 2008 and 2018.

Methods: The Stanford Research Repository (STARR) Tools was used to identify 5,441 patients with International Classification of Diseases (Ninth and Tenth Editions) (ICD) codes for infectious and non-infectious uveitis in one academic institution (Table 1) in patients 18 years or older from 2008 to 2018. Patient demography (age, gender, race, ethnicity), pattern of ICD coding, and types of uveitis was analyzed using custom R scripts.

Results: Of 5,441 unique patients with infectious/non-infectious uveitis, analysis of patient demography revealed that age at first visit significantly increased between 2008 to 2018 ($p<0.001$), with no change in gender, race, ethnicity ($p>0.1$) (Table 1). Analysis of uveitis ICD codes revealed gradual increase in the number of infectious/non-infectious uveitis codes used and marked increase in the complexity of coding. In 2008, there were only 3 ICD codes used to designate infectious/non-infectious uveitis, which increased by 2014. By 2018, there were 9 different ICD codes. The most striking changes in ICD coding was in the frequency of ICD codes 135, 362.18, and 115.92. The most common ICD9 code in the data set was 135 (sarcoidosis); the usage of this ICD code significantly increased over the decade ($p<0.01$). In contrast, ICD9 codes 362.18 (retinal vasculitis) and 115.92 (histoplasmosis retinitis) were not commonly used at the beginning of the decade, but later in the decade, their use significantly increased ($p<0.001$). Despite its introduction in 2016, ICD10 codes were not used frequently. There was only one ICD10 code (B39.9) significantly used ($p<0.05$).

Conclusions: Analysis of patient demography and ICD coding of uveitis between 2008-2018 of uveitis in one academic institution revealed significant increase in age at first visit but not gender, race, and ethnicity and a dramatic increase in the usage of uveitis ICD codes and the complexity of uveitis coding. Despite its introduction in 2016, ICD10 codes are still relatively unused. Given the specificity of ICD10 coding to include laterality, etiology, anatomic parts involved, and severity, improved education and utilization of ICD10 coding can help elucidate the pattern and complexity of uveitis.

CONTROL ID: 3540439

SUBMITTER (NAME ONLY): Jingyun Wang

TITLE: Long-term Stability of Eccentric Fixation Measured by OCT in Children with Unilateral Amblyopia

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Lehman, D. Hendricks, J. Salvin, J. Jin, Nemours/Alfred I. duPont Hospital for Children, Delaware, UNITED STATES|J. Wang, SUNY College of Optometry, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using OCT, we were able to measure eccentric fixation in children with residual amblyopia (Jin et al, 2020). We found that the OCT fixation shift is significantly higher in amblyopic eyes than in fellow eyes, especially in strabismic amblyopia. However, we do not know whether eccentric fixation is stable over time. Here we report long-term follow-up of the OCT fixation shift in children with amblyopia.

Methods: Children with amblyopia (N=24) and normal controls (N=9) were studied. At their first visit (baseline), they ranged from 4 to 16 (8.5 ± 3.1) years old; amblyopia was classified into anisometropic amblyopia subgroup (N=9) and strabismic amblyopia subgroup (N=15). All had baseline and follow-up visits and the follow-up duration from baseline was 2.7 ± 1.8 years (5 months to 6 years). Spectral-domain OCT was used to estimate fixation shift. We asked the participant to focus on the internal dot target of the OCT. OCT fixation shift, i.e. the distance between the fovea and the fixation point, was measured, adjusted for axial length, and converted into visual degrees. Fixation shifts in the amblyopic eye, the fellow eye, and the right eye of the Control Group were compared by ANOVA. Baseline and follow-up results in the strabismic group were compared with the paired t-test. We also compared fixation shift change with visual acuity change between two visits for anisometropic versus strabismic amblyopia.

Results: At the baseline visit, the mean fixation shift was $0.05 \pm 0.10^\circ$ for control eyes, $1.50 \pm 1.87^\circ$ for amblyopic eyes, and $0.28 \pm 0.51^\circ$ for fellow eyes. At the follow-up visit, changes of fixation shift from baseline were $-0.02 \pm 0.06^\circ$ (CI 95%: -0.10, 0) for control eyes, $0.37 \pm 1.48^\circ$ (CI 95%: -0.62, 2.68) for amblyopic eyes, and $0.10 \pm 0.42^\circ$ (CI 95%: -0.25, 0.90) for fellow non-amblyopic eyes. ($F=0.62$, $P=0.54$). Furthermore, in the strabismic subgroup, the difference between baseline and follow-up fixation shift was $0.64 \pm 1.21^\circ$ (CI 95%: -0.62, 3.92), which did not change significantly ($T=1.37$, $P=0.19$). The visual acuity change and the fixation shift change were not significantly correlated ($R=0.24$, $P=0.39$).

Conclusions: Eccentric fixation, assessed by OCT fixation shift, is relatively stable during long-term follow-up of children with unilateral amblyopia.

CONTROL ID: 3540443

SUBMITTER (NAME ONLY): Leon Chea

TITLE: Unfolded Protein Response dysregulation prevents rhodopsin protein clearance and accelerates retinal degeneration in retinitis pigmentosa mouse model

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chea, E. Lee, J.H. Lin, Pathology, Stanford University School of Medicine, Stanford, California, UNITED STATES|L. Chea, E. Lee, J.H. Lin, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|P. Chan, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) causes retinal blindness due to loss of rods and later of cones. The P23H rhodopsin knock-in (P23H-KI) mouse develops retinal degeneration that closely mimics RP patients carrying the orthologous mutation. Previously, we found that P23H rhodopsin protein was robustly degraded in P23H-KI mouse retinas, and that Unfolded Protein Response (UPR) regulator genes promoted P23H rhodopsin protein degradation in heterologous cells in vitro. Here, we investigated the role of the UPR regulator gene, ATF6, in rhodopsin protein homeostasis in P23H-KI mice.

Methods: We compared retinas of ATF6^{-/-} Rho^{+/-}P23H C57BL/6 background mice with littermate control ATF6^{+/-} Rho^{+/-}P23H mice from postnatal days 12-60. Whole retinas were collected for western blotting and qPCR analyses of Rhodopsin (1D4) and UPR gene/protein quantification. Enucleations were cryo-sectioned, H&E stained, and retinal laminar anatomy examined and quantified. Full-field scotopic and photopic electroretinography (ERG) recordings were measured on dark-adapted mice at p60.

Results: Significantly increased rhodopsin protein levels (1.91x; p=0.0406) were found in ATF6^{-/-} Rho^{+/-}P23H retinas compared to ATF6^{+/-} Rho^{+/-}P23H mice at p12. Interestingly, IRE1a and BiP/Grp78 protein levels; and Xbp1s and Hrd1 mRNA levels were also significantly increased in ATF6^{-/-} Rho^{+/-}P23H retinas at early ages without gross changes in ONL thickness while Chop and Rhodopsin mRNA expression levels were not altered. By p60, ATF6^{-/-} Rho^{+/-}P23H mice showed increased retinal degeneration in comparison to control mice in all retinal layers by histology and reduced rhodopsin protein levels by immunoblotting. However, full-field scotopic and photopic ERGs were within normal limits for both ATF6^{+/-} Rho^{+/-}P23H and ATF6^{-/-} Rho^{+/-}P23H mice at p60.

Conclusions: We conclude that ATF6 is required for efficient clearance of P23H rhodopsin protein in rod photoreceptors, and loss of ATF6 leads to hyperactivation of the IRE1-XBP1s signaling pathway of the UPR. Despite these compensatory changes, ATF6^{-/-} Rho^{+/-}P23H mice develop more retinal degeneration as they age. Our findings show that UPR controls rhodopsin proteostasis in the retina and suggests that UPR activity influences the kinetics of retinal degeneration in RP patients expressing misfolded rhodopsin.

CONTROL ID: 3540454

SUBMITTER (NAME ONLY): Cigdem Yasar

TITLE: Novel retinopathy identified in pediatric retinal vasculitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Yasar, W. Matsumiya, A. Akhavanrezayat, H. Ghoraba, M. Halim, G. Uludag, B. Pham, J.J. Hwang, I. Karaca, S. Lajevardi, B.C. Lam, J. Regenold, Y.J. Sepah, Q.D. Nguyen, Ophthalmology, Byers Eye Institute at Stanford University, Palo Alto, California, UNITED STATES|M. Halim, Y.J. Sepah, Ophthalmology, 2. Ocular Imaging Research and Reading Center (OIRRC), Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A unique form of retinopathy was identified during the management of pediatric patients with retinal vasculitis and described in the index case series.

Methods: Pediatric patients diagnosed with uveitis were evaluated between January 2020 and December 2020 at a tertiary uveitis clinic. Wide angle fundus photo (WAFP), fundus autofluorescence (FAF), and optical coherence tomography (OCT) images were analyzed to identify potential retinopathy. Retinal vasculitis was detected by fluorescein angiography (FA). Images from both initial and follow-up visits were registered using image registration software. Subjects whose image quality was not sufficient for analysis were excluded. Boundaries of the lesions pertaining to the retinopathy were manually identified and annotated on WAFP using imaging tool. A custom MATLAB algorithm was utilized to assess the progression of the lesion.

Results: 54 pediatric uveitis patients were identified; 5 were excluded due to unavailability of WAFP and/or FA. Among the 49 patients, 26 were diagnosed with retinal vasculitis and were treated.

The retinopathy was detected in 20 patients (30 eyes) during the course of treatment. Mean age of the 20 subjects was 12.8 ± 3.36 years; 40% were female. Retinal vasculitis was observed in 8 patients with panuveitis, 8 patients with chronic anterior uveitis, 3 patients with posterior uveitis, and 1 patient with intermediate uveitis.

On WAFP, the lesions appeared as dark areas that were diffuse, mid-peripheral or peripheral (Image 1A). All subjects (30 eyes) showed hypoautofluorescence on FAF at the same locations as the WAFP (Image 1B). 8 patients (14 eyes) who had OCT images of the retinopathy area demonstrated ellipsoid zone (EZ) disruption (Image 1C).

Progression of the retinopathy over time was analyzed in 10 eyes; all eyes showed improvement of vasculitis with therapy. Mean area of retinopathy decreased from 670.82 mm^2 (baseline) to 479.92 mm^2 (last follow-up), which was not statistically significant ($p=0.16$).

Conclusions: Pediatric retinal vasculitis may be associated with a unique retinopathy pattern. Improvement in the retinopathy may not necessarily correlate to disease activity. The retinopathy might serve as a marker of previous/ongoing vasculitic events.

CONTROL ID: 3540461

SUBMITTER (NAME ONLY): Joao Leite

TITLE: Optical coherence tomography biomarkers as prognostic factors in diabetic macular edema treatment with ranibizumab – vitrectomized versus non-vitrectomized eyes

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Leite, A. Ferreira, J.H. Marques, J. Coelho, A. Meireles, J. Melo-Beirão, B. Pessoa, Centro Hospitalar Universitario do Porto EPE, Porto, Porto, PORTUGAL|J. Figueira, Centro Hospitalar e Universitario de Coimbra EPE, Coimbra, Coimbra, PORTUGAL|C. Coelho, Universidade de Lisboa Instituto de Saude Ambiental, Lisboa, Lisboa, PORTUGAL|

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ABSTRACT BODY:

Purpose: To evaluate the potential prognostic role of biomarkers in Optical Coherence Tomography (OCT) in vitrectomized and non-vitrectomized eyes treated with intravitreal ranibizumab injections, in patients with diabetic macular edema.

Methods: The eyes were grouped in vitrectomized (group 1) and non-vitrectomized (group 2). OCT biomarkers were assessed at baseline and at 12 months.

Primary endpoint: OCT biomarkers difference between both groups - presence of subretinal fluid (SRF), number of hyperreflective dots (HRD), disorganization of retinal inner layers (DRIL), disruption of outer plexiform layer (OPLd), external limiting membrane (ELMd), ellipsoid layer discontinuity (ELd) and presence of cysts in outer and inner nuclear layers (ONLc and INLc).

Secondary endpoint: OCT biomarkers difference and type of responder: 1) good-earlier responder: when beyond the 24th week of follow-up, there was a complete anatomical response (central foveal thickness, CFT, $\leq 300 \mu\text{m}$) with an increase in best corrected visual acuity, BCVA, ≥ 5 letters; 2) non-responder: CFT $>400 \mu\text{m}$ or $\leq 10\%$ of CFT reduction and BCVA gain <5 letters; 3) partial responder: between good and non-responder criteria.

Results: A total of 45 eyes (10 vitrectomized and 35 non-vitrectomized) from 38 patients completed the follow-up. Mean age was 66.8 ± 8.1 years. Comparing good-earlier responders vs partial/non-responders: 1) at baseline, the presence of INL cysts was lower in good responders (26.5% vs 73.5%, $p=0.035$); 2) at the end of follow-up, good responders maintained a lower percentage of INLc (26.5% vs 73.5%, $p=0.035$) and had a lower percentage of DRIL, OPLd and ONLc (12.0% vs 88.0%, $p=0.001$; 8.7% vs 91.3%, $p<0.001$; 17.4% vs 82.6%, $p=0.013$, respectively). An association between INLc and a higher glycated hemoglobin ($p=0.028$) was also observed at 12 months of follow-up.

Conclusions: This study highlights the prognostic value of some SD-OCT parameters, such as fewer INLc, which were associated with a better therapeutic response.

According to our results, a normalization of the macular anatomy through the disappearance of DRIL, OPLd and ONLc with ranibizumab is most likely to happen in early complete responders.

The association between INLc and higher glycated hemoglobin levels reinforces the relevance of systemic metabolic control in diabetic microvascular manifestations.

CONTROL ID: 3540474

SUBMITTER (NAME ONLY): Francesca Fortenbaugh

TITLE: Retinal Structural Changes Associated with Blast-Induced Mild Traumatic Brain Injury Identified on OCT Imaging

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess retinal morphology differences in Post-9/11 Veterans with and without a history of blast-induced mild TBI (bmTBI) using optical coherence tomography (OCT) retinal segmentation.

Methods: Seventeen participants with a history of bmTBI (33 eyes; bmTBI+ group) and 11 participants without a history of mTBI (22 eyes; bmTBI- group) during military service participated (mean age: 37 ± 9.9 ; 89% male). Participants were recruited from the Translational Research Center for TBI and Stress Disorders (TRACTS) longitudinal cohort study of Post-9/11 Veterans. All TRACTS participants complete the Boston Assessment of Traumatic Brain Injury – Lifetime (BAT-L), a semi-structured interview assessing TBI history prior to, during, and after military service. Military mTBIs are further classified as due to blast or blunt force trauma. An ophthalmic clinical exam was completed in a subset of TRACTS participants returning for a repeat evaluation from 2015 and 2017. This included Heidelberg Spectralis OCT scans of the peripapillary and macular regions. Peripapillary scans were dedicated to the retinal nerve fiber layer (RNFL) thickness. Macular retinal layers were segmented and included RNFL, ganglion cell layer (GCL), inner plexiform layer (IPL), inner nuclear layer (INL), outer plexiform layer (OPL), outer nuclear layer (ONL), and outer retinal layer thickness using an Early Treatment Diabetic Retinopathy Study (ETDRS) grid centered on the fovea (3 concentric rings at 1, 3, 6 mm).

Results: Linear mixed-effects models assessed differences across the bmTBI groups with grid location, eye, and age as fixed factors. The peripapillary RNFL was thinner in the bmTBI+ group ($p = 0.002$), and the difference was greater in the superior/nasal and inferior/nasal segments ($p = 0.007$). In the macular segmentation, the INL showed evidence of thinning in the bmTBI+ group ($p = 0.014$). In contrast, the ONL and outer retinal layer segment containing photoreceptors were found to be thicker in the bmTBI+ group ($p < 0.001$).

Conclusions: Blast mTBI was associated with thinning of inner retinal layers, in particular the peripapillary RNFL and macular INL. In contrast, outer retinal layers were found to be thicker. These results may support the chronic neuroinflammatory sequelae observed in recent animal models of low-level blast exposure on retinal morphology.

CONTROL ID: 3540477

SUBMITTER (NAME ONLY): Breedge Conwell

TITLE: TGFβ1 regulated gene expression in the trabecular meshwork

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Transforming growth factor beta (TGFβ) is a profibrotic cytokine that has been implicated in several disease processes such as cellular growth, differentiation, and extracellular matrix (ECM) synthesis. High levels of both latent and active TGFβ1 are prominent in the aqueous humour of patients with pseudo-exfoliation glaucoma (PXFG). The exact relationship between TGFβ1 induced gene regulation and outflow dysfunction in the TM, contributing to glaucoma development, remains unclear. Here we investigated differential changes in gene expression induced by TGFβ1 in a cell-based model of PXFG.

Methods: Primary normal trabecular meshwork cells isolated from donor human corneal rims (n=5) were treated with 5ng/mL TGFβ1 for 24 hours. RNA was extracted using the Qiagen AllPrep kit and RNA-sequencing was performed commercially. Sequencing libraries were generated using NEBNext® Ultra TM RNA Library Prep Kit on the Illumina platform. Bioconductor was used for primary gene mapping and differential expression. Gene pathways and interaction were analysed using DAVID, Reactome and Cytoscape. Genes from enriched pathways that appeared significant in all three databases were explored.

Results: RNA-sequencing analysis identified a total of 532 significantly ($p < 0.05$) upregulated and 480 downregulated genes in primary TM cells in response to TGFβ1. Significantly differentially expressed genes with a fold increase ≥ 1.5 (n=147) were subjected to a GO and KEGG enrichment analysis. High-ranking gene pathway interactions included TGFβ (PAdj 4×10^{-3}) and SMAD transduction (PAdj 4.9×10^{-7}) signalling, ECM organisation (PAdj 6.1×10^{-7}) and cell to cell communication (PAdj 3×10^{-4}) which strongly correlate to glaucoma.

Conclusions: The interaction between the differentially expressed genes and corresponding pathways, in response to TGFβ1, may play a critical role in PXFG development. Further exploration of the role of the TGFβ1 driven gene expression and pathway activation may elucidate the molecular mechanisms involved in PXFG and aid therapeutic development.

CONTROL ID: 3540484

SUBMITTER (NAME ONLY): Phoebe Shappell

TITLE: Effectiveness of High Concentration (0.05%) Brilliant Blue G for ILM Staining during Macular Hole Surgery

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.E. Shappell, T. Orton, J. Vannavong, A.A. Aziz, F. Siddiqui, A.M. Khanani, Sierra Eye Associates, Reno, Nevada, UNITED STATES|P.E. Shappell, University of Southern California, Los Angeles, California, UNITED STATES|J. Chhablani, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pars plana vitrectomy with ILM peel is a technique used to treat macular holes. The currently accepted technique is to use 0.025% Brilliant Blue G (BBG) dye to stain the ILM, but multiple staining attempts are often needed. Concentrations of 0.05% stain the ILM better, reduce the need for multiple staining attempts, and can thus result in shorter surgical times. Visual and anatomical outcomes were evaluated after use of 0.05% BBG in treatment of macular holes.

Methods: This is a retrospective interventional case study. From Sept. 2014 to July 2017 there were 159 patients identified as having undergone pars plana vitrectomy, 82 of whom were excluded for visually significant pathology including age-related macular degeneration, primary open-angle glaucoma, retinal detachment, retinal tear or other confounding pathology. 25 patients qualified the inclusion and exclusion criteria, and 27 eyes underwent surgical repair for macular hole. Clinical data was collected at baseline, 1, 3, and 6 months post operation. To measure ocular function, best-corrected visual acuity (BCVA), intraocular pressure (IOP), and central macular thickness (CMT) using Optical Coherence Tomography (OCT) were assessed.

Results: Baseline measurements of BCVA, IOP, and CMT were compared to the measurements from each follow-up. The average (standard deviation) baseline BCVA was 58(10) letters, IOP was 16(3), and due to presence of a macular hole there was no baseline data for CMT. 1,3, and 6 months after surgery average CMT was 297(65), 298(81), and 289(61) micrometers respectively. The average BCVA at 1,3, and 6 months was 58(19), 66(14), 67(13) letters respectively with an average change of +6.33 letters post operation. Average IOP measurement for 1,3, and 6 months post operation was 16(5),14(3), and 15(5) mmHg respectively with an average change of -1 mmHg.

Conclusions: Use of high concentration 0.05% BBG appeared to be safe for surgical treatment of macular holes with 100% success rate of closure and significant improvement in BCVA.

CONTROL ID: 3540486

SUBMITTER (NAME ONLY): Ashutosh Jnawali

TITLE: Evaluation of retinal shape and thickness with wide field OCT in young children

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Jnawali, F.A. Vera-Diaz, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P. Bex, Northeastern University College of Science, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Growing evidence suggests that retinal shape and retinal periphery are associated with myopia development and progression, and recent studies implicate a significant role of peripheral retina in emmetropization. However, previous studies on optical coherence tomography (OCT) imaging in children are limited to central 30 degrees retinal and choroidal thickness. We evaluated retinal shape and thickness for retina and choroid up to 55 degrees eccentricity in young children.

Methods: Radial scans (55°, 12 line) centered on the fovea in right eyes were collected with wide-field spectral domain OCT (Heidelberg) in healthy emmetropic children (n=37, ages 7.8±0.9 years) following a thorough vision exam. Images were processed in custom Matlab programs, and corrected for lateral magnification using biometric data collected for each eye (Lenstar) and a 4-surface schematic eye modified for children. Retinal and choroidal thickness were compared across eccentricities of 1, 3, 5, 8 and 12 mm, and across 4 retinal zones using one-way ANOVAs. Retinal curvature in the horizontal (RcH) and vertical meridians (RcV) were correlated with axial length (AXL) and mean corneal curvature (mean K).

Results: Retinae were steeper in the horizontal than the vertical meridian (RcH=12.4±1.8 mm, RcV=14.7±3.8 mm, t=5.31, p<0.001). RcH became steeper with increasing AXL (r=0.38, p<0.05) and mean K (r=0.42, p=0.01), while RcV showed no such relations. There was significant effect of retinal eccentricity for both retinal (p<0.001) and choroidal (p<0.001) thickness (retina central 1 mm: 272.3±21.5 µm, choroid central 1 mm: 366.38±75.13 µm), with the choroid becoming significantly thinner in the periphery. There was significant effect of retinal zone for retinal (p<0.001) and choroidal (p<0.001) thickness, with thinnest retinae temporally and thickest nasally, while the choroid was thinnest nasally and thickest superiorly.

Conclusions: We report asymmetries of ocular shape and retinal and choroidal thickness with wide field OCT in young children that confirm earlier studies and extend measurements to 55° eccentricity. Longer eyes, which are at greater risk of developing myopia, show steeper retinae in the horizontal, but not the vertical, meridian. The asymmetries in the horizontal and vertical meridians may have implications in eye growth and refractive development in children that we are investigating in a longitudinal study.

CONTROL ID: 3540503

SUBMITTER (NAME ONLY): Alex Wright

TITLE: Factors affecting time to recurrence of DME after anti-VEGF treatment

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Wright, J.C. Kuo, D.J. Chen, A.Z. Chuang, E.L. Crowell, Ophthalmology, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recurrent macular edema is of increasing interest in the management of diabetic macular edema (DME). The risk factors for the development of DME are well studied, but those affecting the time to recurrence of DME after treatment have not been well defined. Our objective is to identify factors affecting the time to recurrence of DME after treatment.

Methods: A retrospective chart review was performed on DME patients between 1/2010 to 6/2017 at Lyndon B. Johnson General Hospital. Patients over 18 years with DME and treated with anti-VEGF injection were included. If both eyes were eligible, the left eye was used for data analysis. Demographics and baseline systemic and ocular characteristics were recorded. Presence or recovery of DME, injections, and the last known HbA1C were recorded at each clinic visit. The time to recovery and recurrence were calculated. The cumulative number of anti-VEGF injections at the time of recovery and the Mixed Effect Cox regression was used to identify risk factors and estimate their effect on time to resolution and recurrence of DME.

Results: 114 patients were included in this study. 75 patients (65.8%) were female and 76 (66.7%) were Hispanics, 24 (21.1%) black, and 12 (10.5%) white, and 2 (1.8%) Asians. Mean age at anti-VEGF treatment for DME was 58.6 years (+8.0,27-75) with mean duration of DM 15.2 years (+6.9,1-36), and mean baseline HbA1c 8.8 (+2.1,5.7-15.1). During a mean follow-up period of 3.1 years (+1.7,0.1-7.8), 77 (67.5%) DME eyes were resolved for the first time at a mean of 1.2 years (+1.1,0.1-5.9) with a mean of 3.7 anti-VEGF injections (+2.1,1-10). After resolution, 46/77 eyes had a recurrence with mean of 2.0 years. No risk factors were associated with time to resolution, while males (Hazard ratio (HR) = 2.56 with 95% confidence interval (CI) = [1.30, 5.08], P=0.007) and longer duration of DM (HR=1.06 per year, 95% CI= [1.01, 1.18], P=0.013) significantly shorten the time to recurrence. HbA1c and number of anti-VEGF injections were not significant risk factors for resolution and recurrence of DME.

Conclusions: In our review, the duration of diabetes and male gender were significant factors associated with decreased time to recurrence of DME after treatment with anti-VEGF. HbA1c was not associated with time to recurrence. If confirmed by prospective clinical trials, this could help guide monitoring and treatment approach of DME in patients with a long history of diabetes.

CONTROL ID: 3540520

SUBMITTER (NAME ONLY): Steffen Künzel

TITLE: Low vulnerability of the human retina to SARS-CoV-2 infection - potential role of the choroidal vasculature

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Künzel, Ophthalmology, Charite Universitätsmedizin Berlin, Berlin, Berlin, GERMANY|T. Bürgel, Berlin Institute of Health, Berlin, Berlin, GERMANY|S. Künzel, Ophthalmology, Universitätsklinik Bonn, Bonn, GERMANY|J. Howard, A. Dubrac, Pathology, CHU Ste Justine / UMontreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Ocular manifestations have been described in COVID-19 patients, but it is unknown whether SARS-CoV-2 – the causal agent in COVID-19 – can directly infect posterior ocular tissues. Here, we investigate SARS-CoV-2 host factor gene expression levels and their distribution across retinal and choroidal cell types. The overall aim is to identify particularly vulnerable cell-types to elucidate a potential pathomechanism for observed retinal lesions in COVID-19 patients.

Methods: Datasets from human retina and choroid were retrieved from published datasets. We reprocessed the data from raw quantification matrix following standard Seurat (v.3.1) clustering procedure. To take advantage of the improved Seurat pre-processing and normalization workflow, we used the SCTransform function, thereby we “corrected” log-normalized expression values across datasets. To reannotate the cells, multiple clusterings of different resolutions were generated among which the one best matching published clustering was picked and manual annotation was undertaken using marker genes.

Results: Key genes for SARS-CoV-2 host cell entry are significantly lower expressed in human retinal cell-types compared to choroid. In detail, we observe no expression of ACE2 or TMPRSS2 in the retina, but a scarce co-expression in vessel associated cell-types of the choroid. No differences could be detected between fovea and periphery for both tissues.

Conclusions: Key conclusion:

The human retina is not vulnerable for a direct SARS-CoV-2 infection. Thus, retinal lesions as described in a recent Lancet publication by Marinho et al. are most likely due to a secondary damage (Marinho et al., 2020). However, SARS-CoV-2 entry genes are expressed in vessel-associated cell-types of the choroid. Thus, as described in other organs, the virus might infect the vasculature in terms of an infectious endothelitis, and could subsequently lead to vascular occlusions. Further studies are needed to elucidate whether vascular occlusions of the posterior eye segment correlate with life-threatening cardiovascular complications in COVID-19 patients. Thus, the posterior eye segment might qualify as an in vivo biomarker of systemic vascular disease in COVID-19 patients and imaging techniques of the posterior eye segment could be helpful for manage treatment of COVID-19 patients.

CONTROL ID: 3540543

SUBMITTER (NAME ONLY): Perrine Tami

TITLE: Factors Influencing Follow-up Appointment Delays in Glaucoma Practices

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.G. Tami, Dalhousie University Faculty of Medicine, Halifax, Nova Scotia, CANADA|J.R. Vianna, Ophthalmology & Visual Sciences, Dalhousie University, Halifax, Nova Scotia, CANADA|B.D. Eadie, Ophthalmology & Visual Sciences, Dalhousie University, Halifax, Nova Scotia, CANADA|

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ABSTRACT BODY:

Purpose: Glaucoma specialists provide care for many patients who require regular follow-up appointments. As their practices grow, it can become increasingly difficult to see patients at the recommended follow-up intervals. This study aims to find the factors affecting follow-up delays using computer simulations.

Methods: Three glaucoma specialists were surveyed to estimate the number and severity of glaucoma patients seen in a typical week. Patient severity was categorized as suspects, early, or advanced, and assumed to require follow-up appointments at 52, 26, and 13-week intervals, respectively. Multiple simulations were performed, each creating a new practice for one glaucoma specialist starting with no patients. The survey responses were used to simulate a baseline practice. Further simulations varied multiple parameters to explore their effect on follow-up delays. Simulation parameters included: number of new and maximum follow-up patients per week, patient severity distribution, patient chance of progression and loss of follow-up, proportion of patients discharged, appointment interval spacing (increasing the appointment interval if the patient is stable). For each simulation, we computed the week patients began to have delays and the increasing rate in the weekly mean delay (mean of the delay of patients seen in that week).

Results: The baseline practice had 30 new patients and a maximum of 120 follow-up patients per week. This practice started having follow-up delays at week 111, and the weekly mean delay increases at a rate of 7 weeks of delay per week. Most explored factors had a minor impact on practices delays, including appointment spacing or patient discharging (Fig. 1). The factor most strongly associated with practices delays was the ratio of new to follow-up patients per week (Fig. 2).

Conclusions: Most glaucoma practices are not able to follow patients within the required appointment intervals. While discharging and spacing stable patients reduce practices follow-up delays, these methods are insufficient to avoid large delays over the years. Practices need to reduce the number of new patients to avoid large delays in follow-up appointments; however, this could affect the wait times for initial appointments.

CONTROL ID: 3540544

SUBMITTER (NAME ONLY): Minnah Ahn

TITLE: Cone Contrast Threshold Measurements for Compressive Optic Neuropathies

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ahn, J.J. Wang, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A.N. Vu, J.K. To, A.W. Browne, R.W. Crow, L.S. Ediriwickrema, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A.W. Browne, Department of Biomedical Engineering, Institute for Clinical and Translational Science, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cone contrast test (CCT) is a computer-based contrast sensitivity test that quantifies the type and severity of color vision deficiencies by measuring patient response to varied intensities of visual cues stimulating red, green, and blue cones. Evidence has shown that CCT has greater sensitivity in detecting color vision deficits compared to Hardy Rand and Rittler (HRR) and Ishihara pseudoisochromatic plates. It has also demonstrated clinical utility in evaluating acquired color vision deficiency in glaucoma. In this prospective clinical study, our aim is to use CCT to characterize color vision deficiency in patients with compressive optic neuropathies (ON) secondary to neurological malignancies.

Methods: CCT scores of the right eye (10 control, 8 compressive ON) were included for analysis. Patients with malignancies that led to compression and damage of the optic nerve were included. Patients with glaucoma or other causes leading to ON were excluded. Color vision assessment was performed at 20 inches under photopic conditions using the ColorDx CCT (KonanMedical, Irvine, California USA) as part of normal course of care in a neuro-ophthalmology clinic. CCT provides a numeric, whole number score for each cone class, with lower scores indicating greater color vision deficit. Scores for each group were analyzed by independent sample t-test.

Results: Mean CCT scores for red and green cones were significantly lower in the compressive optic neuropathy group than in the control group. The mean CCT scores for blue cones were also lower in the compressive optic neuropathy group, but the difference was not statistically significant.

Conclusions: This data supports that compressive optic neuropathy is associated with decreased color vision. It reinforces a correlation between optic neuropathy and color vision and the utility of quantifying color vision to follow disease onset and progression. It further highlights that blue cone color quantitation may be less reliable than green and red, as shorter wavelengths can be filtered by anterior segment pathology such as cataracts.

CONTROL ID: 3540545

SUBMITTER (NAME ONLY): Zachary Bergman

TITLE: Attitudes and perceptions toward the use of medical marijuana for glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Bergman, O. Idowu, Ophthalmology, University of Maryland Medical Center, Baltimore, Maryland, UNITED STATES|M. Kaleem, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous work has demonstrated that inhaled tetrahydrocannabinol (THC) can lower intraocular pressure (IOP). The stance of the American Glaucoma Society (AGS) is that medical marijuana is not an acceptable treatment for glaucoma. However, the expanding legality of marijuana for both medicinal and recreational purposes makes it vital that ophthalmologists understand how marijuana can impact their patients. The purpose of this study is to evaluate ophthalmologists' perceptions and attitudes towards the use of medical marijuana for glaucoma.

Methods: An electronic survey was sent to members of the AGS which addressed attitudes and perceptions on the use of medical marijuana in the management of glaucoma. Study questions included practitioner demographics, previous experiences, prescribing patterns, and knowledge regarding the use of medical marijuana for the treatment of glaucoma.

Results: Thirty-seven percent of respondents reported having patients who cited using medical marijuana for their glaucoma, and 38% of respondents were asked about medical marijuana by their patients at least once per week. Fifty-five percent of respondents had patients who asked them for medical marijuana prescriptions. When asked if they felt if there was a role for marijuana in the management of glaucoma patients, 27% of survey takers responded yes. Twenty-eight percent of respondents from states where marijuana is currently legal medicinally and recreationally similarly thought there was a role for marijuana in glaucoma, compared with 14% of respondents from states where marijuana is currently not legal for medicinal or recreational use. Fourteen percent of survey respondents kept information on medical marijuana in their office. Finally, 76% of participants responded they would be interested in additional education on the topic.

Conclusions: Medical marijuana is not recognized as an acceptable treatment option for glaucoma by our professional societies. However, it is likely that the legalization of marijuana for both medicinal and recreational purposes will continue to become more widespread. Thus, it is vital that modern day ophthalmologists understand how marijuana can impact their patients.

CONTROL ID: 3540572

SUBMITTER (NAME ONLY): Shuichi Makita

TITLE: Accurately motion-corrected OCT by Lissajous scan and OCT-and-OCTA based motion correction

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Makita, Y. Yasuno, Computational Optics Group, Tsukuba Daigaku, Tsukuba, Ibaraki, JAPAN|M. Miura, Department of Ophthalmology, Tokyo Ika Daigaku Ibaraki Iryo Center, Inashiki-gun, Ibaraki, JAPAN|T. Mino, S. Azuma, T. Yamaguchi, Kabushiki Kaisha Topcon, Itabashi-ku, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Posterior eye imaging with optical coherence tomography (OCT) and OCT angiography (OCTA) suffers from involuntary eye movements. We have developed a motion-free Lissajous scan OCT method, which enabled accurate assessment of morphology and metrics of diseases. In this paper, further accurate motion correction is enabled by simultaneously using en face OCT and OCTA images for motion estimation. The performance is compared to the previous Lissajous method which uses only OCTA for motion estimation.

Methods: A custom-made 1.0- μm swept-source OCT device with a scan speed of 100,000 A-line/s is used. The OCT probe beam scans along a modified Lissajous pattern, which is designed for both OCT and OCTA. The eye motion is estimated by co-registering small overlapped portions of an en face Lissajous scan. Motion-free three-dimensional volumes and en face maps of OCT images were created by using the estimated motion amounts. The lateral motion estimation was performed by two means; (1) using only en face OCTA and (2) using en face OCT and OCTA. In order to compare the image qualities obtained by the two means, the motion-corrected superficial retinal OCTA images were manually scored from 0 (low) to 5 (high) by an expert.

For this comparison, 73 eyes of 64 patients with retinal abnormalities were scanned over $3 \times 3 \text{ mm}^2$ area.

Results: Figure 1 shows motion-corrected en face OCT and OCTA images of a representative case. The mean scores of the motion-corrected superficial OCTA images are 2.9 for OCTA-only motion estimation and 3.0 for OCT-and-OCTA correction. The score of OCT-and-OCTA correction is statistically significantly better than the OCTA-only correction ($p\text{-value}=0.02$, Wilcoxon's signed-rank test).

Conclusions: The motion-free Lissajous OCT with a newly developed OCT-and-OCTA based motion estimation gave better image quality than that with OCTA-only motion estimation.

CONTROL ID: 3540583

SUBMITTER (NAME ONLY): Jeffrey Cleland

TITLE: Single Subcutaneous Dose of Anti-Angiogenesis Drug Safely Suppresses Choroidal Neovascularization Comparable to Intravitreal Aflibercept

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Cleland, R. Sharma, S. Appiani, M. Sun, S. Kambhampati, Ashvattha Therapeutics, Inc, Redwood City, California, UNITED STATES|J. Prater, D. Culp, Powered Research, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the preclinical efficacy of subcutaneously administered D-4517 in a mouse model of laser-induced choroidal neovascularization (CNV) and its toxicity in a repeat dose rat study.

Methods: D-4517, a novel analog of sunitinib chemically conjugated to a hydroxyl dendrimer, selectively targets inflammation in CNV lesions. D-4517 is not metabolized and is renally excreted. Laser-induced rupture of Bruch's membrane was performed in both eyes of C57BL/6 mice (n=8/group) 24 hr prior to dose administration. Mice were dosed with a single subcutaneous (SC) administration of D-4517 at a total mass dose of 40, 200 or 1000 µg. As a positive control group, a cohort of mice were administered aflibercept intravitreally (IVT; 1 µL, 40 µg). The CNV area was measured 14 days after laser treatment by both fluorescein angiography and flat-mounts of the sclera-choroid/RPE complexes stained with Isolectin. To assess the toxicity of D-4517, a repeat dose study was conducted in Sprague Dawley rats (10 male/10 female per group). Rats were dosed daily for 14 days with 30 mg/kg sunitinib (PO) or 12 mg/kg D-4517 (IP; matched exposure to sunitinib) or a single dose of 168 mg/kg D-4517 (IP). Toxicokinetics, clinical evaluation, pathology, and histology were performed on all animals.

Results: A single SC dose of D-4517 (40 µg) resulted in comparable inhibition of CNV to a single IVT aflibercept dose (40 µg). All doses of D-4517 resulted in a significant inhibition of CNV formation compared to the vehicle control with all three dose levels resulting in comparable levels of CNV lesion area suggesting further dose reductions may be feasible. In the toxicology study, free sunitinib was associated with various clinical and pathological changes in addition to mortality in female rats. D-4517 was well-tolerated following single or repeated dosing with no clinical or histologic indications of toxicity.

Conclusions: After a single SC dose, D-4517 effectively inhibits CNV formation comparable to the same mass dose of aflibercept IVT. Previous studies demonstrated that HDs persist inside cells in the CNV lesion for at least one month after a systemic injection. Repeat dose toxicology in rats support at least an 80-fold safety factor for the effective dose. Taken together, these studies support the development of D-4517 as a potential once per month less invasive SC treatment for wet AMD.

CONTROL ID: 3540598

SUBMITTER (NAME ONLY): Isabela Vale

TITLE: Epidemiological profile of corneal transplant surgeries at Londrina Eye Hospital (HOFTALON), Brazil

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Vale, R.B. Trevisol, I.L. de Oliveira, T. Matsuo, E. Hoyama, Hoftalon Hospital de Olhos, Londrina, Paraná, BRAZIL|

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ABSTRACT BODY:

Purpose: A retrospective observational clinical study was performed to evaluate the characteristics of patients submitted to corneal transplantation surgeries in 2019.

Methods: Medical records of patients submitted to corneal transplantation from January to December 2019 at HOFTALON, Londrina city, Brazil were included. Sociodemographic data, visual acuity, cause of corneal transplant, topographic exam and complications were evaluated and submitted to statistical analysis. Exclusion criteria were incomplete medical records. Visual acuity was separated in categories: legal blindness, subnormal and normal vision.

Results: From 98 medical records evaluated, 91 patients submitted to corneal transplant surgeries were included. The mean age was 49.9 years, 50.5% were male. Glaucoma was the main ocular comorbidity, present in 11 (12.1%) patients.

The causes of corneal transplant were: keratoconus (35/38.5%), post-FACO decompensation (16/17.6%), primary transplant failure (8). The average waiting time from indication to surgery was 125 days. Regarding the surgical technique, 70 patients (76.9%) underwent penetrating keratoplasty (PK), 17 deep anterior lamellar keratoplasty (DALK) and 4 Descemet membrane endothelial keratoplasty (DMEK). 80 patients (87.9%) presented legal blindness (<20/400) before surgery, 6 (6.6%) subnormal vision (20/200-20/60) and 5 (5.5%) normal vision (20/50-20/20). A total of 61 patients (67%) improved vision after transplantation; of these, 11 improved two categories. 50% (35) of patients submitted to PK had improvement and 48.6% (34) maintained the same vision; 58.5% (10) submitted to DALK also showed improvement of vision. 64.8% didn't have complications, 30.8% presented corneal transplant failure and 4.4% developed glaucoma. 11(39.3%) patients had a successful clinical treatment for transplant rejection. The main treatment for rejection was topical corticosteroids, administered to 17 patients (60.7%) and Corneal rejection was proportionally greater in patients who underwent PK, but no statistical significance was observed. Corneal topography was performed in patients after transplantation, with an average K of 42.79.

Conclusions: Penetrating keratoplasty remains the most used technique in our Hospital and Keratoconus was the main cause of indication for surgeries. The most used treatment for corneal rejection was topical corticosteroids with a good response in our patients.

CONTROL ID: 3540602

SUBMITTER (NAME ONLY): Nour Atassi

TITLE: Ocular Graft vs Hosts Disease (oGVHD) After Allogeneic Hematopoietic Stem Cell Transplant (allo-HSCT): A 2 Year Longitudinal, Observational Study

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Atassi, B. Surenkhuu, J. Mun, C. Berek, A. Ahn, N. Dhall, C. Kim, S. Abdul-Hadi, A. Pradeep, C. Mun, S. Jain, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the pre-existing ocular findings that predispose to developing oGVHD in patients following allo-HSCT and evaluate the benefits of early treatment intervention. We performed a 2-year longitudinal, observational clinical study in patients undergoing allo-HSCT (n=105).

Methods: Patients received ocular examination and oGVHD grading in study visits. Examinations included slit lamp biomicroscopy, symptom analysis, Schirmer's I test, Corneal and Conjunctival staining, Bulbar redness scoring, Non-invasive Keratograph Tear Film Break-up Time, MMP-9 test, Lipid Layer Thickness, and Meibomian gland imaging. oGVHD grading was determined using the International Consensus Criteria on chronic oGVHD classification systems.

Results: 61 patients had at least one post-HSCT visit. Of these patients, 74% did not progress to oGVHD. 26% of patients progressed to Probable (n=7) or Definite (n=9) oGVHD. As compared to None oGVHD, greater number of Probable/Definite oGVHD patients had Meibomian gland dysfunction (reduced LLT), ocular surface inflammation (MMP-9 positive), and tear fluid deficiency (Schirmer's <10 mm/5min) in their pre-HSCT examination. Signs and symptoms of oGVHD appeared between 6-9 months post-HSCT. Topical steroid treatment was given in patients with None oGVHD (n=4) or Probable oGVHD (n=3), and these patients did not progress to Definite oGVHD. Topical anti-inflammatory treatment was initiated most commonly due to MMP9 becoming positive. Other common reasons were: (i) tear production reduced to <10 mm/5min; and (ii) increase in OSDI symptom analysis score to >13.6.

Conclusions: Patients who have reduced tear production, Meibomian gland dysfunction, or ocular surface inflammation have a higher likelihood of developing oGVHD after HSCT. Starting anti-inflammatory treatment earlier, based on MMP-9 positivity, increased symptoms of ocular discomfort, or reduced tear production, may prevent progression to Definite oGVHD. Ocular examinations pre-HSCT and every three months post-HSCT, may help to reduce the incidence of oGVHD by facilitating early diagnosis and early therapeutic interventions.

CONTROL ID: 3540608

SUBMITTER (NAME ONLY): Lakshmi Rajagopalan

TITLE: Comparison of visual function in a non-human primate (NHP) model of retinal injury to human age-related macular degeneration (AMD) patients

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Rajagopalan, K. Dhakal, C. Ghosn, B. Anders, M. Engles, Eyecare Research, AbbVie Inc, Irvine, California, UNITED STATES|W.H. Ridder, Basic vision science, Southern California College of Optometry, Fullerton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the visual deficit in NHPs with blue light induced macular injury to a cohort of AMD patients using similar imaging and vision psychophysics testing.

Methods: For the NHP study, 8 cynomolgus monkeys were unilaterally irradiated (study eye, SE) with blue light centered on the macula (8 mm diameter) for 20 to 30 min; contralateral eye (non-study eye, NSE) remained naïve. For the human study, 10 AMD patients with simplified Age-Related Eye Disease Study (AREDS) scores 3 or 4 and 8 age-matched Controls were enrolled. Both, NHP and human subjects were evaluated with fundus autofluorescence (FAF) and optical coherence tomography (OCT) to quantify retinal pigment epithelium (RPE) disruption and outer nuclear layer thickness (ONL). Contrast sensitivity functions (CSF) were used to evaluate visual function using the same custom software suite. NHPs were placed in a primate chair in a custom-made testing chamber. They were trained to hold and then release a lever when a visual stimulus was detected (i.e., “hit”); otherwise non-response was considered a “miss”. Threshold was operationally defined as two successive misses in a descending method of limits (1.5 to 24 cycles per degree (cpd); 5 steps). For the human subjects, a descending method of limits was combined with a 2 Alternate Forced Choice technique (0.75 – 18.50 cpd; 8 steps). The CSF was fit with a double exponential function.

Results: The clinical presentation of the lesions between NHPs and humans was different. In the NHPs, the lesion was diffuse (late stage AMD; GA); in the humans it was multi-focal (early stage AMD). In NHPs, mean log contrast sensitivity (CS) was 1.27 ± 0.06 (NSE) and 0.73 ± 0.08 (SE). Peak reduction was 0.68 log units at 6 cpd. In the human study, mean log CS in the control subjects was 1.34 ± 0.07 while in AMD patients it was 1.28 ± 0.06 . Peak reduction was 0.16 log units at 3 cpd.

Conclusions: Using similar instrumentation, we found a reduction in CS in the NHP model and human AMD patients. The reduction in CS correlated with the severity of the damage. These results demonstrate that vision psychophysics can be used as a valuable tool in evaluating disease models and efficacy prior to clinical study initiation and inform the best selection of sensitive vision endpoints to use with patients.

CONTROL ID: 3540613

SUBMITTER (NAME ONLY): Haig Pakhchanian

TITLE: National Trends of Ophthalmic-Related Procedures during the COVID-19 Pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Pakhchanian, S. Bellur, M. Dalal, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|H. Sen, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has caused significant disturbances as stay-at-home restrictions have prevented adequate healthcare delivery. This investigation aimed to assess the pandemic's impact on the incidence of ophthalmic-related procedures compared to the pre-pandemic period.

Methods: TriNetX (Cambridge, MA, USA) is a real-time, federated healthcare database that was used in this retrospective review. At the time of the study, the database included 60 million unique electronic medical records (EMR) of patients from 41 healthcare organizations (HCOs) across the US. The goal of this study was to analyze the incidence of new ophthalmic procedures that were performed during a period of the COVID-19 pandemic from April 1, 2020 - September 30, 2020. April 2020 was used as the start date as this was the first full month when national lockdown measures were implemented in the USA. Similar incidence data was also extracted from the corresponding time frame of April to July in 2018 and 2019. The 2020 data was then compared to a pooled 2018-2019 data of the same time period through descriptive analyses and an independent samples t-test.

Results: The incidence between fourteen types of ophthalmic procedures experienced a statistically significant reduction between April 1 to September 30, 2020 when compared to overlapping months in 2018 and 2019. Thirteen of the fourteen procedures saw at least a 32.0% decrease in incidence. These procedures included: Keratorefractive surgery (-60.3% change, $p < 0.001$), keratoplasty (-58.4% change, $p < 0.001$), cataract surgery (-50.5% change, $p < 0.001$), pterygium (-49.0% change, $p < 0.001$), oculoplastic (-47.7% change, $p < 0.001$), YAG capsulotomy (-44.3% change, $p < 0.001$), strabismus (-43.2% change, $p = 0.004$), laser trabeculoplasty (-40.1% change, $p < 0.001$), retina surgery (-38.5% change, $p < 0.001$), glaucoma (-36.1% change, $p < 0.001$), panretinal laser photocoagulation (-33.9% change, $p < 0.001$), and intravitreal injection (-32.0% change, $p < 0.001$). The incidence of global trauma during the COVID-19 pandemic was similar to identical months in 2018-2019.

Conclusions: The significant reduction in ophthalmic procedures during the COVID-19 pandemic suggests that patients are delaying ophthalmic care in the US. Further research is necessary to determine the future implications of this disruption in the care of ophthalmic patients during the COVID-19 pandemic.

CONTROL ID: 3540624

SUBMITTER (NAME ONLY): Logan Vander Woude

TITLE: Novel Positive Predictive Factors in Ocriplasmin Efficacy in Symptomatic Vitreomacular Traction

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Vander Woude, G.S. Khurshid, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocriplasmin (OCP) is an enzymatic vitreolysis for symptomatic vitreomacular traction (VMT). Initial trials of OCP yielded tepid results; however, post hoc analysis has provided positive predictive factors for successful outcomes, including age <65 years, phakic eyes, adhesion diameter <1500 microns, and absence of epiretinal membrane (ERM). Continued refinement of positive predictive factors helps to identify optimal patients for OCP treatment. This retrospective case series describes novel positive predictive factors in treating symptomatic VMT.

Methods: This retrospective case series included 11 patients diagnosed with symptomatic VMT and treated with OCP at the University of Florida from 1/1/2015 to 7/1/2020 regardless of their phakic status, presence of ERM, age, or initial visual acuity (VA). Patients were excluded from receiving OCP treatment if they were aphakic, had >8 diopters of myopia or an axial length >28mm, vitreous opacity obscuring posterior pole visualization, diffuse VMT (>1500 microns), stage 2 or greater macular hole, or other concurrent retinal diseases. The de-identified data was then collected and analyzed using Z-test statistical analysis. The primary outcome measured was the resolution of VMT as defined by optical coherence tomography (OCT).

Results: Of the 11 patients treated with Ocriplasmin, 63.6% had resolution of their VMT. Subgroup analysis was conducted for initial visual acuity and adhesion diameter, as measured by OCT. Patients whose initial VA was $\leq 20/50$ all had resolution of their VMT and did significantly better compared to initial VA of $\geq 20/60$ among all patients ($p=0.011$) and when controlling for ERM ($p=0.037$). In subgroup analysis of micro (<500 microns) versus focal VMT (500-1500 microns), micro VMT trended towards greater resolution, 85.7% vs 50%, respectively ($p=0.142$) [Figure 1].

Conclusions: The continued refinement of positive predictor factors is paramount to improving the efficacy of OCP and its cost-effectiveness. The greater resolution rate in micro VMT was not statistically significant in this small case series but warrants further investigation. OCP may have greater efficacy in patients with symptomatic VMT with VA $\leq 20/50$, which may impact useful clinical practice with earlier treatments.

CONTROL ID: 3540644

SUBMITTER (NAME ONLY): Samantha Lee

TITLE: Correcting for axial length in macular thickness analyses

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: When measuring macular thickness using optical coherence tomography (OCT), axial length (AL) is known to affect the size of the scanning area due to transverse magnification effects (TME). However, most studies do not adjust for TME when reporting or analysing macular thickness. In this study, we compared macular thickness with and without TME correction in a large cohort of young adults.

Methods: In a sample of 953 healthy adults in a general population (18-22years; 22% myopes, AL range: 20–28mm), the full retinal thickness at the 9 Early Treatment of Diabetic Retinopathy Study (ETDRS) macular regions (central macula, and the superior, inferior, temporal, and nasal quadrants of the inner and outer macular rings) were obtained using spectral domain OCT. Images were exported into a custom MATLAB program that corrected for TME. Paired t-tests were used to compare TME-corrected and uncorrected measurements. Statistical associations between the TME-corrected or uncorrected measurements with AL and other known predictors of macular thickness (sex, ethnicity, choroidal thickness) were explored using generalized estimating equations.

Results: In the full study sample, failure to account for TME resulted in under-estimation of macular thickness at the central 0.5mm and over-estimation at other regions by 0.1–3.4µm (all $p < 0.001$). Conversely in myopes, uncorrected measurements over-estimated thickness at the central macula and under-estimated at other regions (all $p < 0.001$; difference=1.6–5.9µm). At the central macula, AL was not statistically associated with the uncorrected measurements ($p = 0.77$) but had an inverse relationship with the TME-corrected thickness ($p < 0.001$). At all other macular regions, there were significant associations between AL and uncorrected macular thickness, but not TME-corrected thickness. Sex, ethnicity, or choroidal thickness associations with macular thickness did not differ between the corrected and uncorrected measurements.

Conclusions: In a general population where the majority are non-myopes, the macular thickness measurement error produced by TME is small and may not be clinically significant. However, as the global population becomes more myopic, this measurement error will increase. It is thus important to use TME-corrected macular thickness when exploring associations with AL or when study samples have high rates of ametropia.

CONTROL ID: 3540668

SUBMITTER (NAME ONLY): Dimitrios Ntentakis

TITLE: Vitreoretinal lymphoma: clinical features, treatment, and outcomes

SESSION TITLE: Advances in intra and extra ocular pathologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Ntentakis, S. Bagheri, M. McGarrey, L. Sobrin, I.K. Kim, D. Elliott, M.E. Aronow, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L. Nayak, Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze a large cohort of individuals with primary central nervous system lymphoma (PCNSL) and vitreoretinal lymphoma (VRL) from a tertiary care center.

Methods: A retrospective review of all patients with PCNSL and VRL at Massachusetts Eye and Ear from January 01, 2004 to April 1, 2020 was performed. Demographics, affected site at diagnosis (eye, central nervous system (CNS), or both), lymphoma subtype, MYD88 mutational status, local treatment type (intravitreal chemotherapy vs radiation), local recurrence, and progression from the eye to the CNS or vice versa were analyzed.

Results: 49 patients (46.9% female) with a median age at diagnosis of 64 years (range, 35-91 years) were analyzed. At diagnosis, 30 patients (61.2%) had CNS, 13 (26.5%) had eye, and 6 (12.3%) had eye + CNS involvement. Median time to diagnosis was 2.7 months (eye + CNS), 2.8 months (CNS), and 10.1 months (eye). Eye involvement was bilateral at diagnosis in 78.9%. Common diagnoses prior to confirming VRL were: vitritis (10.2%), uveitis (6.1%), and retinitis (2.0%); 6.1% received prior steroid treatment. Cytopathology confirmed diffuse large B-cell lymphoma in 46 (93.9%), T-cell in 2 (4.1%), and other in 1 (2.0%). MYD88 mutational analysis was performed in 9 out of 19 patients (47.4%) with eye involvement and was positive in 8 out of 9 patients (88.9%). A total of 56 eyes had initial or subsequent VRL, of which 32 eyes (57.1%) received local ocular therapy: 26 eyes (81.3%) with an intravitreal methotrexate-based regimen (MTX, 400 mcg/0.1mL), 2 eyes (6.3%) with radiation (30 Gy), 2 eyes (6.3%) with combination (intravitreal MTX + radiation), and 2 eyes (6.3%) by enucleation. At last follow-up (median 63.1 months), local ocular recurrence occurred in 5 eyes (19.2%) treated with intravitreal therapy and 0 eyes treated with radiation. Nine patients (69.2%) with initial eye only disease progressed to involve the CNS (median time to progression: 28.5 months) and 13 patients (43.3%) with initial CNS disease progressed to involve the eye (median time to progression: 14.1 months). At last follow-up, 33 individuals (67.3%) were alive.

Conclusions: Time to diagnosis was 3.7 times longer for VRL alone, compared to those with CNS involvement. MYD88 testing was helpful for diagnosis (positive in 88.9%). Both intravitreal MTX and radiation achieved excellent ocular control (80.8% and 100.0%, respectively), however 69.2% ultimately progressed to involve the CNS.

CONTROL ID: 3540669

SUBMITTER (NAME ONLY): Michael GUERRA

TITLE: Application of Electric Cell-Substrate Impedance Sensing (ECIS) to investigate the effect of mitochondrial bioenergetics on retinal pigment epithelial barrier functionality

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. GUERRA, T. Yumnamcha, L.P. Singh, A.S. Ibrahim, Department of Ophthalmology, Visual, and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|A.S. Ibrahim, Department of Pharmacology, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Disruption of retinal pigment epithelial (RPE) barrier integrity is a hallmark feature of age-related macular degeneration (AMD), but the underlying causes and pathophysiology are not completely well-defined. One of the most conserved phenomena in biology is the progressive decline in mitochondrial function with aging. This study aimed to investigate the role of mitochondrial bioenergetics in maintaining RPE barrier functionality RPE.

Methods: We used ECIS system to monitor in real time the barrier integrity of RPE cell line (ARPE-19) after treatment with one of four mitochondrial electron transport chain (ETC) inhibitors (Rotenone for complex 1, Oligomycin for Complex IV, trifluoromethoxy carbonyl cyanide phenylhydrazone FCCP for uncoupling ATP synthesis from ETC, and cobalt chloride (CoCl₂) as hypoxia-mimetic agent). We investigated how the resistance across ARPE-19 cells changes in three separate parameters: Rb (paracellular resistance between cells), α (basolateral resistance between RPE and its substrate), and Cs (cell membrane capacitance). Statistical analysis was performed using ANOVA test followed by Tukey post hoc test with $p < 0.05$ considered significant.

Results: Treatment with CoCl₂ and FCCP induced a significant reduction in the total resistance and thus the barrier function of ARPE-19 in a dose dependent manner. Treatment with rotenone decreased barrier function in a non-dose dependent fashion, whereas only treatment with a high dose oligomycin (10 μ M vs 1 μ M) disrupted barrier function. Specifically, the ECIS program's modelling of paracellular resistance, basolateral resistance, and capacitance showed that both CoCl₂-induced hypoxia and FCCP- induced uncoupling decreased paracellular resistance and basolateral resistance, but they both led to increases in membrane capacitance, suggestive of cellular swelling. Sufficient inhibition of ATP-synthase (high dose oligomycin), disrupted both paracellular and basolateral resistances; and finally, complex 1 inhibition only disrupted the basolateral resistance.

Conclusions: Our findings suggest that the ECIS is a powerful tool for measuring in real time how the barrier function of RPE cells changes following mitochondrial dysfunction, and recommend its further use in investigation of RPE dysfunction as it relates to the multifactorial pathogenesis of dry AMD.

CONTROL ID: 3540673

SUBMITTER (NAME ONLY): Jehan Alam

TITLE: Retinoid X receptor alpha (RXRa) mutant Pinkie and vitamin A deficient B6 mice develop similar spectrum of corneal inflammation

SESSION TITLE: Corneal immunology and neovascularization II

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Alam, Z. Yu, R. Ratnapriya, C.S. De Paiva, S.C. Pflugfelder, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test the hypothesis that attenuated retinoid X receptor alpha (RXRa) signaling in the gene mutated Pinkie strain and C57/BL6 (B6) mice with systemic vitamin A deficiency (VAD) develop a similar spectrum of corneal inflammation.

Methods: Cornea immune cells were characterized by flow cytometry, gene expression pattern in the cornea was evaluated by Nanostring immunological array, and immunostaining evaluated expression of cornified envelope (SPRR2) and neovascularization (CD31, LYVE-1) markers and metalloproteinases. Effects of 9-Cis retinoic acid (RA) and all-trans RA (ATRA) on suppression of cyto/chemokine production by stimulated purified monocytes was detected by multiplex immunoassay.

Results: Among the resident CD45⁺ cells in the normal B6 cornea, we found lymphoid (CD45⁺CD3⁺; 21.6%), and myeloid (78.2%) cells which include CD45⁺CD11b⁺Ly6G⁺ (16.9%), CD45⁺CD11b⁺Ly6C^{low}CD64^{high} (13.9%, as macrophages) and CD11b⁺Ly6C^{high}CD64^{low} (19.08%, as classical monocytes). Classical monocytes were the predominant cell population increased in the cornea of Pinkie and VAD strains. Tears cytokines G-CSF, IL-1 α , CXCL-1 and VEGF were significantly upregulated in Pinkie and VAD mice. Both 9-Cis and ATRA attenuated LPS stimulated production of G-CSF, IL-1 α / β , IL-12 and CXCL9 by purified CD11b⁺Ly6C^{high} monocytes in a dose dependent manner. VAD mice lost weight and developed mild to moderate corneal opacity around 12-14 weeks of age. Systemic 9-Cis or ATRA prevented the VAD phenotype. Approximately 20% of Pinkie developed corneal opacification, vascularization and ulceration by age 20 weeks. The ulcerated corneas are densely infiltrated with CD11b⁺ immune cells and have greater immunostaining for SPRR2, blood (CD31+) and lymphatic (LYVE-1+) vessels and MMP-9 compared to age-matched normal B6 corneas. Nanostring RNA expression profiling in the ulcerated cornea revealed high expression of S100a8, S100a9, Plau, Plaur, IL1 β , COX2, CCL2, IL6, CCR4, ICAM1, Pro-Platelet basic protein (PPBP), CCL9, VEGFA, FGF7 and MMP-9.

Conclusions: Corneas from Pinkie with attenuated Rxra signaling and VAD B6 are infiltrated with inflammatory monocytes, have increased expression of proinflammatory and proangiogenic mediators and develop corneal neovascularization and opacification. These findings suggest that RXRa signaling modulates corneal inflammation and maintains corneal health and clarity.

CONTROL ID: 3540683

SUBMITTER (NAME ONLY): Rajendra Gyawali

TITLE: Eyes on guidelines: evaluating the quality of diabetic eye disease clinical practice guidelines

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Diabetic retinopathy is a leading cause of vision impairment globally. Clinical practice guidelines have been developed to assist practitioners in providing evidence-based care to improve vision outcomes. However, the methodological rigor of these guidelines remains largely unknown. This study aimed to systematically review the quality of existing diabetic eye care guidelines.

Methods: A systematic search of guidelines for comprehensive clinical eye care of adult patients with diabetes was conducted on MEDLINE, Scopus PubMed, EMBASE, ProQuest, Web of Science and websites of relevant guideline developers and professional societies. Four reviewers independently rated the quality of the included guidelines using the Appraisal of Guidelines, Research and Evaluation (AGREE II) instrument. Aggregate scores (%) for six domains and overall quality assessment were calculated. A 'good quality' guideline was defined as the one with $\geq 60\%$ score for 'rigour of development' and in at least two other domains.

Results: Eighteen guidelines met inclusion criteria, of which 13 were evidence-based guidelines (involved systematic search and grading of evidence). In general, guidelines scored high in 'clarity of presentation' (Median (interquartile range (IQR)): 86.6% (76.7% to 94.4%)), and 'scope and purpose' (73.6% (54.2% to 80.6%)) and low in 'applicability' (28.6% (18.0% to 37.8%)) and 'stakeholder involvement' (48.6% (29.2% to 71.5%)). The median scores for 'rigour of development' and 'editorial independence' were 60.2% (30.9% to 78.1%) and 67.7% (24.0% to 83.3%), respectively. The median overall score (out of 7) of all guidelines was 5.1 (IQR: 3.7 to 5.8). The evidence-based guidelines scored significantly higher in overall assessment and all domains except for 'clarity of presentation' compared to expert-consensus guidelines. Half (n=9) of the guidelines (all-evidence-based) were of 'good quality'.

Conclusions: A wide variation in methodological quality exists among diabetic eyecare guidelines, with nine guidelines demonstrating 'good quality'. Future iterations of guidelines could improve by appropriately engaging stakeholders, following a rigorous development process, including support for application in clinical practice and ensuring editorial transparency.

CONTROL ID: 3540691

SUBMITTER (NAME ONLY): Alisa Patton

TITLE: T1DM during COVID-19: A Retrospective Analysis on Access to Ophthalmology Care and Health Habits

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Patton, B. Zhou, I. Zhang, C. Ye, B. Szirth, A.S. Khouri, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coronavirus-19 (COVID-19) has had immense effects on access to medical care. Loss of medical care is alarming for individuals with pre-existing conditions like Type 1 Diabetes Mellitus (T1DM) which require uninterrupted care for best outcomes. Consistent care and medication use can reduce risk of developing diabetic retinopathy (DR) by 76% or progression by 54%. Healthy habits have also been linked to reduced risk of DR. The purpose of this study is to assess the effect of COVID-19 on care access and health habits in individuals with T1DM.

Methods: Surveys were administered from July-November of 2020 to multinational groups including the Children with Diabetes Conference (USA) and online groups, the American Diabetes Association and Connected in Motion Canadian Conference for T1DM. Data was collected from 125 patients from the USA, UK, Canada, and Bolivia. Age range was 5-81, and average years with T1DM was 17.9. The survey was online so responder rate is unclear, though response rates from previous surveys with similar groups averaged less than 10%.

Results: While 73.6% of respondents saw an ophthalmologist within 1 year and 98.4% had medication without rationing, 40% postponed medical visits. Reasons for postponement included lack of appointments or transportation, financial issues and safety concerns. The majority (86.4%) were from the US where private insurance is prevalent, 12% were from Europe and Canada, where socialized medicine is common. Of respondents, 90.4% are willing to use telemedicine as an alternative. For most, diet remained the same (48.8%); 25.6% stated their diet was healthier and 20% stated their diet was less healthy. 16.8% had problems accessing their usual foods due to the pandemic. A majority (55.2%) reported decreased exercise with 18.4% reporting more exercise. These overall trends were consistent across countries, and gender trends remained the same as pre-COVID, with women having better lifestyle and medical care adherence.

Conclusions: Though patients delayed appointments, most were able to see an ophthalmologist and access medication. Physical activity levels decreased, though diets were mostly unchanged. In individuals with T1DM, disruptions in medical care and health habits can have negative long-term outcomes on overall and eye health. Telemedicine offers a promising solution for mitigating this risk.

CONTROL ID: 3540693

SUBMITTER (NAME ONLY): Jong Park

TITLE: A comparison of utilization and costs of fluocinolone acetonide and dexamethasone intravitreal implants for the treatment of non-infectious uveitis: A cross sectional study

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare the costs of fluocinolone acetonide (FA) and dexamethasone (DM) intravitreal implants with steroid-sparing systemic therapy in the treatment of non-infectious uveitis (NIU) and to determine the usage patterns and changes in cost over time of FA and DM implants.

Methods: Retrospective claims-based analysis of a study population in IBM MarketScan, a nationally-representative sample of commercial insurance beneficiaries, diagnosed with NIU from 2007-2016 who received intravitreal FA or DM implantation. Cost of procedure, total healthcare costs, follow up to ophthalmology and rheumatology, and number of repeat or crossover procedures (use of the other implant) were analyzed. Costs were also compared to NIU patients receiving steroid-sparing systemic therapy (SSST) with or without intraocular implants.

Results: Over 200,000 patients with NIU were found in the database, and a total of 109 FA patients, 417 DM patients, and 1060 SSST patients were identified. The total cost to the healthcare system of NIU patients who received FA implants was \$57,272, DM implants was \$21,810, and SSST without an implant was \$37,697 at one year ($p < 0.001$). The charged cost of implanting FA decreased from a peak in 2007 at \$40,603 to \$24,292 in 2016. The charged cost of implanting DM in NIU patients was stable over the study period with an average cost of \$2,051. There were no differences in the number of follow up visits to an ophthalmologist or rheumatologist at one, two, or three years between patients with FA and DM. There were more repeat procedures than crossover procedures for both FA (33.0% vs 4.6% at one year, 53.1% vs 14.3% at three years) and DM (60.0% vs 2.9% at one year, 61.6% vs 7.2% at three years).

Conclusions: In NIU patients, total healthcare costs were highest in patients with FA implants, lower with SSST, and lowest with DM implants. FA intravitreal implant use and cost decreased over time, while DM intravitreal implant use increased with stable cost over time. These findings may help clinicians decide which therapies to use in patients with NIU.

CONTROL ID: 3540705

SUBMITTER (NAME ONLY): Camila Albo

TITLE: Is there a shortage of ophthalmologists in the southwestern United States?

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: With an increase in systemic disease leading to ocular manifestations and an expansion of the elderly population, healthcare is experiencing exponential demand and is projected to outgrow the supply of ophthalmologists. We performed a cross-sectional study to determine the prevalence of ophthalmologists and types of ophthalmology subspecialists in the three largest cities of each southwestern (SW) state (Arizona (AZ), New Mexico (NM), Oklahoma (OK) and Texas (TX)) in the United States (US).

Methods: We used the American Academy of Ophthalmology's "Find an Ophthalmologist" online listing, during December 2020, to determine the number and location of ophthalmologists in the SW US. We collected data on each ophthalmologist, including sex, primary subspecialty, practice type, year of board certification, and academic affiliation. We assigned two age groups based on board certification year (Table 1). We compared our data to previous literature demonstrating a mean US national density of 5.68 ophthalmologists per 100,000 persons in 2017. We identified the three largest cities in each state by population.

Results: There were 550 total ophthalmologists in the three largest cities of each SW state. The majority were male (78.5%) and board certified prior to or during 1997 (56.2%). There were 5.48 ophthalmologists per 100,000 persons, i.e., 18,238 persons per one ophthalmologist (P/O), in the SW region. Texas (21,036 P/O) and Oklahoma (13,240 P/O) were the most and least saturated states, respectively (Figure 1). Tucson had the most ophthalmologists per 100,000 persons (10.11); Rio Rancho (0.99) and Houston (3.59) had the least. Retina (N=128) and cornea/external disease (N=45) were the most reported primary subspecialties; oculoplastics (N=33) and neuro-ophthalmology (N=10) were the least reported.

Conclusions: Our results suggest that there are less ophthalmologists per person in the SW region compared to the 2017 mean national density. This data provides important information to younger ophthalmologists seeking job opportunities, the ophthalmic community for resource allocation, and the general public searching for ophthalmologists in the SW US.

CONTROL ID: 3540715

SUBMITTER (NAME ONLY): Timothy Yu

TITLE: Collaborative Diabetic Retinopathy Severity Classification of Optical Coherence Tomography Data through Federated Learning

SESSION TITLE: Deep learning for classification and segmentation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.T. Yu, J. Lo, D. Ma, M.V. Sarunic, Simon Fraser University School of Engineering Science, Burnaby, British Columbia, CANADA|P. Zang, Y. Jia, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|J. Owen, R.K. Wang, A.Y. Lee, University of Washington Department of Ophthalmology, Seattle, Washington, UNITED STATES|R.K. Wang, University of Washington Department of Bioengineering, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is among the most common microvascular complication of diabetes and can lead to sudden loss of vision. Exploration of deep learning for the classification of DR through optical coherence tomography angiography (OCT-A) is limited by the size of the labelled datasets. Data security is fundamental to, yet hinders, collaboration between institutions. We investigate the approach of sharing the deep neural network (DNN) model during training while keeping the images private using a method referred to as federated learning (FL). In this study, we investigate the relative performance of the cross-institution application of FL for the classification of referable DR (RDR) in OCT en face images.

Methods: This IRB approved study consisted of three independent institutions: SFU (n=403 subjects), OHSU (n=323 subjects), and UW (n=54 subjects) using three commercial OCT image acquisition systems. The input for classification consisted of a combination of the en face angiographic and structural images from the deep and superficial vascular complexes. SFU and OHSU allocated 60% for training, 20% for validation, and locked 20% for testing, while the UW data was reserved as an external test set. Transfer learning of a VGG19 architecture initialized with ImageNet weights were used for 4-fold cross-validated classification. Each participating institution trains the DNN model and uploads the weights to a central FL computer. The models are averaged and then redistributed to each of the participants. We compare the FL performance versus each individual institution (internally) trained and tested model, and across institutions (external).

Results: There was no statistically significant ($P < 0.05$) difference in classification observed through two-tailed t-tests between the FL and internal model across every metric for all datasets (representative results shown in Fig. 1). The FL framework achieved an accuracy of 0.762–0.880 with an associated F1 score of 0.677–0.909 and AUC of 0.910–0.979; the internal models attained performances of 0.809–0.908, 0.778–0.921, and 0.884–0.978, respectively.

Conclusions: The FL approach for RDR classification shows comparable performance to internal models. This study demonstrates potential for more generalizable networks through FL that incorporate learning on data from diverse domains.

CONTROL ID: 3540760

SUBMITTER (NAME ONLY): Ian Rubinoff

TITLE: Clinical retinal oximetry with visible-light optical coherence tomography

SESSION TITLE: Advanced imaging technologies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Alterations in retinal oxygen metabolism are implicated in blindness causing diseases, such as diabetic retinopathy and glaucoma. Therefore, a non-invasive clinical tool to assess oxygen saturation (sO_2) in retinal vessels is desirable. Recent development of visible-light optical coherence tomography (vis-OCT) enabled non-invasive sO_2 measurements in retinal blood vessels at micrometer-scale resolution by three-dimensional (3D) spectroscopic analysis. Nevertheless, such measurements are susceptible to spectral contaminants from the complex retina anatomy and vis-OCT signal detection and processing, decreasing measurement reliability. To overcome limitations posed by spectral contaminants, we developed adaptive-spectroscopic OCT (AS-OCT), a processing technique that enables non-invasive, 3D, environment-independent sO_2 measurements in the human retina.

Methods: We used vis-OCT to image the retinas of 18 healthy volunteers. Light exposure in the eye was $< 250 \mu W$ and imaging acquisition time was 5 sec. We used adaptive spectroscopic OCT (AS-OCT) to identify and remove contaminants from retinal tissues, chromatic aberrations, and spectrally-dependent roll-off. Then, we automatically selected the optimal depths in the vessel for sO_2 measurement. Finally, we measured the attenuation spectrum in the blood vessel and used a least-squares regression fit with known spectra to determine the sO_2 value.

Results: We measured sO_2 in 125 unique retinal vessels near the optic disc (vessel diameters ranging from $37 \mu m$ to $176 \mu m$). Major arteries had $sO_2 = 97.9 \pm 2.9 \%$ (mean \pm standard deviation) ($n = 36$), small arteries (diameter $< 100 \mu m$) had $sO_2 = 93.2 \pm 5.0 \%$ ($n = 36$), and veins had $sO_2 = 58.5 \pm 4.3 \%$ ($n = 53$). Repeated measurement standard deviations were 2.21% and 2.32% for all arteries and veins, respectively. Fig. 1 shows an oximetry map of the optic disc in the retina of a healthy 23 year-old volunteer.

Conclusions: AS-OCT enables environment-independent retinal oximetry in the clinical setting. Repeatability in arteries and veins $< 2.5 \%$ indicates robust measurements that are promising for clinical use.

CONTROL ID: 3540765

SUBMITTER (NAME ONLY): Ping Huang

TITLE: Risk factors of Tube exposure in resident performed glaucoma drainage implant surgery

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Huang, A. Djougarian, J. Lee, F. Anwar, A. Djougarian, Northwell Health Eye Institute, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report a series of cases with glaucoma drainage tube exposure and evaluate the possible risk factors for tube exposure in resident performed glaucoma drainage implant surgery.

Methods: The medical records of all patients at the Queens Hospital Center - NYC Health + Hospitals who underwent Ahmed or Baerveldt glaucoma implant surgery by resident physicians from August 1, 2015 to November 1, 2020 were reviewed. Patients who presented with glaucoma drainage tube exposure and required surgical revision of the tube were identified. Demographic factors, past ocular history, past medical history, current treatment, and time to exposure were abstracted from the identified charts and were compared with a similar number of patients without tube exposure identified during the same period.

Results: Five patients (7 eyes) experienced glaucoma drainage tube exposure. The average time to exposure was 46.7 ± 33.6 months. The exposure group had similar mean age of 67.1 ± 11.8 compared to the non-exposure group's mean age of 66.7 ± 15.4 ($P=0.961$). More males 57.1% and fewer African-Americans 42.9% were identified in the exposure group versus 14.3% male and 85.7% African-American in the non-exposure group. All the patients in the exposure group had a diagnosis of primary open angle glaucoma (POAG). In the non-exposure group, four patients had POAG, one had chronic angle closure glaucoma, one had neovascular glaucoma, and one had uveitic glaucoma. In the non-exposure group, all the tubes were located superiorly while in the exposure group 71.4% of the tubes were in the inferior quadrant. The number of previous glaucoma surgeries was significantly higher ($P=0.018$) in the exposure group (2.57 ± 1.51) compared with the non-exposure group (0.57 ± 0.54). The number of intraocular pressure lowering eye drops was higher ($P=0.052$) in the exposure group (3.29 ± 1.11) compared with the non-exposure group (1.71 ± 0.76).

Conclusions: Inferior location of the glaucoma drainage tube, previous glaucoma surgery, and the number of intraocular pressure lowering eye drops are potential risk factors for tube exposure in resident performed glaucoma drainage implant surgery.

CONTROL ID: 3540773

SUBMITTER (NAME ONLY): Anna Britton

TITLE: Retinal vessel density changes in treated and untreated obstructive sleep apnoea

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Obstructive sleep apnoea (OSA) is a risk factor for vascular disease including stroke. Studies have shown OSA alters the retinal arterioles and veins, however studies on the microvasculature have yielded conflicting results and none have assessed the effect of continuous positive airways pressure (CPAP) on retinal vessel density. This prospective cohort study sought to examine the impact of varying severities of OSA on retinal vessel density using optical coherence tomography angiography (OCT-A) and whether CPAP treatment attenuates this change.

Methods: 67 adult patients underwent diagnostic polysomnography and retinal vessel imaging between April 2015 – December 2016. Patients were stratified into four clinical severity groups based on their apnoea-hypopnoea index (AHI, events/hour): controls (<5), mild (≥ 5 to <15), moderate (≥ 15 to <30), and severe OSA (≥ 30). Following their sleep study a subset of patients were offered CPAP at the discretion of a sleep physician. At a 24-month follow up, patients had OCT-A scans taken on Spectralis OCT-A (Heidelberg Engineering, Germany). Vessel density was analysed on images of the macula and optic nerve head (ONH) using ImageJ software. Exclusion criteria included the presence of glaucoma, prior optic neuropathy or retinopathy and media opacities.

Results: Of the 67 participants (45 males; mean age 62.3), there were 9 controls, 16 mild, 18 moderate and 24 severe OSA participants. Vessel density was negatively correlated with clinical severity by AHI but this did not reach statistical significance at the superficial vascular complex (SVC), deep vascular complex (DVC) or optic nerve head (ONH) ($p = 0.072, 0.206, 0.294$, respectively). However, for those not using CPAP, vessel density was significantly and negatively correlated by AHI at the macula (SVC $p = 0.010$, DVC $p = 0.049$). Compliant CPAP use abolishes this trend. Vessel density was also significantly and negatively correlated by AHI for diabetic patients in the cohort (SVC $p = 0.013$, DVC $p = 0.042$).

Conclusions: Our results show that retinal vessel density is negatively correlated with AHI in untreated individuals and that adequate use of CPAP abolishes this trend. Untreated OSA in combination with diabetes has the propensity to significantly worsen vascular outcomes.

CONTROL ID: 3540801

SUBMITTER (NAME ONLY): Ben Brenner

TITLE: Mitochondrial elongation in retinal vascular cells as a result of exposure to high-glucose conditions

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic retinopathy results in the proliferation of endothelial cells and excessive vascularization in the retina, leading to blindness. In diabetic mice, these structural changes succeed changes in oxygen metabolism in the retinal microvasculature. This suggests that changes in mitochondrial function may precede diabetic retinopathy.

Methods: To investigate intracellular mitochondrial changes, we used Stochastic Optical Reconstruction Microscopy (STORM) to visualize mitochondrial morphology variations in primary mouse retinal pericyte (PC) and endothelial cells (EC) with and without five-day incubation in a high-glucose culture medium. This allowed us to visualize mitochondrial morphology down to a ~50nm resolution level. We then segmented and analyzed the images, looking at size, shape, and distributional changes in the mitochondria over different conditions, using an unpaired t-test to compare between groups.

Results: Preliminary results suggest that in primary PC cells treated with glucose, there is a significant level of mitochondrial elongation compared to untreated PC cells. The median length of mitochondria goes increased from 0.41 to 0.90 μm ($p < 0.05$) between the control and glucose treated cells. Furthermore, the median total area of each 2D cell image covered with mitochondria increased from 208 to 298 μm^2 ($p < 0.05$) with no corresponding increase in cytoplasm or nucleus size and with no corresponding increase in the number of mitochondria.

Conclusions: The elongation of mitochondria in the PC suggests an increased metabolic rate in these cells after glucose treatment. Future studies could explore the relationship between PC metabolic rate and the level of vascularization in the retina.

CONTROL ID: 3540811

SUBMITTER (NAME ONLY): Sophia Lam

TITLE: Descriptive Analysis of Cornea Fellowship Program Directors in 2020

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Lam, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|K. Garg, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|W.S. Shalaby, Z.A. Syed, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess demographic qualities, institutional backgrounds, and academic achievements of program directors in Cornea and External Disease, Refractive Surgery, and Anterior Segment fellowships.

Methods: Program directors of Cornea and External Disease, Refractive Surgery, and Anterior Segment fellowships were identified on the San Francisco Match website. Demographic characteristics, educational and training background, and academic productivity were analyzed using the director's institutional profile, PubMed, and Scopus database. Board certification was confirmed using the American Board of Ophthalmology website. Membership in journal editorial board, Cornea Society board, or Heed fellowship was based on the respective websites. Other fellowship qualities reviewed included academic or private practice type, number of cornea faculty, and sex of chairperson.

Results: We reviewed 47 Cornea and External Disease, 29 Refractive Surgery, and 10 Anterior Segment fellowships. Of reviewed programs, 64.0% were considered academic, 34.9% were private practice, and 1.2% were both. Overall, 23.9% of program directors were women and the mean age was 52.6 ± 2.5 years old. More female program directors were in departments with a female chairperson compared to male program directors ($6 \pm 28.6\%$ vs. $4 \pm 6.0\%$, $p=0.011$). Of program directors, 20.5% were Heed Fellows, and the average number of publications was 44.6 ± 11.8 . Mean H-index was 16.5 ± 3.3 and was higher in Cornea, External Disease, and Refractive Surgery than Anterior Segment fellowships (18.2 ± 15.5 vs. 7.1 ± 11.4 , $p=0.008$). Mean H-index was higher in academic than private practice fellowships (19.9 ± 15.1 vs. 11.2 ± 14.7 , $p=0.011$). Of all program directors, 1.1% were Instructors, 14.8% were Assistant Professors, 25.0% were Associate Professors, 34.1% were Full Professors, 18.2% were Endowed Chairs, 12.5% were on the Editorial Boards of the 3 highest impact journals in ophthalmology and cornea, and 6.8% were Cornea Society Board Members.

Conclusions: The majority of fellowships are academic programs led by program directors with a high number of publications, H-index, and level of professorship. Cornea and External Disease and Refractive Surgery fellowship directors had a higher academic productivity than those in Anterior Segment programs. Female program directors remain the minority and are more common in departments with female chairpersons, demonstrating an opportunity for further representation.

CONTROL ID: 3540813

SUBMITTER (NAME ONLY): Karen Torrejon

TITLE: Use of a Novel Potassium Channel Opener in a 3D-Glaucomatous Human Trabecular Meshwork/Schlemm's Canal Tissue Model

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.Y. Torrejon, A. Unser, F. Ahmed, V. Chari, Glauconix Biosciences Inc, Albany, New York, UNITED STATES|T. Htoo, C. Steel, B.M. Wirostko, Qlaris Bio, Massachusetts, UNITED STATES|B.M. Wirostko, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Simulating glaucoma pathology and medication-induced changes to the anatomy and physiology of the conventional outflow pathway presents a unique challenge. In this study, we utilized our proprietary 3D-bioengineered glaucomatous conventional outflow model to investigate the ability of QLS-100 to modulate outflow in vitro. QLS-100 is the active moiety of QLS-101, a novel K_{ATP} channel opener with the unique ability to enhance outflow in the absence of ocular side effects such as hyperemia. The effects of QLS-100 on fibrotic and endothelial junctional markers in human trabecular meshwork/Schlemm's canal co-cultures are also described.

Methods: Bioengineered 3D conventional outflow tract constructs, using 4 donors (ages 47-91), were treated with TGF β -2 (5 ng/mL) for 6 days. Constructs were then treated with QLS-100 (1, 10 or 100 μ M), or Y-27632 (10 μ M). The effect of QLS-100 (1 μ M) on outflow facility (hydraulic conductivity) was assessed by perfusion studies where pressure was constantly recorded at various perfusion rates. Protein expression of α -smooth muscle actin (α -SMA), CD31, endothelin-I, fibronectin, VE-cadherin, Phospho- and total eNOS was analyzed via western blot. Cellular expression of α -SMA, fibronectin, Phospho- and total eNOS was determined by immunocytochemistry and confocal microscopy. Statistical significance was determined by one-way ANOVA with a Tukey's multiple comparisons test, or by two-way ANOVA.

Results: QLS-100 significantly increased outflow facility across all donors, as compared to TGF- β 2 or Y-27632 treated donors ($P < 0.0001$ and $P < 0.05$, respectively). QLS-100 did not affect expression of the cell adhesion proteins CD31 and VE-Cadherin, while Y-27632 significantly decreased their content ($P < 0.01$). Neither compound altered protein expression or distribution of endothelin, fibronectin, α -SMA, or phospho- or total eNOS.

Conclusions: QLS-100 significantly improved outflow facility in glaucomatous tissue constructs without impacting protein expression of fibrotic or endothelial junctional markers. Y27632 decreased expression of endothelial junctional markers, which may explain the hyperemia observed with clinical ROCK inhibition. These results indicate that the novel prodrug QLS-101 is a promising treatment that may lower elevated IOP without altering vessel integrity.

CONTROL ID: 3540815

SUBMITTER (NAME ONLY): Michael Saheb Kashaf

TITLE: IOP-Induced In Vivo Deformation and Strains in the Human Optic Nerve Head using OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Saheb Kashaf, H.A. Quigley, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|T.D. Nguyen, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: We measured in vivo deformation and mechanical strain in the optic nerve head (ONH) in glaucoma patients using optic coherence tomography (OCT) scans of the ONH before and after a short-term change in intraocular pressure (IOP).

Methods: Persons treated for open angle glaucoma underwent imaging by radial ONH OCT scans obtained before and 20 minutes after IOP increase produced by tight-fitting swimming goggles or before and after IOP decrease by laser suturelysis. Bruch's membrane opening and the anterior lamina cribrosa (LC) border were manually marked. Digital volume correlation calculated 3D displacements within the LC, defined as tissue up to 250 μ m posterior to anterior LC border. Displacements were used to calculate anterior lamina depth (ALD) change and LC strains. Generalized estimating equation models accounted for inclusion of both eyes in goggles patients.

Results: In 20 eyes (12 persons, mean field MD= -2.6 dB), goggles-wearing increased mean IOP by 6.6 mm Hg (range 1-16) and produced $-0.32 \pm 0.71\%$ mean compressive anterior-posterior LC strain (Ezz) ($p=0.056$). Suture lysis in 14 eyes (14 persons, mean field MD= -9.5 dB) decreased mean IOP by 13 mm Hg (range: 3-45) and produced $+1.04 \pm 1.37\%$ mean tensile Ezz strain ($p=0.010$). Among suturelysis eyes, greater IOP change was associated with both larger Ezz strain ($p=0.0005$) and larger maximum principal strain (Emax; $p=0.005$). In the goggles group, Emax was significantly smaller with thicker peripapillary nerve fiber layer in corresponding inferior ($p=0.05$) and temporal ($p=0.01$) quadrants. In goggles eyes, a more normal visual field index was associated with a smaller maximum principal strain ($p=0.04$). ALD deepened among goggles eyes (mean = $3.8 \pm 5.98 \mu$ m, $p=0.011$) and moved toward the vitreous after suturelysis (mean = $2.5 \pm 5.93 \mu$ m, $p=0.122$). Greater IOP change was associated with greater ALD change in both goggles ($p < 0.0001$) and suturelysis ($p=0.04$) eyes.

Conclusions: Modest short-term IOP alterations led to measurable changes in anterior LC depth and tissue strains. The association between field damage and strain in goggles wearers may indicate that strains are preexisting correlates of glaucoma susceptibility, or, that strain changes result from glaucomatous injury. Longitudinal studies are planned to elucidate these issues.

CONTROL ID: 3540828

SUBMITTER (NAME ONLY): Ellen Brossart

TITLE: A Retrospective Analysis: Visual Field Progression and Visual Acuity following Administration of Brimonidine Drug Delivery System

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Brossart, B. Bunnell, T. Tepelus, M.Y. Chen, F.J. Lopez, AbbVie Inc, North Chicago, Illinois, UNITED STATES|E. Brossart, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The assessment of functional progression of glaucoma is an important measurement for diagnosing and monitoring the disease. This retrospective study analyzed change from baseline (CFB) in mean deviation (MD) of visual fields (VF) using Humphrey Field Analyzer 24-2 program (HFA 24-2) in glaucomatous eyes from a clinical study evaluating the Brimonidine Drug Delivery System (Brimo DDS).

Methods: A retrospective analysis of CFB in VF MD was performed on a multicenter, randomized, patient-masked, sham-controlled study evaluating the effects on visual function of Brimo DDS in patients with primary open angle glaucoma. Patients that received a single administration (n=70) of Brimo DDS 132 µg, Brimo DDS 264 µg and sham treatment at baseline in the study eye were included in this analysis. VF testing was assessed over 12 months with primary data analysis at 6 months. Subgroup analysis of VF progression and best-corrected visual acuity (BCVA) over time was split by HFA 24-2 baseline median MD (-15.7 dB, above and below). Statistical analysis was conducted using R Software (v3.6.1) under R Studio and verified by an independent group using SAS[®] analytics.

Results: Study eyes administered Brimo DDS 132 µg (n=21), Brimo DDS 264 µg (n=25), and sham (n=24) were analyzed for VF MD and BCVA. At baseline, the VF MD (mean±SEM) were -14.5±0.9, -15.4±1.1, and -18.0±1.0 dB and BCVA (mean±SEM) were 80.6±1.4, 76±1.6, and 77.3±1.6 letters for Brimo DDS 132 µg, Brimo DDS 264 µg, and sham, respectively. At 6 months, the MD CFB in VF (LS means±SE) for patients below median MD were 0.49±1.12, 1.50±0.93, and -1.09±0.73 dB; the CFB in BCVA (LS means±SE) for patients below median MD were 0.27±1.22, 4.06±1.04, and -0.37±1.08 letters for Brimo DDS 132 µg, Brimo DDS 264 µg, and sham, respectively. Brimo DDS 264 µg treated eyes had a significant CFB in VF MD (p<0.05) at 6 months compared to sham treatment indicating a reduction in progressive VF loss. Brimo DDS 264 µg treated eyes had a significant CFB in BCVA at 1 month (p<0.05) and 6 months (p<0.05) compared to sham treatment indicating an improvement in visual acuity. There was no significant difference between treatment groups above the HFA median MD.

Conclusions: In glaucomatous patients with VF MD below the HFA median, Brimo DDS 264 µg significantly reduced VF loss up to 6 months while providing improvement in vision as early as 1 month.

CONTROL ID: 3540835

SUBMITTER (NAME ONLY): Alexander Crane

TITLE: Characterization of Ocular Diseases in an Emergency Setting

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Crane, N. Agi, K. Shah, P.D. Langer, M.A. Zarbin, N. Bhagat, Institute of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Requests for ophthalmic consultations from the Emergency Department (ED) can be due to a wide range of pathology, including urgent ocular diseases. In this study, we characterize ophthalmic consultations from a level-1 trauma ED, representing a high-acuity tertiary care University Hospital setting.

Methods: In this retrospective chart review, 434 consultations to the ophthalmology department over 60 days were identified; 352 (81%) were from ED. Median age was 43 years (interquartile range: 30 to 55 years), and 158 (43%) patients identified as female. Data collected for each subject includes demographic information, reason for consultation, diagnosis, treatment, and follow-up status.

Results: Of the 352 ED consultations identified, 137 (39%) consultations were related to a trauma. Only 102 (29%) of patients were admitted to the hospital. Most common reasons for consultation included: 81 (23%) for eye irritation/pain, 80 (23%) for decreased/blurry vision, 36 (10%) for ocular involvement of trauma, 28 (8%) evaluation of known orbital fracture, 19 (5%) for eyelid/facial laceration, 16 (5%) for red eye, and 15 (4%) for periorbital edema. Most common final ocular diagnoses included: 42 (12%) orbital fracture, 24 (7%) corneal abrasion, 21 (6%) no ocular pathology, 20 (6%) eyelid laceration (including 4 canalicular involving lacerations, and 16 non-canalicular involving laceration), 14 (4%) conjunctivitis, and 13 (4%) uveitis. In total, 69 (20%) received emergent ophthalmic surgery for their presenting condition. Follow up was requested of 334 patients, of which only 165 (49%) returned to clinic.

Conclusions: Ocular involvement of trauma and other acute disease accounted for a significant portion of ophthalmic consultations in this high-acuity care setting. One-fifth of the consultations required emergent ophthalmic surgery.

CONTROL ID: 3540882

SUBMITTER (NAME ONLY): Trisha Miglani

TITLE: Ultrasound biomicroscopy image analysis technique for the human iris

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Miglani, M. Chang, M.R. Levin, J.L. Alexander, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The iris is a highly clinically relevant structure, but most literature on iris pathology is limited to qualitative observations. In this study, we aim to develop novel quantitative assessment tools for evaluation of the iris. We have developed a standardized measurement protocol of iris parameters with reliability analysis using ultrasound biomicroscopy (UBM) and ImageJ software to establish the rigor and reproducibility of these measurements and provide a quantitative description of the human iris in subjects from infancy to young adulthood.

Methods: 14 pediatric control subjects comprising of 25 total eyes (mean age 1.96yrs, standard deviation 1.18yrs, and median age 1.81yrs) were recruited prospectively and underwent UBM imaging. Two observers measured 19 structural iris parameters on four UBM image types per eye using ImageJ. Each image was analyzed by both observers using two methods: Standard and Edge Finder, which uses an edge detector to delineate tissue borders based on changes in intensity. Reliability analysis was comprised of intra-observer repeatability (IOR) and inter-observer agreement (IOA). IOR was determined by calculating the coefficient of variation (CV) and correlation coefficient (r) for each parameter, and IOA was assessed by determining the intra-class correlation coefficient (ICC) for each parameter.

Results: Axial image types resulted in superior ICC, CV and r values for the majority of parameters with the use of an edge finder tool. Longitudinal image types resulted in superior ICC, CV and r values for the majority of parameters using the standard method of image analysis on the raw image.

Conclusions: The use of an edge finder tool increased measurement reliability in axial image types, but it did not increase reliability in longitudinal images.

CONTROL ID: 3540885

SUBMITTER (NAME ONLY): Vladislav Bekerman

TITLE: Adjunctive Use of Netarsudil in Refractory Glaucoma: 1 year Retrospective Analysis.

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Bekerman, B. Zhou, C. Ha, R. Vohra, A.S. Khouri, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Netarsudil is a new class medication targeting rho-kinase inhibition and increasing trabecular meshwork outflow. Published studies have proven its efficacy alone and in combination with latanoprost as primary therapy. This study retrospectively investigated the one year efficacy of adjunctive use of netarsudil in refractory cases of glaucoma at a tertiary care glaucoma clinic. Refractory cases were judged as requiring ≥ 3 topical medications for intraocular pressure (IOP) control.

Methods: Retrospective chart review for patients on ≥ 3 topical medications who received add-on netarsudil was conducted from 01/01/2018 to 08/31/2020. Patients' baseline characteristics prior to add-on therapy were recorded and included type of glaucoma, prior topical, laser, and surgical treatments. A baseline IOP was calculated by taking the average of the two most recent IOP measurements prior to netarsudil add-on treatment. IOP was measured at 3-, 6-, and 12-month intervals ± 4 week windows. A Bonferroni corrected student's T-test was used to test differences between groups with statistical significance set at $p = 0.01$

Results: 69 eyes in 47 patients were included in this analysis. Mean age (\pm SD) was 72.0 ± 12.2 . 22 (47%) African American, 15 (32%) patients were Caucasian, and 10 (21%) Hispanic. Glaucoma diagnosis was as follows: 55 (80%) primary open angle, 4 (6%) uveitic, 4(6%) neovascular, 2 (3%) normal tension glaucoma, 2 (3%) exfoliation. Prior surgeries included: 21 (30%) seton, 13 (19%) trabeculoplasty, 4 (6%) trabeculectomy, 4 (6%) iStent, (1%) iridotomy. Mean IOP mmHg (\pm SD) at baseline was 20.7 ± 5.8 . Follow-up mean IOP mmHg (\pm SD) are as follows: 3-month 17.8 ± 6.7 ($p < 0.008$) in 64 eyes, 6-month 17.8 ± 4.6 ($p < 0.008$) in 56 eyes, 12-month 17.4 ± 6.8 ($p < 0.008$) in 44 eyes.

Conclusions: Adjunctive use of netarsudil in refractory glaucoma showed clinically and statistically significant IOP reductions. This study suggests that adding netarsudil to eyes with previous medical or surgical treatment can provide longer term IOP reduction. Further analysis is required to fully understand the effect of netarsudil in refractory glaucoma.

CONTROL ID: 3540916

SUBMITTER (NAME ONLY): Aditya Gill

TITLE: Improving Refractive Outcomes in Patients with Keratoconus Treated with Superior-Masked Topography-Guided Photorefractive Keratectomy

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gill, S. Greenstein, Ophthalmology, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Aditya Gill: Commercial Relationship: Code N (No Commercial Relationship) | Steven Greenstein: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Topography-Guided photorefractive keratectomy (TG-PRK) is an effective treatment to improve vision, refraction, and corneal contour in patients with keratoconus. Generally, there is a myopic shift after treatment with TG-PRK which may increase manifest refractive spherical equivalent (MRSE) and anisometropia post-operatively. This study aims to evaluate a novel technique, utilizing a superior mask to cover the peripheral ablation profile to reduce a postoperative myopic shift.

Methods: 13 eyes of 13 patients underwent TG-PRK with superior-masking technique. A LASIK eye drain (Wilson Oph Corp, USA) was cut to mask the superior portion of the topography-guided ablation. Topography measurements were obtained on the Pentacam (Oculus, Germany). Preoperative and 12-month post-operative MRSE, uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), maximum keratometry (K_{max}), thinnest pachymetry (P_{thin}), and average anterior and posterior radii of curvature (ARC and PRC) were recorded and analyzed.

Results: Compared to baseline vision, the mean UDVA improved from 1.00 ± 0.35 (SD) to 0.45 ± 0.14 logMar lines (LL) ($P=0.004$) and the mean CDVA improved from 0.48 ± 0.31 LL to 0.19 ± 0.08 LL ($P=0.04$) at the 12 month visit. MRSE improved from baseline of -5.85 ± 3.66 D to -1.82 ± 3.75 D at the 12 month visit ($p=0.02$). K_{max} decreased from 60.78 ± 8.87 D pre-operatively to 51.77 ± 4.62 D at the 12 month visit ($P=0.04$). Finally, P_{thin} decreased from $429.08 \pm 46.07\mu m$ at baseline to $408 \pm 73.72\mu m$ at the 12 month visit ($P=0.33$); however these values were not statistically significant.

Conclusions: TG-PRK with a superior mask is a novel technique to minimize the post-operative myopic shift in treated patients with keratoconus. In addition, this technique appears to improve UDVA, CDVA, and cornea curvature after treatment. Additional data will be presented at ARVO 2021.

CONTROL ID: 3540932

SUBMITTER (NAME ONLY): Naomi Gutkind

TITLE: Outcomes of Resident-Performed Cataract Surgery in a Diverse Veterans Affairs Hospital System Population

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.E. Gutkind, E. Meer, N. Bhatt, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|P. Hua, G. Ying, Center for Preventive Ophthalmology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate visual acuity (VA) outcome and complications, and risk factors for VA outcome from the resident-performed cataract surgery at a diverse Veterans Affairs hospital system population.

Methods: A retrospective chart review was conducted for patients who underwent cataract surgery by residents at the Philadelphia Veterans Administration Medical Center from 01/01/2013 – 12/31/2015. Clinical information including preoperative, intraoperative, and postoperative visual acuity (1 day, month 1, 2-3 and 6) and surgery complications was collected. Descriptive analyses were performed for complication rate, and univariable and multivariable linear regression models were performed for risk factors of VA change from baseline at 1 month and VA change from baseline at all post-operative visits combined.

Results: This study included 1183 patients, with mean (SD) age of 70.8 (9.3) years, 41.7% were African American, 57.6% were Caucasian, and 97.5% were male. The mean (SD) VA in logMAR was 0.69 (0.74) at baseline, and improved to 0.19 (0.36) at 1 month, 0.16 (0.34) at 2-3 months and 0.14 (0.36) at 6 months (Table 1), with 91.3% patients having VA improvement from baseline at 1 month, and 86.5% patients achieved 20/40 or better at 1 month. Analysis by baseline visual acuity levels demonstrated that individuals with baseline visual acuity of worse than 20/40 experienced significant improvement from baseline (Table 1). Complications from cataract surgery were minimal, including hyphema (0.3%), dropped nucleus (1.8%), iris prolapse (0.8%), anterior capsular tears (0.6%), posterior capsular tears (4.0%), zonular dehiscence (1.1%), and vitreous loss (5.4%). In multivariate analysis, younger age ($p < .0001$), worse baseline visual acuity ($p < .0001$) and absence of iris prolapse ($p < .001$) were significantly associated with greater improvement in VA at 1 month.(Table 2)

Conclusions: Resident-performed cataract surgeries achieve significant improvement in visual acuity with a complication rate lower than previously reported in residents, and not substantially greater than in the cataract literature. There is a clear benefit from resident-performed surgery as a means of providing surgery with successful outcomes in this specific population of patients.

CONTROL ID: 3540937

SUBMITTER (NAME ONLY): James Swink

TITLE: Alternative healthcare practitioner use and its association with medical eye care in chronic ocular disease patients

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Swink, B.C. Stagg, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

Commercial Relationships Disclosure (Abstract): James Swink: Commercial Relationship: Code N (No Commercial Relationship) | Brian Stagg: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patient utilization of alternative healthcare providers is on the rise in the United States and the impact of this on chronic ocular disease patients is unknown. We performed a retrospective cross-sectional study using nationally representative data to analyze how patients with chronic ocular disease utilize alternative healthcare providers and determine if there was any association between alternative healthcare use and decreased adherence to prescription medication adherence.

Methods: We used multivariate logistic regression models to evaluate the association between ocular disease, regular eye doctor visits, alternative healthcare provider visits, and skipping or using alternative medications to save money. Our study size was 5,264 participants with self-reported diagnoses of glaucoma, age-related macular degeneration, or diabetic retinopathy. These models were adjusted for potential confounders (gender, age, race, ethnicity, educational attainment, vision impairment, insurance status, poverty level, and presence of other medical conditions). We defined alternative healthcare providers as practitioners of homeopathy, naturopathy, traditional medicine as well as shamans, curanderos, machis, pacheros, yerberos, hierbistas, sobadors, Native American healers, and medicine men. All data came from the 2017 National Health Interview Survey (NHIS) and was analyzed using Stata version 16 (StataCorp, College Station, TX).

Results: Participants with chronic ocular disease who utilized alternative healthcare providers were more likely to have regular eye care appointments (odds ratio [OR]: 1.76, 95% confidence interval [CI]: 1.14-2.72, $P=0.01$). These participants were also more likely to use alternative medications or skip medication doses to save money (OR: 5.31, 95% CI: 3.09-9.14, $P<0.001$ and OR:3.84, 95% CI: 1.84, 7.95, $P<0.001$, respectively).

Conclusions: Regular eye care for patients with chronic ocular disease is important in preventing vision loss. Patients who utilize alternative care providers may be at higher risk for vision loss because of medication nonadherence. The underlying cause of the association of medication nonadherence and alternative healthcare utilization is still not clearly understood. More research is required to understand why patients are utilizing alternative care providers and why they are be more likely to be less compliant with their medication.

CONTROL ID: 3540964

SUBMITTER (NAME ONLY): Lindsey Webb

TITLE: Effects of Stress from COVID-19 on Chronic Central Serous Retinopathy

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Webb, J. Tenewitz, S. Shaikh, University of Central Florida, Orlando, Florida, UNITED STATES|N. Figueroa, G. Kumar, Central Florida Retina, Florida, UNITED STATES|A. Sharma, S. Shaikh, Eye Clinic, Orlando VA Medical Center, Orlando, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: It was hypothesized that stress from COVID-19 would have a negative effect on Central Serous Retinopathy (CSR), a stress associated condition. The purpose of this study was to evaluate the effects of stress from COVID-19 on chronic CSR using a retrospective chart review.

Methods: Charts from 45 patients, 67 eyes, with chronic CSR were evaluated. Data were collected pre COVID-19 shutdown (January 1, 2019 to March 15, 2020) and during COVID-19 shutdown (March 15, 2020 to September 1, 2020) for visual acuity, central subfield thickness (CST), pigment epithelial detachment (PED), and subretinal fluid. Clinical change (improved, stable, or worsened) status was determined by the treating retinal specialist. The data were determined to not be normally distributed via the Shapiro-Wilk test. Statistical significance of the CST and vision data was determined by the sign test. The McNemar Exact test was used to determine statistical significance of PED and subretinal fluid.

Results: Differences in data in pre vs post COVID-19 shutdown were not statistically significant. Clinically, 69% of patients were stable, 14% improved, and 17% worsened. Visual acuity pre COVID-19 shutdown averaged 20/37 (SD 20/46) and during the COVID-19 shutdown averaged 20/37 (SD 20/43); these changes were not statistically significant. CST pre COVID-19 shutdown averaged 281 μm (SD 57 μm) and during the COVID-19 shutdown averaged 288 μm (SD 83 μm); these changes were also not statistically significant. The majority of patients did not change in their presence or absence of PED (94%) or subretinal fluid (85%).

Conclusions: Patients with chronic CSR did not see significant changes to their clinical status, vision, CST, subretinal fluid, or PED when assessed during the COVID-19 pandemic. Stress from onset of the COVID-19 did not appear to have a significant effect on patients with chronic CSR.

CONTROL ID: 3540996

SUBMITTER (NAME ONLY): Rachel Barborek

TITLE: An AAV vector carrying a chimeric photopigment for evaluating gene therapy methods in Old World primates

SESSION TITLE: Photoreceptors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Barborek, J. Rowlan, J. Kuchenbecker, D. Rezeanu, M. Mazzaferri, B. Bembry, J. Neitz, M. Neitz, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|J. Rojas, Y. Tang, C. Romano, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Treating cone disorders by gene therapy via intravitreal injection is challenging because the inner limiting membrane and retinal thickness limit accessibility of photoreceptors to injected agents. Overcoming this requires pre-clinical testing in non-human primates. Blue cone monochromacy is a cone-based disorder with a variety of underlying mutations, a subset of which is likely amenable to gene therapy, however a suitable primate model does not exist. Thus, our goal is to develop a vector optimized for driving robust expression of a photopigment with an absorption spectrum that allows functional detection via ERG and behavioral testing in retinas expressing endogenous primate cone photopigments.

Methods: The vector contains an optimized expression cassette designed to target expression of a passenger opsin gene to primate cones packaged in the AAV-7m8 capsid for an intravitreal route of administration. The opsin gene comprises partial sequence of middle wavelength opsin cDNA of the Mongolian gerbil (*Meriones unguiculatus*) flanked by partial exon 1 and exon 6 sequences of the human OPN1LW gene. The chimeric photopigment is expected to peak ~493 nm, about midway between the absorption maxima of the macaque monkey S and M photopigments (see Figure). Virus was injected into the eyes of mice that had both M and S opsin genes knocked out. Expression of the transgene was evaluated using photopic ERG. Spectral sensitivity was characterized using flicker photometric ERG.

Results: Photopic ERG responses in the cone opsin knockout mice were rescued by gene therapy treatment. Treated mice gave robust photopic ERG responses compared to knockout controls which gave no detectable cone responses. The characteristics of the ERG waveform were comparable to wild-type mice. ERG flicker photometric spectral sensitivity functions were well fit to a single photopigment template with a spectral peak of 493 nm.

Conclusions: We have developed a gene therapy vector designed to be administered intravitreally expressing a photopigment that is well separated in spectral sensitivity from any of the wild-type cone pigments in Old World primates. It should be possible to isolate the responses from this photopigment if it is expressed in macaque cones using silent substitution in ERG and behavioral experiments to evaluate gene therapy success.

CONTROL ID: 3541047

SUBMITTER (NAME ONLY): Rishabh Gupta

TITLE: Using Adaptive Optics to Evaluate Photoreceptor Regularity in a Porcine Laser Model Mimicking Age-Related Macular Degeneration

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gupta, F. BARONE, D. Baker, D. Bose, H. Pakhchanian, I. Bunea, A. Maminishkis, D. Ortolan, R. Sharma, J. Amaral, K. Bharti, Ocular and Stem Cell Translational Research Section, National Eye Institute, Bethesda, Maryland, UNITED STATES|J. Phillips, University of Wisconsin-Madison Waisman Center, Madison, Wisconsin, UNITED STATES|J. Phillips, D. Gamm, McPherson Eye Research Institute, Madison, Wisconsin, UNITED STATES|D. Gamm, Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive Optics (AO) ophthalmic imaging is a rapidly evolving technique that provides ophthalmologists and vision scientists with the ability to resolve characteristics of the retina at a cellular level in vivo. We assessed cone photoreceptor regularity of the porcine retina under varying degrees of laser-induced retinal pigment epithelium (RPE) damage that mimicked age-related macular degeneration (AMD)-like conditions. This tested our hypothesis that AO is a useful imaging technique to evaluate photoreceptor regularity under disease conditions in preclinical porcine models.

Methods: AO was performed in n=4 eyes. The rtx-1 was used to image eyes at baseline and reexamine them at biweekly timepoints after laser intervention. We tested micro pulse laser duty cycles (DC) of 1%, 1.5%, 2%, and 3% in rectangular distributions within the cone dense visual streak of the porcine retina. For image analysis, 80x80 pixel regions of interest were analyzed. MATLAB, AODetect software, and an optimized low-pass filter were utilized in quantifying cone photoreceptors in a semi-automated manner. A custom algorithm aided in calculation of cell region and circularity factor. Cone density was defined by the density of recognized cone photoreceptors within an analyzed image segment. Cell region was defined by the region including the cell and the space abutting the borders of the cell. Cell circularity was defined as a quantitative measurement of the cell border curve from 0.0-1.0, where 1.0 was a perfect circle under healthy conditions.

Results: Following RPE damage with laser, all DCs resulted in decreased cone photoreceptor density and cell circularity factor while cell region increased over the course of 4 weeks. Together, these results suggested an increase in cell morphology irregularity in porcine laser models over 4 weeks.

Conclusions: Our results show AO performed on porcine models may prove to be a useful tool in evaluating cone photoreceptor regularity under disease conditions. Our utilization of the rtx1, an AO instrument designed for clinical settings, optimizes our technique for translational purposes. These findings suggest that cone photoreceptor regularity suffers significantly under conditions that mimic AMD over a 4 week period, and help validate AO as an imaging modality to evaluate photoreceptor health at a cellular level.

CONTROL ID: 3541103

SUBMITTER (NAME ONLY): David Zhang

TITLE: Postnatal growth and neurodevelopment of infants treated with bevacizumab for retinopathy of prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.L. Zhang, S. Rahmani, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: There continues to be uncertainty regarding the systemic effects of anti-vascular endothelial growth factor (anti-VEGF) agents in the treatment of retinopathy of prematurity (ROP). We performed a retrospective clinical study to investigate postnatal systemic outcomes in ROP infants treated with one anti-VEGF agent, intravitreal bevacizumab (IVB).

Methods: All patients who developed ROP at Ann & Robert H. Lurie Children's Hospital of Chicago and Prentice Women's Hospital from 2008-2019 were identified. Three study groups were formed: infants treated with IVB, infants treated with laser photocoagulation, and infants with history of ROP without treatment. Exclusion criteria included infants with nonviable course or hydrocephalus, a source of non-physiologic weight gain. Baseline characteristics, hospital course, and systemic comorbidities were recorded. Neurodevelopment was assessed with Bayley III scores, if available. Weekly weight, length, and head circumference measurements from birth through 50 weeks postmenstrual age (PMA) were compared and plotted on the Fenton preterm growth chart to examine growth trends over time.

Results: 254 infants (139 male, 115 female) were included: 22 treated with IVB, 55 treated with laser, and 177 with ROP that resolved without treatment. Plot of growth measures on the Fenton growth chart showed that the mean weight for both genders started at the 50th percentile but deteriorated to the 14-31st percentile in girls and the 4-12th percentile in boys by 50 weeks PMA in all three groups. Similar trends for length and head circumference were observed in both genders, regardless of treatment status. One-way ANOVA comparing weekly changes in weight, length, and head circumference from birth to 50 weeks PMA showed no significant differences between study groups. Comparison of composite Bayley III scores at 24 months also trended to be not statistically significant.

Conclusions: There were no significant differences in postnatal systemic growth in children treated with IVB compared to those treated with laser and those not requiring treatment in this large retrospective study. These findings further demonstrate safety of bevacizumab treatment for ROP. Our observation that all three groups showed growth percentile deterioration from birth to 50 weeks PMA suggests that ROP development, regardless of treatment status, may be a negative predictor of postnatal growth.

CONTROL ID: 3541107

SUBMITTER (NAME ONLY): Julia Hudson

TITLE: Culture-positive endophthalmitis after open globe injuries with and without retained intraocular foreign bodies

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fan, K. Fan, D. Miller, H.W. Flynn, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|J.L. Hudson, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report on the microbial spectrum and clinical features affecting final visual acuity (VA) outcome in cases of culture-positive endophthalmitis after open globe injury.

Methods: A non-comparative, retrospective, consecutive case series. All patients were diagnosed with endophthalmitis between January 2016 and January 2020 at the Bascom Palmer Eye Institute. Culture-positive isolates from patients with history of open globe injury were identified. Variables included demographic information, time to diagnosis, mechanism of injury, causative organism, and VA outcomes.

Results: Eleven cases of culture-positive endophthalmitis after open globe injury were identified. All patients were male and average age at time of injury was 35.65 years. Penetrating trauma was the mechanism of injury in all cases. Treatment selected included intravitreal antimicrobials in 11 cases, initial pars plana vitrectomy in 8 cases, and silicone oil in 4 cases. Primary evisceration or enucleation was not performed in any patient.

Seven cases of endophthalmitis (64%) were clinically diagnosed prior to open globe repair, whereas 4 cases (36%) developed endophthalmitis after open globe repair. The average time from globe injury to presentation was 7.3 days (range 0 to 42 days). Six cases were associated with an intraocular foreign body (IOFB). Of these, 4 were metallic and 2 were composed of vegetable matter.

Coagulase-negative staphylococcus accounted for the majority of cases (55%, 6/11). Isolates included Staphylococcus epidermidis (n=5) and Staphylococcus hominis (n=1). Virulent organisms represented the remainder of cases and isolates included: Streptococcus mitis (n=1), and Bacillus cereus (n=1), Fusarium (n=1), Colletotrichum gloeosporioides (n=1), and Enterobacter cloacae (n=1).

The mean presenting VA was HM (LogMAR 2.25) and the final average VA was similarly HM (LogMar 2.1) and included 3 enucleations. For patients without an IOFB the mean VA was CF (LogMAR 1.88), as compared to HM (LogMar 2.2) in cases of IOFB.

Conclusions: In agreement with prior studies on open globe injuries, we found coagulase-negative staphylococcus to be the most commonly isolated organism in cases of culture-positive endophthalmitis. In the current study, delayed presentation to care was a common factor in the development of endophthalmitis. VA outcomes for these patients with open-globe related endophthalmitis is generally poor.

CONTROL ID: 3541127

SUBMITTER (NAME ONLY): Aaron Loewen

TITLE: Dark rearing sector RP-associated rhodopsin mutants display variable levels of retinal degeneration in transgenic *Xenopus laevis*

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Loewen, B.M. Tam, R.T. Scharbach, C.N. Chiu, O.L. Moritz, Ophthalmology & Visual Sciences, The University of British Columbia, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: 15% of non-syndromic retinitis pigmentosa (RP) cases belong to a subclass called sector RP. Sector RP is defined by the localization of the disease phenotype to certain quadrants of the retina, usually the inferior. Mutations in RHODOPSIN (RHO) are the primary cause of sector RP, with well-characterized mutations residing in the N-terminal domain (T4K, T17M, and P23H). Dark rearing animals expressing RHO containing sector RP-associated mutations (including T4K, T17M, and P23H) changes the protein's stability, mitigating the retinal degeneration (RD) phenotype; however, many other sector RP-associated RHO mutations have not been investigated in this way. We investigated sector RP-associated mutations outside the N-terminus (T58R and D190G) and an N-terminal mutation that does not interfere with a glycosylation site (L31Q).

Methods: We generated transgenic *Xenopus laevis* by injecting wildtype (WT) oocytes with a mixture of WT sperm nuclei and linearized plasmids containing a human RHO transgene (either WT or containing missense mutations) under control of a *X. laevis* rod opsin promoter. Tadpoles were raised in either cyclic light or constant dark for 14 days before euthanization. Tadpole eyes were enucleated and were either cryosectioned and immunolabelled using anti-mammalian rhodopsin antibodies for confocal microscopy or analysed for rhodopsin levels using a dot blot assay.

Results: We observed mitigated RD in the dark rearing condition for animals expressing the L31Q or T58R RHO transgenes. However, D190G RHO-expressing animals failed to display mitigated RD in the dark rearing condition. Localization of the transgenic rhodopsin in the three mutations was primarily to the outer segment; however, D190G RHO animals display more inner segment localization compared to WT, L31Q, or T58R.

Conclusions: We investigated three sector RP-associated RHO mutations that produced rhodopsin which primarily localized to the outer segment. Similar to previously described models of sector RP, two of these mutations result in RD that is reduced when animals are reared in complete darkness. The localization pattern and the RD of L31Q RHO and T58R RHO mimic the patterns previously seen in T4K RHO and T17M RHO *X. laevis*. However, RD caused by D190G RHO was not alleviated by dark rearing, suggesting that the origin of the sector RP phenotype in D190G RHO patients may be novel.

CONTROL ID: 3541134

SUBMITTER (NAME ONLY): Masumi Asahi

TITLE: Racial differences in outcomes of retinal detachment repair following pars plana vitrectomy in the postoperative period: A TriNetX Analysis

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Asahi, S. Bellur, C.T. Khoo, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|H. Pakhchanian, The George Washington University, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|H. Sen, S. Kodati, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare race-related differences in outcomes following pars plana vitrectomy (PPV) for retinal detachment (RD) in the postoperative period between individuals of black and white descent.

Methods: A retrospective cohort study was conducted using TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple large health organizations in the United States. Patients who underwent PPV for RD were identified by CPT code and stratified into black and white cohorts. Cohorts were matched for age, gender, and medical comorbidities (hypertension, diabetes mellitus, cerebrovascular disease, heart failure, nicotine dependence, alcohol related disorders, and body mass index). The primary outcomes were: retinal tear (RT), RD with retinal break, serous RD, epiretinal membrane (ERM), macular edema (ME), cataract, macular hole (MH), macular degeneration, papilledema, retinal vein occlusion (RVO), retinal artery occlusion (RAO), conjunctivitis, dry eye, optic neuritis, other disorders of optic nerve, decompression of the orbit, and endophthalmitis. Outcomes were compared between the cohorts after propensity score matching using logistic regression and greedy nearest-neighbor matching algorithm.

Results: A total of 3,516 patients were included in analysis with 1,758 in each of the black and white cohorts after propensity matching. The white cohort had a significant greater risk of developing RT (RR, 0.47; 95% CI, 0.26-0.85), RD with retinal break (RR, 0.76; 95% CI, 0.7-0.82), serous RD (RR, 0.65; 95% CI, 0.58-0.73), ERM (RR, 0.52; 95% CI, 0.34-0.79), ME (RR, 0.47; 95% CI, 0.28-0.77), and cataract (RR, 0.56; 95% CI, 0.39-0.8) whereas the black cohort had a significant greater risk of developing a MH (RR, 1.74; 95% CI, 1.2-2.53). No significant difference was seen in rate of development of macular degeneration, papilledema, RVO, RAO, conjunctivitis, dry eye, optic neuritis, other disorders of optic nerve, decompression of the orbit, or endophthalmitis between the black and white cohorts.

Conclusions: Race is an important consideration when evaluating for complications following PPV for RD. Whites were more likely to develop RD, ERM, ME, and cataracts whereas blacks were more likely to develop MH. These differences should be considered when evaluating and discussing outcomes with patients both pre and post-operatively.

CONTROL ID: 3541141

SUBMITTER (NAME ONLY): Jeffrey Yu

TITLE: Vitreous hemorrhage and hypotony with dexamethasone intravitreal implant and new injection technique described

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yu, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|S. Adrean, Retina Consultants of Orange County, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe cases of visually significant vitreous hemorrhage (VH) following dexamethasone (DEX) intravitreal implant in our practice and present two cases which did not clear spontaneously and eventually required surgical intervention, as well as a case of VH and hypotony following DEX implant. We also describe and illustrate a new injection technique in order to minimize incidence of these complications in the future.

Methods: Restrospective case series. In addition, new injection technique is described.

Results: In our practice, the overall incidence of VH was 1.7% (8/467 injections) and those that required surgical intervention was 0.4% (2/467) over a 10 year period, from June 2010 to June 2020. 75% (6/8) VH resolved spontaneously over time, without surgical intervention.

Conclusions: We propose that after the DEX applicator is in the eye, the needle should be pointed up until it is parallel to the IOL. Usually at this point, it can be directly visualized, when standing at the patient's head. The depressor is then slowly depressed and then the DEX implant can be directly visualized slowly entering the eye.

CONTROL ID: 3541179

SUBMITTER (NAME ONLY): Miguel Hernandez-Delgado

TITLE: Patient profile and outcomes regarding intraocular lens type selection in presbyopic hispanic population

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Hernandez-Delgado, M. Salan-Gomez, S. Garza-Gonzalez, M. Herrera-Rodriguez, S. Guevara-Quintanilla, J. Valdez-Garcia, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO]

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ABSTRACT BODY:

Purpose: To describe the patient's profile regarding intraocular lens (IOL) selection, either multifocal or monofocal. And their differences in age, sex, ocular surgery, IOL power and visual acuities.

Methods: Evaluation of 34 randomly selected presbyopic patients that underwent phaco with intraocular lens (IOL) implantation, 17 with multifocal lens (group 1; G1) and the rest with monofocal lens (group 2; G2) in 2020 at Zambrano Hellion Medical Center, Tecnologico de Monterrey. Patients were evaluated for age, sex, previous ocular or refractive surgery, time from surgery proposal to IOL implantation (TSPTI), time to fellow eye surgery, LogMAR preoperative best uncorrected visual acuity (BUVA) and best corrected visual acuity (BCVA), IOL power, tenth day postoperative visual acuity (VA10), and whether residual ametropia was present.

Results: From the total 34 patients, 52.9% (n= 18) were female and 47.06% (n= 16) male. Mean age at surgery was 62.55 ± 11.04 years, 59.35 ± 8.06 for G1 and 65.76 ± 12.83 for G2 ($p= 0.09$). Of all records, 26.4% (n= 9) had previous ocular surgery, 23.5% in G1 and 29.4% of G2 ($p= 0.70$), but six had previous refractive surgery, 17.6% in G1 and 17.6% in G2 ($p= 1.0$).

TSPTI was 46 median IQR days, 51 days in G1 and 35 days in G2 ($p= 0.18$). Half (n= 17, 64.7% of G1 and 35.29% of G2) of patients had fellow eye surgery in 35 MdnIQR days, 35 days for G1 and 40 days for G2 ($p= 0.51$).

BUVA before surgery was 0.5 MdnIQR with a preoperative BCVA of 0.1 MdnIQR. G1 had better BUVA (0.4, $p= 0.015$) and BCVA (0, $p= 0.0007$) in comparison to G2 BUVA (0.9) and BCVA (0.3).

Mean IOL power was 21.50 ± 4.3 D. IOL power was greater ($p= 0.017$) in G1 (mean SD 22.75 ± 3.6 D) than in G2 (mean SD 19.93 ± 4.6 D).

The sample VA10 was 0 MdnIQR. G1 had better ($p= 0.036$) VA10 (0) compared to G2 (0.2).

Residual ametropia was found in 9 patients, 10.7% in G1 and 26.1% in G2 ($p= 0.15$).

Conclusions: Age, sex and previous surgeries were not significant between groups. G2 had a tendency to have a faster TSPTI, but a slower time to fellow eye surgery. G1 had significantly better BUVA and BCVA preoperatively, as well as better VA10 than G2 with less incidence of residual ametropia, at the expense of greater IOL power requirement. IOL type selection is due to the patients perspective and desire to achieve the best possible visual acuity.

CONTROL ID: 3541185

SUBMITTER (NAME ONLY): Yingying Chen

TITLE: Disruption of the pentose phosphate pathway in Müller cells makes them more susceptible to light stress by interfering with the oxidative stress-induced NRF2 response

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, M. Zhang, Department of Ophthalmology, West China School of Medicine, Sichuan University, Chengdu, Sichuan, CHINA|Y. Chen, T. Zhang, S. Zeng, M.C. Gillies, L. Zhu, Save Sight Institute, The University of Sydney Faculty of Medicine and Health, Sydney, New South Wales, AUSTRALIA|K. Jin, X. Fan, Pharmaceutical Informatics Institute, College of Pharmaceutical Sciences, Zhejiang University, Hangzhou, Zhejiang, CHINA|R. Xu, J. Du, Department of Ophthalmology, West Virginia University, Morgantown, West Virginia, UNITED STATES|R. Xu, J. Du, Department of Biochemistry, West Virginia University, Morgantown, West Virginia, UNITED STATES|M. Zhang, Macular Disease Research Laboratory, Department of Ophthalmology, Sichuan University West China Hospital, Chengdu, CHINA|

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ABSTRACT BODY:

Purpose: The Pentose Phosphate Pathway (PPP), a metabolic offshoot of the glycolytic pathway, is essential for cell survival by providing protective metabolites and molecules. Transketolase (TKT) is the critical enzyme that controls the extent of PPP “traffic flow”. Here, we explored the role of PPP in maintaining the health of human Müller cells.

Methods: Immunofluorescence staining (IF) established that TKT was predominantly expressed by Müller cells in the human retina. We validated TKT expression further in human primary Müller cells (huPMCs) by Western Blot (WB). We inhibited the expression of TKT in huPMCs by small interfering RNA (siRNA) to disrupt PPP. The knockdown efficiency was verified by WB, IF and a TKT activity assay. We then explored the metabolic changes after PPP disruption using 1,2-C¹³ glucose as a tracer. We stressed the huPMCs, with or without TKT knockdown, by exposing the cells to 32k lux white light for 4 hours with 5 lux dim light as control. We evaluated the cell viability by AlamarBlue assay, cell death by LDH assay and metabolic states by ATP, NADPH assays. Finally, we performed a transcriptomic analysis of huPMCs after treatments, followed by protein level validation by WB. We used bioinformatic analysis to reveal the molecular pathways with prominent changes in knockdown and control groups.

Results: The Müller cell was the primary cell type expressing TKT in the retina. huPMCs also expressed TKT. siRNA treatment reduced both protein expression and enzyme activity of TKT. TKT knockdown inhibited de novo synthesis of pyruvate from glucose, while the proportion of consumed glucose that went into TCA cycle increased. The cell viability of huPMC was significantly reduced after TKT knockdown by light stress with no detectable cell death. Likewise, ATP levels and the NADPH/NADP⁺ ratio dropped after photic stress, exacerbated by TKT knockdown. According to Ingenuity Pathway Analysis, the NRF2 pathway was activated after photic stress, while one of the downstream targets, NAD(P)H Quinone Dehydrogenase 1, was reduced by TKT knockdown.

Conclusions: Müller cells express TKT abundantly. Knockdown of TKT not only disrupted the PPP but also impaired overall glucose utilization by Müller cells. Knockdown of TKT made the cells more vulnerable to light stress, possibly by impairing NRF2 anti-oxidative responses.

CONTROL ID: 3541187

SUBMITTER (NAME ONLY): Zhenyu Ji

TITLE: Therapeutic effects of recombinant heparin-binding domain protein in a mouse model of diabetic retinopathy

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Ji, Y. Su, A. Mackey, Y. Ng, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Z. Ji, Y. Su, Wuhan University Renmin Hospital, Wuhan, Hubei, CHINA|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is characterized by increased numbers of leukocytes attachment (leukostasis) and vascular hyperpermeability (VP) of the retinal vessels. Previous experimental evidence supports that the heparin-binding VEGF165 isoform, but not the VEGF121 isoform that lacks the heparin-binding domain (HBD), is responsible for inducing retinal leukostasis. Preliminary data showed that the recombinant HBD (rHBD), which likely function as a competitive VEGF165-specific inhibitor for heparan sulfate proteoglycans binding, inhibited VEGF165-induced leukostasis and pathological angiogenesis in an oxygen-induced retinopathy model. Thus, we hypothesize that rHBD also has potential therapeutic effects in a mouse model of DR.

Methods: Streptozotocin (STZ) injection of 6-8 weeks old C57BL/6 male mice were used to induce diabetes (blood sugar levels of at least 250 mg/dL). Retinal VP was measured with the Fluorotron Master Ocular Fluorophotometer (Laboratory Mouse Edition) and retinal leukostasis was quantified by FITC-concanavalin A perfusion assay with retinal flat-mount and fluorescence microscopy. The mice were injected with rHBD (50 pmol) or vehicle control intravitreally 6 months after induction of diabetes. Statistical analysis of data (mean \pm SEM) was performed using t-test and one-way ANOVA.

Results: Retinal VP was significantly increased in diabetic mice compared to non-diabetic mice (29.23 ± 0.90 vs. 17.17 ± 1.06 , $P < 0.0001$). A single intravitreal injection of rHBD significantly reduced retinal VP by about 20% in diabetic mice compared to vehicle injected control (23.78 ± 0.96 vs. 29.41 ± 1.13 , $P < 0.001$). Diabetic mice received vehicle treatment had increased leukostasis compared to non-diabetic mice (9.85 ± 0.74 vs. 3.50 ± 0.31 , $P < 0.0001$), while rHBD injection significantly reduced leukostasis compared to vehicle injected control (3.13 ± 0.38 vs. 9.85 ± 0.74 , $P < 0.0001$), and to the levels comparable to that of the non-diabetic mice.

Conclusions: These data demonstrated that intraocular injection of rHBD significantly suppress retinal vascular hyperpermeability and leukostasis in a mouse model of DR, therefore rHBD could be an efficacious therapeutic for DR.

CONTROL ID: 3541207

SUBMITTER (NAME ONLY): Claude Michael Salva

TITLE: Addition of Mid-peripheral Fields to 2-Field Disc and Macula Handheld Retinal Images Improves Agreement with Early Treatment Diabetic Retinopathy Study (ETDRS) 7-Standard Field Photography

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.G. Salva, L. Aquino, R.P. Salongcay, A.V. Saunar, G.P. Alog, Philippine Eye Research Institute, University of the Philippines Manila, Manila, Metro Manila, PHILIPPINES|R.P. Salongcay, T. Peto, Centre for Public Health, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|L.P. Aiello, P.S. Silva, Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|L.P. Aiello, P.S. Silva, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Claude Michael Salva: Commercial Relationship: Code N (No Commercial Relationship) | Lizzie Anne Aquino: Commercial Relationship: Code N (No Commercial Relationship) | Recivall Salongcay: Commercial Relationship: Code N (No Commercial Relationship) | Aileen Saunar: Commercial Relationship: Code N (No Commercial Relationship) | Glenn Alog: Commercial Relationship: Code N (No Commercial Relationship) | Tunde Peto: Commercial Relationship: Code N (No Commercial Relationship) | Lloyd Aiello: Commercial Relationship: Code N (No Commercial Relationship) | Paolo Silva: Commercial Relationship(s);Hill-Rom:Code F (Financial Support);Optos:Code F (Financial Support);OptoMed:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To determine benefit of 5-field (5F) vs 2-field (2F) mydriatic handheld retinal imaging for assessment of diabetic retinopathy (DR) as compared with standard ETDRS 7-field 30⁰ fundus photographs (ETDRS photos).

Methods: Following standard imaging protocol, 5 fields (macula, disc, superior, inferior and nasal) were acquired using 2 handheld retinal cameras [Aurora (AU), Smartscope (SS)] and ETDRS photos following pupil dilation (Figure 1). Images were evaluated at a centralized reading center independently by masked graders (International DR Classification). Simple (K) and weighted (K_w) kappa statistics assessed agreement for DR. Sensitivity and specificity for any DR, referable DR [(refDR) moderate nonproliferative DR (NPDR) or worse, any DME or ungradable images] and vision threatening DR [(vtDR) severe NPDR or worse, clinically significant DME (CSME) or ungradable images] were calculated.

Results: Images from 177 eyes of 92 patients with diabetes were evaluated. By ETDRS photos: No DR 40.1% eyes, mild NPDR 19.2%, moderate 14.7%, severe 10.2%, proliferative DR 15.8%; No DME 72.9% eyes, DME 6.8%, CSME 17.0%; ungradable 3.4%. Ungradable rate for DR: AU, 2F:1.1%, 5F:0%; SS, 2F:5.0%, 5F: 4.5%; and DME: AU:10.2%, SS:13.0%. DR agreement with ETDRS photos are shown in table 1. 5F imaging increased exact agreement w/ ETDRS photos by 32.5% AU and 19.8% SS and w/in 1-step by 8.9% AU, 6.6% SS. 5F imaging increased k agreement w/ ETDRS photos for DR from moderate to substantial for both AU and SS. Reliability indices are shown in table 1. 5F imaging increased sensitivity for any DR, refDR and vtDR on both AU (0.76 to 0.97, 0.78 to 0.88, 0.83 to 0.86) and SS (0.79 to 0.82, 0.79 to 0.87, 0.83 to 0.89).

Conclusions: The peripheral fields obtained using a 5F protocol with 2 handheld retinal cameras substantially increased agreement with ETDRS-determined DR as compared with only posterior 2F imaging. Sensitivity increased while maintaining specificity for identifying refDR and vtDR. The observed DR grading agreement between 5F handheld imaging and ETDRS photos suggests that handheld retinal imaging performed in this manner may be accurate enough for DR screening programs, where their size, cost and ease of use attributes would allow them to be widely deployed in community-based DR screening programs.

CONTROL ID: 3541208

SUBMITTER (NAME ONLY): Fei Shang

TITLE: Mouse retinal microvessels with single-file blood flow express alpha smooth muscle actin

SESSION TITLE: Blood flow, ischemia, reperfusion

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Shang, Neuroscience, University of Rochester Medical Center, Rochester, New York, UNITED STATES|F. Shang, J.B. Schallek, Center for Visual Science, University of Rochester Medical Center, Rochester, New York, UNITED STATES|J.B. Schallek, Flaum Eye Institute, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Fei Shang: Commercial Relationship: Code N (No Commercial Relationship) | Jesse Schallek: Commercial Relationship(s);University of Rochester:Code P (Patent);Hoffman-LaRoche:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Alpha smooth muscle actin (α -SMA), a contractile protein, mediates retinal vascular tone and neurovascular coupling. Studies report dense α -SMA surrounding retinal arterioles, but microvessel α -SMA is controversial due to complications of immunohistochemistry (IHC) including antibody penetration and rapid histological degradation. Here we characterize the extent of α -SMA expression in the retinal vasculature using ex vivo and in vivo imaging of transgenic mice.

Methods: We used two transgenic mouse strains (FVB JAX #025406; C57BL/6J #032887) to study the structure of α -SMA fluorescence expression in vessels (mCherry or mVermilion, and GCaMP). Ex vivo, we performed epifluorescence microscopy of flat-mount retinas from mice >10 weeks old (n=7 FVB, n=5 C57). In vivo, we used a custom-build adaptive optics scanning light ophthalmoscope (AOSLO) to capture phase-contrast (796/17 nm) and fluorescence images with safe light levels (GCaMP: Ex 488 nm Em 520/35 nm; mVermilion: Ex 561 nm Em 630/92 nm) (n=3 FVB). We quantified the diameter and branch order of all vessels that could be traced to the optic disc.

Results: Arterioles had strong α -SMA expression that diminished at progressive branch orders. Yet ex vivo retinas showed fluorescence in some of the smallest vessels (3 μ m), suggesting heterogeneous organization. 41% of α -SMA+ vessels were <7 μ m. Both strains had similar expression patterns and we detected α -SMA up to 7th order (5.13 \pm 0.83 μ m; mean \pm SD) (Fig1). Similarly, in vivo imaging showed bright α -SMA in arterioles (visible at 5 μ W) while microvessels required more power (134 μ W). This was likely due to lower volumetric α -SMA. We observed fluorescence up to 5th order (10.54 \pm 2.86 μ m). Simultaneous phase-contrast imaging of the same vessels showed luminal diameter of 3.89 \pm 1.19 μ m necessitating single-file blood flow (Fig2).

Conclusions: Many microvessels that accommodate single-file blood flow were α -SMA+. AOSLO imaging corroborates ex vivo findings and further overcomes histological confounds. This finding suggests microvessels have the potential to regulate hemodynamics at the scale of tens of micrometers. This is noteworthy given the retina's high metabolic demand that may be differential in lateral and laminar organization of neural populations. Ongoing work is examining the contractile calcium response (GCaMP) to determine whether differential control exists at this vascular level.

CONTROL ID: 3541217

SUBMITTER (NAME ONLY): Chase Paulson

TITLE: Exfoliation Syndrome in the Baja Verapaz Region of Guatemala

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Paulson, S. Taylor, J. Herrick, K. Curtin, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|S.C. Thomas, Stanford University Department of Medicine, Stanford, California, UNITED STATES|O. Gonzalez, Lions Club Eye Hospital, Salamá, GUATEMALA|C. Swiston, K. Curtin, C.J. Chaya, B.C. Stagg, B.M. Wirostko, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is little epidemiologic data on exfoliation syndrome (XFS) or exfoliation glaucoma (XFG) in Guatemala, especially in the Baja Verapaz region. XFS is an ocular and systemic proteinaceous disorder that causes abnormal fibrillar extracellular material deposition in the eye, heart, brain, lungs and skin (1,2,3). Solar exposure and outdoor occupation have been linked to XFS development (4). This observational study assessing XFS and demographic factors of this region aims to better understand unique exogenous and endogenous risk factors associated with XFS in Guatemala.

Methods: During Moran Eye Center's global outreach cataract trips in 2016 and 2017, 171 patients were evaluated; 46 XFS and 9 XFG patients over age 49 were identified on site and by chart review (Dr. Orlando Gonzalez, Lions Health Club in Salamá). Age, gender, hometown, ancestry (languages spoken by parents and grandparents), past medical history, family medical history and occupational data were obtained for each patient. Under translated informed consent, blood samples from XFS patients and their family members were collected. This research was conducted under Utah IRB (00081512).

Results: Out of 171 total cataract patients and their cataract-free family relatives, 18 lacked a clear diagnosis of either XFS/XFG or control resulting in 153 viable patients. Of these, 66 were male (43%) and 81 were female (53%) and 6 did not indicate gender. The average age of all patients was 64yrs. Those 55 having XFS and XFG were on average 72yrs. The most common occupations were farming and housekeeping. Higher rates of XFS/XFG were noted in individuals of rural (41%) compared to urban settings (24%). Rates of XFS/XFG in Mayan speaking people were 39% compared with 35% in Spanish speakers. Based on this subset of patients, the prevalence of XFS/XFG appeared to be roughly 35%. Blood analysis is underway.

Conclusions: Although study limitations exist (i.e. small sample size and cataract selection bias), this specific population appears to have a high prevalence of XFS compared with other world populations. Further studies are warranted to better understand possible environmental stressors contributing to XFS. Location, higher altitude, along with a farming occupation may contribute to XFS development and subsequent progression to XFG. To our knowledge, this is the first study looking at the epidemiology of XFS/XFG in Guatemalans.

CONTROL ID: 3541243

SUBMITTER (NAME ONLY): Minh Anh Thu Phan

TITLE: EFFECTS OF DHT AND ESTRADIOL ON ROSIGLITAZONE-INDUCED LIPID PRODUCTION IN IMMORTALISED HUMAN MEIBOMIAN GLAND EPITHELIAL CELLS

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Phan, M.C. Madigan, F. Stapleton, M. Willcox, B. Golebiowski, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Human meibomian glands and immortalised human meibomian gland epithelial cells (iHMGEc) contain sex hormone receptors and the molecular machinery required for their biosynthesis, suggesting a role of sex hormones in MG biological function. This study aimed to determine the effects of dihydrotestosterone (DHT) and estradiol (E2) on lipid production in iHMGEc cultured in serum-free medium with rosiglitazone (Rosi, a PPAR γ -agonist), a known inducer of iHMGEc differentiation. We also examined the effect of Rosi on iHMGEc viability.

Methods: iHMGEc were cultured to 80% confluence in keratinocyte serum-free medium, then switched for 2-4 days to serum-free media containing various concentrations of DHT, E2, and Rosi, alone and in combination (n=4 wells/each treatment, n=3 experiments/treatment). Cell viability was assessed using the MTT assay. Accumulation of intracellular lipid droplets was quantified using a Nile Red-cell nucleus (DAPI) spectroscopic assay. Differences between treatments were compared using one-way ANOVA with post-hoc comparisons using Tukey's test ($\alpha=0.05$).

Results: DHT (1-100 nM) or E2 (0.1-10 nM) alone did not significantly affect cell viability. However, treatment with Rosi (alone and in combination with DHT and/or E2) significantly decreased iHMGEc viability by up to 50% when used at 50 μ M ($p<0.001$). Lipid accumulation in iHMGEc treated with Rosi (30 μ M) was significantly higher relative to the medium-only control ($p<0.001$), but the addition of DHT (10 nM) and/or E2 (1 nM) had no further significant effect. DHT (10 nM), E2 (1 nM) and DHT+E2 without Rosi did not affect lipid accumulation in iHMGEc cultured in serum-free medium.

Conclusions: The sex hormones DHT and E2 did not induce lipid accumulation in iHMGEc cultured in serum-free medium, nor affect cell viability. In contrast, treatment with Rosi significantly increased lipid accumulation but adversely affected iHMGEc viability when used at the higher concentration (50 μ M). Further investigations are required to better understand the mechanisms of iHMGEc differentiation, cell survival and lipid secretion.

CONTROL ID: 3541247

SUBMITTER (NAME ONLY): Tara Stonex

TITLE: Peptide Inhibitors of MARCKS Reverse Endotoxin Induced Uveitis in Rats

SESSION TITLE: Cytokines, growth factors, anti-inflammatory

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.M. Stonex, B. Salmon, B.C. Gilger, Clinical Sciences, North Carolina State University, Raleigh, North Carolina, UNITED STATES|K. Adler, Molecular Biomedical Sciences, North Carolina State University, Raleigh, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveitis, the most common form of intraocular inflammation, accounts for 10-15% of preventable blindness in the United States. A potential pathogenic driver (and thus therapeutic target) for uveitis is MARCKS (Myristoylated Alanine Rich C Kinase Substrate) protein. We tested the hypothesis that inhibition of MARCKS, using novel MARCKS inhibitor peptides, would reduce the severity of endotoxin-induced uveitis (EIU) in a rat model.

Methods: EIU was induced in 28 female Lewis rats via subcutaneous administration of 300 µg of lipopolysaccharide (LPS). Three different novel MARCKS inhibitor peptides that mimic the N-terminal region of MARCKS (BIO-11006, or lower molecular weight analogs BIO-91201 or BIO- 91202; Biomarck, Inc., Durham, NC), were administered intravitreally in both eyes at two different concentrations (50µM and 100µM; n=4 rats/treatment group) 4 hours after LPS administration. Phosphate buffered saline (PBS) was injected intravitreally to serve as control (LPS/PBS control group). Ocular inflammation was scored in a blinded manner using slit lamp examinations prior to and following dilation with tropicamide prior to LPS administration, and again at 8, 12, and 24 hours following LPS administration. Optical coherence tomography (OCT) anterior chamber cell counts were done 24 hours after LPS administration. Rats were euthanized 24 hours following EIU induction, aqueous humor collected, and eyes processed for histology.

Results: LPS elicited a significant increase ($p<0.001$) in clinical scores of inflammation at all time points following EIU induction compared to PBS controls. At 12 hours post LPS, the following treatment groups showed significant decreases in clinical scores: BIO-11006 100µM; BIO-91201 50 & 100µM; and BIO-91202 50µM ($p<0.02$). Clinical scores were also significantly decreased at 24 hours post LPS in the following treatment groups: BIO-11006 50 & 100µM; BIO-91201 50 &100µM; and BIO-91202 100µM ($p<0.05$). OCT aqueous humor cell counts were significantly higher ($p<0.001$) in response to LPS at 24 hrs. Each of the peptide treatment groups showed a significant ($p<0.001$) decrease in cell counts at this time point.

Conclusions: MARCKS inhibitor peptides were effective in reducing the clinical severity of ocular inflammation and cellular influx in the EIU rat model of acute uveitis. These results indicate that MARCKS could be an effective therapeutic target to treat uveitis.

CONTROL ID: 3541264

SUBMITTER (NAME ONLY): shuyan zhu

TITLE: Corneal nerve-derived calcitonin gene-related peptide (CGRP) attenuates inflammation in chronic dry eye disease

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. zhu, T. Blanco, K. Pang, R. Dana, J. Yin, Department of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously demonstrated that chronic dry eye disease (DED) leads to decrease in corneal innervation. Calcitonin gene-related peptide (CGRP) is expressed in trigeminal ganglion (TG) neurons, from which corneal nerves originate, and has anti-inflammatory function. In this study, we aim to investigate the role of TG- and corneal nerve-derived CGRP in chronic DED.

Methods: Chronic DED was induced by placing C57BL/6 mice in a controlled environment chamber for 2 weeks, followed non-desiccating standard vivarium for 4 weeks. Corneal nerve density and CGRP expression in the cornea were determined with immunofluorescence of β -tubulin III and CGRP, respectively. Protein levels of CGRP in the TG and corneas were detected with Western blotting. Topical CGRP was given three times daily 1 week after DED induction and corneal fluorescein staining (CFS) was recorded. Expression of inflammatory cytokines in the TG and frequencies of CD45⁺ leucocytes in the cornea were determined with real-time PCR and flow cytometry, respectively.

Results: In chronic, but not acute, DED, central corneal subbasal nerve density was decreased by 20% (P=0.005) and CGRP expression in the cornea (64% decrease, P=0.002) and TG (50% decrease, P=0.026) were significantly reduced, compared to age-matched control mice. Topical application of CGRP led to a decrease in CFS, compared to albumin-treated control mice (11.4 vs 8.7, P=0.04). CGRP treatment led to lower expression of TNF- α (P= 0.031), IL-1 β (P= 0.017) and IL-6 (P= 0.011) in TG. Frequencies of CD45⁺ cells decreased by 23.7% in CGRP-treated corneas

Conclusions: CGRP expression in the cornea and TG is decreased in chronic, but not acute, DED. Topical application of CGRP alleviates clinical signs of DED and inflammation in the cornea and TG, suggesting a critical role of nerved-derived CGRP in DED and its therapeutic potential

CONTROL ID: 3541276

SUBMITTER (NAME ONLY): Bin Lin

TITLE: Effect of immunosuppression on hESC-derived retina organoids in vitro and in vivo

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lin, R. Sims, Y. Xue, R.T. Fouda, J.A. Santoso, R. Aramant, M.J. Seiler, Sue and Bill Gross Stem Cell Research Center, University of California Irvine, Irvine, California, UNITED STATES|Y. Xue, A.W. Browne, Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|B. McLelland, G. Nistor, H. Keirstead, AIVITA Biomedical, Irvine, California, UNITED STATES|A.W. Browne, Institute for Clinical and Translational Science, and Ophthalmology, Gavin Herbert Eye Institute, University of California Irvine, Irvine, California, UNITED STATES|M.J. Seiler, PM&R, Ophthalmology, Anatomy & Neurobiology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The effect of immunosuppression on the development of human embryonic stem cell (hESC) derived retina organoids (ROs) produced by a scalable cGMP compatible process was studied in vitro and after transplantation to the subretinal space of immunocompetent retinal degeneration (RD) rats.

Methods: A Working Cell Bank (WCB) of CSC-14 hESCs (NIH 0284) was established using a scalable cGMP compatible process. ROs differentiated from hESCs were characterized by immunohistochemistry (IHC), flow cytometry, qPCR and a two-way mixed lymphocyte reaction (MLR). Functional and structural imaging of organoids was obtained using fluorescence lifetime imaging microscopy (FLIM) and hyperspectral imaging (HSPEC). Retina organoid sheets were transplanted to the RD hosts and monitored by Optical Coherence Tomography (OCT). Immunosuppressants (20-30mg Tacrolimus [TAC] pellet implant in combination with oral mycophenolate mofetil [MMF]) were applied to the rats. TAC levels in blood were determined by LC-MS. Cytostatic effects on target lymphocyte populations were evaluated by flow cytometry. Visual function was accessed by optokinetic tests and superior colliculus electrophysiology. Sections through transplants were stained with hematoxylin & eosin (H&E) and IHC. The effect of TAC (3 ng/ml) and MPA (0.5 µg/ml) on retinal organoids was tested by FLIM after 1 and 4 weeks exposure.

Results: The WCB of hESCs meets the FDA requirements. In vitro immunogenicity tests showed that ROs are not likely to induce an immune response. IHC of ROs shows early lamination and development of retinal cell progenitors. At 2-3 mo. of differentiation, organoids switched their metabolic status from more glycolytic to more oxidative which remained stable at 4 months. Immunosuppressants TAC and MPA showed no influence on the metabolic activity of retinal organoids after 1 and 4 weeks of exposure. OCT revealed transplant development and photoreceptor rosettes. The transplants developed different retinal cells including photoreceptors; and integrated with the host retina. Therapeutic levels of immunosuppressant remained in the blood and helped transplants survive in the host.

Conclusions: Retina organoids matured and developed photoreceptors in long-term culture and after transplantation. Immunosuppressants did not measurably alter the metabolic status of organoids, and prevented rejection of retinal organoid transplants.

CONTROL ID: 3541278

SUBMITTER (NAME ONLY): Jennifer Liao

TITLE: The Decline of Ophthalmology in General Medical Education and Strategies to Overcome Barriers to Learning

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Liao, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jennifer Liao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: As the U.S. population ages, it is expected that demand for visual care will significantly rise in the next few decades. However, there has been a continuous decline of ophthalmology education in medical school curriculum. This literature review aims to explore research and conceptual pieces on the state of ophthalmology education and investigate potential ways to address current challenges and better prioritize ophthalmology curriculum time in undergraduate and graduate medical education.

Methods: A search was conducted in PubMed and ERIC with the search terms: ((Ophthalmology[Title]) AND (Education[Title])) AND ((Medical student) OR (Resident)). Irrelevant articles and articles published before 2000 were eliminated, yielding 30 final articles.

Results: Five primary themes were identified: challenges to ophthalmological education around the world, potential remedies for optimizing ophthalmology curriculum, competency-based ophthalmology education, utilization of technology in ophthalmology education, and ophthalmology service, ethics, and empathy. Major challenges included the lack of a standardized curriculum and inadequate clinical exposure. A number of remedies were proposed, such as increasing adherence to curriculum guidelines, encouraging relationships between ophthalmology faculty and medical school administration committees, and extending utilization of extracurricular activities. Other recommendations included the incorporation of competency-based education, technology-based curriculum, and self-regulated learning. Programs also explored humanistic aspects of ophthalmology education and its role in expanding underserved care.

Conclusions: In light of challenges in ophthalmology education, ophthalmology programs have increasingly proposed solutions to optimize limited curriculum time. In order to ensure all core competencies are met, there are three major areas to tackle, including: 1) adjusting current curriculum to address learner needs, 2) maximizing learning opportunities by promoting crossover between ophthalmology and other disciplines, and 3) cultivating empathy and service motivation to improve care and increase underserved outreach. Valuable addition to ophthalmology education research would be more qualitative studies engaging the students' and educators' perspectives of ophthalmology curriculum, in order to provide a more holistic view of ophthalmology education.

CONTROL ID: 3541281

SUBMITTER (NAME ONLY): Brian Nguyen

TITLE: Assessing Interest in Point-of-care Diabetic Retinopathy Screening in Primary Care

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of this study was to determine the willingness of patients to undergo point-of-care diabetic eye screening with primary care providers (PCPs) by means of non-mydriatic fundus photography (nFP).

Methods: An anonymous ten-question survey was mailed out to a random sample of patients overdue for diabetic retinopathy screening examinations. The survey was designed to measure self-reported health status, diabetic and eye-health literacy, perceived barriers to in-person eye examinations, and willingness to undergo nFP. Demographic data was limited to age and gender. Chi-Square Test-Cramer's V, Pearson's correlation coefficients, and linear regression were used in the statistical analyses.

Results: Out of 390 patients surveyed, 62 participants (16%) returned a completed questionnaire by mail. Roughly half of participants were over the age of 65 (56%). Participants generally rated themselves in above-average health (7.0 ± 1.8). The participants' overall rating of health was inversely correlated with concern about losing vision because of diabetes ($F_{4,55} = 2.931$, $p = 0.029$). Ability to drive (79%) was positively associated with the frequency of eye examinations ($F_{3,58} = 6.61$, $p < 0.001$). In contrast, driving had no impact on frequency of seeing PCPs ($p=0.446$ [KMR1]). Despite the survey being sent to patients identified as being overdue for screening examinations for diabetic retinopathy (an average of 731 ± 413 days), more than 90% of participants reported that they obtained eye checkups at least annually despite evidence to the contrary. The most common disincentives reported for obtaining in-person eye examinations were: difficulty in scheduling or inconvenient location (27%); reluctance to have eyes dilated or finding eye examinations uncomfortable (11%); and high out-of-pocket costs (11%). Respondents who cited barriers to obtaining eye examinations were more likely to be interested in nFP compared to those who cited none ($V = 0.360$, $p=0.023$). Patients who stated that they saw their eye doctor frequently were more likely to continue to do so after nFP screening ($V = 0.335$, $p=0.015$).

Conclusions: Diabetic eye screening by means of nFP is likely to be accepted by a majority of patients as a point-of-care test, if offered by PCPs. Patients who experience barriers in accessing traditional in-person eye care services are more likely to favor diabetic eye screening by nFP.

CONTROL ID: 3541295

SUBMITTER (NAME ONLY): Sophie Kim

TITLE: Bactericidal effect of povidone-iodine solution and swabs through lidocaine gel

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The use of lidocaine gel was reported as a potential independent risk factor in the development of post-intravitreal injection endophthalmitis. Previously, we reported that 10% povidone-iodine (PVI) swabs were able to penetrate lidocaine gel to yield comparable PVI concentration to 5% PVI solution without gel. This follow up study aimed to directly determine the bactericidal effectiveness of various PVI applications by demonstrating growth inhibition of *Staphylococcus epidermidis*.

Methods: Mueller Hinton agar plates were inoculated with *S. epidermidis* (ATCC 12228) from a tryptic soy agar slant. 6mm diameter discs were punched from cellulose filter paper. In the control group, 50 µL of 5% PVI was applied to the discs. 5 variable groups were treated with (1) 3.5% lidocaine gel plus 50 µL 5% PVI, (2) gel with 10% McKesson PVI swab, (3) gel with 10% PDI PVI swab, (4) gel with 5% PVI soaked cotton-tip applicator (CTA), and (5) gel with 10% soaked CTA. An additional plate with a plain disc, disc with lidocaine gel, and PDI PVI 10% swab directly applied served as controls. The discs were placed on the inoculated plates and incubated for 24 hours. Zones of inhibition (ZOI) were measured for each plate.

Results: 10 discs were plated for each group. The gel + 5%, gel + McKesson swab, gel + 5% CTA, and gel + 10% CTA groups yielded smaller ZOIs compared to the control, no gel + 5% (all $p < 0.001$), and to gel + 10% PDI swab (all $p < 0.001$). There was no significant difference between the ZOI of the control versus gel + 10% PDI swab. Both McKesson and PDI swabs yielded a greater ZOI than gel + 5% ($p < 0.001$), however PDI swabs produced a greater ZOI than McKesson swabs ($p = 0.0004$).

Conclusions: The results redemonstrated that the gel barrier significantly decreases the amount of 5% PVI solution in contact with the treated surface. The data suggests that the mechanical force of application with 10% PVI swabs can penetrate the gel barrier with enough PVI to produce a bactericidal effect similar to the control. However, the amount of PVI is dependent on the manufacturer and amount of PVI loaded into the swab.

The main limitation of this study lies in its in vitro nature. Major differences between our model and the human eye may affect interaction with topical PVI. Further investigation with randomized controlled trials are needed to elucidate the relationship between post-injection endophthalmitis and prep method.

CONTROL ID: 3541300

SUBMITTER (NAME ONLY): Kendra Hong

TITLE: Hemiretinal vessel density asymmetry supplements diagnostic accuracy of retinal nerve fiber layer thickness for glaucoma

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.L. Hong, B. Burkemper, A. Urrea, R. Chang, J. Lee, V. LeTran, B. Xu, B. Wong, B.J. Song, X. Jiang, G. Richter, Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|Z. Chu, X. Zhou, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R. Varma, Southern California Eye Institute, CHA Hollywood Presbyterian Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study investigates hemiretinal asymmetry in radial peripapillary capillary vessel area density (VAD) of healthy, glaucoma suspect, and primary open angle glaucoma (POAG) eyes of varying severity, and its diagnostic utility, alone and in combination with other ocular parameters, for POAG.

Methods: 6x6-mm optic disc scans were collected on optical coherence tomography angiography to obtain VAD and on OCT to measure circumpapillary retinal nerve fiber layer (RNFL) thickness. Hemiretinal difference in VAD (hdVAD) was defined as the absolute difference between superior and inferior hemiretinal VAD. Age-adjusted multivariable linear regression of hdVAD on POAG severity was performed. Area under curves (AUCs) were calculated from predicted probabilities generated by multiple logistic regression of POAG severity on age-adjusted values of either a single parameter or a combination of parameters. DeLong's test was used to determine the statistical significance of differences in AUCs from various models, thus identifying parameters with the greatest diagnostic accuracy.

Results: 1069 eyes of 1069 participants (602 healthy, 275 glaucoma suspect, and 192 POAG classified into 70 mild, 56 moderate, and 66 severe POAG) were included. After adjusting for age, mean hdVAD was similar between healthy and suspect ($\beta = 0.002$, $P = 0.253$), higher in mild versus suspect ($\beta = 0.013$, $P < 0.001$), higher in moderate versus mild ($\beta = 0.010$, $P = 0.009$), but lower in severe versus moderate ($\beta = -0.012$, $P = 0.001$). AUCs of hdVAD were qualitatively highest for mild (0.674) and moderate (0.685) POAG (versus 0.515 for suspect, 0.602 for severe POAG, 0.655 for any POAG). A combination of hdVAD and global RNFL (gRNFL) had the highest AUC of all parameters for mild (0.809) and any POAG (0.851), which were greater than AUCs of either hdVAD ($P < 0.001$ for both comparisons) or gRNFL ($P = 0.041$ for mild, $P = 0.048$ for any POAG) alone.

Conclusions: hdVAD is higher in early POAG and may help with early detection when damage is focal, but its diagnostic ability appears to be less robust in advanced POAG when damage is diffuse. Combination of hdVAD and gRNFL yielded the best diagnostic accuracy of all parameter permutations for mild and any POAG, suggesting the potential of hdVAD to supplement gRNFL and other ocular parameters in the diagnosis of early POAG.

CONTROL ID: 3541301

SUBMITTER (NAME ONLY): Soraiya Thura

TITLE: Risk of posterior subcapsular cataract development among uveitis patients treated with topical difluprednate

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Thura, P. Janardhana, Ophthalmology, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|S. Thura, P. Janardhana, Ophthalmology, UMass Memorial Medical Center, Worcester, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We sought to investigate the risk of posterior subcapsular cataract development amongst patients treated for uveitis with 0.05% topical difluprednate.

Methods: This is a retrospective cohort study assessing patients with uveitis who were treated with topical difluprednate from January 1st, 2016 through October 30th, 2020 at an academic medical center. Thirty patients (forty eyes) were evaluated through a chart review to collect clinical data which was then analyzed. Patients that received cataract surgery before being treated with difluprednate for uveitis were excluded.

Results: Twelve eyes (30%) were observed to have had development or progression of PSC. For the eyes that developed a PSC, both the duration (mean of 17.3 weeks versus 13.7 weeks) and total cumulative dose (mean of 334 drops versus 271.6 drops) of topical difluprednate were higher compared to patients who did not develop a PSC. The average time to development of a PSC noted on eye exam after the initiation of difluprednate was 12.9 months. Nine eyes (30%) were noted to have ocular hypertension at some point during the follow-up period, and all of these eyes were controlled with pressure-lowering drops. The current data collection and analysis will continue to include information on confounding variables such as additional topical and oral steroid use, posterior sub-tenon kenalog injections, presence of active uveitis, as well as a stratification of daily drop use and duration of treatment.

Conclusions: In our cohort of uveitis patients, we have found that an increased duration and cumulative dosing of difluprednate treatment is associated with an increased risk of posterior subcapsular cataract formation. Based on our current collected data, we predict that this finding will be significant when controlling for other variables associated with formation of PSC. This is one of only a few studies that have assessed the impact of topical difluprednate on cataract formation in an adult uveitic population. We believe this study will provide further clinical insight into the safety profile and dosing of difluprednate, as well as contribute to our knowledge of topical steroid treatment regimens for patients with uveitis.

CONTROL ID: 3541330

SUBMITTER (NAME ONLY): Sushmitha RAJA

TITLE: Influence of anesthesia and electrode type on dual-eye mouse electroretinogram

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. RAJA, W. Jiang, M. Cameron, School of Medicine, Western Sydney University, Penrith South, New South Wales, AUSTRALIA]

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ABSTRACT BODY:

Purpose: A combination of ketamine and xylazine has been used as the choice of anesthetic to record electroretinogram (ERG) in rodents, however, an increase in the sudden death of animals has been reported in recent years. Replacing xylazine with medetomidine, an $\alpha 2$ agonist reports higher survival rates and isoflurane has also been shown to be a suitable alternative, with a much lower mortality rate. In this study, we aimed to assess the suitability of ketamine/medetomidine and isoflurane on mouse ERG. Furthermore, we aimed to determine the best electrode type to minimize crosstalk while recording from both eyes simultaneously. A new conductive material "StaticotTM" (polyester/cotton blended with 8 μ m stainless steel fibers) was trialed as an ERG electrode and compared to highly conductive platinum electrodes.

Methods: ERGs were recorded from mice anaesthetised with either ketamine (72 mg/kg)/ medetomidine (0.5 mg/kg) or 1.75% isoflurane. Both males and females were used with ages ranging between 12-18 weeks. Electrodes (platinum, staticotTM) were embedded in contact lenses and placed on both eyes simultaneously. Dark- and light-adapted ERG responses to a range of light stimuli were recorded.

Results: No differences were observed in either a-wave amplitude or implicit time but ketamine/medetomidine injected animals displayed a reduction in b-wave amplitude and a large increase in b-wave implicit time in comparison with the isoflurane cohort in dark and light-adapted ERGs. Overall, isoflurane ERG parameters were more similar to published values for the ketamine/xylazine than ketamine/medetomidine suggesting that medetomidine significantly suppresses second/third order processing. Recovery from ketamine/medetomidine was longer, even following $\alpha 2$ antagonist reversal (atipamezole 1 mg/kg), and the mortality rate was 37.5% (n=8). The isoflurane cohort showed rapid recovery and no mortality (n=9). Recordings conducted using platinum electrodes showed some cross-communication between the electrodes in the dual-eye ERG, while no such crosstalk was observed with staticot electrodes.

Conclusions: Isoflurane is a viable alternative to the traditional ketamine/xylazine combination and displays rapid recovery and enhanced survival of animals. Staticot conductive fiber is a suitable and cost-effective replacement of traditional electrodes for dual-eye ERG recordings.

CONTROL ID: 3541358

SUBMITTER (NAME ONLY): Angela Yim

TITLE: Clinical validation of Age-Related Macular Degeneration remote monitoring device

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Yim, L. Azzouz, A. Yu, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|Y.M. Paulus, Ophthalmology, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in industrialized countries. While treatments are available, prompt identification of conversion to wet AMD is necessary for optimal patient outcomes. A digital, handheld standalone device using shape discrimination hyperacuity to identify a patient's minimum distortion-detection threshold has been described. This study performs a clinical validation of that device.

Methods: Using a prototype device (KaIEYEdoscope) with an injection-molded 3D printed shell, two tactile buttons, a battery, a processing unit (Raspberry Pi 3), and a 1.5 inch RGB OLED screen, a clinical validation was conducted on 15 patients after approval of the University of Michigan IRB. Patients were presented with a series of circle-like images and, after each image, asked whether the image previously displayed was a perfect circle. The duration of the test and responses to a post-test questionnaire were recorded.

Results: All patients were able to complete the test (n=15, 100%). The total duration of the test took a mean of 70 seconds (standard deviation 9.1 seconds), with a range from 32 seconds to 2 minutes and 23 seconds. Compared to other home monitoring products, ForeseeHome and myVisionTrack (mVT), this device reduced test time by 67% on average. On a Likert scale from 1 to 5 with 1 being the easiest and 5 the hardest, patients rated the test as a mean of 1.545 in difficulty. All 15 patients found the device comfortable to hold for the duration of the test (100%). The device was devised to accommodate refractive errors from +5 D to -10 D and accommodated 100% of the evaluated patients, whom had refractive errors ranging from +1.25 D to -7.0 D.

Conclusions: This clinical validation demonstrates that a digital, handheld standalone device using shape discrimination hyperacuity to identify a patient's minimum distortion-detection threshold can provide a rapid, easy, comfortable testing solution for a range of patients. Further validation and trials are necessary to demonstrate that this device results in improved outcomes of patients with AMD.

CONTROL ID: 3541376

SUBMITTER (NAME ONLY): Kin Ho Chan

TITLE: Changes in Refractive Components After a Short Exposure to Astigmatic Blurs in Young Adults

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Chan, J. Leung, H. Shik, W. Kwok, C. Kee, School of Optometry, The Hong Kong Polytechnic University, Kowloon, HONG KONG

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ABSTRACT BODY:

Purpose: Astigmatism is a very common refractive error in Native American and Asian Chinese. Recent studies have reported the effects of optically imposed astigmatism on ocular parameters in humans and chickens. This study investigated the effect of astigmatism on refractive changes in young Chinese adults.

Methods: Nineteen non-/ low-myopic young adults (age: 18-24 years; spherical-equivalent error: 0DS to -5.00DS, cylindrical error ≤ 0.75 DC) with unremarkable ocular health were recruited. Participants wore a trial frame to watch a movie for 60 minutes, with one eye chosen randomly as the treated eye and the fellow eye served as control. In three separate visits, while the control eye was fully corrected optically, the treated eye was exposed to one of three defocused conditions in random sequence :

1. Myopic defocus (SPH): +3.00 DS
2. With-The-Rule (WTR) astigmatism: +3.00 DC x 180°
3. Against-The-Rule (ATR) astigmatism: +3.00 DC x 90°

Before and after watching the movie, spectacle over-refractions were measured by a Shin Nippon open-field autorefractor.

Results: A significant interaction effect (treatment*time) was found for the interocular difference in J0 astigmatic component ($p < 0.001$): the interocular difference significantly reduced in magnitude for both the WTR condition (Change: -0.25 ± 0.10 D, $p = 0.022$) and the ATR condition (Change: $+0.39 \pm 0.15$ D, $p = 0.017$), suggesting an active refractive compensation to reduce the difference in the perceived astigmatic blur between fellow eyes. However, the change was not significant in the SPH condition ($p = 0.129$). There was also no such effect in the J45 astigmatic component, spherical-equivalent error, and other biometric parameters (all $p > 0.372$).

Conclusions: Optically imposed astigmatic blur for an hour led to bi-directional changes in the astigmatic component, suggesting that young adults are susceptible to refractive changes in response to orientation-dependent astigmatic blur.

CONTROL ID: 3541379

SUBMITTER (NAME ONLY): Sahar Ashrafzadeh

TITLE: Implementation of teleretinal screening using optical coherence tomography in the Veterans Health Administration: A pilot study

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ashrafzadeh, B. Gundlach, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|S. Ashrafzadeh, B. Gundlach, I. Tsui, Ophthalmology, VA Greater Los Angeles Healthcare System, Los Angeles, California, UNITED STATES|I. Tsui, Ophthalmology, Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Use of optical coherence tomography (OCT) in optometry and ophthalmology clinics has improved screening for potential retinal diseases and leads to increased retina clinic referrals and patient travel burden. We evaluated the impact of a pilot tele-OCT program offering remote, asynchronous retina specialist consultation on reducing in-person retina clinic visits and on patient adherence to the recommended follow-up plan.

Methods: We performed a retrospective cohort study of all tele-OCT consults originating from optometry and non-retinal ophthalmology clinics in the Greater Los Angeles Veterans Health Administration from January to December 2019. A retina specialist evaluated tele-OCT consults within three days of each consult and recommended patient-specific follow-up plans, including necessity of in-person retina specialist evaluation. Data on patient demographics, consult notes, and eye care visits were collected from electronic medical records. Patient adherence to the follow-up plan, defined as following up at the recommended clinic within twice the recommended time interval, was calculated. Logistic regression analyses were performed to identify factors associated with patient adherence to the follow-up plan.

Results: In 2019, 158 tele-OCT consults were conducted, of which 44.3% of patients were white, 34.8% were Black, and 10.1% were Hispanic/Latino; 97.5% were male; and mean (SD) age was 70.6 (11.3) years. The most common retinal diagnoses were age-related macular degeneration (n=43, 27.2%) and diabetic retinopathy (n=30, 19.0%). After tele-OCT consultation, 113 (71.5%) patients were recommended continued monitoring in their originating eye clinic, 27 (17.1%) were referred to intravitreal injection clinic, 12 (7.6%) to in-person retina clinic, and 6 (3.8%) to another location. Patient adherence to tele-OCT follow-up plans was 76.4%. Compared to non-adherent patients, patients adherent to follow-up plans were more likely to have ocular symptoms (e.g. decreased central vision, metamorphopsia, or scotoma) (OR 3.53, 95% CI 1.57-7.94, p=0.002) or an intravitreal injection clinic referral (OR 4.61, 95% CI 1.04-20.46, p=0.043).

Conclusions: A tele-OCT program improved clinic efficiency when implemented in a large multidisciplinary eye care practice. Having ocular symptoms or requiring treatment led to patient adherence to tele-OCT follow-up plans.

CONTROL ID: 3541385

SUBMITTER (NAME ONLY): Hsu-Hang Yeh

TITLE: PhacoTrainer: Deep Learning for Activity Recognition in Cataract Surgical Videos

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The use of deep learning in surgical training is promising but applications in ophthalmology are scant. The purpose of this study was to train a deep neural network to recognize cataract surgical steps, including routine and complex steps such as use of trypan blue or iris expansion devices.

Methods: We collected 268 resident cataract surgical videos routinely recorded during the residency training of 12 surgeons across 6 sites. Videos were downsampled and cropped to 256x256 at 1 frame/second. Trained annotators labeled 13 steps of surgery: create wound, injection into the eye, capsulorrhexis, hydrodissection, phacoemulsification, irrigation/aspiration, place lens, remove viscoelastic, close wound, stain with trypan blue, manipulating iris (e.g. malyugin ring/iris hooks), subconjunctival/SubTenon's injections, and other (e.g. anterior vitrectomy, placement of capsular support devices). A deep learning model based on the VGG16 architecture was customized and trained to predict the class probabilities that each frame depicted. The model was evaluated on a held-out test set using frame-by-frame top-N accuracy, defined as the proportion of frames where the true class was among the highest N predicted class probabilities. Per-class and micro-averaged area under receiver-operating and precision-recall curves (AUROC, AUPRC) were determined. To evaluate which frame areas were most important for model predictions, class activation maps were visualized using gradient-weighted class activation mapping.

Results: Overall top-1 prediction accuracy was 77.4% (93.2% for top-3 accuracy). The overall AUROC was 0.97 and the AUPRC was 0.85. Evaluation of class activation maps revealed the model was appropriately focused on the instrumentation used in each step to predict. Challenges remain in prediction of rare steps or steps with diverse appearances, including subconjunctival/subTenon's injections, iris manipulation, anterior vitrectomy, for which prediction had poor recall.

Conclusions: Deep learning models can classify cataract surgical activities on a frame-by-frame basis with remarkably high accuracy, especially routine surgical steps. An automated system for recognition of cataract surgical steps could have broad applications, including providing automated feedback metrics to residents on their surgical videos.

CONTROL ID: 3541396

SUBMITTER (NAME ONLY): Konrad Pesudovs

TITLE: Cataract-related blindness and vision impairment in 2020 and trends over time in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study.

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To contribute to the WHO initiative, VISION 2020: The Right to Sight, we report extensively updated estimates of global vision loss burden due to cataract presenting estimates for 2020, including changes over time.

Methods: Population-based surveys of eye disease from January, 1980, to October, 2018 were collated by the Vision Loss Expert Group of the Global Burden of Disease Study in the Global Vision Database. We fitted hierarchical models to estimate age-standardised prevalence (with 95% uncertainty intervals [UIs]) of moderate and severe vision impairment (MSVI; presenting visual acuity from <6/18 (20/60) to 3/60 (10/200)) and blindness (<3/60 (10/200) and/or less than 10° visual field around central fixation) caused by cataract by age, global region, and year. Data sparsity at younger ages required the analysis focused on adults aged ≥50 years.

Results: In 2020, worldwide an estimated 15.2 million (12.7-17.9) people aged 50+ years were blind, and a further 78.8 million (67.2-91.4) had MSVI, due to cataract. There had been an increase of 29.7% in cases of cataract blindness and 93.1% in cases of MSVI since 2000. Over the same period, age-standardised prevalence of cataract blindness decreased by 27.5% and MSVI increased by 7.2%. Between 2000 and 2020, the age-standardised prevalence of cataract blindness in males decreased to a greater extent than in females (-31.8% vs -24.8%); similarly the increase in cataract MSVI was less for males (+4.7%) than females (+8.9%). Among GBD super-regions, South Asia had the highest cataract blindness and MSVI burden in 2020 (blind: 2.23%; 1.89-2.61, MSVI: 9.46%; 8.11-10.93). The most profound reductions in cataract blindness rates between 2000 and 2020 occurred in Southeast Asia, East Asia and Oceania (-43.0%), North Africa and Middle East (-40.0%), and South Asia (-36.5%).

Conclusions: The World Health Assembly Global Action Plan target of a 25% reduction from 2010 to 2019 in avoidable vision impairment (WHA 66.3 24/5/2013) was met for cataract blindness but not for MSVI. However,

decreases in prevalence were more than offset by global population growth and aging, leaving more people cataract blind and visually impaired than ever before. Globally, immense increases in resource mobilization for treating cataract are required.

CONTROL ID: 3541398

SUBMITTER (NAME ONLY): Kelly Murrell

TITLE: Using directional OCT to analyze photoreceptor visibility over AMD-related drusen

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dysfunction in AMD is mostly a result of photoreceptor loss. Many clinical and adaptive optics optical coherence tomography (AO-OCT) investigators report reduced cone photoreceptors visibility over associated drusen. Two possibilities explanations are angular disorientation and cell structure disorganization. Our study uses directional OCT to measure contribution of these two factors, potentially guiding future research into early AMD.

Methods:

Three AMD subjects were recruited and dilated. Large drusen were identified using OCT images. The imaging beam was positioned at a series of horizontally displaced locations in the pupil, all imaging the same retinal location. 1200 B-scans of drusen and healthy adjacent retina were acquired at each pupil location. The apparent tissue slope indicates illumination angle. Between 20-50 cross-correlated B-scans were registered and averaged, producing one composite B-scan per subject, per retinal position. In each B-scan, abnormal and apparently-healthy tissues were delineated. Next, the inner-segment-outer-segment junction (ISOS) bands were segmented using a semi-automated procedure, resulting in a trace through both tissue types. Their reflectance and slope were computed at each A-scan in each B-scan. Separately for data from healthy and drusen-affected parts of ISOS segmentation, the relationship between slope and intensity was fit with a three-parameter (directionality, non-directional component B, directional component A) Gaussian equation to quantify angle-dependent and independent components of ISOS reflectance. Healthy and drusen-affected retina were compared for each.

Results: Between healthy and drusen-affected retina, large differences were found in parameters ($p=0.011$) and B ($p=0.004$), and small differences found in A ($p=0.130$). Values were lower in drusen-affected areas of retina than healthy for each.

Conclusions: Reduction in fitted values of A and B values in drusen-affected tissue indicates gross attenuation of ISOS backscattered light. Reduction in indicates a widening of the acceptance angle of drusen-affected cones, suggesting changes in diameter and/or refractive indices of inner segment. Reduced reflectance and directionality of the inner-segment may underlie the low visibility of cones in adaptive optics imaging.

CONTROL ID: 3541470

SUBMITTER (NAME ONLY): minjuan bian

TITLE: Magnetic nanoparticles for subcellular organelle manipulation

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Labelling cells with magnetic nanoparticles (MNPs) has gained increasing interest due to their wide biological and medical applications. Magnetic forces used to control MNPs can thereby target or even manipulate specific cell types or organelles during drug delivery, cell imaging and cell tracking. The primary uptake pathway of MNPs is endocytosis, which leads to extracellular excretion or lysosomal degradation, preventing the targeted localization to cytosol and other organelles. Here we explore methods to bypass endocytosis and thereby enhance organelle targeting.

Methods: We generated MNPs conjugated with Alexa Fluor 647 enclosed in cell-membrane-fusogenic liposomes was labeled with lipophilic dye 1,1'-dioctadecyl-3,3,3',3'-tetramethylindocarbocyanine perchlorate (DiI) in the lipid leaflets. Lipid-to-MNP ratio was varied to generate optimal liposome-MNPs based on transmission electron microscope (TEM), dynamic light scattering and zeta potential analysis. The delivery efficiency of liposome-MNPs into the cells was confirmed by Prussian blue staining. The fraction of free MNPs was identified at different time points after delivery of liposome-MNPs to the retinal pigment epithelial ARPE-19. Targeting to endosomes and lysosomes was assessed using CellLight reagents targeting Rab5a and Lamp1, respectively, as well as TEM imaging. A focal magnetic field was applied to assess the movement of intracellular MNPs.

Results: TEM showed liposome coating core-shell structure compared to bare MNPs when the initial lipid-to-MNP ratio increased. Highest MNP delivery efficiency into ARPE-19 cells was observed when the initial ratio of lipid:MNP (w/w) was 1:1. The amount of free MNPs peaked at 70% 24 hours after application of liposome-coated MNPs, indicating separation of MNPs from liposomal coatings. Whereas MNP uptake resulted in endocytosis, confocal microscopy revealed early endosome-localized MNPs from liposome-coated MNPs decreased from 14.4% right after administration to 6.9% after 4 hours, and 6.2% after 24 hours, demonstrating escape from endocytosis. TEM results verified cytosolic and lysosomal location of liposome-coated MNPs. Local magnetic force generated from an electromagnetic probe demonstrated corresponding movement of intracellular MNPs.

Conclusions: This novel fusogenic liposome-MNP delivery can bypass endocytosis to achieve efficient delivery of MNPs to the cytosol, allowing for external control by focal magnetic fields.

CONTROL ID: 3541495

SUBMITTER (NAME ONLY): Noriko Terada

TITLE: Clinical relevance of intercapillary spaces on optical coherence tomography angiography in diabetic retinopathy

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Terada, T. Murakami, A. Uji, Y. Dodo, K. Nishikawa, A. Tsujikawa, Kyoto Daigaku Daigakuin Igaku Kenkyuka Igakubu, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: The transient or persistent disturbance of blood flow is one of several clinical findings of vascular lesions and exacerbate neuronal impairment in diabetic retinopathy (DR). Optical coherence tomography angiography (OCTA) allows us to quantify vascular density or vascular density length, which are modestly associated with DR severity. In this study, we characterized the intercapillary spaces on OCTA images and investigated their clinical significance in DR.

Methods: In this retrospective study, we reviewed 88 eyes of 76 patients with treatment-naïve DR, for whom 3x3 mm OCTA images centered on the macula were acquired using PLEX Elite 9000 (Carl Zeiss Meditec). The superficial slab images with a 2-mm diameter were prepared and processed by binarization. The intercapillary spaces were automatically detected and quantified using 'Analyze Particles' function in ImageJ (NIH, Bethesda, MD). The number of intercapillary spaces was applied to receiver operating characteristics (ROC) curve analyses to discriminate DR from nondiabetic subjects.

Results: The intercapillary spaces were detected in the superficial capillary layer, although they were rarely found in the deep layer. The numbers of intercapillary spaces were 540 ± 117 , 421 ± 162 , 365 ± 145 , 256 ± 162 , 283 ± 109 , and 236 ± 154 in nondiabetic subjects, no apparent retinopathy (of diabetic patients), mild nonproliferative diabetic retinopathy (NPDR), moderate NPDR, severe NPDR, and proliferative diabetic retinopathy (PDR). The numbers of intercapillary spaces were greater in nondiabetic subjects than those in diabetic eyes ($P < 0.001$). Eyes with DR had more spaces than those with no apparent retinopathy ($P = 0.001$). The area under ROC curve (AROC) was better for discriminating diabetic eyes from nondiabetic subjects (AROC = 0.895) than that for discriminating no apparent retinopathy from DR (AROC = 0.771).

Conclusions: The numbers of intercapillary spaces decreased according to the DR severity. The ROC analyses suggested that the number of intercapillary spaces in the macula has a diagnostic significance in diabetic eyes.

CONTROL ID: 3541556

SUBMITTER (NAME ONLY): Christian Pompoco

TITLE: Association of Non-Melanoma Skin Cancer with Exfoliation Syndrome:
The Utah Project of Exfoliation Syndrome

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The Utah Project on Exfoliation Syndrome (UPXFS) was created to investigate the association between systemic disorders and exfoliation syndrome (XFS). Given the data suggesting an association between non-melanoma skin cancer (NMSC), i.e. basal and squamous cell cancer (cancers most often located in areas of sun exposure) and XFS based on the ocular UV exposure hypothesis, a retrospective cohort study was conducted to evaluate the relationship between NMSC and XFS.

Methods: NMSC and malignant melanoma diagnoses (based on ICD-O-3 and ICD-9/10 codes) were obtained from the Utah Cancer Registry (UCR) and University of Utah Healthcare (UUHC) patient records from 1966-2016 and linked to individuals in the Utah Population Database (UPDB) with XFS and without XFS. The occurrence of a melanoma or basal/squamous cell skin cancer diagnosis was estimated in 2,659 XFS patients compared with randomly selected 13,294 participants without XFS in the population matched 1:5 on sex and birth year using a logistic regression model accounting for sex and age from individual matching and adjusting for race and ethnicity.

Results: Among the 2,659 XFS cases, the mean age of XFS diagnosis was 74 years, and 67% were women. Of the 2,659 XFS patients and the 13,294 individuals without XFS, 227 patients (8.5%) and 829 (6.2%) without XFS were diagnosed with basal or squamous cell skin cancer respectively. Compared with those without XFS, in those with XFS, there was an approximate 1.5-fold increased risk of basal or squamous cell skin cancers (odds ratio of 1.46, 95% confidence interval: 1.25-1.71; $p < 0.0001$). We observed no association between XFS and malignant melanoma.

Conclusions: XFS is a systemic disorder related to elastosis, and this data suggests that individuals with XFS may have an increased risk of a NMSC history. These data are consistent with the findings from another study that reported an association between those with NMSC and incident XFS⁷. We hypothesize based on these findings that an underlying pathogenesis of NMSC and XFS may stem from a common triggering event – ultraviolet exposure.

CONTROL ID: 3541572

SUBMITTER (NAME ONLY): Roy Schwartz

TITLE: Are we doing better? Impact of treatment paradigm change on neovascular age-related macular degeneration treatment outcomes over the past decade. A big data analysis.

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Management of neovascular age-related macular degeneration (nAMD) has evolved over the last decade with several treatment regimens and different medications. This study describes the treatment patterns and visual outcomes over ten years in a large cohort of patients.

Methods: This was a retrospective analysis of electronic health records from 27 National Health Service (NHS) secondary care healthcare providers in the UK. Treatment-naïve patients receiving at least three intravitreal anti-vascular endothelial growth factor (VEGF) injections for nAMD in their first six months of follow-up were included in the study. Patients with missing data for age or gender and those aged less than 55 were excluded. Eyes with at least three years of follow-up were grouped by years of treatment initiation, and three-year outcomes were compared between the groups. Data were generated during routine clinical care between 09/2008 and 12/2018. Main outcome measures included visual acuity (VA), number of injections, and number of visits.

Results: A total of 15,843 eyes of 13,734 patients receiving 195,238 injections were included. VA improved from baseline during the first year, but dropped thereafter, resulting in loss of visual gains. This trend remained consistent throughout the past decade. Although an increasing proportion of eyes remained in the driving standard, this was driven by better presenting visual acuities over the decade. The number of injections dropped substantially between the first and subsequent years, from a mean of 6.25 in year 1 to 3 in year 2 and 2.5 in year 3, without improvement over the decade. In a multivariable regression analysis, final VA improved by 0.24 letters for each year since 2008, and younger age and baseline VA were significantly associated with VA at three years.

Conclusions: Our findings show that despite improvement in functional VA over the years, primarily driven by improving baseline VA, patients continue to lose vision after the first year of treatment, with only marginal change over the past decade. The data suggest that these results may be related to suboptimal treatment patterns, which have not improved over the years. Rethinking treatment strategies may be warranted, possibly on a national level or through the introduction of longer-acting therapies.

CONTROL ID: 3541579

SUBMITTER (NAME ONLY): Kellyn Bellsmith

TITLE: Validation of home visual acuity tests for telehealth in the COVID-19 era

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.N. Bellsmith, M.J. Gale, S. Yang, I. Nguyen, C.J. Prentiss, L. Nguyen, A.I. Summers, M. Thomas, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: One of the most important clinical data points in evaluating ophthalmology patients is visual acuity (VA). During the COVID-19 pandemic, eye health providers are utilizing telehealth to decrease patient and provider risk related to in-person clinic visits, while still providing high-quality care. This study sought to compare at-home VA tests with in-office clinical VA measurements to determine the validity of at-home VA testing for telehealth visits.

Methods: Patients from 1 comprehensive and 3 subspecialty ophthalmology clinics had VA greater than or equal to 20/200 in the study eye. The patients were prospectively randomized to perform 2 of 3 at-home VA tests (printed chart – University of Arizona/Banner Eye Care Letter Distance Chart; mobile phone app – VeranaTM Vision Test; website test – Farsight.care) within 3 days of their standard of care clinic visit. Patients also completed a survey to assess usability of home tests. At the clinic visit, best corrected Snellen distance acuity was measured to serve as the reference standard.

Results: Of the 44 patients (84 eyes) enrolled, 60% were female and the mean age was 66 years (range 22 to 80). The mean difference between printed chart and Snellen, website test and Snellen, and mobile app and Snellen acuity data was 0.10 (95% CI: 0.09-0.11), 0.13 (95% CI: 0.12-0.14), and 0.12 (95% CI: 0.11-0.13) LogMAR, respectively. The highest degree of correlation was between the website and Snellen tests (0.74, 95% CI: 0.59-0.84) (Table 1).

Patients found the tests easy to perform at home and were neutral regarding confidence in their results and desire to continue with home testing. In the survey, there was no significant difference for between the 3 tests regarding any of the 4 questions ($P = 0.32-0.62$), although there was a trend toward a more positive response with the printed chart (Table 2).

Conclusions: These data suggest that some at-home visual acuity tests are comparable in accuracy to in-clinic Snellen visual acuity tests (within 1 line of difference). Patient surveys indicated the tests were easy to understand and complete at home. Further development and validation of at-home vision testing modalities are needed to provide accurate and accessible tele-ophthalmology care.

CONTROL ID: 3541587

SUBMITTER (NAME ONLY): Yu Fujinami-Yokokawa

TITLE: Prediction of Causative Genes in Inherited Retinal Disorders from Fundus photography and Fundus Autofluorescence Imaging Utilising Deep Learning Techniques

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Fujinami-Yokokawa, X. liu, L. Yang, N. Pontikos, K. Fujinami, Laboratory of Visual Physiology, Division of Vision Research, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, Tokyo 152-8902, Japan., Meguro, Tokyo, JAPAN|Y. Fujinami-Yokokawa, H. Ninomiya, H. Miyata, Department of Health Policy and Management, Keio University School of Medicine, Tokyo, 160-8582, Japan., JAPAN|X. liu, L. Yang, Department of Ophthalmology, Keio University of Medicine, JAPAN|N. Pontikos, K. Fujinami, UCL Institute of Ophthalmology, UNITED KINGDOM|K. Yoshitake, T. Iwata, Division of Molecular and Cellular Biology, National Institute of Sensory Organs, National Hospital Organization Tokyo Medical Center, JAPAN|Y. Sato, Department of Preventive Medicine and Public Health, Keio University School of Medicine, JAPAN|T. Hashimoto, Sports Medicine Research Center, Keio University, JAPAN|

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ABSTRACT BODY:

Purpose: Inherited retinal disorders (IRDs) are rare intractable diseases, and the access to specialists is difficult world widely. The purpose of this study is to investigate the utility of a data-driven deep learning approach in patients with IRDs, to predict the causative genes based on fundus photography and fundus autofluorescence (FAF) imaging.

Methods: Clinical and genetic data from 156 Japanese subjects with IRDs or no ocular diseases registered to the database of the Japan Eye Genetics Consortium were reviewed. Three categories of genetic diagnosis were selected, based on the highest prevalence of their causative genes: Stargardt disease (ABCA4), retinitis pigmentosa (EYS), and occult macular dystrophy (RP1L1). Fundus photographs and FAF images were cropped in a standardised manner with a macro algorithm. Algorithms for pipeline analyses, based on TensorFlow Inception V-3 were determined with learning parameters (provided by Medic Mind). Images for learning/testing were selected with a randomised 4-fold cross-validation method. The application program interface was established to reach the learning accuracy of concordance (aimed >80%) between the genetic diagnosis and the machine diagnosis (ABCA4, EYS, RP1L1, and normal).

Results: A total of 417 images were examined. The mean overall test accuracy for fundus photographs and FAF images was 88.2% (range, 81.5%-94.4%) and 81.3% (range, 73.5%-87.8%), respectively. The mean overall sensitivity/specificity for fundus photographs and FAF images were 88.3%/97.4% and 81.8%/95.5%, respectively. The mean test sensitivity/specificity per gene category for fundus photographs and FAF images was 88.2%/100% and 97.5%/94.8% for ABCA4-retinopathy, 88.4%/98.1% and 70.7%/99.2% for EYS-retinopathy, 94.4%/92.9% and 64.9%/96.3% for RP1L1-retinopathy, and 82.9%/96.7% and 92.9%/96.3% for normal.

Conclusions: A novel application of deep neural networks in the prediction of the causative gene in IRD from fundus photographs and FAF was highlighted, with a high prediction accuracy of over 80%. These achievements will extensively promote the quality of medical care by facilitating early diagnosis, reducing the cost for referrals, and

allowing unnecessary clinical and genetic testing to be avoided.

CONTROL ID: 3541616

SUBMITTER (NAME ONLY): Cem Kesim

TITLE: Biocompatibility and neural stimulation capacity of aluminum antimonide nanocrystals biointerfaces for use in artificial vision

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Colloidal inorganic nanocrystals have great potential as photosensitive biointerfaces that might be used as retinal stimulation devices. We introduced the aluminum antimonide nanocrystals (AISb NCs) as a cell interfacing layer for light-induced capacitive neural stimulation in the blue spectrum.

Methods: A four-layer photovoltaic biointerface was fabricated by sequential planar deposition of indium tin oxide (ITO), zinc oxide (ZnO), organic poly(3-hexylthiophene) (P3HT) and AISb NCs that is excitable under 445 nm blue LED illumination. Biocompatibility tests were performed in vitro on rat primary hippocampal neurons (PHN) and in vivo by subretinal implantation of the biointerface into adult rat eyes. In vitro electrophysiology for AISb NCs based photostimulation of PHN were measured by whole cell patch clamp method.

Results: The AISb NCs based biointerface generated a photovoltage increase from 52 to 98 mV.cm⁻² with a rise time of ~55 µs upon stimulation. MTT viability assay showed no significant decrease in PHN metabolic activity (P>.05). No increase of TUNEL-positive cells was observed in biointerface implanted retinas when compared with sham group (P>.05). The biointerface effectively induced action potential in PHN with >90% success rate when stimulated by LED illumination frequencies up to 10 Hz under ocular safety limits.

Conclusions: The AISb NCs based biointerfaces hold high promise for future bioelectronics. With their high performance and biocompatibility, AISb nanocrystals prove to be applicable candidates for nanoengineered prostheses to rescue vision.

CONTROL ID: 3541620

SUBMITTER (NAME ONLY): Gregory Ghahramani

TITLE: Deep learning survival analysis on the progression to late AMD in the Age-Related Eye Disease Study

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Accurately predicting a patient's risk of progressing to late age-related macular degeneration (AMD) is crucial for personalized medicine. We conduct deep learning survival analyses to predict AMD progression and to identify which sets of features, derived from Age-Related Eye Disease Study (AREDS) fundus photographs, are key predictors. While existing algorithms consider data from the present visit only, we evaluate how adding data from prior visits improves predictive performance.

Methods: The dataset comprised 3,768 AREDS participants without late AMD in either eye by year 3. Four survival models were trained and evaluated (Figure 1) to predict progression to late AMD at year 5 (2-year risk) and year 8 (5-year risk), based on data from year 3 only (Model 1) or years 0, 2, and 3 (Models 2-4). Models 1 and 2 were Cox proportional-hazard models (CoxPH). Models 3 used a deep neural network by concatenating visit information using a multilayer perceptron (MLP). Model 4 used a deep neural network to model the time-dependencies of visits using Long-Short-Term Memory (LSTM). Models were trained and evaluated using (a) drusen size and pigmentary abnormalities (i.e., akin to the 5-step AREDS Simplified Severity Scale, the clinical standard), or (b) drusen size, RPE depigmentation, retinal detachments, hemorrhages, and fibrosis, and geographic atrophy (Figure 2).

Results: Figure 2 conveys the results using the two sets of risk factors. We observe that: 1) using deep learning to model the time-dependencies (LSTM) of feature set b outperformed all other models (AUC@2year: 0.918, AUC@5year: 0.930, c-index: 0.902) (Figure 2b); 2) incorporating data from prior visits improved predictive performance (up to 2% in AUC@2year, 1% in AUC@5year, 1% in c-index); 3) using feature set b improved performance over using drusen/pigment only (up to 6% in AUC@2year, 4% in AUC@5year, 3% in c-index), suggesting that the 5-step AREDS Simplified Severity Scale overlooks useful risk factors.

Conclusions: Existing algorithms for predicting progression to late AMD consider data from one time-point only. We demonstrate that incorporating AREDS grading features from previous years in a deep learning framework provides more accurate predictions than the existing clinical standards and basic survival models.

CONTROL ID: 3541630

SUBMITTER (NAME ONLY): Kaoru Fujinami

TITLE: The clinical and genetic spectrum of cone-dominated retinal dystrophies with normal funduscopy appearance

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There are several cone-dominated dystrophies (CDD) that show normal funduscopy appearance; however, the prevalence of each causative gene and the phenotypic overlap caused by each gene within the CDD are still uncertain. We illustrate the clinical/genetic spectrum of CDD with normal funduscopy appearance (CDD-NF) in a nationwide cohort.

Methods: 1302 patients with available genotype-phenotype correlation analysis results registered to the Japan Eye Genetic Consortium database were surveyed. Patients were classified into one of the three disease categories based on the electrophysiological findings: occult macular dysfunction syndrome (OMDS: confined macular dysfunction, including hereditary occult macular dystrophy (OMD) and occult maculopathy), cone (-rod) dystrophy with normal funduscopy appearance (CORD-NF: progressive generalized cone (-rod) dysfunction), and cone dysfunction syndrome (CDS: non-progressive generalized cone dysfunction). The clinical parameters were compared among the three disease categories, and the overlap of causative genes was investigated in genes identified in multiple families.

Results: 192 patients from 150 families with CDD-NF were recruited, including 76 families with OMDS, 43 families with CORD-NF, and 31 families with CDS. The median age of onset was 30.0 years for OMD, 30.0 years for CORD-NF, and 0.0 years for CDS, respectively. The median LogMAR visual acuity (VA) was 0.52 for OMD, 0.70 for CORD-NF, and 0.80 for CDS, respectively. The causative genes were RP1L1, GUCY2D, and CRX for OMD, POC1B,

GUCY2D, CRX, PDE6C, and CRB1 for CORD-NF, and CNGA3, PDE6C, GNAT2, KCNV2, and RGS9BP for CDS. Out of eight genes identified in multiple families, four genes were found only in a single disease category: RP1L1 (OMD; Miyake disease), CNGA3 (CDS), GNAT2 (CDS), and KCNV2 (CDS); while four genes overlapped the disease categories; POC1B, PDE6C, GUCY2D, and CRX.

Conclusions: The clinical spectrum of CDD-NF was first identified in a large well-characterized cohort: OMD with later-onset and moderate VA decrease, CORD-NF with later-onset and severe VA impairment, and CDS with early-onset and more severe VA decline. The heterogeneous genetic background of CDD-NF was revealed; meanwhile distinct genotype-phenotype relations such as RP1L1-OMD, CNGA3-CDS, and GNAT2-CDS were confirmed.

CONTROL ID: 3541632

SUBMITTER (NAME ONLY): Charumathi Sabanayagam

TITLE: Circulating metabolites and onset of diabetic retinopathy: a prospective study of two population-based cohorts

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the prospective association of circulating metabolites with incidence of diabetic retinopathy (DR) in two Asian cohorts who are at high-risk for diabetes.

Methods: We included 424 Malay and 515 Indian adults with diabetes but were free of DR at baseline who participated in the baseline (2004-2009, aged 40-80 years) and the 6-year follow-up visits (2011-2017) of two population-based cohort studies: the Singapore Malay Eye Study and the Singapore Indian Eye Study. Serum metabolites at baseline (n=225) were quantified using high-throughput nuclear magnetic resonance profiling. DR was assessed from retinal photographs and graded using the Early Treatment Diabetic Retinopathy Study (ETDRS) severity scale. Based on the worse eye score, we defined incident any-DR as ETDRS ≥ 20 , moderate/above DR as ETDRS > 43 and vision-threatening DR (VTDR) as the presence of severe nonproliferative or proliferative DR, or clinically significant macular edema (CSME). Associations between each metabolite (per SD increase) and outcomes were evaluated using logistic regression models adjusting for age, systolic blood pressure, duration of diabetes, HbA1c and follow-up period in each cohort followed by random-effects meta-analysis corrected for multiple testing.

Results: Incidence of any-DR, moderate/above DR and VTDR in Malays were: 13.7%, 6.2% and 3.7%. Corresponding estimates in Indians were 18.3%, 7.7% and 4.2%. After Bonferroni correction, higher levels of four high-density lipoprotein (HDL) metabolites (free cholesterol and total cholesterol in large HDL, phospholipids in very large HDL and concentration of very large HDL particles) were protectively associated with any DR ($p \leq 0.0042$); tyrosine, an aromatic aminoacid showed an inverse association while 3-hydroxy butyrate (ketone body) showed a positive association with moderate/above DR ($p \leq 0.0125$); aminoacid, histidine showed an inverse association with VTDR in the meta-analysis.

Conclusions: We found higher levels of HDL-related metabolites, tyrosine and histidine to be associated with reduced risk of DR while 3-hydroxy butyrate to be associated with increased risk of DR implying the involvement of HDL, aminoacid and ketone metabolism in the pathogenesis of DR.

CONTROL ID: 3541658

SUBMITTER (NAME ONLY): Ifat Sher-Rosenthal

TITLE: Novel flavonoid-based eye drops for the treatment of retinal degeneration

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Sher-Rosenthal, E. Bubis, Z. Goldberg, Y. Rotenstreich, Goldschleger Eye Institute, Sheba Medical Center at Tel Hashomer, Tel Hashomer, ISRAEL|I. Sher-Rosenthal, E. Bubis, Z. Goldberg, Y. Rotenstreich, Goldschleger Eye Institute, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|A. Elmann, Department of Food science Agricultural Research Organization, Agricultural Research Organization Volcani Center, Bet-Dagan, ISRAEL|M. Samara, The Interinstitutional Analytical Instrumentation Unit, Agricultural Research Organization Volcani Center, Bet-Dagan, ISRAEL|

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ABSTRACT BODY:

Purpose: To assess the safety and efficacy of a novel flavonoid (TTF)- based eye drops formulation for retinal degeneration treatment.

Methods: Eye cups of 21 day-old RPE65/rd12 mice were incubated in media supplemented with 8nM TTF or the same volume of vehicle solution for 18 hours. Sections were stained with antibodies directed against cone opsins and counter-stained with DAPI. The number of positively stained cells/mm retina was recorded. Rabbits were treated with TTF eye drops and TTF concentration in anterior chamber tap removed at 5, 45, and 180 minutes was determined by HPLC to determine corneal permeability. RPE65/rd12 mice were treated twice daily, 6 days/week, for 12 weeks with eye drops containing either TTF (12.5mg/ml, n=16) or vehicle (n=16). RPE /retina flat mounts were stained with Iba-I to assess microglial activation and retinal sections were stained with TUNEL to assess treatment effect on photoreceptor apoptosis. Retinal function was determined by electroretinogram (ERG).

Results: Supplementation of 8nM TTF rescued cones photoreceptors from degeneration in the eye cups cultures in vitro. TTF penetrated the corneal barrier in rabbit eyes. The maximal concentration of TTF in anterior chamber taps was 1.7 μ M, 45 minutes following eye drops instillation. Three-week treatment with TTF eye drops significantly reduced microglial activation and migration into the sub retina compared to vehicle (mean \pm SD: 42 \pm 14 microglia cells/retina vs. 143 \pm 28 microglia cells/retina, p=0.0063). The number of TUNEL positive cells in the photoreceptor layer was significantly lower in treated mice compared with control (mean \pm SE: 2 \pm 0.4 apoptotic cells/mm retina vs. 6 \pm 0.8 apoptotic cells/mm, p=0.0013). A significantly higher scotopic ERG a-wave was recorded in treated mice 3 weeks following treatment initiation (p=0.005).

Conclusions: TTF eye drops may present a novel simple treatment for retinal degeneration, reducing microglial activation and inflammation, preventing photoreceptor cell death, and preserving retinal function in a mouse model of RP. No side effects were observed following 12 weeks of daily treatment with the TTF eye drops, supporting the potential feasibility for clinical application as a treatment for incurable blinding diseases.

CONTROL ID: 3541690

SUBMITTER (NAME ONLY): Janya Grainok

TITLE: Modulation of CNOT3 expression using antisense oligomers to treat retinitis pigmentosa 11

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa 11 (RP11) is an inherited degenerative retinal disease caused by heterozygous mutations in pre-mRNA processing factor 31 (PRPF31) for which there is currently no effective treatment available. RP11 features incomplete penetrance within affected families; the level of PRPF31 expression from the healthy allele determines whether mutation carriers develop symptoms. The CCR4-NOT transcription complex subunit 3 (CNOT3) is a major disease modifier that regulates PRPF31 levels via transcription inhibition. Higher CNOT3 levels are observed in RP11 cases. In this study, we aim to lower CNOT3 expression and function to indirectly upregulate functional PRPF31 from the healthy allele and rescue RP11 disease phenotypes.

Methods: Seventy-four antisense oligomers (ASO) were designed to target exonic splice enhancers to mediate exclusion of selected CNOT3 exons to (i) induce translational frameshift and mRNA decay or (ii) produce truncated low/non-functional CNOT3 isoform(s). PRPF31 expression and function were assessed in RP11 iPSC-derived retinal pigment epithelial (RPE) cells.

Results: We observed an inverse correlation between CNOT3 and PRPF31 mRNA levels in healthy fibroblasts (n=20). In iPSC-RPE cells, we found 10% higher expression of CNOT3 with 17% lower PRPF31 expression in a patient compared to an asymptomatic relative, both carrying a PRPF31 c.1205 C>A nonsense mutation. Fewer and shorter primary cilia were observed in the symptomatic patient RPE compared to asymptomatic, healthy RPE. Lowering CNOT3 levels and function with ASOs demonstrated a 1.7-fold increase in PRPF31 expression in patient RPE and significantly improved cilia number and length. Healthy cilia play an integral role in phagocytosis and are crucial for normal retinal function.

Conclusions: Subtle changes in CNOT3 and PRPF31 levels in retinal cells determine disease penetrance in PRPF31 mutation carriers within an affected family. Modulating expression levels of these proteins can reverse the cellular disease phenotype in RP11. ASOs are effective modulators of CNOT3 expression and function with the ability to increase PRPF31 transcription from the unaffected allele to an expected therapeutic level. Future studies will assess the restoration of transcriptional profiles linked to improved PRPF31 levels in patient derived iPSC-retinal organoids and RPE compared to healthy controls.

CONTROL ID: 3541716

SUBMITTER (NAME ONLY): Maria Cabrera-Aguas

TITLE:

The Bacterial Ocular Surveillance System (BOSS): 2017 report

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Antimicrobial resistance (AMR) globally threatens the treatment outcomes of patients with any medical condition. AMR surveillance programs have been recommended by the World Health Organisation (WHO) to support disease prevention and control strategies. A bacterial ocular surveillance program (BOSS) was initiated in Sydney, Australia in 2016. We aimed to report the spectrum and AMR of bacteria isolated from corneal scrapings in bacterial keratitis in 2017 from different areas of the Sydney metropolitan area.

Methods: A retrospective analysis of bacteria isolated from corneal scrapings from patients with bacterial keratitis from four centers across Sydney, New South Wales, Australia, from January 1 to December 31, 2017 was conducted. Sydney Eye and Prince of Wales Hospitals are in the east side of the city, and Westmead and Liverpool Hospitals in the west side. All specimens were processed at NSW Health Pathology. Antimicrobial resistance data were available for specimens from the eastern hospitals.

Results: There were 288 episodes of clinical bacterial keratitis. Of these, 161 inoculated plates isolated 189 organisms (positive culture rate of 56%). There were 127 (67%) Gram-positive organisms and 62 (33%) Gram-negative organisms. Most of the episodes (n = 155, 82%) presented to the eastern hospitals.

Coagulase-negative staphylococci (CoNS) 37% (70/189), *Staphylococcus aureus* 12% (23/189), including four methicillin-resistant (MRSA), and *Pseudomonas aeruginosa* 18% (34/189) were the most common organisms. AMR was found for: CoNS to cefalotin 18%, chloramphenicol 15%, gentamicin 9%, and ciprofloxacin 3%; methicillin-sensitive *Staphylococcus aureus* (MSSA) to chloramphenicol 8%; MRSA to ciprofloxacin 75% and gentamicin 25%; and *Corynebacterium* spp. to chloramphenicol 40%, and ciprofloxacin 40%. All Gram-positive organisms were susceptible to vancomycin. *Pseudomonas aeruginosa* isolates were susceptible to ciprofloxacin, gentamicin, and tobramycin

Conclusions: CoNS were the most commonly culprit of bacterial keratitis and of these, about one-fifth were resistant to cefalotin, a common antibiotic used to initially treat bacterial keratitis. Most MRSA were resistant to ciprofloxacin. Although the BOSS was established in Sydney, a wider system should be implemented across Australia for providing more comprehensive data from different geographic areas to inform both clinical decision-making and empiric treatment strategies

CONTROL ID: 3541721

SUBMITTER (NAME ONLY): Anand Vinekar

TITLE: Development and validation of a Deep Learning (DL)-based screening tool for 'Plus disease' detection on retinal images captured through a tele-ophthalmology platform for Retinopathy of prematurity (ROP) in India

SESSION TITLE: Retinopathy of prematurity/vein occlusion

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Plus disease denotes a severe vascular abnormality in cases of ROP, which may portend to requiring treatment to prevent blindness but its assessment is subjective. Bringing in Artificial Intelligence (AI) automation can not only improve diagnostic consistencies but can also help scale up ROP screening services to remote and underserved regions of the world. We developed and assessed the performance of an AI algorithm to automatically detect the presence of Plus disease in retinal images of premature babies.

Methods: We trained a deep learning (DL) algorithm with 42,641 disc and macula centered images from a tele-ROP screening program in India. The model was trained to indicate the presence of Plus in the images. Since the dataset contained 0.5% of Plus images, it was trained using metric learning, a technique improving DL performance under datasets with strong class imbalance. Pre-Plus images were not presented to the AI during training. The algorithm was tested on two distinct datasets. Test set A consists of 10,976 images, with 169 pre-plus, 70 plus images and rest no plus images. Test set B consists of 108 images, with 39 pre-Plus, 45 Plus images and rest no plus images. The reference standard for training and test sets was the interpretation of ROP specialists.

Results: The sensitivity on test set A was 95.7% (95% CI: 88.0% to 99.1%), with 3 Plus images being misclassified. Specificity with pre-plus as non-referable was 99.6% (95% CI: 99.4% to 99.7%), and 99.9% (95% CI: 99.8% to 100%) if pre-plus images were excluded. The sensitivity on test set B was 97.8% (95% CI: 88.2% to 99.9%) with one Plus image being misclassified. The specificity was 68.3% (95% CI: 55.3% to 79.4%) with pre-plus, and 100% (95% CI: 85.8% to 100%) without.

Conclusions: The DL tool for ROP Plus detection has excellent sensitivity in picking up Plus disease and thus can potentially be used as a triaging tool for infants with ROP requiring immediate treatment. A prospective clinical validation in a real-world setting is under consideration.

CONTROL ID: 3541735

SUBMITTER (NAME ONLY): Eri Kubo

TITLE: Elevated expression of Decorin inhibits injury-driven epithelial-mesenchymal transition in mouse lens

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Decorin (Dcn) is a dermatan sulfate proteoglycan which belongs to the small leucine-rich proteoglycan family and plays critical roles in controlling extracellular matrix assembly homeostasis. This is highly upregulated in mouse and rat posterior capsular opacification (PCO) tissues after extracapsular lens extraction surgery. Herein, we aim to explore the biological role of decorin in the development or prevention of PCO in mice lenses overexpressing human DCN (hDCN).

Methods: All animal and recombinant DNA experiments were approved by the Kanazawa Medical University Ethics Committee. We generated lens-specific hDCN-transgenic mice (hDCN-Tg) using a plasmid in which Pax6-human alpha crystallin (P6a) composite promoter drives hDCN cDNA. Histological analysis of postnatal day (PD) 2, 8 and 48 weeks-old hDCN-Tg and wild type (WT) mice were performed by using Hematoxylin & Eosin (H&E) staining. Expression of DCN in hDCN-Tg on PD2 was confirmed by histochemical staining for lacZ with 5-Bromo-4-chloro-3-indolyl- β -D-galactoside (X-gal) and immunostaining using anti-Dcn Ab. The lens injury model as mouse PCO model was generated in 14 weeks-old hDCN-Tg and WT mice. The histological patterns were evaluated by H&E staining and immunohistochemical analysis using anti- α smooth muscle actin (α SMA) antibody.

Results: X-gal was stained in cytoplasm of lens epithelial cells (LECs) at equatorial to bow region and primary lens fiber from PD2 hDCN-Tg mice. hDCN protein was expressed in LECs and surface fibers in lens sections from PD2-hDCN-Tg. However, X-gal staining and DCN expression was not observed in lens from PD2-WT mice. In histological observation of eye lens in PD2, adult 8 and 48 weeks-old hDCN-Tg, morphological changes were not observed compared to wild type as control. Importantly, overexpression of DCN inhibited fibroblastic EMT changes and α SMA expression observed in mouse wound healing of lens surface in hDCN-Tg.

Conclusions: Our findings reveal that enhanced expression of DCN play a role in preventing EMT of LECs and has potential beneficial effect in the intervention of PCO progression.

CONTROL ID: 3541741

SUBMITTER (NAME ONLY): Avigail Beryozkin

TITLE: Clinical characterization and genotype-phenotype correlation in RPGRIP1 patients with autosomal recessive early onset retinal degeneration

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: RPGRIP1 encodes a ciliary protein expressed in photoreceptor cilia. It contains a C-terminal RPGR interacting domain and two C2 domains, which are known to be involved in signal transduction or membrane trafficking. Mutations in this gene are known to cause ~5% of Leber congenital amaurosis (LCA) worldwide, but are also associated with cone-rod dystrophy (CRD) and retinitis pigmentosa (RP) phenotypes. Our purpose was to clinically characterize RPGRIP1 patients in the Israeli and Palestinian populations, perform an extensive literature search to collect clinical data of additional RPGRIP1 patients. From this combined data set we attempted to identify common clinical features and sought genotype-phenotype correlations.

Methods: Clinical data from 16 patients from our cohort and 175 RPGRIP1 patients previously reported by other groups was collected including (when available) family history, best corrected visual acuity (BCVA), refraction, full ocular examination, ocular coherence tomography (OCT) imaging, visual fields (VF) and full-field electroretinography (ffERG).

Results: Out of 191 patients, the majority (158, 83%) were diagnosed with LCA, 9% with CRD, and 8% with RP. Age of onset in all patients for whom this data was reported was during childhood (n=121), all had moderate myopia (n=49, Mean of -4.8D), and average BCVA was 0.06 Snellen (n=116; only 10 patients had VA>0.1). On funduscopy, narrowing of blood vessels was noted early in life. Most patients had mild bone spicule-like pigmentation starting in the midperiphery and later encroaching upon the posterior pole. OCT shows thinning of the ONL, while cystoid changes and edema are relatively rare. VF are usually very constricted from early-on. FFERG responses were non-detectable in the vast majority of cases. Most of the mutations are predicted to be null (297 alleles) and 85 alleles harbored missense mutations. Missense mutations were identified only in two regions: the RPGR interacting domain and the C2 domains. Patients with 2 missense mutations tended to show a milder course of disease (CRD/RP and not LCA).

Conclusions: RPGRIP1 usually causes severe retinal degeneration at an early age, with rapid disease progression. Most patients manifest a LCA phenotype. Missense changes in the conserved domains are usually associated with a less severe disease phenotype (CRD/RP) than null-predicted mutations.

CONTROL ID: 3541754

SUBMITTER (NAME ONLY): Jenni Hakkarainen

TITLE: Maturation of retinal pigment epithelium cells in vitro enhances the endogenous antioxidant defense system

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of the study was to evaluate the endogenous antioxidant defense system in human induced pluripotent stem cell (hiPSC)-derived retinal pigment epithelium (RPE) cells.

Methods: hiPSC-RPE cells were differentiated according to the manufacturer's instructions for different times in vitro (days in vitro, DIV) on Matrigel[®]-coated 96-well cell culture plates. Oxidative stress was applied using different concentrations of tert-butyl hydroperoxide (tBHP) for 22 h. Resistance of hiPSC-RPE cells to oxidative stress was measured using the general cell viability assays, resazurin assay and lactate dehydrogenase (LDH) release assay. In addition, production of reactive oxygen species (ROS) in cells was quantified using the ROS indicator, chloromethyl 2',7'-dichlorodihydrofluorescein diacetate (CM-H₂DCFDA).

Results: Cell viability as assessed by resazurin assay was similar from DIV13 to DIV19 with IC₅₀ values for tBHP of approx. 0.4 mM. IC₅₀ values started to shift significantly on DIV26 and DIV28, increasing to 0.7 - 0.9 mM. LDH release and CM-H₂DCFDA assays confirmed the shift of IC₅₀ value with concomitantly increased levels of LDH release and ROS generation.

Conclusions: hiPSC-RPE cells have a strong endogenous antioxidant defense system, as evident by strong cellular resistance to exogenous oxidative stress insult. Maturation periods longer than 26 days induce sudden, increased resistance against exogenous oxidative stress in hiPSC-RPE cells. Our results necessitate careful and precise characterization of individual hiPSC-RPE cell pools, as rapid changes in the endogenous antioxidant defense pose a significant confounding factor in experimental designs that utilize hiPSC-RPE cells for drug discovery.

CONTROL ID: 3541764

SUBMITTER (NAME ONLY): Jos Rozema

TITLE: Refractive Correction and Visual Strehl in Keratoconus

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: It is notoriously difficult to determine optimal refractive corrections for keratoconus patients. To investigate the underlying reasons, we compared how visual image quality, in the form of Visual Strehl (VSX), changes over a range of spherocylindrical spectacle and scleral lens corrections in eye models with and without keratoconus.

Methods: Starting from the previously published SyntEyes models, the ocular biometry sets of 20 healthy and 20 keratoconic eyes were generated, including corneal tomography and all intraocular structures. Using Matlab, these eyes underwent simulated spherocylindrical spectacle or scleral lens correction, followed by ray tracing to determine the residual wavefront aberrations, which were used to calculate VSX to assess resulting visual image quality. For each eye, refractive corrections were applied over the entire range of the phoropter, referred to as 'correction space'; an area of 'optimal correction' (i.e. maximized VSX) is called a 'focus'. To speed up calculations, a smart scanning algorithm was used, consisting of three consecutive scans over increasingly finer grids, considering only those points neighboring a previously calculated point with a VSX above 0.01.

Results: In all 20 healthy eyes the VSX pattern in correction space resembled an hourglass for both the spectacle and scleral lens corrections, with a distinct focus at the narrowest point and a quick drop in VSX away from the focus (Figure). For 18/20 keratoconic eyes the VSX pattern of spectacle corrections resembled a shell. In 9/20 of these cases two foci could be distinguished, separated by a large mean dioptric distance ($13.3 \pm 4.9D$) and a mean orientation difference of $96.4 \pm 32.1^\circ$. In keratoconic eyes scleral lenses always produced an hourglass pattern with a single focus with a VSX lower than in healthy eyes.

Conclusions: Based on the hourglass pattern found in healthy eyes, it is easily understood how the refracting process automatically funnels practitioners towards the optimal correction. The shell pattern of the spectacle correction in keratoconus, on the other hand, presents a far more complex shape with multiple foci. Hence, depending on the starting point, refracting procedures can often lead away from the optimal correction.

CONTROL ID: 3541765

SUBMITTER (NAME ONLY): Erdost Yildiz

TITLE: Generative Adversarial Network Based Automatic Segmentation of Corneal Subbasal Nerves on In vivo Confocal Microscopy Images

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In vivo confocal microscopy (IVCM) is non-invasive, reproducible, and inexpensive diagnostic tool for corneal diseases, which also helps to detect neurological and metabolic diseases. However widespread and effortless image acquisition with IVCM creates also a serious workload of image processing and analysis for clinicians. Deep learning algorithms are possible solutions for this heavy workload. In our study, we have produced a novel deep learning algorithm based on generative adversarial network (GAN) and we compare its accuracy for automatically segmentation of subbasal nerve plexus in IVCM images with ophthalmology experts and a convolutional neural network(U-Net) based method.

Methods: We have collected IVCM images from various patient groups and anonymized patient information for segmentation procedures. Three graders, U-Net based conventional algorithm and our GAN-based nerve segmentation system traced nerve plexus for each IVCM images. Results for GAN and U-Net based nerve segmentation methods in IVCM images compared with the graders and analyzed with Pearson's r correlation, Bland-Altman analysis, and receiver operating characteristics (ROC) curves. Lastly, different types of noises applied on IVCM images and segmentation performance of GAN-based and U-Net based methods observed under these different noise types.

Results: The GAN-based algorithm demonstrated similar correlation and Bland-Altman analysis results compared to U-Net-based algorithm. When ROC curves applied to both methods, the GAN-based segmentation method showed significantly higher sensitivity and higher specificity compared to U-Net based algorithm for corneal nerve segmentation in IVCM images ($p<.001$). Lastly, the performance of the U-Net-based algorithm deteriorates significantly with real world noise simulation, especially in speckle type noise, compared to GAN-based algorithm ($p<.001$).

Conclusions: This study is the first study for application of GAN-based algorithms on IVCM images. The GAN-based algorithm demonstrated higher accuracy compared to the experts and the U-Net based algorithm for corneal nerve segmentation in IVCM images. The GAN-based algorithm is more reliable than the U-Net based method in IVCM images with different types of noise. In the near future, the GAN-based segmentation method could be used as a facilitative diagnostic tool in ophthalmology clinics.

CONTROL ID: 3541766

SUBMITTER (NAME ONLY): Ying Li

TITLE: Blue light induces impaired autophagy through nucleotide-binding oligomerization domain 2 activation on the mouse ocular surface

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, R. Jin, L. Li, J. Kim, H. Yoon, K. Yoon, Chonnam National University, Gwangju, Jeollanam-do, KOREA (THE REPUBLIC OF)

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ABSTRACT BODY:

Purpose: To investigate the effect of blue light (BL) exposure on nucleotide-binding oligomerization domain 2 (NOD2) expression on the mouse ocular surface and to evaluate the role of NOD2 signaling in BL-induced cell death.

Methods: Wild or NOD2 knock-out (KO) C57BL/6 mice were exposed to BL (410nm) twice a day for 10 days at an energy capacity of 100 J/cm² and divided into the WT+BL and NOD2-KO+BL groups. Mice in the WT and NOD2-KO groups were not exposed to BL and served as control. Corneal fluorescein staining scores were measured after 10 days of BL stimulation. 2'7'-dichlorofluorescein diacetate for reactive oxygen species (ROS), enzyme-linked immunosorbent assay for malondialdehyde (MDA), and terminal deoxynucleotidyl transferase-mediated dUTP-nick end labeling for apoptosis were performed 10 days after exposure to BL. In addition, expression of NOD2, ATG16L1, LC3-||, and p62 were evaluated using Western blot.

Results: After exposure to BL, increased ROS and MDA were observed in the WT+BL and NOD2-KO+BL groups, and the WT+BL group showed a higher expression of NOD2 and ATG16L. Mice in the WT+BL and NOD2-KO+BL groups showed a significant increase in the expression of LC3-|| and p62, whereas the NOD2-KO+BL mice had lower LC3-|| expression and higher p62 expression compared to WT+BL mice. In addition, NOD2-KO+BL mice had significantly lower corneal epithelial damage and apoptosis than WT+BL mice.

Conclusions: BL exposure can induce impaired autophagy by activation of NOD2 on the ocular surface. In addition, the ROS-NOD2-ATG16L signaling pathway may be involved in the BL-induced autophagy responses, resulting in corneal epithelial apoptosis.

CONTROL ID: 3541774

SUBMITTER (NAME ONLY): Helen Kuht

TITLE: A machine learning solution to predict foveal development and visual prognosis in retinal developmental disorders

SESSION TITLE: Pediatric ophthalmology and Systemic Disorders

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.J. Kuht, V. Sheth, Z. Tu, M. Hisaund, R.J. McLean, R. Purohit, S. Teli, F.A. Proudlock, I. Gottlob, M.G. Thomas, Ulverscroft Eye Unit, Ophthalmology Department, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|G. Nishad, G. Varma, International Institute of Information Technology Hyderabad, Gachibowli, INDIA|S.S. Wang, Department of Mathematics, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|S.S. Wang, Y. Zhang, Department of Informatics, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|G. Maconachie, Academic Unit of Ophthalmology and Orthoptics, The University of Sheffield, Sheffield, Sheffield, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Detecting and grading abnormal retinal development has important diagnostic and prognostic implications in children. The foveal hypoplasia (FH) grading system is based on the stage at which retinal development ceases, and can be described as grade 1 to 4 FH and atypical FH. Correctly identifying the degree of arrested retinal development requires an understanding of the retinal developmental sequence and thus can be challenging for the non-expert. We therefore proposed the development of the first artificial intelligence (AI) based system to accurately identify and grade FH using optical coherence tomography (OCT).

Methods: A representative sample (n=5078) of paediatric OCT scans demonstrating varying degrees of arrested retinal development (normal, grade 1-4 FH and atypical FH) were obtained from the Leicester paediatric OCT database. Foveal scans were acquired from table mounted OCT (n=3037) (Copernicus, Optopol Technology S.A., Poland) and handheld OCT (n=2041) (Envisu 2300; Leica Microsystems, Germany) devices to ensure a high-performing, device agnostic system. The foveal B-scans were extracted, annotated, and segmented. A high-yield training dataset (n=3555) was inputted through a customised convolutional neural network (CNN) (Resnet50) for the training stage. Following the training and fine-tuning of the customised Resnet50, a validation stage to test the accuracy of the model was implemented. The foveal scans in this stage were new and unseen scans to the CNN.

Results: Our binary classification (normal and abnormal foveal morphology) and six-point classification (normal, grade 1-4 FH and atypical FH) achieved 98.1% and 95.0% validation accuracy, respectively.

Conclusions: We have demonstrated, for the first time, the proof-of-concept for the use of a device agnostic, automated AI system in paediatric OCT interpretation. Our system can help to eliminate inter-examiner variability and augment the clinical pathway by increasing time efficiency during busy clinics. The introduction of OCT to routine clinical assessment is imminent. Therefore, our AI system provides a strong foundation for the development of a real-time, frontline diagnostic tool for retinal developmental disorders.

CONTROL ID: 3541776

SUBMITTER (NAME ONLY): Rujun Jin

TITLE: Efficacy of 0.1% Cyclosporin A Cationic Emulsion in Murine Dry Eye with Different Severity

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Jin, Y. Li, L. Li, J. Kim, H. Yoon, K. Yoon, Chonnam National University, Gwangju, Jeollanam-do, KOREA (THE REPUBLIC OF)

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ABSTRACT BODY:

Purpose: To compare the therapeutic effects of 0.1% cyclosporin A cationic emulsion (CsA CE) with that of 0.05% CsA emulsion for ocular surface damage and inflammation in murine dry eye (DE) with different severity.

Methods: After exposure to desiccating stress and subcutaneous injection of scopolamine for 5 days, C57BL/6 female mice were divided into the severe dry eye (SDE) and non-severe dry eye (NSDE) groups based on corneal fluorescein staining scores (CFS). Mice from both groups were topically treated with 0.05% CsA emulsion or 0.1% CsA CE for 10 days. Tear volume, tear film break-up time, and CFS were measured at 5 and 10 days. Western blot for NF- κ B, multiplex immunobead assay for inflammatory cytokines, flow cytometry for CD4+ T cells, histology for goblet cell density, and TUNEL staining for apoptosis were performed at 10 days.

Results: 0.1% CsA CE-treated mice in the SDE and NSDE groups showed a significant improvement in all clinical parameters. Furthermore, in the SDE group, CFS in 0.1% CsA CE-treated mice was lower than that in 0.05% CsA-treated mice at 10 days. In the SDE and NSDE groups, remarkably improved expression of NF- κ B, levels of TNF- α , IL-6, and IL-17, percentage of CD4+ IFN- γ + and CD4+ IL-17+ T cells, density of goblet cells, and number of apoptotic cells on the ocular surface were observed. Specifically, in the SDE group, 0.1% CsA CE-treated mice had significantly decreased NF- κ B activation, inflammatory infiltrations, and apoptosis on the ocular surface and increased conjunctival goblet cell density compared to 0.05% CsA-treated mice.

Conclusions: 0.1% CsA CE was more effective than topical 0.05% CsA emulsion in improving corneal epithelial injury and decreasing inflammatory cytokines and T cells in SDE.

CONTROL ID: 3541785

SUBMITTER (NAME ONLY): Jesse Panthagani

TITLE: Tear Film Biomarkers in Patients with Ocular Mucous Membrane Pemphigoid

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Panthagani, R.C. Vincent, A. Sekaran, J.M. Romero del Hombre, G.R. Wallace, S. Rauz, Ophthalmology, Birmingham and Midland Institute, Birmingham, Birmingham, UNITED KINGDOM|N. Barnes, University of Birmingham Institute of Clinical Sciences, Birmingham, West Midlands, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mucous membrane pemphigoid (OcMMP) is an immunobullous disease characterised by a progressive conjunctival fibrosis driven by inflammation. In over 50% of cases, disease progresses in the absence of clinically visible inflammation. The purpose of this study was to analyse tear washings to identify components of inflammation and fibrosis that could be used as putative biomarkers of disease activity and response to therapy.

Methods: Tear washings were obtained by applying 100µL 0.9% NaCl onto the ocular surface and aspirating with a lacrimal canula from 21 OcMMP patients (42 eyes; mean age 74.6(±8.9 SD) years, 14(66%) female, 17(81%) biopsy-positive) and 15 age-matched cataract patient controls(30 eyes; age 72.3(±10.9) years, 8(53%) female). Total protein content (DC Protein Assay (BioRad, USA)) was used to correct for the variation in sample volume. Matrix metalloproteinases (MMP) 8 and 9, myeloperoxidase (MPO), epithelial growth factor (EGF), interleukin (IL)-1β, 6, 8, 10, 13 and TNF-α were quantified with a Luminex Assay (Thermo Fisher Scientific, USA). Total aldehyde dehydrogenase (ALDH) activity was measured using BioVision PicoProbe™ ALDH assay. Statistical analyses were performed using GraphPad Prism 8 (Mann Whitney U non-parametric test).

Results: Based upon the cicatrising conjunctivitis assessment tool (CCAT[®] Score) the majority of OcMMP eyes had none/minimal inflammation (mean score 0.79±1.58SD) at the time of sampling and 29(69.0%) had >50% symblepharon. MMP8, MPO and IL-6 were significantly elevated whereas EGF was significantly lower in OcMMP versus controls (p=0.025, p=0.010, p=<0.001 and p=0.001 respectively, Figure 1). There was no significant difference in the other measured cytokines. Mean ALDH activity was higher in OcMMP eyes (0.4 vs 0.05 mAU/mg, p=0.025, Figure 2).

Conclusions: Despite the absence of clinically visible conjunctival inflammation significant differences in tear film MMP8, MPO, IL-6, EGF and ALDH expression were observed in OcMMP eyes compared to controls. MMP8 and MPO are primarily produced by neutrophils and macrophages. IL-6 is a pro-inflammatory cytokine playing a role in chronic inflammation. ALDH has been linked to progressive conjunctival fibrosis in OcMMP. Taken together, these data could represent a pharmacodynamic biomarker panel for OcMMP to enable measurement of treatment response to novel therapies, and as predictors of disease progression in quiescent eyes.

CONTROL ID: 3541786

SUBMITTER (NAME ONLY): Ivan Lee

TITLE: Clinical characterization of autosomal dominant and autosomal recessive PROM1 mutation with a report of novel mutation.

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Lee, J. Odom, A. Jones, M. Leys, West Virginia University Eye Institute, Morgantown, West Virginia, UNITED STATES|C. Bebout, V. Ramamurthy, School of Medicine, West Virginia University, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prominin 1 is a transmembrane domain glycoprotein, ubiquitously expressed in plasma membranes, namely at the protrusion of rod and cone outer segments of the retina. While dominant variants usually take a milder, slowly progressive course, recessive variants are associated with early-onset and progressive retinal degeneration. We performed a retrospective chart review of patients with pathogenic PROM1-variants to improve our understanding of this rare disease and to report two novel mutations.

Methods: Records of 208 patients with inherited retinal disease (IRD) seen at the West Virginia University Eye Institute who had genetic testing between March 2015 and December 2020 were reviewed. We retrieved 6 patients with pathogenic PROM1 variants. Their clinical findings, retinal images, and electrodiagnostic tests were reviewed.

Results: Pathogenic PROM1 variants were found in 6 patients (2.9%) of the genotyped IRD patients.

1. A father and 2 sons were identified with AD variant c.1117C>T. The Ganzfeld ERG was decreased in the father.
2. Two affected siblings diagnosed with cone rod dystrophy harbored two new novel PROM1 heterozygous variants: 1) c.1909C>T (p.Gln637*) and 2) c.2050C>T (p.Arg684*) and a previously reported mutation of ABCA4 c.4793 C>A (p.Ala1598Asp). Parental testing confirmed recessive inheritance. Visual acuity, visual field and ERG significantly deteriorated over 23 years.
3. The sixth patient had PROM1 variant c.642T>A(p.Tyr214*) . He displayed a Best phenotype with normal EOG and visual acuity and imaging remained stable over 4 years of follow up.

Conclusions: We report six patients with pathogenic PROM1 mutations, characterized via genotyping, electrodiagnostic testing as well as imaging studies, corroborating reports on the general trend of AR variant taking a more severe and progressive phenotype. We also report novel AR variants of PROM1 mutation: c.1909C>T and c.2050C>T. These mutations produce premature stop codons in an extracellular domain of prominin 1, resulting in a truncated protein and loss of prominin activity. PROM1 is a key regulator of ABCA4 expression. In that regard, the presence of mutations in PROM1 and ABCA4 in our AR variants is important. Further studies are needed to elucidate the need for PROM1 in ABCA4 expression.

CONTROL ID: 3541787

SUBMITTER (NAME ONLY): Michael Grinton

TITLE: Delayed follow up in Retinal Vein Occlusion and Diabetic Macular Oedema Patients due to COVID-19: Impact on Disease Activity and Visual Acuity

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Grinton, L.G. Stone, J.S. Talks, Ophthalmology, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The coronavirus pandemic has prompted unprecedented delays to treatment with anti-VEGF intra-vitreous injections due to the need to reduce hospital attendances and prioritize the patients at highest risk of vision loss. This study aims to quantify the effect of these delays on visual acuity (VA) outcomes and optical coherence tomography (OCT) features for retinal vein occlusion (RVO) and diabetic macular oedema (DMO) patients.

Methods: A retrospective data analysis of an electronic medical record was performed on a random sample of eyes receiving anti-VEGF injections for RVO and DMO between 1 January and 23 March 2020. Patients with RVO and DMO were identified and data collected included whether the review was delayed (defined as delayed by 8 weeks or more from planned) and VA at baseline and follow up. For those patients not delayed, a VA at 20 weeks was recorded to provide a control group as this was the mean number of weeks until the delayed group were seen. For the delayed group, the OCT features at follow up were also noted.

Results: 300 eyes were analysed, of which 176 had RVO and 124 had DMO. 65 out of 176 eyes (36.9%) with RVO and 39 out of 124 eyes (31.5%) with DMO had their review delayed by 8 weeks or more. The mean number of weeks delay was 13.3 and 13.7 weeks for RVO and DMO respectively. Mean change in VA for eyes with RVO where their appointment was delayed was worse compared to those not delayed. For delayed RVO eyes, VA changed from 59.7 to 54.5 (-5.2) letters and for non-delayed RVO eyes VA changed from 63.5 to 61.6 (-1.9) letters ($P=0.363$). Mean change in VA for eyes with DMO was comparable between delayed (63.0 to 61.1 letters, -1.9) and non-delayed groups (63.7 to 61.0 letters, -2.7). For the delayed group, mean CMT (μm) changed from 374 to 451 (+77) in RVO eyes and 395 to 387 (-8) in DMO eyes. By November 2020, 23.1% of eyes with RVO and 8.6% of eyes with DMO had not returned to within 5 letters of their baseline vision.

Conclusions: Delayed appointments due to COVID-19 affected a significant proportion of RVO and DMO patients receiving intra-vitreous injections. Delayed reviews in RVO eyes had a greater impact than for DMO eyes, with a higher proportion losing vision both in the short and long term. VA loss was associated with worsening of OCT features in RVO patients.

CONTROL ID: 3541794

SUBMITTER (NAME ONLY): Li Guo

TITLE: VSN16S, an agonist of the cannabinoid receptor, reduces IOP profiles and exhibits neuroprotective properties in a rat model of glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Guo, V. Luong, M. Cordeiro, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Cordeiro, ICORG, Western Eye Hospital, London, London, UNITED KINGDOM|A. Gregson, D. Selwood, Medicinal Chemistry, Wolfson Institute for Biomedical Research, University College London, London, London, UNITED KINGDOM|D. Baker, Neuroimmunology Unit, Blizard Institute, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: There is an unmet need for new drugs in glaucoma that can effectively prevent glaucoma progression. We assessed the effects of VSN16S and AG-020, the agonists of the cannabinoid receptor, on intraocular pressure (IOP) and neuroprotection using a rat model of ocular hypertension (OHT).

Methods: 20 male Dark Agouti (DA) rats aged 8-10 weeks were randomly located into four groups (n=5): OHT-only, OHT+vehicle, OHT+VSN16S, and OHT+AG-020. All animals had IOP surgically elevated in the left eye (OS) by injection of hypertonic saline into the episcleral veins. Except for OHT-only, animals in the other three groups have received eye drops in OS either vehicle or VSN16S or AG-020 at 10mg/ml, twice daily for 3 weeks following OHT-induction. IOPs were recorded in both eyes at baseline (BL), day1, week1, 2, and 3 using a Tonopen. Animals were in vivo imaged for retinal ganglion cell (RGC) apoptosis in both eyes using DARC (Detection of Apoptotic Retinal Cells) at BL and week3 before culled. Retinal whole-mounts were immunostained with a Brn-3a antibody to assess RGC survival. DARC spots and RGC counts were assessed by blinded algorithm analysis.

Results: Surgical procedure induced a significant increase in IOP profiles in all animal groups compared to the contralateral eye (OD), and peak levels occurred at day1 ($p<0.001$). In the OHT eyes treated with VSN16S, IOPs at week1 exhibited a sharp reduction ($p<0.05$), and integrate IOP at week3 was significantly lower than vehicle controls ($p<0.01$). However, AG020 showed no effect on IOP. Surgically induced IOP elevation resulted in a significant increase in DARC counts (RGC apoptosis) in all groups, compared to the baseline. DARC counts revealed a significant reduction in the OHT eyes treated by VSN16S, compared to the OHT-only and vehicle groups ($p<0.01$), but less of a reduction of DARC counts was observed with AG-020 treatment ($p<0.05$). A significant reduction of Brn-3a⁺ RGC density was seen in the OHT-only group compared to naïve controls ($p<0.05$), and VSN16S treatment demolished the difference although no significance was found on Brn-3a⁺ RGC density between VSN16S and controls.

Conclusions: VSN16S exerted neuroprotective properties in OHT-induced RGC loss, which may be associated with lowering IOP profiles. DARC is a useful tool in the assessment of drug efficacy in retinal neurodegenerative diseases.

CONTROL ID: 3541796

SUBMITTER (NAME ONLY): Michael Whitehead

TITLE: Immunogenicity of phosphodegrogen mutant AAV2 vectors in the ocular compartment

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Whitehead, P. Yu-Wai-Man, Department of Clinical Neuroscience, University of Cambridge, Cambridge, Cambridgeshire, UNITED KINGDOM|P. Yu-Wai-Man, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Michael Whitehead: Commercial Relationship: Code N (No Commercial Relationship) | Patrick Yu-Wai-Man: Commercial Relationship(s);Gensight:Code C (Consultant)

ABSTRACT BODY:

Purpose: Adeno-associated virus serotype 2 (AAV2) is a viral vector that can be used to deliver therapeutic genes to the retina. AAV2 capsids can be altered in order to improve the efficiency of gene transfer, for instance, by mutating surface-exposed residues that mediate intracellular phosphorylation and degradation of viral particles. Whilst this strategy has demonstrated promise in terms of improving retinal transduction, the possibility of immune activation following the incorporation of phosphodegrogen mutations into AAV2 has not been explored.

Methods: Adult male C57BL/6J mice were injected intravitreally with either 2E8 viral particles (VP)/eye AAV2, AAV2 (Y444F), AAV2 (Y444F, K556E, S662V), 2E10 VP/eye AAV2 or PBS vehicle. After three weeks, mice were sacrificed, serum samples were extracted and eyes were enucleated for analysis. Serum neutralising antibody (NAb) titres were calculated using an in vitro neutralisation assay. Transduction efficiency was assessed via analysis of reporter expression (GFP), and immunohistochemical analysis was used to identify activation of adaptive and innate immune systems. An in vitro heparan binding assay was used to assess whether phosphodegrogen mutant AAV2 may bind to heparan sulphate proteoglycan (HSPG) with lower affinity than prototypical AAV2.

Results: AAV2 (Y444F) and AAV2 (Y444F, K556E, S662V) exhibited higher transduction efficiency in the retina than wild type capsids. Both mutant capsids induced higher serum NAb titres and levels of CD4+ and CD8+ T-cell infiltration into the retina than wild type AAV2. We also observed elevated immunoreactivity of CD68 and Iba1, suggesting that microglia activation was induced by the mutant capsids. Similarly, we saw morphological changes and increased immunoreactivity in GFAP+ fibrils, suggesting that Muller glia were involved in the immune response to the mutant capsids. Finally, we showed that AAV2 (Y444F) and AAV2 (Y444F, K556E, S662V) exhibit slightly reduced binding affinity to heparan sulphate.

Conclusions: Our results suggest that incorporation of phosphodegrogen mutations in AAV2 results in elevated immune activation vs. wild-type capsids. The underlying molecular basis of this requires further investigation, however, increased permeation of virions into the neural retina due to attenuated heparan binding in the inner limiting membrane may be involved.

CONTROL ID: 3541798

SUBMITTER (NAME ONLY): Maria Luísa Ribeiro

TITLE: Characterization of one-year progression in risk phenotypes of diabetic retinopathy

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ribeiro, I. Marques, M. Lopes, S. Simão, P. Barreto, T. Santos, P. Basile, J. Figueira, R. Silva, M.H. Madeira, A. Santos, C.F. Lobo, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|I. Marques, J. Figueira, R. Silva, M.H. Madeira, A. Santos, C.F. Lobo, J.G. Cunha-Vaz, Universidade de Coimbra Faculdade de Medicina, Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To identify one-year progression of two nonproliferative diabetic retinopathy phenotypes B and C associated with risk of developing sight-threatening complications in type 2 diabetes (T2D).

Methods: Patients with type 2 diabetes were followed in a one-year longitudinal study. The following systemic factors were evaluated: age, sex, diabetes duration, lipidic profile, inflammatory cytokines and hemoglobin A1c (HbA1c). Ophthalmological examinations were performed at baseline, 6 months and at one-year, and included visual acuity (BCVA), color fundus photography (CFP) and optical coherence tomography (OCT and OCTA). Phenotype classification was performed based on microaneurysm turnover (MAT, on CFP) and central retinal thickness (CRT, on OCT). Only risk phenotypes were included; Phenotype B identified by low MAT (< 6) and increased CRT; and Phenotype C identified by higher MAT (≥ 6) with or without increased CRT. ETDRS grading of seven fields CFP was performed at the initial visit.

Results: To evaluate the relative risks associated with the two phenotypes, B and C, associated with increased risk of developing sight threatening complications, 1421 individuals with T2D and NPDR were recruited (81 eyes classified as phenotype B and 60 eyes classified as phenotype C), and followed for one year. Of these, 136 completed the one-year follow-up or developed DME (considering both clinically significant macular edema (CSME) and center-involved macula edema (CIME). Nineteen eyes (14%) developed either CSME (1) or CIME (18). Eleven eyes with phenotype B (14%) and 7 eyes with phenotype C (12%) developed CIME. One eye with phenotype C developed CSME. During the period of one-year, phenotype C showed a decrease in BCVA ($p=0.008$), in ganglion cell layer (GCL) thinning ($p=0.022$) and in macular vessel density in the inner ring ($p=0.004$), particularly in the deep retinal capillary plexus. No significant changes were detected in CRT in both phenotypes during one-year period of follow-up.

Conclusions: In one-year period of follow-up, phenotype C is the only risk phenotype that is associated with vision loss and shows disease progression at both microvascular level, represented by capillary closure, and neurodegeneration, represented by GCL thinning.

CONTROL ID: 3541804

SUBMITTER (NAME ONLY): Katja Hatz

TITLE: Efficacy and outcome predictors of long-term intravitreal anti-VEGF therapy in neovascular age-related macular degeneration following a strict treat-and-extend regimen.

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.B. Hatz, Vista Klinik AG, Binningen, SWITZERLAND|K.B. Hatz, Universitat Basel Medizinische Fakultat, Basel, BS, SWITZERLAND|

Commercial Relationships Disclosure (Abstract): Katja Hatz: Commercial Relationship(s);Novartis Switzerland:Code F (Financial Support);Bayer Switzerland:Code F (Financial Support);Roche:Code F (Financial Support);Allergan:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To determine functional and morphological long-term outcomes and outcome predicting factors in patients with neovascular age-related macular degeneration (nAMD) applying a treat-and-extend regimen (TER).

Methods: Consecutive retrospective case series of treatment-naïve subjects with nAMD starting treatment with either ranibizumab or aflibercept in a strict TER without loading dose and exit strategy.

Results: Two hundred-eleven (211) eyes of 187 patients with a mean follow-up of 60.3 ± 20.9 months were included. Mean BCVA increased from initially 63.9 ± 15.5 ETDRS letters (20/55) to 70.0 ± 14.7 (20/40) after one year (+6.1 letters, $p < 0.001$) and to 68.5 ± 18.1 (20/43) (+4.6 letters, $p = 0.028$) at 5 years. Mean number of injections decreased from 9.9 ± 2.1 during the first year to 7.54 ± 3.6 ($p < 0.001$) at year 5. During follow-up 30.3% of eyes reached exit criteria. Significant predictors of BCVA gain at 5 years were a worse baseline BCVA ($p = 0.001$), a better external limiting membrane (ELM) disruption score ($p = 0.019$) and the absence of central geographic atrophy at diagnosis ($p = 0.006$). The probability of reaching the exit criteria was significantly predicted by a low central retinal thickness (CRT) ($p = 0.025$), a better ELM disruption score at baseline ($p = 0.044$) and the absence of a central pigment epithelial detachment (PED) ($p = 0.05$).

Conclusions: Significant visual gains were sustained after 5 years of follow-up in a TER in a real-world setting. Integrity of ELM at baseline was associated with BCVA gain and anatomic disease stability at 5 years of treatment.

CONTROL ID: 3541812

SUBMITTER (NAME ONLY): Fiona Cunningham

TITLE: The role of placental growth factor (PlGF) in retinal pigment epithelial (RPE) barrier integrity and outer retinal integrity in geographic atrophy

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Cunningham, I. Lengyel, A. Stitt, Wellcome-Wolfson Institute for Experimental Medicine, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|T. van Bergen, J. Feyen, Oxurion, BELGIUM|

Commercial Relationships Disclosure (Abstract): Fiona Cunningham: Commercial Relationship(s);Oxurion NV:Code F (Financial Support) | Tine van Bergen: Commercial Relationship(s);Oxurion NV:Code E (Employment) | Jean Feyen: Commercial Relationship(s);Oxurion NV:Code E (Employment) | Imre Lengyel: Commercial Relationship: Code N (No Commercial Relationship) | Alan Stitt: Commercial Relationship(s);Oxurion NV:Code F (Financial Support)

ABSTRACT BODY:

Purpose: PlGF has been widely investigated as a target for the mitigation of neovascular age-related macular degeneration (AMD). Previous investigations suggest PlGF inhibition may also be an effective target for the treatment of outer retinal degeneration seen in geographic atrophy (GA). However, this has only been reported in the light-induced retinal atrophy mouse model. This study tested the hypothesis that PlGF inhibition might protect RPE and the outer retina in the sodium iodate (NaIO_3) mouse model.

Methods: PlGF-2 (50ng/mL) was applied to human foetal RPE (hfRPE) for 24 hours in culture. Barrier integrity was assessed by transepithelial electrical resistance (TEER) and staining for ZO-1 and f-actin. Retinal degeneration was induced in mice by intraperitoneal delivery of 50mg/kg NaIO_3 . PlGF and VEGFR1 expression were assessed by in situ hybridisation (ISH) and immunohistochemistry (IHC). Anti-PlGF antibody (5D11D4) was delivered via intravitreal injection. Control conditions were untreated; PBS vehicle control; and IgG antibody control. Retinal degeneration was assessed by optical coherence tomography and post-mortem analyses of retinal sections and RPE/ choroid flatmounts.

Results: PlGF reduced hfRPE barrier resistance by 66.96% \pm 7.78% compared to untreated RPE (mean \pm SD, p-value \leq 0.0005). There was fragmentation of the ZO-1 network and increased cells with stress fibres. In vivo, 50mg/kg NaIO_3 induced outer retina thinning and RPE and choroidal atrophy. Increased VEGFR1 mRNA was detected in the inner retina of NaIO_3 -treated mice by ISH and in the RPE and choroid by IHC. PlGF was detected in the NaIO_3 -treated choroid by IHC. 5D11D4 treatment significantly preserved portions of intact RPE after 24 hours NaIO_3 exposure compared to vehicle and IgG control groups (p-value \leq 0.005 and \leq 0.05 respectively). At the same time, 5D11D4 treatment improved choroidal vascular area after 72 hours NaIO_3 treatment compared to a vehicle control group, although this was not significant. However, 5D11D4 did not prevent RPE atrophy seen at 72 hours, nor retinal thinning.

Conclusions: These results suggest that while PlGF signalling suppresses RPE barrier activity in vitro, this growth factor does not play a significant role in RPE dysfunction observed during oxidative stress induced-retinal degeneration in vivo, in contrast to previous studies.

CONTROL ID: 3541821

SUBMITTER (NAME ONLY): Mungunshur Byambajav

TITLE: A survey of practitioners' awareness of Dry Eye in Diabetes in the UK and Mongolia

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Byambajav, S. Hagan, Vision Sciences, Glasgow Caledonian University, Glasgow, Glasgow, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Mungunshur Byambajav: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Hagan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Dry Eye Disease (DED) in diabetes mellitus (DM) is common. Although, there have been no studies published that evaluate the awareness of DED in DM in the practices of eye care professionals in different regions. In this study, the clinical practice behaviours of eye care professionals based in the UK and Mongolia were compared, with respect to the diagnosis and management of DED in DM.

Methods: An online survey was sent to eye care professionals in the 2 countries (UK and Mongolia). Respondents provided information about practice modality, preferred diagnosis and management of DED in DM.

Results: Only the completed responses (128 from the UK and 68 from Mongolia) were analysed. In the clinical experience of respondents, the mean prevalence of DED in patients with DM was reported as 61.6% (± 21.1) and 57.2% (± 21.7) in the UK and Mongolia, respectively. In addition, the mean prevalence of asymptomatic DED in DM was reported as 50.5% (± 19) and 48.6% (± 18) in the UK and Mongolia, respectively. When comparing the reported prevalence, there were no statistical significant differences detected between the countries ($p > 0.05$). A significant higher proportion ($p < 0.001$) of UK respondents (57.8%; $n = 74$) than Mongolia-based respondents (35.3%; $n = 24$) agreed that the prevalence of DED in DM was higher than those without DM. The majority of UK (71.9%) and Mongolian respondents (61.8%) saw between 1-5 DM patients with DED per week. Both countries reported that DED in DM was diagnosed with the same clinical tests as DED without DM. For DED treatment, respondents mainly prescribed artificial tear supplements (69.4% in the UK; 90% in Mongolia), followed by warm compress and lid scrubs (19.4% in the UK and 6.7% in Mongolia). Half of respondents from both countries agreed that DED in DM receives less attention than diabetic retinal complications during ophthalmic examinations. In addition, they agreed that there needs to be increase in practitioners' awareness of DED in DM. Undergraduate and postgraduate studies were acknowledged as the main source of information for DED in DM among UK and Mongolian respondents, respectively (see Figure 1).

Conclusions: Eye care professionals in both regions had similar practice behaviours for diagnosing and treating DED in DM. According to the responses from the UK and Mongolia, DED was considered as being prevalent in DM.

CONTROL ID: 3541844

SUBMITTER (NAME ONLY): Greg Hofmann

TITLE: Pilot study: Examining relationship among CLDEQ-8 defined classes, blink intervals, and tear film metrics

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Hofmann, V. Korde, N. Franklin, P. Martin, J. Xu, J.R. Buch, Johnson and Johnson Vision Care Inc, Jacksonville, Florida, UNITED STATES|A. Fogelton, Blinkingmatters.com, Trenčín, SLOVAKIA|

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ABSTRACT BODY:

Purpose: To investigate the association between CLDEQ-8 classes, blink frequency during digital device use, tear film metrics, and a metric that emphasizes blinks that occur after the tear film has destabilized.

Methods: A bilateral, dispensing, randomized, double-masked 2x2 cross over study with a 2-week washout was executed. Two silicone hydrogel investigational soft contact lenses were employed, differing only by hydration method. The study included 6 visits: a baseline evaluation and lens fitting, a 1-week follow-up (FU) after 8 hours of lens wear, and a 2-week FU after 8 hours of lens wear. After a 2-week washout with habitual contact lens wear, this was repeated using the second investigational lens. A total of 37 subjects completed the study. At both 1-week FUs, 2 measures of tear stability were evaluated using the Oculus Keratograph 5M and a customized dynamic iDesign wavefront system, and the interblink interval (IBI) was measured while the subject watched a 5-minute video on a tablet. During this measurement, a video of each subject was recorded and analyzed using custom software to yield the IBIs. Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) was also administered at these 1-week FUs, however this questionnaire is not validated at the 1-week wear timepoint. Classes were defined using CLDEQ-8 scores, as follows. Poor and fair ≥ 15 ; 7 < good and very good < 15; excellent subjects ≤ 7 .

Descriptive statistics, by class, were calculated for the IBI, NIKBUT, wavefront RMS, and ocular protection index (OPI) calculated using the NIKBUT and IBI.

Results: Mean or median IBI and mean NIKBUT, plotted by class, did not point to a relationship between the metrics and classes. Plots of the wavefront RMS suggested an increase of RMS and plots of the OPI suggested a decrease in OPI with increasing symptom class.

Conclusions: Combining the NIKBUT tear stability and IBI (OPI metric) appeared to provide better agreement with symptom classes defined by CLDEQ-8 as compared to using IBI or NIKBUT alone. Further investigation of dryness symptoms and discomfort during digital device use, and the interaction between the blink frequency and tear film metrics are warranted.

CONTROL ID: 3541847

SUBMITTER (NAME ONLY): Mahi Muqit

TITLE: Safety of multiple intravitreal injections of ocriplasmin in subjects with non-proliferative diabetic retinopathy (NPDR): Results of the CIRCLE study.

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Muqit, NIHR Moorfields Biomedical Research Centre, London, Greater London, UNITED KINGDOM|R. Tadayoni, Hopital Lariboisiere, Paris, Île-de-France, FRANCE|J. Hamouz, Fakultni nemocnice Kralovske Vinohrady, Praha, Praha, CZECHIA|V.H. Gonzalez, Valley Retina Institute, McAllen, Texas, UNITED STATES|J. Montero, Hospital Universitario Rio Hortega, Valladolid, Castilla y León, SPAIN|D. Scales, Foresight Studies, LLC, San Antonio, Texas, UNITED STATES|G.V. Menon, Frimley Health NHS Foundation Trust, Frimley, Surrey, UNITED KINGDOM|P. Abraham, Black Hills Regional Eye Institute, Rapid City, South Dakota, UNITED STATES|T.L. Jackson, King's College Hospital, London, London, UNITED KINGDOM|I. Fiser, Evropska očni klinika Lexum, CZECHIA|P. Kozma-Wiebe, Oxurion NV, Leuven, BELGIUM|

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ABSTRACT BODY:

Purpose: The CIRCLE study was conducted to assess the efficacy and the safety of up to 3 intravitreal (IVT) injections of ocriplasmin to induce total posterior vitreous detachment (PVD), in order to reduce the risk of disease progression to proliferative diabetic retinopathy (PDR). A single intravitreal injection of ocriplasmin 0.125mg is approved for the treatment of symptomatic vitreomacular adhesion (VMA)/vitreomacular traction (VMT).

Methods: The CIRCLE study was a multicenter, sham-controlled, double-masked study. Subjects were randomized 2:2:1 to receive up to 3 IVT injections of ocriplasmin 0.0625mg, ocriplasmin 0.125mg, or a sham procedure, 1 month apart. They were followed for 24 months.

Results: Recruitment in the study was stopped early due to a slow recruitment rate. As a result, the study was not powered for its primary endpoint (total PVD by Month 3) and the main goal became the assessment of the safety of up to 3 IVT injections of ocriplasmin. Forty-eight (48) subjects were randomized: 20 to ocriplasmin 0.0625mg, 19 to ocriplasmin 0.125mg and 9 to sham. The subjects were mostly white and male. The mean age at Baseline was 56.2 years. The mean time since the diagnosis of diabetes was 16.9 years. There were no relevant imbalances between treatment arms. The most frequently reported treatment-related adverse events (AEs) in the study eye were Conjunctival Haemorrhage in the ocriplasmin 0.0625mg arm (3 events in 3/20 [15.0%] subjects) and Vitreous Floaters in the ocriplasmin 0.125mg arm (5 events in 3/19 [15.8%] subjects). This is similar to the most frequently observed treatment-related AEs following a single injection of ocriplasmin 0.125mg in patients with symptomatic VMA/VMT. No new type of AE was identified. The majority of AEs were mild or moderate in intensity, started within the first week after injection and resolved within a few days. The frequency or intensity of AEs did not increase following the second or third injection with ocriplasmin.

Conclusions: Up to three (3) IVT injections with ocriplasmin were considered safe, given that no new type of AE unknown to ocriplasmin was identified, as compared to a single injection of ocriplasmin 0.125mg in patients with symptomatic VMA/VMT. Neither the frequency nor the intensity of the AEs increased following the second or third injection with ocriplasmin.

CONTROL ID: 3541849

SUBMITTER (NAME ONLY): Aleksandra Parka

TITLE: Changes in visual processing during progression of Tau accumulation and neurodegeneration in a mouse model of human tauopathy

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Parka, F. Sotty, B. Laursen, H Lundbeck A/S, Valby, Hovedstaden, DENMARK|A. Parka, M. Nedergaard, Center for Translational Neuromedicine, Kobenhavns Universitet, Kobenhavn, DENMARK|

Commercial Relationships Disclosure (Abstract): Aleksandra Parka: Commercial Relationship: Code N (No Commercial Relationship) | Maiken Nedergaard: Commercial Relationship: Code N (No Commercial Relationship) | Florence Sotty: Commercial Relationship: Code N (No Commercial Relationship) | Bettina Laursen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Neurodegeneration in Alzheimer Disease (AD) is caused by aggregation of amyloid- β plaques and formation of tau neurofibrillary tangles (NFT). While NFTs are a hallmark of AD, the misfolding and oligomerization of tau protein can start up to 15 years before the first symptoms of dementia. Detecting the disease at an early stage can be complicated and costly. Evidence shows that the visual system follows the pathology in the brain. Indeed, studies have shown significant changes in the visual evoked potentials (VEPs) in patients with mild cognitive impairment as well as AD. The aim of our study was to evaluate whether changes in visual processing may represent an early biomarker of pathological Tau accumulation.

Methods: An animal model of tauopathy, Tg4510, exhibits progressive accumulation of pathological Tau species and neurodegeneration. Transgenic mice at ages of 6, 9 and 16 months were studied against their age matched controls. Retinal response to a white light stimulus was recorded using electroretinography (ERG). Electroencephalography was simultaneously performed to record VEPs. The stimulus was applied at eight different intensities with an appropriate interval in between flashes.

Results: While ERG responses at 6, 9 and 16 months did not differ between transgenic (tg) and control animals, an age-dependent decline in retinal response was observed regardless of genotype. On the other hand, VEP responses to a light stimulus were significantly more pronounced in 6 month tg animals compared to age matched control mice. At 9 months, the difference between tg and control animals was slightly diminished. By 16 months of age, the VEPs in tg mice were weaker compared to their age matched controls, possibly reflecting extensive neuronal loss.

Conclusions: Our findings in younger animals (6 months) may indicate that compensatory mechanisms precede extensive neuronal loss and Tau accumulation. Further histological analysis will help establish the level of correlation between tauopathy and visual processing, which would further strengthen its value as a biomarker

CONTROL ID: 3541857

SUBMITTER (NAME ONLY): Felix Datlinger

TITLE: Long-term results following indocyanine green angiography-guided laser therapy of teleangiectatic capillaries in diabetic macular edema utilizing intraprocedural OCT monitoring to determine the immediate treatment response

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Datlinger, A. Pollreisz, S. Sacu, U. Schmidt-Erfurth, Ophthalmology, Medizinische Universität Wien, Wien, Wien, AUSTRIA|A. Datlinger, Medizinische Universität Wien, Wien, Wien, AUSTRIA|P. Datlinger, Praxis Datlinger, Mattersburg, AUSTRIA|

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ABSTRACT BODY:

Purpose: To evaluate the functional and morphological long-term outcome of ICGA-guided laser therapy of teleangiectatic capillaries (TC) and to assess their immediate as well as their subsequent morphological response to laser treatment.

Methods: In this retrospective study, the presence of TCs was evaluated in patients with treatment naive or pretreated diabetic macular edema (DME). TCs, presenting as hyperfluorescent spots in late-phase ICGA (>10minutes), were targeted with laser. Customized OCT scans were used to monitor changes in the reflectivity of the TCs lumina during and immediately after laser therapy as well as during follow-up. Additionally, patients were treated with intravitreal anti-vascular endothelial growth factor (anti-VEGF) as needed.

Results: 13 eyes of 10 patients with DME were followed-up for a mean of 24 months (± 8). After targeted laser therapy of only 2 TCs per eye on average mean best-corrected visual acuity (BCVA) improved from 0.25 logMar (± 0.19) at baseline to 0.13 (± 0.10 ; $p=0.035$) at months 12-15 and remained stable at 0.14 (± 0.12 ; $p=0.042$) at each patient's last visit. Mean central subfield thickness (CST) decreased from 406 μ m (± 82) at baseline to 295 μ m (± 39) at months 12-15 ($p<0.001$) and remained stable at 291 μ m (± 50) at the last visit ($p<0.001$). The immediate darkening of the TCs lumina, observed in 11 out of 13 eyes at the first laser session was followed by shrinking of the TCs after a mean of 1.3 months, followed by their full resolution after a mean of 4 months in all of these cases. In the two eyes where no darkening of the TCs lumina was observed, re-treatment was necessary after 6 months due to persistence of the TCs and an increase of the edema. Within a mean follow-up of 2 years additional treatment with anti-VEGF was indicated in only 2 of 13 eyes (1 eye 1 injection, the other 4 injections).

Conclusions: The darkening of the TCs lumina visible in OCT as immediate reaction to focal laser therapy resulted in successful closure of these lesions in all cases. Consequently, a statistically significant improvement in BCVA and reduction in CST could be achieved with targeted laser therapy of only two lesions per eye on average. No anti-VEGF injections were needed in the vast majority of eyes during a mean follow-up of 2 years.

CONTROL ID: 3541860

SUBMITTER (NAME ONLY): Deirdre Harford

TITLE: Elucidating the role of inner blood retina barrier integrity in the development of dry AMD

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The initiating pathophysiological events in the development of early AMD still remain unclear. Inner blood retina barrier integrity in young, healthy adult humans has been shown to cycle in a circadian manner, mirroring tight junction protein claudin-5 cycling. As circadian rhythm disturbance has previously been associated with other neurodegenerative disorders, we conducted a case controlled observational study to test the hypothesis that inner blood retina barrier circadian kinesis is arrested in AMD patients.

Methods: Patients with AMD over the age of 65 (n=16) and age matched controls (n=11) were recruited and informed consent obtained. Participant's chronotype was established by way of the Munich Chronotype Questionnaire (MCTQ). Time points in the morning and evening were defined and OCT, FFA and fundal photos were performed. Quantification of FFA images was performed by a bespoke MatLab based software platform. These findings are part of a longitudinal study named the "Irish Circadian Retina Project" which is still recruiting participants with AMD and age matched controls.

Results: In young healthy subjects, fluorescein signal was evident and more prolonged in the evening compared to the morning and this was significantly increased in the inner macula^{***}, outer macula ^{***} and total area^{**}(n=33 subjects, ^{***}p<0.0005, ^{**}p <0.0026). Analysis of melatonin and cortisol revealed variations as expected, with cortisol elevated in the morning and melatonin increased in the evening. Upon OCT volume analysis of the macula, no significant differences between AM and PM were observed. Similarly, preliminary data from AMD patients compared to age matched controls suggests a region-dependent fluorescein signal differential, with a more prolonged signal in AMD patients.

Conclusions: The preliminary findings of this study suggest that the iBRB is highly dynamic. We have previously demonstrated the potential size-selective passive diffusion from the inner retinal vasculature to the retinal parenchyma with diffusion towards the outer retina and RPE in young, healthy controls. Now, we have demonstrated that this phenomenon appears to be attenuated with age and absent in AMD patients. We suggest that disruption in the circadian mediated integrity of the iBRB may be an early initiating event in AMD development and progression. To our knowledge, this is the first time the iBRB has been implicated in AMD pathogenesis.

CONTROL ID: 3541869

SUBMITTER (NAME ONLY): Rebecca Leighton

TITLE: Association between peripheral refractive error and 12-month changes in central refraction and axial length in Caucasian children

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Controversy exists regarding the influence of peripheral visual experience on axial ocular growth in humans. This longitudinal, observational study evaluates the relations between baseline relative peripheral refraction (RPR), change in central refraction and ocular biometry in children aged 6-7 and 12-13 years.

Methods: Cycloplegic autorefraction at horizontal retinal eccentricities of 0° and ±30° were recorded from right eyes (Shin Nippon SRW-5000). The Zeiss IOLMaster 700 measured central axial length (AL) and lens thickness (LT). Measurements were repeated after 12-months. Refractive data were transposed into spherical equivalent refraction (SER). RPR was calculated by subtracting central from peripheral SER. Correlations between baseline RPR and 12-month change in central SER and AL were explored. Multiple regression analyses evaluated the hypothesis that baseline RPR predicts central SER change.

Results: Baseline myopia was associated with more hyperopic RPR and baseline hyperopia and emmetropia with more myopic RPR (all negative correlation $r/\rho > 0.325$, $p < 0.074$). More hyperopic temporal RPR at 12-13 years was significantly correlated with greater myopic shift in central SER ($r = -0.388$, $p = 0.0008$) and greater axial elongation ($r = 0.376$, $p = 0.011$) over 12-months. More hyperopic nasal RPR at 12-13 years was significantly correlated with greater axial elongation ($\rho = 0.333$, $p = 0.025$) but not with central SER change ($r = -0.158$, $p = 0.301$). Neither nasal nor temporal RPR at 6-7 years were correlated with 12-month change in central SER or AL ($p > 0.675$). Multiple regression analyses indicated that baseline central SER, nasal and temporal RPR and AL at 12-13 years explained 21.8% of the variance in 12-month change in central SER ($r^2 = 0.218$, $p = 0.04$) with temporal RPR the strongest predictor of myopic shift ($\beta = -0.449$, $p = 0.029$). Multiple regression analyses suggest neither RPR, AL or LT at 6-7 years are helpful in predicting subsequent 12-month central SER change.

Conclusions: More hyperopic temporal RPR at 12-13 years is associated with greater short-term myopic progression. This relationship is not seen in younger children. These data suggest that temporal RPR may be a useful metric for eyecare clinicians to consider when developing intervention and review plans for teenage children but are less informative when examining younger children.

CONTROL ID: 3541873

SUBMITTER (NAME ONLY): Karen Peynshaert

TITLE: ICG-mediated photoporation of the ILM to enhance retinal drug delivery after intravitreal injection

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Peynshaert, K. De Clerck, F. Sauvage, A. Minnaert, K. Braeckmans, S. De Smedt, K. Remaut, Laboratory of General Biochemistry & Physical Pharmacy, Universiteit Gent, Ghent, BELGIUM|K. Peynshaert, K. De Clerck, F. Sauvage, A. Minnaert, K. Braeckmans, S. De Smedt, K. Remaut, Ghent Research Group on Nanomedicines, Universiteit Gent, Ghent, BELGIUM|

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ABSTRACT BODY:

Purpose: The inner limiting membrane (ILM) is the primary barrier hindering effective drug delivery to the retina after intravitreal injection. Therefore, we aim to create therapeutic entryways into the retina by puncturing the ILM using photoporation. To explore our concept, we applied indocyanine green (ICG) at the ILM surface of bovine and human retinal explants followed by laser scanning of the retina with 800 nm laser light (Figure).

Methods: To perforate the ILM, we applied varying concentrations of ICG (0,1 mg – 1mg/ml) on top of bovine and human retinal explants followed by scanning of the laser beam at lower and higher laser energies (0,24 and 0,4 J/cm²). For the latter, an Nd:YLF laser was applied to generate 800 nm single laser pulses of a 2 picosecond pulse width and frequency of 1 kHz. Following laser treatment, 100 nm sized PEGylated nanoparticles (NPs) were applied on top of the explants prior to their culture for 24 hours. Finally, retinal cryosections were prepared and immunostained for Collagen IV to check for ILM integrity as well as NP entry into the retina with confocal microscopy.

Results: Bovine retinal explants treated with laser only (0,4 J/cm²) showed an intact ILM. In explants treated with both ICG and laser light, however, the ILM was clearly affected: high ICG concentration and laser energy led to full ILM ablation, while lower conditions led to partial ILM destruction. As anticipated, 100 nm sized NPs were largely unable of crossing the intact ILM of untreated and laser-treated explants. By contrast, complete treatment (ICG and laser) resulted in a massive entry of NPs into the retina for all conditions. Additionally, we effectively ablated the ILM of human explants of patients with varying age (27 – 70 years) which indicates that our approach is also effective for treating the thicker and more complex human ILM.

Conclusions: We have successfully ablated the ILM of bovine and human explants by means of ICG-mediated photoporation. In addition, this ILM damage resulted in extensive entry of NPs into the retina. Future plans include fine-tuning of our approach in accordance with the limitations set by toxicity evaluations ex vivo and in vivo.

CONTROL ID: 3541879

SUBMITTER (NAME ONLY): Christopher Girkin

TITLE: Comparison of the 3D morphology of the optic nerve head measured in vivo with OCT and ex vivo by autofluorescence histology

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Girkin, J.C. Downs, G. Bianco, M.A. Fazio, Ophthalmology and Vision Sciences, University of Alabama at Birmingham/Callahan Eye Hospital, BIRMINGHAM, Alabama, UNITED STATES|L. Bruno, Department of Mechanical, Energy and Management Engineering, University of Calabria, Arcavacata di Rende, ITALY|S.K. Gardiner, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the degree of agreement in morphological parameters of the human optic nerve head (ONH) measured with in vivo OCT with ex vivo three-dimensional (3D) histology

Methods: The ONH of 6 eyes from 3 brain-dead organ donors (4 healthy and 2 with glaucomatous eyes) were imaged by OCT with IOP set to 10 mmHg by anterior chamber cannulation. After organ recovery, the eyes were enucleated and fixed at 10mmHg, then high-resolution episcopic 3D histomorphometric reconstructions were created. The surfaces of: Bruch's membrane (BM) and opening (BMO), anterior sclera (AS) and scleral canal opening (ASCO), and anterior lamina cribrosa surface (ALCS), were delineated and then interpolated by analytical 3D fitting models in both the OCT and histology volumetric reconstructions. ALCS visibility area was quantified as the sum of the areas of the Delaunay mesh elements connecting the delineation points. Spearman correlations tested the agreement between in vivo vs. ex vivo measures. Limits of agreement (LOA) were calculated for the relative difference between the two measures, and expressed as % of the mean.

Results: Bland-Altman plots of the relative difference between in- and ex-vivo 3D measurements are shown in the Figure. Spearman correlations are shown in the Table. Good correlation and agreement was seen with parameters defining the canal size ($R \sim 1$, Table), with very narrow LOA ($<10\%$ in band width). ALCS depth ($R \sim 0.8$) and choroidal thickness ($R \sim 0.9$) had good correlation between ex- and in-vivo measurements. However, the ALCS was 20-50% deeper and the Choroid was 50-100% thicker when measured in vivo. ALCS global shape index metrics showed moderate correlation (R of 0.6 and LOA of $\sim 30\%$ in width). On average, 31% of the ALCS defined histologically was visible using in-vivo OCT.

Conclusions: While there is a good agreement between in vivo and ex vivo measurements of the anterior ONH canal morphology and moderate agreement in ALCS shape, in vivo imaging provides limited visualization of the entire ALCS.

CONTROL ID: 3541883

SUBMITTER (NAME ONLY): Aya Barzelay

TITLE: Retinal lineage specific therapeutic effect of human Orbital and Abdominal adipose-derived mesenchymal stem cells

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study compared the therapeutic potential for retinal regeneration of human mesenchymal stem cells derived from abdominal subcutaneous fat (ABSCs) or from orbital fat (OASCs) due to their accessibility and mutual embryonic origin with retinal tissue, respectively.

Methods: Human ABASCs and OASCs were harvested from sub cutaneous and orbital fat by collagenase digestion. Conditioned medium was collected to treat RPE cells under oxidative stress, and was studied for content by cytokine array. Differentiation towards RPE was assessed by qRT-PCR and immunostainig after a co culture system. OASCs, ABASCs, or PBS were transplanted in the sub retinal space of sodium iodate mice, retinas were analyzed By Immunohistochemistry after 3 weeks.

Results: OASCs conditioned medium prevented RPE cell death compared to cells treated with standard medium ($40\% \pm 3.85$ decrease, $p < 0.01$). OASCs and ABASCs showed secretion of anti-apoptotic and neuroprotective cytokines, however, ABASCs showed stronger secretion of immunomodulatory chemokines (threshold > 1.4 folds). OASCs exhibited a potential to differentiate towards RPE lineage evident by upregulation of nuclear OTX2 and PAX6 (929.7 ± 76.2 , 57.6 ± 5.6 folds respectively). ABASCs exhibited a broader differentiation potential into retinal precursors with cytoplasmic localization of OTX2. ABASCs have specifically restored photoreceptor of sodium iodate (SI) mice, exhibited by higher ONL thickness and rhodopsin intensity when compared to PBS (ONL: ABASCs- 51.8 ± 11.7 , PBS- 31.1 ± 5.76 μm . rhodopsin: ABASCs- 27.4 ± 4.09 , PBS- 21.5 ± 2.57 , $p < 0.05$). This effect was correlated with higher retinal infiltration of Iba1+ cells compared to PBS (ABASCs 50.9 ± 14.5 , PBS 28.2 ± 8.17 cells/area, $p < 0.05$). SI induced RPE injury was salvaged by OASCs demonstrated by higher RPE65 intensity (OASCs- 50.2 ± 20.5 , PBS- 23.4 ± 5.51 , $p < 0.05$).

Conclusions: In summary, OASCs exhibited in vitro protective effect on RPE cell death, and differentiation potential to RPE, which translated to salvage of RPE layer in vivo. ABASCs showed immunomodulatory chemotactic secretion in vitro, as well as differentiation ability to retinal precursors, translated to restoration of photoreceptors in vivo. These data suggest a lineage specific therapeutic potential of OASCs and ABASCs in the treatment of retinal degeneration and distinguishes the potential of using each population for future cell therapy application.

CONTROL ID: 3541887

SUBMITTER (NAME ONLY): Charlotte Ernst

TITLE: Differential involvement of adenosine triphosphate (ATP) in hypoxia-induced dilatation of larger and smaller porcine retinal vessels ex vivo

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Adenosine triphosphate (ATP) is involved in hypoxia-induced vasodilatation of larger retinal vessels, but the effect on smaller retinal vessels has not been studied in detail. Therefore, the purpose of the present study was to investigate the effect of purinergic antagonists on hypoxia-induced dilatation of porcine retinal arterioles, pre-capillary arterioles and capillaries.

Methods: Porcine superior hemiretinas (n=30) were mounted in a specially designed perfusion chamber, and the diameter of retinal arterioles, pre-capillary arterioles and capillaries were studied during hypoxia with and without the presence of antagonists to ATP-degradation (AOPCP), P2-purinergic receptors (PPADS) and the A2B-adenosine receptor (MRS1754).

Results: Hypoxia induced dilatation of both arterioles, pre-capillary arterioles and capillaries ($p < 0.01$ for all comparisons). The dilatation of arterioles was antagonized by both AOPCP, PPADS and MRS1754 ($p < 0.03$ for all comparisons), whereas dilatation of pre-capillary arterioles and capillaries were antagonized by PPADS ($p < 0.03$) but not by AOPCP or MRS1754 ($p > 0.50$ for both comparisons).

Conclusions: Hypoxia-induced dilatation of retinal vessels is regulated differentially in larger arterioles, pre-capillary arterioles and capillaries. This may form the basis for selective interventions on the diameter of retinal vessels at different branching level.

CONTROL ID: 3541893

SUBMITTER (NAME ONLY): Recivall Salongcay

TITLE: Comparison of Mydriatic Handheld Retinal Imaging with Early Treatment Diabetic Retinopathy Study (ETDRS) 7-Standard Field Photography for Diabetic Retinopathy (DR) and Diabetic Macular Edema (DME)

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare mydriatic handheld retinal imaging with standard ETDRS 7-field color 30-degree fundus photography (ETDRS photos) for assessment of DR/DME

Methods: Following standard imaging protocol, mydriatic retinal images were acquired using handheld retinal cameras [Aurora (AU), Smartscope (SS), RV700 (RV) and InView (NV)] and dilated ETDRS photos (Figure 1). All images were evaluated at a centralized reading center independently by 4 graders (2 certified retinal image/graders, 1 ophthalmologist, 1 retina specialist). All differences were adjudicated by a senior retina specialist. Kappa statistics [simple (K), weighted (K_w)] assessed agreement for DR/ DME. Sensitivity/specificity for any DR, referable DR [(refDR) moderate nonproliferative DR (NPDR) or worse, any DME or ungradable images] and vision threatening DR [(vtDR) severe NPDR or worse, clinically significant DME (CSME) or ungradable images] were calculated.

Results: Images from 177 eyes of 92 patients with diabetes were evaluated. Severity by ETDRS photos: no DR 40.1%, mild NPDR 19.2%, moderate 14.7%, severe in 10.2%, proliferative DR 15.8%; no DME 72.9%, DME 6.8%, ciDME 17.0%; ungradable 3.4%. Ungradable rate for DR/DME for AU: 0%/0.56%; SS: 4.5%/5.7%; RV:4.0%/5.7%; and NV:7.3%/35.6%. Kappa statistics and agreement rates with ETDRS photos for DR/DME are shown in Table 1. Agreement with DR was highest with the AU (K_w =0.79) and lowest with NV (K_w =0.53). DME agreement was similar across all devices (K_w = 0.79-0.83). Agreement for DR severity with ETDRS photos was highest with AU (68.9% exact, 96.6% 1-step). Sensitivity/Specificity for any DR, refDR and vtDR are shown in Table 1. The established standards (0.80 sensitivity,0.95 specificity) were met by AU, SS and RV for any DR and refDR.

Conclusions: Following a standardized protocol, handheld retinal imaging devices have substantial levels of agreement for DR/DME and meet accepted standards for sensitivity and specificity in identifying any DR and refDR. However, the ungradable rate varies greatly, exceeding 35% even with pupil dilation in some devices. None of the handheld devices met the established 95% specificity for vtDR.

CONTROL ID: 3541897

SUBMITTER (NAME ONLY): Joanna Przybek-Skrzypecka

TITLE: Morphological features of Acanthamoeba keratitis as visualized with laser-scanning In Vivo Confocal Microscopy at diagnosis.

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Przybek-Skrzypecka, Department of Ophthalmology, Warszawski Uniwersytet Medyczny, Warszawa, POLAND | J. Przybek-Skrzypecka, Department of Ophthalmology, SPKSO Ophthalmic Hospital, Warsaw, POLAND | M. Armstrong, Microbiology Department, Manchester Royal Infirmary, Manchester, Manchester, UNITED KINGDOM | L. Au, A. Brahma, F. Carley, Cornea Department, Manchester Royal Eye Hospital, Manchester, Manchester, UNITED KINGDOM | J. Chidambaram, Fungal Infection Group, The University of Manchester Faculty of Biology Medicine and Health, Manchester, Manchester, UNITED KINGDOM |

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ABSTRACT BODY:

Purpose: To identify in vivo confocal microscopy (IVCM) cellular features in Acanthamoeba keratitis (AK) at diagnosis.

Methods: Retrospective observational study of patients aged ≥ 16 years diagnosed with AK at Manchester Royal Eye Hospital from 2012 to 2018. AK diagnosis made by microbiology, IVCM-positive for double-walled cysts/bright spot sign/trophozoite or signet ring sign by experienced grader, or clinical suspicion of Acanthamoeba with improvement after anti-amoebal treatment. IVCM images were graded for morphological features by 2 ophthalmologists masked to clinical features and microbiological diagnosis. Statistical analysis performed in Stata 13.1, with Fisher's exact test for group comparisons.

Results: Of the 27 patients included: 41% were male ($n=11/27$) with median age 29 years (range 16-71 years); 74% were Acanthamoeba culture-positive ($n=20/27$), 81% were IVCM positive for Acanthamoeba ($n=22/27$), 16 were both IVCM and culture-positive, 6 were culture-negative but IVCM-positive, and 1 was clinically diagnosed as AK (culture and IVCM negative). The main risk factor was contact lens wear ($n=21/21$). Median symptom duration at first presentation was 9 days (range 2-42 days), with average BCVA at presentation of logMAR 0.25 (range 0.0-Hand movements). Acanthamoeba appeared in IVCM as bright-spots (86%; 19/22: see image), double-walled cysts (59%; 13/22), signet-ring (23%; 5/22), trophozoites (18%; 4/22) and as lines/clusters in 1 patient. The main epithelial changes detected were: koilocyte appearance with perinuclear halo (64%; 14/22; see image) and hyper-reflective cell borders (59%, 13/22). Nerve beading in basal nerve plexus was observed in 27% (6/22), seen mainly with A. polyphaga ($n=5/6$, $p=0.054$). For both, anterior and posterior stroma, activated keratocytes (65%, $n=15/23$, and 72%, $n=8/11$, respectively) were the most prominent feature. Microtubules connecting adjacent keratocytes were visible in 52% ($n=12/23$), and mostly in A. polyphaga ($n=8/12$, $p=0.036$).

Conclusions: Here we report novel IVCM features in AK of koilocyte appearance of epithelial, and microtubules between keratocytes. These may be initial morphological features of AK infection and could be used as an aid for earlier diagnosis. Larger studies are required to evaluate whether these features are specific to AK, and may therefore be clinically useful as diagnostic or prognostic biomarkers.

CONTROL ID: 3541898

SUBMITTER (NAME ONLY): Roos Wennink

TITLE: Human Leukocyte Antigen mapping of paediatric uveitis

SESSION TITLE: Uveitis: Clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Wennink, S. Hiddingh, A. Haasnoot, V. Kalinina Ayuso, T. de Hoop, E. Spierings, J. van Setten, J. Kuiper, J. de Boer, Universitair Medisch Centrum Utrecht, Utrecht, Utrecht, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Paediatric uveitis is a potentially blinding disease. To date, the aetiology of childhood uveitis is poorly understood. Genome-wide association studies have linked peptide motifs in HLA molecules to susceptibility of paediatric uveitis. Our aim was to comprehensively map the association of HLA alleles with childhood uveitis.

Methods: Whole gene next generation sequencing of all classical HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 loci was performed in 280 children with different forms of uveitis. Dense genotype data from 499 Dutch controls from Genome of The Netherlands were imputed using the SNP2HLA pipeline, using 5,225 samples from European-ancestry from the Type 1 Diabetes Genetics Consortium as reference panel. Cases and controls were compared using logistic regression models adjusting for sex.

Results: In total, 179 unique classical alleles were determined at second field resolution or higher. For cases with juvenile idiopathic arthritis associated uveitis, we ascertained the strong association to HLA-DRB1*08:01 (OR = 11.12, 95% CI 5.76-21.43; $P = 6.51 \times 10^{-13}$) and HLA-DQB1*04:02 (OR = 10.11, 95% CI 5.32-19.22; $P = 1.69 \times 10^{-12}$). There was no HLA-wide significant association signal for intermediate uveitis (lead allele, HLA-DRB1*15:01; OR = 2.18, 95% CI 1.26-3.77; $P = 0.005$). In contrast, we detected HLA-DRB1*01:02 (OR = 9.98, 95% CI 4.47-22.28; $P = 1.9 \times 10^{-8}$) as the primary association in patients with panuveitis. No unique HLA amino acid polymorphisms were associated with the different forms of uveitis.

Conclusions: These findings suggest distinct genetic susceptibility in paediatric uveitis and might help classifying different forms of uveitis in the future.

CONTROL ID: 3541903

SUBMITTER (NAME ONLY): Michael Fliotsos

TITLE: Global Preferred Practice Patterns for the Management of Central Retinal Artery Occlusion

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Fliotsos, S. Miller, A. Chen, L. Thangamathesvaran, S. Zafar, F. Woreta, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: While central retinal artery occlusion (CRAO) is relatively rare, it is associated with vision loss in over 75% of cases. Despite these severe outcomes, there continues to be significant controversy over best treatment practices. Our objective is to summarize global preferred practice patterns for the management of central retinal artery occlusions.

Methods: An online survey was distributed to trauma centers throughout the world to assess institutional management practice patterns for central artery occlusions.

Results: Responses were collected from 33 institutions (response rate 33/42, 78.6%) distributed across Asia (39.4%), North America (33.3%), South America (12.1%), Africa (9.1%), and Europe (6.1%). Approaches to manage CRAO diverged amongst respondents. The majority of respondents performed an anterior chamber (AC) paracentesis (n=31, 93.9%) after the diagnosis was made. The reported permissible time range from onset of CRAO to performing AC paracentesis varied, with 11 centers (33.3%) performing the procedure within 6 hours of onset, 2 centers (6.1%) within 12 hours, and 2 centers (6.1%) within 24 hours. Hyperventilation and/or an ocular massage were each performed at 57.6% of centers (n=19). 39.4% of respondents administered a beta blocker (timolol, n=13). Two centers reported administering tissue plasminogen activator (tPA, n=2, 6.1%); one through an intra-arterial approach and the other through an intravenous route. Only one center (3.0%) routinely uses non-invasive oxygenation for CRAO patients.

Conclusions: Conventional treatment paradigms for central retinal artery occlusions differ considerably. Evidence-based guidelines for the management of CRAO are needed to resolve controversies in care.

CONTROL ID: 3541909

SUBMITTER (NAME ONLY): Mohammed Alnawmasi

TITLE: Visual attention deficits after traumatic brain injury: A systemic review and meta-analysis

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Alnawmasi, S. Khuu, Optometry and Vision Science, University of New South Wales Faculty of Medicine, Sydney, New South Wales, AUSTRALIA|M. Alnawmasi, Optometry and Vision Science, Qassim University College of Science, Buraidah, Qassim, SAUDI ARABIA|

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ABSTRACT BODY:

Purpose: Traumatic brain injury (TBI) is frequently associated with a variety of cognitive deficits, primarily attention and memory deficits. Typically, vision is used as an index of attention deficits following TBI and this study focussed on understanding the impact of TBI on visual attention and the degree to which the different attentional components and processes visual attention (such as selective, sustained, divided, and covert orientation of visual attention) are affected differently following TBI.

Methods: A systematic and meta-analytic review was conducted from research examining visual attention following TBI. A literature search before May 2020 was undertaken on different databases for studies that assessed visual attention using different tasks that target specific or multiple aspect or component of visual attention. Two hundred eighty-seven potentially relevant articles were identified through the literature search and the application of the inclusion and exclusion criteria yielded a total of 16 studies.

Results: A total of 103 effect sizes were estimated from 16 studies using the random effect model from 424 cases and 437 controls. The overall combined effect size suggests considerable impact of TBI on visual attention as it was statistically significant and large TBI, but with high heterogeneity (Effect size=0.92, $Q = 563.84$, $p < 0.0001$, $I^2 = 81.91\%$). Sources of heterogeneity may be due to TBI severity, the aspect of visual attention under investigation, and the use of different tasks and paradigms used to investigate them. Combined effect sizes for severe TBI was significantly higher than mild TBI ($t(92) = 2.63$, $p = 0.009$), indicating greater deficits in visual attention with more injury severity. The combined effect sizes for different aspects of visual attention were significantly different ($F(2, 100) = 9.682$, $p = 0.0001$). A subgroup analysis comparing outcome measures (for different aspects of attention) showed that reaction time was significantly more affected compared to performance accuracy ($F(1, 96) = 25.98$, $P < 0.0001$).

Conclusions: Large and significant deficit in visual attention was found following TBI which can last for years after the initial injury. However, different aspects of visual attention were not affected to the same extent. Future TBI studies and clinical approaches should consider this when investigating potential attentional deficits following TBI.

CONTROL ID: 3541925

SUBMITTER (NAME ONLY): Karla Alejandra Ruiz Ceja

TITLE: Definition of the organization of the ABCA4 transcriptional unit by meta-analysis of transcriptome data

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Ruiz Ceja, M. Pinelli, M. Karali, A. Iuliano, M. Failli, L. Di Filippo, D. di Bernardo, S. Banfi, Telethon Institute of Genetics and Medicine, Napoli, Campania, ITALY|D. di Bernardo, Department of Chemical Engineering and Industrial Engineering, Universita degli Studi di Napoli Federico II, Napoli, Campania, ITALY|S. Banfi, Department of Precision Medicine, Universita degli Studi della Campania Luigi Vanvitelli, Naples, Campania, ITALY|

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ABSTRACT BODY:

Purpose: To gain insight into the genomic organization and transcript composition of ABCA4, the gene responsible for Stargardt disease type 1, using publicly available human retina RNA-Seq datasets.

Methods: A total of 177 bulk RNA-Seq human retina data from non-visually impaired post-mortem donors were retrieved from publicly available expression databases (Pinelli et al., PMID:27235414 and Ratnapriya et al., PMID:30742112). We re-analysed the whole dataset using an ad-hoc designed pipeline. We removed samples with reported RNA integrity number (RIN) values lower than 5.0. Reads were then aligned and mapped to the GRCh38 release of the human genome. Samples with less than 10 million reads mapped and/or less than 70% of reads aligned to the reference genome were discarded. RNA-Seq alignments were assembled to generate an Observed Transcriptome allowing us to create a single set of assembled transcripts and to identify putative novel transcripts. To identify more abundant transcripts, we quantified transcript expression levels by scaling TPM abundance estimates per sample (scaled TPM). We selected ABCA4 transcripts with a median value higher than 50 scaled TPM counts.

Results: After quality control evaluation, we analysed a total of 161 bulk RNA-Seq samples. We focused our analysis of the ABCA4 genomic region, and identified 26 different ABCA4 transcripts, 14 of which are novel. The latter ones are the result of several partial intron retentions, exon skipping and extension along with a few putative novel exon additions.

Conclusions: This is, to the best of our knowledge, the most comprehensive and extended meta-analysis of the ABCA4 locus carried out relying on RNA-Seq data. Our work yielded a reliable expression quantification of the ABCA4 transcripts in the human mature retina, including 16 putatively novel ones, and paves the way towards a better understanding on the organization of this transcriptional unit and on the molecular mechanisms underlying ABCA4-related diseases.

CONTROL ID: 3541926

SUBMITTER (NAME ONLY): John McDermott IV

TITLE: Assessing risk factors for retinal vein occlusions using the NIH All of Us Research Program

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. McDermott IV, T. Lee, A. Chan, G. Ye, B. Shahrivini, B. Radha Saseendrakumar, S.L. Baxter, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, UCSD, University of California San Diego, La Jolla, CA, US, academic, La Jolla, California, UNITED STATES|J.J. McDermott IV, T. Lee, A. Chan, G. Ye, B. Shahrivini, B. Radha Saseendrakumar, S.L. Baxter, UCSD Health Department of Biomedical Informatics, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vein occlusions (RVOs) are known to be associated with several cardiovascular risk factors, but social determinants have been studied less frequently. Additionally, most studies have been conducted on predominantly white, Asian or local populations. Here, we assessed medical and socioeconomic risk factors for developing retinal vein occlusions (RVO) in a diverse nationwide population.

Methods: We performed a case-control study with data in All of Us, comparing 301 adults diagnosed with RVO to controls sampled from >250,000 participants matched by age, gender, and race/ethnicity. Data were extracted regarding demographics, co-morbidities, income, housing, insurance, and substance use. Multivariable logistic regression with bi-directional stepwise variable selection was performed to assess risk factors for RVO. Statistical significance was defined as $p < 0.05$.

Results: The mean (standard deviation) age of 301 adults with RVO in All of Us was 68.1 (12.2) years. The majority (58.7%) were female. Cases were diverse: 24.2% Hispanic or Latino, 25.5% Black or African American, 3.55% Asian and 46.1% white. Most (69.9%) were not currently employed, 38.5% had an annual income of \$25,000 or less, and 22.3% had Medicaid insurance. Traditional risk factors such as hypertension, glaucoma and diabetes mellitus were significantly associated with increased risk of RVO diagnosis (Table 1). Increasing annual income, increasing education level, and all forms of health insurance were associated with decreased risk of RVO, whereas current employment and past street opioid use were associated with increased risk of RVO (Table 1).

Conclusions: In addition to previously associated medical risk factors, multiple social determinants were found to be significant for RVO risk stratification. Past street opioid use was also a novel risk factor that merits further investigation. As a diverse national-level dataset, All of Us offers opportunities for a better understanding of social determinants of eye health, which can inform patient outreach and prevention efforts.

CONTROL ID: 3541935

SUBMITTER (NAME ONLY): Mirzi Grace Byrnes

TITLE: Comparative analysis of the osmoprotective effects of a novel contact lens packaging solution on human corneal epithelial cells

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Contact lens wear (CLW) can change the balance of the ocular surface environment by increasing evaporation and tear osmolarity. Maintaining ocular surface homeostasis during CLW is an important consideration for clinicians. A novel silicone hydrogel daily disposable (SiHy DD) lens has been developed to help reinforce the balance through integration of osmoprotective erythritol and glycerin polyols into the material and packaging solution. The purpose of this study was to use a transformed human corneal epithelial cell (THCEpiC) model to compare metabolic activity and inflammatory responses of the kalifilcon A(KA) packaging solution and 6 other SiHy DD packaging solutions subjected to hyperosmotic conditions.

Methods: THCEpiC were seeded in a 96 well plate, incubated for 72 hours, media was replaced with fresh basal medium, and the cells were incubated for 24 hours. The packaging solutions of kalifilcon A(KA), delefilcon A(DE), narafilcon A(NA), senofilcon A(SE), somofilcon A(SO), stenofilcon A(ST), verofilcon A(VE) were prepared at 25% and adjusted to a hyperosmolar condition (400 mOsm) with NaCl. 25% HBSS was used as the control. The THCEpiC were exposed to each packaging solution for 24 hours and the cell culture supernatant collected. An alamarBlue assay was performed to evaluate THCEpiC metabolic activity after exposure to the solutions. The cell culture supernatants were quantitated with ELISA specific immunoassays for the detection of inflammatory cytokine (IL-6) and chemokines (IL-8 and MCP-1).

Results: There was a reduction in THCEpiC metabolic activity with SE and SO solutions adjusted to 400 mOsm ($p<0.05$). For THCEpiC cells exposed to 400 mOsm adjusted solutions, there were significantly elevated levels of IL-6 with DE, NA, SE, and SO solutions, significantly elevated IL-8 with DE, NA, SE, SO, ST, and VE solutions and significantly elevated levels of MCP-1 with DE, SO, ST, and VE ($p<0.05$). Cytokine levels of THCEpiC cells exposed to KA 400 mOsm adjusted solution were not significantly elevated.

Conclusions: The novel KA solution exhibited better overall osmoprotective properties as compared to the six other SiHy DD solutions under hyperosmotic conditions. These results suggest that erythritol and glycerin polyols may have utility in reducing corneal epithelial cell response to hyperosmotic conditions associated with CLW.

CONTROL ID: 3541940

SUBMITTER (NAME ONLY): Timothy Janetos

TITLE: Effect of the rho-kinase inhibitor Netarsudil on established corneal neovascularization in a PAX-6 knockout mouse model

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Janetos, T. Kume, S. Basti, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|T. Liu, P.R. Norden, T. Kume, Feinberg Cardiovascular and Renal Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: RhoA and its downstream effector ROCK play an important role in proangiogenic endothelial cell polarity, motility, and apoptosis, which are all processes involved in the development of neovascularization. Previous research has shown the use of inhibitors for both rhoA and ROCK to reduce corneal neovascularization (CNV) in alkali-burn induced mouse models. These studies demonstrate the use of these agents in corneal wound healing. Our study is designed to evaluate the effect of a commercially available rho-kinase inhibitor (Netarsudil) on established CNV in a PAX-6 knockout mouse model as regression of established CNV has the potential for visual improvement.

Methods: PAX-6 knockout mice are characterized by congenital iris hypoplasia, foveal hypoplasia and the development of CNV secondary to limbal stem cell deficiency, similar to PAX-6 aniridia in ophthalmic patients. 8 mice (16 eyes) will be divided into two treatment (8 eyes) and a placebo group (8 eyes). The study group is treated with Netarsudil ophthalmic solution (0.02 mg/mL). The placebo group is treated with balanced saline solution. Mice are randomized to be treated once daily or twice daily in one eye, with the opposite eye serving as the placebo. At the start of treatment, anterior segment photography is taken to document baseline CNV. Treatment lasts four weeks. At the end of treatment, mice will be euthanized for corneal immunostaining to quantify CNV.

Results: Two PAX-6 knockout mice are currently undergoing treatment. Two-week treatment results with slit lamp photography show significant CNV and opacification in both the treatment and control eyes (Figure 1). Ongoing treatment with additional mice as the colony grows will continue for 8 mice, based on a power analysis of a 20% expected decrease. The final outcome is percent area of CNV on corneal immunostaining.

Conclusions: This pilot study is designed to evaluate whether inhibition of rho-kinase using a topical, commercially available treatment can regress established CNV in an in vivo mouse model. Final results have the potential to impact future research directions for treatment of CNV.

CONTROL ID: 3541947

SUBMITTER (NAME ONLY): Vita Dingerkus

TITLE: Increased Risk of Severe Rise in Intraocular Pressure after Intravitreal Injection of Aflibercept with Prefilled Syringes

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.L. Dingerkus, G.M. Somfai, F.M. Heussen, S. Kinzl, M.D. Becker, Eye clinic, Stadtspital Triemli, Zurich, Zürich, SWITZERLAND|G.M. Somfai, F.M. Heussen, Werner H Spross-Stiftung, Zurich, SWITZERLAND|M.D. Becker, Eye Clinic, Ruprecht Karls Universität Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Intravitreal injections (IVI) with prefilled syringes (PFS) are supposed to reduce procedure time and the risk of endophthalmitis. Postoperative rise in intraocular pressure (IOP) is suspected to lead to glaucomatous changes and there are informal reports that IOP can increase greatly following injections by the aflibercept PFS. Therefore, our aim was to analyze the emptying volumes (EV) of the aflibercept PFS depending on the injection technique.

Methods: The amount of the EV was assessed using 40 aflibercept PFS. We measured the EV in four different groups with 10 injections in each group: In the first two groups, the cone was set precisely at the indication line (Normal Volume, NV) and the fluid was ejected without (nP) or with forced pressure (wP) at the end of emptying the syringe (NVnP and NVwP groups). In two further groups, the plunger was set right below the line (High Volume, HV) and was ejected without or with forced pressure (HVnP and HVwP groups). A laboratory weighing scale (AX105 DeltaRange®, Mettler Toledo, Ohio) was used for the measurements of EV calculated with a density of 1.034 mg/ml. The EV data of the four groups were compared by one-way ANOVA test followed by post hoc Tukey HSD test.

Results: The EV values in the NVnP, NVwP, HVnP and HVwP groups were 56.06 ± 10.32 , 70.69 ± 4.56 , 74.22 ± 7.41 and 81.63 ± 3.67 µl, respectively. The EV was significantly different in the four groups (ANOVA $p < 0.001$, $F = 23.56$), the NVnP group was statistically significantly lower compared to all other groups ($p < 0.001$ in all comparisons). The EV in three cases (30%) was below 50 µl in the NVnP group (40.62, 42.35 and 45.64 µl) while in the NVwP group all values were above 64 µl, with 7 values (70%) exceeding 70 µl. In the HVwP group 8 measurements (80%) exceeded an EV of 80 µl.

Conclusions: Our results point toward the importance of the right injection technique with the aflibercept PFS to ensure the correct amount of drug intravitreally. With the right injection technique the drug can be underdosed in one third of the cases. 60% (30 µl) excess volume can be achieved by using suboptimal settings and injection technique. One explanation could be the design including the relatively high syringe diameter of the aflibercept PFS. This should be taken into consideration when applying them in the daily routine and might be addressed in future development of further PFS.

CONTROL ID: 3541950

SUBMITTER (NAME ONLY): Luis Alarcon-Martinez

TITLE: Pericyte dysfunction promotes neurovascular deficits in glaucoma

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Alarcon-Martinez, Y. Shiga, N. Belforte, D. Villafranca-Baughman, J. Cueva Vargas, H. Quintero, F. Dotigny, A. Di Polo, Neuroscience, Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Major vascular defects are observed in glaucoma patients, but the mechanisms underlying these alterations are poorly understood. Pericytes, the contractile cells that wrap along capillaries, regulate blood flow in response to metabolic demand. We recently identified inter-pericyte tunneling nanotubes (IP-TNTs), fine tubular processes that connect two distally-located pericytes and are essential for neurovascular coupling. Here, we asked whether pericytes/IP-TNTs contribute to neurovascular dysfunction in glaucoma.

Methods: Ocular hypertension (OHT) was induced by injecting magnetic microbeads into the anterior chamber of mice. Two-photon laser scanning microscopy was used for live imaging of retinal pericytes, IP-TNTs, calcium (Ca^{2+}) signals, light-evoked capillary dynamics and blood flow changes. Ca^{2+} influx induces pericyte contraction, thus we generated mice carrying a pericyte-specific Ca^{2+} indicator (NG2-GCaMP6), and mice with a pericyte-specific conditional deletion of the voltage-dependent Ca^{2+} channel alpha 1C subunit (Cav1.2) (CACNA1Cnull) for analysis of microvascular responses.

Results: Our data show early and sustained reduction of capillary diameter and blood flow at pericyte locations in eyes subjected to OHT relative to sham-operated controls (blood flow - sham: 15 ± 0.6 red blood cell (RBC)/s, OHT-2 weeks: 11.6 ± 0.8 RBC/s, $n=58-86$ capillaries, $N=5-6$ mice/group, Student's t-test $p<0.01$). Vascular deficits correlated with a substantial increase in the number of pericytes with elevated Ca^{2+} , visualized in NG2-GCaMP6 mice (sham: 11.9 ± 2.1 pericytes, OHT-2 weeks: 41.6 ± 2.4 pericytes, $n=167-235$ pericytes, $N=5-13$ mice/group, Student's t-test $p<0.001$). OHT led to IP-TNT rupture with consequent deficits in light-evoked neurovascular coupling (blood flow change - sham: 16.2 ± 3.6 %, OHT-2 weeks: 4.7 ± 1.0 %, $n=29-32$ capillaries, $N=5-6$ mice/group, Student's t-test $p<0.01$). Remarkably, selective blockage of Ca^{2+} influx to pericytes (CACNA1Cnull mice) restored capillary dynamics, blood flow, and light-evoked neurovascular coupling in glaucomatous retinas.

Conclusions: Early calcium-induced pericyte contraction in glaucoma leads to reduced capillary diameter/blood flow and IP-TNT rupture leading to neurovascular impairment. Our data reveal a critical role for pericytes in OHT-related vascular deficits, and suggest that restoration of Ca^{2+} homeostasis in pericytes is effective to rescue neurovascular function in glaucoma.

CONTROL ID: 3541953

SUBMITTER (NAME ONLY): Avril Reddy

TITLE: The Role of inner Blood-Retina Barrier Integrity in Macrophage Recruitment to the Retina

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Reddy, N. Hudson, C. Delaney, K. Byrne, M. Campbell, Smurfit Institute of Genetics, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Claudin-5, a tight junction protein enriched in retinal capillary endothelial cells, is a key modulator of inner blood-retina barrier (iBRB) integrity and paracellular permeability. Persistent suppression of claudin-5 in mice fed a high cholesterol diet (HCD) for several weeks has been shown to induce a geographic atrophy (GA) like phenotype. Here, we aim to characterise a potential new model of GA and further investigate the role of claudin-5 cycling at the iBRB. Claudin-5 expression levels were disrupted by inducing heterozygosity at the *Cldn5* locus in endothelial cells using the Cre-loxP system.

Methods: *Cldn5*^{Flx/wt}; Tie2-cre⁺ mice were generated using the Cre-loxP system. Specific expression of Cre recombinase, driven by the endothelial cell promoter, Tie2, allows *Cldn5* heterozygosity to be induced at the iBRB. Heterozygous mice were fed a normal or HCD, and after 6-10 weeks retinal cryosections were imaged and compared to wild-type littermate controls. Additionally, retinal macrophages and microglia were examined using immunohistochemistry and detected using F4/80, Cd68, and Iba1 staining. ImageJ software was used to quantify the relative level of staining in wild-type and heterozygous animals.

Results: Retinal claudin-5 was found to be decreased and an accompanying increase in macrophage markers were detected in the heterozygous mice. Histological analysis showed an accumulation of subretinal cells in heterozygous animals fed a HCD for 10 weeks. Additionally, some of these subretinal cells were CD68⁺, potentially indicating the presence of subretinal immune cells in these mice. A notable disruption of the RPE was evident.

Conclusions: Our results show that the integrity of the iBRB may influence macrophage recruitment to the retina. Claudin-5 has been shown to cycle under the control of the circadian clock transcription factor, BMAL1. It is hypothesised that disruption of this cycling pattern, a process that may occur with age or due to genetic risk factors, could perturb iBRB function, eventually leading to GA. Subretinal immune cell accumulation is another known hallmark of AMD. Therefore, this study further illustrates the important role of claudin-5 cycling and how a disruption in this process may be a key initiating factor in the development of AMD.

CONTROL ID: 3541955

SUBMITTER (NAME ONLY): Samuel Berchuck

TITLE: Identifying risk factors for blindness from glaucoma at first presentation to a tertiary clinic

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Berchuck, S. Hunt, A. Shi, G. Singh, A.A. Jammal, F.A. Medeiros, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blindness is a crippling disability, resulting in higher risks of chronic health conditions. To better understand disparities in blindness risk, we identify risk factors upon first presentation using a large clinical database.

Methods: We performed a retrospective cross-sectional study using the Duke Glaucoma Registry (DGR). The DGR consists of electronic health records (EHR) of over 100,000 patients seen at the Duke Eye Center from 2009 to 2018. Our cohort included patients with glaucoma and a minimum of one good quality visual field and visual acuity measure recorded within 90 days of a first glaucoma encounter (defined as baseline). International Classification of Diseases codes were used to identify glaucoma and exclude concurrent diseases. Patients were classified as being blind by the definition of legal blindness (i.e., central visual acuity less than or equal to 20/200 with correction or a visual field less than or equal to 20 degrees in the better eye). Baseline risk factors included gender, race (Caucasian vs. African American/Black), marital status (married vs. single), intraocular pressure (IOP; measured by Goldmann applanation tonometry), and a history of diabetes. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for risk factors using both univariable and multivariable logistic regression.

Results: Our cohort consisted of 8,694 glaucoma patients with a complete set of covariates, with 324 (4%) blind upon first presentation. In univariable models, African American/black race (OR: 2.16; 95%CI 1.71, 2.74), single marital status (1.68; 1.32, 2.13), a 10-year increase in age (1.20; 1.10, 1.32), and a standard deviation increase in IOP (1.23; 1.11, 1.35), were all associated with an increased risk of presenting with legal blindness. These associations remained significant in a multivariable regression, with male gender becoming significant (1.42; 1.12, 1.79).

Conclusions: Using a large real-world clinical database, we identified risk factors associated with presentation to blindness among glaucoma patients. Our results highlight disparities in healthcare outcomes and indicate public health outreach for vulnerable communities can reduce differential outcomes in blindness.

CONTROL ID: 3541979

SUBMITTER (NAME ONLY): Assel Talaspayeva

TITLE: The diagnostic accuracy of Optic Coherent Tomography Angiography (OCTA) in Central Asians with primary open angle glaucoma (POAG) suspects, POAG and normal subjects.

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Khujatova, Corporate fund University medical center, Nazarbayev University School of Medicine, Nur-Sultan, KAZAKHSTAN|A. Talaspayeva, M. Khujatova, Department of Ophthalmology, Republican Diagnostic Center, Nur-Sultan, KAZAKHSTAN|A.S. Khouri, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Assel Talaspayeva: Commercial Relationship: Code N (No Commercial Relationship) | Madina Khujatova: Commercial Relationship: Code N (No Commercial Relationship) | Albert Khouri: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To test and identify diagnostic accuracy of a single OCTA in Central Asians for differentiating among normal subjects, POAG suspects and POAG compared to clinical examination.

Methods: Data from Central Asians (Kazakh, Korean, N=59) with confirmed POAG, POAG suspects and healthy subjects age 27 -76 yr were collected. Patients with different stages of glaucoma were included. Visual acuity, refraction, IOP (non contact tonometer, Shin-Nippon NCT -200), slit lamp and fundus examination, ultrasound biometry of lens and vitreous (Alcon Ultrascan B-Scan + A-scan), visual field (HFI 750i, Carl Zeiss), anterior segment (AngioVue OCTA ,Optovue Inc.) were obtained. Anterior chamber parameters were measured. The optic nerve was measured and analyzed in all patients with OCTA (AngioVue, Optovue Inc.). Parameters included RNFL analysis, ONH analysis, GCC analysis, TSNIT NDB Reference.

OCTA images interpretation with a single-page report were exported and analyzed by independent, experienced glaucoma imaging expert, according to a specified grading protocol. The OCTA reader was blinded to any clinical patient information, such as the patient's medical history, visual acuity, IOP, fundus examination, etc.. The OCTA reader assessment was compared to the standard of care clinical examination which had access to exam and all ancillary testing.

Results: An OCTA analysis gave an overall classification rate of 85%.

With two outputs (normal subject, POAG suspect) of OCTA analysis the specificity was 87% and sensitivity 91.4%. The specificity of OCTA for the detection of POAG was 86.6% with sensitivity of 92.5%

Conclusions: A single OCTA assessment demonstrated good diagnostic accuracy when compared to comprehensive exam in its ability to differentiate glaucoma patients from glaucoma suspect and normal subjects in Central Asians. This findings demonstrates that OCTA is a valuable adjunctive tool to assist in glaucoma diagnosis and may provide a method for diagnosis remotely which has value during the COVID pandemic.

CONTROL ID: 3541997

SUBMITTER (NAME ONLY): Jingjing Huang

TITLE: Oxidative stress in Anterior Segment of Acute Primary Angle-Closure Eyes and Its Correlation with Senescence-Associated Secretory Phenotype

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Huang, D. Ye, Y. Xu, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA]

Commercial Relationships Disclosure (Abstract): Jingjing Huang: Commercial Relationship: Code N (No Commercial Relationship) | Dan Ye: Commercial Relationship: Code N (No Commercial Relationship) | Yue Xu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Sudden and dramatic elevation of intraocular pressure (IOP) in acute primary angle closure (APAC) can lead to pathological changes of anterior segment. So far, the mechanisms that connect the two processes are still unknown. We performed a cross-sectional study to evaluate the levels of oxidative stress in anterior segment of APAC eyes and its correlation with senescence-associated secretory phenotype (SASP).

Methods: This study includes 21 patients with APAC, 22 age-matched control patients with age-related cataract (ARC) patients and 5 healthy age-matched donors. Aqueous humor (AqH) samples and iris tissues were collected. Oxidative stress markers in AqH were estimated by relevant reagent kits. The levels of SASP-related cytokines were measured by the multiplex bead immunoassay technique. Immunofluorescence staining was performed to examine the intensity of oxidative stress markers and senescence-associated markers in the iris.

Results: The levels of ROS, MDA, 8-OHdG, SOD and GSH/GSSH ratio were significantly elevated in APAC eyes ($p < 0.001$). ROS levels were increased in older and higher preoperative IOP eyes ($p < 0.01$). Besides, several SASP-related cytokines (GRO α , VEGF- α , TNF- α , IL-1 α , IL-6, IL-8, MMP-10, MMP-10, IGFBP5, IGFBP7, MCP-1, MIP-1 α , TGF- β 1, CCL-2; $p < 0.5$) significantly elevated in the AqH of APAC eyes. Among those cytokines, ROS and MDA were positively correlated with some SASP-related cytokines ($p < 0.01$), while SOD and GSH/GSSH ratio did the opposite. Increased positive cells of oxidative mtDNA damage marker 8-OHdG, apoptosis related marker (Bcl-2, Bax, Bcl-xl, CREB, cleaved caspase-3), and senescence-associated marker (p16, p21 and p53) were detected in the iris tissues of APAC group ($p < 0.001$).

Conclusions: Collectively, we first found that the increase of oxidative stress and premature senescence in the anterior segment of APAC patients. Additionally, the levels of oxidative stress were positively correlated with age, highest preoperative IOP and levels of SASP-related cytokines. These results suggested that there is an important relationship between oxidative stress and premature senescence, and the two factors may be involved in the development of anterior segment pathological changes in APAC eyes.

CONTROL ID: 3541999

SUBMITTER (NAME ONLY): Katrin Wacker

TITLE: Hyperosmolar eye drops for diurnal corneal edema in Fuchs endothelial dystrophy: a double-blind randomized-controlled trial

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Wacker, D. Zander, D. Böhringer, M. Fritz, V. Grewing, T. Lapp, P. Maier, T. Reinhard, Eye Center, Faculty of Medicine, Albert-Ludwigs-Universität Freiburg, Freiburg im Breisgau, GERMANY|

Commercial Relationships Disclosure (Abstract): Katrin Wacker: Commercial Relationship(s);ProQR Therapeutics:Code C (Consultant) | Daniel Zander: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Böhringer: Commercial Relationship: Code N (No Commercial Relationship) | Marianne Fritz: Commercial Relationship: Code N (No Commercial Relationship) | Viviane Grewing: Commercial Relationship: Code N (No Commercial Relationship) | Thabo Lapp: Commercial Relationship: Code N (No Commercial Relationship) | Philip Maier: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Reinhard: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the efficacy of hyperosmolar eye drops on corneal edema resolution.

Methods: The double-blind randomized-controlled Eye Drops for Early Morning-Associated Swelling (EDEMAS) trial included participants without ocular comorbidities other than Fuchs' dystrophy scheduled for Descemet membrane endothelial keratoplasty (DMEK). One eye was randomized to hyperosmolar eye drops (treatment), while the fellow eye was randomized to artificial tears (placebo). After a baseline exam in the afternoon, participants' corneas were examined using Scheimpflug tomography after eye opening in the hospital in the morning. Imaging was repeated every 30 minutes up to four hours. Participants received eye drops twice. Primary endpoint was decrease in central corneal thickness one hour after eye opening. Secondary endpoints were corneal thickness, subjective visual function, glare, visual acuity, and adverse events over the duration of the study.

Results: 68 participants received the allocated intervention (59 eyes treatment, 55 eyes placebo). Corneal thickness was 626 μm in the treatment arm and 622 μm in the placebo arm after eye opening, indicating an early-morning edema compared to baseline of +21 μm and +24 μm , respectively. Decrease in corneal thickness after one hour was -10.5 μm in the treatment arm (95% CI, -12.8 to -8.2) and -11.2 μm (95% CI, -13.6 to -8.9) in the placebo arm (between-arm difference, 0.7 μm , 95% CI, -2.0 to 3.5; $p = 0.59$), indicating no effect of hyperosmolar eye drops on early-morning associated corneal edema. Corneal thickness decrease, and improvement of visual acuity and glare over the entire course of the study duration were not different between treatment and placebo. Subjective visual function tended to be worse in the treatment arm. Adverse events, most commonly burning after eye drop application, were more common with treatment (30 eyes) than placebo (1 eye; risk difference, 49 percentage points; 95% CI, 36 to 62).

Conclusions: In the double-blind randomized-controlled EDEMAS trial, resolution of early-morning associated edema was not accelerated by hyperosmolar eye drops, which frequently caused adverse events. These results are not compatible with a clinically meaningful effect of hyperosmolar eye drops in Fuchs' dystrophy and do not support their routine use.

CONTROL ID: 3542000

SUBMITTER (NAME ONLY): Ana Chucair-Elliott

TITLE: Inducible Cell-Specific Mouse Model for Paired Epigenetic and Transcriptomic Studies of Müller Glia in Age-Related Macular Degeneration

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chucair-Elliott, S. Ocañas, M. Van Der Veldt, W. Freeman, Genes & Human Disease Research Program, Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma, UNITED STATES|S. Ocañas, M.H. Elliott, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|J. Gurley, M.H. Elliott, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|W. Freeman, Oklahoma City VA Medical Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ana Chucair-Elliott: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Ocañas: Commercial Relationship: Code N (No Commercial Relationship) | Michael Van Der Veldt: Commercial Relationship: Code N (No Commercial Relationship) | Jami Gurley: Commercial Relationship: Code N (No Commercial Relationship) | Michael Elliott: Commercial Relationship: Code N (No Commercial Relationship) | Willard Freeman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aging is the major risk factor for age-related macular degeneration (AMD) but how 'normal' aging contributes to AMD pathogenesis is unclear. Epigenetic mechanisms, mainly methylcytosine (mC) and hydroxymethylcytosine (hmC), affect DNA accessibility, regulate genomic organization and gene expression, and are altered with aging. DNA methylation analyses of AMD patient blood and retinas suggest differential methylation resulting in gene expression changes during development/progression of AMD. In addition, Müller glia are activated in AMD patient retinas. The aim of this study is the validation of a cre/ERT2-NuTRAP mouse model to allow the parallel interrogation of differential mC/hmC genome-wide and the transcriptome specifically in Müller glia with retinal aging.

Methods: Female NuTRAP^{flox/flox} and male Aldh111-cre/ERT2^{+/-wt} mice were bred to generate Aldh111-cre/ERT2^{+/-wt}; NuTRAP^{flox/wt} (Aldh111-cre/ERT2⁺; NuTRAP⁺) mice. At 5 months old, mice received single intraperitoneal injections of tamoxifen (Tam) for 5 consecutive days (100 mg/kg) or were left untreated as controls. After Tam induction mice were euthanized and their retinas harvested and processed for: immunohistochemistry of mCherry, EGFP, GS, and GFAP expressions on retina sagittal sections via confocal microscopy; ribosome bound RNA isolation via TRAP protocol, qPCR validation and stranded RNA-Seq profile; and nuclei suspension preparation and DNA isolation via INTACT method for bisulfite amplicon sequencing (BSAS).

Results: Specific co-localization of EGFP, mCherry, and the Müller glia marker GS was observed in the Aldh111-cre/ERT2⁺; NuTRAP⁺ retinas. RNA-seq bioinformatic analysis revealed enrichment of Müller marker genes and pathways and depletion of other cell type markers in the positive TRAP fraction of Aldh111-cre/ERT2⁺; NuTRAP⁺ retinas, compared to input profiles. qPCR validated enrichment and depletion of selected transcript expressions. BSAS showed site-specific decrease of mC in the promoter region of selected Müller glia-specific genes in INTACT-DNA positive fraction relative to input.

Conclusions: The selective recombination in Müller glia, cell-specific transcriptome enrichments found via TRAP-RNAseq and qPCR, and BSAS findings, suggest the Aldh111-cre/ERT2; NUTRAP model is suitable for the study of Müller glia and its contributions to the transcriptome/epigenome of the aging retina.

CONTROL ID: 3542001

SUBMITTER (NAME ONLY): Anna Paula Nassaralla

TITLE: Impact of visual changes on falls and postural control in patients diagnosed with senil cataract in Anápolis, Goiás, Brazil

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Nassaralla, D.A. Oliveira, Medical, UniEVANGELICA Centro Universitario de Anapolis, Anapolis, GO, BRAZIL|

Commercial Relationships Disclosure (Abstract): Anna Paula Nassaralla: Commercial Relationship: Code N (No Commercial Relationship) | Deise Oliveira: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The aim of this study is to compare the risk of falls, depression symptoms and postural balance in the elderly before and after facectomy.

Methods: This is a cross-sectional study consisting of 17 individuals of both sexes aged ≥ 40 years, diagnosed with cataracts. Data collection was carried out in two phases (the first phase before and the second after facectomy) using the same questionnaires and tests in both of them. They were performed from January 2020 to March 2020. In each phase, all patients responded to two tests of balance and locomotion, identification, quality of life related to visual function and analysis of questionnaires of depressive symptoms. In all analyzes, the same level of significance was used ($p < 0.05$).

Results: Regarding the general characteristics of the sample, 17 patients were analyzed, with a mean age of 65 years, 70.6% of whom were female. Of the total number of patients, 11 of them were afraid of falling and, after the procedure, this number decreased by 8. When analyzing the depressive symptoms, which can induce falls, 82.3% of the patients showed improvement, punctuating before the facectomy an average of 32.06 (SD ± 6.67) and after the facectomy an average of 30.53 (SD ± 8.22), being statistically significant ($p < 0.05$). As for the quality of life related to routine activities, such as climbing stairs and identifying environmental obstacles, all patients reported levels of difficulty in the preoperative period, but in the post-facectomy, 64.7% and 58.8% of the patients had no difficulty to climb stairs and identify environmental obstacles, respectively, with an average score of 92.88 (SD ± 15.61) in the first application of the questionnaire and resulting in an average score of 98.18 (SD ± 12.71), being statistically significant ($p < 0.05$).

Conclusions: It is primordial to analyse a multicausal risk factors for falls , however, it was found with the data raised that cataracts is an independent factor for falls. The surgical procedure increased patients' dexterity and confidence when referring to walking.

CONTROL ID: 3542003

SUBMITTER (NAME ONLY): Ivan Rebutini

TITLE: PEDF protects photoreceptors via a CRX-dependent mechanism

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Rebutini, S. Becerra, Section on Protein Structure and Function, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ivan Rebutini: Commercial Relationship: Code N (No Commercial Relationship) | S Patricia Becerra: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pigmented Epithelium-Derived Factor (PEDF) is a neuroprotective peptide expressed and secreted by the Retinal Pigmented Epithelium (RPE) and protects photoreceptors from apoptosis during genetic- related retinal degeneration such as Retinitis Pigmentosa (RP). PEDF-derived peptides protect photoreceptors from apoptosis in rd10 mice, a RP model with mutated Phosphodiesterase 6b (PDE6b). Many forms of RP are also associated with dysregulation of Cone and Rod Homeobox (CRX), which is a transcription factor necessary for photoreceptors differentiation and regulates the transcription of more than 700 genes associated with photoreceptors function, among them the Phosphodiesterase 6a (PDE6a), which is involved in the visual phototransduction system in the photoreceptors. Although rod photoreceptors express both PDE6a and PDE6b phosphodiesterase subunits, it is unclear whether there is a compensatory mechanism involving PEDF signaling and CRX expression in mouse models of RP. The purpose of this study is to address whether the mechanisms of PEDF-induced photoreceptor protection involves CRX expression and its regulatory gene network.

Methods: We employed a wild-type mouse retinal explant model and Zaprinstat, a broad-range phosphodiesterase inhibitor to establish a model of general induction of photoreceptor cell death and define the molecular mechanisms of PEDF as neuroprotective to photoreceptors. We used whole mount immunofluorescence after treating the mouse retinal explants with combinations of PEDF and Zaprinstat, to characterize cellular processes such as apoptosis via TUNEL and the expression of CRX and various photoreceptor markers by confocal microscopy super resolution imaging.

Results: We established a quantitative imaging methodology to assess photoreceptors maintenance and survival in mouse retinal explants by using super resolution confocal microscopy, and found that PEDF treatment increased CRX expression in surviving photoreceptors in Zaprinstat-treated retinal explants and decreased apoptosis, suggesting that PEDF signaling regulates photoreceptors survival via a CRX-dependent mechanism.

Conclusions: We postulate that CRX expression is downstream to PEDF signaling and is a regulatory key component for photoreceptor survival upon retinal degeneration disease induction.

CONTROL ID: 3542004

SUBMITTER (NAME ONLY): Diana Mitchell

TITLE: Compensatory phagocytic function and effects on Müller glia in the absence of microglia

SESSION TITLE: Glial Cells

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.M. Mitchell, Z. Blume, R. Dimico, Biological Sciences, University of Idaho College of Science, Moscow, Idaho, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Diana Mitchell: Commercial Relationship: Code N (No Commercial Relationship) | Zachary Blume: Commercial Relationship: Code N (No Commercial Relationship) | Ren Dimico: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Both microglia and Müller glia have been shown to phagocytose dying cells in the vertebrate retina, but the phagocytic activities and respective loads of these two cell types appear to differ depending on context. In the zebrafish retina, microglia appear to act as the primary phagocytes during development (Blume et al., 2020, Dev Dyn) while both cell types may phagocytose dying cells in contexts of disease or injury. Müller glia (MG) act as the source of regenerated retinal neurons in zebrafish, and there is a possible link between MG phagocytic activity and the regenerative response. In addition, microglia appear to influence the outcome of retinal regeneration though their functions in this regard are not well understood. We hypothesized that in the absence of microglia, Müller glia take on the primary phagocytic role to clear apoptotic cells during retinal development and that increased phagocytic load may result in changes in MG-expressed genes known to be associated with damage and regenerative responses.

Methods: Developing retinas from microglia deficient mutant zebrafish and wildtype (wt) siblings were stained and imaged by confocal microscopy to visualize apoptotic cells (TUNEL) and MG (GS). Total numbers of TUNEL+ cells and those phagocytosed by MG were quantified in whole retinas (n=11-13). To analyze MG entry into the cell cycle, retinal cryosections were stained for PCNA and GS and the total number of PCNA+MG were quantified in images from microglia-deficient and wt siblings (n=4-6). Expression of gfap and ascl1a were determined by qPCR (1 pooled sample from 5-10 embryos per genotype).

Results: We found increased accumulation of TUNEL+ cells in microglia deficient retinas compared to wt ($p<0.0001$), and increased numbers but not proportions of TUNEL+ cells engulfed by MG ($p<0.0001$). There was a modest increase in numbers of PCNA+MG in microglia deficient retinas (n=4-6, $p=0.008$). Preliminary data indicated a modest increase in gfap (~1.8 fold), but not ascl1a in microglia deficient retinas compared to wt.

Conclusions: In the absence of microglia, Müller glia increase phagocytic load to clear dying cells from the developing retina. However, it appears they are less efficient than microglia at clearance of engulfed cells. Increased phagocytic activity may induce Müller glia proliferation and increase expression of gfap, however phagocytosis alone does not induce a robust regenerative response.

CONTROL ID: 3542006

SUBMITTER (NAME ONLY): Daniel Moverman

TITLE: Chromatic pupilloperimetry for diagnosis and monitoring of patients with brain tumors with no apparent contact with the visual or pupil light reflex systems

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Moverman, I. Sher, A. Hamburg, S. Zorani, Y. Rotenstreich, Sheba Medical Center The Goldschleger Eye Institute, Tel Hashomer, Tel Aviv, ISRAEL|D. Moverman, I. Sher, A. Hamburg, S. Zorani, E. Derazne, A. Wohl, Z. Cohen, Y. Rotenstreich, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|A. Wohl, Z. Cohen, Department of Neurosurgery, Sheba Medical Center, Tel Aviv University, Israel, Tel Aviv-Yafo, ISRAEL|

Commercial Relationships Disclosure (Abstract): Daniel Moverman: Commercial Relationship: Code N (No Commercial Relationship) | Ifat Sher: Commercial Relationship(s);Sheba Medical Center:Code P (Patent) | Amit Hamburg: Commercial Relationship: Code N (No Commercial Relationship) | Shlomit Zorani: Commercial Relationship: Code N (No Commercial Relationship) | Estela Derazne: Commercial Relationship: Code N (No Commercial Relationship) | Anton Wohl: Commercial Relationship: Code N (No Commercial Relationship) | Zvi Cohen: Commercial Relationship: Code N (No Commercial Relationship) | Ygal Rotenstreich: Commercial Relationship(s);Sheba Medical Center:Code P (Patent)

ABSTRACT BODY:

Purpose: To characterize the pupil light responses (PLR) for small focal chromatic light stimuli presented in peripheral and central retinal locations in patients with a mass effect due to brain tumors with no apparent contact with the visual or PLR systems.

Methods: The PLR for small (0.43°) blue and red-light stimuli presented at peripheral (21°) and central (4.2°) visual field (VF) locations were measured using chromatic pupilloperimetry in 6 patients with brain tumors with no apparent contact with the visual or PLR systems and 32 age-similar controls. All subjects underwent a complete ophthalmic exam, standard Humphrey automated perimetry (24-2), color vision test, best-corrected visual acuity, refraction and Spectral-Domain Optical Coherence Tomography (SD-OCT) imaging. All patients underwent brain MRI before and following tumor removal surgery.

Results: The SD-OCT thicknesses of macular ganglion cell and inner plexiform layers, as well as peripapillary retinal nerve fiber layer, were within normal limits in all patients. Differences in cone-mediated PLR were statistically insignificant between patients and controls. By contrast, rod-mediated percentage of maximal pupil contraction was significantly lower in patients compared to controls in the center of the VF (mean \pm SD: 11% \pm 4 % vs. 16 % \pm 5 %, $p=0.028$, ROC AUC=86.6%, $p=0.005$). Melanopsin-mediated PLR was attenuated in the peripheral VF ($p=0.005$, ROC AUC=95.3% $p=0.001$). The rod- but not the melanopsin-mediated PLR recovered by 4 weeks post-OP.

Conclusions: Chromatic pupilloperimetry may present a fast, objective non-invasive test for diagnosis and monitoring of patients with brain tumors with no apparent contact with the visual or PLR systems. Short and long term mass effects on PLR pathways can be identified by multiparametric analysis of the PLR for focal chromatic stimuli at central and peripheral VF. Localized melanopsin-mediated sustained PLR may provide a novel surrogate biomarker for mass effects.

CONTROL ID: 3542008

SUBMITTER (NAME ONLY): Amy Babiuch

TITLE: Characterization of real-world progression from non-proliferative to proliferative diabetic retinopathy in patients with diabetes

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Babiuch, T.F. Conti, A. Kalur, A. Iyer, T. Greenlee, J. Muste, R.P. Singh, Center for Ophthalmic Bioinformatics, Cole Eye Institute, Cleveland Clinic, Ohio, UNITED STATES|S.L. Gale, L. McLaughlin, R. Gan, D. Ferrara, G.J. Spicer, J.J. Hopkins, Genentech Inc, South San Francisco, California, UNITED STATES|D. Ferrara, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize baseline, follow-up, and testing attributes of a real-world population with non-proliferative diabetic retinopathy (NPDR) and to report progression to proliferative diabetic retinopathy (PDR).

Methods: Retrospective study of patients with diagnosis of diabetes and NPDR based on clinical exam performed at Cleveland Clinic Cole Eye Institute from January 2012 to February 2020. Patients must have had at least 365 days of follow-up after the NPDR index date, and at least two ophthalmic visits during follow-up. Basic descriptive stats were used for a survival analysis with time to PDR. Diagnosis of PDR was determined by initiation of treatment with anti-VEGF or panretinal photocoagulation (PRP) and an ICD-9 or 10 PDR diagnosis.

Results: The cohort consisted of 4555 patients; 10% (435/4474) developed PDR (23.6 cases per 1000 person-years) during follow-up [median, interquartile range (IQR) = 2.9 years (1.8, 4.1)]. The median age of patients was 66 years at baseline; half were female; 25% were Black, and 4053 (89%) had a diagnosis of type 2 diabetes. 1595 patients (35%) had concurrent eye diseases. On average, each patient had approximately 8 retinal images collected (optical coherence tomography, color fundus photographs and/or fluorescein angiography). Of the patients who received anti-VEGF treatment in the first year after NPDR index date (n=572), the median (IQR) real-world frequency of anti-VEGF injections was 5 (2, 9) in the first year. Of the patients who received PRP in the first year after NPDR index date (n=134), the median (IQR) real-world frequency of PRP was 2 (1, 3) in the first year. Over 80% of patients had 20/40 or better visual acuity (VA) in the right (83%) or left eye (82%) at index date.

Conclusions: Real-world data may provide meaningful insights to the characterization of patients and eyes with NPDR and higher risk of progression to PDR. Further data analysis in this cohort as well as future studies to elucidate how retinal imaging and VA correlate in diabetic retinopathy (DR) may lead to better characterization of DR disease phenotypes and aide in further development of algorithms or therapeutics for DR management at all stages.

CONTROL ID: 3542015

SUBMITTER (NAME ONLY): Warren Lewis

TITLE: Assessing different combinations of B-scan repetitions to improve detection of flow in optical coherence tomography angiography

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Lewis, S. Kubach, L. De Sisternes, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|T. Bacci, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal optical coherence tomography angiography (OCTA) is based on the comparison between successive B-scans taken in the same location. Differences between these repetitions are usually due to moving blood. This study examines the effect of using longer time intervals on the detection of flow.

Methods: High resolution retinal OCTA scans usually comprise sets of 4 repeated B-scans, which may be arranged in 3 pairs and processed and averaged to make flow B-scans. In this study, the B-scans in each of these pairs were separated by a time interval ($\Delta t_0 \approx 3.2$ msec) equal to the time between successive B-scans. In addition to this approach, we also used different pair definitions to achieve longer time intervals.

3x3mm OCTA scans were acquired with a PLEX® Elite 9000 (ZEISS, Dublin, CA) and exported as raw amplitude and phase data. 17 eyes from 14 patients were included in the analysis. These scans were processed using a custom angiography algorithm that allowed selection of the repetitions combined to produce the flow signal.

In addition to using sequential scans to calculate flow, new flow B-scans were created by averaging results from comparing repetitions 1- 3, 2- 4, and 1- 4, with time intervals $2\Delta t_0$, $2\Delta t_0$ and $3\Delta t_0$ respectively. The resulting images were compared, and vessel density was calculated in the 4 zones of the inner ETDRS ring.

Results: Figure 1 shows vasculature visualized from combining pairs of temporally adjacent B-scans and the results of redefining these pairs. There is better detection of flow in small vessels, along with some increase in noise, when using pairs having larger values of Δt . Figure 2 shows increased vessel density in the latter method for this test set.

Conclusions: Using B-scan pairs with longer time intervals results in increased sensitivity to flow and better visualization of vascular structure.

CONTROL ID: 3542029

SUBMITTER (NAME ONLY): Arun Upadhyay

TITLE: OCU200 (transferrin-tumstatin fusion protein): A potential therapeutic for DME, DR, and wet-AMD

SESSION TITLE: Cytokines, growth factors, anti-inflammatory

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Upadhyay, R. Arumugham, P. Naha, D. Singh, R&D, Ocugen, Inc., Malvern, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose of this study was to evaluate efficacy of OCU200 in in-vitro and in-vivo models for ocular neovascular diseases. Angiogenesis and neovascularization are hallmarks for diabetic macular edema (DME), diabetic retinopathy (DR), and wet age-related macular degeneration (wet-AMD). Most approved therapeutics target vascular endothelial growth factor (VEGF), a pro-angiogenic factor with neurotrophic and neuroprotective effects. However, these therapies are effective only in about 50% of patients. OCU200 is a fusion protein designed to have improved efficacy in DME, DR, and wet-AMD patients.

Methods: Effect of OCU200 on in-vitro cell proliferation, invasion and tube formation were assessed by MTT assay, scratch assay and endothelial cell culture on basement membrane matrix, respectively. In -vivo efficacy was evaluated in an oxygen-induced retinopathy (OIR) mouse model (age-P12), dosed intravitreally with various doses of OCU200 (2.5, 5.0, and 10 µg/eye) and compared to an approved anti-VEGF positive control (aflibercept, 20 µg/eye). Retinal tissues were collected at P18 age to assess avascular areas (AVAs) and neovascular tufts (NVs) areas of Isolectin GS IB4 immunostained retinal flat mounts. AVA and NVs regression in retina indicate therapeutic benefit of test compound. Quantitative data was analyzed by paired Student's t test or One-Way ANOVA followed by Dunnett's or Tukey's multiple comparisons test.

Results: OCU200 inhibited cell proliferation, cell invasion and tube formation by endothelial cells. In OIR mice, OCU200 significantly reduced avascular areas at low dose (68% reduction, $P < 0.05$) and high dose (68% reduction, $P < 0.05$), and significantly reduced neovascular tufts (NVs) at low dose (59% reduction, $P < 0.05$) and high dose (58% reduction, $P < 0.05$) compared to vehicle-treated eyes. Aflibercept reduced NVs by 77% ($P < 0.01$). OCU200 showed comparable activity to aflibercept at 2 to 8-fold lower doses.

Conclusions: OCU200 acts on endothelial cells specifically to decrease cell proliferation, cell invasion, and tube formation. In addition, the in vivo results suggest that OCU200 is efficient in reducing neovascularization and damage to retina in mouse OIR model and has comparable/slightly improved activity to aflibercept. These findings demonstrate OCU200 as a potential therapeutic for the treatment of DME, DR, and wet-AMD.

CONTROL ID: 3542037

SUBMITTER (NAME ONLY): Bryce Buchowicz

TITLE: Identification of Barriers to Timely Diagnosis of Central Retinal Artery Occlusion and Treatment with Tissue Plasminogen Activator

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Buchowicz, L. Vander Woude, S.S. Iyer, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|J. Wiese, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Central retinal artery occlusions (CRAOs) are newly characterized as stroke equivalents and may benefit from tissue plasminogen activator (tPA); however, barriers to presentation and evaluation in the timeframe for tPA administration limit our ability to study potential treatments. We performed an observational study to identify and quantify barriers to timely diagnosis of CRAOs.

Methods: This study included 41 newly diagnosed CRAO patients who presented to the University of Florida Emergency Department (ED) or Ophthalmology Clinic between 1/1/2012 and 3/23/2020 as identified using the ICD-9 and ICD-10 codes for "CRAO". Patients were excluded if they presented with concurrent stroke symptoms, had a clearly identified surgical or traumatic etiology, or had decreased mental capacity affecting the accuracy of reported symptoms. Primary outcomes measured were time to presentation after symptom onset, and times from arrival to exam by ED physician, ophthalmology consult, and ophthalmology exam. Statistical analysis included the mean and standard deviation of these outcomes, including further stratification at the 4-hour mark (the requirement for possible tPA administration).

Results: The average time to presentation after onset of vision loss was 38.16 ± 54.43 hours. 11 of 41 of patients presented within 4 hours with an average presentation time of 148 ± 47.82 minutes; however, only 4 of those patients were diagnosed by an ophthalmologist within the window for tPA administration. Of those presenting within 4 hours, the average time from arrival to exam by ED physician, ophthalmology consult, and ophthalmology exam were 28 ± 20.85 , 65 ± 26.2 , and 108 ± 28.79 minutes, respectively. Among all patients, these times were 35 ± 45.69 , 101 ± 26.0 , and 127 ± 61.46 minutes, respectively.

Conclusions: The barriers to timely diagnosis of CRAO include early identification of symptoms and realization of systemic severity by patients and emergency medical services. In addition, there are delays in triage and evaluation by ED and ophthalmology teams, for which we propose a novel protocol to hasten diagnosis (Figure 1). This protocol has been adapted at the University of Florida Shands Emergency Department; further studies will be conducted using this protocol to examine its utility.

CONTROL ID: 3542048

SUBMITTER (NAME ONLY): James Liu

TITLE: Investigating the genotype-phenotype relationships of patient specific PNPLA6 mutations

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Liu, C. Lwin, B. Guan, R.B. Hufnagel, Medical Genetics and Ophthalmic Genomics Unit, National Eye Institute, Bethesda, Maryland, UNITED STATES|L.A. Huryn, R.B. Hufnagel, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|C. Lwin, Department of Biostatistics, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|Y. He, Fermentation Facility, Biochemistry and Biophysics Center, National Heart Lung and Blood Institute, Bethesda, Maryland, UNITED STATES|A.T. Moore, Joint Library of Ophthalmology Moorfields Eye Hospital and UCL Institute of Ophthalmology, London, London, UNITED KINGDOM|A.T. Moore, Ophthalmology Department, University of California San Francisco, San Francisco, California, UNITED STATES|G. Arno, A. Webster, UCL Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|G. Arno, A. Webster, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Pathogenic variants in the PNPLA6 gene cause a broad spectrum of neurological disorders such as spastic paraplegia type 39 (SPG39), Gordon-Holmes syndrome (GHS), Boucher-Neuhauser syndrome (BNHS), Laurence-Moon syndrome (LMS), and Oliver-McFarlane syndrome (OMS). PNPLA6 encodes Neuropathy Target Esterase (NTE), yet it's unclear why NTE enzymatic dysfunction causes early childhood onset retinopathy in a subset of patients. Here, we investigate the relationship between PNPLA6 genotype-associated enzymatic activity and risk of retinal degeneration.

Methods: PNPLA6 variants were detected by NGS, sanger sequencing, and digital droplet PCR. Clinical meta-analysis was performed on 133 previously reported patients by literature search (PubMed, 2008-2020). Statistical analysis was performed in Prism. DNA constructs containing full length NTE underwent site directed mutagenesis to produce the patient specific proteins. NTE activity was determined as previously published (PMID:12791540). Intronic variants were assessed for splice alterations by minigene assay.

Results: Biallelic pathogenic PNPLA6 variants were detected in ten patients with clinical diagnosis of SPG39, BNHS or OMS, including 7 novel variants. Clinical meta-analysis of these and 75 previously reported genotyped patients indicated significant differences in ophthalmic and endocrinologic symptom onset between clinical diagnosis categories. Intriguingly, patients with early onset retinopathy were not more likely to harbor truncating variants, and no differences in disease onset or tissues affected were found between those with and without truncating variants. To examine effects of missense alleles on phenotype, we measured activity in 17 variants observed in two or more patients with the same clinical diagnosis. Residual esterase activity of recurrent missense variants observed in patients with retinopathy was significantly lower compared to those without reported visual symptoms.

Conclusions: Molecular determinants of retinal disease onset is different among clinical diagnoses of PNPLA6-opathies. Enzyme activity of recurrent disease-associate missense variants indicates a relationship between enzymatic activity and likelihood of retinopathy, implicating missense variants as drivers of tissue-specific disease onset. This supports a genotype:activity:phenotype relationship among PNPLA6-opathies that may be valuable for both diagnosis and prognosis.

CONTROL ID: 3542049

SUBMITTER (NAME ONLY): Wenjie Zhu

TITLE: Toll-like receptor 2 signaling in $\gamma\delta$ T cells is required for immune responses to commensal bacteria at the ocular surface

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Zhu, X. Xu, A. St. Leger, F. Almaghrabi, R. Yamane, R.R. Caspi, Lab of Immunology, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. St. Leger, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Conjunctiva of the eye is a mucosal immune tissue and harbors a variety of immune cells. It is exposed to diverse microorganisms that come in contact with the ocular surface. Previously, we demonstrated that colonization of the ocular mucosa with the commensal bacterium, *Corynebacterium mastitidis* (C. mast), results in increased resistance of the ocular surface to infectious fungal and bacterial pathogens, and that this effect is mediated by IL-17A produced by $\gamma\delta$ T cells that respond to C. mast. In this study, we investigate the role of TLRs in this process.

Methods: TLR on immune cells at the ocular surface before and after C. mast inoculation in WT, TLR2^{-/-} and TLR4^{-/-} mice. After 28 days, immune cells and their IL-17A production were quantitated in the conjunctiva and eye-draining lymph nodes (DLN) by flow cytometry. To investigate the function of TLRs on $\gamma\delta$ T cells, we co-cultured TLR^{-/-} $\gamma\delta$ T cells with WT CD11c⁺ APC and heat killed C. mast. IL-17A production was quantitated by ELISA and by intracellular cytokine staining. Transcriptomic analysis by RNA-Seq and cellular metabolism by Seahorse assay were performed to confirm pathway analysis results.

Results: Significant increase of TLR2 expression was observed on $\gamma\delta$ T cells in WT mice after C. mast inoculation. TLR2^{-/-} mice failed to recruit $\gamma\delta$ T cells and neutrophils to the conjunctiva upon C. mast inoculation, and IL-17A-producing $\gamma\delta$ T cells were reduced in DLN. In vitro, IL-17A production in response to C. mast by $\gamma\delta$ T cells was dependent on TLR2 expression in both $\gamma\delta$ T cells and APCs. Exogenous IL-1 β or WT APC only partly restored IL-17A production by TLR2^{-/-} $\gamma\delta$ T cells, indicating a need for another TLR2-dependent signal. Kinetic experiments and RNA-Seq analyses demonstrated the dependence of IL-17A production and IL-17A-related gene expression on $\gamma\delta$ -expressed TLR2, which was higher in the V γ 6 than in the V γ 4 subset. Notably, transcriptomic analysis implicated dysregulation of mitochondrial pathways as a result of TLR2^{-/-} deficiency in $\gamma\delta$ T cells, which was functionally confirmed by the Seahorse assay.

Conclusions: Sensing of the commensal C. mast by $\gamma\delta$ T cells requires cell-intrinsic TLR2 expression to maintain their metabolism and function, in order to drive local IL17 response and maintain immune homeostasis at the ocular surface.

CONTROL ID: 3542050

SUBMITTER (NAME ONLY): norihiko misawa

TITLE: Reduction of choroidal thickness was not associated with the outcomes of photodynamic therapy for pachychoroid spectrum diseases

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. misawa, A. kyo, K. hirayama, M. Yamamoto, T. Kohno, S. honda, ophthalmology, Osaka Shiritsu Daigaku, Osaka, Osaka, JAPAN|M. hirabayashi, Shiraniwa Byoin, Ikoma, Nara, JAPAN|

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ABSTRACT BODY:

Purpose: A reduction of choroidal thickness is generally thought to be associated with the outcomes of photodynamic therapy (PDT) for pachychoroid spectrum diseases (PSD). We performed a retrospective chart review to investigate whether the reduction of choroidal thickness after PDT may influence the visual and anatomical outcomes in PSD.

Methods: Fifty-three eyes of 53 patients (male 40, female 13) who underwent initial PDT were included in this study. Patients were diagnosed with pachychoroid neovascularopathy (PNV) (n= 20), polypoidal choroidal vasculopathy (PCV) (n=24) and central serous chorioretinopathy (CSC) (n=9). The subjects were divided into two groups according to the reduction ratio of central choroidal thickness (CCT) more than 15% (group A) or not (group B) at 3 months post-PDT. The best corrected visual acuity (BCVA), central retina thickness (CRT), and CCT were compared between the groups. For statistical analysis, each clinical factor was evaluated by paired or unpaired t-test where applicable between any two groups.

Results: The group A and group B contained 24 eyes and 29 eyes, respectively. The mean age, the baseline BCVA, CRT, CCT in the group A and group B were 68.0±13.2 vs 71.4±13.6 years, 0.25±0.29vs0.26±0.40(logMAR),301.0±117.0vs319.1±111.8µm and 310.0±111.9 vs 292.5±111.8µm, which showed no significant difference between the groups (P=0.39, 0.85, 0.57 and 0.57, respectively). No significant differences were observed in the post-PDT BCVA 0.18±0.32 vs 0.26±0.42(logMAR) (P=0.46) and post-PDT CRT 207.2±81.8 vs 237.8±102.9µm (P=0.24) between the group A and group B. A multiple regression analysis showed no significant variables associated with the reduction of CCT after PDT.

Conclusions: None of the pre-treatment BCVA, CCT, and CRT was associated with a reduction of CCT after PDT. The reduction of CCT was not associated with an improvement in visual acuity or CRT after the treatment. Decreased CCT might be a result, not a therapeutic role of PDT over the management of PSD.

CONTROL ID: 3542052

SUBMITTER (NAME ONLY): Kevin Carbajal

TITLE: Novel corticosteroid class reduces inflammation and lowers IOP in animal models

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Carbajal, M.V. Zaretskaia, C.L. Lichorowic, J.M. Sturdivant, M. Weksler, A. McDougal, C. Lin, M.A. deLong, C. Kopczynski, D.A. Hollander, J. White, Aerie Pharmaceuticals Research and Development, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Risks associated with topical corticosteroid (CS) treatment limit their long-term use for controlling inflammatory conditions of the ocular surface and anterior segment. One of their most common side effects is steroid-induced elevated intraocular pressure (IOP). It is believed that CS cause this by promoting fibrosis and collagen deposition in the trabecular meshwork (TM). Rho kinase inhibitors (ROCKi) have been shown to reduce deposition of collagen and fibronectin in TM cell cultures and reverse fibrotic changes in the TM of mice with steroid-induced elevated IOP. We set out to design a new class of CS with ROCKi activity with the hypothesis that such compounds could protect the TM while maintaining anti-inflammatory efficacy. A CS with fewer ocular side effects would be an invaluable tool for the treatment of patients with a variety of ocular inflammatory conditions.

Methods: CS covalently linked to AR-13503, the active metabolite of netarsudil, were designed to deliver physiologically relevant levels of each drug to tissues of the ocular surface. The anti-inflammatory activity of one of these compounds was assessed following topical treatment in a mouse allergic eye disease (AED) model. The AED model has robust ocular surface inflammation and meibomian gland (MG) plugging, two common features of dry eye. Anti-inflammatory activity was further tested in a mouse cornea wound healing (CWH) model that also served to understand the compound's effect on the recovery rate of the corneal epithelium following injury. Lastly, we treated rabbits topically with this compound to assess tolerability and to determine if its ROCKi activity could lower IOP, thereby reflecting a potential to protect the TM from CS activity.

Results: Our novel CS with ROCKi-activity controlled inflammation on the ocular surface in mice with AED and reduced the formation of MG plugs. This activity was comparable to treatment with standard CS used in the clinic. Treatment also reduced inflammation in the CWH model and did not significantly impair corneal re-epithelialization. Importantly, treatment resulted in a moderate IOP reduction and no tolerability issues in rabbits.

Conclusions: CS are invaluable tools in ophthalmology but carry significant risks with long-term use. Our new class of CS with ROCKi activity demonstrated a reduced risk of inducing elevated IOP while retaining anti-inflammatory efficacy comparable to CS used in the clinic.

CONTROL ID: 3542053

SUBMITTER (NAME ONLY): Rose Gilbert

TITLE: Collaborative Development of a Novel Patient-centred App (MyEyeSite): Transforming Researcher Access to Rare Inherited Retinal Disease Data

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gilbert, Medical Ophthalmology, Addenbrooke's Hospital, Cambridge, Cambridgeshire, UNITED KINGDOM|R. Gilbert, N. Pontikos, A. Webster, Medical Retina, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|N. Pontikos, R. Young, A. Webster, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|D. Sumodhee, Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London, London, London, UNITED KINGDOM|C. Hollyhead, A. Patrick, MyEyeSite IRD Patient Advisory Group, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|J. Cammack, Moorfields Eye Hospital & UCL Institute of Ophthalmology, National Institute for Health Research, London, London, UNITED KINGDOM|S. Scarles, S. Van Der Smissen, N. Nettleton, Loft Digital Limited, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Inherited Retinal Disease (IRD) data are, by definition, rare and research in this area has historically been constrained by the lack of such data. To date, the challenge has been to identify these data and make them available to researchers in the most productive way. MyEyeSite is an early stage research collaboration in the United Kingdom (UK), aiming to design and develop a digital platform for people with rare IRDs that enables patients, doctors and researchers to aggregate and share specialist eye health data. The proposed infrastructure is designed to accelerate research into IRD by curating and making available highly specific data from consenting patients. The ability for this data to be accessed by appropriate researchers will facilitate the planning of disease-specific trials and the development of cost-effective treatments, such as gene therapies.

Methods: A pilot feasibility study was carried out, informed by qualitative data (generated through focus groups and workshops) and quantitative data obtained by survey from patients with IRD. Participants were recruited through ophthalmology clinics at Moorfields Eye Hospital National Health Service (NHS) Trust, UK, and databases managed by the Moorfields Biomedical Research Centre.

Results: 87% of surveyed participants (n=82) were motivated to have a more active role in their eyecare, and to share their data for research purposes using a secure application technology. 94% of our IRD focus group sample (n=50) highlighted themes of: 'frustration with the current system' regarding data sharing within the UK's NHS; positive 'expectations' of the potential benefits of the MyEyeSite app for this patient community with increased access to these specialised data; and concerns about data security and potentially unethical use of data by those outside the NHS. Detailed patient input was also given into the functionality and accessibility of the application prototype.

Conclusions: This pilot study demonstrates that IRD patients wish to be actively involved in managing their own data for both research use and their own eyecare. It reveals their willingness to engage with the detailed design of a technological solution to the issue of the paucity of these datasets and the potential benefits to research and care, not only for the IRD patient community, but for others with rare diseases.

CONTROL ID: 3542057

SUBMITTER (NAME ONLY): Valeria Marigo

TITLE: New in vitro model of photoreceptor degeneration based on the 661W cell line

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Marigo, L. Huang, M. Kutluer, E. Adani, Life Sciences, Università degli Studi di Modena e Reggio Emilia, Modena, Emilia-Romagna, ITALY]

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) is an inherited degenerative disease characterized by photoreceptor cell death. Several studies, mostly in Pde6b mutant retinas, identified the mechanisms of rod photoreceptor cell death involving excess of intracellular calcium and cGMP, activation of calpain and PKG and nuclear translocation of AIF. One of the limits that hamper the development of novel therapeutic strategies resides on the lack of a reliable in vitro system for high-throughput drug screenings. The purpose of this study was to generate a genetically modified cell line, derived from 661W photoreceptor progenitor cells, able to model the disease in vitro.

Methods: 661W cells were genetically modified to stably express the neural retina leucine zipper (NRL) rod specific transcription factor. qPCR and immunofluorescence were used to select a clone, highly expressing rod specific genes. Cell differentiation was achieved with a culture medium containing retinoic acid (RA), basic fibroblast growth factor (bFGF), taurine and sodium butyrate. A stress protocol for mimicking photoreceptor degeneration was based on the PDE6 inhibitor zaprinast.

Results: 661W cells were infected with a retrovirus expressing the NRL transcription factor. Out of 14 cell clones, one was selected based on expression of Nrl and Cnga1 genes. qPCR analyzed rod-specific gene expression, such as Rho, Pde6b, Cngb1, Gnat, Guca, Crx, and showed significant higher levels in this clone compared to the 661W cell line. Cone-specific genes, otherwise, did not change level of expression. We developed a differentiation protocol based on FBS withdrawal and exposure to bFGF, RA, Taurine and sodium butyrate. After differentiation, based on qPCR and immunofluorescence, cells showed an elongated shape and augmented expression of rod specific genes, when compared to not differentiated cells. To mimic the degeneration process caused by increased cGMP, we exposed the cells to zaprinast, an inhibitor of PDE6, and found an increased cell death accompanied by increased intracellular calcium and calpain activation. The effects of known, previously published, neuroprotective agents were tested in the new in vitro model.

Conclusions: The new in vitro model for rod photoreceptor degeneration will be instrumental for high-throughput screenings and testing of new compounds that can act as novel therapeutic approaches for this blinding disease.

CONTROL ID: 3542059

SUBMITTER (NAME ONLY): Sean Kim

TITLE: Barriers to Attendance among Patients Scheduled for Appointments at an Academic Ophthalmology Practice

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.D. Kim, E.M. Bowie, I.U. Scott, M.C. Chen, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|S. Athukorala, O. Waldron, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|I.U. Scott, Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: No-show appointments may be associated with significant detriments to patient outcome, practice efficiency, and practice financial status. The purpose of this study is to investigate reasons patients failed to attend scheduled appointments at an outpatient ophthalmology clinic at an academic medical center.

Methods: The study protocol was reviewed and deemed exempt from further review by the Penn State College of Medicine Institutional Review Board. A scheduling software was used to identify all adult patients who did not attend their scheduled ophthalmology clinic appointments at Penn State Eye Center from 11/9/20 to 12/16/20. Potential subjects were contacted by phone to conduct a brief phone interview. Subjects willing to participate were asked to specify the reason(s) they did not attend their appointment, and to suggest interventions that would help them attend. Descriptive statistical methods were used to describe the reasons for missed appointments and suggested interventions.

Results: Of the 325 patients identified, 160 (49.2%) were reached by telephone and participated in the phone survey. The most common reason for non-attendance reported was forgetting the appointment (35.6%), followed by being unaware of appointment (20.6%), scheduling conflict (13.1%), and illness (11.9%). Eighteen patients (11.3%) reported transportation difficulty and two patients (1.3%) reported financial burden. Six patients (3.8%) reported concern for the COVID-19 pandemic as the reason for non-attendance. Fifty-seven patients suggested potential interventions that would help them attend their visits, with the most common being the provision of a reminder (49.1%), followed by providing aid with transportation (15.8%) and sending multiple modalities of reminders (14.0%).

Conclusions: In this study conducted at an outpatient ophthalmology clinic at an academic center, the most common reasons for non-attendance were patients forgetting about the appointment and being unaware of the appointment. This finding is supported by the interventions suggested by the patients, which consisted primarily of providing appointment reminders. Patients also noted difficulty with transportation and suggested assistance with transportation to the clinic. These findings may facilitate the development and implementation of specific interventions to decrease the patient no-show rate.

CONTROL ID: 3542060

SUBMITTER (NAME ONLY): WEILIANG WANG

TITLE: Quantitative comparison of changes in vessel characteristics post retinopathy of prematurity treatment with bevacizumab versus laser

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. WANG, Duke-NUS Medical School, Singapore, SINGAPORE|G.J. Hong, S.F. Freedman, S.G. Prakalapakorn, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|S.F. Freedman, S.G. Prakalapakorn, Duke University Department of Pediatrics, Durham, North Carolina, UNITED STATES|D.K. Wallace, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness in high- and middle-income countries. Appropriate screening and timely treatment are critical and can reduce the risk of blindness due to ROP. Plus disease is a certain degree of vascular dilation and tortuosity that is usually present in treatment indicated (type 1) ROP. This study uses the semiautomated software ROPttool to quantitatively compare posterior pole vascular changes after bevacizumab versus laser treatment.

Methods: This retrospective study used prospectively-collected narrow-field retinal images from preterm infants screened and treated for ROP. We included retinal images acquired in the session just prior to and in all sessions post-treatment. Using quadrant-level methodology where ≤ 3 images/session were included, we used ROPttool to trace and analyze ≤ 2 vessels/quadrant, following the same vessels over time (Figure 1). For each imaging session, these ROPttool indices were calculated: tortuosity index (TI), dilation index (DI), and combination dilation/tortuosity indices: sum of adjusted indices (SAI) and tortuosity-weighted plus (TWP). We used Wilcoxon signed-rank test to compare each average ROPttool index before and after treatment, and Wilcoxon rank sum test to compare the rates of percent change of each index between bevacizumab versus laser.

Results: Of 15 eyes with type 1 ROP, 6 were treated with bevacizumab and 9 with laser. We included a median of 5 imaging sessions/eye. Compared to pre-treatment values, all ROPttool indices significantly decreased 1 week after bevacizumab ($p=0.03$) and 1 month after laser ($p=0.05$). Those treated with bevacizumab versus laser had higher rates of percent change in TI ($p=0.01$), SAI ($p=0.02$), and TWP ($p=0.01$) 1 week after and in SAI ($p=0.03$) and TWP($p=0.01$) 1 month after treatment (Figure 2).

Conclusions: Regression of vessel dilation and tortuosity in type 1 ROP occurs earlier after bevacizumab versus laser. The quantification of retinal vascular characteristics post-treatment helps guide clinical expectations after bevacizumab versus laser.

CONTROL ID: 3542062

SUBMITTER (NAME ONLY): Rhonda Walters

TITLE: Antimicrobial Efficacy of Hydrogen Peroxide Contact Lens Care Products in the Presence of Contact Lenses

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Walters, E. Miller, C. McAnally, M.M. Gabriel, P. Shannon, M. Crary, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Rhonda Walters: Commercial Relationship(s);Alcon Research LLC:Code E (Employment) | Elise Miller: Commercial Relationship(s);Alcon Research LLC:Code E (Employment) | Cindy McAnally: Commercial Relationship(s);Alcon Research LLC:Code E (Employment) | Manal Gabriel: Commercial Relationship(s);Alcon Research LLC:Code E (Employment) | Paul Shannon: Commercial Relationship(s);Alcon Research LLC:Code E (Employment) | Monica Crary: Commercial Relationship(s);Alcon Research LLC:Code E (Employment)

ABSTRACT BODY:

Purpose: Hydrogen peroxide (HP) based contact lens care products (CLC) offer outstanding antimicrobial efficacy against a range of pathogenic microorganisms. HP CLCs function using a strong disinfectant that is neutralized over time. HP CLCs are recognized in the market for their enhanced efficacy to preserved multipurpose solutions. In this study, HP CLCs were evaluated for antimicrobial efficacy against strains of Staphylococcus, Pseudomonas, Serratia, Fusarium, Candida, as well as Acanthamoeba trophozoites and cysts in the presence of silicone hydrogel (SH) contact lenses (CL).

Methods: Two CLCs (3% hydrogen peroxide) were tested against ISO strains as well as clinically relevant strains including Fusarium, and Acanthamoeba trophozoites and cysts using a modified version of ISO 18259. Testing was conducted using SH lenses in the manufacturer's contact lens case so that neutralizing discs could be utilized per the instructions for use. Aliquots of 10^4 - 10^6 CFU/mL of each organism were inoculated onto two SH lenses. Organisms were allowed to adhere for three minutes then CLs were submerged in the lens case containing 10mL of hydrogen peroxide product until disinfection time (DT). After DT (6 hours), contents of the lens case as well as both lenses were placed in a glass tube and vortexed vigorously. CLC/CL combinations were sampled and organisms recovered depending on their individual growth requirements. Log reductions were calculated based on inoculum controls generated at time 0 and test samples recovered at disinfection time.

Results: CLCs (3% hydrogen peroxide) showed a high level of efficacy in the presence of SH lenses against all organisms tested. For bacteria, and yeast, both products had >5.0 log kill while for Fusarium, the CLCs had >4.0 log kill with SH lenses. The log reduction for Acanthamoeba trophozoites was >4.5 and for Acanthamoeba cysts, log kill ranged from 2.5-3.7 for both products and all CLs tested. The presence of CL did not negatively affect the antimicrobial efficacy of HP products. HP products can effectively clean CL lenses of a wide range of microorganisms.

Conclusions: Hydrogen peroxide CLCs demonstrated a high level of antimicrobial efficacy against all microorganisms including Acanthamoeba in the presence of SH lenses. Hydrogen peroxide products maintain their antimicrobial efficacy in the presence of contact lenses.

CONTROL ID: 3542063

SUBMITTER (NAME ONLY): Giulia Ascari

TITLE: Long-read sequencing to unravel complex structural variants of CEP78 leading to Cone-Rod Dystrophy and Hearing Loss

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Ascari, M. De Bruyne, M. Van Heetvelde, A. Dueñas Rey, B. Menten, E. De Baere, Center for Medical Genetics Ghent, Ghent University Hospital, BELGIUM|G. Ascari, M. De Bruyne, M. Van Heetvelde, A. Dueñas Rey, B. Menten, E. De Baere, Department of Biomolecular Medicine, Universiteit Gent, Gent, BELGIUM|N. Rendtorff, M. Bertelsen, L. Tranebjærg, Department of Clinical Genetics, Copenhagen University Hospital, The Kennedy Center, DENMARK|J. De Zaeytijd, Department of Ophthalmology, Ghent University Hospital, BELGIUM|M. Van Lint, Department of Ophthalmology, Antwerp University Hospital, BELGIUM|G. Arno, UCL Institute of Ophthalmology, UNITED KINGDOM|G. Arno, Moorfields Eye Hospital, UNITED KINGDOM|J. Jacob, Department of Ophthalmology, Leuven University Hospital, BELGIUM|D. Creytens, J. Van Dorpe, Department of Pathology, Ghent University Hospital, BELGIUM|D. Creytens, J. Van Dorpe, Department of Diagnostic Sciences, Ghent University, BELGIUM|L. Tranebjærg, Institute of Clinical Medicine, University of Copenhagen, DENMARK|M. Strazisar, Neuromics Support Facility, VIB Center for Molecular Neurology, VIB, BELGIUM|M. Strazisar, Neuromics Support Facility, Department of Biomedical Sciences, University of Antwerp, BELGIUM|M. Bertelsen, Department of Ophthalmology, Rigshospitalet-Glostrup, University of Copenhagen, Glostrup, DENMARK|

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ABSTRACT BODY:

Purpose: Inactivating sequence variants as well as a unique missense variant in the centrosomal CEP78 gene have been identified in autosomal recessive Cone-Rod Dystrophy with Hearing Loss (CRDHL), a rare syndromic inherited retinal disease (IRD) clearly distinct from Usher syndrome. Apart from this, a complex structural variant (SV) implicating CEP78 has been reported in CRDHL. Here we aimed to expand the genetic architecture of typical CRDHL by the identification of complex SVs and characterization of their underlying mechanisms.

Methods: Approaches used, for SVs identification, are shallow whole genome sequencing (sWGS) combined with quantitative PCR (qPCR) and long-range PCR, or ExomeDepth analysis on whole exome sequencing data. Targeted or whole genome Nanopore long-read sequencing (LRS) was used to delineate breakpoint junctions at the nucleotide level. For all SV cases, the effect of the SVs on CEP78 expression was assessed using qPCR on patient-derived RNA. Data mining of human single cell (sc), bulk retinal and cochlear transcriptional datasets was used to further characterize the CEP78 expression profile.

Results: Apart from two novel canonical CEP78 splice variants and a frameshifting variant, three SVs affecting CEP78 were identified in three unrelated individuals with CRDHL: a heterozygous total gene deletion of 235kb and a partial gene deletion of 12kb in heterozygous and homozygous state respectively. Assessment of the molecular consequences of the SVs on patient's materials displayed a loss-of-function effect. Delineation and characterization of the 12kb deletion using targeted LRS revealed the previously described complex CEP78 SV, suggestive for a recurrent genomic rearrangement. A founder haplotype was demonstrated for the latter SV in three cases of Belgian and British origin respectively. The novel 235kb deletion was delineated using whole genome LRS. Breakpoint

analysis showed microhomology and pointed to a replication-based mechanism behind CEP78 SV formation.

Moreover, we correlated CEP78 sc expression with the phenotypic presentation of CRDHL.

Conclusions: Overall, this study supports that the CEP78 locus is prone to distinct SVs and that SV analysis should be considered in a genetic work-up of CRDHL. Finally, it demonstrated the power of sWGS and both targeted and whole genome LRS in identifying and characterizing suspected complex SVs in patients with IRD.

CONTROL ID: 3542069

SUBMITTER (NAME ONLY): Sofia Gonçalves

TITLE: Mobile models for AMD and DR screening

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gonçalves, L. Mendes, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|R. Silva, Universidade de Coimbra, Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: The identification of lesions in color fundus photography (CFP) to detect and characterize ocular pathologies requires specialized professionals to manually perform this task. In this study, we explore two different CNN architectures, Inceptionv3 (Iv3) and MobileNetv2 (MbNv2), and test their performance on identifying pathologies in CFPs.

Methods: We gathered 29,329 fovea-centered CPFs from the Epidemiologic (NCT01298674) and Incidence (NCT02748824) studies, previously classified regarding three targets: age-related macular degeneration (AMD), Diabetic Retinopathy (DR) and both AMD and DR. Given the unbalanced nature of data, we split the dataset into 5 balanced sets and tested a majority voting ensemble approach. For each architecture, three experiments (E1, E2, E3) were conducted. In E1, training was performed with non-augmented data, in E2, images were treated with a color correction software developed by Harvard Medical School that standardizes brightness, contrast, and color balance, and in E3 we studied the impact of horizontal flips, brightness changes, and small rotations and translations on the model performance.

Results: Iv3 achieved the best performance in E3 for all the targets with an AUC above 85%, and high sensitivity (>0.67) and specificity (>0.82) for the targeted class. As for MbNv2, each experiment presents different results depending on the target. When targeting AMD, E1 and E2 show similar performance with AUC reaching 0.78, but a slightly smaller sensitivity in E2. As for DR, E2 shows a high value for AUC but a low value for sensitivity (0.41). Finally, targeting AMD+DR, the AUC is equal in all experiments, however, sensitivity is higher (0.64) in E1 and specificity is higher in E2.

Conclusions: MbNv2 is a highly efficient basic architecture that ensures good accuracy in low computational budget and energetically economic devices. The use of the MbNv2 architecture opens the possibility of processing data in mobile devices and may come as an advantage on the screening of blinding age-related diseases in remote and rural areas with weak healthcare infrastructure and systems.

CONTROL ID: 3542083

SUBMITTER (NAME ONLY): Jeffrey Wigdahl

TITLE: Automatic image stitching of video frames captured during indirect retinopathy of prematurity examinations using a condensing lens and camera phone

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wigdahl, E. Barriga, VisionQuest Biomedical, Albuquerque, New Mexico, UNITED STATES|S. Wilson, M. Barley, Keeler, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Jeffrey Wigdahl: Commercial Relationship(s);Keeler:Code F (Financial Support);VisionQuest Biomedical:Code E (Employment) | Sam Wilson: Commercial Relationship(s);Keeler:Code E (Employment) | Maya Barley: Commercial Relationship(s);Keeler:Code E (Employment) | E Simon Barriga: Commercial Relationship(s);VisionQuest Biomedical:Code E (Employment)

ABSTRACT BODY:

Purpose: To demonstrate software that automatically generates wide-field images of neonates' retinas using videos captured with a low-cost, narrow field smartphone fitted to a headset and an indirect ophthalmoscopy lens. Accurate determination of plus disease is critical for achieving favorable outcomes in infants with ROP. However, given the narrow field of a smartphone-based imager, it can be difficult to judge vascular changes present in an infant's posterior pole. To meet the needs of the developing world, low-cost tools and software need to provide equally actionable information as more expensive counterparts that capture larger field of view images.

Methods: To generate a mosaic, videos must be stripped of extraneous information:

Lens Detection: Circle Hough transform is used to detect the most likely lens candidate in each frame.

Image Quality: A deep neural network was trained with over 100,000 images from three classes (outlier, low, high).

The model is used to determine which frames will be used to create the mosaic.

Grouping: During the ROP exam, the lens is out of frame when the doctor moves to a different area of the retina. The initial grouping of usable frames exploits this so that each group represents a contiguous view of the retina.

Image Stitching: Each group is stitched together, then an attempt is made to stitch the group outputs into a final mosaic. Stitching is performed using FAST key point detection and Rotated BRIEF descriptors to find correspondence between images.

Results: 20 videos were used to test the algorithms with success criteria being the retinal field of view present in the output mosaics. The full field of view, as determined by an independent grader, was manually extracted from the videos and visually compared against the automatic output. The full field of view was found to be present in 18 videos, with only a single view underrepresented in each. An example output and processing pipeline is provided in Fig.1.

Conclusions: We demonstrated an automatic approach that can extract the usable retinal information from a video and create one or more widefield images that can be used for documentation, education, or making an accurate ROP diagnosis.

CONTROL ID: 3542095

SUBMITTER (NAME ONLY): Zhuolin Liu

TITLE: Impaired cone function in drusen regions revealed by phase-sensitive adaptive optics OCT

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Liu, F. Zhang, D. Hammer, CDRH/OSEL, US Food and Drug Administration, Silver Spring, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zhuolin Liu: Commercial Relationship(s);Indiana University:Code P (Patent) | Furu Zhang: Commercial Relationship(s);Indiana University:Code P (Patent) | Daniel Hammer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study how cone photoreceptor function is affected by drusen.

Methods: Three subjects with no diagnosed ocular disease were imaged with the FDA adaptive optics (AO) imager [1]. Two subjects were found to have drusen in the macula from previous AO imaging. Brief synchronous flashes of visible stimulus were delivered to the retina with a Maxwellian view illumination channel co-aligned to the AO-OCT beam. Two stimulus sources (centered at 530 nm and 625 nm) were selected to change the relative response of the cones. Seven 1° field of view AO-OCT videos were acquired with each stimulus. The phase difference between cone IS/OS and COST signals was calculated and converted to optical path length change (Δ OPL). We then analyzed cone response using principal component analysis and classified cone types (L-, M-, and S-) following the methods described by Zhang et al. [2]. To avoid inter subject variability, cone responsivity and outer segment (OS) length were compared between non-drusen and drusen regions.

Results: Despite the presence of drusen, both IS/OS and COST reflections were present above regions of small drusen (Fig.1 A). The responses of the three cone types were distinctly separated in this study (Fig.1 B-C). In S1, the cones above a ~150- μ m diameter drusen (drusen 1) have significant weaker response compared to the non-drusen region for both L- (drusen: 639.4; non-drusen: 680.7; $p=0.04$) and M- (drusen: 309.6; non-drusen: 402.5; $p<0.01$) cones (Fig.1 C-D). The weaker cell response also prevented separation of the third (S-) cluster from the other two in the drusen region. Intriguingly, the L-cones above drusen 1 had a weaker response to green stimulus compared to the cones in the non-drusen region, suggesting the L- cones spectral sensitivity is affected by drusen. Weaker cone response was also found in the drusen 2 region, with no change in cone spectral sensitivity. Cones in the drusen area also tended to have shorter OS length, suggesting a structure-function correspondence. Similar results were found in S2, but no regional difference in cone functionality was evident in S3, who had no observable drusen.

Conclusions: The presence of drusen results in a weaker cone response to visible stimulation. The ability to measure individual cone function in drusen regions may lead to new functional biomarkers for detection of early age-related macular degeneration.

CONTROL ID: 3542097

SUBMITTER (NAME ONLY): Kitiya Ratanawongphaibul

TITLE: Detecting glaucoma progression using optic nerve volume scans with three-dimensional spectral-domain optical coherence tomography

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Ratanawongphaibul, Ophthalmology, Chulalongkorn University, Bangkok, Bangkok, THAILAND|K. Ratanawongphaibul, T.C. Chen, E. Tsikata, M. Margeta, C. Ondeck, B. Pan, P. Petrakos, Ophthalmology, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|M. Zemlenyi, Biostatistics, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|T.C. Chen, E. Tsikata, H. Lee, M. Margeta, C. Ondeck, J. Kim, B. Pan, P. Petrakos, Harvard Medical School, Boston, Massachusetts, UNITED STATES|H. Lee, Medicine, Massachusetts General Hospital, Boston, Massachusetts, UNITED STATES|A.L. Coleman, F. Yu, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|J. de Boer, Ophthalmology, Vrije Universiteit Amsterdam, Amsterdam, Noord-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To determine whether three-dimensional (3D) spectral-domain optical coherence tomography (SD-OCT) neuroretinal rim measurements detect glaucoma progression earlier than current standard of care clinical testing i.e., disc photography (DP), visual field (VF) testing, and two-dimensional (2D) retinal nerve fiber layer (RNFL) thickness measurements.

Methods: In this 5-year prospective longitudinal cohort study, 124 eyes of 124 open angle glaucoma patients had yearly DP, VFs, SD-OCT RNFL thickness scans, and optic nerve volume scans (Spectralis, Heidelberg Engineering, Heidelberg, Germany) which were performed on the same day. From high-density optic nerve volume scans, custom-built software calculated the minimum distance band (MDB) thickness, a 3D neuroretinal rim parameter, which quantifies the amount of tissue in the neuroretinal rim. Patients were classified as glaucoma progressors or non-glaucoma progressors using event-based analysis. Progression by DP and VF were determined when 3 masked glaucoma specialists unanimously concurred. Progression by RNFL and MDB thickness were determined if there was change greater than test-retest variability. Kaplan-Meier curves were constructed to analyze time-to-progression data.

Results: Global MDB neuroretinal rim thickness detected glaucoma progression earlier either DP (23 versus 44 months; $P < 0.001$) or global RNFL thickness (23 versus 33 months; $P < 0.001$). Global MDB thickness also detected progression slightly earlier than visual fields (23 versus 32 months), but the difference was not statistically significant ($P = 0.15$).

Conclusions: High-density 3D SD-OCT neuroretinal rim measurements detected glaucoma progression approximately 1-2 years earlier compared to current clinically available structural tests (i.e., DP and 2D RNFL thickness measurements).

CONTROL ID: 3542107

SUBMITTER (NAME ONLY): Shiju Thomas

TITLE: Assembly of epithelial basement membrane (EBM) in vitro in a 3D organotypic cornea model

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Thomas, R. de Oliveira, L. Sampaio, G. Hilgert, S.E. Wilson, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To use a 3D corneal organotypic model to study which cell types, either alone or in combination, contribute to the assembly of the epithelial basement membrane (EBM).

Methods: A 3D corneal organotypic model was established by culturing the rabbit corneal epithelial cells with either corneal fibroblasts or myofibroblasts embedded in collagen type I for 18 or 30 days. The myofibroblasts were derived either from bone marrow or differentiated from corneal fibroblasts. Fresh rabbit corneas had overnight enzymatic digestion to collect the keratocytes/corneal fibroblasts. The fibroblast were differentiated into myofibroblasts by incubating in TGFb1 (20 ng/ml) and mature myofibroblasts were confirmed with ICC for markers alpha-SMA, vimentin, desmin and vinculin. Immunohistochemistry for laminin alpha-5, laminin beta-3, perlecan, nidogen-1 and collagen IV was performed on cryofixed sections to detect EBM generation and IHC staining for vimentin and alpha-SMA was used to differentiate the fibroblasts and myofibroblasts. Each experiment was repeated at least 3 times.

Results: Expression and localization of EBM components laminin alpha 5, laminin beta 3, perlecan, nidogen 1 and collagen IV at the interface of the epithelial cells and corneal fibroblasts confirmed generation of a normally-assembled EBM in 3D organotypic cultures of epithelial cells and corneal fibroblasts. The presence of vimentin+, SMA– cells in the organotypic culture of corneal fibroblasts with epithelial cells revealed that corneal fibroblasts retained their phenotype after 18 days of culture. Epithelial cells or corneal fibroblasts alone in culture did not produce EBM. EBM was not observed in 3D organotypic cultures of myofibroblasts (either cornea- or bone marrow-derived) with epithelial cells, even with a long term (30 days) organotypic culture. However, a thickened EBM was observed in epithelial cell-corneal fibroblast organotypic cultures when incubation was continued for 30 days.

Conclusions: Corneal EBM assembly is mediated by the coordinated action of epithelial cells and corneal fibroblasts—with both cell types producing EBM component proteins. This in vitro organotypic model can be used to further elucidate EBM assembly in the cornea and to study other functions such as regeneration of epithelial barrier function after injury.

CONTROL ID: 3542111

SUBMITTER (NAME ONLY): Yihe Chen

TITLE: Antigen-specific memory CD4⁺ T cells are uveitogenic in chronic autoimmune uveitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, N. Fan, S. Wang, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|N. Fan, Ophthalmology, Taipei Veterans General Hospital, Taipei, TAIWAN|R.M. Huckfeldt, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|S. Wang, Ophthalmology, Harbin Medical University, Harbin, Heilongjiang, CHINA|

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ABSTRACT BODY:

Purpose: Chronic autoimmune uveitis (CAU) is often a treatment-resistant disease, and the underlying pathogenesis remains poorly understood. Our previous work demonstrates the presence of CD44^{hi}IL-7R⁺IL-15R⁺IL-17A⁺CD4⁺ memory Th17 cells in the retina, draining lymph nodes, and spleen in a mouse model of CAU. In the present study, we further determined the pathogenicity of these memory T cells in CAU.

Methods: CAU was induced in wild-type C57BL/6 mice by immunization with 150 µg interphotoreceptor retinoid-binding protein (IRBP) peptide 161–180 plus 300 µg IRBP 1–20 emulsified in 0.2ml Complete Freund's Adjuvant (CFA). Mice also received 0.2µg Bordetella pertussis toxin. Establishment of CAU was confirmed by digital fundus imaging at week 12. CAU mice were sacrificed, draining lymph nodes and spleen were collected, and CD44^{hi}CD4⁺ (memory T cells) and CD44^{-/low}CD4⁺ (control T cells) were isolated using CD4⁺ negative MACS sorting combined with FITC-CD44 FACS sorting. The sorted cells were stimulated with 20 µg/mL IRBP in the presence of 1 µg/ml anti-CD28 antibody in vitro. Next, the cultured cells were evaluated for (i) proliferation profile using fluorescence-based dilution assay (Violet CellTrace™ Cell Proliferation Kit), (ii) activation profile using flow cytometry-based PE-CD154 antigen-specific activation assay, and (iii) cytokine profile using ELISA kit for IL-17A detection in cell culture supernatant. Finally, the sorted cells were also adoptively transferred to normal Rag1^{-/-} mice, and clinical disease in recipients was followed up for 2 weeks using fundoscopy.

Results: The CAU-derived CD44^{hi}CD4⁺ memory T cells showed 2-fold higher proliferation and 20-fold higher CD154 expression upon IRBP re-stimulation compared to control CD44^{-/low}CD4⁺ T cells. The IL-17A expression levels in CD44^{hi}CD4⁺ memory T cell cultures (15.5 ± 0.6 pg/mL) were significantly higher than that in CD44^{-/low}CD4⁺ T cell cultures (8.8 ± 0.4 pg/mL). In addition, Rag1^{-/-} mice receiving CD44^{hi}CD4⁺ memory T cells developed multiple retinal lesions by 2 weeks post-transfer; in contrast, those receiving control T cells showed normally appearing retina.

Conclusions: Our data demonstrate that memory CD4⁺ T cells in CAU are antigen-specific pathogenic effector memory T cells.

CONTROL ID: 3542116

SUBMITTER (NAME ONLY): TIANXI WANG

TITLE: The roles of SOCS3 in myeloid cell-derived neovascular endothelium formation in a laser-induced choroidal neovascularization mouse model

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. WANG, D. Tsiрукis, S. Cho, Y. Sun, ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): TIANXI WANG: Commercial Relationship: Code N (No Commercial Relationship) | Demetrios Tsiрукis: Commercial Relationship: Code N (No Commercial Relationship) | Steve Cho: Commercial Relationship: Code N (No Commercial Relationship) | Ye Sun: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pathological choroidal neovascularization (CNV) is a common cause of blindness in age-related macular degeneration (AMD). We aim to investigate the underlying molecular mechanism by identifying a novel immunoregulator suppressor of cytokine signaling 3 (SOCS3) which controls the development of myeloid lineage cells into endothelial cells to form the pathological vascular endothelium using a laser-induced CNV mouse model.

Methods: We generated SOCS3 gain-of-function and loss-of-function mice using the Cre/loxP system to modulate endogenous Socs3 levels. Myeloid and endothelial-specific Cre mice and ROSA^{mT/mG} reporter mice were used to trace the origin of neovascularization in the AMD mouse model. Bone marrow from GFP transgenic mice was injected into irradiated mice. Mature endothelial cell markers CD31 and VWF were used for immunostaining. CNV was quantified using image J. Results are presented as mean \pm SEM and were compared using the 2-tailed unpaired t-test. Statistical analyses were performed with GraphPad Prism (v6.0).

Results: Our data showed that bone marrow-derived GFP-positive cells gathered at the neovascularization site, and most of them were Iba-1 positive, which means myeloid cells were involved in CNV. We also found in the endothelial-specific promoter-driven GFP mice with CNV, only partial pathological CNV is GFP positive, indicating that endothelial lineage is not the only origin of pathological CNV. In addition, myeloid specific promoter-driven GFP mice, some of the pathological CNV is GFP positive, indicating that myeloid lineage may contribute to pathological CNV. In laser-induced CNV, myeloid specific deletion of SOCS3 increased CNV by 30-40% ($p < 0.001$, $n = 40-46$ lesions from 10 mice/group), and myeloid specific overexpression of SOCS3 reduced CNV by ~25% ($p < 0.001$, $n = 30$ lesions from 8 mice/group). This data suggests that SOCS3 in myeloid lineage controls pathological CNV formation in the laser-induced CNV.

Conclusions: Our data suggests that the myeloid lineage may contribute to pathological neovascularization and the process was modulated by SOCS3 in neovascular AMD mouse model. This finding provides a novel understanding of pathological neovascularization.

CONTROL ID: 3542118

SUBMITTER (NAME ONLY): Bogale Aredo

TITLE: Analysis of cell type-specific responses to retinal injury in the fundus camera delivered-light induced retinal degeneration (FCD-LIRD) model

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Aredo, C. Zhao, R. Ufret-Vincenty, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|B. Chen, Tongji Hospital of Tongji Medical College of Huazhong University of Science and Technology, Wuhan, Hubei, CHINA|Y. Ding, The Central Hospital of Wuhan, Wuhan, Hubei, CHINA|A. Kumar, C. Xing, McDermott Center for Human Growth and development, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal light injury models can be useful in understanding aspects of retinal degeneration and retinal oxidative stress. We recently developed the FCD-LIRD model of light-induced retinal degeneration and demonstrated some retinal recovery from the original damage. In the current study, our aim was to perform cell-type specific analyses using single cell RNA sequencing of the acute and subacute retinal responses to light injury using this FCD-LIRD model.

Methods: C57BL/6J mice (4m old) were exposed to FCD-LIRD. Eyes were collected from control mice and from mice that had been exposed to light injury 4 h, 48h and 5d prior. Retinas were peeled off from the posterior eyecups and 2 mm posterior retina, centered on the optic disc spot, was cut out using a trephine. These retinal samples were then prepared for retinal single-cell suspensions using a Papain Dissociation System. Droplet-based single cell RNA-seq of dissociated retinal cells was performed with the GemCode Single Cell Platform (10X Genomics, Pleasanton). Libraries were sequenced on an Illumina NextSeq 500. Cell Ranger 3.0.0 (10X Genomics) was used to process and analyze the raw sequencing data. Seurat R package (v3.0.0) was used for downstream gene expression analysis. Cell clusters were then identified and named on the basis of known gene markers specific to various cell types found in the retina. Differential gene expression, pathway analyses and trajectory analyses of each cluster were performed, using Seurat and Ingenuity Pathway Analysis software.

Results: Our analysis generated 23 clusters with a resolution of 0.5. In addition to confirming previously published gene markers for retinal cell types, we were able to identify new ones. Using both unbiased and marker-based methods for data processing we identified genes that were significantly altered in each cell type after light injury. Using trajectory analysis we were able to identify several differentiation fates, including some suggestive of activation of pathways for cellular recovery.

Conclusions: Photo-oxidative/photo-inflammatory retinal injury leads to acute and subacute cell type-specific responses. A better understanding of these responses may be helpful in identifying therapeutic approaches to minimize retinal damage and maximize recovery after exposure to injury.

CONTROL ID: 3542119

SUBMITTER (NAME ONLY): Elaheh Shirneshan

TITLE: Assessing Presbyopia Impacts and Coping Behaviors with a de Novo PRO Instrument in a Phase 3 Study of AGN-190584 (Pilocarpine 1.25%)

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shirneshan, S. Lee, J. Campbell, Allergan, an AbbVie Company, California, UNITED STATES|D. Wirta, Eye Research Foundation, California, UNITED STATES|W. Christie, Scott & Christie and Associates, Pennsylvania, UNITED STATES|J. Tauber, Tauber Eye Center, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: This report presents results of a de novo, validated patient-reported outcomes instrument, the Presbyopia Impact and Coping Questionnaire (PICQ), in assessing effects of an optimized formulation of pilocarpine (1.25%; AGN-190584) on daily life, emotional impact and compensatory coping mechanisms in individuals with presbyopia.

Methods: In this multicenter, double-masked, 30-day study (NCT03804268; n=323), individuals with presbyopia were randomized to bilateral treatment with AGN-190584 or vehicle (placebo) once daily. Secondary efficacy endpoints included mean change from baseline in PICQ Coping (8 item) and Impact (6 item) domain scores evaluating use of presbyopia coping behaviors or impacts on daily life during the past 7 days. In prespecified analyses of PICQ domain scores (Day 30 Hour 3 [3 hours after dosing]), the cumulative distribution of change scores from baseline was depicted and the proportion of responders to AGN-190584 (those achieving meaningful change threshold of ≥ 1 point reduction from baseline in PICQ domain scores) assessed.

Results: Baseline PICQ Coping and Impact scores were generally comparable between treatment groups. At Day 30 Hour 3, the mean score differences (95% confidence interval [CI]) between groups for the Coping and Impact domain scores were -0.5 points (-0.6, -0.3) and -0.3 points (-0.4, -0.1), respectively ($P=.011$ for both vs vehicle). The cumulative proportion of participants reporting change in use of coping behaviors showed consistent separation between the two groups, favoring the AGN-190584 arm. Of the AGN-190584 group, 20.2% (95% CI: 10.5, 29.9; $P<.001$) more participants reported a ≥ 1 point reduction in PICQ Coping score vs vehicle. The difference in impact response rates was not significant.

Conclusions: Analyses of PRO efficacy endpoints demonstrated significant improvement in participants' subjective experiences with presbyopia. Participants who received AGN-190584 reported a clinically meaningful reduction in use of presbyopia coping mechanisms, versus participants receiving vehicle, supporting the value of this pharmacologic treatment option.

CONTROL ID: 3542121

SUBMITTER (NAME ONLY): Laura Krueger

TITLE: Expression pattern of Chd7 suggests a role in retinal and photoreceptor development

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Krueger, A.C. Morris, Biology, University of Kentucky, Lexington, Kentucky, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Laura Krueger: Commercial Relationship: Code N (No Commercial Relationship) | Ann Morris: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Mutations in the chromatin remodeling factor CHD7 are the predominant cause of CHARGE syndrome, a congenital disorder that frequently includes ocular coloboma. Although CHD7 is known to be required for proper ocular morphogenesis, its role in retinal development has not been thoroughly investigated. In this study, we characterize the expression pattern of chd7 in the developing zebrafish retina and begin to study its function using two chd7 mutant lines.

Methods: All animal procedures were performed in accordance with IACUC and guidelines established by the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Wild-type and transgenic zebrafish embryos or larvae were collected at 24, 48, 72 hours post fertilization (hpf) and 4, 5 days post fertilization (dpf). Retinas were sectioned, followed by immunohistochemistry with a Chd7 antibody or RNAscope with a chd7 mRNA probe, and imaged with fluorescent and confocal microscopy. A CRISPR chd7 mutant line was obtained and genotyped by Sanger sequencing to identify a 2 base pair deletion. A second mutant line generated by ENU mutagenesis was outcrossed four times, and genotyped by Sanger sequencing to identify a single point mutation.

Results: Chd7 was expressed throughout the developing zebrafish retina at 24 and 48 hpf, when retinal progenitors are actively proliferating and early cells of the retina are beginning to differentiate. At 72 hpf, when most retinal cell types have terminally differentiated, Chd7 expression remained strong in the ganglion cell layer and in some cells in the inner nuclear layer. Strong expression of Chd7 was also observed in the photoreceptor cells of the outer nuclear layer (ONL). By 4 and 5 dpf, when the zebrafish larvae display active swimming and visual behaviors, Chd7 expression remained strong in the ONL, where it co-localized with markers of cone and rod photoreceptors. Incrosses of chd7 heterozygous adults yielded homozygous mutant progeny suggesting that the mutations are not early embryonic lethal in zebrafish.

Conclusions: Our results demonstrate that Chd7 is expressed throughout development of the zebrafish retina and remains expressed in some newly differentiated retinal cell types, including the photoreceptors. Further work is ongoing to investigate this specific patterning of Chd7 and chd7 mutant fish will be used to understand the function that this factor plays in retinal development.

CONTROL ID: 3542124

SUBMITTER (NAME ONLY): Leyla Yavuz Saricay

TITLE: Corneal Nerve Alterations of Neuropathic Corneal Pain Patients with Underlying Autoimmune Conditions: Comparative In Vivo Confocal Microscopy Study in Patients with and without Anti-Neuronal Antibodies

SESSION TITLE: Corneal immunology and neovascularization II

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Yavuz Saricay, B. Bayraktutar, P. Hamrah, 1Center for Translational Ocular Immunology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|L. Yavuz Saricay, B. Bayraktutar, V. Atocha, P. Hamrah, Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare corneal nerve alterations in patients with neuropathic corneal pain (NCP) and positive serology for autoimmune antibodies (Ab) with and without IgM against neuronal trisulfated heparin disaccharide (TS-HDS) and IgG against fibroblast growth factor receptor 3 (FGFR3).

Methods: Retrospective chart review of NCP patients (n=35) with autoimmune Ab (those having a positive result for ANA, SS-A, SS-B, c-ANCA, p-ANCA, anti-gliadin IgA, anti-TS-HDS IgM and/or anti-FGFR3 IgG were included in the study). Laser in vivo confocal microscopy (HRT3/RCM) images were analyzed using corneal nerve alterations using Neuron J in a masked fashion, comparing patients with or without anti-neuronal TS-HDS IgM/FGFR-3 IgG. The control group consisted of age- and sex-matched subjects (n=35) from a reference normative database.

Results: The mean age was 50.3 ± 19.0 (20-88) years for patients without anti-neuronal Abs (n=19, 4 males, 15 females) and 48.1 ± 18.7 (27-74) years for patients with anti-neuronal Abs (n=16, 1 male, 15 females), and 47.5 ± 13.5 (27-74) years (n=35, 5 males, 30 female) for controls. The overall pain intensity in the anti-TS-HDS IgM/FGFR-3 IgG (+) group was 5.67 ± 2.99 (1.0-10.0) and similar to 5.20 ± 2.26 (1.0-10.0) in the anti-TS-HDS IgM /FGFR-3 IgG (-) group (p=0.66). The mean total, main and branch subbasal corneal nerve densities in patients with anti-TS-HDS IgM/FGFR-3 IgG were $9,944.7 \pm 1,085.0$ mm/mm², $6,542.7 \pm 563.2$, and $3,402.0 \pm 579.2$, and were significantly lower (p=0.01, p=0.01, p=0.03 respectively) compared to patients without anti-neuronal Abs with $14,406.7 \pm 1,192.1$, $9,046.2 \pm 684.8$, and $5,360.6 \pm 592.9$, and controls ($20,896.0 \pm 697.4$, $9,097.4 \pm 460.6$, and $11,778.6 \pm 564.4$, p=0.001, p=0.005, p<0.001 respectively). The number of mean total and branch subbasal corneal nerves in patients with or without anti-TS-HDS IgM/FGFR-3 IgG were significantly lower compared to healthy controls (p<0.001). The number of mean main subbasal corneal nerves was lower in patients with anti-neuronal Abs compared to anti-TS-HDS IgM/FGFR-3 IgG (-), (p=0.07).

Conclusions: NCP patients with autoimmune conditions demonstrate reduced nerve density compared to controls. NCP patients with anti-neuronal TS-HDS IgM and/or FGFR-3 IgG demonstrate significant corneal nerve fiber loss compared to other autoimmune-mediated NCP patients.

CONTROL ID: 3542125

SUBMITTER (NAME ONLY): Susanna Koenig

TITLE: Effect of trabeculectomy on the rate of progression of visual field damage

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Jayaram, J. Clarke, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|J. Clarke, Glaucoma Service, NIHR Biomedical Research Centre at Moorfields Eye Hospital, London, UNITED KINGDOM|H. Jayaram, Glaucoma Service, NIHR Moorfields Biomedical Research Centre, London, Greater London, UNITED KINGDOM|G. Montesano, D. Crabb, City, University of London, London, London, UNITED KINGDOM|S. Koenig, G. Montesano, C. Fang, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To quantify the effect of trabeculectomy on the rate of progression (RoP) of visual field (VF) damage.

Methods: Clinical and VF data from 199 patients that were randomly selected from the cohort of patients that underwent trabeculectomy between 2015 and 2016 were extracted from clinical charts and digital archives at the network of sites of Moorfields Eye Hospital NHS Foundation Trust. Of these, we selected 80 patients who met our criteria of at least three reliable VFs before and after surgery. Reliability was defined by a false positive rate < 15%. The change in RoP was tested using total deviation (TD) values through a mixed effect model with random effects on both intercepts and slopes. The fixed effects modelled a broken-stick regression of TD over time, with a breakpoint at the day of surgery. We used two nested levels of random effects (patient and location within the VF, example in Figure 1). The fixed effect component of the model provided an estimate of the average change in slope between the pre and post-operative period.

Results: We analysed 10 [9, 12] VFs per subject (Median [Interquartile Range]). At surgery, the age was 67 [57, 72] years, the mean deviation was -10.84 [-14.68, -5.56] dB and the intraocular pressure (IOP) was 18 [15, 20] mmHg. One year after surgery, the IOP was 10 [8, 13] mmHg ($p = 0.002$). The mean RoP before surgery was -0.82 [-0.58, -1.07] dB/year (Mean [95% Confidence Intervals]) and it was slowed down by 0.56 [0.23, 0.89] dB/year ($p = 0.001$, Figure 2) after surgery.

Conclusions: Glaucoma patients who underwent trabeculectomy in 2015/16 showed a significant reduction in the rate of progression of the visual fields postoperatively throughout their follow-up.

CONTROL ID: 3542131

SUBMITTER (NAME ONLY): Rebecca Kaye

TITLE: Choroidal Vascularity in Chronic Central Serous Chorioretinopathy

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Kaye, A.J. Lotery, Ophthalmology, University Hospital Southampton NHS Foundation Trust, Southampton, Southampton, UNITED KINGDOM|R. Kaye, A.J. Lotery, University of Southampton, Southampton, Hampshire, UNITED KINGDOM|T. Peto, Queens University Belfast, Belfast City Hospital, Belfast, Belfast, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Rebecca Kaye: Commercial Relationship: Code N (No Commercial Relationship) | Tunde Peto: Commercial Relationship: Code N (No Commercial Relationship) | Andrew Lotery: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patients with central serous chorioretinopathy (CSC) are reported to have dilated, hyper-permeable choroidal vessels with leakage into the interstitial space. The vascular component of choroidal tissue can be assessed using the choroidal vascularity index (CVI), a ratio of the luminal component of the choroid to the cross-sectional choroidal area.

The aim of this study was to test for differences in the CVI in patients with chronic (cCSC), fellow eyes and healthy controls. Patients were genotyped for single-nucleotide polymorphisms (SNPs) associated with CSC and their relationship with a patient's CVI analysed.

Methods: Patients were included with cCSC, treatment naive, with a visual acuity of ≤ 79 EDTRS letters, OCT evidence of sub-foveal sub-retinal fluid, and fluorescein/ICG angiography evidence of active CSC. Age-matched controls were included. The central, foveal, EDI-OCT image was agreed upon by 2 ophthalmologists. Images were analysed in ImageJ and binarised. The central sub-foveal choroidal area was selected with a width of 1,500 μ m, the upper border at the retinal pigment epithelium and lower border at the choroid scleral interface. The total selected sub-foveal choroidal area, luminal area (dark pixels), stromal area (light pixels) and CVI were calculated (Fig1). cCSC patients were genotyped for risk SNPs associated with CSC. ANOVA used for statistical analysis.

Results: 106 patients with cCSC and 106 control eyes were included. There was a significant increase in the sub-foveal choroidal area in cCSC patients $2.35 \pm 0.56 \text{ mm}^2$ vs controls $1.82 \pm 0.54 \text{ mm}^2$ ($p < 0.0001$), and in fellow eyes $2.23 \pm 0.58 \text{ mm}^2$ vs controls ($p < 0.0001$). The CVI was reduced in cCSC patients $63.45 \pm 3.10\%$ vs controls $65.43 \pm 2.61\%$ ($p < 0.0001$) and in their affected vs fellow eyes $64.55 \pm 2.90\%$ ($p < 0.01$). There was a significant association between CVI and the presence of the risk SNP rs2379120 at GATA5 ($p < 0.01$) in cCSC patients after Bonferroni correction.

Conclusions: These results suggest the sub-foveal choroidal area is increased in both eyes of patients with cCSC. The relative reduction in CVI in cCSC may suggest a persistence of vessel hyper-permeability over dilation; resulting in an increase in stromal area. Tracking a patient's CVI and relative stromal area could be used to monitor disease. GATA5 may play a role in choroidal vascularity in cCSC.

CONTROL ID: 3542135

SUBMITTER (NAME ONLY): Brian Patterson

TITLE: Microbial Ingress Risk Evaluation of NOVELIA Package Containing Systane Ultra

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Patterson, M. Crary, P. Shannon, R&D Microbiology, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Brian Patterson: Commercial Relationship(s);Alcon Research, LLC:Code E (Employment) | Monica Crary: Commercial Relationship(s);Alcon Research, LLC:Code E (Employment) | Paul Shannon: Commercial Relationship(s);Alcon Research, LLC:Code E (Employment)

ABSTRACT BODY:

Purpose: Microbial keratitis is a risk for all users of topical ophthalmic solutions due to microbial proliferation within the formulation upon accidental contamination of the product. Historically, preservatives added to the formulation are included to inhibit the growth of microbes introduced from repeated use. Preservative-free products are viable alternatives for individuals who are sensitive, or have reservations about using traditional preservatives. To mitigate microbial growth without the use of preservatives, a multi-dose packaging system must present a physical barrier to contamination throughout the use period. This study evaluates the potential of microbial ingress into Systane Ultra presented in the NOVELIA® Multi-Dose Preservative Free package over a 30-day use period.

Methods: Two challenge methods were evaluated for 30 days per Note for Guidance on In-Use Stability Testing of Human Medicinal Products (CPMP/QWP/2934/99) to simulate consumer use. First, the tip was challenged daily with low levels (10^2 CFU) of *Brevundimonas diminuta* (ATCC 19146) after actuation to simulate the tip routinely contacting a contaminated surface. Second, after four days of dispensing, the tip was submerged in a high level (10^6 CFU/mL) susp. of *B. diminuta* and actuated to simulate routine use of the product followed by a gross contamination event similar to falling into a heavily contaminated liquid.

Following each 30-day simulation, the internal contents of replicate samples were evaluated for sterility per USP<71>. A passing result indicates the packaging system was able to prevent microbial ingress into the bottle, while a failing result indicates ingress into the packaging system.

Results: For all simulations, a passing USP<71> sterility result was obtained following the 30-day use simulations and microbial challenges of the NOVELIA package.

Conclusions: Systane Ultra Preservative Free when presented in the NOVELIA package with the PureFlow™ 200 nozzle remains contaminate-free over a 30-day use period, even when subjected to extreme cases of accidental contamination. Users who suffer from dry eye disease now have the option of Systane Ultra Preservative Free in a unique multi-dose package.

CONTROL ID: 3542139

SUBMITTER (NAME ONLY): Jessica Jasien

TITLE: Effect of Spaceflight and Lower Body Negative Pressure on Intracranial Pressure

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.V. Jasien, CVL - NASA, JES Tech, Texas, UNITED STATES|S. Laurie, S.M. Lee, K. Marshall-Goebel, PhD, D.J. Ebert, A. Sargsyan, KBR, Texas, UNITED STATES|M.B. Stenger, B. Macias, NASA, Texas, UNITED STATES|D. Kemp, University College London, London, London, UNITED KINGDOM|A. Hargens, University of California San Diego, La Jolla, California, UNITED STATES|S.A. Dulchavsky, Henry Ford Hospital, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The head-to-foot hydrostatic pressure gradient causes intracranial pressure (ICP) to be ~0 cmH₂O during upright posture on Earth, but the gradient is absent during spaceflight, resulting in a cephalad shift of blood and cerebrospinal fluid. It has been hypothesized that ICP is elevated during spaceflight and may contribute to development of optic disc edema which occurs in some astronauts; invasive ICP measures have not been obtained during spaceflight. On Earth, use of lower body negative pressure (LBNP) redistributes fluid caudally and lowers ICP, so may be capable of lowering ICP during spaceflight. The purpose of this study was to assess ICP during spaceflight using 3 noninvasive techniques (nICP) and to determine if LBNP can lower ICP during spaceflight to levels similar to upright posture on Earth.

Methods: Twelve astronauts were tested three months before spaceflight (preflight) in the seated and supine posture, and ~150 days (FD150) into spaceflight with and without 25 mmHg LBNP. Optic disc edema was determined using fundoscopy and optical coherence tomography (OCT) images. We assessed ICP using 3 noninvasive techniques: ultrasound measures of optic nerve sheath diameter (ONSD), cerebral and cochlear fluid pressure (CCFP) tympanic membrane displacement, and otoacoustic emission (OAE) phase shift. Mixed effects models were used to detect differences between conditions.

Results: One astronaut developed Frisen grade 1 optic disc edema, while OCT imaging showed subclinical retinal thickening in 8 of 12 astronauts. Measures of nICP after 150 days of spaceflight were not greater than nICP measured in either the seated or supine postures preflight. During spaceflight, the use of LBNP resulted in a reduction in nICP assessed by CCFP (94.7 -nL, $p < 0.02$), compared to -39.1 and 66.4 -nL changes in the seated and supine postures related to FD150, respectively. No changes were detected by the other nICP measures.

Conclusions: Despite development of subclinical and Frisen grade optic disc edema in some astronauts, our data suggest spaceflight results in a mild, chronic elevation of ICP similar to the supine position on Earth, and that LBNP did not result in changes indicative of ICP values similar to those of upright posture on Earth. Invasive measures of ICP may clarify these findings. Research is needed to determine if small reductions in ICP induced by LBNP would be sufficient to prevent optic disc edema.

CONTROL ID: 3542144

SUBMITTER (NAME ONLY): Eric Thee

TITLE: The effect of antidiabetic drugs in age-related macular degeneration: the Rotterdam study.

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E.F. Thee, C.C. Klaver, Ophthalmology and Epidemiology, Erasmus MC, Rotterdam, NETHERLANDS|J. Vergroesen, F. Ahmadizar, M. Kavousi, Epidemiology, Erasmus MC, Rotterdam, NETHERLANDS|J.R. Vingerling, W.D. Ramdas, Ophthalmology, Erasmus MC, Rotterdam, NETHERLANDS|B.H. Stricker, Internal Medicine and Epidemiology, Erasmus MC, Rotterdam, NETHERLANDS|C.C. Klaver, Institute of Molecular and Clinical Ophthalmology, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Recent studies suggest that the antidiabetic drug metformin has a significant protective effect on age-related macular degeneration (AMD). These studies were based on large registries, were retrospective, mostly case-control designed, and not specific to AMD stage. Here, we evaluated the association between diabetes, metformin, other antidiabetic medications and incident any or late AMD in a large prospective, population-based study.

Methods: In total, 12,939 individuals aged 45+ years from the population-based Rotterdam Study were available for analyses. Diabetes diagnosis was based on general practitioners' records, hospital discharge letters and serum glucose measurements. Diabetic medication data were obtained through linkage with the computer network of pharmacies in the study district and were categorized as monotherapy of metformin, monotherapy of insulin, monotherapy of sulfonylurea, any monotherapy and any combination therapy. AMD features and diagnosis of late AMD were assessed by the EyeNED Reading Center on multimodal imaging. Associations between diabetes, the treatment groups, and incident AMD were determined by Cox regression adjusted for age, sex, BMI, use of statins, antihypertensives and fasting serum glucose.

Results: A total of 1,723 participants were diagnosed with diabetes, of them 688 (40%) used metformin as monotherapy. 1,091 participants were diagnosed with incident any AMD, and 172 with late AMD during a mean follow up time of 6.6 (SD 5.5) years. Diabetes was associated with a lower risk of any AMD (HR 0.74, 95%CI 0.63-0.85), but not significantly associated with late AMD (HR 0.99, 95%CI 0.67 - 1.46). Monotherapy of metformin was borderline associated with any AMD (HR 0.57, 95%CI 0.29 – 1.04), not significant for late AMD (HR 0.51, 95%CI 0.12– 2.27). None of the other medications were significantly associated with any or late AMD, but also had risk estimates which seemed slightly protective (HRs 0.7-0.9).

Conclusions: Our study shows that it is challenging to dissect the effect of treatment from that of the indication in the study of antidiabetic drugs and AMD. If any, metformin has a greater protective effect on AMD than other medications in diabetic patients, but the clinical significance remains to be elucidated in large prospective studies.

CONTROL ID: 3542145

SUBMITTER (NAME ONLY): Ashkan Eliasy

TITLE: Evaluation of Stress-Strain Index (SSI2) in Healthy and Keratoconic corneas

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Eliasy, B.T. Lopes, A. Abass, R. Vinciguerra, A. Elsheikh, University of Liverpool Faculty of Science and Engineering, Liverpool, Liverpool, UNITED KINGDOM|R. Vinciguerra, Department of Ophthalmology, Humanitas San Pio X Hospital, Milan, ITALY|S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|A. Elsheikh, Beijing Advanced Innovation Centre for Biomedical Engineering, Beihang University, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: To evaluate the performance of a new Corvis ST parameter denoted the Stress-Strain Index (SSI2) as an in-vivo measure of material stiffness of healthy and keratoconic corneas.

Methods: A large parametric study was conducted on realistic ocular finite element models. The input and output parameters were recorded in a database and used to develop an algorithm for SSI2, which involved the central corneal thickness (CCT), the intraocular pressure (IOP) along with a number of the dynamic corneal response parameters provided by the Corvis ST including the integrated inverse radius (IIR) and the Stiffness Parameter (SP). The algorithm was validated using data obtained by Vincieye Clinic (Milan, Italy) for 414 healthy participants, 79 forme-fruste keratoconus (FFKC) subjects and 222 patients with confirmed keratoconus. IOP was measured with the Corvis ST (OCULUS Optikgeräte GmbH; Wetzlar, Germany), whose measurements also allowed calculation of the SSI2 values using a custom Matlab code. The results were statistically analysed and correlations were evaluated for SSI2 with CCT and age. Topography data obtained using a Pentacam (OCULUS) were also acquired for the same participants, and analysed using Topographic Keratoconus Classification (TKC) (Chen, JCRS, 2019) to categorise the eyes into healthy, FFKC, mild, moderate and advanced keratoconus. IRB approval in the form of written and informed consent was obtained to use the data in scientific research. The study followed the tenets of the Helsinki Declaration revised in 2013.

Results: The mean SSI2 was 1.08 ± 0.21 , 1.02 ± 0.18 , 0.79 ± 0.17 , 0.70 ± 0.21 and 0.63 ± 0.15 in healthy participants and patients with FFKC, mild KC, moderate KC and advanced KC, respectively, showing gradual, consistent and significant decreases with keratoconus progression ($p < 0.05$). As expected, the correlation between SSI2 and CCT was not significant in both the healthy population ($p = 0.552$) and the KC population ($p = 0.205$), while the correlation with age was significant in healthy eyes ($p < 0.05$). The correlation with age in KC eyes was not significant ($p = 0.141$) possibly due to the biomechanical changes in the tissue caused by the disease.

Conclusions: The results revealed consistent reductions in SSI2 with keratoconus progression and independence of corneal thickness. This parameter may be used for personalised medicine to optimise procedures such as corneal cross-linking.

CONTROL ID: 3542150

SUBMITTER (NAME ONLY): Oliver Voecking

TITLE: Single cell transcriptome analysis of periocular mesenchyme during anterior segment development

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O. Voecking, J.J. Smith, J. Famulski, Biology, University of Kentucky, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Periocular mesenchyme (POM) is a subgroup of neural crest cells, responsible for forming anterior structures, including the anterior segment of the eye. Despite the importance for the development of a healthy eye, knowledge about this cell group is limited. Particularly, only very few genetic markers and their respective roles are known. The purpose of this study is to identify formerly unknown markers of POM cells, to further understand their role in eye development and the genetic interactions required for AS formation. To do so, we employed newly available scRNA analysis over the course of AS development.

Methods: Larval eyes of transgenic zebrafish Tg(Foxc1b:GFP) and Tg(Lmx1b:GFP) were collected every 24 hours between 48hpf and 144hpf. GFP+ cells were isolated via FACS cell sorting and processed with the 10x genomics chromium single cell transcriptome kit. The resulting Illumina sequencing single cell transcriptomes were processed with the Cell Ranger pipeline. Analysis was done with the Cell Loupe Browser 5.0 and Monocle3. Gene expression was studied via in situ hybridization and gene function via Morpholino and Alt R CRISPR induced knockouts.

Results: We collected a total of more than 40,000 Foxc1b+ and Lmx1b+ cells from eyes only, including one biological replicate for each individual time point. Transcriptome analyses showed that these cells were organized in re-occurring clusters during zebrafish anterior segment development. These clusters are partly localized to different structures within the eye, including the cornea, iridocorneal angle, retina and retinal pigment epithelium. Additionally, we found several new markers with specific expression within these spatially limited areas with apparent importance for general eye development, as proven by genetic knockout. These genes include hgd, si:ch211-251b21.1, slc22a7a, ppil1, stmn1a, seta, hmgb2a and b.

Conclusions: Our results provide a base for a single cell transcriptome atlas for anterior segment development in zebrafish. Not only do they reveal previously unknown and uncharacterized genetic markers, but they also give a first insight into potential genetic interactions necessary anterior segment development. This new knowledge might further enable clinicians to increase their genetic screening for anterior segment related diseases and treatment of ocular diseases such as glaucoma.

CONTROL ID: 3542167

SUBMITTER (NAME ONLY): Ariela Gordon-Shaag

TITLE: Ethnic differences in the prevalence of myopia in Israeli college students

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gordon-Shaag, R. Doron, E. Shneor, Dept. of Optometry, Hadassah Academic College, Jerusalem, Jerusalem, ISRAEL|L.A. Ostrin, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetics, as well as behavioral factors, such as near work and light exposure, are known to play a role in the etiology of myopia. Education is often used as a proxy for near work, with more educated populations showing a higher prevalence of myopia. Two distinct ethnic populations, Jews and Arabs, study at Israeli colleges. Given that all students are admitted on similar criteria, educational background of these populations is believed to be comparable. This study aimed to assess the prevalence of myopia in college students in Jerusalem and to determine its association with gender and ethnicity (Jew or Arab).

Methods: First year college students (from 2011-2019) underwent a vision screening that included non-cycloplegic auto-refraction (Luneau L80 or VX130) and a questionnaire to assess age, gender, and ethnicity. Students who had undergone refractive surgery were excluded. Myopia was defined as spherical equivalent ≤ -0.50 D and high myopia as ≤ -6.00 D. Prevalence and 95% confidence interval (CI) were calculated, and groups were compared using Chi-square or Fisher test. Odds ratio to evaluate risk factors were calculated.

Results: The study included 807 students (652 women, 377 Jews) with a mean age of 22.1 ± 2.6 (range: 17-30) and mean spherical equivalent of -1.7 ± 2.2 (range: -13.3-+5.7). The prevalence of myopia and high myopia were 66.3% (95% CI: 63.0-69.6%) and 4.6% (95% CI: 4.4-4.8%), respectively. Women had significantly higher prevalence of myopia than men (68.1% vs. 58.7%, $p < 0.03$), but not of high myopia (5.1% vs. 2.6%, $p = 0.28$). Jewish students had significantly higher prevalence of myopia (69.2% vs. 60.3%, $p < 0.02$) and high myopia (5.9% vs. 1.9%, $p < 0.02$) than Arab students. Female gender emerged as a risk factor for myopia (OR=1.54, 95% CI 1.07-2.21, $p < 0.02$), but not for high myopia. Jewish ethnicity emerged as a risk factor for both myopia and high myopia (OR=1.51, 95% CI 1.11-2.05, $p < 0.01$ and OR=3.52, 95% CI 1.35-9.19, $p < 0.01$, respectively).

Conclusions: The prevalence of myopia, approximately 66%, in college students in Israel is higher than the global average. Jewish ethnicity, compared to Arab ethnicity, was a risk factor for myopia and high myopia in this population. As all students had a similar academic background, findings suggest that genetic factors play a role in the refractive differences between Arabs and Jews.

CONTROL ID: 3542168

SUBMITTER (NAME ONLY): Bernardo Lopes

TITLE: A New Method to Describe Cone Shape in Keratoconic Corneas

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.T. Lopes, A. Abass, A. Eliasy, H. Zhang, A. Elsheikh, University of Liverpool, Liverpool, Merseyside, UNITED KINGDOM|H. Zhang, School of Biomedical Engineering, Capital Medical University, Beijing, CHINA|A. Elsheikh, NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To introduce and validate a novel method to describe the cone features in keratoconic corneas.

Methods: Corneal anterior and posterior surfaces were described using a spherical coordinate system to generate a new spherical height map to allow the detection of the cone apex. Cone boundaries were objectively estimated using second derivatives of spherical height in an iterative process. Corneal topography exams of 309 keratoconic patients with different disease severities were evaluated with the new automated method as its first validation. In addition, 12 cornea specialists blindly evaluated the tangential and elevation maps relative to the best-fit sphere of 6 patients. Their estimations were cross-checked and compared with the results of the new automated method in order to evaluate the subjective variability and provide a second validation of the method.

Results:

The main cone features in the anterior and posterior surfaces were evaluated in the large clinical dataset. There was strong correlation between the cone height and the disease severity in both surfaces ($R=0.71$, $p<0.01$), while the disease stage did not show significant correlation with cone area in any of the surfaces ($R=0.01$, $p=0.77$). The height of the posterior cone was, on average, larger than the corresponding anterior cone height by $37 \pm 24 \mu\text{m}$ (0–158). In relation to the experts' assessment, there was high inter-subject variability, up to 55%, among experts' estimations of the cone area and low intra-subject agreement in cone apex location using different maps ($p<0.05$). However, there was no statistically significant difference between the automated estimation and the specialists' estimations in both maps ($p>0.05$). The cone boundaries estimated by the automated method were within the range of the specialists' estimations in all cases.

Conclusions:

An objective automated method able to determine the cone's 3D features was developed and validated in a large clinical dataset and against worldwide corneal specialists' estimations. The method's results were in agreement with disease severity and independent of the subject variability observed among different experts. The objective method provided a reliable and unique evaluation of keratoconus features that is independent of maps' type or color-scale.

CONTROL ID: 3542171

SUBMITTER (NAME ONLY): Fang Chai

TITLE: Regulatory role of GRP78 in oxidative stress of Trabecular meshwork cells induced by tunicamycin

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Chai, XIAN FOUTH HOSPITAL, XIAN, CHINA|

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ABSTRACT BODY:

Purpose: To clarify the regulatory effect of tunicamycin on endoplasmic reticulum stress by affecting GRP-78

Methods: In this study, the endoplasmic reticulum stress model of trabecular reticulum cells (HTMC and GTM3) was established by tunicamycin, and the cells were treated with GRP78. The morphological changes of cells were observed by electron microscope, apoptosis and ROS content were detected by flow cytometry, and the expression of GRP78, PERK-eIF2a-ATF4/CHOP signal pathway and apoptosis-related proteins were detected.

Results: Tunicamycin could significantly increase the content of ROS in HTMC and GTM3 and increase the rate of apoptosis. The determination of calcium concentration in cells showed that tunicamycin could increase the flow of calcium ions in cells. Tunicamycin can increase the expression of GRP78,IP3R,ATF4,PERK,sXBP1,eIF2a,CHOP,PDI-1. Overexpression of GRP78 can protect cells during stress and reduce the rate of apoptosis. And Co-IP test shows that there is a direct binding effect between GRP78 and eIF2. It is suggested that GRP78 may play a regulatory role by regulating eIF2.

Conclusions: This study proves that tunicamycin can induce oxidative stress in trabecular meshwork cells, and the increase of GRP78 expression can protect cells during stress, and GRP78 may play a protective role by regulating eIF2.

CONTROL ID: 3542181

SUBMITTER (NAME ONLY): Sheldon Rowan

TITLE: Manipulation of Gut Microbiota Affects Diet- and Age-Related Retinal Degeneration

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Rowan, S. Francisco, C. Tsai, K. Barger, D. Smith, A. Taylor, K.M. Smith, JM-USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts, UNITED STATES|S. Rowan, A. Taylor, Dept. of Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|C. Zhou, E.I. Paschalis, Dept. of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diet has an important role in risk for age-related eye diseases, including AMD and diabetic retinopathy. Humans that adhere to Western and high glycemic index dietary patterns have increased risk for AMD. We have previously shown that aged mice that consumed high glycemic (HG) diets developed AMD-like retinopathy that could be prevented by a low glycemic (LG) diet. We also showed a role for gut microbiota in mediating protection by a LG diet, which we coined the gut-retina axis. Altered gut microbiota have also been associated with human AMD, but experimental evidence and mechanisms for this association are lacking.

Methods: 12-month male C57BL/6J mice were fed HG and LG diets for 12-months. Gut microbiota were manipulated either by continuous oral antibiotic ablation of commensal bacteria (Ampicillin + Neomycin) or via weekly fecal microbiota transplants from mice consuming opposite diets. Eye health was evaluated using fundus imaging and angiography, immunohistochemical detection of retinal microglial/macrophages, histology, and electron microscopy of the RPE. Bacterial 16S rRNA sequencing was used to determine the fecal microbiome composition.

Results: Mice that consumed HG diets developed multiple retinal lesions, consistent with greater retinal damage scores. There were fewer lesions in mice consuming LG diet, or in HG-fed mice receiving fecal transplants from LG mice. Lesions were associated with infiltration of retinal microglia/macrophages in the choroid and outer retina. Ablation of commensal microbiota was associated with retinal and RPE degeneration in some mice. Microbiome analysis revealed that retinal neuroprotection was associated with increased levels of Akkermansia, a commensal bacteria with known beneficial metabolic functions. HG-fed mice receiving LG fecal microbiota transplants also had improved glycemic control relative to HG-fed mice.

Conclusions: Our studies confirm previously observed roles for commensal gut microbiota in mediating protection against diet-induced AMD. Importantly, these protective effects could be transferred via fecal microbiota transplantation, indicating that microbiome-based therapies have therapeutic potential for AMD. Neuroprotection was associated with improved glycemic control, suggesting that metabolic reprogramming may be a critical component of the gut-retina axis, possibly via modulation of innate immune system function.

CONTROL ID: 3542198

SUBMITTER (NAME ONLY): Sudhir Ranganath

TITLE: Hypothermia breaks down the barrier function of the corneal endothelium

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.H. Ranganath, M. Thanuja, M. T D, Chemical Engineering, Siddaganga Institute of Technology, Tumkur, Karnataka, INDIA|S.P. Srinivas, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: The donor corneal endothelium (CE) is exposed to hypothermia during cold storage, which is inevitable before transplantation. Here, we have examined the impact of hypothermia on the barrier function of CE with a goal to enhance the success of corneal transplantation.

Methods: Primary cultures of porcine CE or freshly isolated porcine corneas were employed for the experiments. Since hypothermia is known to cause microtubule (MT) disassembly, which causes a breakdown of barrier integrity in CE (Srinivas, EER, 2012), we immunostained and imaged MT and ZO-1 with and without prior exposure to epothilone B (a microtubule-stabilizing agent; EpoB). To ensure sustained intracellular levels of the agent, we also formulated EpoB-loaded PLGA nanoparticles (ENPs; coated with poly-L-lysine; zeta potential 25 mV). ENPs were spherical ($\sim 95 \pm 10$ nm) with a drug entrapment efficiency of 91% and drug loading of 5% (w/w). The ENPs showed a burst release of EpoB, but the subsequent slow release phase sustained for up to 4 weeks.

Results: An exposure to hypothermia (15 h; 4 °C) led to MT disassembly in cultured CE. The effect was also evident in CE cells associated with ex vivo corneas. Moreover, the impact was similar to that observed in response to TNF- α (20 ng/mL; 24 hrs). Exposure to EpoB (100 nM) or ENPs (0.25 mg/mL) for > 24 h induced MT stabilization with minimal toxicity and importantly opposed the hypothermia-induced MT disassembly. Prior exposure to SB-203580 (a p38 MAPK inhibitor; 20 μ M; 1 hr) reduced the hypothermia-induced MT disassembly. The effect of SB-203580 was similar to the inhibition of the response to TNF- α , which activates p38 MAPK (Srinivas, EER, 2012). Concomitant with the impact on MT, hypothermia led to a disruption of the contiguous ZO-1 at the cellular periphery (Fig. 1B; Fig. 1D shows response to TNF- α), indicating a loss of barrier integrity. However, pre-treatment with EpoB (Fig. 1C), ENPs, or SB-203580 opposed the ZO-1 disruption, indicating that MT disassembly underlies the hypothermia-induced breakdown of tight junctions.

Conclusions: Hypothermia induces MT disassembly via activation of p38 MAPK and subsequently breaks down the barrier function of CE. Sustained exposure to MT stabilizers overcomes the hypothermia-induced barrier failure. The ENPs could serve as a modality to obtain sustained protection of CE against hypothermia-induced stress and TNF- α -induced damage to MT in case of allograft rejection.

CONTROL ID: 3542200

SUBMITTER (NAME ONLY): Zhe Liu

TITLE: Ascertainment of Age-related Macular Degeneration (AMD) Status in the Second Carotenoids in Age-Related Eye Disease Study (CAREDS2), an Ancillary Study of the Women's Health Initiative (WHI)

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Liu, A. Domalpally, B. Blodi, Y. Liu, C. Hurtenbach, J.A. Mares, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|S. Bailey, J. Maykoski, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K.M. Gehrs, Department of Ophthalmology and Visual Sciences, The University of Iowa, Iowa City, Iowa, UNITED STATES|R. Gangnon, Department of Population Health Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|K. Wood, Ocular Services On Demand, Madison, Wisconsin, UNITED STATES|T. Lawler, Department of Nutritional Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|R.B. Wallace, Department of Epidemiology, The University of Iowa, Iowa City, Iowa, UNITED STATES|L. Tinker, Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES|C. Blomme, Prevention Services, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: We report a multi-pronged strategy for ascertaining AMD status in the CAREDS cohort and the prevalence of AMD in CAREDS2 (2016-2019).

Methods: AMD was assessed in CAREDS1 (2001-2004), primarily, from stereoscopic fundus photographs, among 2,005 women aged 53 to 86 years, who attended three study centers in the U.S. (Iowa, Oregon, and Wisconsin). Fifteen years later, in CAREDS2 639 women had died, and surviving women resided in 21 states, requiring updated protocols to assess AMD presence and severity. In CAREDS2 we ascertained AMD in 697 women who either participated in person (487), or by mail (198), or whose AMD status could be additionally assessed from Medicare billing records accessed via the WHI Virtual Data Enclave (12). A multipronged approach was used to reconcile AMD status for each woman, integrating AMD features from: 1) graded stereoscopic fundus photos taken in study visits, or by providers according to study specification, 2) spectral domain-optical coherence tomography (SD-OCT), 3) AMD features abstracted from medical records or questionnaires completed by providers, and from 4) International Classification of Diagnoses-10 codes for AMD in Medicare billing records.

Results: In CAREDS2, participants aged 69 to 101 years, intermediate AMD (n=135) or late AMD (n=38) were identified from fundus photographs. SD-OCT captured an additional 55 women with intermediate AMD (large or reticular pseudodrusen or nascent geographic atrophy). Further capture of AMD outcomes from participants' eyecare providers, either directly or via ICD-10 AMD diagnoses, increased the prevalence of documented clinically significant AMD by an additional 27 cases, for a total of 255 cases. Overall, 37% of women had either intermediate (n=202) or late AMD (n=53). The prevalence of clinically significant AMD (intermediate or late), by age tertile, was 30%, 44%, and 61%, in women <78, 73-83, and >83 years old, respectively.

Conclusions: The multi-pronged approach to ascertaining AMD prevalence, maximizes capture of clinically significant AMD outcomes, which steeply increased in prevalence with age in older women.

CONTROL ID: 3542203

SUBMITTER (NAME ONLY): Sam Kushner-Lenhoff

TITLE: Capillary Flow Characteristics Vary with Hematocrit on SS-OCTA

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kushner-Lenhoff, X. Jiang, Ophthalmology, USC Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|A.H. Kashani, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|Y. Li, Q. Zhang, R.K. Wang, Bioengineering and Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the associations of capillary density and flow with hematocrit, blood pressure and medical comorbidities using OCTA.

Methods: A cross-sectional study using 3 x 3 mm SS-OCTA images to measure vessel skeleton density (VSD) and flow (flux) in the superficial retinal layer (SRL). Flux is a relatively new measure that approximates the number of red blood cells moving through a vessel segment per unit time. Complete blood count, blood pressure, self-reported/medical-record based history including diabetes status, hypertension status, hypertensive medication use, cigarette smoking and retinopathy status (including edema) were obtained. A generalized linear mixed-effects model was used to evaluate the relationship with OCTA parameters after considering the correlation between eyes. Least-square means were estimated.

Results: A total of 154 eyes from 83 participants [56 women and 27 men, mean [SD] age, 66.2 (8.9) years, 22 with diabetes, 63 with hypertension] were included. Mean VSD was 0.147 ± 0.009 and mean flux was 0.156 ± 0.016 . VSD showed a negative correlation with age ($p=.001$) and retinopathy ($p=.016$), but no significant correlation with hematocrit ($p=.86$) or signal strength ($p=.51$). Flux showed a positive correlation with hematocrit ($p = .006$) and signal strength ($p<.001$), as well as a negative correlation with age ($p=.005$) and diabetes status ($p=.050$). These associations remained even after accounting for hypertensive status, and smoking status. Mean flux was 0.010 lower in OCTA scans with a signal strength of 9 compared with those with a strength of 10, and 0.006 lower for the following comparisons: participants age 65 and above with younger participants, participants having hematocrit of less than 40% with those having higher hematocrit, and diabetics with non-diabetics. A one percent decrease in hematocrit was approximately equivalent to 1.8 years of aging in its effect on the calculated flux.

Conclusions: Retinal blood flow is independently affected by hematocrit and diabetes status even when accounting for known determinants of capillary density such as age and retinopathy status. This effect by hematocrit is not found in OCTA measurements of vessel skeletal density.

CONTROL ID: 3542204

SUBMITTER (NAME ONLY): Tao Liu

TITLE: High-resolution imaging of cone photoreceptors and retinal pigment epithelial cells in Chediak-Higashi Syndrome

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Liu, N. Aguilera, A.J. Bower, J. Liu, L.A. Huryn, W.M. Zein, R.B. Hufnagel, B.P. Brooks, J. Tam, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|W.J. Introne, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chediak-Higashi Syndrome (CHS) is a rare inherited disorder with ophthalmological manifestations that include reduced pigmentation and foveal hypoplasia. We characterized the status of cone photoreceptor and retinal pigment epithelial (RPE) cells in CHS in comparison with foveal hypoplasia arising from oculocutaneous albinism type 1 (OCA1) and Waardenburg syndrome type 2A (WS2A).

Methods: Patients were recruited for high resolution retinal imaging (CHS, 2 eyes from 2 patients; OCA1, 3 eyes from 3 patients; WS2A, 6 eyes from 3 patients). Adaptive optics (AO) imaging was performed from which measurements of cone density (all eyes) and RPE cell-to-cell spacing (CHS and OCA1, 5 eyes from 5 patients) were obtained over a range of retinal eccentricities from the fovea out to ~5 mm. Foveal hypoplasia grades were assigned according to optical coherence tomography (Ophthalmology 118:1653–1660, 2011) and compared to peak cone density wherever possible.

Results: There was considerable variation in the number of cones and RPE cells near the fovea as observed using AO. Cone density near the fovea (eccentricity < 1 mm) was reduced inversely with the foveal hypoplasia grade (IOVS 55:4186-4198, 2014) which ranged from 1 to 3 (lower peak cone densities seen in higher foveal hypoplasia grades). At larger eccentricities, cone densities were mostly normal, with no apparent differences observed between CHS, OCA1, WS2A, or published normative data. RPE cells in CHS imaged using AO-ICG (IOVS 57:4376-4384, 2016) exhibited the characteristic heterogeneous fluorescence signal, similar to OCA1 and healthy controls. RPE cell spacing near the fovea was variable (either within normal ranges or slightly enlarged), with no apparent differences between CHS and OCA1. At larger eccentricities, RPE cell spacing appeared to be normal.

Conclusions: Our preliminary data shows the in vivo status of cone photoreceptors and RPE cells suggesting that foveal hypoplasia associated with CHS, OCA1, and WS2A result in anatomically consistent reductions in peak cone density pursuant to the degree of hypoplasia. Although impacted to a lesser degree, the RPE cells may also play a role in foveal specialization. Additional patients are needed to further explore these findings.

CONTROL ID: 3542217

SUBMITTER (NAME ONLY): Jan Skerswetat

TITLE: The effect of visual feedback on perceptual and oculomotor performance in a gaze-contingent simulated scotoma paradigm

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Skerswetat, A. Sharma, H. Jefferis, K. Costa, T. Arango, P. Bex, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|N.C. Ross, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gaze-contingent simulated scotomas have been used in normally-sighted individuals to mimic central vision loss (CVL) and to study perceptual and ocular-motoric processes. We investigated the effect of visual feedback on eccentric viewing training assessed with fixation stability (Bivariate Contour Ellipse Areas, BCEAs), contrast sensitivity (CS) Area-Under-the-Curve (AUC) and acuity (highest visible spatial-frequency).

Methods:

Performance was measured in phases of 25-50 CS trials/session (≥ 25 correct) in which participants used their peripheral vision to identify 26AFC band-pass-filtered letters. An adaptive algorithm controlled spatial frequency and contrast of the letters. A gaze-contingent binocular scotoma simulated 6° or 9° CVL. Baseline learning (n=8) was measured in six free-viewing trials. Two separate four-phase-protocols investigated two types of visual feedback (target cue, n=10; and scotoma boundary, n=8) across fixation eccentricity and orientation. One freeview session at the start (Phase1) and end (Phase4), and four counterbalanced orientation (eight 45° steps) and eccentricity (6° or 9°) cued sessions with (Phase3) and without (Phase2) visual feedback were performed. Feedback employed letter-surrounding dots (Target-cue) or a scotoma-surrounding ring (scotoma boundary).

Results: Linear regression models identified a significant increase in Acuity ($p < 0.01$) and AUC ($p < 0.01$) and a non-significant trend of BCEAs reduction during baseline. Pre-trial cueing and both feedback types significantly reduced BCEAs ($p < 0.05$) and improved eccentricity-dependent acuity ($p < 0.05$), while AUC results were mixed. Eccentricity-dependent learning was retained in Phase 4 ($p < 0.05$).

Conclusions: Eccentric fixation training delivers sustained functional benefits through both oculomotoric and perceptual learning. The current findings may be transferable into rehabilitation of CVL patients.

CONTROL ID: 3542219

SUBMITTER (NAME ONLY): Kevin Emmerich

TITLE: Dendrimer-targeted immunosuppression of microglia reactivity super-accelerates photoreceptor regeneration kinetics in the zebrafish retina

SESSION TITLE: Microglia and other Macrophages in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Emmerich, J.S. Mumm, 1.McKusick-Nathans Institute of the Department of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|K. Emmerich, D.T. White, S.P. Kambhampati, G.Y. Lee, A. Sahoo, M.T. Saxena, R.M. Kannan, J.S. Mumm, 2.Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|S.P. Kambhampati, R.M. Kannan, The Center for Nanomedicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|T. Fu, E. Betzig, Howard Hughes Medical Institute - Janelia Farm Research Campus, Ashburn, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously showed that microglia are key regulators of retinal regeneration in zebrafish. Microglia reactivity to induced rod photoreceptor death stimulates Müller glia to mount a regenerative response. Ablating microglia or suppressing microglia reactivity with dexamethasone (Dex) prior to induction of cell death inhibited regeneration. However, suppressing microglia reactivity after induction of rod death enhanced regeneration kinetics. These data support the concept that microglia play stage-dependent roles during retinal regeneration and that immunosuppression could be a viable therapeutic approach for promoting repair in retinal degenerative disease. Here, we used intravital time-lapse imaging to investigate how post-injury Dex treatment altered microglia reactivity. We also tested what effect targeted delivery of Dex to reactive immune cells following induction of rod cell death had on regeneration kinetics.

Methods: Metronidazole (Mtz) induced rod cell death was enabled by a transgenic line expressing bacterial nitroreductase (NTR) and a fluorescent reporter in rod photoreceptors. A novel intravital imaging technique, Adaptive Optics-Lattice Light Sheet Microscopy (AO-LLSM), was used to capture fast subcellular dynamics of microglia. Imaris was used to quantify aspects of microglia behavior during regeneration \pm Dex. Dendrimer conjugated Dex (Dendrimer-Dex) was evaluated for effects on rod cell regeneration kinetics using an established plate reader assay.

Results: AO-LLSM time-lapse imaging showed that post-injury Dex represses reactivity to rod cell death by reducing the speed of microglia migration rather than altering morphology (sphericity). Compared to free Dex controls, Dendrimer-Dex formulations led to: 1) reduced toxicity, 2) targeted delivery of Dex to reactive microglia, and 3) a further enhancement of regeneration kinetics, from +33% (free Dex controls) to +67% (Dendrimer-Dex treated fish).

Conclusions: These results increase our understanding of the roles microglia play during retinal regeneration and advance the therapeutic potential of immune suppressing drugs and dendrimer-based immune cell targeting in retinal disease settings.

CONTROL ID: 3542221

SUBMITTER (NAME ONLY): Amber Wilkerson

TITLE: Sterol O-acyltransferase 1 (Soat1) is critical for cholesteryl ester production in mouse Meibomian glands

SESSION TITLE: Lacrimal gland and Meibomian gland

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Wilkerson, S. Yuksel, I.A. Butovich, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|I.A. Butovich, The Graduate School of Biomedical Sciences, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cholesteryl esters (CE) are the second most abundant class of lipids produced by the Meibomian glands (MG). The Soat1 gene is encoding a SOAT1 enzyme that is responsible for the formation of cholesteryl esters (CE) from cholesterol (Chl) and fatty acids, and is highly expressed in MG of humans and mice. The purpose of this study was to determine the impact of Soat1 ablation on meibum composition and the homeostasis of the ocular surface and adnexa in mice.

Methods: The ocular surface of 2- to 4-month old male and female knockout (Soat1^{-/-}) and wild-type (WT) mice was assessed via a slit lamp. Their eye geometry was evaluated. Phenol red thread test was used to assess tear production. Tarsal plate (TP) anatomy was evaluated by hematoxylin and eosin staining. Lipid profiling was conducted by liquid chromatography and mass spectrometry (LC/MS). Melting temperature of meibum (T_m) was measured by hot stage cross-polarized light microscopy (HSPLM).

Results: Soat1^{-/-} had noticeably smaller, slit-eye openings (p= <0.001) when compared with WT mice. Slit lamp examination of Soat1^{-/-} mice revealed thick meibum accumulations and meibum protrusions from the MG orifices. Tear production was increased in Soat1^{-/-} mice (p=0.002). Excised TP of Soat1^{-/-} mice had visible MG, central ducts and connecting ductules, but lacked discernible acini. The histology displayed abnormal acini and dilated central ducts. Lipid profiling of Soat1^{-/-} meibum revealed an upsurge of free Chl (reaching 30% of all MG lipids) and an almost complete loss of CE. HSPLM experiments revealed that Soat1^{-/-} meibum had highly elevated T_m: only half of lipids melted at 50°C, requiring temperatures in excess of 100°C to be completely melted. WT meibum melts 50% at 34°C and 100% at 50°C.

Conclusions: Soat1 is essential for the conversion of free Chl into CE in the MG. The increased Chl and lack of CE had detrimental effects on the physical and biochemical properties of meibum leading to an abnormal ocular phenotype. The changes in meibum and the ocular phenotype resemble characteristic signs of MG dysfunction in humans and demonstrate the importance of Soat1 in MG lipid homeostasis.

CONTROL ID: 3542226

SUBMITTER (NAME ONLY): Zhiyi Cao

TITLE: Galectin-3 Inhibition by a Small-Molecule Inhibitor Downregulates Fibrosis-Related Genes and Signaling Pathways in a Mouse Model of Corneal Fibrosis

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Cao, A. Ramadan, N.A. Panjwani, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|F. Zetterberg, Galecto Biotech AB, Gothenberg, SWEDEN|

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ABSTRACT BODY:

Purpose: Previously, studies in our Lab have shown that the treatment with a galectin-3 inhibitor, GB1265, reduces corneal fibrosis. To detect the impact of GB1265 treatment specifically on fibrosis-related genes, we analyzed differentially expressed genes by Nanostring technology using the fibrosis panel.

Methods: Corneal fibrosis was induced by alkali-burn injury in C57B/6 mice. Vehicle alone or GB1265 (10µl of 10mg/ml in vehicle) were topically applied to the eye twice per day from day 1 until day 14. Corneal opacity was scored by slit lamp examination at day 7 and 14 post-injury. On day 14, corneas were harvested, isolated RNA was processed for Nanostring analysis using a mouse fibrosis panel that profiles 770 genes across 51 annotated pathways. Differentially expressed genes were analyzed using nCounter gene expression platform analysis. Subset of genes involved in fibrosis pathway were confirmed by Q-PCR and immunohistochemical staining.

Results: Of the 770 genes in the panel, 230 genes were not expressed above background, 9 genes were not expressed in all replicates (n = 3), 128 genes were not affected by GB1265 treatment. Of the remaining 540 genes, 11.5% were differentially expressed in GB1265-treated corneas compared to vehicle-treated corneas (fold change >2.0; false discovery rate q <0.05). Of the 55 differentially expressed genes in the inhibitor treated group, 52 were downregulated, and 3 were upregulated. MMP-9 and -12, Collagen I and V, LOXL-1 and -2 and Itgb3 were among the significantly downregulated genes. Pathway analysis of differentially expressed genes revealed that three fibrosis-related pathways i.e. TGFβ pathway, Th17 differentiation, and collagen biosynthesis were downregulated whereas none of the pathways were upregulated in the GB1265-treated corneas.

Conclusions: Our data indicated that galectin-3 inhibitor plays an important role in reducing corneal fibrosis by downregulating fibrosis-related genes in the corneas treated with GB1265. This leads us to conclude that GB1265 is an effective galectin-3 inhibitor and could be a potential candidate for developing a new drug to halt the progression of fibrosis after injury.

CONTROL ID: 3542228

SUBMITTER (NAME ONLY): Junaid Bhatti

TITLE: Complementary and Alternative Medicine for Glaucoma in Social Media

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Bhatti, R. Swamy, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|M. Kaleem, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Social media has been increasingly utilized by both patients and providers to receive and deliver medical information. The lack of regulation of posts pose a threat of misinformation, making monitoring social media platforms a necessity. In this project we performed a cross-sectional study surveying social media content regarding Complementary and Alternative Medicine (CAM) and its usage for glaucoma.

Methods: Social media posts from Twitter and Facebook were analyzed using a systematic approach. Specific search queries with multiple hashtags were used to identify top posts over the past 10 years for popular CAM types. Descriptive and quantitative information were collected for each post, including account type, credibility, tone, among others. Data was collected using a standardized online form and was organized into spreadsheets which were used for further analysis.

Results: Overall, the data showed most posts to be general discussion (42.9%), article presentation (21.2%), and promotional (14.7%). The majority of posts were by companies (40.4%), medical professionals (32.0%), and unaffiliated individuals (17.9%), with variation between CAM types.

Most posts had no article references (61.5%), while fewer had non peer-reviewed (24.4%) and peer-reviewed (14.1%) articles cited. Posts with peer-reviewed articles were mainly by medical professionals (59.1%). Posts without citations were mainly by companies (42.7%).

Ophthalmologists mostly had article presentation posts (50.0%). Companies mostly had either general discussion posts (46.0%) or promotional material (20.6%), with the majority not referencing articles (65.1%).

Facebook had a higher proportion of medical professionals compared to Twitter (49.2% vs 19.8%). More articles were referenced in Twitter (46.2% vs 27.7%); however, Facebook had the higher portion of peer-reviewed articles (18.5% vs 11.0%).

Conclusions: Patients should be cautious about information they gain on social media as a lack of credibility and financial intentions make many posts, specifically promotional material from companies, potential sources of misinformation. Medical professionals have reliable posts with article citations, however, also tend to have a smaller social media engagement. The results of this study can help educate ophthalmologists and other eye care providers about the source and type of information being presented to their patients on CAM and can counsel their patients accordingly.

CONTROL ID: 3542230

SUBMITTER (NAME ONLY): Maria del Mar Schilt-Catafal

TITLE: QUANTITATIVE ANALYSIS OF THE THREE MACULAR CAPILLARY PLEXUSES IN OPEN ANGLE GLAUCOMA AND OCULAR HYPERTENSION USING OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY (OCTA)

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schilt-Catafal, V. Pérez-Torregrosa, A. Duch-Samper, Ophthalmology Department, Hospital Clínic Universitari de València, València, València, SPAIN|A. Duch-Samper, Associated Professor, Universitat de Valencia, València, València, SPAIN|

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ABSTRACT BODY:

Purpose: A decrease in macular vessel density (VD) has been described in glaucoma eyes (GE). This study aims to investigate whether VD changes occur in all three macular capillary plexuses in GE and in ocular hypertension eyes (OHE).

Methods: A prospective observational study was performed with 111 open-angle GE, 107 OHE and 106 gender-age matched control eyes (CE). Macula was imaged with a 6x6mm scan using DRI-OCT Triton (Topcon), and VD was automatically defined by OCTARA algorithm. Statistical analysis was performed using Kruskal-Wallis Test, Bonferroni Post Hoc analysis and Spearman rank correlation.

Results: Superficial capillary plexus (SCP) VD in GE was lower than OHE and CE (-4,93% and -10,20%), being the temporal sector the most affected. Deep capillary plexus (DCP) VD in GE was lower than OHE and CE (-4,05% and -10,21%), being the nasal sector the most affected. In OHE, SCP and DCP VD was also lower than CE (-5,54% and -6,41%). Choriocapillaris plexus (CCP) VD in GE was lower than OHE and CE (-1,7% and -1,1%), being the nasal sector the most affected ($p<0.01$ for all pairwise comparisons). However, CCP VD in OHE was not significantly different than CE ($p=0,119$).

Correlation analysis showed that SCP VD was low positive correlated with ganglion cell layer thickness (GCL) ($r=+0,366$) and moderate positive correlated with visual field mean deviation (VFMD) ($r=+0,597$), being the superior and the inferior sectors the most correlated ones. DCP VD was negligible correlated with GCL ($r=+0,149$) and low positive correlated with VFMD ($r=+0,303$). The correlation between CCP VD and VFMD was low positive ($r=+0,287$) ($p<0,01$ for all), however the correlation with GCL was not statistically significant ($p=0,59$).

Conclusions: In GE and OHE, the decrease of macular VD can be visualized in both SCP and DCP. However, decreased VD in CCP can only be objectivized in GE. This finding suggests that the vascular damage may occur concurrently among the three plexuses; but at initial phases of the disease, vascular abnormalities may occur specially at the SCP and DCP. Eventually, the SCP VD resulted to be correlated with GCL and VFMD. Therefore, quantitative OCTA may have value in the future to evaluate or follow up GE and OHE. Nevertheless, further research is needed to obtain stronger results.

CONTROL ID: 3542233

SUBMITTER (NAME ONLY): Madeline Sparks

TITLE: Pediatric Rhegmatogenous Retinal Detachments: Etiologies, Clinical Course, & Surgical Outcomes

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sparks, The University of Texas Southwestern Medical Center Medical School, Dallas, Texas, UNITED STATES|P. Davila, Y. He, A. Wang, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|Y. He, A. Wang, Children's Health Children's Medical Center Dallas, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pediatric rhegmatogenous retinal detachments (RRD) make up a small percentage of all retinal detachments and typically present late with poor visual outcomes. We performed a retrospective clinical study to better characterize the predisposing factors, clinical course, surgical methods, and outcomes of pediatric RRD at a major children's hospital in Dallas.

Methods: We performed an IRB-approved, retrospective review of data for patients under 18 years old who underwent surgical repair for RRD from January 1, 2004 to December 31, 2019. Exclusion criteria included a history of retinoblastoma, the presence of persistent fetal vasculature or active retinopathy of prematurity, and those who had follow-up of less than 6 months. Patient's age, race, gender, laterality, etiology, risk factors, presenting symptoms, fellow eye findings, exam findings at diagnosis, type and location of break, presence or absence of proliferative vitreoretinopathy (PVR), surgical procedures, post-op complications, initial and final best corrected visual acuities, and anatomic success were recorded.

Results: A total of 93 eyes of 87 patients were included. The majority of the patients were male (n = 65; 74.7%) and the median age was 11 (+/- 4.25) years. 90.3% of eyes had at least one predisposing factor of pediatric RRD, including prior ocular surgery (n = 49, 52.7%), trauma (n= 44, 47.3%), myopia (n=35, 37.6%), and congenital anomaly (n=19, 20.4%). 58% of eyes had greater than one predisposing factor. 78.4% (n=73) had macula-off detachments and 36.6% (n=34) had PVR grade C or worse at the time of presentation. 52.7% (n=49) achieved anatomic success after the first operation. Overall, 71.0% (n=66) achieved anatomic success after their final surgery.

Conclusions: The majority of the cases of pediatric RRD in this study are associated with the risk factors of congenital/developmental anomalies, myopia, trauma, or previous ocular surgery. Pediatric patients with RRD often present late as shown by the high incidence of macula-off detachments, as well as the presence PVR Grade C or worse. The majority of patients were able to achieve anatomic success after surgical repair using scleral buckle and/or vitrectomy.

CONTROL ID: 3542238

SUBMITTER (NAME ONLY): Ajay Kuriyan

TITLE: Intravitreal HC-HA/PTX3, a soluble matrix component of amniotic membrane, inhibits proliferative vitreoretinopathy (PVR) in a mouse model of PVR

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Kuriyan, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|A.E. Kuriyan, A. Heffer, V. Wang, S.E. Feldon, R.T. Libby, C. Woeller, Flaum Eye Institute, University of Rochester Medical Center, Rochester, New York, UNITED STATES|H. He, M. Mahabole, S.C. Tseng, Tissue Tech Inc., Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) occurs in 10% of retinal detachments and is the most common cause of failure of retinal detachment surgery. There are currently no approved treatments for inhibiting PVR. We studied the ability of intravitreal HC-HA/PTX3, a soluble matrix component of amniotic membrane, to inhibit PVR in a mouse model. Additionally, we assessed the safety of intravitreal HC-HA/PTX3 on the mouse retina.

Methods: PVR was induced in 38 control and 43 treatment eyes of 6-8 week old female C57BL/6J mice. A posterior vitreous detachment was induced by intravitreal injection of 0.5µL SF₆ gas. One week later, immediately prior to injection, freshly harvested ARPE-19 cells (immortalized retinal pigment epithelial cells [RPE]) were mixed with PBS alone (control) or PBS with HC-HA/PTX3 to yield solutions containing 2×10^4 RPE cells and 0.15 (n=15), 0.30 (n=15), or 0.6 (n=13) µg/ml HC-HA/PTX3 per microliter. 1µL of the solution was injected intravitreally and weekly fundus photos were used to grade PVR development for 4 weeks. Additionally, mice received intravitreal injection of PBS (n=2) or 0.6 µg/ml HC-HA/PTX3 (n=5) and ERG a- and b-wave amplitudes compared after 4 weeks to assess safety. Mann-Whitney U test was used to compare PVR grades.

Results: After 4 weeks, eyes injected with RPE/PBS (control mice) developed a mean PVR grade of 2.75 out of 6 (SD: 1.35), which was significantly higher than mice treated with intravitreal 0.6 µg/ml HC-HA/PTX3 (1.77, SD: 0.73, p = 0.018). The difference in PVR grade compared to control mice approached statistical significance in mice treated with intravitreal 0.3 µg/ml HC-HA/PTX3 (1.93, SD: 1.16, p = 0.062) and was not significantly different compared to mice treated with intravitreal 0.15 µg/ml HC-HA/PTX3 (2.93, SD: 1.44, p = 0.803). There was no difference in a or b wave ERG amplitudes after 4 weeks in mice treated with intravitreal PBS or 0.6 µg/ml HC-HA/PTX3.

Conclusions: Intravitreal HC-HA/PTX3 (0.6 µg/ml) inhibits PVR in a pre-clinical mouse model without any deleterious effects on ERG amplitude measurement.

CONTROL ID: 3542241

SUBMITTER (NAME ONLY): MD Imam Uddin

TITLE: Quantitative and Qualitative Analysis of Retinal Hypoxia in a Mouse Model of Retinal Artery Occlusion (RAO)

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Uddin, S. Jamal, G.W. McCollum, J.S. Penn, Ophthalmology, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: To demonstrate the quantitative and qualitative analysis of tissue hypoxia from a single retinal artery occlusion (RAO). Also, to demonstrate the utility of HYPOX-4 for early detection of retinal hypoxia in RAO in real time.

Methods: A major retinal artery was occluded in mice using laser-induced retinal artery occlusion using Rose Bengal. Real time imaging of the retinal hypoxia was achieved using HYPOX-4, a molecular imaging probe developed in our laboratory. Pimonidazole-adduct immunostaining was used as an ex vivo method to characterize retinal hypoxia in RAO. Retinal vasculature was imaged using fluorescein angiography (FA) and IB4 staining. Retinal tissue morphology was evaluated using spectral domain OCT (SD-OCT).

Results: Retinal hypoxia was observed in a mouse model of RAO within few hours of laser-induced retinal artery occlusion in mice. We also observed that occlusion of an artery near the optic disk caused a 'pie-shaped' tissue hypoxia covering about $1/8^{\text{th}}$ of the entire retina. We also observed that occlusion of a vein in the same eye at about same distance from optic disk caused a 'cascade-shaped' tissue hypoxia covering about half of the entire retina (hemi-retinal ischemia). Retinal hypoxia was confirmed ex vivo using standard pimonidazole-adduct immunostaining method. Interestingly, we observed that the total hypoxic retina is about the same (~12% of the entire retina) from a single retinal artery occlusion compared to single retinal vein occlusion (RVO). This study provides the first quantitative and qualitative evidence of retinal hypoxia from single RAO and compared with single RVO in mice at early stage.

Conclusions: This study demonstrated the utility of a new hypoxia sensitive molecular imaging probe, HYPOX-4, to detect retinal hypoxia in RAO in real time at an early stage. This study also demonstrated that the pattern of tissue hypoxia is very different in RAO compared to RVO. Also, HYPOX-4 could be a powerful method to detect retinal hypoxia at an early stage that occurs in RAO and other vascular diseases.

CONTROL ID: 3542245

SUBMITTER (NAME ONLY): Pamela Capellan

TITLE: Myopic, Congenital, and Secondary Focal Choroidal Excavation Morphologic Phenotypes, Associations, and Prognostic Implications

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Capellan, L.A. Gonzalez, M. Mahrous, S. Weiss, B. Botsford, T. Lenis, M.C. Ryan, A. Orlin, T.D. Papakostas, S. Kiss, D.J. D'Amico, K.D. Kovacs, Department of Ophthalmology, Retina Service, Weill Cornell Medical College, New York, NY, Weill Cornell Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize and classify the morphological, clinical, and tomographic characteristics of focal choroidal excavation (FCE) lesions to determine their longitudinal prognostic implications.

Methods: Retrospective, consecutive case series of all patients with FCE who underwent ophthalmologic assessment with multimodal imaging including spectral domain optical coherence tomography (OCT) and fundus autofluorescence, with additional fluorescein, indocyanine, and OCT angiography as indicated. FCE was classified into three subtypes: Type 1 - myopic eyes with small FCE; Type 2 - FCE with larger "U" shape, presumed congenital lesions with no signs of other adjacent ocular pathology; and Type 3 - "V" shaped FCE associated with other chorioretinal pathology. Imaging characteristics, tomographic measurements, and clinical course (development of choroidal neovascular membrane (CNVM) and vision loss) were compared between types.

Results: The study included 36 eyes from 32 patients. 80.6% of eyes were followed longitudinally (26.8 ± 18.8 months). There were 9 Type 1 (myopic) FCE, 10 Type 2 (U-shaped, congenital) FCE, and 17 Type 3 (V-shaped, secondary) FCE. The mean FCE distance to the fovea was greatest in Type 1s ($1791.2 \pm 655.8 \mu\text{m}$) and shortest in Type 3s ($921.2 \pm 718.1 \mu\text{m}$), which was significantly different from each other ($p < 0.006$). The mean choroid thickness both under and adjacent to the FCE was greatest in Type 3s, whereas Type 2 lesions were found to be wider compared to other types. Type 3s were most commonly associated with central serous chorioretinopathy or pachyvessels (52.9%), but also were seen in pattern dystrophy, geographic atrophy, inactive choroiditis, torpedo maculopathy, and adult-onset vitelliform dystrophy. CNVM and breaks in Bruch's membrane was more prevalent in type 3 (41.2% compared with 11.1% for Type 1 and 0% for Type 2, which was significant).

Conclusions: FCE lesions from all three types demonstrated distinct morphological characteristics from one another. Morphological distinction held prognostic implications as type 3 lesions with V-shapes were all associated with other chorioretinal conditions and were more likely to also contain breaks in Bruch's membrane and develop CNVM during longitudinal follow-up. Further long-term analysis of each FCE type is warranted.

CONTROL ID: 3542247

SUBMITTER (NAME ONLY): Minjie Chen

TITLE: PEGylated TRAIL alleviates alkali burn induced rat corneal fibrosis by targeting DR5

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chen, H. Lin, S. Seo, S. Lee, S.C. Yiu, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|Y. Oh, S. Lee, D&D Pharmatech, Gaithersburg, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal fibrosis and neovascularization are inevitable outcome of corneal alkali burn injury. Here we determine whether TLY012, a PEGylated TNF-related apoptosis-inducing ligand (TRAILpeg) could provide preventive effects against corneal fibrosis through death receptor 5 (DR5) dependent pathway in a murine alkali burn model.

Methods: To induced corneal fibrosis, ten (10) Sprague-Dawley rats (age 6-8 weeks, male) were treated by applying 0.5N NaOH to the cornea for 90 seconds. After 7 days, rats were randomly assigned into treatment (TLY012, 10 mg/mL, 50uL subconj) or control (PBS 50ul subconj) groups and treated twice a week for the following 14 days. Corneal opacity, neovascularization, edema, and flare were recorded. Analysis of DR5 and α -smooth muscle actin (α -SMA) immunofluorescent staining of rat cornea were performed after rat euthanizing at 21 days.

Results: TLY012 significantly decreased corneal opacity score (0.9 ± 0.19 vs 1.9 ± 0.33 , $*p \leq 0.05$) and neovascularization score (1.0 ± 0.22 vs 2.4 ± 0.33 , $**p \leq 0.01$) compared to PBS group in alkali burn injured rat cornea at D21. TLY012 facilitated corneal flare clearness and transiently slowed corneal edema recovery, but there was no detectable difference between two groups at D21. DR5 were present in corneal epithelium and stroma in PBS treatment group at D21, and its expression was attenuated with TLY012 treatment. Correspondingly, α -SMA staining were noticeably reduced in epithelium and stroma layer with TLY012 treatment. Additionally, TLY012 decreased blood vessel density in corneal stroma induced by alkali injury.

Conclusions: Our experiment showed that TLY012 prevents corneal neovascularization and fibrosis induced by ocular alkali burn injury. These results demonstrated that TLY012 could be a novel candidate for treating corneal fibrotic disease.

CONTROL ID: 3542252

SUBMITTER (NAME ONLY): Giorgia Scapin

TITLE: CRISPR/Cas9-mediated gene-editing of TAPBP to alleviate antigenicity of human corneal-limbal epithelial cells

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Scapin, S. Chauhan, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G. Scapin, S. Chauhan, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human Corneal-Limbal Epithelial (HCLE) cells express high levels of Human Leukocyte Antigens Class I (HLA-I), which make them a target for alloimmune rejection. The chaperon Tapasin (coded from the TAPBP gene) is not only important for the proper folding of the HLA-I molecules, but it also plays a vital role in loading the HLA-I with the antigenic peptides before its exposure on the cell surface. The goal of the project is to analyze how the deletion of the TAPBP gene in HCLE cells affects their expression of HLA-I.

Methods: We used the CRISPR/Cas9 gene-editing method to generate the TAPBP gene knockout (KO) in HCLE cells. Specifically, we electroporated the HCLE cells with the Cas9 enzyme and 2 guide RNAs targeting the TAPBP gene. After the recovery of the cells, we performed limiting dilution to generate monoclonal cell lines. We screened such lines by PCR-based genotyping and Sanger-sequencing to uncover the TAPBP-KO clones. We next performed qRT-PCR to verify the abolished expression of TAPBP. To test the ability of the TAPBP-KO cells to express the HLA-I molecules, we performed FACS analysis and compared the HLA-I expression levels with the HCLE wild type (WT) cells.

Results: The comparison of the HLA-I expression in HCLE and in human immune cells (monocytes) demonstrated that both cell types express comparable levels of HLA-I even after the IFN- γ stimulation. Next, we embarked upon the CRISPR/Cas9-mediated KO of the TAPBP gene in the HCLE and tested how TAPBP KO affects the HLA-I expression. We found that 2 electroporation pulses at 1400V gave us 55.7% efficiency and 89% of cell viability. After limiting dilution, we selected 3 monoclonal lines for further analysis. FACS analysis showed a substantial decrease in the HLA-I ABC expression in TAPBP-KO cells (66% vs 99% of WT cells), suggesting that TAPBP-KO cells might escape CD8⁺ T cell-mediated cell death. In contrast, the levels of universally expressed HLA-I E in TAPBP-KO and WT cells remained comparable (93% vs 99%), suggesting TAPBP-KO cells retained their ability to escape from NK cell cytotoxicity.

Conclusions: The deletion of chaperon Tapasin selectively downregulates HLA-I expression in the corneal-limbal epithelial cells, which could prevent their rejection by the immune system.

CONTROL ID: 3542256

SUBMITTER (NAME ONLY): Lennart Husvagt

TITLE: Applying nnU-Net to the segmentation of microaneurysms in OCTA data in patients with non-proliferative diabetic retinopathy

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Husvagt, J. Schottenhamml, S.B. Ploner, K. Breininger, A.K. Maier, Pattern Recognition Lab, Friedrich-Alexander-Universitat Erlangen-Nurnberg, GERMANY|L. Husvagt, E. Moul, J.G. Fujimoto, Research Laboratory for Electronics, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|O. Abu-Qamar, E. Levine, N.K. Waheed, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of vision loss in working age populations worldwide. Patients may not notice any symptoms during the early non-proliferative stage (NPDR) while microaneurysms (MA) can still be detected using fluorescein angiography or optical coherence tomography angiography (OCTA). The purpose of this contribution is to automatically detect MA from OCTA en face images to aid in the early detection and diagnosis of NPDR.

Methods: Patients were enrolled at the New England Eye Center at Tufts Medical Center in Boston. We collected data from 90 eyes (70 patients) with NPDR who were imaged using the OptoVue Avanti system using a field size of 3x3 mm. The system software automatically performs a segmentation of the retinal layers. The OCTA en face images of the superficial capillary layer were used. Two expert graders at the Boston Imaging Reading Center manually labeled MA in these images using custom software. The labeled data were divided into 73 training and 16 testing images. We then trained a 2D nnU-Net to segment the MA. nnU-Net is a self-configuring deep learning tool that can automatically generate 2D and 3D U-nets and uses heuristic and data-based rules to choose suitable hyper-parameters. nnU-Net runs a five-fold cross-validation on the training data, which allows to use the resulting five trained nets as an ensemble.

Results: 12 of the 16 test images contained MA. The number of expert-labeled MA was 21. 11 of those MA were correctly found by nnU-Net. There were 4 false positives, but no false MA were detected on the 4 test images without labeled MA.

Figure 1 shows four of the test images. The top row shows the images without, the bottom row with marked aneurysms. The images show undetected MA (false negatives) marked in red, correctly detected areas in green and false positives in pink. Sub-figure A shows one detected aneurysm and one false negative. B shows two correctly detected MA. C shows a false positive in the center and a not correctly detected aneurysm in the upper image. Both are located directly near a saccade. D shows a correctly identified MA.

Conclusions: nnU-Net detected 11 out of 21 labeled MA. Future work will focus on improving these results by optimizing loss, data augmentation and training of the generated U-Net.

CONTROL ID: 3542259

SUBMITTER (NAME ONLY): Paula Subirada Caldarone

TITLE: The neurotrophin receptor p75^{NTR} as a new player in the development of choroidal neovascularization

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Choroidal neovascularization (CNV) is a key feature in the wet form of age related macular degeneration (AMD). Current treatments are inefficient, therefore a better understanding of the pathophysiology of AMD is necessary to develop novel therapeutic approaches. The p75 neurotrophin receptor (p75^{NTR}) is recognized as one of the main surface proteins involved in the transduction of death signals and recently also vascular changes. Here, we aim to determine if p75^{NTR} participates in the development of neuronal and vascular alterations in a mouse model of laser-induced CNV.

Methods: Briefly, mice were anesthetized and their pupils were dilated, then 4 injuries were performed in the retina using a photocoagulation laser with a 532nm wavelength slit lamp. 7 days after laser mice were subjected to electrorretinography (ERG) studies, and posterior sacrifice. Retinas and RPE-Choroid were processed separately for Western blot and immunofluorescence assays in whole mounts and cryosections. Colocalization was analysed in tissues double labeled with p75^{NTR} and one of the following cell markers: F4/80 (macrophages), NG-2 (pericytes), Isolectin IB-4 (blood vessels), glial fibrillary acid protein (glial cells) or β -actin (neurons). WT (N=17) and p75^{NTR} KO (N=12) mice were included in the experimental design and animals without CNV were used as control. GraphPad Prism program was employed for statistical analysis and one way ANOVA or t-test analysis was performed accordingly.

Results: In WT rodents, Western blot of neural retinas of CNV mice exhibited an increased expression of p75^{NTR} protein levels respect to control ($p < 0.05$). Confocal images showed overexpression of p75^{NTR} in macrophages in the RPE-Choroid, and in Muller glial cells around the injured area in the retina. These alterations in the CNV model were accompanied with neuronal dysfunction observed as a reduction in the amplitude of the a-wave by ERG, which was preserved in p75^{NTR} KO mice. In accordance, p75^{NTR} KO mice showed a reduction in the area and perimeter of choroidal neovessels ($p < 0.05$) as well as a decreased macrophage infiltrate by immunostaining.

Conclusions: Altogether these preliminary findings suggest that p75^{NTR} would participate in the development of CNV.

CONTROL ID: 3542261

SUBMITTER (NAME ONLY): Gil Torten

TITLE:

3D Ultrastructural Deconstruction of Rod Synapses after Retinal Detachment.

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Torten, D.S. Williams, Ophthalmology and Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|K.A. Linberg, G. Luna, S.K. Fisher, Neuroscience Research Institute, University of California Santa Barbara, Santa Barbara, California, UNITED STATES|G.A. Perkins, M.H. Ellisman, National Center for Microscopy and Imaging Research and Department of Neuroscience, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have shown structural remodeling of rod photoreceptor synaptic terminals (rod spherules, RS) in response to experimental retinal detachment (RD, Erickson, et al., 1983, IOVS, 24: 927). However, these studies relied on conventional electron microscopy, which is limited for 3-D analyses. Here we used the advanced imaging capabilities of electron microscope tomography (EMT) to study the 3-D complexities of the RS in feline retina during remodeling after experimental RD. Our aim was to generate a high-resolution 3-D analysis of the time-course of RS remodeling, and thus enhance our understanding of this process and its potential for reversibility.

Methods: All tissue used in this study was generated in previous studies of experimental RD (Erickson et al., 1983). Here we generated tomograms from RDs of 30min, 1hr, 24hr, 48hr, 72hr, 7d duration and from a control eye without RD. Tomograms were generated from imaging of either single 400nm sections, at 400KeV, or serial 200nm-thick sections, at 120KeV. 3D models were constructed using the software IMOD3D.

Results: At 7d, the RS no longer form a solid layer of terminals across the outer plexiform layer (OPL). Those that remain show several signs of severe degeneration including their transformation into an elongated “teardrop” shape, loss of some post-synaptic processes, changes in the geometry of the synaptic invagination with enlargement of the opening (hilus) through which post-synaptic processes pass, fragmentation of synaptic ribbons, the accumulation of large cytoplasmic vesicles, and a loss of branches from horizontal cell axon terminals within the synaptic invagination. In addition, Müller cells show many ultrastructural changes associated with their hypertrophy throughout the OPL. Within 1hr of RD there is minor restructuring of the synaptic invagination and postsynaptic processes, and a severe loss of synaptic vesicles. The degenerative phenotype becomes more severe as the length of the RD increases.

Conclusions: Our data indicate that RS undergo both pre- and post-synaptic changes that begin within 1hr after a RD. This is much earlier than previously thought. Clearly, it will now be critical to determine at what stage these early changes cease to be reversible, in order to understand the limitations of surgical reattachment for the return of vision in RD patients.

CONTROL ID: 3542263

SUBMITTER (NAME ONLY): Sidharth Mahotra

TITLE: Detecting Glaucoma Progression using Deep Archetypal Analysis of Retinal Nerve Fiber Layer Thickness Measurements

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Mahotra, X. Huang, S. Yousefi, Department of Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|M.V. Boland, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|L. Pasquale, Department of Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|T. Elze, M. Wang, Eye Research Institute of Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J.E. Majoor, K.A. Vermeer, H. Lemij, Rotterdam Ophthalmic Institute, Rotterdam Eye Hospital, Rotterdam, NETHERLANDS|K. Nouri-Mahdavi, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|C.A. Johnson, Department of Ophthalmology and Visual Sciences, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an artificial intelligence framework for detecting glaucoma progression using retinal nerve fiber layer (RNFL) thickness measurements obtained from optical coherence tomography (OCT) imaging of the optic disc.

Methods: We developed a deep archetypal analysis (DAA) framework and applied it to RNFL thickness measurements (circle scans with 768 A-scans) of 691 eyes of 691 patients and identified 16 prevalent patterns of RNFL loss. We then developed a framework to detect glaucoma progression using the deep archetypes discovered. We simulated a stable dataset by randomly shuffling the longitudinal visits of another dataset with 254 eyes of 127 subjects (Average of 9 visits). We selected the critical slopes of no-progression from this dataset at 95th percentile and subsequently used an independent longitudinal dataset with 254 eyes (mean 9 visits) to compare the detection rate of the proposed model against linear regression of RNFL summary parameters.

Results: Deep archetypal analysis discovered 16 patterns of RNFL loss which explained over 70% of the total variation in the RNFL data (Fig. 1). The critical slopes were selected in such a way to maintain 95% specificity for each model using the simulated stable dataset. The sensitivity of the overall DAA model was 54.7% while the detection rate of the linear regression of RNFL in global, superior, and inferior hemifields were 16.1%, 13.0% and 16.9%, respectively. Most of the eyes progressed across deep archetypes number 10 and 12 (Fig. 2).

Conclusions: The proposed deep archetypal analysis framework identifies major patterns of RNFL loss in patients with glaucoma. It also provides a more sensitive model in detecting glaucoma progression compared to linear regression of the summary parameters. This model may aid clinicians in detecting structural progression and identifying the corresponding pattern of RNFL loss, which in turn could improve disease monitoring and treatment planning.

CONTROL ID: 3542267

SUBMITTER (NAME ONLY): Kaito Narimoto

TITLE: Deep neural network by transfer learning for the analysis of guttae in the patients with Fuchs endothelial corneal dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Narimoto, N. Okumura, S. Yamada, K. Okamura, N. Koizumi, Department of Biomedical Engineering, Doshisha University, Kyotanabe, JAPAN|A. Izumi, ActualEyes Inc., Kyotanabe, JAPAN|T. Tourtas, F.E. Kruse, Department of Ophthalmology, University of Erlangen-Nurnberg, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: Transfer learning (TL) is a method in deep learning where knowledge is transferred from one model to another. It allows for generation of artificial intelligence (AI) by 1) limited amounts of data and 2) shortened time. We previously generated AI for analyzing guttae in a Fuchs endothelial corneal dystrophy (FECD) model mouse (Yamada, S, et al., ARVO, 2020). Here we report the use of TL to generate AI for analyzing human guttae from a mouse-model AI.

Methods: Of corneal endothelial images obtained from 20 patients with FECD via contact specular microscopy, 26 focused images were selected and the guttae area was manually annotated as ground truth. Our previously reported AI for analyzing mouse guttae, which was generated by using the FECD mouse-model data (n=2538), was then used to predict the area of human guttae. Next, training/testing was performed to accommodate the AI for mouse guttae to AI for human guttae via application of U-Net, a fully convolutional network architecture for biomedical image segmentation. TL AI was then evaluated by predicting the guttae areas of the human subjects and comparing it with the ground truth.

Results: The AI for mouse guttae severely underestimated the guttae of human subjects, and Pearson correlation coefficient showed no significant correlation between the guttae area predicted by AI and ground truth ($r = 0.21$, $p = 0.384$). Thought sensitivity, specificity, and F-measure of the mouse-model AI was 84.6%, 99.8% and 88.8%, respectively, for analyzing mouse guttae and 5.8%, 99.9% and 10.9%, respectively, for analyzing human guttae. However, the AI for human subjects, which was generated by TL from the mouse-model AI, successfully recognized human guttae, and sensitivity, specificity, and F-measure were 86.6%, 94.7%, and 81.5%, respectively. Pearson correlation coefficient showed that guttae area predicted by TL AI for human subjects was strongly associated with manually annotated ground truth ($r = 0.96$, $p = 1.60 \times 10^{-11}$). Brand Altman analysis showed that the mean systematic error of the TL AI was $-2.25 \pm 10.7\%$.

Conclusions: TL allowed for accommodation of AI for analyzing mouse guttae to AI for analyzing human-subject guttae. Our findings suggest that TL will be applicable in multiple ophthalmology fields; e.g., the generation of AI for device A from data set obtained by device B, C, and D.

CONTROL ID: 3542268

SUBMITTER (NAME ONLY): Joshua Katuri

TITLE: Ophthalmology resident on-call performance at a tertiary referral center in Texas

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Katuri, J. Wong, N. Tran, S. Lahoti, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|H. Nguyen, R. Jones, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Post-clinic emergency room and inpatient ophthalmic consultations ("on call") allow unique insights due to increased resident autonomy. We use these encounters to evaluate resident performance in relation to multiple systemic variables to help optimize training and patient care.

Methods: A retrospective study used electronic medical records to collect logistics, clinical data, and resident variables for resident on-call encounters between 7/2019 – 7/2020. Resident data was anonymized and initial encounters were compared with serial follow-up visits for accuracy. Performance was scored by a modified ACR RADPEER system of review. Diagnostic accuracy = 0/1. Diagnostic difficulty = 1/2/3. Management accuracy = 0/1. Management difficulty = 1/2/3, where 2 should involve a senior resident and 3 should involve faculty. Disposition appropriateness = 0/1. Adverse outcome = 0/1 if results were secondary to management and disposition appropriateness.

Results: 209 of 501 encounters had serial follow-up data to use for grading. 23/501 patients were triaged to a later clinic appointment without direct encounter. 9/209 patients followed up 7.1 ± 6.8 days after indirect encounters. Of the 200 direct encounters (difficulty 1.6 ± 0.7), 191 diagnoses were accurate (difficulty 1.6 ± 0.6). 9 were inaccurate (difficulty 2.2 ± 0.8) and encountered a late PGY-2 on average. 2/11 inaccurate diagnoses led to suboptimal management, although both had appropriate follow-up triage and no adverse outcomes. 194/200 had appropriate initial management (difficulty 1.7 ± 0.7). 6/200 were suboptimal (difficulty 1.8 ± 0.4) and encountered a late PGY-2 on average but had no adverse outcomes. 199/200 had appropriate disposition (location and duration). 3/209 were marked as adverse outcomes, one from each level of training: 2 were from delayed IOP management and 1 was a mistriage based on ED staff evaluation.

Conclusions: Sub-optimal performances occurred infrequently in our current redundancy-designed safety escalation system. Performance scores did not statistically vary with different residents, clinical difficulty, or call logistics. Due to appropriate follow-up, suboptimal performances were not associated with worse visual outcomes, but rare cases show the need for prudent high IOP management and reliable ED physician sign out of ocular vitals.

CONTROL ID: 3542269

SUBMITTER (NAME ONLY): Kieva Byrne

TITLE: Claudin 5 expression has distinct impacts on the Immune profiles of mouse models of AMD

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Byrne, N. Hudson, C. Delaney, A. Reddy, M. Campbell, Smurfit Institute of Genetics, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The role of claudin-5 as a key mediator of the inner Blood Retinal Barrier (iBRB) and Blood Brain Barrier (BBB) are well established. However, the role of this Tight Junction (TJ) protein in diseases affecting retinal homeostasis, remains poorly understood. In this study we analyse the effects of Claudin-5 expression disruption on Age-Related Macular Degeneration (AMD) pathology through the analysis of the immune profiles of two novel mouse models of the disease.

Methods: The first model analysed is created through a Cldn5 flox Tie2cre system in which endothelial Cldn5 expression is heterozygosity is established. RNA samples were isolated from the retinas of these mice for qPCR analysis. Cre negative animals were used as controls.

The second model under investigation utilised AAV vectors expressing an shRNA targeting claudin-5 to decrease Cldn5 expression levels in the retinal endothelium. These mice were fed a high cholesterol diet (HCD) to further induce AMD pathogenesis. RNA samples were isolated from the RPE of these mice and subjected to a PCR array of 35 genes representing various inflammatory markers, markers of endoplasmic reticulum (ER) stress, and oxidative stress markers. Controls used were mice administered with non-targeting shRNA.

Results: Analysis of Cldn5 tie2-cre⁺ retinas show a significant decrease in expression of TJ genes, Marvel2 and Lsr concomitant to Cldn5 suppression, (*p=0.048, *p=0.0493, respectively). Numerous inflammatory markers also show downregulation including Il-1β (*p=0.0455) and macrophage markers such as Tmem119 (**p=0.0089).

Results from the RPE qPCR panel show that inflammatory markers are significantly upregulated in Cldn5 deficient mice. Such markers included cytokines such as Cxcl10 (**p=0.0038), components of the complement system, Traf6, (*p=0.0197) and Toll like receptor 2 (Tlr2, **p=0.0039).

Conclusions: The immune profile of these two disease models show trends towards two distinct inflammatory outcomes. This disparity in inflammatory phenotypes may be attributed to the synergistic effect of a HCD with decreased claudin 5 expression, resulting in the differential recruitment and activation of immune cells within the retina. Therefore, these results provide an interesting insight into the immunological implications of the disruption of claudin-5 expression in such disease contexts.

CONTROL ID: 3542270

SUBMITTER (NAME ONLY): Anneka Joachimsthaler

TITLE: Combining temporal white noise stimulation and silent substitution technique: wnERGs driven by single photoreceptor types in LIAIS mice

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Joachimsthaler, N. Stallwitz, J.J. Kremers, Ophthalmology, University Hospital Erlangen, Erlangen, GERMANY|A. Joachimsthaler, Biology - Animal Physiology, FAU Erlangen-Nürnberg, Erlangen, GERMANY|

Commercial Relationships Disclosure (Abstract): Anneka Joachimsthaler: Commercial Relationship: Code N (No Commercial Relationship) | Nina Stallwitz: Commercial Relationship: Code N (No Commercial Relationship) | Jan Kremers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the Impulse response functions (IRFs) to luminance and photoreceptor-isolating stimuli in mice expressing a human L*-opsin instead of M-opsin.

Methods: After dark adaptation over night, anesthetized animals were adapted for 2 min to the mean luminance (ML) of the following stimulus.

ERGs to temporal white noise modulation (wnERGs: containing all frequencies up to 20 Hz with equal amplitudes and random phases) were recorded. Both luminance and photoreceptor-isolating stimuli were used.

Responses were recorded at 7 mean luminances (MLs) between -0.7 and $1.2 \log \text{cd/m}^2$ with luminance and at 4 MLs (between -0.8 and $1 \log \text{cd/m}^2$) with rod and cone isolating stimuli.

For each stimulus condition, two recordings of 200 sweeps were performed. IRFs were calculated by a cross correlation of the recordings and the stimulus luminance or photoreceptor excitation. Amplitudes and latencies of the IRF trough and peak were measured at each ML.

Results: Recordings measured with equal stimulus conditions displayed similar time courses, indicating that wnERGs gave reproducible results. IRFs of luminance stimulation showed an initial (a-wave-like) trough followed by a positive (b-wave-like) peak for all MLs. Trough and trough-to-peak (T-P) amplitudes increased monotonously with increasing ML. Latencies of trough and peak decreased with increasing ML up to $0.3 \log \text{cd/m}^2$ and were constant for higher MLs. IRFs of L*-cone and S-cone isolating stimuli displayed similar time courses and dependency on ML. T-P amplitudes increased by a factor of 10^2 for L*-cones and by a factor of 2.5 for S-cones. Maximal S-cone-driven responses were 2.7 times smaller than maximal L*-cone-driven responses. In contrast to cone-driven responses, IRFs of rod-driven recordings decreased in amplitude with increasing ML by a factor of 1.7. In none of the recordings, oscillatory potentials were observed.

Conclusions: wnERGs can be reliably recorded in mice with luminance stimulation and photoreceptor-isolating stimuli. Cone-driven responses grow with increasing ML, whilst rod-driven responses were larger at low ML.

Luminance stimulation shows a rod-cone transition below $0.3 \log \text{cd/m}^2$. Although the IRFs resemble flash ERGs superficially, they are fundamentally different and offer a novel procedure to study retinal physiology.

CONTROL ID: 3542276

SUBMITTER (NAME ONLY): Michelle McCall

TITLE: Impact of fundus pigmentation on retinal layer and choroidal scleral junction visibility on investigational bedside OCT in preterm infants

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dark fundus pigmentation (FP) can limit fundus photography quality in eyes being evaluated for retinopathy of prematurity. We sought to determine the impact of FP on retinal layer and choroid-scleral junction (CSJ) visibility and scan quality for investigational bedside swept source (SS) optical coherence tomography (OCT) imaging.

Methods: We analyzed investigational SS-OCT images captured between 30-42 weeks post menstrual age in 188 eyes of 94 preterm infants enrolled in BabySTEPS study (NCT02887157). Trained ophthalmologists, masked to OCT findings, determined FP (dark/medium/blond). Expert graders, masked to FP, evaluated OCT images for: 1) age-appropriate retinal layers visible (yes/no), 2) CSJ visible (yes/no), and 3) overall OCT quality (excellent/acceptable/poor/unusable). To assess the association of FP with retinal layer and CSJ visibility and OCT quality, we performed multivariable logistic regression modeling, adjusting for biologic and demographic confounders and correlations from repeated OCT scans and paired eyes.

Results: Mean gestational age was 27.8±2.6 (SD) weeks, mean birthweight was 964±283 grams; 51 (54%) infants were non-white, and 48 (51%) infants were male. FP was dark in 24 (13%) eyes, medium in 92 (49%), and blond in 72 (38%). All age-appropriate retinal layers were visible in 781 of 846 scans (92%), CSJ was visible in 701 (83%), and OCT quality was excellent/acceptable in 725 scans (86%). Compared to eyes with blond FP, eyes with medium and dark FP did not have higher odds of inability to see all age-appropriate retinal layers on OCT (adjusted OR 1.17 [95% CI 0.39-3.51] and 0.57 [95% CI 0.15-2.20], respectively) or poor/unusable OCT scan quality (adjusted OR 0.87 [95% CI 0.50-1.48] and 0.49 [95% CI 0.16-1.55], respectively). Conversely, eyes with medium and dark FP had higher odds of inability to visualize the CSJ (adjusted OR 2.8 [95% CI 1.49-5.31] and 4.8 [95% CI 1.48-15.48], respectively).

Conclusions: Medium and dark FP affected visibility of CSJ but did not affect overall scan quality or age-appropriate retinal layer visibility on investigational bedside OCT in preterm infants. This study supports the feasibility of using OCT to analyze retinal microanatomy in diverse populations of preterm infants with a range of fundus pigmentation. Further imaging methods/system enhancement could be pursued to improve CSJ imaging.

CONTROL ID: 3542280

SUBMITTER (NAME ONLY): Marco Nassisi

TITLE: PHENOTYPE-GENOTYPE CORRELATION AND PROGRESSION MODELING APPLIED TO MUTATIONS IN RPGR-RELATED ROD-CONE DYSTROPHY.

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Nassisi, G. De Bartolo, S. Mohand-Said, V.M. SMIRNOV, A. Antonio, C. Condroyer, J.A. Sahel, C. Zeitz, I. Audo, Institut de la vision, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: to characterize a large cohort of patients with RPGR-related rod-cone dystrophy (RCD) and compare the phenotypes of patients with mutations on the RPGR-ORF15 isoform and on the RPGR(1-19) isoform.

Methods: male patients with RPGR-related RCD were recruited at the “Center of rare diseases” at “Quinze-Vingts” Hospital, Paris, France. Phenotypic data were collected retrospectively including age of onset, best corrected visual acuity (BCVA), presence of high myopia, kinetic visual field (VF), presence and size of a central hyper-reflective ring on short-wavelength fundus autofluorescence (SW-FAF), presence and width of central preserved ellipsoid zone (EZ) on optical coherence tomography (OCT). All available visits were considered for each patient and an estimation of the progression was done for each quantitative parameter through the analysis of the regression slopes which were then compared between the two genotypic groups. Finally, a correlation between BCVA and all other parameters was done using a linear regression analysis with the cross-sectional data from the last visit available.

Results: 28 patients (age: 42.73 ± 22.27 years) with RPGR(1-19)-related RCD and 84 (age: 37.57 ± 15.03 years) with mutations on the RPGR-ORF15 isoform were included. The age of onset was significantly earlier in the RPGR(1-19) group than the RPGR-ORF15 group (76.4% vs 50.8% in the 1st decade respectively). In both groups a progressive decline of all quantitative parameters was observed along the available follow-up (maximum 18 years for RPGR(1-19); maximum 14 years for RPGR-ORF15). When comparing the respective regression slopes for BCVA, VF, SW-FAF and OCT parameters, no significant differences were found between the two genotypic groups. In all the cohort (as well as in both RPGR(1-19) and RPGR-ORF15 cohorts separately), age was a strong predictor for BCVA (standardized β coefficient: 0.404, $p < 0.001$) as well as the preserved EZ on OCT (standardized β coefficient: -0.450, $p < 0.001$).

Conclusions: longitudinal data on a large cohort of RPGR-related RCD showed no differences in progression between patients carrying mutations on different isoforms of the gene. Overall, the comprehensive analysis of RPGR(1-19)- and RPGR-ORF15-related RCD will help clinicians in assessing the visual prognosis of these patients. This will also constitute an important guidance in the design of therapeutic clinical trials.

CONTROL ID: 3542287

SUBMITTER (NAME ONLY): Joshua Disatham

TITLE: Multiomic identification of genome-wide DNA binding sites and target genes identifies HIF1 α as a hypoxia-dependent master regulator of lens gene expression

SESSION TITLE: Lens Development and Differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Disatham, L.A. Brennan, M. Kantorow, Biomedical Sciences, Florida Atlantic University, Boca Raton, Florida, UNITED STATES|D. Chauss, B. Afzali, NIDDK, National Institutes of Health, Bethesda, Maryland, UNITED STATES|J. Kantorow, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hypoxia-inducible factor 1 (HIF1 α) is a critical transcription factor known to govern vascularization. The lens contains an oxygen gradient that parallels the surface to core differentiation of lens epithelial cells into fiber cells. The presence of this oxygen gradient suggests that HIF1 α could mediate gene expression events required for lens cell differentiation and fiber cell function. Consistently, we have recently identified HIF1 α to be an essential regulator of BNIP3L that we have shown initiates the hypoxia-dependent elimination of non-nuclear organelles during fiber cell maturation. Here, we employed a multiomics approach to map the genomic complement of HIF1 α DNA binding sites and target genes in the lens and identify HIF1 α as a novel master regulator of lens gene expression.

Methods: HIF1 α DNA binding was induced in embryonic primary chick lens cells through exposure to dimethylallyl glycine (DMOG). HIF1 α -DNA binding complexes were identified by CUT&RUN (Cleavage Under Targets and Release Under Nuclease). Expression levels of activated or repressed HIF1 α -target genes were identified by parallel RNA sequencing analysis. Sites were mapped to putative promoter or enhancer sequences and analyzed for chromatin configuration by analysis of ATAC sequencing data.

Results: CUT&RUN analysis revealed 8,375 HIF1 α -DNA binding complexes across the chick lens genome. 1,190 HIF1 α -DNA binding complexes were significantly clustered within open chromatin regions ($p < 1e-55$) identified by ATAC sequencing. Formation of the identified HIF1 α -DNA complexes parallels the direct activation or repression of 526 genes, 202 of which contained HIF1 α binding sites within 100kbp of the transcription start site. The identified genes were associated with multiple key cellular processes including glycolysis, cell cycle control, chromatin remodeling, Notch and Wnt signaling, lens cell differentiation, development, and cataract formation.

Conclusions: The data establish a functional genomic map of novel HIF1 α -regulated lens genes. They further support the hypothesis that hypoxia is critical for lens fiber cell differentiation, structure and function and they identify novel HIF1 α -dependent pathways and genetic components important for lens differentiation, homeostasis and cataract formation.

CONTROL ID: 3542288

SUBMITTER (NAME ONLY): Adnan Alawami

TITLE: Visual Outcomes and Complications of Corneal Transplant With and Without Previous Glaucoma Surgery

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Alawami, H. Liu, I. Kherani, F. Mostofian, S. Ziai, G. Mintsioulis, K. Baig, Ophthalmology, Ottawa Hospital, Ottawa, Ontario, CANADA]

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ABSTRACT BODY:

Purpose: The purpose of this study is to assess change in visual outcomes and graft survival for patients undergoing corneal transplantation (PKP, DSAEK, UT-DSAEK, DMEK) with a previous history of glaucoma surgery compared to those with a history of glaucoma without glaucoma surgery.

Methods: This is a retrospective single center, case-control study. 71 consecutive patients (mean age = 72.3 ± 14.8 years, M:F = 1.1) who underwent corneal transplantation procedures with a history of glaucoma filtering surgery (trabeculectomy and/or tube shunt) compared to 83 controls (mean age = 72.1 ± 13.9 years, M:F = 0.89) at the University of Ottawa Eye Institute. Patient demographics, surgical technique for corneal transplantation, indication for transplantation, donor endothelial cell density (ECD), death to enucleation and graft times were recorded. The primary outcome of the study was number of letters gained from baseline to 12 months. Secondary outcome was incidence of graft failure and time to graft failure. Analysis was conducted using t-test and chi-squared test with a significance level of 0.05.

Results: Overall, the proportion of patients in each corneal transplant group was as follows: 23 (14.9%) PKP, 70 (45.5%) DSAEK, 9 (2.6%) UT-DSAEK and 52 (33.8%) DMEK. No difference was observed between the two groups with respect to graft status including donor and recipient age, donor ECD, and death to enucleation and graft times ($p > 0.05$). No difference was observed between the two groups with respect of IOP control at baseline ($p > 0.3$) and at 12 months follow up ($p > 0.05$). Baseline BCVAs were 1.56 ± 0.62 LogMAR and 1.26 ± 0.76 LogMAR for the case and control groups respectively ($p = 0.01$). BCVA was improved significantly from baseline to follow-up at 12 months in both case ($p = 0.02$) and control ($p < 0.01$) groups. There was no difference in the number of letters gained from baseline to 12 months between the two groups ($p > 0.05$). Average time to graft failure was 10.6 months, with better overall graft survival rates in the control group (78.3%) compared to the case group (59.2%) ($p = 0.01$).

Conclusions: Although there was no difference in the number of letters gained between the two groups at 1 year, patients with pre-existing glaucoma surgery had worse pre-operative BCVA and overall corneal graft survival rates compared to patients with pre-existing glaucoma on medical therapy.

CONTROL ID: 3542289

SUBMITTER (NAME ONLY): Celia Bisbach

TITLE: Monocarboxylate Transporters Facilitate Succinate Export, but not Import, in Ocular Tissues

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Bisbach, D. Hass, J. Hurley, Biochemistry, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retina tissue exports succinate, while eyecup tissue (containing sclera, choroid, and retinal pigment epithelium) imports succinate. This study aims to determine which transporters facilitate export of succinate from the retina and import of succinate into the retinal pigment epithelium.

Methods: Retina and eyecup tissue from male and female C57Bl6/J mice was incubated in Krebs-Ringer Bicarbonate buffer with ^{12}C - and ^{13}C -labeled metabolites. Incubation medium was sampled at 0, 20, and 40 minutes, and gas chromatography-mass spectrometry was used to measure the rates of metabolite release into and depletion from the media. Experiments were conducted with a variety of transporter inhibitors and competing metabolic substrates to determine conditions under which succinate import or export was diminished.

Results: Succinate export by retinas was diminished by the MCT1 inhibitor AZD3965 and the MCT4 inhibitor bindarit. Although eyecups also express MCT1 (and MCT3), succinate import by eyecups was completely insensitive to the MCT1 inhibitor AZD3965 and was unaffected by including the MCT1 substrates lactate and pyruvate in the incubation medium. However, eyecup succinate import was severely diminished when assayed in sodium-free buffer, indicating that succinate import into eyecups might instead occur through a sodium-linked transporter, such as one of the SLC13 family members.

Conclusions: Both MCT1 and MCT4 contribute to export of succinate from retinas. Although MCT1 is present on the apical side of the RPE, inhibiting MCT1 does not affect import of succinate into eyecups. Import of succinate into the RPE instead appears to occur through a sodium-linked transporter. It is possible that the different role MCT1 plays in succinate export and uptake in our ex vivo system could be due to physiological differences between the cytoplasm of the retina and the incubation medium that eyecups are exposed to. Since transport of substrates by MCTs is proton-linked, the high rate of glycolysis in retinas could acidify the retinal cytosol to an extent which is sufficient to activate MCT-mediated succinate export. Further experiments to determine 1) the extent to which aerobic glycolysis and succinate export are linked in retinas, and 2) if lowering the pH of eyecup incubation media can cause MCT1 to participate in succinate import will be required to test this hypothesis.

CONTROL ID: 3542290

SUBMITTER (NAME ONLY): Rait Parmann

TITLE: Shared Features in Retinal Diseases with Primary Involvement of Retinal Pigment Epithelium

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Parmann, R. Jauregui, R. Allikmets, S. Chang, S.H. Tsang, J.R. Sparrow, Department of Ophthalmology, Harkness Eye Institute, Columbia University, New York, New York, UNITED STATES|R. Allikmets, S.H. Tsang, J.R. Sparrow, Department of Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: We compared fundus features in patients carrying mutations in ABCA4 (16 patients) and peripherin-2/RDS (PRPH2/RDS) (7), both of which are associated with fundus flecks; retinol dehydrogenase 5 (RDH5) (1) and retinaldehyde-binding protein 1 (RLBP1) (2) that display white-dot lesions and patients (9) manifesting reticular pseudodrusen (RPD) in association with age-related macular degeneration (AMD).

Methods: This retrospective study included spectral domain optical coherence tomography (SD-OCT); near infrared fundus autofluorescence (NIR-AF) that originates from melanin; short-wavelength fundus autofluorescence (SW-AF) originating in bisretinoid lipofuscin; and ultrawide-field pseudocolor fundus images.

Results: At positions of flecks, dots and RPD in en face images, hyperreflective lesions were detected in SD-OCT scans. These lesions presented as corrugated thickenings of interdigitation zone (IZ) and ellipsoid zone (EZ) or in later stages as rectangular or pyramidal shaped foci that extended radially through photoreceptor cell-attributable bands interrupting the IZ, EZ in association with a thinned outer nuclear layer (ONL). Hypertransmission of OCT signal, a sign of non-intact retinal pigment epithelium (RPE) was observed with dot-lesions and RPD. Dots, flecks and RPD were typically (but not always) hypoautofluorescent in NIR-AF images, and hyperautofluorescent (flecks, dots) or hypoautofluorescent (RPD) relative to the surround in SW-AF images. Flecks profiles were larger in NIR-AF than in SW-AF images. In wide-field pseudocolor images acquired from an RLBP1-patient, depigmented dot-like foci were organized into peripheral radial arrays resembling patterns in ocular albinism indicative of RPE clones. Target configurations were observed in NIR-AF images associated with dots (RDH5, RLBP1) and RPD.

Conclusions: Common to these disorders are hyperreflective lesions that extend anteriorly and progressively incorporate photoreceptor-attributable OCT bands. We suggest that these deposits may be left by degenerative processes in groups of photoreceptor cells, the degeneration beginning in inner and outer segments and being preceded by RPE dysfunctioning, thinning or atrophy. Differences in en face appearances of these lesions may be accounted for by disease-associated levels of retinoids and bisretinoid, melanin, sensitivity settings and image normalization.

CONTROL ID: 3542292

SUBMITTER (NAME ONLY): Andrew Taylor

TITLE: Retinal regulation of antigen presentation and processing

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.W. Taylor, J. Gardiner, K. Dawit, Y. Wu, T. Ng, Ophthalmology, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Andrew Taylor: Commercial Relationship(s);Palatin Technologies, Inc.:Code F (Financial Support);Palatin Technologies, Inc.:Code C (Consultant);Mallinckrodt Pharmaceuticals:Code C (Consultant) | John Gardiner: Commercial Relationship: Code N (No Commercial Relationship) | Kaleb Dawit: Commercial Relationship: Code N (No Commercial Relationship) | Yalan Wu: Commercial Relationship: Code N (No Commercial Relationship) | Tat Fong Ng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously reported that retinal pigment epithelial cells (RPE) through melanocortin pathways suppress phagosome maturation within antigen presenting cells (APC). This suppression would significantly affect APC activation of CD4⁺ T cells. Therefore, we assayed for suppression of APC antigen-activation of CD4⁺ T cells by RPE from mice with experimental autoimmune uveitis (EAU) and treated with alpha-melanocortin stimulating hormone (α -MSH).

Methods: Experimental autoimmune uveitis (EAU) was induced in C57BL/6 mice immunized with IRBP peptide in adjuvant, and the mice were treated with α -MSH when EAU reached the chronic phase. At clearance of uveitis, RPE-eyecups were made by making a circumferential cut just under the ciliary body, and discarding the anterior chamber, lens, and neuroretina leaving the RPE monolayer, choroid, and sclera. The RPE-eyecups were incubated in serum-free media for 24 hrs. The conditioned media was removed and used to treat the naive peritoneal macrophages with opsonized ovalbumin for 24 hours. Opsonized rat serum albumin was used as irrelevant antigen control. The APC were washed, and CD4⁺ T cells isolated from draining lymph-nodes of mice immunized to OVA were added. After 48 hrs incubation, the culture supernatant was assayed by ELISA for IFN- γ , IL-17, and IL-10, and the T cells assayed by flow cytometry for Treg cell markers CD25 and FoxP3.

Results: APC treated with the conditioned media of RPE-eyecups from naive and α -MSH-treated EAU mice, but not from untreated-EAU mice significantly suppressed IL-17, while significantly enhancing IL-10 production by CD4⁺ T cells with all RPE-eyecup conditioned media suppressing APC-stimulation of IFN- γ production. While APC treated with the conditioned media of RPE-eyecups from EAU mice significantly enhanced by 2.5-fold the number of CD25⁺ FoxP3⁺ T cells, it was 80% suppressed by RPE-eyecup conditioned media from α -MSH-treated EAU mice that were neither statistically different from the effects of EAU or naive RPE-eyecup conditioned media on APC. None of the RPE-eyecup conditioned media induced APC to expand the population of CD25⁺ FoxP3⁺ Treg cells.

Conclusions: The results demonstrated that APC are influenced by RPE soluble molecules and demonstrated that RPE promote APC maintenance of Treg cells while suppressing expansion of effector T cells. Treatment of EAU with α -MSH supports recovery of RPE regulation of immune cell activity.

CONTROL ID: 3542293

SUBMITTER (NAME ONLY): Jennifer Chang-Wolf

TITLE: Cost Comparison of Reusable versus Disposable Equipment for Retinopathy of Prematurity Screening Rounds

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Chang-Wolf, S.F. Freedman, S.G. Prkalapakorn, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|S.F. Freedman, Department of Pediatrics, Duke University, Durham, North Carolina, UNITED STATES|E.R. Myers, Department of Women's Community and Population Health, Department of Obstetrics & Gynecology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of Prematurity (ROP) screening rounds have been linked to infection transmission and serious adverse outcomes in the neonatal intensive care unit (NICU). The purpose of this study is to compare the cost of using reusable versus disposable equipment (i.e. indirect lenses, eyelid speculums, and scleral depressors) and identify the least costly strategy for maintaining sterile equipment for use on ROP rounds based on the gestational age (GA) distribution of a NICU.

Methods: Based on institutional data of infants examined on ROP screening rounds (2015-2019) and published data from a neonatal network on United States NICU admissions by GA category and NICU type (2015-2019), we modeled cost estimates of maintaining sterile equipment for use on ROP rounds over a 5-year (yr) period. Cost considerations included purchasing enough equipment/day and processing/autoclaving equipment (assuming 5-yr equipment lifetime). We performed separate Monte Carlo microsimulations for per-infant (1) lenses and (2) speculum/depressor sets to quantify uncertainty about whether using reusable or disposable equipment is least expensive.

Results: Over 5 yrs, the median cost of using reusable versus disposable lenses was less (Figure 1A) and the median cost of using reusable speculum/depressor sets was less than the first quartile cost of using disposable speculum/depressor sets regardless of NICU level (Figure 1B). Using Monte Carlo simulations, in level I-IV NICUs, using reusable versus disposable lenses was cheaper in 65.7%, 60.5%, 63.1%, and 63.3% of scenarios, respectively, and using reusable versus disposable speculum/depressor sets was cheaper in 74.8%, 77.2%, 80.4%, and 81.4% of scenarios, respectively. At our academic institution (a level IV NICU), using reusable versus disposable lenses became and remained cheaper after ~2.08 yrs, or 1960 examinations.

Conclusions: Using reusable versus disposable equipment is more likely less expensive for maintaining sterile equipment at all level NICUs for ROP rounds, assuming ≥ 5 yr instrument longevity. Our findings help inform those choosing between these strategies, taking into consideration cost, infection control, and efficiency.

CONTROL ID: 3542294

SUBMITTER (NAME ONLY): Reza Kianian

TITLE: Efficacy of netarsudil in veterans with severe glaucoma on maximally tolerated medical therapy

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Kianian, S.W. Hulbert, E.G. Villalpando, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|S.K. Law, J. Giaconi, Ophthalmology, Ronald Reagan UCLA Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Netarsudil is a newly approved intraocular pressure (IOP) lowering agent with a novel mechanism of action. Although the efficacy of netarsudil has been shown in clinical trials, its real-world effectiveness is uncertain. This study assesses netarsudil's effectiveness in reducing IOP in patients with advanced glaucoma already on maximally tolerated medical therapy.

Methods: Medical records of all patients who received netarsudil between 6/1/2018 and 4/30/2020 from the West Los Angeles Veterans Administration Medical Center were retrospectively reviewed. Exclusion criteria included laser trabeculoplasty and glaucoma surgery within 6 months of initiation of netarsudil, ocular conditions interfering with reliable IOP measurement, documented noncompliance with baseline medical therapy, initiation of netarsudil prior to first visit, or if netarsudil was discontinued due to intolerability prior to first post-treatment visit. One eye per patient was enrolled. If both eyes were qualified, the more severely affected eye based on visual field was selected. Baseline average IOP was compared to average IOP within 4 months and more than 4 months after initiation of netarsudil with paired t-tests. Intolerability was reported.

Results: Sixty-six out of the 202 patients that were prescribed netarsudil met the inclusion criteria. Mean age (\pm SEM) was 74.6 ± 1.1 years. 98.5% were male, 65.2% were black, and 80.3% had open angle glaucoma. The mean LogMAR acuity score was 0.78 ± 0.10 (equivalent to 20/120), cup/disc ratio was 0.87 ± 0.01 , the central corneal thickness was 527.4 ± 6.2 μ m, and the total number of medications at baseline was 3.6 ± 0.1 . Mean IOP was reduced from 17.2 ± 0.4 at baseline to 15.0 ± 0.5 within 4 months ($n=66$) and 15.0 ± 0.5 mmHg between 4-18 months ($n=40$) after netarsudil initiation ($p<0.0001$). Thirty-three patients (50%) within 4 months and 18 patients (45%) between 4-18 months had $\geq 15\%$ IOP reduction. There was no significant difference in absolute or percent IOP reduction between patients on ≤ 2 and >2 baseline glaucoma medications. Three patients could not tolerate and stopped netarsudil during follow-up, and 18 of the 136 excluded patients discontinued netarsudil before the first post-treatment visit. Total discontinuation rate was 10.4% (21/202).

Conclusions: Netarsudil is moderately effective in lowering IOP even among patients who have exhausted all other pharmacologic options.

CONTROL ID: 3542301

SUBMITTER (NAME ONLY): Stefanie Seo

TITLE: Monitoring corneal change in a murine dry eye disease model using in vivo confocal microscopy

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Seo, M. Chen, S.C. Yiu, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|W. Schubert, Bayer AG, Leverkusen, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: While dacryoadenectomy is a commonly employed method to establish animal dry eye disease model, there is limited research in systematically monitoring its development longitudinally. In vivo confocal microscopy (IVCM) is a powerful tool to examine the cornea in vivo. Here we applied the Heidelberg Retina Tomograph III with Rostock Cornea Module (HRT III-RCM) to a murine double dacryoadenectomy model to examine the effect of dry eye disease on the cornea.

Methods: Five (5) Sprague-Dawley rats (aged 8-9 weeks, male) underwent double dacryoadenectomy to remove the intraorbital and extraorbital lacrimal glands. Male rats were chosen in this study due to a lesser influence of hormone cycle. A modified Schirmer's tear test, blink tests and IVCM images were acquired pre-surgery and at 1, 2 and 4 weeks post-surgery. Location and depth of up to three nerves per eye were randomly selected in the sub-basal nerve plexus (SNP). Same areas were identified by locating them in SNP layer and re-imaged as volume acquisition in subsequent weeks. Data were presented as Mean+SEM, and p values were calculated by Student's t test.

Results: After double dacryoadenectomy, aqueous tear production measured by Schirmer's test were reduced by 45% ($1.03 \pm .04$ vs. $1.88 \pm .19$ mm/5 min, $*p=0.024$) and blink rate increased to 237% (24.9 ± 3.5 vs. 10.5 ± 2.2 blinks/5 min, $**p<0.001$) compared to pre-surgery value. We observed distinct differences between pre- and post-surgery corneal morphologies using IVCM. Starting from 1 week after surgery, massive inflammatory cell infiltration was observed throughout the SNP which peaked at week 1 and subsided at week 2. Nerve branches swelled and showed noticeable nerve sprouting. These trends were also seen in nerve trunks located in the stroma. Furthermore, in the stroma, we noticed that activated keratocytes were present through week 4. Blood vessels and fibrous elements were also more prominent in post-surgery than pre-surgery corneas.

Conclusions: Here we demonstrated that the HRT III-RCM could be employed to non-invasively monitor pathophysiological changes of dry eye disease. It revealed that differential changes in corneal nerves as well as corneal epithelia and stroma.

CONTROL ID: 3542303

SUBMITTER (NAME ONLY): Khob Bhandari

TITLE: Objectively Measured Near Work and Light Exposure in Adults

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.R. Bhandari, H. Mirhajianmoghadam, L.A. Ostrin, Optometry, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Evidence supporting a role for near work in myopia prevalence and progression is conflicting, likely due to the subjective nature in which behaviors are traditionally quantified. Additionally, potential mechanisms have not been elucidated. Animal studies suggest that temporal patterns of myopiagenic stimuli may be significant. Continuous objective measurement of viewing behavior and light exposure may help to better understand contributing factors. Here, a novel sensor, the Clouclip, is further validated in adults.

Methods: Five adults wore a spectacle-mounted Clouclip during waking hours and wrist-worn Actiwatch Spectrum continuously for 7 days. Working distance and illuminance were recorded by the Clouclip every 5 seconds (s) and 2 minutes (min), respectively. Activity and illuminance were recorded by the Actiwatch every 1 min. Subjects maintained a log of activities. Data were analyzed in MATLAB. Near work was defined as viewing distances of 10 to <60 cm, and intermediate work 60 to <100 cm. Near work episodes were defined as >1 min near viewing with no interruption >20 s. Continuous near work was defined as 30 min with no interruptions >60 s. Clouclip- and Actiwatch-measured illuminances were compared, and shifts from indoors to outdoors were quantified.

Results: Clouclip wear time was 14.4 ± 0.6 hours (h) per day. Activities noted in subject logs correlated well to Clouclip-measured distance and illuminance. Mean daily duration of near work was 5.0 ± 2.8 h, and intermediate work was 2.1 ± 1.5 h. Mean daily number of near work episodes was 57.1 ± 31.7 with duration of 4.6 ± 1.2 min each and distance of 33.0 ± 4.2 cm. Mean daily number of continuous near work episodes was 1.7 ± 1.2 . Clouclip-measured mean daily light exposure (281 ± 210 lux) was not significantly different than Actiwatch-measured light exposure (125.1 ± 119.8 lux, $P=.09$). Mean daily wake time spent in illuminance <30 lux, 30 to <1000 lux, >1000 lux, >2000, and >3000 lux were 6.1 ± 2.2 h, 6.6 ± 2.1 h, 0.8 ± 0.8 h, 0.5 ± 0.6 h, and 0.4 ± 0.5 h respectively. The number of shifts between indoors and outdoors was 4.9 ± 4.5 (range: 0-15).

Conclusions: The Clouclip provided continuous, objective data for viewing distance and illuminance that correlated well with subject logs and with the Actiwatch, a widely used light sensor. These findings suggest that the Clouclip will be a valuable tool for quantifying behaviors that have been linked to myopia.

CONTROL ID: 3542313

SUBMITTER (NAME ONLY): Steven Bailey

TITLE: Quantitative evaluation of type 1 and type 2 choroidal neovascularization components under treatment with projection-resolved optical coherence tomography angiography

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the response of type 1 and type 2 choroidal neovascularization (CNV) components under anti-vascular endothelial growth factor (VEGF) treatment in age-related macular degeneration (AMD) using projection-resolved optical coherence tomography angiography (PR-OCTA).

Methods: Eyes with treatment naïve exudative AMD were enrolled in a prospective, year-long longitudinal cohort study while under PRN anti-VEGF injections. Macular PR-OCTA was obtained at baseline, 6-month, and 1-year visit. PR-OCTA signal between outer plexiform layer to Bruch's membrane generated total CNV angiogram. PR-OCTA signal was further separated by RPE and projected onto type 1 (above RPE) and type 2 (below RPE) CNV angiograms. CNV vascular area was segmented and measured by a convolutional neural network (CNN) based algorithm. Individual CNV were classified as pure type 1 CNV, all vascular area was type 1 CNV component; predominantly type 2 CNV, at least 75% of the vascular area was type 2 CNV component; or mixed type CNV, with type 2 component accounting for 75% or less of the lesion. Change in CNV vascular area between visits were assessed with Friedman's analysis of variance (ANOVA).

Results: Of 18 total eyes, 13 eyes (72%) were pure type 1 CNV, 2 eyes (11%) were predominantly type 2 CNV, and 3 eyes (16%) were mixed type CNV at baseline. Total CNV vascular area did not change over the 1-year follow-up ($P=0.45$). CNV vascular area of type 1 increased ($P=0.0034$), whereas CNV vascular area of type 2 decreased during the 1-year follow-up ($P=0.0015$). At 6-month and 12-month visit, type 2 CNV was undetectable and all cases were graded as pure type 1 CNV. Of 5 eyes with type 2 CNV component at baseline, 4 eyes (80%) had RPE envelopment which converted type 2 CNV component into a type 1 pattern. CNV vascular area of pure type 1 CNV increased, but not significantly ($P=0.0753$).

Conclusions: PR-OCTA with CNN based algorithm demonstrated after one year of treatment, all Mixed type CNV and predominantly type 2 CNV converted to pure type 1 CNV. In these eyes, type 1 CNV vascular area increased at one year. Pure type 1 at baseline had non-significant increase in CNV vascular area at one year.

CONTROL ID: 3542318

SUBMITTER (NAME ONLY): Heberto Quintero

TITLE: Increased DISC1 expression restores mitochondrial axonal transport and rescues RGC function in glaucoma

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Quintero, N. Belforte, L. Alarcon-Martinez, F. Dotigny, S. El Hajji, A. Di Polo, Neuroscience, Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Adequate distribution of mitochondria in retinal ganglion cells (RGCs) is crucial for energy balance and synaptic function. Here, we tested the hypotheses that: i) early deficits in mitochondrial transport in glaucoma contributes to RGC loss, ii) the adaptor protein Disrupted in Schizophrenia 1 (DISC1) is an essential regulator of mitochondrial trafficking along RGC axons, and iii) restoring mitochondrial transport is beneficial for RGCs survival and function.

Methods: Ocular hypertension was induced by intracameral injection of magnetic microbeads in Thy1-CFP-MitoS mice, a strain that allows mitochondria visualization in RGCs. Two-photon laser scanning microscopy (TPLSM) was used to image mitochondrial transport along RGC axons, followed by kymograph analysis. Levels of transport adaptor proteins were analyzed by qPCR using mRNA from FACS-sorted RGCs. DISC1 levels in RGCs were modulated using siRNA or recombinant adeno-associated virus serotype 2 (AAV2.DISC1). RGC function was assessed by measuring positive scotopic threshold responses (pSTR).

Results: Live imaging using TPLSM revealed a selective reduction of anterograde mitochondrial transport along RGC axons soon after glaucoma induction (50% decrease vs. sham control, Student's t-test $p < 0.001$, $n = 35$ axons/group, $N = 12-14$ mice/group). Analysis of mitochondrial trafficking genes in RGCs showed reduced DISC1 transcript levels after glaucoma (Student's t-test, $p \leq 0.01$, $n = 4$ /group). DISC1 protein, which is abundantly expressed by naïve RGCs, was also downregulated by ocular hypertension (Student's t-test $p \leq 0.05$, $n = 6$ /group). siRNA-mediated silencing of DISC1 further reduced mitochondrial transport and exacerbated RGC death (14% reduction vs. control siRNA, ANOVA $p < 0.05$, $n = 6$ /group). In contrast, AAV2.DISC1 fully restored mitochondrial mobility and promoted RGC survival in glaucomatous eyes (30% increase vs. control AAV, ANOVA $p < 0.001$, $n = 6$ /group). AAV2.DISC1 also restored light-evoked pSTR amplitudes, indicative of RGC functional recovery.

Conclusions: Ocular hypertension triggers mitochondria axonal transport deficits and limits the availability of trafficking proteins, notably DISC1. Restoration of DISC1 levels is sufficient to rescue mitochondrial mobility, enhance RGC survival and light-evoked responses. These findings suggest that mitochondrial transport recovery is beneficial to improve RGC viability and function in glaucoma.

CONTROL ID: 3542323

SUBMITTER (NAME ONLY): Kirk Stephenson

TITLE: Target 5000: Evolution of the Irish National Program for Inherited Retinal Degenerations

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Inherited retinal degenerations (IRD) are rare genetic eye diseases with >300 implicated genes, many manifesting as progressive visual loss in children/young adults. The IRD population was historically underserved and disillusioned with healthcare services due to lack of interventions. Many novel therapies (e.g., gene and cell-based therapies) will require accurate genetic/clinical diagnosis, thus an efficient and effective pathway for assessment and management of IRDs is required. Here we describe the development of a national pathway for the management of the Irish IRD population.

Methods: Surveys of past Irish practice and international experts advice were used to design an all-Ireland IRD service (Target 5000). Assessment included clinical phenotyping (history, examination, multimodal imaging, perimetry, and electrophysiology) and next generation genetic sequencing in research-grade and accredited laboratories. Unresolved pedigrees underwent further studies (whole gene/whole exome/whole genome sequencing). Novel variants were interrogated for pathogenicity (cascade screening, in silico analysis, functional studies). Weekly multidisciplinary team (MDT; ophthalmologists, physicians, clinical and molecular geneticists, genetic counsellors) meetings reconciled phenotype with genotype. Bespoke care plans were created for each patient comprising supports, existing interventions, and novel therapies/clinical trials.

Results: The survey revealed that, prior to Target 5000, a significant cohort of patients were not engaging with healthcare and support services due to lack of effective interventions. Pathogenic/likely-pathogenic genetic variants in IRD-implicated genes were confirmed in 62.3% of cases, with 11.6% had variants of unknown significance. The genotyping strategy (research grade testing with validation in an accredited laboratory) of Target 5000 saved 42.73% vs independent testing, not accounting for MDT expertise access, which is unavailable outside the program. This has leveraged funding from government resources, where previously this was largely charitably sourced.

Conclusions: The Target 5000 program has demonstrated a move toward a more efficacious & efficient model of care. This enables harmonized clinical & genetic diagnosis while investigating novel genes/variants, disease mechanisms and therapies. This template could be helpful in developing similar IRD program in small/medium nations.

CONTROL ID: 3542331

SUBMITTER (NAME ONLY): Parth Patel

TITLE: Functional and morphological differences in old and young Brown Norway rat optic nerves: Implications for glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is the leading cause of irreversible blindness in the world. Two risk factors are elevated intraocular pressure and increased age. The Brown Norway (BN) rat has emerged as an important pre-clinical model to study glaucoma. Here, we investigated changes in ON structure and function with age. We hypothesized that in vivo screening of the visual system would correlate with ON morphology.

Methods: Male and female BN rats, 11 (average age 15.5 months) and 11 (average age 2.8 months) were used. Prior to sacrifice, pattern electroretinography (PERG), optokinetic response (OKR), and optical coherence tomography (OCT) were assessed. ONs harvested 1.5 mm posterior to the globe, were fixed (4% paraformaldehyde, 2% glutaraldehyde in 0.1-M sodium cacodylate buffer), postfixed (2% osmium tetroxide), and embedded. Semithin (0.5–1 μ m) sections stained with 1% toluidine blue were imaged by light microscopy (63x oil). QuPath software was used for automated analysis of axon numbers, densities, and size distributions, percent gliotic area, and ON cross sectional area. Statistical significance ($P < 0.05$) was determined by two-way ANOVA followed by Sidak's multiple comparison test or two-tailed Student's t-test.

Results: Overall, ON axon numbers in old and young rats were not statistically different although young female rats had fewer numbers of detected axons. Old rats had significantly lower axon densities and higher ON cross sectional areas than young rats. Old rats had significantly increased NFL thickness but smaller total retinal thickness than young rats. Old rat axon distributions had more small (0.25 μ m) and large (>2 μ m) diameter axons than young rats. Functional analyses showed significant increases in N2 wave timing in old rat PERGs. Old and young rats had similar visual acuity assessed by OKR but contrast sensitivity trended lower in old rats. Correlations of axon numbers and densities with PERG, OKR, and OCT parameters did not show significant trends.

Conclusions: Old and young rats have subtle but significant differences in ON structure and function. Lack of correlation between in vivo screening and ON morphology suggest that PERG, OKR, and OCT did not predict variations in axon numbers or axon densities at baseline. Examination of other biochemical markers of aging and neurodegeneration may offer a clearer picture of how age affects the propensity to develop glaucoma.

CONTROL ID: 3542335

SUBMITTER (NAME ONLY): Katelyn Robillard

TITLE: Gene therapy and gene-editing approaches to treat vision loss in a murine model of Acadian Usher syndrome

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Usher syndrome Type 1C (USH1C) is an inherited deaf-blinding disease that affects Acadian populations in the United States and Canada. Specifically, the USH1C c.216G>A mutation encodes a truncated harmonin protein that disrupts photoreceptor and hair cell function. The goal of this study was to develop genetic approaches for long-term vision improvements in a murine model of USH1C. We hypothesized that AAV-mediated gene therapy and gene-editing approaches would increase full-length Ush1c expression and restore visual function in USH1C mice.

Methods: An AAV vector co-expressing Ush1c-a1 and GFP was delivered via subretinal injection to USH1C mice at different postnatal (P) ages (P17, P22, P98). Transgene expression was determined by confocal scanning laser ophthalmoscopy (cSLO), immunohistochemistry (IHC), and polyacrylamide gel electrophoresis (PAGE). Changes in retinal structure, function, and visual behavior were assessed using optical coherence tomography (OCT), electroretinography (ERG), and a visual cliff assay, respectively. As an alternative approach, multiple gene-editing systems targeting the 216A mutation were developed and introduced into 293T cells alongside an USH1C minigene or into USH1C murine fibroblasts. Editing efficiency was determined by restriction fragment length polymorphism (RFLP) and sequencing analyses.

Results: AAV-treated retinas showed increased full-length Ush1c mRNA and GFP fluorescence localized to the outer nuclear layer (ONL) and photoreceptor inner/outer segments (IS/OS) up to 6 months of age. Although cSLO showed GFP in approximately 20% of the fundus, these molecular changes did not correlate with improvements in retinal structure, function, or visual behavior. Multiple combinations of gene-editing plasmids yielded high rates of on-target editing (up to 46% in sorted 293T cells) with minimal off-target effects in the protospacer region.

Conclusions: This study demonstrated successful AAV-mediated transgene expression in USH1C murine retina and successful gene editing of the human USH1C c.216G>A mutation, in vitro. Future studies will modify viral dose, Ush1c variant, gene promoter, and capsid structure to optimize long-term improvements in retinal structure, function, and visual behavior. We are currently optimizing the transfection protocol for murine fibroblasts to determine editing efficiency at the genomic 216A site.

CONTROL ID: 3542342

SUBMITTER (NAME ONLY): Suchismita Acharya

TITLE: The anti-inflammatory and neuroprotective activity of novel hybrid molecule SA-10 in in vitro ischemic models

SESSION TITLE: Blood flow, ischemia, reperfusion

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Embolism and/or high intraocular pressure lead to poor retinal circulation, reactive oxygen species (ROS) production, microglial activation and retinal ganglion cell (RGC) death. Previously we reported, a small hybrid molecule, SA-10 with both anti-oxidant and nitric oxide donating activity protect retina in a mouse model of ischemia/reperfusion (I/R) injury. Here, we determined the anti-inflammatory and angiogenic effects of SA-10 using in vitro primary human endothelial and rat retinal neuronal cells.

Methods:

Tube formation assay: Human umbilical vascular endothelial cells (HUVECs) were seeded on Matrigel with H_2O_2 (200 μM) and with or without SA-10. Formation of microtubules were captured at 12h and analyzed by Angiogenesis analyzer on ImageJ. I/R cell assays: Primary and immortalized (R28) rat retinal mixed neurons (Oxygen Glucose Deprivation model) and primary rat retinal microglial cells (activated with TII: TNF- α IL- β and IFN- γ) were used with or without SA-10 (1.0, 10, 100 μM). ROS scavenging (DCFDA) and cytoprotective (LDH) activities were measured at 24h. Inhibition of microglial activation by SA-10 was evaluated by measuring inflammatory cytokines from cell supernatant using multiplex ELISA. Data represented as Mean \pm SEM. N = 4.

Results: In HUVECs, SA-10 dose dependently increased microtubule formation with an EC_{50} of 0.125 μM . SA-10 (10 μM) significantly attenuated cell death in both microglia and R28 cells (43% vs 13% and 52 % vs 17% respectively) and decreased ROS (68% to 38%) production in retinal microglial cells. OGD induced cell death is attenuated in primary retinal neurons (66% vs 10%) by SA-10. In microglia after TII insult, there was significant increase in inflammatory cytokines IL-4, IL-1 β , IL-6, TNF- α and decrease in anti-inflammatory cytokine IL-10 as compared to control. SA-10 (10 μM) significantly decreased (2-3-fold) all inflammatory cytokines and increased IL-10 (2.5-fold).

Conclusions: Our results are consistent with our hypothesis that the compound SA-10 is protective to retinal neurons and microglia by decreasing oxidative stress, inflammation with possibility to improve retinal blood perfusion by forming new blood vessels. We predict SA-10 as a possible therapeutic candidate in treating I/R injury in retina and diseases associated with microglia activation and inflammation.

CONTROL ID: 3542347

SUBMITTER (NAME ONLY): Volha Malechka

TITLE: Clinical and Molecular Findings in a CDHR1 Retinal Dystrophy Cohort

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Malechka, B.G. Jeffrey, L.A. Huryn, W.M. Zein, OGVFB, National Eye Institute, Bethesda, Maryland, UNITED STATES|D. Blain, E. Ullah, R.B. Hufnagel, Medical Genetics and Ophthalmic Genomics, National Eye Institute, Bethesda, Maryland, UNITED STATES|B.P. Brooks, Pediatric, Developmental and Genetic Eye Disease Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|C.A. Cukras, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cadherin-related family member 1 is a transmembrane photoreceptor protein encoded by CDHR1 (OMIM 609502). Mutations in CDHR1 are associated with cone-rod dystrophy (CRD 15), retinitis pigmentosa (RP 65) and late-onset macular dystrophy. This work aims to:

1. Describe the clinical and molecular findings in a retinal dystrophy cohort attributed to autosomal recessive CDHR1 variants.
2. Report novel pathogenic CDHR1 variants in ethnic/racial groups not previously known to be affected by disease associated with this gene.

Methods: Ten retinal dystrophy patients harboring biallelic CDHR1 variants were identified from the National Eye Institute clinic records. Pertinent demographic and historical data as well as genetic testing results were collected. Initial visit and follow-up data were analyzed including visual acuity, color vision, Goldman visual field (GVF) testing, color fundus photography (CFP), fundus autofluorescence (FAF), optical coherence tomography (OCT), electroretinography (ERG).

Results: Six males and four females (mean age at the most recent clinic visit 49.0 ± 13.7 years) from nine families of African American, Asian, and European (including Greek) origins were identified. Age at the time of initial symptoms showed a bimodal distribution with peaks in the second (for RP patients) and fifth (for CRD patients) decades of life. Vision loss was the most common presenting symptom. Best corrected visual acuity at last visit ranged from 20/20 to 20/2000 (average LogMAR 0.8 or 20/125). Notable asymmetry of the degree of macular atrophy was present in two patients. Color vision deficits were more severe in patients with larger areas of macular atrophy. GVF testing revealed constriction of visual fields in three patients diagnosed with RP, while seven patients with maculopathy or CRD had central scotoma that mirrored the degree of macular atrophy. Macular involvement was noted in all patients on CFP, FAF, and OCT. Unrecordable scotopic ERG responses distinguished the RP patients. Novel pathogenic variants included a 7-bp deletion common to three patients of Greek origin.

Conclusions: Despite the variable phenotype of CDHR1-associated retinal dystrophies, an involvement of the macula is a common manifestation in this patient cohort. Notable asymmetry in macular involvement is highlighted in two patients. Novel mutations affecting patients of African American and Greek background are reported.

CONTROL ID: 3542351

SUBMITTER (NAME ONLY): Xuan Bao

TITLE: Expression and localization of exon-skipping RGR-d protein in cultured RPE cells

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Bao, H. Xu, H. Cui, M. Zhao, Department of Ophthalmology, Peking University People's Hospital, Beijing, CHINA|H.K. Fong, USC Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The exon-skipping isoform of RGR opsin (NM_001012722.1, RGR-d) has been reported to be associated with human age-related macular degeneration (AMD) and AMD-like pathology in gene-editing mouse models. RGR-d is considered an abnormal protein that undergoes different intracellular processing from the normal RGR protein. Here, we studied the expression and subcellular localization of RGR and RGR-d protein.

Methods: ARPE-19 cells were transfected with FLAG labeled lentiviral vectors expressing RGR or RGR-d and cell lines with stable expression were selected by puromycin. Cells were treated with 4 μ M MG132, a 26S proteasome inhibitor, for 0, 4, 12, and 20 h. The expression of RGR and RGR-d was detected by real-time PCR and western blot. After the cells were treated with 2 μ M MG132 for 10 h, double-labeling immunofluorescence was used to detect the co-localization of RGR/RGR-d and the markers of organelles or autophagy-lysosomal pathway, including calnexin, GM130, LAMP-2, and Rab7.

Results: After the transfection, the mRNA expression of both RGR and RGR-d were hundreds of times higher than that of the negative control. The protein expression of RGR was significantly elevated. But inconsistent with the mRNA expression, RGR-d expression was barely detected by western blot. After the cells were treated with MG132, the protein expression of RGR-d was detected after 4 h, and gradually increased after 12 h and 20 h, indicating an intracellular proteasome degradation of RGR-d. MG132 of a low concentration was then used for the enrichment of intracellular RGR and RGR-d protein. Double-labeling immunofluorescence showed that compared with RGR, RGR-d had less co-localization with calnexin, a marker of the endoplasmic reticulum (ER), and better co-localization with LAMP-2 and Rab7, markers of the autophagy-lysosomal pathway. Neither RGR nor RGR-d had significant co-localization with GM130, a marker of the Golgi apparatus.

Conclusions: In transfected cells, RGR-d was normally transcribed but was almost completely degraded through the ubiquitin-proteasome pathway after translation, while the full-length RGR was normally expressed at both mRNA and protein levels. With the treatment of MG132, RGR-d was less likely to undergo the post-translational modification in the ER and Golgi apparatus and was prone to lysosomal degradation. The findings may provide insights into the processing of abnormal RGR-d protein in the aged population.

CONTROL ID: 3542352

SUBMITTER (NAME ONLY): Sharad Mittal

TITLE: Mesenchymal stem cells enhance suppressive function of T regulatory cells and promote corneal graft survival

SESSION TITLE: Corneal immunology and neovascularization I

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Mittal, W. Cho, E. Elbasiony, S. Chauhan, Department of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mesenchymal stem cells (MSCs) regulate adaptive immune responses in various inflammatory disorders. Here, we investigate whether MSCs directly interact with T regulatory cells (Tregs) to promote their suppressive function in corneal transplantation.

Methods: Bone marrow MSCs (CD45⁻CD34⁻SCA1⁺CD29⁺) and CD4⁺CD25⁺ Tregs (purity: >95% Foxp3⁺) from spleen and lymph nodes (LNs) of Balb/c mice were used. MSC-Treg co-cultures were set up in the presence or absence of Transwells (1 µm pore size) for 48h. Flow cytometry was performed to assess (i) Tregs for Foxp3 levels and frequencies of Foxp3^{high} Tregs and (ii) MSCs for CD80 expression. Results were calculated as fold change from normal controls. To evaluate the contribution of MSC-expressed CD80 on Treg function, MSC-Treg co-cultures were neutralized with anti-CD80 antibody (1 mg/ml), and CD80-silenced MSCs were intravenously administered to transplanted allogeneic mice (Balb/c grafted with B6 corneas). Corneal opacity was evaluated to assess graft survival.

Results: A significant increase was observed in frequencies of Foxp3^{high} Tregs (fold change: 4.8 ± 0.6; p<0.01) and their FoxP3 expression (fold change in MFI: 3.4 ± 0.7; p<0.01) in direct co-cultures of MSCs and Tregs compared to Tregs cultured alone. Inhibition of cell-cell contact via Transwell mitigated this effect (p<0.05). Data showed significant expression of CD80 on MSCs, and neutralization of CD80 in the co-cultures resulted in a decrease of Foxp3^{high} Treg frequencies (fold change: 2.8 ± 0.8; p<0.04) and levels of Foxp3 in Tregs (fold change in MFI: 1.6 ± 0.6; p<0.05). Mice treated with CD80-silenced MSCs did not show augmented frequencies of Tregs with high Foxp3 levels (fold change: 1.3 ± 0.3) and enhanced graft survival (p<0.02) compared to control shRNA/MSC-treated controls (fold change: 2.4 ± 0.3; p<0.03).

Conclusions: MSC-expressed CD80 directly amplifies function of regulatory T cells and promotes corneal graft survival.

CONTROL ID: 3542362

SUBMITTER (NAME ONLY): Ze Zhang

TITLE: Slow release antibiotic medication delivery system in an animal model of ophthalmic surgery

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Zhang, D. Blake, Ophthalmology, Tulane University, New Orleans, Louisiana, UNITED STATES|D. Blake, Biochemistry, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|N. Sahiner, R. Ayyala, Ophthalmology, University of South Florida, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The most common ophthalmic surgery performed in the world is cataract surgery, as cataracts affect the aging population and is an inevitable part of life. Standard post-operative care after all ophthalmic surgery involve the use of eye drops to prevent infection. One of the major challenges including the postoperative infection prevention after ophthalmic surgery is the difficulty in administering topical medications into the patients' eyes. Studies have shown that up to 50% of prescribed drops are incorrectly instilled or not used at all. When used correctly, only a minor fraction of the instilled medication can effectively get into eyes. In this study, we examine the safety and efficacy of an in vitro safe sustained release formulation of antibiotics in prevention and treatment of ocular infections. This could revolutionize infection control and treatment regimens, and significantly improve patient's outcomes and quality of life, while also reducing the cost of care.

Methods: Hyaluronic acid conjugated polymers of ciprofloxacin and vancomycin were created using biocompatible chemical linkers with stable release profile and safety in vitro. 10,000 colony forming units of bacteria were injected into the anterior chamber of New Zealand white rabbit eyes to simulate potential inoculation from bacteria during surgery and compared to standard topical antibiotic therapy using ciprofloxacin and vancomycin. Daily clinical anterior segment and fundus exams were performed. Animals were followed daily for 2 weeks or until any evidence of endophthalmitis.

Results: Hyaluronic acid-antibiotic polymers provide effective prophylaxis and treatment of potential bacterial inoculation of *Staphylococcus aureus* and *Pseudomonas aeruginosa* in a rabbit model for ophthalmic surgery that is non-inferior to current standard of care using topical antibiotics. Rabbit eyes are able to clear the infection at similar rates in both groups.

Conclusions: The hyaluronic acid and antibiotic polymers provide effective and predictable release of antibiotics that are safe and effective in vitro and in vivo. These particles provide a novel way to deliver drugs in an ophthalmic setting that could replace the need for post-operative drops and make surgery dropless. These sustained release particles could also be used to treat corneal keratitis, removing the need for hourly drops, improving both efficacy and patient quality of life.

CONTROL ID: 3542368

SUBMITTER (NAME ONLY): Sasha Kravets

TITLE: Associations between Large Optic Nerve Cupping, Related Genetic Risk Scores and Cognitive function

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The optic nerve and the brain share anatomy and pathophysiology of the neurodegenerative process. This study investigates if genetic risk scores (GRS) for large optic nerve cupping (CDR) mediates the association between CDR and cognitive function.

Methods: We used data from the Women's Health Initiative (WHI)-Sight Exam and WHI-Memory Study, excluding women with ocular hypertension (intraocular pressure > 23 mmHg) or glaucoma medication use. Large CDR was defined as > 0.6 in either eye. To form the GRS, we used the log odds ratio (OR) estimated from a previously identified single nucleotide polymorphisms (SNP) logistic regression model adjusted for age and two principle components. Cognitive function was measured by the Modified Mini-Mental State Examination (3MSE). We used multiple logistic regression to evaluate the association of the weighted GRS with large CDR, then a generalized linear model to assess the association between weighted GRS and 3MSE scores, and between weighted GRS, CDR, and 3MSE scores, adjusted for age, education, smoking, diabetes, body mass index, cardiovascular disease, diabetic retinopathy, and hormone therapy randomization. As 3MSE scores were non-normally distributed, a log-transformed function of scores, $\log(102-3MSE)$, was used.

Results: Final analyses included 1201 White women; mean age (\pm SD) was 69.59 ± 3.62 years. Of those, 7.24% had large CDR. The mean GRS in women with and without a large CDR was 1.51 ± 0.31 vs. 1.41 ± 0.36 , $p = 0.004$, and the odds of large CDR for a one unit increase in GRS is 2.29 (95% CI: (1.21, 4.34), $p = 0.011$). There was no association between weighted GRS and 3MSE scores ($p = 0.964$). The final adjusted model showed that women without large CDR had significantly lower 3MSE scores than those with large CDR, yielding a predicted mean difference in 3MSE of 0.838 (p -value=0.0071). Adding GRS in the model, women with large CDR still had statistically significantly lower 3MSE scores than those without large CDR, yielding a predicted mean difference in 3MSE scores of 0.844 ($p = 0.0069$).

Conclusions: Prior work showed a mean difference of 0.21 3MSE units was associated with a 76% increased hazard for dementia. This analysis suggests independent of the GRS, women who had large CDR, without glaucoma or ocular hypertension had a lower cognitive function. Further investigation is warranted.

CONTROL ID: 3542370

SUBMITTER (NAME ONLY): Riccardo Sacconi

TITLE: Characterization of macular neovascularization in geographic atrophy

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To characterize macular neovascularization (MNV) developing in eyes affected by geographic atrophy (GA).

Methods: In this multicentric longitudinal study, patients previously affected by GA that developed an active MNV were included in 3 retina referral centers. Patients were investigated using structural optical coherence tomography (OCT), fundus autofluorescence, OCT-angiography, and dye angiographies. Patients were treated with ProReNata (PRN) anti-vascular endothelial growth factor (VEGF) injections and were reevaluated after treatment.

Results: Among 512 patients previously diagnosed with GA, 40 eyes of 40 patients (mean age 80.8 ± 7.9 years, mean GA area $8.73 \pm 7.39 \text{ mm}^2$) presented with treatment-naïve exudative MNV (accounting for an estimated prevalence of 7.81%; 5.49 - 10.13, 95% confidence intervals) and thus were included in the analysis. 67.5% of MNVs were classified as type 2 MNV, 25% as type 1, 2.5% as type 3, and 5% as mixed phenotype. In 92.5% of cases, active MNV in GA showed subretinal hyperreflective material (SHRM) with or without evidence of sub-/intra-retinal hyporefective exudation. During a mean follow-up of 28 ± 25 months, patients were treated with 6.6 ± 6.3 anti-VEGF injections, with 2.9 ± 1.4 injections in the first year of treatment. No patient developed GA enlargement in the area of MNV.

Conclusions: MNVs in GA showed different multimodal imaging features and therapeutic response in comparison to previously reported features of MNV in age-related macular degeneration (AMD) without GA. For these reasons, the combined phenotype (i.e. GA with neovascular AMD) should be considered as a distinct entity in the research and clinical setting.

CONTROL ID: 3542374

SUBMITTER (NAME ONLY): Fatema Ghasia

TITLE: Fixation Eye Movements in Amblyopia during Binocular and Dichoptic viewing conditions

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.F. Ghasia, J. Murray, K. Garg, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patching and dichoptic amblyopia therapies aid recovery of vision through distinct mechanisms and require different viewing conditions. We have previously characterized abnormalities of fixation eye movements of the fellow and amblyopic eye during monocular and binocular viewing conditions. The purpose of the study was to assess the fixation stability of the fellow and amblyopic eye and quantify eye misalignment in dichoptic environment when the contrast of the fellow eye was rebalanced to facilitate reduction in the inter-ocular suppression.

Methods: We recruited 20 amblyopic and 10 control subjects. Fixation eye movements were measured with high-resolution video-oculography during A) binocular and B) dichoptic viewing as the brightness of the fellow eye fixation target varied from full to low contrast. Fixation eye movements and BCEA of fellow and amblyopic eye and vergence BCEA were analyzed.

Results: We found increased instability of the amblyopic eye during both eye viewing conditions. We also found increased instability in both controls and amblyopes under dichoptic viewing especially at low fellow eye contrasts. BCEA values increased from -0.12 ± 0.07 at full contrast to -0.07 ± 0.12 at low contrast in the dichoptic environment in controls. Amblyopes responded more dramatically, with mean BCEA values increasing from 0.02 ± 0.38 at full contrast to 0.1 ± 0.36 at low contrast for the fellow eye and from 0.32 ± 0.29 at full contrast to 0.54 ± 0.45 at low contrast for the amblyopic eye. Dichoptic viewing also affected eye alignment, with 4 of the 6 strabismic subjects experiencing pronounced increases in strabismus angle as compared with binocular viewing. Vergence BCEA increased from 1.93 ± 0.925 to 3.15 ± 2.99 at 100% contrast in amblyopes, rising to 4.84 ± 3.31 at low contrast. There was no such increase in controls.

Conclusions: Even for simple stimuli, dichoptic presentation presents challenges for amblyopes. Although, the contrast rebalance to the fellow eye is likely reducing the inter-ocular suppression, the eye misalignment and disconjugacy are increased in the dichoptic environment for amblyopic subjects. This could account for the variability of treatment outcomes seen with dichoptic therapies.

CONTROL ID: 3542379

SUBMITTER (NAME ONLY): Hanieh Mirhajianmoghadam

TITLE: Behavioral Changes During the COVID-19 Pandemic in Myopic and Non-Myopic Adults

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Mirhajianmoghadam, A.B. Pina, L.A. Ostrin, College of Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic began in the United States in early 2020, affecting day to day life for adults and children. Secondary to quarantine and lockdown measures, many people have had to spend more time in their home and carry out activities virtually, not only for work, but also for social interactions and daily tasks, such as grocery shopping. Increased time indoors and electronic device use may ultimately impact sleep/wake patterns and, in younger adults, potentially eye growth and myopia progression. Our goal was to compare subjective measures of daily behaviors in myopic and non-myopic adults during the summer COVID-19 pandemic to their behaviors prior to the pandemic.

Methods: Adults (ages 40.5 ± 5.5 years, $n=66$) completed a questionnaire regarding their demographics, ocular history, and behaviors for summer 2020, as well as for before the COVID-19 pandemic. Subjects were asked to estimate the time spent per day on various activities, such as hand held and traditional electronic device use, time spent outdoors, and sleep. Data were analyzed with repeated measures ANOVA for session (COVID-19 vs pre-COVID-19), day of week (weekdays vs weekends), and refractive error group (myopic vs non-myopic).

Results: During the COVID-19 pandemic, participants spent more time doing near work compared to pre-COVID-19 (4.5 ± 0.4 vs 4.1 ± 0.3 hours per day, respectively, $P=.026$). Additionally, on weekdays, participants demonstrated increased electronic device use during COVID-19 compared to pre-COVID-19 (9.9 ± 0.5 vs 8.9 ± 0.5 hours per day, respectively, $P=.008$). On weekdays, sleep duration significantly increased by 36 minutes during COVID-19 ($P<.001$). Time spent outdoors and in physical activities were not significantly different between sessions ($P>.05$ for all). For all metrics, there were no significant differences by refractive error group.

Conclusions: COVID-19-related quarantine measures changed adults' behaviors compared to before the COVID-19 pandemic. Based on self-report, near work and use of electronic devices increased during COVID-19, whereas physical activity and time outdoors were not significantly different compared to pre-COVID-19. There were no differences in behaviors between myopes and non-myopes. Depending on temporal characteristics of artificial light exposure from the reported increase in electronic device use, sleep/wake patterns and circadian rhythm may ultimately be affected.

CONTROL ID: 3542381

SUBMITTER (NAME ONLY): Quinn Lee

TITLE: Inhibition of EB3 prevents choroidal neovascularization in AMD model of non-human primates

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Lee, X. Qu, A.B. Malik, Y. Komarova, Pharmacology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|M. Sanders, Laurel Therapeutics, Inc., Houston, Texas, UNITED STATES|M. Rosenblatt, Ophthalmology, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vascular leakage and aberrant neovascularization in eyes are major causes of blindness affecting diverse patient groups. Current treatments require regular intravitreal injections of anti-VEGF biologics. Here, we demonstrated the therapeutic benefits of a topically administered inhibitor of End-Binding protein 3 (EB3), herein EBIN, in treating leaky choroidal neovessels.

Methods: The efficacy of topical administration of EBIN was evaluated in a CNV model of AMD in African green monkeys compared to topical vehicle and single IVT administration of aflibercept. Six laser spots were symmetrically placed within the perimacular region employing an Iridex Oculight TX 532 nm laser with laser duration of 100 ms, with a spot size of 50 μm and power of 750 mW. All animals received 30 μL topical instillation of vehicle or 150 μg EBIN twice daily on days 1-7 and once a day on days 8-21. An additional cohort received IVT injections of 2 mg Eylea® per eye. Fluorescein leakage was graded using angiograms of CNV lesions. The CNV complex area was measured using Optical Coherence Tomography images.

Results: The incidences of clinically relevant grade IV CNV was 23.08% and 16.42% of the total lesions from the vehicle treated group and 11.94% and 7.35% in EBIN treated group at days 14 and 21, respectively. The Fisher's Exact Probability Test revealed significantly lower incidence of grade IV lesions in EBIN versus vehicle groups at day 14 ($p=0.0288$). No significant difference was observed between vehicle and EBIN groups on day 21, and EBIN and aflibercept treated groups on days 14 and 21. The mean CNV lesion size was 50,471, 39,512 and 23,838 μm^2 at day 14, and 34,621, 33,884 and 19,739 μm^2 at day 21 for vehicle, EBIN, and aflibercept groups, respectively. Compared to the vehicle group, the mean CNV complex area was significantly smaller in EBIN-treated eyes at day 14 ($p=0.0146$), but not at day 21 ($p=0.9791$). The mean CNV complex area was smaller in the aflibercept group compared to EBIN group at days 14 ($p=0.0003$) and 21 ($p=0.0014$).

Conclusions: Mean CNV complex size was significantly smaller in the EBIN group at day 14 and aflibercept group on days 14 and 21 when compared with the vehicle-treated animals. This was consistent and aligned with observed reduction in incidence of grade IV lesions.

CONTROL ID: 3542393

SUBMITTER (NAME ONLY): Eitan Katz

TITLE: Exosomes as a Novel Multitarget Approach to Promote Growth of Corneal Sensory Neurons

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Katz, V.H. Guaiquil, E. Ivakhnitskaia, D. Lara, K. Anwar, E. Jalilian, M. Rosenblatt, A.R. Djalilian, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Several growth factors, lipids and microRNAs can influence the regeneration of corneal nerves after injury. However, they have been primarily used as single entities with variable results. Here we propose the use of exosomes, which carry as “cargo” many of these regenerative factors, as a multitarget approach to enhance nerve growth.

Methods: Exosomes from cultured human corneal mesenchymal stem cells (cMSCs) and bone marrow mesenchymal stem cells (BM-MSCs) were isolated using ultracentrifugation. Trigeminal ganglia neurons from adult mice were cultured in neurobasal A media alone (negative control), supplemented with nerve growth factor (NGF) as a positive control, or supplemented with exosomes derived from cMSCs or BM-MSCs. Neurons were observed for four days and subsequently fixed with paraformaldehyde (PFA) and stained with beta-tubulin to evaluate neurite growth. Treatment conditions were masked to prevent bias and neurons were imaged and traced using Neurolucida software. Finally, branched-length and Sholl analysis were performed. Experiments were repeated for each treatment condition (n=3).

Results: Neurons treated with exosomes derived from BM-MSCs had an average neurite length of 576 um, while those in the control and NGF group had an average length of 288 and 529 um respectively. Additionally, Sholl analysis indicated that neurons from the BM-MSC exosome group had greater complexity than controls. Exosomes derived from cMSCs did not show as strong of an effect, with an average neurite length of 433 um.

Conclusions: Our results indicate a possible neurotrophic effect of exosomes. Neurons treated with exosomes displayed greater neurite growth and complexity than controls. Additional work will evaluate the effects of stem cell derived exosomes on in-vivo models of corneal nerve injury.

CONTROL ID: 3542394

SUBMITTER (NAME ONLY): Katarzyna Komar

TITLE: The effect of cataract on two-photon visual thresholds

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Komar, A. Matuszak, M. Wojtkowski, Uniwersytet Mikołaja Kopernika w Toruniu Wydział Fizyki Astronomii i Informatyki Stosowanej, Torun, POLAND|K. Komar, M.J. Marzejon, M. Wojtkowski, International Centre for Translational Eye Research, Instytut Chemii Fizycznej Polskiej Akademii Nauk, Warszawa, POLAND|M.J. Marzejon, Faculty of Electronics, Telecommunications and Informatics, Politechnika Gdanska, Gdansk, Województwo pomorskie, POLAND|B. Sikorski, Department of Ophthalmology, Uniwersytet Mikołaja Kopernika w Toruniu Collegium Medicum im Ludwika Rydygiera w Bydgoszczy, Bydgoszcz, POLAND|B. Sikorski, Oculomedica Eye Research & Development Center, Bydgoszcz, POLAND|

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ABSTRACT BODY:

Purpose: Two-photon vision is associated with the perception of short pulses of near-infrared (NIR) laser radiation as a visible (VIS) light. It is caused by the nonlinear process of two-photon absorption by visual pigments. The longer wavelength of the stimulating radiation suggests that this phenomenon may be beneficial for functional visual examination in cataract patients compared to normal, one-photon based, perception of light. To verify this hypothesis, we performed measurements of the one-photon (VIS) and two-photon (IR) visual thresholds for a group of cataract patients before and 6 months after the intraocular lens (IOL) implantation.

Methods: We used custom-built two-photon perimeter with NIR pulsed laser ($\lambda_c = 1028.4$ nm, $\tau_p = 12.2$ ps, $F_{rep} = 19.17$ MHz) and VIS continuous wave laser ($\lambda = 520$ nm) as a source of stimulating light. Due to two-photon vision effect both sources are perceived as green. The sensitivity of central part of the macula (10 deg diameter) was tested in 32 patients aged 53-84 years, under scotopic conditions. The examined patients were qualified for IOL surgery because of cataract with no diagnose of diabetes and retinal diseases. 6 months after the surgery 25 patients were tested again. The retinal sensitivity assessment was the same as described in [1] except smaller number of tested locations (17) to shorten examination time. The visual function of the patients before and after IOL implantation was also tested by commercial MAIA microperimeter (photopic version) on the same retinal area. The study was approved by the Ethics Committee of the Collegium Medicum, NCU.

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Results: The mean difference of sensitivity after the cataract surgery was equal to: 6.6 ± 1.3 dB (SEM) for VIS laser, 2.8 ± 0.7 dB (SEM) for IR laser and 2.0 ± 0.6 dB (SEM) for MAIA. There is significant difference between VIS and IR result (p-value 0.014) and between VIS and MAIA result (p-value 0.004).

Conclusions: The obtained results indicate that presence of cataract stronger affects the sensitivity of retina as measured by VIS- than IR-laser-based perimetry under scotopic conditions. It supports the hypothesis that two-photon visual sensitivity of cataract patients is limited less by the changes that occur in the lens than normal visual sensitivity. Surprisingly, the photopic visual sensitivity measured by MAIA also has changed slightly, which may be explained by wide spectral range of stimulus used in the device.

CONTROL ID: 3542395

SUBMITTER (NAME ONLY): WonKyung Cho

TITLE: Ocular surface distribution of mast cells functionally contributes to asymmetrical angiogenic response

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Cho, S. Mittal, E. Elbasiony, S. Chauhan, Department of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Asymmetrical neovascularization has been reported in the pathogenesis of multiple ocular conditions such as pterygium and pinguecula. Here, we investigated whether distribution of ocular surface mast cells are functionally associated with angiogenic response.

Methods: Corneal neovascularization was induced by placing a single figure-8 intrastromal suture on the nasal or temporal side of the cornea using 11-0 nylon suture. Growth of blood vessels were observed clinically using a slit-lamp biomicroscope and at the molecular level by immunohistochemistry (IHC) analysis of CD31+ vascular endothelial cells in harvested corneas on day 7 post-suture. Distribution and activation of mast cells in the nasal and temporal corneas were evaluated by IHC analysis of avidin stained corneas and by quantification of tryptase and β -hexosaminidase levels in tear and corneal lysates. Mast cell deficient cKitw-sh mice and cromolyn (2% in PBS) treated mice were used to study the effect of mast cell distribution on asymmetrical corneal angiogenesis.

Results: A nasally placed suture resulted in more extensive corneal neovascularization compared to one placed temporally, as evidenced by slit lamp ($p=0.01$) and IHC analysis ($p=0.04$). IHC analysis showed a 2-fold increase in number of avidin+ mast cells in the nasal cornea compared to the temporal cornea. Moreover, 4.3-fold increase in tryptase levels and 2.1-fold increase in β -hexosaminidase levels were observed following suture placement on the nasal side, compared to the naive cornea. Suture on the temporal side resulted in significantly less increase in tryptase (1.4-fold ($p=0.0002$)) and β -hexosaminidase levels (1.1-fold ($p=0.006$)). Mast cell deficiency and cromolyn-mediated inhibition of mast cell activation abrogated the disproportionate growth of blood vessels, resulting in comparable nasal and temporal neovascularization, as evidenced by slit-lamp and IHC.

Conclusions: Our novel findings demonstrate that the spatial distribution and function of mast cells regulate pathological angiogenesis.

CONTROL ID: 3542396

SUBMITTER (NAME ONLY): Nicholas Konopek

TITLE: Hemodynamic retinal changes in diabetic macular edema after anti-vascular endothelial growth factor injection on optical coherence tomography angiography

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Konopek, P.L. Nesper, A.A. Fawzi, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nicholas Konopek: Commercial Relationship: Code N (No Commercial Relationship) | Peter Nesper: Commercial Relationship: Code N (No Commercial Relationship) | Amani Fawzi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate retinal hemodynamic response to anti-vascular endothelial growth factor (anti-VEGF) injection in diabetic macular edema (DME) eyes evaluated before and 1 month after the injection using optical coherence tomography angiography (OCTA).

Methods: We used a previously validated thresholding method based on the skeletonized deep capillary plexus (DCP) of each eye. We then analyzed the following parameters in the parafoveal area (3mm annulus with 1mm inner circle): Adjusted Flow Index (AFI), Vessel Density (VD), Skeletal Vessel Density (SVD) in addition to the Fovea Avascular Zone (FAZ), and Central Foveal Thickness (CFT). We assessed longitudinal changes using a generalized linear model correcting for image quality (SSI).

Results: Our pilot study examined 6 eyes (4 female, age 51 ± 15.7 years). Compared to baseline, follow up imaging revealed significantly reduced superficial capillary plexus (SCP) VD ($p=0.036$), FAZ area ($p=0.001$) and CFT ($p=0.001$). Although not significant, overall trends showed increased AFI in the full retina and middle capillary plexus (MCP), contrasted with reduced AFI in the SCP and DCP slabs.

Conclusions: FAZ and CFT decrease significantly after anti-VEGF injection, consistent with reduced DME. Only the VD in the SCP was significantly reduced on follow up. Ongoing active recruitment is underway to further confirm the results of this pilot study and will be reported at the ARVO 2021 Annual Meeting.

CONTROL ID: 3542398

SUBMITTER (NAME ONLY): Hye Jin Kim

TITLE: Vitamin A aldehyde-aurine adduct and the visual cycle

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Kim, J. Zhao, J.R. Sparrow, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J.R. Sparrow, Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Hye Jin Kim: Commercial Relationship: Code N (No Commercial Relationship) | Jin Zhao: Commercial Relationship: Code N (No Commercial Relationship) | Janet Sparrow: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Continued light sensitivity necessitates the regeneration of 11-cis-retinal via a series of enzyme-catalyzed steps within the visual cycle. During this process vitamin A aldehyde is shepherded within photoreceptors and retinal pigment epithelial cells by retinoid-binding proteins and NRPE to facilitate retinoid trafficking, to prevent non-specific aldehyde reactivity and to conserve the 11-cis configuration. Least understood is a Schiff base adduct (A1T) that forms non-enzymatically and reversibly from reactions between taurine and vitamin A-aldehyde and is abundant in neural retina of humans and mice.

Methods: Retinoids (derivatized with O-ethylhydroxylamine (100 mM) in DPBS) and bisretinoids, taurine and β -alanine (derivatized with NBD-F) were quantified by HPLC and UPLC with reference to authentic standards. A1T was synthesized by reacting retinaldehyde with taurine (1:1 molar ratio of retinal isomers and taurine) in dehydrated methanol containing sodium methoxide. ONL area was calculated as the sum of the ONL thicknesses in superior and inferior retina (0.2–2.0 mm) multiplied by the measurement interval of 200 microns.

Results: Reduction in cellular taurine by treatment with the taurine transport inhibitor β -alanine (in drinking water, 2%; 2 months) accentuated the thinning of outer nuclear layer (ONL) expected in albino $Abca4^{-/-}$ mice. β -alanine-treatment reduced bisretinoid levels. When mice were treated with taurine (2.5% in drinking water for 2, 4 and 6 months) ONL thinning in albino $Abca4^{-/-}$ mice was reduced.

Conclusions: We previously observed that A1T is more abundant under conditions in which 11-cis-retinaldehyde is present at higher levels, including black versus albino mice, dark-adapted versus light-adapted mice and mice carrying the Rpe65-Leu450 versus Rpe65-450Met variant. The accentuated ONL thinning indicative of photoreceptor cell loss, is consistent with previous reports of photoreceptor cell death in the presence of taurine deficiency; perhaps the worsening of ONL thinning occurs due to inadequate 11-cis-retinal handling. The reduction in bisretinoid levels with β -alanine treatment suggests that the intent of A1T formation is not to protect against unwanted bisretinoid formation as might be supposed. Rather A1T may serve to preserve retinaldehyde.

CONTROL ID: 3542401

SUBMITTER (NAME ONLY): Andres Serrano

TITLE: Intraocular Inflammasome Activation in Pseudophakic Bullous Keratopathy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Serrano, A. Gomez-Bedoya, E. Salero, A. Tovar, P. Persad, G. Amescua, F. Cabot, A.L. Sabater, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|R. Hadad, R.W. Keane, J. de Rivero Vaccari, Neurological Surgery, University of Miami Miami Project to Cure Paralysis, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: High intraocular levels of proinflammatory cytokines have been associated with low corneal endothelial cell density in pseudophakic bullous keratopathy (PBK). However, it is unknown which mechanism is involved in this interaction. The adaptor protein apoptosis-associated speck-like protein containing a caspase-recruitment domain (ASC) is part of the inflammasome, a protein complex responsible for triggering the activation of the pro-inflammatory cytokine IL-1 β and the inflammasome-mediated cell death process of pyroptosis. In the present study, we measured the intraocular levels of ASC among patients with PBK and Fuchs' dystrophy to assess the role of pyroptosis-mediated endothelial cell death and correlate them with clinical parameters such as central corneal thickness (CCT) and ocular surface inflammation.

Methods: Aqueous humor (AqH) samples from 17 patients were analyzed. These samples were collected at the beginning of surgery from patients with PBK (5) and Fuchs' dystrophy (4) who underwent cornea transplantation, and healthy patients undergoing cataract surgery (8). The presence of the inflammasome was assessed by measuring ASC levels of the AqH samples via Simple Plex technology (Protein Simple). Additionally, a correlation between ASC concentrations and clinical parameters (CCT measured by ultrasound pachymetry and ocular surface inflammation measured by InflammaDry[®] tear immunoassay) among the subjects was made.

Results: Protein levels of ASC were significantly higher in the AqH of patients with PBK compared with both Fuchs' dystrophy [Mann-Whitney U, or Wilcoxon, (MWW) test $p=0.016$] and the control group (MWW test $p=0.001$). Fuchs' dystrophy and controls did not show significance when compared to each other. Regarding clinical measurements, there was a positive correlation between the levels of ASC in AqH and the InflammaDry[®] assay severity (Kendall's tau correlation coefficient=0.55, $p=0.020$). Also, the CCT positively correlated with protein levels of ASC in the AqH (Spearman's rank correlation coefficient=0.53, $p=0.028$).

Conclusions: Significantly higher levels of ASC in the AqH of patients with PBK suggest that the inflammasome may play an important role in the disease and should be further studied for therapeutic purposes. Moreover, protein levels of ASC in the AqH could aid to a better management of the PBK patient population in combination with the parameters used during standard clinic visits.

CONTROL ID: 3542402

SUBMITTER (NAME ONLY): Sehar Riaz

TITLE: PCDH15-associated retinopathy in an orthologous Usher mouse and evaluation of potential therapies for progressive vision loss

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Riaz, S. Sethna, Z. Ahmed, Department of Otorhinolaryngology head & neck Surgery, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|L.H. Vandenberghe, Dept of Ophthalmology, Harvard Medical School and Mass Eye and Ear, Grousbeck Gene Therapy Center, Ocular Genomics Institute, Boston, Massachusetts, UNITED STATES|L. Carvalho, Lions Eye Institute, University of Western Australia, Centre for Ophthalmology and Vision Science, Nedland, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Usher syndrome type I (USH1) is characterized by congenital deafness, vestibular areflexia, and progressive retinal degeneration. The protein-truncating p.Arg245* founder variant of PCDH15 has ~2% carrier frequency among Ashkenazi Jews, accounting for nearly 60% of their USH1 cases. Here we will investigate the precise role of protocadherin-15 in light transduction and mechanism of visual deficits and rescue of vision in the Pcdh15^{KI/KI} mouse model (Pcdh15^{R250X}; equivalent to human p.Arg245*) by two different modalities.

Methods: Pcdh15^{KI} mice were generated using CRISPR/Cas9. Retinal function was assessed by electroretinography (ERG), structural integrity by optical coherence tomography (OCT). Light-dependent translocation of phototransduction cascade proteins was determined using immunostaining. RPE65 and CRALBP levels by immunoblot. Rescue strategies included exogenous retinoids delivery via intraperitoneal injections, and AAV mediated gene delivery via subretinal injections.

Results: Our results showed Pcdh15^{KI} mutants recapitulates human p.Arg245* visual deficit phenotype. ERG showed attenuated a- and b-wave amplitudes and OCT showed no gross retinal degeneration. We found light-dependent translocation of arrestin and transducin was perturbed in mutant mice, indicating protocadherin-15 has an important role in rapid shuttling of proteins from outer segments to inner segments and vice versa, under light adapted conditions. We found lower levels of visual retinal cycle proteins RPE65 and CRALBP. For the rescue of retinal phenotype, administration of exogenous 9-cis retinal, improved ERG amplitudes in these mutant mice. We evaluated dual AAV PCDH15 mediated expression of full length PCDH15 in Pcdh15^{KI/KI} MSC's (Mesenchymal stem cells). Currently, we are evaluating the impact of subretinal injections of dual AAV vector containing full length PCDH15 gene in Pcdh15^{KI} mutant mice. Results of these studies will be presented in the meeting.

Conclusions: Our current findings support a role for visual retinoid cycle dysfunction in Pcdh15^{R250X} mutant mice suggesting a basis for a clinical trial of exogenous FDA approved retinoids to preserve vision in USH1F patients. Finally, dual AAV PCDH15 vectors mediated gene replacement therapy is one of the treatment modalities to rescue vision function in USH1F patients at the early stage.

CONTROL ID: 3542403

SUBMITTER (NAME ONLY): Debora Nickla

TITLE: Wearing blue-green blocking lenses in the evening inhibits ocular growth rate in chicks

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.L. Nickla, W. Chen, C.P. Taylor, F.J. Rucker, Biosciences and Disease, New England College of Optometry, Boston, Massachusetts, UNITED STATES|C. Barrau, T. Villette, K. Baranton, R&D, Essilor International Creteil, Creteil, Île-de-France, FRANCE|

Commercial Relationships Disclosure (Abstract): Debora Nickla: Commercial Relationship(s);Essilor International:Code F (Financial Support) | William Chen: Commercial Relationship(s);Essilor International:Code F (Financial Support) | Christopher Taylor: Commercial Relationship(s);Essilor International:Code F (Financial Support) | Coralie Barrau: Commercial Relationship(s);Essilor International:Code E (Employment) | Thierry Villette: Commercial Relationship(s);Essilor International:Code E (Employment) | Konogan Baranton: Commercial Relationship(s);Essilor International:Code E (Employment) | Frances Rucker: Commercial Relationship(s);Essilor International:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Blue light in the evening phase-delays the dim light melatonin onset rhythm, and is associated with various pathologies. Blue-blocking lenses prevented the phase-delay in humans (2019 ARVO E-Abstract #5269). In chicks, while rearing in blue light inhibited ocular growth, brief daily exposures to blue light in the morning or evening stimulated ocular growth (2020 ARVO E-Abstract 3407), which, if translatable, might predispose children to myopia. We tested the effects of blue-green blocking lenses (Essilor: block 70% in the circadian band of 460-510nm; Tv(D65) = 77%) on ocular growth rates in chicks.

Methods: Experiments began at age 12-14 days. The light cycle was 12L/12D in all experiments. Lens Conditions: White light: Chicks wore binocular lenses for 4 hours in the morning (n=11) or evening (n=8) in white light (588 lux). Extra blue light: Chicks wore lenses for 4 hours in the evening, with the addition of 4 hours blue light (575 lux; 460 nm) in the morning (n=6). Control conditions: Blue light: chicks were exposed to 4 hours blue light (200 lux) in the morning (ZT0-ZT4; n=9) or evening (ZT8-ZT12; n=16). White light: chicks were not exposed to blue light (n=23). Growth rates ($\mu\text{m}/9\text{d}$) were determined using A-scan ultrasonography; rhythm parameters were determined by measures at 6-hr intervals over 24 hours on the last day of the experiment.

Results: Wearing lenses in the evening inhibited ocular growth relative to "white controls" (670 vs 766 $\mu\text{m}/9\text{d}$; ANOVA $p=0.025$; $p<0.05$); there was no significant effect of morning lens-wear (708 vs 766 $\mu\text{m}/9\text{d}$). The addition of blue light in the morning did not reduce the efficacy of the evening lens-wear: growth was inhibited relative both to white controls and to morning blue (no lens) controls (592 $\mu\text{m}/9\text{d}$ vs 766 μm and 830 $\mu\text{m}/9\text{d}$ respectively; $p<0.05$ for both comparisons). 4 hours of blue light in the evening (without lenses) increased the amplitude of the rhythm in choroidal thickness relative to white controls (71 μm vs 47 μm ; $p<0.05$); wearing lenses in the evening prevented this effect (34 μm ; $p<0.01$ for lens vs blue evening light).

Conclusions: The evening-wear of lenses that block light spectra in the circadian range inhibited eye growth in white light, and when "extra" blue light was added to the light cycle. These results suggest that such lenses may be beneficial in preventing the development of myopia in children.

CONTROL ID: 3542404

SUBMITTER (NAME ONLY): Paul Grosrenaud

TITLE: Etiology, characteristics, and outcomes of oculomotor apraxia in children

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Grosrenaud, M. Borchert, M. Chang, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M. Borchert, M. Chang, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Paul Grosrenaud: Commercial Relationship: Code N (No Commercial Relationship) | Mark Borchert: Commercial Relationship: Code N (No Commercial Relationship) | Melinda Chang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Oculomotor apraxia (OMA) is a rare disorder characterized by inability to initiate saccades. In children, OMA may be congenital and idiopathic or secondary to an underlying genetic or neurologic diagnosis. We describe clinical and radiographic findings and outcomes in children with OMA in the modern era of neuroimaging and genetic testing.

Methods: We conducted a retrospective chart review of all children (<18 years) diagnosed with OMA at our institution from 2010-2020. OMA was diagnosed in children with impaired horizontal and/or vertical saccade initiation during optokinetic nystagmus testing. Children with developmental delays underwent neuroimaging; those with additional medical comorbidities underwent genetic testing. OMA was considered improved if saccades could be generated in the affected direction with or without blinking. We compared children with congenital idiopathic OMA (CIOMA) to those with acquired or congenital OMA secondary to a genetic or neurologic disorder (SOMA).

Results: 37 patients were included. 17 (46%) were congenital and idiopathic, and 20 (54%) were secondary to a genetic or neurologic condition. Among SOMA cases, 17 (85%) had a genetic disorder (6 with Joubert syndrome), 2 had hypoxic-ischemic encephalopathy (10%), and 1 (5%) occurred after encephalitis. Neuroimaging abnormalities (90% vs. 18%, $p<0.001$) and developmental delays (100% vs. 59%, $p=0.002$) were more frequent in children with SOMA than CIOMA. Endocrine disorders (most commonly growth hormone deficiency) were diagnosed in 12% of CIOMA and 15% of SOMA cases ($p=0.77$). Strabismus (45% vs. 12%, $p=0.03$), nystagmus (30% vs. 0%, $p=0.02$), and vertical saccade involvement (25% vs. 0%, $p=0.05$) were significantly more common in SOMA than CIOMA. Improvement occurred more frequently in CIOMA than SOMA (77 vs. 35%, $p=0.02$). Follow-up time did not significantly differ (median 3.5 vs. 3.2 years in CIOMA and SOMA groups, respectively, $p=0.77$).

Conclusions: Consistent with prior literature, we report a high frequency of developmental delays, neuroimaging abnormalities, and genetic and neurologic disorders in children with OMA. Additionally, we found that children with both CIOMA and SOMA had a higher rate of endocrine disorders than the general pediatric population, which has not been previously reported. Compared to children with CIOMA, those with SOMA were more likely have vertical involvement, strabismus, nystagmus, and poor oculomotor outcomes.

CONTROL ID: 3542412

SUBMITTER (NAME ONLY): Brian Vohnsen

TITLE: A possible link between age-dependent photoreceptor cone density and the onset of myopia driven by low luminance

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Vohnsen, Physics, University College Dublin, Dublin, IRELAND|

Commercial Relationships Disclosure (Abstract): Brian Vohnsen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Time outdoor is a critical parameter for emmetropization and to prevent the onset of myopia. Here, the purpose is to analyze whether oblique ray angles at the retina may cause photoreceptor light leakage and contrast reduction in low luminance conditions. If so, this will give an optical understanding to mechanisms that halt myopia and why dim light may trigger excessive eye growth.

Methods: Reported age-dependent changes in axial length for emmetropes and myopes (Jones et al., IOVS 2005), cone inner and outer segments (Lee et al., IOVS 2015) and cone densities (Yuodelis and Hendrickson, Vision Res. 1986) are used to evaluate the degree of photoreceptor light leakage, as well as cross-coupling, in terms of visual contrast as a function of pupil size for typical outdoor and indoor conditions. The impact of age-dependent changes in axial length, cone photoreceptor density and geometry is evaluated using ray optics in a scalable eye model to determine which parameters matter most for infants, children and adolescents from 0 to 20 years.

Results: The analysis reveals two distinct phases: (i) In the infant, post-natal photoreceptor parameters change significantly in the first 4 years of life while the foveal pit matures with denser cone packing. (ii) For the child and adolescent, photoreceptor dimensions remain stable while axial length and foveal cone density increase at a balanced pace in the emmetropic eye. A typical outdoor pupil of 2.4 mm is small enough to ensure that rays cannot leak from foveal cones whereas a larger indoor pupil increases the likelihood of leakage before traversing the entire outer segment. For the infant eye, the reduction in calculated contrast is less than 20% when the pupil increases to 4 mm. In turn, the dropoff is faster for the adult eye with denser cone packing and a corresponding contrast reduction by up to 70%.

Conclusions: The study shows that leakage of light presents a serious challenge for emmetropization when foveal cone density reaches that of the adult eye. Myopia-induced eye growth reduces the ray angle in ideal conditions and lowers the foveal cone density thereby limiting leakage-associated contrast loss. The same concept may also explain why form-deprivation myopia with a diffuser stimulates open-loop eye growth as an ocular mechanism to search for improved contrast as the retina is moved further from the pupil.

CONTROL ID: 3542416

SUBMITTER (NAME ONLY): Omar Halawa

TITLE: Factors associated with lower self-reported quality of life among glaucoma patients

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: O.A. Halawa, R.S. Meshkin, N. Zebardast, D.S. Friedman, Harvard Medical School, Boston, Massachusetts, UNITED STATES|O.A. Halawa, A.M. Roldan, R.S. Meshkin, N. Zebardast, D.S. Friedman, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|E.L. Lamoureux, E.K. Fenwick, Singapore Eye Research Institute, Singapore, SINGAPORE|E.L. Lamoureux, E.K. Fenwick, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Factors associated with poor quality of life (QoL) in glaucoma are not well understood. In this study, we used the Glaucoma Computerized Adaptive Testing System (GlauCAT) to identify clinical and sociodemographic factors associated with lower scores in five QoL domains reported by patients with glaucoma.

Methods: 138 English-speaking adults presenting to an outpatient glaucoma clinic at a tertiary eye center were enrolled in this study. Patients with a history of intra-ocular surgery 90 days prior to enrollment, and/or who met criteria for cognitive impairment were excluded. GlauCAT is a tablet-administered survey that uses computerized adaptive testing and item banking to measure QoL in five domains (Table 1). Scores for each domain range from 0 to 100, with higher scores indicating better QoL. Multivariable linear regression analyses were used to identify clinical and sociodemographic factors associated with domain scores. Covariates associated with domain scores with a significance at p-value <0.1 on univariate analyses were included in the multivariable models.

Results: Low visual acuity was associated with lower scores on activity limitation (3.1 points lower with each 0.1 worse logMAR, 95% CI -4.8 to -1.4) and mobility (2.5 points lower with each 0.1 worse logMAR, 95% CI -4.1 to -0.9). Factors associated with lower emotional well-being scores were worse visual field mean defect (2.7 points lower with each 5 dB worse visual field mean defect, 95% CI -5.2 to -0.2), low visual acuity (1.9 points lower with each 0.1 worse logMAR, 95% CI -3.5 to -0.4), history of a glaucoma laser procedure and/or surgery (13.3 points lower vs no treatment, 95% CI -24.3 to -2.3) and female gender (6.8 points lower vs male, 95% CI -12.9 to -0.7). No significant clinical or demographic correlates of the ocular comfort symptoms and concerns domains were found.

Conclusions: Worse visual acuity was associated with greater self-reported activity limitation and worse mobility and emotional well-being. Worse visual field mean deviation, history of glaucoma laser and/or surgery and female gender were associated with worse emotional well-being.

CONTROL ID: 3542421

SUBMITTER (NAME ONLY): Sukhvinder Singh

TITLE: Myeloid deletion of AMPK α worsen the pathobiology of bacterial endophthalmitis by promoting inflammatory milieu

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Singh, P. Singh, A. Kumar, Ophthalmology, Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|S. Giri, Department of Neurology, Henry Ford Health System, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: AMP-activated protein kinase (AMPK) is a critical regulator of fundamental cellular processes such as growth, proliferation, and survival. Previously, using AMPK α knockout mice, we reported their increased susceptibility to endophthalmitis. To dissect the role of AMPK in residential versus infiltrating cells, in this study, we sought to determine the pathobiology of bacterial endophthalmitis in mice lacking AMPK α in myeloid cells.

Methods: Endophthalmitis was induced in wild-type (WT), C57BL/6, and myeloid deleted AMPK α (LysM AMPK α ^{-/-}) mice by intravitreal (IVT) injection of *S. aureus* strain RN6390 (500 CFU/eye). Disease progression was evaluated by both non-invasive (ophthalmoscopy exam, ERG analysis), and invasive (histology, bacterial burden) methods. In-vitro studies were performed using mouse bone marrow-derived macrophages (BMDMs). Activation of inflammatory mediators was measured using qPCR and ELISA.

Results: *S. aureus* endophthalmitis was resolved in WT mice, in contrast, the LysM AMPK α ^{-/-} mice showed a time-dependent increase in endophthalmitis severity. The intraocular bacterial burden was significantly higher in LysM AMPK α ^{-/-} vs WT mice at 24, 48, and 72h post-infection. The ERG analysis revealed a transient decline in retinal function in WT mice, whereas LysM AMPK α ^{-/-} mice exhibited a rapid decline. Analysis of inflammatory mediators showed significantly higher levels of IL-1 β , TNF- α , and IL-6 in the eyes of LysM AMPK α ^{-/-} mice as compared with WT mice at all-time points. Mechanistically, LysM AMPK α ^{-/-} mouse exhibited the inflammatory, M1 phenotype (Cox2, iNos, and IL12p40), whereas the WT mice retina showed the M2 phenotype (Arg1, Ym1, Fizz1, and IL10) during *S. aureus*-induced endophthalmitis resolution.

Conclusions: Our findings demonstrated that myeloid-specific AMPK α deficiency impairs the resolution of inflammation in endophthalmitis by skewing to M1 macrophage phenotype. Therefore, therapies directed to restore or enhance AMPK activity could be used to improve visual outcomes in endophthalmitis.

CONTROL ID: 3542422

SUBMITTER (NAME ONLY): Zhiqi Chen

TITLE: OCT Denoising Performance Comparison on 2D and 1D Approaches

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Current Optical Coherence Tomography (OCT) denoising techniques mainly focus on denoising 2-dimensional (2D) B-scans, especially for deep learning (DL) methods, which assume spatial integrity among neighboring samplings. However, OCT signal is essentially one dimensional (1D), and eye movements during scanning often violate the assumption. The purpose of this study was to see if 1D denoising is a feasible approach for clinical OCT imaging.

Methods: 3D SD-OCT data within 6x6x2mm volumes centered on optic nerve head were obtained from 121 eyes (79 patients). Clean reference scans were constructed by registering and averaging 6 OCT scans obtained on the same day using ANTs software. As shown in Figure 1, we used a 5-layer U-shape net (UNet) for both 2D denoiser (Figure 1.(a)) and 1D denoiser (Figure1.(b)). In addition, both 2D and 1D approaches are combined by using the 2D denoised B-scan as a mask to selectively remove high signal peaks in the 1D denoised B-scan (Figure 1.(c)). Peak signal-to-noise ratio (PSNR) and contrast-to-noise ratio (CNR) were calculated to compare the performance.

Results: Subjectively, the 2D denoiser generated smoother edges but tended to over-smooth textual information within the retinal layers, while the 1D denoiser preserved more textual information but caused more jittering at retinal edges due to the lack of structural information from neighboring A-scans. Quantitatively, the 1D denoiser showed similar PSNR to the 2D denoiser, while outperforming in CNR (PSNR: 31.20 (1D) V.S. 31.20 dB (2D), $p=0.963$; CNR: 4.23 (1D) V.S. 3.90 dB (2D), $p<0.001$, paired t-test, Table 1). The combined denoiser further improved CNR (4.39 (combined) V.S. 3.90 dB (2D), $p<0.001$). Combining 1D and 2D denoisers, the denoised B-scan showed more continuous edges compared to the 1D denoiser and did not lose the texture information compared to the 2D denoiser (Figure 2).

Conclusions: Quantitatively, 1D denoiser performance is as good as 2D denoiser or even better. A combination of 1D and 2D approaches may provide well-balanced image enhancement in clinical applications.

CONTROL ID: 3542428

SUBMITTER (NAME ONLY): Tsung-Han Chou

TITLE: Potency study of high-titer AAV2 gene therapy for treating Leber Hereditary Optic Neuropathy (LHON) in a preclinical mouse model.

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chou, R.D. Koilkonda, W.J. Feuer, H. Yu, V. Porciatti, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|R.D. Koilkonda, Lacerta Therapeutics, Inc., Alachua, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test the efficacy of high-dose of AAV2(Y444,500,730F)-P1ND4v2 vector obtained from Children's Hospital of Philadelphia (CHOP) to rescue retinal ganglion cell (RGC) structure and function in a mouse model of LHON.

Methods: Thirty DBA/1J mice were separated into three groups: Naive Controls (NC, n=10); Mock LHON controls (MC, n=10) intravitreally injected in both eyes with ScAAV2-HSP-ND4(G11778A) (4.32×10^{12} vg/ml, 1 μ l) followed by a second injection ScAAV2-mCherry (4.32×10^{12} vg/ml, 1 μ l); Gene Therapy (GT, n=10) intravitreally injected in both eyes with ScAAV2-HSP-ND4(G11778A) (4.32×10^{12} vg/ml, 1 μ l) followed by a second injection with CHOP test article (TA) ScAAV2-(Y444,500,730F)-P1ND4v2 (High Dose, 4.5×10^{12} vg/ml, 1.5 μ l). Pattern electroretinograms (PERG) were recorded between 3- and 12-months post injections. At one-year post-injection, cell density in RGC layer (H&E staining) and axon density in the optic nerve (TEM) were determined (n=3 in each group).

Results: While in the MC group the mean PERG amplitude decreased by about 20 % over time (GEE, $p=0.01$) it did not change in the GT and NC groups (GEE, $p<0.05$: NC>MC; GT>MC). At endpoint, the mean RGC layer cell density and optic nerve axon densities were on average reduced in the MC group by about 9% and 10%, respectively, compared to NC and GT groups.

Conclusions: High titer CHOP TA appeared to have a protective role on RGC function and structure in mice with optic neuropathy induced by mutant ND4.

CONTROL ID: 3542441

SUBMITTER (NAME ONLY): CHI SUN

TITLE: Redundant functions of MLL1 and MLL2 in retinal development and cone cell maintenance

SESSION TITLE: Glial Cells

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. SUN, X. Zhang, S. Chen, Ophthalmology and Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: MLL1 (KMT2A) and MLL2 (KMT2B) are closely related members in the mixed-lineage leukemia (MLL) family of histone methyltransferases. They form a core complex for epigenetic regulation of gene expression. The previous study showed MLL1 is essential for retinal neurogenesis and horizontal cell integrity. This research aimed to unveil MLL1/MLL2 collaboration, whether by distinct pathways or through redundancy, in the retinal development and maintenance.

Methods: Cre/loxP-mediated Mll2 and Mll1/Mll2 deletions were specifically targeted in retinal progenitors (Chx10-Cre), developing rods (Nrl-Cre) and cones (HRGP-Cre), respectively. Electroretinography (ERG) detected functional deficits caused by Mll1 and Mll2 deficiency. Hematoxylin and eosin (H&E) staining of retinal cross-sections showed morphological defects at various postnatal (P) ages. EdU labeling and immunostaining of cell-type specific markers reported changes in cell composition between mutant and control retinae. Quantitative PCR (qPCR) determined gene expression differences of cell type-specific markers, phototransduction cascade components and transcriptional factors.

Results: Mll2 knockout (KO) in progenitors produced similar retinal thinning and functional decline to Mll1KO retinae at all ages. Mll1/Mll2 double-KO mice showed severe flaws, including null ERG responses, retinal thinning at P14 and P30, reactive gliosis at 1 month old (MO), followed by rapid degeneration within 2MO. Progenitor cell proliferation was moderately affected in all mutants. In addition, double-KO retinae had decreased numbers of M-cones, horizontal and amacrine neurons. qPCR results confirmed the cellular changes in mutants and explained the ERG deficits. In contrast, rod-specific double-KO mice showed normal retinal morphology and function, suggesting that Mll1/Mll2 are not functionally required for rod development and survival. Cone-specific double-KO mice had M-cone number reduced by 50% and decreased cone ERG responses.

Conclusions: Our results identified the redundant roles of MLL1 and MLL2 in the retinal development and maintenance of M-cones. Mll1/Mll2 deficiency results in retinal degeneration and reactive gliosis as well as gene silencing at young adulthood. Future efforts are underway to determine the underlying molecular mechanisms.

CONTROL ID: 3542443

SUBMITTER (NAME ONLY): Clara Llorens Quintana

TITLE: Accuracy and repeatability of net corneal astigmatism measured with a novel OCT topography algorithm compared to two commercial devices

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Llorens Quintana, E. Pavlatos, O.C. Thaware, D. Huang, Y. Li, Department of Ophthalmology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the accuracy of net corneal astigmatism (NCA) measured with a spectral-domain optical coherence tomography (SD-OCT, Avanti, Optovue Inc), a Scheimpflug imaging device (Pentacam HR, Oculus Optikgerate GmbH) and a swept-source optical biometer (IOLMaster 700, Carl Zeiss Meditec AG) and to determine the repeatability for Avanti and Pentacam HR derived astigmatism.

Methods: Sixty pseudophakic eyes from 39 subjects (39 eyes post-LASIK, 16 eyes post-radial keratectomy and 5 eyes post-photorefractive keratectomy) with monofocal non-toric intraocular lens (IOL) were measured with Avanti, Pentacam HR and IOLMaster 700. Avanti topography was measured using a 16-meridian scan pattern that was repeated 10 times in less than 1.50 sec. Motion error was reduced by comparison of the 10 redundant scan sets and NCA was obtained by Zernike decomposition of the vertex-centered 4 mm diameter area of anterior and posterior corneal surfaces using a custom algorithm. For Pentacam HR and IOLMaster 700, true net and total keratometry readings were used, respectively. Vector analysis was used by decomposing astigmatism into cardinal and oblique components. Repeatability was assessed by means of the coefficient of repeatability ($CR = S_w * 2.77$, where S_w is the within-subject standard deviation of three repeated measures). To assess accuracy, NCA was compared to manifest refraction (MR) converted to the corneal plane. Vectors difference between NCA and MR were calculated and the average of the absolute magnitude of the difference vectors (mean absolute difference) and the mean difference vector reported.

Results: The repeatability of NCA measurement was significantly better (F test, $p < 0.01$) for Avanti (total vector CR = 0.29 D) than for Pentacam HR (total vector CR = 0.67 D). The accuracy of NCA measurement was best for Avanti compared to Pentacam HR and IOLMaster 700 (Fig. 1) – the mean absolute difference with MR was significantly lower ($p < 0.01$ by mixed effect model using gamma distribution).

Conclusions: In post refractive surgery patients, NCA measured by high-speed SD-OCT can achieve better accuracy than current commercial Scheimpflug and swept-sourct biometer devices. This may be useful in toric IOL selection.

CONTROL ID: 3542448

SUBMITTER (NAME ONLY): Elizabeth Whitcomb

TITLE:

Control of lens fiber cell denucleation by CDK1 regulation in mouse and chick

SESSION TITLE: Lens Development and Differentiation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The lens of the eye undergoes a regulated differentiation process whereby organelle removal in the fiber cells is necessary for lens clarity. A critical step in this process is the removal of the fiber cell nucleus. The mechanisms by which this occurs are unclear. Previous work in our lab demonstrated that impaired lens fiber cell denucleation (LFCD) was associated with increased levels of the CDK inhibitor p27. Additionally, deletion of CDK1 in the lens impaired LFCD indicating that CDK activity is crucial for LFCD. In this study, we test CDK activators and inhibitors in the denucleation process.

Methods: We examined lens differentiation in the mouse and embryonic chick by histology and immunofluorescence. We used three different mouse models to ask whether increased p27 levels affects lens differentiation. The first model expresses a drug inducible p27 transgene. We induced expression of the transgene during pregnancy to increase p27 during a crucial phase of lens differentiation. The second model is a Skp2^{-/-}. Skp2 is part of a ubiquitin ligase complex that is known to ubiquitinate p27 and target it for proteasomal degradation; these mice constitutively express high levels of p27. The third model expresses a degradation resistant mutant p27. To determine how CDK1 regulators are involved in LFCD, we used an organ culture system and treated isolated chick lenses with small molecules that inhibit the activities of CDK1 and Cdc25, which activates CDK1. Additionally, we examined LFCD in lenses in which we inhibited CDK1 inhibitors, Wee1 and PP2A.

Results: Expression of increased levels of p27 led to impaired LFCD in all three mouse models. Inhibition of the CDK1 activator Cdc25 inhibits LFCD, whereas inhibition of the CDK1 inhibitors Wee1 and PP2A potentiate LFCD in chick lenses. PP2A inhibits CDK1 activity: activation of PP2A inhibits LFCD while inhibition of PP2A increases LFCD.

Conclusions:

Increasing p27 levels in lenses or inhibiting CDK1 in lenses by genetic and pharmacologic mechanisms results in impaired LFCD. CDK1 activity is a crucial regulator of LFCD in the chick as well as the mouse.

CONTROL ID: 3542450

SUBMITTER (NAME ONLY): Nevin El-Nimri

TITLE: Agreement between Compass Fundus Perimeter New Grid and 10-2 Testing Protocols for Detecting Central Visual Field Defects

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the agreement between Compass New Grid (NG) and Compass10-2 test protocols for detecting early glaucomatous defects in the central 10 degrees of the visual field (CVFD).

Methods: 123 eyes of 14 healthy individuals, 17 glaucoma suspects and 32 glaucoma patients performed NG and 10-2 automated perimetry measurements within one week and macular scans using Spectralis OCT within 12 months. For both test protocols total deviation (TD) or pattern deviation (PD) plot CVFDs were defined in either superior or inferior hemifields by three contiguous points with probabilities of <5%, <2%, <2% or <5%, <1%, <1%. Cohen's Kappa (k) statistic was used to assess agreement between NG and 10-2 for identifying CVFDs. The Spectralis GMPE Hood Glaucoma Report (investigational software version) macula deviation analysis was used to identify macular defects as areas of thickness with $p \leq 0.05$ covering three or more contiguous 10-2 test points in the superior and inferior hemiretina for calculating sensitivities and specificities of all test protocols.

Results: Low to moderate agreement was observed between NG and 10-2 protocols for detecting presence of superior CVFDs on TD ($k=0.566$) and PD ($k=0.256$) plots and for detecting inferior CVFDs on TD (0.487) and PD (0.272) plots. Specificity of NG and 10-2 TD plots for detecting superior CVFDs was 0.82 and 0.65, respectively. Specificity of NG and 10-2 TD plots for detecting inferior CVFDs was 0.92 and 0.84, respectively. Specificity of NG and 10-2 PD plots for detecting superior CVFDs was 0.81 and 0.36, respectively. Specificity of NG and 10-2 PD plots for detecting inferior CVFDs was 0.86 and 0.52, respectively. Sensitivity of NG and 10-2 plots ranged from 0.20 for NG PD plot inferior defects to 0.78 for 10-2 PD plot superior defects.

Conclusions: Because agreement between the detection of central visual fields defects using Compass New Grid and 10-2 is fair to moderate, the visual field test results may be complementary and are not interchangeable.

CONTROL ID: 3542452

SUBMITTER (NAME ONLY): Rupert Bourne

TITLE: Burden of Global Vision Loss due to Glaucoma: Temporal and Regional Changes 2000-2020

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To update estimates of the global vision loss burden due to glaucoma, presenting temporal change since the beginning of VISION 2020 and distribution by sex and region.

Methods: Data gathered from population-based surveys of eye disease from January, 1980, to October, 2018 were collated. We fitted hierarchical models to estimate prevalence (with 95% uncertainty intervals [UIs]) of moderate and severe vision impairment (MSVI; presenting visual acuity from <6/18 to 3/60) and blindness (<3/60) caused by glaucoma, by age, sex, region, and year.

Results: In 2020, 3.60 million (95% UI 2.80-4.41) people aged 50+ years were blind due to glaucoma, and a further 4.13 million (3.24-5.17) had MSVI, a 41.0% increase in cases of blindness and 91.9% increase in cases of MSVI since 2000. Over the same period, age-standardised prevalence of glaucoma blindness decreased by 23.3% but for MSVI it increased by 5.9%. The age-standardised ratio of women to men for glaucoma blindness was 0.71:1.00 in 2020 and 0.67:1.00 in 2000. For MSVI, this ratio was 0.87:1.00 in 2020 and 0.84:1.00 in 2000. Sub-Saharan Africa was the super-region with the highest 50+ age-standardised glaucoma blindness and MSVI rates in 2020 (blind: 0.66%; 0.52-0.81, MSVI: 0.46%; 0.36-0.57), followed by North African and Middle East (blind: 0.57%; 0.44-0.71, MSVI: 0.38%; 0.29-0.48) and Latin America and the Caribbean (blind: 0.26%; 0.20-0.32, MSVI: 0.39%; 0.30-0.48).

Conclusions: Raw prevalence of vision impairment from glaucoma has grown due to population aging since 2000. The decline in age-adjusted glaucoma blindness (compared to MSVI) suggests successful targeting of the most severe cases or earlier detection. Further reduction in the burden of VI from glaucoma can be realised by improved access and affordability of topical medications and laser, and a focus on high quality glaucoma surgery and postoperative care. Screening must be cost-effective and sustainable and this may be possible in some populations, but in most areas of the World there is a reliance on opportunistic case detection. Heightening awareness of glaucoma among family members of cases and in primary care and within existing eyecare programs such as cataract and

diabetic retinopathy screening may slow the rise in numbers of people with irreversible vision loss due to glaucoma.

CONTROL ID: 3542454

SUBMITTER (NAME ONLY): Yaniv Barkana

TITLE: Improved sensitivity of microperimetric outcomes for clinical studies in age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate sensitive outcome measures based exclusively on abnormal points in microperimetry testing of eyes with intermediate age-related macular degeneration (iAMD)

Methods: 25 eyes of 25 subjects with iAMD had undergone 2 successive tests of mesopic microperimetry with the Macular Integrity Assessment Microperimeter (MAIA), using a custom grid of 33 points spanning the central 14 degrees of the macula. Each point was defined as abnormal if its threshold sensitivity was lower than 1.65 standard deviations (SD) (5%) or 2 SD (2.5%) than the expected threshold in healthy eyes according to the MAIA internal database. We analyzed the number of abnormal points in each test, their mean sensitivity and deviation from normal values, and compared the repeatability of these measures with those of all the points in the grid.

Results: Among the 25 eyes there were 11.8 ± 9 and 8.4 ± 8.2 abnormal points at $<5\%$ and $<2.5\%$, with mean deviation of thresholds from normal -4.9 ± 1.2 dB and -5.8 ± 1.5 dB, respectively. These deviations were greater, and their SD smaller, compared with the mean deviation of all points in the microperimetry grid which was -2.3 ± 2.0 dB. The number of eyes with at least 5 abnormal points was 19 (76%) and 14 (56%) using the two criteria. The 95% limits of agreement for average threshold between the 2 successive tests were smaller when only abnormal points were included compared with the complete grid, 3.2 vs 4.2 dB, implying better repeatability.

Conclusions: We propose a framework for the construction of an outcome measure for clinical trials of visual function improvement in iAMD that consists only of microperimetry points that are abnormal at baseline. Despite limiting the analysis to a particular subset of points, most subjects in this iAMD cohort could be enrolled. Advantages include a greater average deviation allowing more ample opportunity for observable effect of any intervention, a more homogenous dataset, and excellent test-retest variability.

CONTROL ID: 3542456

SUBMITTER (NAME ONLY): Joshua Glass

TITLE: RNA-Seq reveals IL-6 trans-signaling mediated regulation of paracellular permeability in human retinal endothelial cells

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The blood retinal barrier (BRB) breakdown in diabetic retinopathy (DR) is induced in part by increased paracellular permeability. Interleukin-6 (IL-6) plays an important role in the regulation of paracellular permeability in human retinal endothelial cells (HRECs). This pleiotropic cytokine acts via two distinct mechanisms, including “classical” signaling through a membrane-bound IL-6 receptor and “trans-signaling” through a soluble IL-6 receptor. The purpose of this study was to compare the effects of these two IL-6 pathways on paracellular permeability in HRECs.

Methods: To activate IL-6 classical signaling, HRECs were treated with IL-6 (50 ng/mL), and to activate IL-6 trans-signaling, cells were treated with IL-6 (50 ng/mL) and sIL-6R (150 ng/mL) overnight. Trans-endothelial electrical resistance (TEER) was measured using electrical cell impedance sensing (ECIS). Gene expression changes were determined using RNA-Seq.

Results: IL-6 trans-signaling activation caused a significant drop in TEER, while there was no effect of classical signaling. Among the 3 parameters of endothelial barrier function, paracellular resistance was significantly decreased, cell membrane capacitance was significantly increased, and no change was observed in basal adhesion. We found distinct effects on gene expression with each treatment, with more genes significantly altered following trans-signaling activation. Significant changes in the expression of 7 tight junctions were observed after trans-signaling activation: CLDN1 (-3.27-fold), CLDN3 (-4.44-fold), CLDN11 (-1.85-fold), CLDN12 (1.25-fold), CLDN14 (-1.36-fold), TJP1 (1.17-fold) and TJP2 (-1.31-fold). Among the adherens junctions, genes which showed significant changes were CDH6 (-1.66-fold), CDH11 (1.74-fold), CDH12 (1.97-fold), CDH24 (-1.67-fold), CTNNAL1 (-1.21-fold), and CTNNBIP1 (-1.29-fold). The 3 differentially expressed gap junctions included GJA1 (1.49-fold), GJA4 (-2.41-fold) and GJC1 (-1.19-fold). Only CLDN15 (1.48-fold) was significantly upregulated by classical signaling.

Conclusions: IL-6 trans-signaling caused a significant increase in paracellular permeability in HRECs, while classical signaling had no significant effect. Specific gene expression changes in intercellular junctions were identified that will aid our future understanding of the molecular mechanisms of IL-6 trans-signaling mediated BRB breakdown in HRECs.

CONTROL ID: 3542458

SUBMITTER (NAME ONLY): Mohammad Sharifian Gh.

TITLE: Lacritin Bactericidal Peptide N-104 Binds Surface-Exposed Lipoprotein YaiW, a Known Peptide Transporter

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sharifian Gh., G.W. Laurie, Cell Biology, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|M.G. Gadjeva, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G.W. Laurie, Biomedical Engineering, University of Virginia School of Medicine, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mohammad Sharifian Gh.: Commercial Relationship: Code N (No Commercial Relationship) | Mihaela Gadjeva: Commercial Relationship: Code N (No Commercial Relationship) | Gordon Laurie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Lacritin C-terminal proteoform 'N-104' is a main source of tear bactericidal activity. By screening for N-104 resistance, we recently discovered the importance of respective putrescine and iron transporters PotH and FeoB as likely virulence factors for *P. aeruginosa* (PA14) ocular pathogenesis. PotH and FeoB are constituents of the inner bacterial membrane, whereas N-104 is in tears and not membrane disruptive. How then does N-104 bactericidal activity involve PotH and FeoB? Here we search for N-104 binding proteins in the outer membrane of PA14.

Methods: N-104, and negative control lacritin peptide C-95, synthesized with cysteine added to the N-terminus, were coupled to beads of SulfoLink® Coupling Resin with an efficiency of 0.7 mmole peptide to ml resin, and then blocked with L-cysteine. Overnight cultures of PA14, either without or with prior surface biotinylation, were washed in PBS, resuspended in lysis buffer containing 200 mM octyl β -D-glucopyranoside ('OG') with rocking overnight at 4°C to allow membrane proteins to insert into OG vesicles, and centrifuged. Supernatant was passed through PierceTM Agarose Resin precolumns and then onto N-104 or C-95 columns with rocking overnight at 4°C. After washing with 20 ml of running buffer containing 20 mM KCl, proteins were eluted by progressive addition of 50, 75, 100, 125, 150, 300, 500 or 1000 mM KCl. 500 mM KCl eluted proteins from N-104 and C-95 columns were subjected to mass spectrometry.

Results: 'YaiW' was the sole outer membrane protein hit with 7.4x higher enrichment from N-104 vs negative control C-95 columns, and mutants lacking YaiW resistant to N-104 with a slope ratio threshold of 0.7. YaiW contributes to the transport of proline-rich Bac7 peptides across the outer membrane. No hits were obtained from biotinylated cells, in keeping with amine-reactive interference.

Conclusions: YaiW is a candidate outer membrane receptor for N-104 with the potential capability to transport N-104 into the periplasm, and thus in proximity to inner membrane PotH and FeoB.

CONTROL ID: 3542459

SUBMITTER (NAME ONLY): Rebekah Robinson

TITLE: β -catenin partially mediates IL-6 trans-signaling induced barrier dysfunction in retinal endothelial cells

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Robinson, J. Bloom, H. Iyer, S. Sharma, Center for Biotechnology and Genomic Medicine, Augusta University, Augusta, Georgia, UNITED STATES|S. Sharma, Department of Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Interleukin 6 (IL-6) plays a role in the endothelial barrier dysfunction seen in diabetic retinopathy (DR). Our recent studies have shown that the primary IL-6 signaling modality in retinal endothelial cells is IL-6 “trans-signaling”, which utilizes a soluble form of the IL-6 receptor (sIL-6R). The molecular mechanisms underlying this dysfunction, however, have not been fully elucidated. Adherens junctions play a critical role in the formation of cellular barriers, and the purpose of this study is to evaluate the contribution of adherens junction components to IL-6 trans-signaling induced barrier dysfunction.

Methods: Expression of VE-cadherin, β -catenin, α -catenin, and p120-catenin were measured in human retinal endothelial cells (HRECs) by RT-PCR following overnight treatment with IL-6 (50 ng/mL) \pm sIL-6R (150 ng/mL). Protein expression was measured by western blotting and immunofluorescence (IF). β -catenin gene knockdown in HRECs was performed using siRNA, and endothelial barrier function was measured using electric cell-substrate impedance sensing (ECIS).

Results: IL-6 trans-signaling significantly decreased expression of VE-cadherin (0.7-fold) and β -catenin (0.6-fold), but not α -catenin or p120-catenin. IF showed that β -catenin was primarily junctional, and trans-signaling led to gaps in membrane coverage. Activation of IL-6 trans-signaling significantly decreased endothelial barrier function (0.76-fold vs. untreated). β -catenin knockdown with siRNA resulted in a baseline decrease in barrier function (0.85-fold vs. wildtype), and IL-6 trans-signaling activation further reduced barrier function (0.73-fold vs. wildtype untreated), suggesting that β -catenin loss can partially explain IL-6 trans-signaling induced barrier dysfunction. Furthermore, β -catenin knockdown did not alter expression of β -catenin-regulated genes involved in tight junctions and the formation of capillary fenestrae. IL-6 trans-signaling, however, induced changes in expression of several permeability-associated genes, including CLDN1 (0.28-fold), CLDN3 (0.58-fold), OCLN (0.69-fold), and PLVAP (1.4-fold).

Conclusions: Our findings suggest that loss of β -catenin and adherens junctions partially explain the mechanism of IL-6 trans-signaling-induced endothelial barrier dysfunction and provide further support for the role of IL-6 trans-signaling in the pathology of diabetic retinopathy.

CONTROL ID: 3542466

SUBMITTER (NAME ONLY): Stela Vujosevic

TITLE: Three-year longitudinal changes in patients with diabetes mellitus type 1 and type 2 without signs of diabetic retinopathy: a quantitative OCT-Angiography study

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vujosevic, E. Villani, University Hospital San Giuseppe, Milan, ITALY|C. Toma, S. DeCilla', University Hospital Maggiore della Carita', Novara, ITALY|E. Torti, Electrical, Computer and Biomedical Engineering, University of Pavia, Pavia, ITALY|M. Brambilla, Medical Physics, University Hospital Maggiore della Carita', Novara, ITALY|E. Villani, P. Nucci, Clinical Sciences and Community Health, University of Milan, Milan, ITALY|S. DeCilla', Health Sciences, University East Piedmont, Novara, ITALY|

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ABSTRACT BODY:

Purpose:

Three-year evaluation and comparison in microvascular and neuronal macular parameters in patients with type 1 and 2 diabetes mellitus (DM1/DM2) and no clinical signs of diabetic retinopathy(DR).

Methods:

Ninety-two eyes/patients(20 with DM1, 48 with DM2, 24 healthy controls) were included in this prospective longitudinal study. Main inclusion criteria were: absence of any sign of DR in both eyes, good image quality. The right eye was chosen for analysis unless poor quality of imaging. OCT/OCT-angiography (OCT-A) images of the macula were taken using DRI swept source-OCT Triton plus. Following OCT parameters were evaluated: thickness of retinal nerve fiber layer(NFL), ganglion cell layer(GCL+) and NFL + GCL+ (GCL++). On 3x3 mm OCT-A images: foveal avascular zone(FAZ) parameters, perfusion/vessel density(PD/VD), fractal dimension(FD) at the superficial and deep capillary plexus (SCP/DCP); choriocapillaris flow voids(CC-FV) using MATLAB, version 2017b. Changes over time were evaluated by means of repeated measures ANOVA.

Results: At baseline, in DM1 in the SCP a decrease in FAZ circularity index(CI, $p<0.001$), PD($p=0.05$) and FD($p<0.001$) vs controls was detected; in the DCP a decrease in FAZ CI and FD($p<0.001$) and an increase in FAZ perimeter($p=0.03$) vs controls; and in the CC a decrease in FV($p=0.02$) vs DM2 were documented. In DM2, central subfield-GCL++ and GCL+ and inner ring-GCL+ thickness were reduced vs DM1($p\leq 0.01$); in the SCP a decrease in FAZ CI and FD($p\leq 0.001$) and an increase in FAZ area and perimeter($p\leq 0.01$) vs controls were detected; in the DCP a decrease in FAZ CI and FD($p<0.001$) vs controls and an increase in FAZ area and perimeter vs controls and DM1($p\leq 0.02$) were detected. During the follow-up 14 eyes(20.6%) developed mild DR. After 3 years, no significant changes were observed in OCT parameters; FAZ area and perimeter in the DCP and FV($p<0.05$ for all) significantly increased in DM2.

Conclusions: Specific microvascular changes in SCP, DCP and CC were documented in both DM1&2 without clinical signs of DR. GCL thickness was more reduced in DM2 vs DM1. FAZ parameters in the DCP and FV in the CC significantly increased in DM2 in patients that progressed to mild DR vs those who remained stable(no clinical signs of DR). Further longitudinal studies should evaluate the role of DCP and CC in development of clinical signs of DR.

CONTROL ID: 3542468

SUBMITTER (NAME ONLY): Camille Robinson

TITLE: Glaucoma knowledge and disease severity in a veteran population with poor adherence

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Robinson, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|A. Williams, K. Muir, J.A. Rosdahl, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|S. Woolson, M. Olsen, Durham VA Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a lifelong disease that requires treatment adherence and active patient engagement. Poor patient adherence is associated with lower levels of understanding of the disease. However, little is known about the relationship between patient glaucoma knowledge and level of glaucoma severity. The purpose of this study is to evaluate a correlation between glaucoma knowledge scores and disease severity among veterans with glaucoma who had poor adherence enrolled in a randomized controlled trial.

Methods: Patients treated for glaucoma who had poor adherence at the Durham Veterans Affairs Eye Clinic were recruited to participate in the medication adherence in glaucoma to improve care (MAGIC) study, which measured adherence following an educational intervention (NCT03052257). As part of that study, participants completed a glaucoma knowledge assessment using the 10-question Eye-Q glaucoma knowledge test. Glaucoma severity was assessed using visual field criteria. Demographics and clinical history were recorded. Comparisons were made between glaucoma severity levels, categorized as mild, moderate, severe, and indeterminate. Continuous variables were compared using analysis of variance and categorical characteristics using the chi-square statistic; alpha was 0.05.

Results: Two hundred participants were included with a mean age of 68 ± 8 years and representation across all glaucoma severity categories (53 mild, 56 moderate, 74 severe, and 17 indeterminant). The majority (57%) reported a glaucoma duration of 5 years or more. The mean Eye-Q score was poor across all categories and did not differ based on severity (6.0 ± 1.6 , 6.2 ± 1.5 , 6.3 ± 1.8 , and 5.9 ± 1.9 for mild, moderate, severe, and indeterminate visual field severity, respectively; $p=0.779$).

Conclusions: Glaucoma knowledge did not differ across disease severity categories in this population of glaucoma patients with poor adherence. Glaucoma knowledge was generally poor, supporting the need for interventions to educate glaucoma patients about their disease.

CONTROL ID: 3542473

SUBMITTER (NAME ONLY): Michael De Ieso

TITLE: Caveolin-1 mediates relaxation of trabecular meshwork cells to chronic mechanical stretch via protein kinase C

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.L. De Ieso, M. Kuhn, D.W. Stamer, Duke University, Durham, North Carolina, UNITED STATES|M.H. Elliott, Department of Ophthalmology/Dean McGee Eye Institute, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Polymorphisms at the Cav1/2 gene loci impart increased risk for ocular hypertension and primary open-angle glaucoma (POAG). Caveolae are specialized cellular domains that form invaginations in the plasma membrane, and Cav1 is required for caveolae biosynthesis. The mechanism by which Cav1 contributes to intraocular pressure (IOP) homeostasis is unknown. Interestingly, protein kinase C (PKC) interacts with Cav1 and plays a key role in trabecular meshwork (TM) contractility; an important mediator of conventional outflow resistance, and subsequently IOP. Thus, we used pharmacological modulators of PKC to test the hypothesis that caveolae serve as mechanosensors in the TM, which respond to changes in IOP by modulating PKC signaling.

Methods: Experiments were conducted using cultures of 8 different human TM cell strains. Adenoviruses encoding shRNA targeted to Cav1 were used to silence expression. Western blotting was used to determine relative protein levels, phosphorylation status, and PKC activity. Gö6983 (1 micromolar) was used as a selective PKC inhibitor. For cyclic stretch experiments, TM cells were plated on type IV collagen-coated flexible silicone bottom plates and subjected to 20% stretch, 1 Hz for 24 h. Data are expressed as mean \pm SEM.

Results: Using phosphorylated myosin light chain (pMLC) as a surrogate indicator for Rho/ROCK activity and contractile tone, we found that pMLC/MLC levels in TM cells were reduced in stretched versus unstretched conditions ($58.2 \pm 12\%$ vs. $100 \pm 19\%$, $n=8$, $p=0.005$). When Cav1 expression was decreased by knockdown (efficiency= $56 \pm 5.7\%$), pMLC/MLC levels were unaffected in stretched versus unstretched conditions ($81.5 \pm 16\%$ vs. $100 \pm 19\%$, $n=8$, $p=0.28$). Levels of pMLC/MLC were also lower in TM cells treated with the PKC inhibitor, Gö6983, for 24 h compared to control ($74.1 \pm 5.6\%$ vs. 100% , $n=7$, $p<0.004$). Interestingly, PKC activity trended downward in 24 h stretched, Cav1-competent TM cells ($90.3 \pm 9.5\%$ vs. $100 \pm 9.3\%$, $n=7$, $p=0.057$). This effect was not present in Cav1-deficient cells ($94.5 \pm 4.8\%$ vs. $100 \pm 9.7\%$, $n=7$, $p=0.55$), likely because PKC colocalizes with Cav1 at plasma membrane in TM cells.

Conclusions: Caveolae act as scaffolds that compartmentalize PKC at the membrane in TM cells, enabling signal transduction to downstream effectors in response to chronic stretch (Figure 1).

CONTROL ID: 3542475

SUBMITTER (NAME ONLY): Zhihong Hu

TITLE: Comparison of OCTA Axial Profiles in Healthy Eyes and Eyes with AMD

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Hu, F. Corvi, Z. Wang, Z. Mishra, S.R. Sadda, Retina, Doheny Eye Institute, Los Angeles, California, UNITED STATES|Z. Wang, S.R. Sadda, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|J. Weichsel, M. Teussink, Heidelberg Engineering, GERMANY|

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ABSTRACT BODY:

Purpose: Eye disease analysis using en-face maps over predefined retinal vascular slabs in optical coherence tomography angiography (OCTA) has been a popular approach. However, such approach relies on high lateral resolution and is rather insensitive to decrease of OCTA signal (flow density) axially due to diseases. In contrast, axial profiles are averaged over the flow density in lateral directions which are then analyzed in depth and may be more sensitive to detect changes of microvasculature with diseases. The purpose of this pilot study is to compare axial profiles in healthy eyes and eyes with age-related macular degeneration (AMD).

Methods: The study cohort includes 19 eyes of young adults, 11 eyes of elderly adults, and 33 eyes of AMD patients. Among the 33 AMD eyes, 7 has intermediate AMD; 6 has geographic atrophy (GA); and 20 has macular neovascularization (MNV). OCTA macular images were captured with Spectralis OCT2 (Heidelberg Eng.) using scan pattern 3mm x 3mm (10° x 10°; 512 x 512 pixels). Axial signals were quantified from specific retinal layers (NF - nerve fiber, GC - ganglion cell, IP - inner plexiform, IN - inner nuclear, OP - outer plexiform) within fovea-centered concentric rings in radii 1.5° - 2° (paracentral) , 3° - 3.5° (pericentral), and 4.5° - 5° (peripheral).

Results: Fig.1 shows comparison of axial profiles in eyes from healthy young and elderly adults, and AMD patients. Fig. 2 shows that from AMD sub-category eyes. Blunting of axial signal peaks in GCL in paracentral ring and in IPL-INL (intermediate capillary plexus) in pericentral ring was observed in elderly and AMD eyes compared to young eyes. Both intermediate and deep (INL-OPL) peaks were blunted in AMD eyes compared to elderly eyes in paracentral ring. Significant differences were not observed in eyes with different AMD stages.

Conclusions: Axial profile analysis may reveal differences between healthy and diseased eyes, providing new insights into disease pathophysiology. AMD eyes show a reduction in parafoveal OCTA signal in intermediate and deep flow layers. These findings require replication in larger studies.

CONTROL ID: 3542476

SUBMITTER (NAME ONLY): Kendall Goodyear

TITLE: Dance training to improve medical student ophthalmologic surgical skills

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Goodyear, H. DeLisser, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|D.N. Sarlo, A.K. Jensen, G. Binenbaum, Ophthalmology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|A. Swain, Penn Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Technical skills are critical to the practice of ophthalmology and other surgical fields. Visuospatial ability is associated with technical competency and outcome quality in spatially complex surgeries. While surgical instruction and practice improve technical skills, medical education does not provide explicit training to improve visuospatial abilities. Dance training has been associated with improved visuospatial abilities. We sought to evaluate the effects of formal ballet training on the technical surgical competence of medical students.

Methods: Twenty pre-clinical medical students naive to dance or surgical training were divided 1:1 into dance-training and control groups. Students in the dance-training group received six 1.5-hour ballet lessons over a 2-month period at Koresh Dance Studio in Philadelphia. All subjects completed pre- and posttesting, in which they performed a wet lab bovine extraocular muscle recession. Procedure videos were graded by two ophthalmologists using a modified version of a previously validated surgical skills assessment tool, the Objective Structured Assessment of Technical Skill, and masked to group assignment and pretesting/posttesting status.

Results: Technical surgical ability, as measured by wet lab skills lab testing, improved significantly in the dance group (mean change +12.6 points) compared to the control group (mean change +5.2 points), $p=0.042$. In a poststudy questionnaire, students in the dance group reported improvement in awareness of their body positioning in space as well as control over their own movements.

Conclusions: Dance training for pre-clinical medical students can improve ophthalmology technical surgical ability. Principles from the field of dance, which focus on body awareness and intention, can successfully be applied to surgical training. Further studies can examine the extent of impact of dance training on surgical ability.

CONTROL ID: 3542477

SUBMITTER (NAME ONLY): Chloe Li

TITLE: Sex-specific changes in choroid vasculature of schizophrenia and bipolar disorder patients

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.Y. Li, I. Garg, M. Kasetty, R. Katz, J. Wang, J.B. Miller, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|D. Bannai, I. Adhan, M. Keshavan, P. Lizano, Department of Psychiatry, Beth Israel Deaconess Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior studies of schizophrenia (SZ), schizoaffective (SZA) and bipolar disorder (BD) patients have identified retinal layer abnormalities, but none have closely investigated their choroidal vasculature. We compared choroidal vascularity in patients with SZ, SZA, BD, and healthy controls using swept-source optical coherence tomography angiography (SS-OCTA) in a cross-sectional pilot study.

Methods: 51 subjects were recruited, including 19 healthy controls (HCs) and 18 SZ, 9 SZA, and 5 BD patients. SS-OCTA images were obtained using Triton DRI OCT-1 Atlantis. Choroidal thickness (CT) was obtained using native device software (Topcon Fastmap). Choroid vascular enface images (12mm x 9mm) were exported every 2.6 μ m from Bruch's membrane to the choroid-scleral interface from Topcon to ImageJ. Images were binarized using Otsu's method, signal from the optic disk and retinal vasculature was removed, and average choroid vascular density (CVD) was calculated as the average of percent area occupied by choroidal vasculature across images in the stack. Choroid vascular volume (CVV) was calculated as the CVD multiplied by maximum CT and image area. Data was analyzed in R, with mixed-effect linear regression modeling to test for group differences and post-hoc multivariate analysis to test for group-by-sex interactions. Tukey's HSD test was used to adjust for multiple comparisons.

Results: Among patients with a psychiatric diagnosis, 64% were male, median age was 34 years, and median body mass index (BMI) was 29.4. Compared with same-sex controls, male psychiatric patients had significantly lower CVD. Compared with same-sex controls, female psychiatric patients had significantly lower maximum CT with correspondingly decreased CVV, after adjusting for age. When all psychiatric patients were compared with all healthy controls, no significant differences in CT, CVD, or CVV were noted. Neither race nor BMI were predictors of maximum CT, CVD, or CVV.

Conclusions: We report sex-specific changes in choroid thickness and choroid vascularity among patients with SZ, SZA, and BD. Further investigation of sex-specific pathologic differences in these patients is needed, as similar sex-specific changes in SZ and BD patients' cortical imaging have also been reported.

CONTROL ID: 3542482

SUBMITTER (NAME ONLY): Alireza Kamalipour

TITLE: Artificial Intelligence Characterization of Spatial Patterns of Microvascular Dropout in Glaucoma

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kamalipour, S. Moghimi, J.A. Proudfoot, H. Hou, T. Nishida, A. Yarmohammadi, R.C. David, N.W. El-Nimri, J. Rezapour, C. Bowd, L.M. Zangwill, R.N. Weinreb, Ophthalmology, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|M. Jazayeri, San Diego State University, San Diego, California, UNITED STATES|P. Khosravi, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the spatial patterns of microvascular dropout in glaucoma using an unsupervised artificial intelligence approach.

Methods: This retrospective cohort study included a total of 1899 Angiovue optic nerve head optical coherence tomography angiography (OCTA) scans of 707 eyes of 397 healthy, glaucoma suspect and glaucoma patients from the Diagnostic Innovations in Glaucoma Study. An unsupervised artificial intelligence technique "Archetypal Analysis" was applied to pre-processed en-face OCTA images obtained at the level of the retinal peripapillary capillary density network. Correlations of OCTA derived spatial patterns with 24-2 visual field (VF) mean deviation (MD), 24-2 VF pattern standard deviation (PSD), 10-2 VF-MD, and 10-2 VF-PSD were evaluated. Diagnostic accuracy of spatial patterns to detect past glaucoma progression was calculated and compared with those of circumferential capillary density (cpCD) and retinal nerve fiber layer thickness (cpRNFLT) using 310 eyes (of 195 glaucoma suspect and glaucoma patients) with a minimum of 3 years of follow-up and 5 reliable 24-2 VF tests before their last OCTA image. Progression was defined based on an event-based glaucoma progression analysis (GPA) criterion. Generalized mixed-effects model was used to adjust for correlations of different metrics at the patient and eye levels.

Results: Eleven distinct spatial patterns were identified across the spectrum of disease severity (Figure 1). Notably, 10 of the 11 patterns of microvascular loss preserved the less vulnerable papillomacular area. Eight (1,5,6,7,8,9,10,11), 5 (1,7,8,10,11), 5 (1,8,9,10,11) and 5 (1,3,8,10,11) spatial patterns were significantly associated with 24-2 MD, 24-2 PSD, 10-2 MD and 10-2 PSD, respectively ($P < 0.05$ for all). The archetypal model (area under the receiver operating characteristic curve [AUC]=0.75) outperformed cpCD (AUC=0.66) and cpRNFLT (AUC=0.65) in detecting past glaucoma progression ($P=0.017$).

Conclusions: Unsupervised artificial intelligence techniques are capable of identifying patterns of microvascular dropout in glaucoma using OCTA images. These patterns show promise not only in qualitative evaluation but also in the quantitative assessment of glaucomatous microvascular dropout associated with VF damage and VF progression.

CONTROL ID: 3542483

SUBMITTER (NAME ONLY): Huey Cai

TITLE: Differences in gene expression and metabolism among AMD and non-AMD patients arise only after iPSC are differentiated into RPE

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Cai, J. Gong, L.J. Rizzolo, L.V. Del Priore, M.A. Fields, Department of Ophthalmology and Visual Sciences, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have reported previously that retinal pigment epithelium (RPE) differentiated from induced pluripotent stem cells (iPSC) generated from fibroblasts of patients with age-related macular degeneration (AMD) exhibit a retinal degenerative phenotype and a distinct transcriptome compared to age-matched controls. Since the genetic composition of the iPSC and RPE are inherited from fibroblasts we investigated whether differential behavior was present in the parental fibroblasts and iPSC prior to differentiation of the cell lines into RPE.

Methods: Induced pluripotent stem cells (iPSCs) were generated from fibroblasts isolated from AMD patients or age-matched (normal) controls. Fibroblast, iPSC and iPSC-derived RPE cells from normal and AMD patient donors were studied with DNA microarrays and Seahorse analysis for mitochondrial functions.

Results: Principal component analyses revealed no significant differences in the transcriptome of fibroblasts harvested from skin biopsies of AMD patients versus controls. After reprogramming, there was no significant difference in the transcriptome of iPSC generated from AMD versus normal donors. In contrast, hierarchical clustering analysis reveals that the transcriptome of iPSC-derived RPE segregated into two distinct clusters of AMD-derived cells versus controls. Interestingly, mitochondrial dysfunction in AMD-derived RPE was evident after approximately two months in culture. Moreover, these differences in mitochondrial dysfunction were not evident in the parental fibroblasts and iPSC. This study demonstrates an altered transcriptome and impaired mitochondrial function in RPE derived from AMD patients versus controls, and demonstrates these differences are not present in the original fibroblasts or iPSC.

Conclusions: These results suggest that the initial pathological changes in RPE seen in AMD may develop only after fibroblasts and the subsequent iPSC are differentiated into RPE, and that mitochondrial function is significantly affected in these cells. Additional study is required to advance the current understandings of the etiology of AMD and the development of novel therapeutic targets.

CONTROL ID: 3542486

SUBMITTER (NAME ONLY): Nicholas Besley

TITLE: ST266 Improves Survival and Mitochondrial Function in Human RPE Cells Under Oxidative Stress

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.A. Besley, P. Yang, S.W. Lallier, G.J. Jaffe, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|H. Wessel, L. Brown, Noveome Biotherapeutics Inc, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress is a potent contributor to the loss of retinal pigment epithelial (RPE) cell function observed with age-related macular degeneration (AMD). ST266 is the biological secretome produced by a novel population of amnion-derived multipotent progenitor cells. ST266 has been previously reported to improve retinal ganglion cell survival and cellular function in optic neuritis and optic nerve crush mouse models. Herein, we investigated the effect of ST266 on RPE cell survival and mitochondrial function after cells were treated with hydroquinone (HQ) and hydrogen peroxide (H_2O_2), oxidants related to cigarette smoke, and all-trans Retinal (atRal), a pro-oxidant component of the retinoid cycle.

Methods: Cultured human RPE cells were labeled with 10 μ M JC-1 dye (a mitochondrial membrane potential, $\Delta\psi$ m, indicator) for 30 minutes followed by treatment with HQ (175-250 μ M), H_2O_2 (1000-1200 μ M), or atRal (17.5-30 μ M) for 90 minutes. Media were then replaced with ST266 or STM100 (control) for 24 hours at 37°C. A fluorescent plate reader was used to determine the ratio of red JC-1 aggregate/ green JC-1 monomer. Cell viability was measured with WST-1 reagent.

Results: ST266 significantly improved cell viability on average by 20%, 23.2%, and 18.6% for HQ, H_2O_2 , and atRal treated cells, respectively, compared to control ($P<0.05$). Additionally, ST266 significantly reduced the percent decrease of $\Delta\psi$ m after 24 hours, on average, by 14.7% for atRal treated cells compared to control ($P<0.05$).

Conclusions: RPE cells subjected to varied sources of oxidative stress had reduced cell viability and mitochondrial membrane potential. ST266 inhibited these deleterious effects caused by atRal; however, it did not similarly impact the reduction in mitochondrial membrane potential induced by HQ and H_2O_2 . Therefore, the mechanism through which ST266 acts may be oxidant-specific and requires further study.

CONTROL ID: 3542490

SUBMITTER (NAME ONLY): Miguel Seabra

TITLE: FORMATION OF LIPOFUSCIN-LIKE AUTOFLUORESCENT GRANULES IN THE RETINAL PIGMENT EPITHELIUM REQUIRES LYSOSOME DYSFUNCTION

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Seabra, C. Escrevente, A. Falcão, M. Lopes-da-Silva, P. Antas, M. Mesquita, I. Ferreira, H. Cardoso, A. Fradinho, S. Tenreiro, Cedoc - Chronic Diseases Research Center, Universidade Nova de Lisboa Faculdade de Ciencias Medicas, Lisboa, Lisboa, PORTUGAL|M. Seabra, M.J. Hall, C.E. Futter, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: We aim to characterize the pathways required for autofluorescent granule (AFG) formation by retinal pigment epithelium (RPE) cells using cultured monolayers.

Methods: We fed RPE monolayers in culture with a single pulse of photoreceptor outer segments (POS). After 24h the cells started accumulating AFGs similar to lipofuscin in vivo. Using this model, we used a variety of light and electron microscopical techniques, flow cytometry and western blot to analyze the formation of AFGs. We also generated a mutant RPE line lacking Cathepsin D by gene editing.

Results: AFGs appear to derive from incompletely digested POS-containing phagosomes and after 72h are surrounded by a single membrane containing lysosome markers. We show by various methods that lysosome-phagosome fusion is required for AF granule formation but that impairment of lysosomal pH or catalytic activity, particularly Cathepsin D activity, enhances AF intensity.

Conclusions: We conclude that lysosomal dysfunction results in incomplete POS degradation and AFG accumulation.

CONTROL ID: 3542491

SUBMITTER (NAME ONLY): Brahim Chaqour

TITLE: The matricellular protein CCN2/CTGF is an extrinsic cue essential for retinal progenitor cell growth and diversification

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Chaqour, Cell Biology and Ophthalmology, SUNY Downstate Health Sciences University College of Medicine, Brooklyn, New York, UNITED STATES|A. Bulakhova, G. Mohiuddin, S. Lee, SUNY Downstate Health Sciences University, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal progenitor cell (RPC) specification into appropriate retinal cell types is temporally and spatially coordinated by well-characterized intrinsic signals endowing RPCs with neurogenic or gliogenic potential. The cellular communication network 2 (CCN2), also known as connective tissue growth factor or CTGF, is a secreted extracellular matrix protein with regulatory functions in vasoproliferative and fibrotic diseases. Although CCN2 expression extends to developmental processes in the central nervous system, the role of such extrinsic signal in retinogenesis is unknown. Herein, we used mouse genetics and omic approaches to determine the functional importance of CCN2 in retinogenesis.

Methods: A CCN2-green fluorescent protein bacterial artificial chromosome transgenic mouse was used as a proxy to analyze CCN2 expression pattern during retinogenesis. Moreover, mice with global deletion of CCN2 were generated by crossing CCN2 floxed and cytomegalovirus promoter-driven Cre mice. RPC growth and differentiation were analyzed in transverse cryosections of retinas by immunohistochemical methods at embryonic stages E11, E14, E16, and E18. Transcriptomic changes were determined by RNA-sequencing analysis of retinas from CCN2-deficient and control littermate mice at E18.

Results: At E11, CCN2 was expressed in the outer neuroblastic layer, which consists of RPCs and differentiating photoreceptors (PRs). At E14, 45 and 23% of CCN2 producing cells were positive for the RPC markers Sox2 and CHX10, respectively. From P1 onwards, CCN2 expression was restricted to Müller glia and vascular cells. Meanwhile, CCN2 deficiency in mice resulted in retinal hypocellularity with reduced RPC pool and impaired competence of remaining RPCs to generate immediate-early and late-born retinal cell types. CCN2 deficiency induced a dramatic reduction of Sox2 to Pax6 ratio, which is key to the maintenance of RPC neurogenic competence and multipotency. CCN2 gene inactivation caused down-regulation of marker and transcription regulator genes of retinal ganglion cells, PRs, and Müller glia.

Conclusions: CCN2 expression is required for the generation of neuronal and glial diversity in the retina. Understanding the regulation and function of CCN2 in retinal neurogenesis is of key importance toward optimization of cellular replacement therapy in congenital retinal diseases.

CONTROL ID: 3542495

SUBMITTER (NAME ONLY): Jay Oh

TITLE: Parthanatos operates intraocularly during murine cytomegalovirus (MCMV) retinitis in mice with acquired immunodeficiency syndrome (MAIDS): An investigation of possible cell-type specificity

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Oh, Biology, Georgia State University, Atlanta, Georgia, UNITED STATES|R.D. Dix, Biology, Georgia State University, Atlanta, Georgia, UNITED STATES|R.D. Dix, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jay Oh: Commercial Relationship: Code N (No Commercial Relationship) | Richard Dix: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Parthanatos is a caspase-independent cell death pathway whose contributions to retinal tissue destruction during the progression of AIDS-related human cytomegalovirus retinitis have yet to be explored. We have previously shown that key parthanatos proteins are stimulated within MCMV-infected eyes of retinitis-susceptible mice with MAIDS of 10-weeks duration (MAIDS-10) (Oh et al, J Med Virol, 2019) but not within MCMV-infected eyes of retinitis-resistant mice with MAIDS of 4-weeks duration (MAIDS-4) (unpublished data). That stimulation of parthanatos during MCMV-related MCMV retinitis might be cell-type specific prompted us to perform a pilot study to test this hypothesis using mouse embryo fibroblasts (MEF) and mouse lung fibroblasts (MLg), both non-ocular cells known to be susceptible to MCMV infection.

Methods: Monolayers of MEF and MLg were inoculated with MCMV (moi = 1) or maintenance medium (control). Cell lysates of MCMV-infected and mock-infected cells were harvested at 24, 36, and 72 hrs after infection and subjected to western blot analysis for detection of parthanatos-associated PARP-1, PAR, and PARG proteins.

Results: Whereas MCMV-infected MEF showed stimulation of PAR and PARG when compared with mock-infected cells, stimulation of these two key parthanatos-associated proteins was not observed within MCMV-infected MLg at all times investigated. In comparison, PARP-1 protein showed significantly reduced stimulation within MCMV-infected MLg when compared with MCMV-infected MEF, but equivalent amounts of PARP-1 protein production were also observed within mock-infected MEF at all times investigated suggesting its stimulation was due to trauma associated with the inoculation procedure.

Conclusions: Our findings support the hypothesis that stimulation of the parthanatos cell death pathway during MCMV infection is cell-type specific. This proof-of-principle finding supports further investigations by us to determine if parthanatos operates within individual cell types of the retina during MAIDS-related MCMV retinitis with a focus on the retinal pigmented epithelium.

CONTROL ID: 3542497

SUBMITTER (NAME ONLY): Christopher Bowd

TITLE: Deep-learning enface image classifier analysis of optical coherence tomography angiography images improves classification of healthy and glaucoma eyes.

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Bowd, A. Belghith, M. Christopher, M.H. Goldbaum, R. Fan, J. Rezapour, S. Moghimi, A. Kamalipour, H. Hou, L.M. Zangwill, R.N. Weinreb, Hamilton Glaucoma Center, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|M.H. Goldbaum, Jacobs Retina Center, Viterbi Family Department of Ophthalmology and Shiley Eye Institute, University of California San Diego, La Jolla, California, UNITED STATES|J. Rezapour, Department of Ophthalmology, University Medical Center of the Johannes Gutenberg University, Mainz, GERMANY|

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ABSTRACT BODY:

Purpose: To compare gradient boosting classifier model (GBM) machine learning analysis of instrument-based OCTA vessel density measurements with deep learning convolutional neural network (CNN) classifier analysis of radial peripapillary capillary (RPC) enface vessel density images for classifying healthy and glaucomatous eyes.

Methods: 100 eyes from 51 healthy participants and 264 glaucomatous eyes from 185 patients from the Diagnostic Innovations in Glaucoma Study who underwent OCTA imaging of the optic nerve head (ONH) were enrolled in this observational cross-sectional study. Classification performance of a GBM trained and tested on standard OCTA ONH measurements was compared to performance of a pre-trained ResNet-50 CNN trained and tested on enface OCTA high density (HD) and non-HD optic nerve head 4.5 mm x 4.5 mm images. Images from 69 healthy eyes (of 35 subject) and 188 glaucomatous eyes (of 130 subjects) were used to train both models and an independent test set containing images from 31 healthy eyes (of 16 subjects) and 76 glaucomatous eyes (of 55 subjects), with no patient overlap between training and test sets, were used to compare model performance. Areas under the receiver operating characteristic (AUROC) curves adjusted for age and the inclusion of both eyes per subject were calculated.

Results: The glaucoma test subjects were significantly older (mean [95% CI], 71.9 [68.7, 75.1] years and 59.5 [53.4, 65.6] years; $P < 0.001$) and glaucoma test eyes had a significantly worse visual field MD (-6.9 [-8.5, -5.2] dB and -0.53 [-0.2, 0.8] dB; $P < 0.001$) compared to the healthy test eyes. The adjusted AUROC using GBM was 0.82 (0.77, 0.84) for RPC vessel density measurements, 0.85 (0.80, 0.87) for RPC capillary density measurements and 0.86 (0.81, 0.87) for combined vessel and capillary RPC density measurements. The adjusted AUROC using CNN analysis of RPC enface vessel density images was 0.91 (0.88, 0.94) resulting in improved classification compared to all GBM results ($P < 0.05$ for all comparisons). Two randomly selected images from the test set with associated probabilities of glaucoma by CNN analysis are shown below .

Conclusions: Deep learning enface OCTA measured vessel density image analysis can improve on instrument-based GBM models for classifying healthy and glaucoma eyes.

CONTROL ID: 3542500

SUBMITTER (NAME ONLY): Sarah Roy

TITLE: Membrane affinity of different segments of lecithin retinol acyltransferase

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Roy, O. Gosselin, S. Gagne, C. Salesse, Universite Laval, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Lecithin retinol acyltransferase (LRAT) is responsible for transforming all-trans retinol into all-trans retinyl ester in the visual cycle. Our preliminary nuclear magnetic resonance data of a truncated form of LRAT (residues 30-196) suggests the presence of an amphiphilic segment (residues 96-107) which could bind membranes. In addition, other authors have postulated that a segment near this amphiphilic segment (residues 71-103), which is found uniquely in LRAT, could be involved in its membrane binding. However, no evidence was shown to support their hypothesis. The objectives of this study are therefore to determine the secondary structure and the membrane binding of these segments of LRAT.

Methods: The amphiphilic segment of LRAT was synthesized commercially. In addition, the human and murine forms of the unique segment were synthesized by the Plateforme de Chimie Médicinale du Centre de Recherche du CHU de Québec. The secondary structure of these peptides was determined by circular dichroism (CD) and their membrane binding was studied using Langmuir monolayers.

Results: The CD spectra show that all segments have a predominantly α -helical structure in methanol. However, in an aqueous medium, the secondary structure of the amphiphilic segment and the murine unique segment is mostly in random coil, whereas the human unique segment is insoluble. All segments bind strongly to monolayers of different types of phospholipids. Indeed, maximum insertion pressure (MIP) values of 44 ± 2 , 47 ± 3 and 57 ± 5 mN/m were obtained for the amphiphilic segment in the presence of dioleoylphosphocholine, dioleoylphosphoethanolamine and distearoylphosphocholine, respectively. MIP values of 36 ± 2 , 40 ± 1 , 35 ± 1 and 40 ± 2 mN/m were obtained for the murine unique segment in the presence of dioléoylphosphocholine, dioléoylphosphoéthanolamine, palmitoyl-arachidonoyl phosphocholine and palmitoyl-arachidonoyl phosphoethanolamine, respectively.

Conclusions: The amphiphilic segment and the murine unique segment both have a high affinity for membranes since all the MIP values obtained are superior to the estimated lateral pressure of membranes (30 mN/m). This suggests that these segments could be involved in the membrane binding of LRAT. This study gives a better understanding of the role of these segments in the function of LRAT. Langmuir monolayer measurements of the human unique segment are in progress.

CONTROL ID: 3542514

SUBMITTER (NAME ONLY): Manoj Mohan Kulkarni

TITLE: The Rod Pathway Contributes to Aberrant Ganglion Cell Activity in Early Retinal Degeneration

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Kulkarni, W.R. Taylor, T. Puthussery, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|M. Kulkarni, W.R. Taylor, T. Puthussery, Helen Wills Neuroscience Institute, Berkeley, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Manoj Mohan Kulkarni: Commercial Relationship: Code N (No Commercial Relationship) | William Taylor: Commercial Relationship: Code N (No Commercial Relationship) | Teresa Puthussery: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aberrant tonic and oscillatory spike activity emerges in retinal ganglion cells (RGCs) during the progression of inherited photoreceptor degenerations. This aberrant activity degrades residual vision and may impede the success of vision restoration. In this study, we tested whether the rod pathway drives aberrant activity in All amacrine cells (All-ACs) and RGCs during early degeneration in the rd10 mouse.

Methods: We used rd10 mice at postnatal (P) day 21-60, an age range when rod bipolar cells (RBCs) undergo morphological and functional changes. Age-matched C57BL6/J mice (WT) were used as controls. Whole-cell recordings were made from All-ACs in retinal slices and spike recordings were made from alpha-like RGCs in wholemount. Two-photon imaging was used to record spontaneous calcium signals from RGCs after bulk-loading of Cal520 AM. The Ca^{2+} -permeable AMPA receptor blocker, IEM1460 (IEM, 50 μM), was used to block RBC input to All-ACs, while sparing cone-driven input. Paired and unpaired t-tests were used for statistical analyses.

Results: We observed periodic voltage fluctuations (frequency: ~3-12 Hz) in 14/20 All-ACs in rd10 retina as early as P21-25, which were rarely seen in WT (1/10 All-ACs). These fluctuations were suppressed by IEM in 6/9 rd10All-ACs, suggesting they were driven in part by the rod pathway. Since All-ACs relay signals to RGCs, we tested whether IEM could suppress aberrant RGC activity in the rd10 retina at a timepoint after complete rod degeneration (P44-55). On-type RGCs had higher spontaneous spike rates in rd10 compared to WT (rd10, 31.3 Hz \pm 19.3, n=12 cells; vs WT, 3.6 Hz \pm 3.7, n=10 cells; mean \pm S.D., p=0.003). IEM significantly reduced spontaneous firing in rd10 On-RGCs (~62% suppression; n=12 cells, p=0.001) and unmasked residual cone-driven light-evoked activity. Ca^{2+} imaging in the rd10 (n=2 mice; P45-55) revealed spontaneous sustained Ca^{2+} events lasting >30s (~7.5% of 293 imaged cells), which were blocked by IEM. Similar spontaneous Ca^{2+} events were absent from WT retina (n=2327 cells, 3 mice; P30-60).

Conclusions: Our results suggest that the rod pathway drives aberrant spontaneous excitatory activity in a sub-population of RGCs in the rd10 retina. Blocking the rod bipolar to All-AC synapse may improve detection of residual cone signals in the degenerating retina by silencing much of the aberrant spontaneous activity.

CONTROL ID: 3542516

SUBMITTER (NAME ONLY): Ramesh Periasamy

TITLE: Development of rAAV capsid mutant vectors with improved tropism for retinal vascular endothelial.

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Periasamy, D. Patel, D.M. Lipinski, Department of Ophthalmology and Visual Science, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D. Patel, Cell Biology, Neurobiology, Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|S.E. Boye, S.L. Boye, Department of Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|D.M. Lipinski, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinal vascular endothelial cells (VECs) are critical for maintaining retinal-homeostasis and play a key role in mediating vascular permeability, tone and contractility. Dysfunction of the vascular endothelium negatively affects the integrity of the blood-retinal barrier and underlies pathogenesis in vascular diseases affecting the eye, such as diabetic retinopathy (DR) and exudative age-related macular degeneration (AMD). As such, VECs represent a promising therapeutic target for the development of future gene therapy treatments, but remain particularly challenging to transduce using existing viral vectors. In this study, we investigate whether the incorporation of endothelial targeting peptides into the rAAV capsid increases VEC transduction efficiency in an ex vivo primary culture model.

Methods: rAAV2/2, 2/2[QuadYF-TV] and rAAV2/9 serotype vectors (n=10 capsid mutants per serotype) packaging a ubiquitously expressing GFP reporter construct were generated by inserting heptameric peptides (7AA) at position 588 (2/2 and 2/2[QuadYF-TV] or 589 (2/9) of the virus protein (VP1-3). The packaging and transduction efficiency of the VEC targeting vectors was first assessed on HEK293T cells using a picogreen dsDNA quantitation assay, fluorescence microscopy, and flow cytometry. After isolating and culturing primary bovine VECs, all vectors were subsequently applied at MOI=75,000. After 72 hours, cells were stained with CD31, and transduction efficiency quantified using flow cytometry.

Results: All VEC targeting mutants packaged successfully and vectors at MOI=10,000 were found to be infectious in HEK293T cells, resulting in widespread GFP expression. Flow cytometry revealed that capsid mutant 5 demonstrated significantly increased normalized GFP expression in CD31+ primary bovine VECs in all serotypes, with 1.7-fold, 2.7-fold and 3.6-fold higher transduction efficiency in rAAV2/9, 2/2 and 2/2[QuadYF-TV], respectively.

Conclusions: Generating rAAV vectors capable of efficiently targeting retinal VECs is an essential first step towards the development of a successful gene therapy treatment for ocular diseases such as DR and AMD. Our initial findings indicate that incorporation of endothelial targeting peptides in the rAAV capsid is well tolerated and able to significantly alter vector tropism, leading to increased VEC transduction efficiency.

CONTROL ID: 3542517

SUBMITTER (NAME ONLY): Ahmad Abdel-Aty

TITLE: Differences in the management of scleritis among ophthalmologists and non-ophthalmologists

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abdel-Aty, N. Kombo, Department of Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ahmad Abdel-Aty: Commercial Relationship: Code N (No Commercial Relationship) | Ninani Kombo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We performed a retrospective, observational clinical study to identify differences in treatment utilization for acute scleritis across medical specialties.

Methods: The records of 256 patients (302 eyes) with scleritis who presented to the Yale New Haven Health System between January 1, 2013 to January 1, 2018 were retrospectively reviewed. Data was collected on treatments utilized and the specialty of the provider caring for the patient. The primary outcome was quiescence of inflammation at three months. The study was approved by the Institutional Review Board (IRB).

Results: We identified 256 patients (302 eyes), including 232 patients (90.6%) with diffuse anterior scleritis, 10 (3.9%) with nodular anterior scleritis, 5 (2%) with necrotizing scleritis, and 9 (3.5%) with posterior scleritis. 173 patients (67.2%) had an ophthalmologist involved in their care, 19 (4.6%) were managed by their rheumatologist alone, 16 (6.3%) were managed by their primary care physician, and 15 (5.9%) were managed by an emergency medicine physician. Patients seen by ophthalmologists were overall more likely to receive acute treatment than those not seen by ophthalmologists (91.9% compared to 50.6%, $p<0.05$). Patients seen by an ophthalmologist were more likely to receive topical steroids (61.3% compared to 10.8%, $p<0.05$), systemic non-steroidal anti-inflammatory drugs (NSAIDs) (43.4% compared to 14.5%, $p<0.05$), or systemic steroids (38.7% compared to 24.1%, $p<0.05$). Patients seen by an ophthalmologist were more likely to resolve within three months (49.5% compared to 10.0%, $p<0.05$). All patients with necrotizing or posterior scleritis were seen and managed by an ophthalmologist, as were the majority of those with systemic disease (61.1%).

Conclusions: There were differences in medication utilization among specialty types, and patients with an ophthalmologist involved with their care were more likely to have resolution of symptoms. Patients with scleritis may benefit from ophthalmologic consultation.

CONTROL ID: 3542519

SUBMITTER (NAME ONLY): Monichan Phay

TITLE: Differentiation of tree shrew iPSC-derived retinal ganglion cells using 3D organoid approach

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: *Tupaia belangeri* [tree shrew (Ts)] is a small para-primate mammal that have been successfully used as an animal model for progressive myopia and glaucoma due to the close resemblance of their eye to human. Having a large eye size with low lens-to-vitreous ratio, a cone-dominant retina, and an optic nerve head with collagenous lamina cribrosa, Ts is an excellent model to study retina ganglion cell (RGC) replacement. To enable allotransplantation in Ts retina, we explored a 3D differentiation approach for deriving RGCs from Ts induced pluripotent stem cells (iPSCs).

Methods: Ts iPSC were derived from Ts neural progenitor cells (Kandoi et. al 2021). Prior to differentiation, Ts iPSCs were first enriched for cells with the highest self-renewal capacity through transient glutamine starvation. Ts iPSC lines were then assessed for alkaline phosphatase (ALP) activity and pluripotency markers by immunofluorescence (IF). To derive RGCs, Ts iPSCs were aggregated to form embryoid bodies and subsequently differentiated into retinal organoids (ORs) using matrigel and sequential inhibition of WNT signaling pathway by IWR1e and activation of hedgehog signaling pathway by SAG. On day 35 of differentiation, Ts ORs were analyzed for RGC markers using IF. RGCs were then isolated using L1CAM-conjugated magnetic microbeads and plated onto PDL and laminin coated glass cover slips for further analysis.

Results: Ts iPSCs treated with transient glutamine starvation maintained rounded dome shaped colony morphology showing high ALP activity and are positive for pluripotency markers, OCT3/4, SOX2, and KLF4 after >50 passages. In contrast, untreated cells displayed rapid differentiation \leq 3 passages. On day 9 of differentiation, Ts neuro-retinal organoids were positive for neuroectoderm marker, PAX6, and neuroretina marker, SIX6. By day 35, RGC markers, RBPMS and THY1 were spatially detected within the organoids. Cultured cells of L1CAM specific RGCs extend neurite outgrowth by day 2 in culture and display typical morphology similar to that of mouse and human RGCs.

Conclusions: Ts RGCs expressing surface marker L1CAM were successfully derived from Ts iPSCs using 3D differentiation strategy. Our success in the generation and isolation of Ts iPSC-derived RGCs enables allotransplantation study and could potentially help to overcome challenges relating to acute rejection of donor RGCs in tree shrew model of glaucoma.

CONTROL ID: 3542520

SUBMITTER (NAME ONLY): Samantha Lin

TITLE: Fixational Eye Movements depend on Fixation Task

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Even when fixating on a stationary target, the eye is in constant motion. These fixational eye movements (FEM) consist primarily of drifts (slow, random-walk-like movements) and microsaccades (fast, ballistic movements). Understanding these movements is important for two reasons (i) determining their role in normal vision and (ii) to learn optimal strategies for maintaining stable fixation for imaging and/or vision testing. Here we compare FEMs during active and passive fixation tasks. Five fixation targets were selected: Maltese cross, Annular disk, Dynamic concentric circles, a two-bar Vernier target, and an E-letter. The Maltese cross and disk targets were stationary (passive) while the Vernier and E-letter targets varied in presentation and time, requiring subject response (active). The concentric circle target was an attention-grabbing task with continual inward moving rings but required no subject response.

Methods: An Adaptive Optics Scanning Laser Ophthalmoscope system (AOSLO) was used to present the fixation target and to collect retinal videos for subsequent retrieval of eye motion and fixated image position on the retina. This instrument provides high spatial (~ 0.1 arcmin) and temporal (960Hz) resolution. Data was collected on 8 subjects with normal. Five 30-second videos of the fixated target moving on the retina were collected for each condition. FEMs were extracted from the videos and analyzed using custom software. Saccades and drifts were automatically marked and any missed or mislabelled saccades were manually amended.

Results: Important differences between passive and active fixation targets were observed. FEMs were overall larger for active tasks, marked with larger saccades but lower saccade rate, larger and longer drifts, and a larger ISOA. Conversely, passive tasks had smaller FEMs, with more saccades and faster/shorter/smaller drifts. Furthermore, each subject consistently used the same preferred retinal locus for all targets.

Conclusions: The lower saccade rate for active tasks suggests saccadic suppression. This suppression, in turn, leads to longer drift segments, larger saccade magnitudes and an overall larger distribution (ISOA) for fixation. Passive fixation targets (eg Maltese cross or disk) are recommended if minimal FEMs are desired. This study emphasizes that the choice of fixation target is important when studying the fine structure and functional role of eye movements for human vision.

CONTROL ID: 3542525

SUBMITTER (NAME ONLY): Andy Shao

TITLE: Revealing Candidate Inherited Retinal Disorder Genes through Genome-wide Screening of Knockout Mice

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Identify candidate inherited retinal disorder (IRD) genes through International Mouse Phenotyping Consortium (IMPC) generated single gene knockout mouse strains with retinal abnormalities, with particular interest in Usher Syndrome and heritable retinal vascular disorders such as Familial Exudative Vitreoretinopathy (FEVR).

Methods: The IMPC database currently contains phenotypic data for approximately 7,000 mice with targeted single gene knockouts. We investigated all strains with abnormal retinal phenotypes and further enriched our search for strains with concomitant hearing or retinal vascular abnormalities. Candidate genes were then analyzed for potential protein-protein interactions via bioinformatic analysis with STRING and PANTHER proteomics databases and cross-referenced against established IRD-causative genes as presented by the RETNET database.

Results: Initial interrogation revealed 182 knockout strains with retinal abnormalities, 153 of which have not been associated with retinal pathology to date. Of these 182 knockout strains, 15 had concomitant impaired auditory function, none of which have been implicated with Usher syndrome to date. Furthermore, 108 strains had vascular phenotypes, 106 of which were novel for retinal vascular anomalies based on search of literature. Bioinformatic analysis revealed two clusters of predicted protein-protein interactions between the 108 candidate vascular disorder genes from IMPC mice and established angiogenesis/vascular pathology genes. These clusters presented 13 candidate genes for retinal vascular disorders, 12 of which have not been implicated in retinal disorders. Analysis of gene clusters revealed evidence for involvement of Wnt/Notch/PDGFR/Rac1 signaling pathways.

Conclusions: We present 153 targeted gene deletions previously unknown to cause retinal pathology. Fifteen of these 153 are candidate Usher Syndrome genes. Thirteen of these 153 are candidates for heritable retinal vascular disorders such as FEVR. These genes are of interest not only for improving screening of human IRD patients, but also for elucidating novel biological mechanisms involved in retinal development.

CONTROL ID: 3542527

SUBMITTER (NAME ONLY): Philipp Steven

TITLE: Adverse Environmental Stress is a Risk Factor for Ocular Graft-Versus-Host Disease

SESSION TITLE: Dry eye and microbiome clinical

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Ocular graft-versus-host disease (oGVHD) is a rapidly progressing, sight-threatening condition of the eye following allogeneic hematopoietic stem cell transplantation (aSCT). Previously we reported in a small case-series that adverse environmental stress (AES) during allogeneic hematopoietic stem cell transplantation (aSCT) may be a risk factor for chronic oGVHD. To strengthen these findings and to identify pathomechanisms, consecutive retrospective analysis of all clinical files of our clinic since 2014 was performed in addition to experimental simulation of AES in a mouse model of oGVHD.

Methods: Comprehensive review of all files from all patients undergoing aSCT between 2014-2018 was performed. Collected data included Schirmer test scores, corneal fluorescein staining, onset of GVHD of the eyes, skin and gut. Statistical analysis included Pearson's Chi2 and Kruskal-Wallis Test.

A minor mismatch-mouse model (129S2->C57BL/6) was used where mice either remained in standard housing or were subjected to AES (35% humidity, constant air flow) for 18 days after bone marrow transplantation (BMT). Systemic and ocular GVHD was monitored for up to 28 days and histological and flow-cytometry analyses of ocular tissue, lacrimal gland, ocular draining-lymph nodes and spleen were performed.

Results: From 444 patients (n=181 female, n=263 male) undergoing aSCT, 211 surviving patients presented with systemic GVHD and n=126 (53 %) developed chronic oGVHD. Humidity of less than 30% during aSCT was significantly higher correlated with oGVHD (73%), whereas humidity above 50% lead to a lower rate of oGVHD (30%). Acute skin GVHD, but not gut GVHD was an AES-independent risk factor for oGVHD.

In the mouse GVHD model, AES led to a significant higher systemic and ocular GVHD score than in the GVHD without AES at days 7 and days 14 after BMT. Corneal staining and blepharitis remained significant elevated after discontinuation of AES until day 28.

Conclusions: Both clinical and experimental data confirm the hypothesis that AES is an independent risk factor for ocular GvHD. In particular humidity below 30% during aSCT increases the risk for oGVHD significantly. Low humidity conditions after aSCT in the mouse model worsened the severity of systemic GVHD in the mouse model, implicating that AES has not only a local effect. In general, AES could be an avoidable risk factor for oGVHD.

CONTROL ID: 3542528

SUBMITTER (NAME ONLY): Sophie Bonnin

TITLE: Retinal capillary and choriocapillaris assessment using Beam Expander module

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the effect of an increase in the lateral resolution of the OCT beam, on the retinal and choriocapillaris optical coherence tomography angiography (OCTA) en face images .

Methods: Prototype software was used on the PLEX® Elite 9000 Swept-Source OCT instrument (ZEISS, Dublin, CA) in combination with the beam expander (BE) module in the OCT path, which produces a wider beam at the pupil plane. This configuration provides a 17 μm optical resolution at the retina compared to the standard 24 μm resolution. This retrospective study involved 23 healthy subjects imaged with 3 \times 3 mm and 2.25 \times 2.25 mm OCTA scans repeated at least 3 times for each subject. The 3x3 mm and 2.25x2.25 mm scans were acquired without and with the BE respectively.

The angiograms were aligned and cropped to keep the part common to both images. Two graders analyzed the images. Perfusion density (PD), vessel density (VD), and foveal avascular zone (FAZ) measurements were also compared.

Results: Qualitative analysis of retinal angiograms acquired with the BE showed significantly better vessel sharpness ($p=0.0005$), better peripheral image quality ($p=0.0001$) and a decrease in segmentation errors ($p=0.04$) compared to scans acquired without the BE.

Mean VD was significantly higher for BE angiograms compared to classic angiograms ($25.86 \pm 1.12 \text{ mm}^{-1}$ and $21.5 \pm 1.13 \text{ mm}^{-1}$, respectively, $p<0.0001$), whereas mean PD was not significantly different between the 2 groups.

Mean FAZ circularity was found to be significantly lower in BE angiograms ($0.65 \pm 0.14 \text{ mm}^{-1}$ and 0.69 ± 0.08 , $p=0.0067$) whereas mean FAZ area was not significantly different between the 2 groups.

Repeatability of VD, PD and FAZ measurements were higher for BE angiograms (ICC : 0.662 ; 0.536 and 0.874 with BE, vs 0.439; 0.435 and 0.804 without BE).

Choriocapillaris image quality was found to be significantly superior with BE, and flow deficits were more visible in all BE scans compared to “classic” scans.

Conclusions: An increase in lateral resolution of the OCT beam resulted in higher quality of retinal and choriocapillaris OCTA images. Improved vessel sharpness and higher mean VD were significant in the scans acquired with the BE.

The improvement was also very significant for choriocapillaris definition, particularly in the visualization of flow deficits

CONTROL ID: 3542530

SUBMITTER (NAME ONLY): Ulrich Kellner

TITLE: Autosomal dominant gyrate atrophy-like choroidal dystrophy revisited: 45 years follow-up and association with a novel missense variant

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To present long-term follow-up in autosomal dominant gyrate atrophy-like choroidal dystrophy (adGALCD) in two distantly related families and propose a possible genotype/phenotype correlation.

Methods: Clinical findings from two families, each with three affected patients, are presented. One of the families had been reported in part previously (Kellner et al 1997, doi: 10.1097/00006982-199709000-00008). Visual field testing, multifocal and full-field ERG recording according to ISCEV standards, as well as non-invasive retinal imaging (fundus photography, near-infrared reflection, fundus autofluorescence, optical coherence tomography) were performed in most patients. Diagnostic genetic testing was performed in two patients of each family using whole genome sequencing. Haplotype analysis was performed by genotyping SNPs and microsatellites in order to establish whether both families were distantly related.

Results: All affected patients presented with large confluent areas of choroidal atrophy beginning in the far periphery as well as peripapillary. Peripheral atrophy was first observed in the second decade of life. During progression, these areas continued to grow towards the foveal area, reaching the fovea at about 60 years of age. The fundus findings resemble gyrate atrophy, no or minimal pigmentary alterations were seen. In addition, subretinal lesions or choroidal neovascularization were not detected in these patients. Diagnostic genetic testing revealed a novel missense variant in a known gene in the heterozygous state in all affected family members. Haplotype analysis showed that the variant found in both families is identical by descent.

Conclusions: adGALCD presents a distinct phenotype with gyrate atrophy-like choroidal dystrophy, with early onset in the second decade of life and slow progression with preservation of the foveal area until late adulthood.

CONTROL ID: 3542531

SUBMITTER (NAME ONLY): Sara Thomasy

TITLE: Chromatic pupillometry as an effective screening tool for heritable retinal disease in rhesus macaques

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRD) are important causes of blindness in humans and animals. Non-human primates (NHP) are useful animal models for human retinal disease due to similar retinal morphology and function. Identification of spontaneous disease models in NHP colonies requires quick screening tools due to the laborious, expensive nature of individual examination. Chromatic pupillometry is a noninvasive method of identifying IRD in humans; however, standard protocols employ time-consuming dark adaptation. We used this tool to compare chromatic pupillary light reflex characteristics utilizing a shortened dark adaptation protocol as well as standard dark-adaptation in rhesus macaques with PDE6C associated achromatopsia to controls with normal retinal function.

Methods: This prospective study evaluated red-, blue-, and white-light chromatic pupillometry following a shortened 1-minute versus standard 20-minute dark adaptation in rhesus macaques with PDE6C associated achromatopsia and sex- and age-matched controls without IRD. Pupil latency, degree of pupil constriction, pupil constriction time, and average constriction velocity were measured and compared between groups.

Results: Nine rhesus macaques (7 females and 2 males) homozygous for the PDE6C mutation and nine age-, sex-matched normal controls were used in this study. Pupil constriction latency was significantly longer in achromats versus controls with red- and blue-light stimulation ($P<0.05$); but did not differ between groups with white-light stimulation ($P=0.2$). Degree of pupil constriction was significantly less in achromats compared to controls with red-, blue-, and white-light stimulation ($P<0.0001$). Pupil constriction time was significantly shorter in achromats versus controls with red- and white-light stimulation ($P<0.05$), but did not significantly differ between groups following blue-light stimulation ($P=0.9$). Pupil constriction velocity was significantly slower in achromats versus controls with red-, blue-, and white-light stimulation ($P<0.001$). Dark adaption time was only a significant factor for degree of pupil constriction ($P=0.008$) and pupil constriction time ($P=0.02$) following blue-light stimulation.

Conclusions: Chromatic pupillometry is an effective tool for screening NHPs for achromatopsia. A 1-minute dark adaptation protocol was sufficient to discern NHPs with and without achromatopsia.

CONTROL ID: 3542533

SUBMITTER (NAME ONLY): Eugene Hsu

TITLE: Quantification of Corneal Collagen Cross-Linking in Keratoconus with Inverse Spectroscopic Optical Coherence Tomography

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optimization of corneal collagen cross-linking (CXL) is hindered by the inability to immediately measure treatment effects. Inverse spectroscopic optical coherence tomography (IS-OCT) is an emerging technique capable of non-invasively detecting nanoscale ultrastructural changes. The IS-OCT output measure D was previously found to increase with increased collagen cross-linking in vitro. We performed a pilot study to measure changes in keratoconus patient eyes before and after CXL by IS-OCT in vivo.

Methods: With IRB approval, keratoconus patients scheduled to undergo CXL were consented and enrolled. Standard epi-off CXL was performed in one eye (Glaukos, San Clemente, CA). Immediately preceding, and one month after unilateral CXL, both central corneas were imaged with dual channel visible and near-infrared light OCT. D was calculated and compared between eyes. A two-tailed paired Students t-test was used for statistical analysis.

Results: The change in corneal D before and after CXL was $+1.78 \pm 0.36$ ($n = 3$), compared to -0.22 ± 0.34 ($n = 3$) in the contra-lateral non-CXL cornea ($p = 0.03$). Delta D in the anterior half of the cornea was $+1.83 \pm 0.12$ in CXL eyes vs. -0.21 ± 0.68 in non-CXL eyes ($p=0.047$). Delta D in the posterior half of the cornea was $+1.68 \pm 0.47$ in CXL eyes vs. -0.19 ± 0.37 in non-CXL eyes ($p=0.03$). The increase in D after CXL appeared more consistently higher in the anterior corneal stroma and diminished in the posterior-most region (Figure 1).

Conclusions: In this preliminary study, we found that IS-OCT can be used to image corneas quickly and non-invasively in patients. D was increased in corneas following CXL. IS-OCT could help quantitate CXL in vivo, but further study with additional patients and methods for improved data normalization are needed to validate these preliminary results.

CONTROL ID: 3542534

SUBMITTER (NAME ONLY): Jade Liu

TITLE: Evaluation of the novel Foraging Interactive D-prime (FInD) CSF Test

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Liu, A. Jnawali, F.A. Vera-Diaz, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P. Bex, Northeastern University, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the repeatability and reliability of the novel Foraging Interactive D-prime (FInD) test for the contrast sensitivity function (CSF) against a standard Two-Alternative Forced Choice (2AFC) method. Compared to other tests, FInD is self-administered, generalizable, and user-friendly for patients of all ages, cognitive status, language backgrounds, and literacy levels.

Methods: FInD was used to present three charts of 4*4 cells, a random subset of which contain band-pass filtered noise targets (peak spatial frequency 0.5, 1, 2, 4, 8, and 16 cpd) that observers are required to mouse-click. The contrast of each target is selected from a range spanning difficult ($d'=0.1$) to easy ($d'=4.5$), that is adaptively updated after each chart based on a decision function fit to Hit/Miss/Correct_Rejection/False_Alarm scores for each cell. Fourteen adult observers with varying visual acuities performed the FInD CSF and 2AFC CSF in random order at 40 cm and at 4 m. The FInD CSF test was repeated twice at both viewing distances. Repeatability was assessed using mixed linear models and Bland-Altman analysis. Reliability was assessed using mixed linear models.

Results: The FInD CSF test was completed significantly more quickly than the 2AFC (4.98 ± 1.52 min vs 10.86 ± 0.91 min at 40 cm; 4.93 ± 2.00 min vs 12.69 ± 2.11 min at 4 m). A mixed linear model repeated measures ANOVA with Huynh-Feldt correction showed good repeatability for the FInD CSF test at 4 m ($F=0.044$, $p=0.877$, $\eta^2=0.002$) and 40 cm ($F=0.633$, $p=0.498$, $\eta^2=0.024$). Posthoc analysis showed a significant difference in test-retest repeatability for 0.5 cpd only at 4 m. Bland-Altman analysis showed proportional biases for 0.5 cpd at 40 cm ($p=0.003$), and 16 cpd at 4 m and 40 cm ($p=0.008$, $p=0.002$). The mixed linear model showed no overall significant difference between the FInD CSF and 2AFC CSF tests at 4 m ($F=0.913$, $p=0.366$, $\eta^2=0.034$) and 40 cm ($F=2.130$, $p=0.123$, $\eta^2=0.098$). Posthoc analysis showed significant differences at 0.5 cpd ($p<0.001$), 1 cpd ($p=0.001$), and 2 cpd ($p=0.025$) at 4 m. At 40 cm, posthoc analysis showed differences for 4 cpd ($p=0.032$), and 8 cpd ($p=0.002$).

Conclusions: Good repeatability and reliability were found for the FInD CSF test at 4 m and 40 cm viewing distances. Completion of data collection (aim is $n=50$) will conclude whether the FInD CSF test is indicated for use in clinical practice.

CONTROL ID: 3542535

SUBMITTER (NAME ONLY): Sarah Palko

TITLE: Genetic ablation of PAD4 in the Accelerated Mouse Model of AMD Results in Reduced Citrullinated Products

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Protein citrullination is catalyzed by the peptidyl arginine deiminases (PADs). PAD4 has emerged as an important biomarker in mouse and human wet-AMD (IOVS June 2020, Vol.61, 3689). Here we have investigated the contribution of PAD4 to pathological citrullination in the mouse model of wet-AMD, as well as in human wet-AMD maculae.

Methods: PAD4 homozygous deficient (PAD4 KO) mice were generated by breeding PAD4^{flox/flox} mice with GFAP-Cre^{ERT2} mice and progeny treated with tamoxifen. PAD4 KO mice and litter mates were subjected to focal laser burns of the retinal pigment epithelium using the Meridian Merilas 532 nm laser coupled to the Micron III fundus imaging system. Mouse eyes were cryosectioned and stained with antibodies against F95 antibody (citrullination) and glial fibrillary acidic protein (GFAP). Mouse retino-choroidal tissue was lysed in RIPA buffer for western blot (WB) analyses. Human donor AMD eyes (n=2) and age-matched normal eyes (n=2; male and female) were subjected to SD-OCT, as described (Pang et al., Ophthalmology 2015). A circular 8 mm retino-choroidal button centered at the macula was cryosectioned and stained with antibodies to PAD4, GFAP and citrullinated GFAP (CTGF-1221) and analyzed by confocal microscopy.

Results: PAD4 KO 7-day-laser injured mice showed decreased citrullination of specific species, as well as high molecular weight species compared to injured litter mates in WB analysis. PAD4 KO mice also showed reduced filamentous citrullinated protein in Muller glia compared to wildtype mice. In human female AMD maculae, the CTGF-1221 antibody recognizing citrullinated arginine (R270 and R416) on GFAP showed increased positive staining in the astrocyte layer, as well the inner nuclear layer. The male AMD retina also showed modest increase of citrullinated-GFAP. The citrullinated-GFAP species are in the cell body in both layers and have decreased filamentous structure compared to age matched controls.

Conclusions: Increased retinal citrullination in the mouse AMD model is driven by Muller cell expression of PAD4. Providing proof of the importance of this enzyme, PAD4 genetic ablation results in reduced citrullination. Human wet-AMD maculae that show increased PAD4 expression revealed corresponding increased citrullinated GFAP species. These findings illuminate PAD4 as an important druggable target in AMD and its attenuation for pathological citrullination.

CONTROL ID: 3542536

SUBMITTER (NAME ONLY): Christopher Le

TITLE: Automated Vessel Segmentation in Adaptive Optics – Optical Coherence Tomography Images

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To demonstrate automated capillary segmentation in adaptive optics – optical coherence tomography (AO-OCT) images.

Methods: AO-OCT volumes were acquired from the FDA multimodal AO imager focused on the inner retina. A trained grader generated the vessel plexus projections from the averaged AO-OCT volumes. We trained a UNet-based convolutional neural network to segment retinal capillaries in en face projections of the superficial vascular plexus (SVP), intermediate capillary plexus (ICP), and deep capillary plexus (DCP). The network was trained with random 128x128 pixel patches from 177 automatically contrast-corrected projections of each plexus from 18 eyes in 18 subjects with a 20% validation split. We trained four models: one with all-plexus images and three with plexus-specific images only. The models' results were compared with a trained grader's manual capillary segmentation. We evaluated segmentation performance based on Dice coefficient (DC), pixel-wise precision, recall, and accuracy on a held-out 20% test split.

Results: Our all-plexus model achieved good segmentation results with an overall DC of 0.701, precision of 0.686, recall of 0.749, and accuracy of 0.929. All-plexus and plexus-specific model performance had comparable results for each plexus, with slightly better DC in the all-plexus model in SVP and ICP, but worse in DCP projections.

Conclusions: This is the first application of deep learning techniques for automated vessel segmentation in AO-OCT projections, achieving a good DC, precision, recall, and accuracy and demonstrating the applicability of segmentation techniques to this imaging modality. Difference in results across plexus-specific models may reflect a trade-off in training sample size and task-relevance; however, statistical significance of these results is not determined from this study. Future work is needed to further understand whether automated segmentation should be optimized for each plexus.

CONTROL ID: 3542540

SUBMITTER (NAME ONLY): Reece Mazade

TITLE: Cortical ON and OFF pathway mechanisms of visual brightness

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Mazade, J. Jin, C. Pons, J. Alonso, SUNY College of Optometry Department of Biological and Vision Sciences, New York, New York, UNITED STATES|R. Mazade, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The strength of visual responses in primary visual cortex varies with stimulus luminance and size. However, the relative contribution of ON and OFF cortical pathways to signaling luminance remains poorly understood. Here, we investigated how the responses from ON and OFF cortical neurons change with the spatial structure and brightness of the stimulus.

Methods: We measured the responses from ON and OFF neurons in cat visual cortex to light-dark pattern stimuli (white noise, gratings) and light or dark homogenous surfaces. Cortical neurons were classified as ON or OFF based on the contrast polarity ratio of their maximum response to light and dark small features, $CP = (light - dark) / (light + dark)$, where $CP < 0$ indicates OFF pathway dominance and $CP > 0$ indicates ON pathway dominance.

Results: When stimulated with patterns, ON and OFF neurons had similar response strength (42.9 ± 1.1 vs. 41.9 ± 1.0 spk/s, $p=0.30$, Wilcoxon test). OFF neurons responded to small dark stimuli aligned with their receptive field centers, and were suppressed by small light stimuli, and the opposite was found for ON neurons. As stimulus luminance increased, the responses from ON and OFF neurons became stronger ($R^2=0.84$, $p<0.001$) and ON neurons increased their ON dominance while OFF neurons increased their OFF dominance, a change that may help to distinguish better small dark stimuli from small light stimuli. Surprisingly, both ON and OFF neurons showed strong spatial summation to large bright surfaces and strong spatial suppression to large dark surfaces (dark vs. light size suppression ratio; OFF: 0.46 ± 0.03 vs. 0.16 ± 0.03 ; ON: 0.39 ± 0.05 vs. 0.08 ± 0.04 ; $p<0.001$, Wilcoxon tests). Additionally, as stimulus luminance increased, cortical responses from both ON and OFF neurons, and the combined ON-OFF response, became stronger.

Conclusions: Our results reveal a cortical mechanism for stimulus size-luminance interactions that may underlie brightness perception. Brightness of small features is signaled with an increase in ON pathway strength but brightness of large surfaces is associated with a strong ON-OFF combined response. This is explained if both ON and OFF neurons have opposite receptive field centers but the same ON extended surrounds. With this structure, small features drive opposite ON and OFF center responses while large surfaces drive the same extended surround, increasing response to light surfaces and suppressing response to dark surfaces.

CONTROL ID: 3542548

SUBMITTER (NAME ONLY): Zahra Souri

TITLE: Expression of immune checkpoint LAG3 is associated with high risk uveal melanoma

SESSION TITLE: Advances in Diagnosis and Treatment of Uveal Melanoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Souri, G. Luyten, M.J. Jager, Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NL, academic/hospital, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Uveal melanoma is a rare malignancy of the eye originating from the uveal tract. While treatment with immune checkpoint inhibitors such as anti-PD1 is often effective in the treatment of cutaneous melanoma metastases, no effective treatment for UM metastases has as yet been developed. A potential new target for immune checkpoint inhibitors is Lymphocyte-activation gene 3 (LAG3). LAG3 is an immune inhibitory receptor which is expressed on T cells and shows a great affinity for MHC Class II. Another ligand of LAG3 is Galectin-3. As LAG3 is known as an indicator of T cell exhaustion in tumors, we set out to investigate which Uveal Melanoma express this immune checkpoint and its ligands, MHC Class II and Galectin-3, in order to get a better insight in possible immunotherapeutic approaches.

Methods: The mRNA expression of LAG3, MHC II, Galectin-3, PD1, markers of tumor-infiltrating lymphocytes (TIL) and tumor-associated macrophages (TAM) was determined using an Illumina HT12V4 array in 64 primary UM. In order to confirm our analysis, the mRNA expression of the same markers was studied using 80 UM samples from the TCGA cohort.

Results: When comparing the level of LAG3 expression with clinic-pathological characteristics in the Leiden set of 64 tumors, a higher expression was associated with the presence of epithelioid cells ($P=0.05$), ciliary body involvement ($P=0.05$) and loss of BAP1 staining ($P=0.001$); the level of LAG3 expression was significantly higher in monosomy 3 tumors compared to disomy 3 ($P=0.004$). Furthermore, LAG3 showed a positive correlation with TILs and TAMs (CD3, CD4, CD8, CD68, all $P<0.001$). LAG3 expression correlated positively with expression of HLA-DP ($P<0.001$), HLA-DQ ($P<0.001$), two probes for HLA-DR ($P<0.001$; $P<0.001$), Galectin3 ($P<0.001$) and PD1 ($P<0.001$). When looking at the TCGA data, similarly, LAG3 ($P<0.001$), HLA-DP ($P=0.001$), HLA-DQ ($P<0.001$), HLA-DR ($P=0.001$), and Galectin3 ($P<0.001$) were significantly higher in M3 compared to D3 UM tumors.

Conclusions: We show that LAG3 is highly expressed in M3 UM tumors; LAG3 is strongly associated with expression of its ligand MHC Class II, and with the presence of TILs and TAMs. We suggest that LAG3 might have a potential role for the exhaustion of T cells present in the UM tumor environment and propose that due to its association with high risk tumor characteristics, LAG3 may be a good target for immunotherapy in UM.

CONTROL ID: 3542552

SUBMITTER (NAME ONLY): Han Peng

TITLE: Vitamin D3 and HDL nanoparticles: novel ocular therapeutics for the acute inflammatory response following mustard exposure

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Peng, N. Kaplan, A.E. Calvert, K.M. McMahon, J. Wang, W. Yang, V. Onay, K. Lu, C.S. Thaxton, R. Lavker, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The eye is the most susceptible part of the body to the effects of chemical warfare agents, nitrogen and sulfur mustard (NM and SM). Steroidal and/or non-steroidal anti-inflammatory drugs are the accepted treatments for the acute and prolonged phases of mustard injury. However, there have been warnings against the use of topical steroids in SM ocular injuries. Thus, additional therapies to prevent the SM-induced ocular deterioration is a major unmet need.

Methods: Mouse corneas were exposed to NM (2%, 5 min) an analogue of SM. After exposure, corneas were topically treated with high-density lipoprotein like nanoparticles (HDL NPs), or Vitamin D3 (Vit D3, 5 ng i.p.) that was systemically injected. Cy3-labeled HDL NPs were used to determine penetration of HDL NPs through corneal epithelium. To evaluate corneal clarity, mouse corneas were imaged for haze scoring. To determine epithelial integrity, corneas were stained with fluorescein and imaged. Immunostaining and qPCR were performed to examine gene expression.

Results: After NM exposure, Vit D3 treatment significantly (>60%) reduced: (i) the amount of corneal fluorescein staining; (ii) degree of haze; (iii) pro-inflammatory cytokine and chemokine expression; and (iv) angiogenic signaling. This indicates that Vit D3 treatment results in marked alleviation of NM-induced corneal damage. Furthermore, we have demonstrated that following topical treatment, HDL NPs can penetrate into corneal epithelial cells. After NM injury, topical treatment of HDL NPs (1 μ M) significantly attenuated the expression of several inflammatory factors including Il6, Il1b, Cox2, and Ccl2. Additionally, factors that affect the stroma and normal repair process were reduced including Mmp9, Mmp12, Vegfa, Tgfb, and Pdgfb.

Conclusions: Collectively, our findings strongly suggest that systemic delivery of Vit D3 or topical delivery of HDL NPs to the cornea and limbus have vast treatment potential for corneal mustard keratopathy. Furthermore, the beneficial properties of HDL NPs as well as Vit D3 argues for the development of a "super" HDL NP-Vit D3 eye drop in order to reduce inflammation in the anterior segment.

CONTROL ID: 3542560

SUBMITTER (NAME ONLY): Ryan Gallo

TITLE: Targeting the Notch transcriptional activation complex with a novel PRAG1 inhibitor to attenuate reactive gliosis

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In response to neurodegenerative diseases and injury to the retina, astrocytes and Müller glia (MG) undergo reactive gliosis. Chronic reactive gliosis exacerbates neurodegeneration by promoting inflammation and scar formation. Studies report that Notch signaling enhances gliosis and neuronal death. Current compounds that target this pathway, including non-specific inhibitors of presenilin-dependent γ -secretase, do not effectively treat central nervous system (CNS) disease and injuries. Recently, PEAK1 Related, Kinase-Activating Pseudokinase 1 (PRAG1) was identified as a novel Notch transcriptional coactivator (and given the alternate name Notch Activation Complex Kinase [NACK]). Our team identified a first-in-class PRAG1 inhibitor to target Notch1 activity directly and specifically. Given the activation of Notch1 signaling upon CNS injury and the critical role of PRAG1 in the activation of this signaling pathway, we hypothesize that directly modulating Notch1 transcriptional activity via PRAG1 inhibition will mitigate reactive gliosis and neuropathic progression.

Methods: Human and mouse MG were stimulated with Notch ligands then treated with the PRAG1 inhibitor UM74 for Western blot and real-time PCR. We also studied changes in Notch signaling and the effects of UM74 following ischemia/reperfusion (IR) injury in 2-month-old C57BL/6J mice. Retinal ischemia was induced for 1 hour by elevating intraocular pressure above systolic blood pressure with normal saline (to 120 mmHg). Intravitreal injection of UM74 was performed immediately after IR injury. Mice were sacrificed 7 days after injury and their eyes were enucleated for Western blot, real-time PCR, and immunofluorescence staining.

Results: Notch-1 signaling was upregulated in human and mouse MG after Notch ligand treatment as confirmed by an increase in activated Notch-1 and Hes1. Notch-1 signaling was also upregulated after 7 days post IR-mediated retinal gliosis. Blockade of Notch signaling with PRAG1 inhibitor UM74 attenuated astrocytic and MG hypertrophy and GFAP expression as assessed by immunofluorescence staining and Western blot, respectively. Longitudinal retinal ganglion cell functional studies are underway.

Conclusions: Notch-1 signaling is induced after IR-mediated reactive gliosis, and its direct blockage by PRAG1 inhibition may be a potential therapeutic strategy.

CONTROL ID: 3542564

SUBMITTER (NAME ONLY): Ahmed Abass

TITLE: Corneal Stress-Strain Index (SSI) Map

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abass, A. Eliasy, H. Zhang, B.T. Lopes, R. Vinciguerra, A. Elsheikh, School of Engineering, University of Liverpool, Liverpool, Merseyside, UNITED KINGDOM|H. Zhang, School of Biomedical Engineering, Capital Medical University, Beijing, CHINA|R. Vinciguerra, Department of Ophthalmology, Humanitas San Pio X Hospital, Milan, ITALY|A. Elsheikh, Beijing Advanced Innovation Centre for Biomedical Engineering, Beihang University, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: To introduce a novel method to map the mechanical stiffness of healthy and keratoconic corneas.

Methods: Numerical modelling based on the finite element method was used to carry out inverse analysis of simulated healthy and keratoconic corneas to determine the regional variation of mechanical stiffness across the corneal surface based on established trends in collagen fibril distribution. The Stress-Strain Index (SSI), developed and validated in an earlier study and presented as a parameter that can estimate the overall stress-strain behavior of corneal tissue, was adopted in this research as a measure of corneal stiffness. The regional variation of SSI across the corneal surface was obtained using inverse analysis while referring to the common features of collagen fibrils' distribution obtained from earlier x-ray scattering studies. Additionally, for keratoconic corneas, a method relating keratoconic cone features and cornea's refractive power to the reduction in collagen fibril density inside the cone was implemented in the development of SSI maps.

Results: SSI values varied slightly across the corneal surface in healthy eyes. In contrast, keratoconic corneas demonstrated substantial reductions in SSI values inside the cone, Figure 1. These SSI reductions depended on the extent of the disease and increased with more considerable simulated losses in fibril density in the cone area. SSI values and their regional variation showed little change with changes in IOP, corneal thickness and curvature.

Conclusions: SSI maps provide an estimation of the regional variation of biomechanical stiffness across the corneal surface. The maps could be particularly useful in keratoconic corneas, demonstrating the dependence of corneal biomechanical behavior on the tissue's microstructure and offering a tool to fundamentally understand the mechanics of keratoconus progression in individual patients.

CONTROL ID: 3542566

SUBMITTER (NAME ONLY): Sarah Sunshine

TITLE: Combinatorial Therapy with Immunosuppressive, Immunomodulatory and Tear Substitute Eyedrops ('Triple Play') in Recalcitrant Immunological Ocular Surface Diseases

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sunshine, Ophthalmology, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|E. Katz, C. Mun, J. Mun, C. Berek, A. Pradeep, B. Surenkhuu, S. Jain, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current paradigm for therapy of immune mediated ocular surface diseases (i OSD) consists of targeting innate or adaptive immune system pathways in a sequential, step-up treatment approach. A combinatorial topical therapy (anti-inflammatory/immunosuppressive pharmaceutical [steroid] with immunomodulatory [pooled human immune globulin] and tear substitute [serum] biologics) that simultaneously targets several immunological pathways may be more efficacious. This combinatorial therapy targets distinct albeit overlapping pathways of the immune system to affect several inflammatory mediators (eicosanoids, autoantibodies, complement system and cytokines/chemokines).

Methods: We performed a retrospective, case study of patients receiving topical formulations of methylprednisolone, pooled human immune globulin, and serum tears to evaluate if the 'triple play' therapy resulted in clinical benefit in recalcitrant OSD cases (n=10). Patients included one male and nine females ranging in age from 27 to 87 years old. Patients were included if they suffered from recalcitrant OSD, received the three therapies, and had slit lamp photographs prior to starting the 'Triple Play' therapy and a subsequent photograph following at least a month of treatment. Outcome measures were individualized by case and included visual acuity, ocular surface disease index (OSDI), ocular discomfort score, subjective global assessment (SGA), and slit lamp photographs.

Results: Pathologies included ocular graft-versus-host disease, Sjögren's syndrome, ocular cicatricial pemphigoid, neurotrophic keratitis, pemphigus vulgaris, peripheral ulcerative keratitis, Stevens-Johnson syndrome, and giant papillary conjunctivitis. All patients were 'much improved' on SGA after 'Triple Play' therapy. Additionally, three patients had improvement in their visual acuity (one from 20/400 to 20/20). All patients had clinically meaningful improvement in signs (reduction in bulbar redness and corneal staining).

Conclusions: Combinatorial 'Triple Play' therapy provides a clinical benefit by reducing the symptoms and signs in recalcitrant i OSD. Our study provides the rationale for performing prospective clinical trials to evaluate the efficacy of combinatorial 'Triple Play' therapy for treating i OSD.

CONTROL ID: 3542567

SUBMITTER (NAME ONLY): Yik Tung Tracy Ling

TITLE: Computational Model of the Stress and Deformation Response of the Mouse Astrocytic Lamina to Intraocular Pressure

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Ling, A. Korneva, T.D. Nguyen, Mechanical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|A. Korneva, H.A. Quigley, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a computational biomechanical model of the mouse astrocytic lamina (AL) and investigate the effect of the AL network structure on the local stress and strain response to increased intraocular pressure (IOP).

Methods: An unmyelinated optic nerve section of a 6-month old GFP-GLT1 mouse was immunolabeled for GFAP and stained for actin and nuclei(Ling et al. 2020, Fig 1a). The non-GFAP and non-actin regions in the acquired confocal image were segmented as axonal compartments(ACs). A finite element model(FEM) was created using the GFAP, actin and AC labels in Gibbon Toolbox(Fig 1b). Nodal displacements were applied to the side surface of the AL using average of measured boundary displacements from 7 mouse eye explants that were inflated from 10 to 30 mmHg(Korneva et al. 2020). A pressure of 20 mmHg was applied on the anterior surface of the model to simulate the inflation test(Fig 1c). The GFAP, actin and ACs were assumed to be incompressible Neo-Hookean materials with shear moduli of 2.4MPa(Guzman et al. 2006), 21.2MPa(Janmey et al. 1991) and 1.9kPa(Budday et al. 2015), respectively. Bulk modulus for each material was assumed to be 100 times larger than the shear modulus. The effect of axonal area on strains simulated in FEBio was analyzed using a linear regression model in MATLAB.

Results: Preliminary results showed that the average nasal-temporal strain($E_{xx}=0.033$, Fig 2a) in the AL was higher than the inferior-superior strain($E_{yy}=0.026$), while the anterior-posterior strain was compressive($E_{zz}=-0.021$). This agreed with the inflation test results. The maximum principal strain(E_{max}) was larger in the ACs(0.03 ± 0.10) compared to that experienced by GFAP and actin structures in the astrocyte processes(0.01 ± 0.02 and 0.02 ± 0.01 , $p<0.01$, Fig 2b&d). However, the maximum principal stress(σ_{max}) was lower in the ACs (0.0058 MPa) when compared to that in GFAP(0.77 MPa) and actin(1.64 MPa, $p<0.01$, Fig 2c). Greater tensile strains E_{xx} and E_{yy} and greater compressive strains E_{zz} were obtained for larger ACs(Fig 2e&f, $p<0.05$). The model will be applied to examine the effects of fiber tortuosity and aspect ratio on the stress and strain response in the astrocyte processes and AC.

Conclusions: A specimen-specific FEM of the AL suggested that larger ACs experienced higher strain magnitudes. Variations in AL network structure may be related to the susceptibility of axonal damage in glaucoma.

CONTROL ID: 3542568

SUBMITTER (NAME ONLY): Joseph Bechay

TITLE: Hemorrhagic Complications Following Trabecular Bypass Microstent Surgery in the Setting of Antithrombotic Therapy

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bechay, S. Patel, S. Lam, I. Zadrozny, J. Reyes, W.S. Shalaby, D. lee, J. Myers, M. Pro, M. Moster, A. Shukla, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the incidence of postoperative hemorrhagic complications in patients on antithrombotic therapy (ATT), including antiplatelet (AP) or anticoagulant (AC) therapy, and controls following combined trabecular stent implantation and phacoemulsification.

Methods: This single center, retrospective, case-control study included patients on chronic ATT who underwent iStent/iStent inject (Glaukos Corp., Laguna Hills, CA) or Hydrus (Ivantis Inc., Irvine, CA) with phacoemulsification between 2013-2019 and had ≥ 3 -month follow-up. The primary outcome measure was hemorrhagic complications within the 3-month postoperative period. Changes were not made to ATT therapy during this time. Secondary measures included visual acuity (VA), intraocular pressure (IOP), and number of glaucoma medications.

Results: Of 333 patients (435 eyes), 161 patients (211 eyes) were on ATT, and 172 patients (224 eyes) were controls. Baseline characteristics including age, sex, VA, IOP, cup-to-disc ratio, and number of glaucoma medications were similar between groups. Hyphema, the only hemorrhagic complication, was seen in 94 eyes (21.6%). Hyphema incidence differed by stent type (21.8% in iStent, 11.8% in iStent inject, and 42.4% in Hydrus ($P=0.002$)).

Incidence and duration of hyphema did not vary between ATT and control groups ($P=0.827$) (Figure 1). Of 35 ATT eyes with hyphema, 7 eyes (20.0%) were on AC therapy, 29 eyes (82.9%) were on AP therapy, and 1 eye was on combined therapy. Of the 102 patients who had two eyes included, hyphema was present in both eyes in 18 patients (17.6%). Hyphema was associated with an IOP increase of ≥ 10 mmHg from baseline in 22 ATT eyes (10.4%) and 25 control eyes (11.2%) ($P=0.878$). Reoperations were not required for hyphema or associated IOP spike. At month 3, VA improvement, reduction of IOP, and number of glaucoma medications were similar between the ATT and control groups ($P<0.001$ for all).

Conclusions: Hyphema was present in 21.6% of eyes, and was most common following Hydrus microstent and least common following iStent inject. ATT was not identified as a risk factor for the presence or prolonged duration of hyphema. Although hyphema was associated with an IOP increase of ≥ 10 mmHg from baseline in approximately one-tenth of eyes, reoperations were not required for this indication, and nearly all hyphemas resolved by postoperative month 1.

CONTROL ID: 3542569

SUBMITTER (NAME ONLY): Eric Ritchey

TITLE: Pediatric Assessment of Peripheral Visual Acuity

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.R. Ritchey, A. Ravikumar, College of Optometry, The University of Houston, Houston, Texas, UNITED STATES|K.A. Butler, M&S Technologies, Inc., Niles, Illinois, UNITED STATES|C. Hunt, Visioncare Research, Ltd., Farnham, UNITED KINGDOM|J. Rappon, SightGlass Vision, Inc., Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Increasing use of optical methods for controlling myopia progression has raised questions regarding the potential long-term effects of these treatments on peripheral vision; however, there is currently no available clinical methodology for measuring peripheral visual acuity. We examined the ability to measure peripheral visual acuity in myopic children using standard spectacle lenses over a 12-month period in a prospective clinical trial using a novel measurement system.

Methods: Sixty-three myopic subjects aged 6 to 10 years old were evaluated using a novel, electronic system to measure peripheral acuity over two study visits, baseline (BL) and 12 months (12M). Subjects were seated 40 cm from a computer display wearing standard spectacle lenses, with the non-test eye patched. The test eye fixated on a numerical target while HOTV optotypes were presented at 25° eccentricity in 4 quadrants: Superior Temporal (ST), Superior Nasal (SN), Inferior Temporal (IT) & Inferior Nasal (IN). Varying optotype sizes were presented using a staircase method and responses recorded until threshold acuity was determined.

Results: Mean BL age and spherical equivalent refraction (\pm SD) were 8.1 ± 1.21 years and $-2.05 \pm 0.80D$ (range: -0.75 to -4.25). Mean BL peripheral visual acuity (\pm SD) in logMAR were: ST 0.99 ± 0.30 , SN 0.94 ± 0.30 , IT 1.06 ± 0.30 and IN 0.99 ± 0.25 . Mean 12M logMAR peripheral visual acuity were: ST 0.88 ± 0.27 , SN 0.88 ± 0.29 , IT 0.89 ± 0.28 and IN 0.87 ± 0.27 . Statistically significant differences in logMAR acuity between BL and 12M (paired t-test) were observed for the ST ($p = 0.015$), IT ($p = 0.002$) and IN ($p = 0.006$) quadrants. No difference was observed in the SN quadrant ($p = 0.20$).

Conclusions: Peripheral visual acuity in children wearing standard spectacle lenses can be measured effectively with this novel peripheral acuity system. While approximate 1-line improvements in mean logMAR peripheral visual acuity were observed in 3 of 4 visual field quadrants and may reflect increased subject familiarity with the test procedure and increasing subject age, these differences are not clinically significant and should be considered clinically stable. This measurement methodology may be an effective tool to monitor for changes in peripheral visual acuity over time in children in a clinical setting.

CONTROL ID: 3542571

SUBMITTER (NAME ONLY): Roberto Gonzalez-Salinas

TITLE: Safety and Efficacy of Lotilaner Ophthalmic Solution 0.25% for the Treatment of Demodex Blepharitis: The EUROPA Study

SESSION TITLE: Dry eye clinical treatments

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Gonzalez-Salinas, H. Quiroz-Mercado, N. Ramos-Betancourt, C. Corredor-Ortega, J. Ceballos Galvez, M. Massaro-Corredor, Department of Research, Asociación para Evitar la Ceguera (APEC), Mexico City, MEXICO|E. Yeu, Virginia Eye Consultants, Norfolk, Virginia, UNITED STATES|S.N. Baba, M.J. Holdbrook, Tarsus Pharmaceuticals, Inc., Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: There are no FDA-approved treatments for blepharitis due to Demodex infestation. We performed a prospective, randomized, vehicle-controlled Phase IIb clinical trial to evaluate the safety and efficacy of topical lotilaner ophthalmic solution 0.25% (TP-03, Tarsus Pharmaceuticals, Inc.) in patients with Demodex blepharitis.

Methods: Fifty-four adult participants were randomized 1:1 to the active (A) or vehicle (V) groups. One eye of each patient was defined as the analysis eye. To be included, participants had to have >10 collarettes (cylindrical dandruff) on the upper lid, at least mild upper lid margin erythema, and ≥ 1.5 mites per lash on the upper and lower lids combined. Lid hygiene treatment and topical antibacterial, antiparasitic or anti-inflammatory agents were not permitted during or 2 weeks before the study. Participants applied 1 drop of TP-03 in both eyes twice daily for 42 days. Primary outcome measures were the percentage of eyes achieving collarette cure (≤ 2 lashes with collarettes on the upper eyelid), mite eradication (mite density of 0), and a composite of collarette cure and grade 0 erythema. A one-sided Fisher's exact test with an α of 0.025 was used to compare the proportions between treatment groups.

Results: Collarette cure (Fig 1) was achieved in 72% of the A group and 11% of the V group at 28 days ($p < 0.001$) and 80% of the A group vs. 16% of the V group at 42 days ($p < 0.001$). Mites were eradicated in 56% of the A group and 11% of the V group at 28 days ($p = 0.006$) and in 73% of the A group and 21% of the V group at 42 days ($p = 0.003$). A composite collarette/erythema cure was achieved in 67% of the A group and 11% of the V group at 28 days ($p < 0.001$) and in 73% of the A group and 11% of the V group at 42 days ($p < 0.001$). There were no serious adverse events and no discontinuations due to adverse events. There was little to no change in mean CDVA or mean IOP in either group. In a post hoc analysis, 93% of the A group had collarette density of Grade 1 (2-10 total collarettes) or less by Day 42. Reduction in mite density by > 50% was seen in 87% of the A group by Day 14.

Conclusions: Treatment with TP-03 for 42 days is safe and shows promising efficacy for the treatment of blepharitis due to Demodex infestation.

CONTROL ID: 3542573

SUBMITTER (NAME ONLY): Cris Martin Jacoba

TITLE: Comparisons of Handheld Retinal Imaging Devices with Spectral Domain Optical Coherence Tomography (SDOCT) in the Identification of Macular Pathology

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Jacoba, A. Rageh, J.K. Sun, L.P. Aiello, P.S. Silva, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|J.K. Sun, L.P. Aiello, P.S. Silva, Harvard Medical School, Boston, Massachusetts, UNITED STATES|R. Salongcay, L. Aquino, C.G. Salva, Philippine Eye Research Institute, University of the Philippines Manila, Manila, Metro Manila, PHILIPPINES|R. Salongcay, T. Peto, Centre for Public Health, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To compare monoscopic macula centered images taken by mydriatic handheld retinal imaging with SDOCT for detection of macular pathology in diabetic patients.

Methods: Mydriatic macular images of 177 eyes of 92 diabetic patients were taken with 3 handheld retinal imaging devices [Aurora (AU), Smartscope (SS), RV700 (RV)] and compared with the Cirrus 6000 SDOCT taken during the same visit. Images were evaluated for the presence of diabetic macular edema (DME) on monoscopic fundus photographs adapted from Early Treatment Diabetic Retinopathy Study (ETDRS) definitions [no DME, noncenter-involved DME (non-ciDME) and center-involved DME (ciDME)]. Presence of DME on SDOCT used DRCR Retina Network Cirrus gender-based thresholds of central subfield thickness. Sensitivity and specificity were calculated for each device with the SDOCT as gold standard.

Results: Mean age was 56.6±10.8 years and 38% were male. Severity by ETDRS grading: No DR 40.1%, mild NPDR 19.2%, moderate 14.7%, severe 10.2%, proliferative 15.8%, ungradable for DR 0%; no DME 72.9%, non-ciDME 6.8%, ciDME 17.0%, ungradable for DME 3.4%. Gradable images by SDOCT (N=174, 98.3%) showed no DME in 84.7%, non-ciDME in 4.9%, and ciDME in 10.4%. Epiretinal membranes (ERM) were the second most common pathology, present in 11.9% of eyes. Ungradable rate for images (poor visualization in >50% of the macula), was AU:12.3%, SS:16.0%, RV:8.6%. Summary results are shown in table 1. For non-ciDME, sensitivity and specificity were similar across devices (0.71 – 0.78, 0.93 – 0.96) but sensitivity for ciDME was highest with AU(0.76). For nondiabetic macular pathology across all devices, sensitivity was highly variable (0.13 – 0.67) but highly specific (0.99 – 1.00). Sensitivity for ERM was lowest across all devices (0.13 – 0.46).

Conclusions: Compared to SDOCT, monoscopic handheld macular imaging attains high specificity but low sensitivity in identifying macular pathology. Without stereopsis, 22-29% of eyes without DME on monoscopic photos have DME on SDOCT, and 28-37% of eyes with DME on monoscopic handheld imaging will have no DME on SDOCT. Additionally 54-87% of eyes with macular ERM are missed without SDOCT imaging. This suggests the importance of SDOCT integration to improve detection of macular pathology, leading to appropriate referrals in large-scale DR screening programs.

CONTROL ID: 3542575

SUBMITTER (NAME ONLY): Maciej Oseka

TITLE: Leucocyte esterase activity in the conjunctival sac as a marker of the bacterial ocular surface inflammation.

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.K. Oseka, Oftalabs Sp. z o.o., POLAND|P. Maciejewicz, Department of Ophthalmology, Warszawski Uniwersytet Medyczny, Warszawa, POLAND|

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ABSTRACT BODY:

Purpose: Red eye (RE) is one of the most common ophthalmic disease induced by various factors as: bacteria, fungi, viruses or environmental conditions. The treatment of RE should be focused on an elimination of the primary cause and a reduction of symptoms. Topical antibiotics are prescribed in many cases of RE without a clear evidence on a bacterial etiology what can be a reason of an antibiotic resistance. During the inflammatory process caused by bacteria neutrophilic leucocytes are activated and release a leucocyte esterase enzyme (LE). The purpose of the study was to evaluate an activity of LE in the conjunctival sac of patients with acute RE.

Methods: The study was performed on 17 eyes of patients with subjective (itching, tearing, foreign body sensation, discharge) and objective (conjunctival redness and edema, discharge color, eyelid edema) symptoms of the acute RE. The discharge was collected from the lower conjunctival sac by a sterile swab and used for an assessment of LE activity and bacteria identification in microbiological cultures. LE activity was measured in a color chemical reaction with pyrrole amino acid ester and diazonium salt. An intensity of the pink-purple color of the reaction was divided into six grades (0 – lack of any color, 1 – light pink, 5 - dark purple).

Results: The activity of LE was the highest (grade 4-5) in 3 eyes and it correlated with the presence of the purulent discharge. Staphylococcus aureus was found in 2 of those eyes. There were not purulent discharges and any bacteria in 11 eyes with grade 0-1 of LE activity. There were 3 eyes with grade 3 of LE activity and without purulent discharge. Staphylococcus aureus was identified in 1 eye and Staphylococcus epidermidis in 2 eyes.

Conclusions: LE can be a useful marker for the identification the bacterial cause of ocular surface inflammations. LE activity measurement seems to be a quicker, easier and more precise diagnostic method in RE than bacterial culture. It can help to choose a proper treatment and reduce the usage of topical antibiotics in non-bacterial RE.

CONTROL ID: 3542576

SUBMITTER (NAME ONLY): Ava Bittner

TITLE: Practice Patterns and Visual Improvements following Optometric Vision Rehabilitation Services at an Ophthalmologic Medical Center

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Bittner, J. Kageyama, M. Chun, Ophthalmology; Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ava Bittner: Commercial Relationship: Code N (No Commercial Relationship) | Jennie Kageyama: Commercial Relationship: Code N (No Commercial Relationship) | Melissa Chun: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A previous records review at a low vision rehabilitation (LVR) service in a department of ophthalmology revealed a relatively low rate of improvement in distance visual acuity (VA) by ≥ 2 lines with refraction for 11% of low vision (LV) patients, and did not consider improvements at near or LV assistive devices. We hypothesized that this published data may underestimate the potential benefits of LVR.

Methods: A retrospective review of electronic health records was conducted for 230 patients seen by three optometrists at the UCLA Vision Rehabilitation Center within the past six years with best-corrected VA ≥ 0.18 logMAR in the better eye at baseline. Presenting mean VA was 0.69 logMAR, half were female, and mean age was 69 years (range 5-98), 24% had congenital or retinal dystrophy, while 42% had age-related macular degeneration.

Results: To improve distance and/or near vision, a new spectacle prescription and/or LV devices were recommended for the vast majority (92%). LV devices were recommended to 61% of all patients: 43% were for near tasks and 18% were telescopic devices for distance; 54% of these devices were dispensed. For the 90% in whom refraction was completed, VA improved in either eye by ≥ 2 lines at distance for 24%, or at distance and/or near for 43%. Odds of post-refraction distance VA improvement by ≥ 2 lines was not significantly related to age, gender, whether they had any habitual correction or previous LVR exam, but was significantly more likely for those with worse presenting distance VA (OR: 2.6; 95% CI: 1.2-5.8; $p=0.02$). VA improved with refraction by ≥ 1 line at distance for 53%, or at distance and/or near VA in 67%. Nearly half (47%) had mild VA loss (0.18-0.54 logMAR), of whom 40% were prescribed a high add $\geq +4D$ for near, 48% were recommended LV devices, and 63% were recommended high adds and/or LV devices. There was a significant increase in the chief complaint of reading digital devices: 6% pre-pandemic ($n=3$ of 50) vs. 30% during the pandemic ($n=15$ of 50) ($p=0.002$).

Conclusions: To help increase referrals for LVR, it is important to promote the success rate for LVR services, which was greater in the present study than reported in the literature. Mild VA loss patients were also recommended LV strategies. Future studies should be conducted at other centers to determine whether these findings are similar to outcomes for other LVR practitioners.

CONTROL ID: 3542582

SUBMITTER (NAME ONLY): Lucas Rowe

TITLE: Choriocapillaris Vascular Flow Area as a Biomarker of Diabetic Retinopathy Severity

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.W. Rowe, M. Scheive, K. Reinhart, A.R. Hajrasouliha, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lucas Rowe: Commercial Relationship: Code N (No Commercial Relationship) | Melanie Scheive: Commercial Relationship: Code N (No Commercial Relationship) | Kathryn Reinhart: Commercial Relationship: Code N (No Commercial Relationship) | Amir Hajrasouliha: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCT-A) offers the opportunity to safely and routinely image the choriocapillaris (CC), which is unable to be visualized by the established technique of fluorescein angiography. We performed a retrospective cohort study to compare the CC vascular flow area between diabetic patients with differing degrees of clinical diabetic retinopathy (DR) severity. We hypothesize that blood flow area in the CC can be used as a biomarker to correlate with clinical severity of DR.

Methods: This retrospective cohort study analyzed the measured flow area of the CC on quality OCT-A scans in non-diabetic control patients (n=206), diabetic patients without retinopathy (n=47), and diabetic patients with mild non-proliferative DR (NPDR) (n=40), moderate to severe NPDR (n=144), and proliferative DR (PDR) (n=81). A two-sample t-test was completed to compare CC flow area between control patients and diabetic patients with at least one quality OCT-A scan. A multivariate linear regression analysis was performed to compare CC flow area to clinical DR diagnosis when controlling for age, gender, and visual acuity in patients with at least one quality OCT-A scan.

Results: There was found to be a statistically significant decreased CC flow area ($p<0.05$) in diabetic patients compared to patients without diabetes. In comparison to diabetic patients without retinopathy, mild NPDR patients revealed an insignificantly increased CC flow area of 0.253 ($p=0.53$), while moderate to severe NPDR patients revealed a significantly decreased CC flow area of 0.691 ($p=0.04$) and PDR patients revealed a significantly decreased CC flow area of 1.11 ($p<0.01$).

Conclusions: CC vascular flow area, as measured by OCT-A, shows promise for the diagnosis and monitoring of DR as a biomarker of clinical disease severity. Future studies investigating longitudinal CC blood flow changes after anti-VEGF injections may be helpful in better understanding the treatment's effects.

CONTROL ID: 3542584

SUBMITTER (NAME ONLY): Chung Shen Chean

TITLE: Aqueous misdirection syndrome masking as myopic surprise: a case report and review of literature

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Chean, D. Gabadage, S. Mukherji, Ophthalmology, Northampton General Hospital, Northampton, Northamptonshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Aqueous misdirection syndrome, also known as malignant glaucoma, is a rare but serious condition that can present after routine uncomplicated phacoemulsification procedure. Clinical presentations can be subtle and its fluctuating and recurrent nature makes diagnosis difficult. Its pathophysiology is not fully understood, posing therapeutic challenge. We report a case of aqueous misdirection-like presentation in a pseudophakic patient.

Methods: Case report

Results: A 68-year-old Caucasian woman with previous narrow anterior chamber (AC) angle treated with bilateral peripheral iridotomies on Brinzolamide eye drops presented with symptoms of anisometropia and a left eye (LE) myopic surprise a few months after an uncomplicated LE phacoemulsification procedure. Repeat biometry did not show shallow AC and intraocular pressure (IOP) was normal at initial presentation. However, 2 years and 7 months after the operation, IOP was raised. Topical cycloplegic and anti-glaucoma medications relieved signs and symptoms, but effect was temporary with fluctuating IOP. Nd: YAG laser capsulotomy with subsequent cyclodiode laser were performed with good effect on IOP control.

Conclusions: Clinical presentation of aqueous misdirection syndrome may be subtle and can occur weeks to years after routine uncomplicated phacoemulsification surgery. Short axial lengths, hypermetropia, female gender and shallow anterior chamber depths (ACD) are known risk factors. Myopic surprise may be the only initial presenting sign, and measurements of ACD, IOP and gonioscopic examination are essential when clinicians are suspecting aqueous misdirection syndrome on patients who has had recent uneventful cataract surgery.

CONTROL ID: 3542588

SUBMITTER (NAME ONLY): OLIVIA KILLEEN

TITLE: Retrospective Analysis of Demographic and Clinical Data from a School-Based Eye Clinic in Southeastern Michigan

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. KILLEEN, C. Dewey, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure (Abstract): OLIVIA KILLEEN: Commercial Relationship: Code N (No Commercial Relationship) | Courtney Dewey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Limited data exists on the role of school-based eye clinics. An optometrist from the University of Michigan (UM) holds a biweekly clinic at Ypsilanti Community High School. We performed a retrospective analysis of clinical and demographic data to describe the population and design interventions to improve care.

Methods: Students presenting to clinic received comprehensive eye exams. We collected demographic and ocular data from initial visits 2/2015-7/2019. Follow up visits were excluded. Statistical analysis was performed using SAS 9.4. The UM IRB approved the study.

Results: 429 patients visited during this period. Average age was 14.2 ± 2.7 years. 55.7% were female, 59.7% Black, 17.9% White, and 10.9% Hispanic. 61.7% had Medicaid, 23.6% had private health insurance, and 14.8% were uninsured. 69.0% had a previous eye exam; there was no relationship between insurance and prior exam ($P=0.41$). Medical eye concerns included 4.2% with elevated intraocular pressure, 8.7% with amblyopia, and 0.23% with a cataract. For refractive error, 56.0% had myopia and 31.9% had hyperopia. 52.9% had presenting visual acuity (PVA) worse than 20/40 in both eyes and 15.0% had PVA 20/100 or worse in at least one eye. 58.4% had improvement in best corrected visual acuity (BCVA) of 2 or more lines; 62.7% of Black patients had 2 or more line improvement compared to 42.9% of White patients ($P=0.013$). There was no difference in BCVA improvement by insurance ($P=0.22$). 60.8% wore glasses previously; 24.1% were still wearing glasses. 56.9% of former glasses wearers reported glasses were lost or broken. There was no difference in glasses wear by insurance ($P=0.078$) or race ($P=0.10$). There was no difference in rates of myopia ($P=0.28$) or hyperopia ($P=0.052$) by race. 21 students were referred to UM for further care; 13 (61.9%) attended the appointment, 3 (14.3%) scheduled but did not attend, and 5 (23.8%) never scheduled.

Conclusions: The school-based clinic identified important pathology. Over half wore glasses previously, but less than a quarter still wore glasses. Glasses wear was not correlated to race or insurance, suggesting barriers to glasses beyond access to care. Many students referred for further care did not attend; barriers to follow up must be addressed.

CONTROL ID: 3542592

SUBMITTER (NAME ONLY): Yanxiu Li

TITLE: Comprehensive retinal safety evaluation of photoacoustic microscopy in rabbits

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, V. Nguyen, N. Khan, Y.M. Paulus, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|Y. Li, X. Xia, Eye Center of Xiangya Hospital, Central South University, Changsha, Hunan, CHINA|W. Zhang, X. Wang, Y.M. Paulus, Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether photoacoustic microscopy (PAM) retinal imaging is safe and whether PAM causes damage to retinal structure or function in rabbit eyes.

Methods: 12 pigmented rabbit eyes received 5 consecutive days of PAM imaging with 5% of the ANSI limit laser energy to achieve high quality PAM imaging of more than 50% of the retinal surface area. One rabbit used for positive control by using 500% of the ANSI limit laser energy. Retinal morphology was examined by ophthalmic examination, fundus photography, red-free photography, fundus autofluorescence (FAF), fluorescein angiography (FA), indocyanine green angiography (ICGA), and optical coherence tomography (OCT). Retinal function was assessed by full field electroretinography (ff-ERGs). Retinal structure was evaluated by histopathology and transmission electron microscopy (TEM). Retinal cells apoptosis was examined by TUNEL assay. Evaluation was performed at 3 days, 1, 2, 3, and 4 weeks post PAM imaging.

Results: Retinal morphologic analyses showed no retinal hemorrhage, edema, detachment, vascular, or pigmentary abnormalities in the retina or choroid after PAM imaging. ff-ERG showed no significant difference in scotopic or photopic a- and b-wave amplitudes or implicit times between the control and experimental eyes. Retinal ultrastructural evaluation using TEM showed normal cellular structure after PAM. TUNEL assay showed no evidence of cells undergoing apoptosis. Retinal histopathology indicated that the architecture and thickness of the retinal layers was well preserved in all experimental eyes. The positive control at 500% of the ANSI limit demonstrated significant damage.

Conclusions: A comprehensive retinal safety evaluation demonstrates no damage to retinal structure or function for 4 weeks after retinal PAM imaging.

CONTROL ID: 3542594

SUBMITTER (NAME ONLY): Amrita Saha

TITLE: High mobility group box 1 mediated crosstalk between infected corneal epithelial cells and stromal keratocytes

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Saha, A. Ismail, X. Zhou, J. Chodosh, J. Rajaiya, Department of Ophthalmology, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular surface infection by viruses within human adenovirus species D (HAdV-D) causes epidemic keratoconjunctivitis (EKC). Subepithelial infiltrate (SEI) formation in the cornea is the most significant long-term complication of EKC, and presents in about one-third of cases. However, the mechanism of SEI formation after adenoviral infection of the cornea remains uncertain. High-mobility group box protein 1 (HMGB1) is an endogenous danger signal molecule and chemokine that variably regulates inflammatory responses. Although HMGB1 has been implicated previously in viral infections, and may play a role in bacterial keratitis, its role in EKC has not been studied.

Methods: hTERT-immortalized human corneal epithelial (THE) cells and primary human corneal fibroblasts (HCFs) were infected with HAdV-D37 or HAdV-C5 at MOI = 5, and cell supernatants were collected through 48 hours post infection. Mass spectrometry (LC-MS/MS) analysis was performed on infected human corneal cells. Immunoblotting was performed on infected cell supernatants, and on cytoplasmic and nuclear cellular fractions, using acetylated HMGB1 antibody. ELISA for secreted HMGB1 was conducted on cell-free supernatants, and HMGB1 gene expression was studied using real-time qPCR. Confocal microscopy was performed to visualize HMGB1 translocation. Cytokine expression by HCFs treated with rHMGB1 was analyzed using human cytokine protein arrays.

Results: HAdV-D37 infection resulted in HMGB1 translocation from the nucleus to the cytoplasm and then to the extracellular space in THE cells, but not in HCFs. HAdV-C5, a virus not associated with EKC, did not induce secretion of HMGB1 from either cell type. Finally, recombinant active HMGB1 treatment of HCFs triggered expression of pro-inflammatory mediators.

Conclusions: This study provides insights into possible mechanism of corneal SEI formation in EKC. Our results suggest that HMGB1 expressed by adenovirus infected corneal epithelial cells could induce underlying stromal cells to express pro-inflammatory mediators, leading indirectly to the development of SEI. HMGB1 may be a viable therapeutic target for preventing the corneal stromal complications of EKC.

CONTROL ID: 3542595

SUBMITTER (NAME ONLY): Kenzo Tomishige

TITLE: Comparison of depressive symptoms between age-related macular degeneration and glaucoma patients who live in a developing country.

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.S. Tomishige, C.S. Germano, P.A. Ottaiano, R.M. Maccione, N. Kasahara, Oftalmologia, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Depression is a serious and often under diagnosed medical condition in older people. Visual impairment increases the risk of depression to almost two-fold and it is prevalent in both glaucoma and age-related macular degeneration (AMD) patients. This topic has not been extensively studied in patients with eye diseases especially in low-middle income countries. The purpose of this cross-sectional, case-control study was to compare depressive symptoms between primary open-angle glaucoma (POAG) and AMD Brazilian patients.

Methods: Patients with AMD, POAG, and normal controls underwent a complete eye examination including measurement of best-corrected visual acuity, biomicroscopy, tonometry, eye fundus evaluation, and all participants answered the Portuguese short version of the Geriatric Depression Scale (GDS-15). This is a 15-item questionnaire with binary answer (yes or no) and a cut-off value of 6/7 has an optimal balance between sensitivity and specificity. The summed score was compared among the three groups with the ANOVA test.

Results: The sample comprised 48 patients with AMD, 56 with POAG, and 53 controls. All groups were matched for age, gender, ethnic distribution, and comorbidities. The mean score for AMD, POAG, and controls were 3.7 ± 2.9 , 4.3 ± 2.8 , and 2.4 ± 1.7 , respectively ($P = 0.006$). More AMD patients (28.5%) presented scores >5 as compared to 25% of POAG patients, and only 3.3% of controls ($P = 0.07$).

Conclusions: AMD and POAG patients are at higher risk for depression. This poses a challenge to Brazilian healthcare authorities and strategies to help patients maintain independence and good quality of life should target depression.

CONTROL ID: 3542597

SUBMITTER (NAME ONLY): Tal Carmy-Bennun

TITLE: Use of quantitative proteomic analysis to identify potential mechanisms of neuroprotection from myeloid differentiation factor 88 (MyD88) inhibition in the retinal degeneration (rd) 10 mouse

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Carmy-Bennun, C. Myer, S.K. Bhattacharya, A. Hackam, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: MyD88 mediates inflammatory signaling in the retina. MyD88 inhibition delayed rod photoreceptor death in two mouse models of retinal degeneration. In this study, we performed quantitative proteomic analysis using liquid chromatography-tandem mass spectrometry iTRAQ to characterize early protein changes that may contribute to the protective effects of inhibiting MyD88 in rd10 mouse retinas.

Methods: Rd10 mice (male and female, PN day 18) were injected IP with 2 mg/Kg MyD88 inhibitor (neuroprotective dose) or control peptide (n=4 each). Retinas were collected 3 days later, proteins were extracted then trypsin digested, and incubated with 8-PLEX iTRAQ Reagents followed by analysis using Q Exactive mass spectrometer. Proteins were identified and quantified using Proteome Discoverer 2.2 software, bioinformatics enrichment analysis used PANTHER v.15.0 and interaction networks used the STRING database v.11. QPCR was used to confirm gene expression.

Results: A total of 332 proteins were identified with high (FDR<0.01) and medium confidence (FDR<0.05) with >2 unique matching peptides. Forty-two proteins were differentially expressed (fold change >1.2 or <0.83; p<0.05): 20 proteins were upregulated in the MyD88 inhibitor group and 22 were downregulated. The top biological processes were metabolic, developmental and regulation, and the top molecular functions were catalytic activity, binding and structural molecules. The upregulated proteins were enriched in crystallins, unfolded protein binding and structural molecular activity, and decreased proteins were enriched in pyrophosphatase activity, small molecule binding, and peptide biosynthesis. Notably, MyD88 inhibition led to upregulation of 7 stress-response crystallins. STRING analysis on the upregulated proteins showed 3 distinct physical interaction networks (p=1.94e-05): crystallins, cytosolic small ribosome subunit and aminopeptidase activity. Retinal expression of the crystallin genes was confirmed by QPCR.

Conclusions: This study provides a foundation for understanding molecular mechanisms regulating retinal homeostasis in rd10 mice. A novel link was identified between anti-apoptotic crystallins and MyD88 inflammatory pathway inhibition.

CONTROL ID: 3542599

SUBMITTER (NAME ONLY): Issahy Cano

TITLE: Galectin-3 requires VEGF to activate VEGF receptor 2 in retinal endothelial cells

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Cano, Z. Hu, D. Abusamra, M. Saint-Geniez, Y. Ng, P. Argueso, P.A. D'Amore, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Z. Hu, D. Abusamra, M. Saint-Geniez, Y. Ng, P. Argueso, P.A. D'Amore, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Galectin-3 is a carbohydrate-binding protein that modulates vascular endothelial growth factor receptor 2 (VEGFR2) signal transduction, but the molecular mechanism of Gal3 in VEGF/VEGFR2 signal transduction has not been fully elucidated. To better define the role of VEGF in Gal3-induced VEGFR2 signaling, we determined whether exogenous Gal3 requires VEGF to activate VEGFR2 signaling and if exogenous VEGF requires any Gal3 to activate VEGFR2.

Methods: To examine the interaction between Gal3 and VEGFR2, Gal3 was conjugated to cyanogen beads and used for immunoprecipitation (IP). VEGFR2 activation was inhibited using the small molecule VEGFR2- selective tyrosine kinase inhibitor, sunitinib malate (10 μ M). Semi-quantitative PCR was used to measure the expression levels of E-selectin and VCAM-1 mRNA, genes that are downstream of VEGFR2. The knockdown of Gal3 was achieved in human retinal microvascular endothelial cells (HRECs) using siGal3, with nontargeting siRNA as a control. HREC surface proteins were labeled with NHS-SS-biotin and isolated using avidin beads. VEGF neutralization was attained with ranibizumab (10 μ g/ml). The ability of exogenous Gal3 (50 μ g/ml) to activate VEGFR2 kinase was measured at 0, 5, 10, 30, and 60 min after addition. Levels of total and phosphorylated VEGFR2 (Y1175), CD31, and tubulin were examined using western blot. HREC migration was determined using a wound-healing assay, in which confluent HRECs were mechanically scratched and cell migration was measured 15 hours after the addition of VEGF (10 ng/ml) or Gal3 (50 μ g/ml).

Results: VEGFR2 was IP-ed with Gal3. Exogenous Gal3 induced an increase in E- selectin (0.99 ± 0.07 vs 15.3 ± 1.2 , $p < 0.004$. N=3) and VCAM-1 (1 ± 0.03 vs 3.4 ± 0.3 , $p < 0.02$. N=3) expression compared to the control. Inhibition of VEGFR2 activation by sunitinib significantly reduced exogenous Gal3-induction of E-selectin (91%, $p < 0.001$. N=3) and VCAM-1 (67%, $p < 0.02$. N=3). Gal3 was knockdown by over 90% (0.064 ± 0.001 vs 1 ± 0.14 , $p < 0.05$. N=3). Loss of endogenous Gal3 did not alter VEGF-induced VEGFR2 internalization or migration in HRECs. Neutralization of VEGF significantly inhibited the migration of exogenous Gal3-induced HREC migration compared to the control (1.17 ± 0.059 vs 0.97 ± 0.066 , $p < 0.05$. N=6).

Conclusions: Any VEGF is necessary for Gal3 induced kinase activation and HREC migration but endogenous Gal3 is not sufficient for VEGF/VEGFR2 signal transduction.

CONTROL ID: 3542607

SUBMITTER (NAME ONLY): Mahmoud KhalafAllah

TITLE: Longitudinal positional changes of anterior scleral canal opening versus Bruch's membrane opening during high myopia development in juvenile tree shrews

SESSION TITLE: Role of choroid and sclera in myopia development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.T. KhalafAllah, Vision Science Graduate Program, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|P. Fuchs, F. Nugen, M. El Hamdaoui, B.C. Samuels, R. Grytz, Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|A. Levy, Department of Biomedical Engineering, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate positional changes of the Bruch's membrane opening (BMO) relative to the anterior scleral canal opening (ASCO) during high myopia development in juvenile tree shrews.

Methods: Juvenile tree shrews were randomly assigned to two groups: normal visual experience (n=9) and monocular -10D lens treatment to induce high myopia, where the other eye served as a control (n=12). Lens treatment started at 24 days of visual experience (DVE). Refractive (Nidek ARK-700A, Marco Ophthalmic) and biometric (Lenstar LS-900, Haag-Streit) measurements were obtained daily. Optical coherence tomography (OCT) of optic nerve head (ONH) (Spectralis, Heidelberg Engineering) was performed weekly. BMO and ASCO were manually segmented and analyzed after nonlinear distortion correction (Grytz R, et al. IOVS 2020; 61: ARVO E-Abstract 4778) of each OCT scan.

Results: Offset between ASCO/BMO centroids gradually increased during axial elongation and high myopia development in the lens treated eyes. These positional changes were significantly different from control and normal eyes at 59 DVE (two-sided Wilcoxon rank sum test; $0.05 \pm 1.9\mu\text{m}$, $-0.05 \pm 1.4\mu\text{m}$ and $3.46 \pm 3.5\mu\text{m}$, mean \pm SEM in normal, control and myopic eyes respectively; $p < 0.05$). Largest changes in ASCO/BMO centroid offset occurred in myopic eyes towards the inferior-nasal quadrant with BMO points located outside the ASCO boundary. BMO/ASCO areas and ovality indices were not significantly different among the three groups.

Conclusions: Our results show relative deformations of BMO and ASCO that gradually increase during high myopia development in juvenile tree shrews. These morphological changes during juvenile myopia development may contribute to subsequent ONH remodeling and increased risk of glaucoma later in life.

CONTROL ID: 3542608

SUBMITTER (NAME ONLY): Lisa Hernandez-Denlinger

TITLE: Developing Methotrexate-Induced Immune Tolerance in a Rabbit Model of Persistent Retinal Vascular Leak

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Hernandez-Denlinger, M. Mason, M. Tian, L. Andrews-Jones, M. Shah, K.A. Luhrs, G. Rodrigues, L. Christie, Research, Non-Clinical and Translational Sciences, AbbVie Inc, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Preclinical testing of biologics is complicated by immunogenicity, which differs from immunogenicity in humans. It is necessary to mitigate immunogenic responses in order to effectively test the pharmacodynamics and pharmacokinetics of novel biologics, especially for repeat administration. The persistent retinal vascular leak (PRVL) rabbit model is a valuable tool for testing intravitreal (IVT) therapies; however, rabbits frequently mount a strong anti-drug antibody (ADA) response. We developed an antigen-independent immune tolerance protocol to 1) reduce ocular inflammation, and 2) reduce systemic production of ADAs while maintaining the model's vascular phenotype.

Methods: DI- α -amino adipic acid was administered IVT in rabbit eyes to induce the PRVL model (Rodrigues et al., 2018, IOVS). Daily administration of methotrexate (MTX; 30mg/kg s.c.; N=10) or PBS (N=10) was initiated 3 days prior to IVT challenge with a biologic and continued for 21 days. Ocular examinations, fundus angiography, and blood collections were conducted from weeks 2 through 12 to evaluate the effect of MTX on systemic ADA levels and incidence of ocular inflammation. Eyes were enucleated and fixed for histopathological assessment.

Results: The MTX dosing regimen was well tolerated. Incidence of moderate-severe ocular inflammation was eliminated in MTX-treated rabbits, which coincided with significantly reduced systemic ADA titer levels compared to PBS-treated controls. Histologic evaluation determined that 4/10 eyes of PBS-treated rabbits showed substantial lymphoplasmacytic infiltrate following IVT administration of the biologic while eyes of MTX-treated rabbits did not.

Conclusions: The reduction of systemic ADAs in the MTX group demonstrates that induction of immune tolerance in the PRVL rabbit model is feasible. A coinciding decrease in incidence of gross ocular inflammation was observed in vivo, and histologic results confirmed that MTX treatment eliminated infiltrate signatures typically associated with activation of adaptive immunity. This immune tolerance protocol can be used in future studies to reduce ocular inflammation, minimize study attrition, and increase confidence in drug exposure levels.

CONTROL ID: 3542610

SUBMITTER (NAME ONLY): Jae Lee

TITLE: Longitudinal changes in optical coherence tomography angiography (OCTA) parameters versus retinal nerve fiber layer (RNFL) in glaucomatous and non-glaucomatous eyes

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, B. Burkemper, A. Jain, V. LeTran, B.J. Song, B. Wong, B. Xu, G.M. Richter, USC Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|X. Zhou, Z. Chu, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study explores the longitudinal rates of change between peripapillary optical coherence tomography angiography (OCTA) parameters and retinal nerve fiber layer thickness (RNFL) of glaucomatous and non-glaucomatous eyes.

Methods: A retrospective, longitudinal study collected 6x6mm optic disc OCTA scans (Cirrus HD-OCT 5000) of glaucomatous and non-glaucomatous eyes with at least 2 visits between 12 to 24 months apart. Non-glaucomatous eyes included healthy and glaucoma suspects from an academic glaucoma clinic. A commercially provided automatic segmentation software was used to create en face OCTA images of the radial peripapillary capillary (RPC) layer. Images with poor quality, segmentation error or motion artifacts were excluded. Furthermore, subjects with non-glaucomatous optic neuropathy, cystoid macular edema, diabetic retinopathy, and other retinal disease were excluded. Images were quantified using a research-oriented quantification software to measure OCTA parameters: vessel area density (VAD), vessel skeleton density (VSD), and flux; a commercial quantification software measured perfusion density (PD) and flux index (FI). RNFL scans (Cirrus HD-OCT 5000) were also collected. The rates of change of OCTA parameters and RNFL were estimated using multivariable linear mixed-effects models.

Results: RPC OCTA images from 151 eyes of 96 subjects (81 non-glaucomatous eyes and 70 glaucomatous eyes) were included. RNFL OCT scans from 139 eyes of 87 subjects (78 non-glaucomatous and 61 glaucomatous eyes) were included. With a mean follow-up of 16 months, there was significant reduction in all OCTA parameters for both non-glaucomatous and glaucomatous eyes (Table 1) with a trend of faster reduction in the glaucomatous group. In contrast, there was no significant change in RNFL over time for either the non-glaucomatous or glaucomatous eyes.

Conclusions: OCTA images of the RPC layer showed significant annual rates of decrease in vessel parameters in both non-glaucomatous and glaucomatous eyes followed for 12-24 months. In contrast, the rate of change in RNFL thickness of the same eyes within the same time period was not significant. OCTA may have greater clinical utility than RNFL for monitoring progression in eyes at risk for and with glaucoma.

CONTROL ID: 3542611

SUBMITTER (NAME ONLY): Atieh Yousefi Koupaei

TITLE: Characterization of droplet formation with high-speed video in noncontact tonometry

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Yousefi Koupaei, Y. Ma, C.J. Roberts, M.A. Reilly, Ophthalmology, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|C.J. Roberts, M.A. Reilly, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess tear dynamics in response to air puff deformation with two noncontact tonometers (NCTs).

Methods: The interaction between air puffs from two NCTs and the tear film were characterized using Phantom VEO 340s high-speed camera at a spatial resolution of 20 microns and a frame rate of 1500 fps. Exams were performed on right eyes of 20 healthy human volunteers with no history of dry eye or tear film instability. Each subject was examined before and after administration of one lubricant eye drop to the lower lid. 10 subjects received Ocular Response Analyzer (ORA) first followed by CorVis ST, while the rest received CorVis ST first followed by ORA. High-speed videos were further analyzed using Phantom Camera Control (PCC) software to quantify droplet size, instantaneous droplet velocity, and eyelid motion.

Results: No droplets were detected for first NCT device used (both ORA and CorVis ST). Among the 40 exams with an eye drop administered, two exams resulted in droplets with a predominant forward motion (one from each device), while 11 exams showed droplet formation where the drop had a downward trajectory and did not remain suspended in the air. All droplets were emitted from lashes whether predominantly forward or downward motion. No droplets originated from the corneal surface. The average droplet diameter among all exams with eye drop administration was $502.9 \pm 195.2 \mu\text{m}$ (range 210-970 μm). For the two exams with predominantly forward motion, two in-focus, forward-moving droplets were detected with each exam. Droplet velocities were 0.93 and 0.50 m/s for ORA and 1.72 and 1.32 m/s for CorVis ST exams.

Conclusions: As the air puff arrives at the corneal surface, the tear film is pushed radially away from the apex while remaining attached to the corneal surface (Figure 1). This behavior, explained by the Coanda effect¹, occurs due to the tendency of the tear film to follow the cornea curvature during deformation and results in droplets leaving the eye only at the eyelid boundary which interrupts tear flow. Droplet formation during NCT exams with different air puff strategies occurs only with eye drop administration, consistent with literature reports.

¹D. J. Tritton, Physical Fluid Dynamics, 2012

CONTROL ID: 3542615

SUBMITTER (NAME ONLY): Lyne Racette

TITLE: Racial disparity in the impact of the COVID-19 pandemic on adherence to ocular hypotensive medication among patients of African and European descent

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Racette, S.L. Abu, T. Thomas, C.A. Girkin, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|S. Poleon, School of Optometry, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|N. Sabbagh, Internal Medicine, The University of Alabama at Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Emerging evidence suggests that the COVID-19 pandemic, which has disproportionately affected people of African descent (AD), is disrupting health behaviors such as medication adherence. Studies have not yet assessed, however, whether medication adherence is differentially affected in people of AD, a population shown to have poorer adherence prior to the pandemic. We examined whether racial disparities exist in the impact of the COVID-19 pandemic on medication adherence in people of AD and European descent (ED).

Methods: We used a controlled interrupted time series design in which the interruption was the declaration of the COVID-19 pandemic in the United States on March 13, 2020. The 300-day follow-up period, which bracketed this declaration, started on October 16, 2019 and ended on August 10, 2020. Patients were selected from an ongoing longitudinal NIH-funded study initiated prior to the onset of the pandemic, if they had primary open-angle glaucoma, were prescribed ocular hypotensive medication and had adherence data spanning the 300 days of the study. The primary outcome was daily adherence defined as the number of doses taken divided by the number of doses prescribed, expressed as a percentage. Adherence was measured objectively using Medication Event Monitoring System (MEMS). Segmented regression analysis using the "slope change following a lag" impact model was performed and the Davies test was used to compare the slopes in the periods preceding and following the pandemic.

Results: 72 patients (35 of AD and 37 of ED) were included. Prior to the pandemic, mean adherence was $75 \pm 25\%$ in patients of AD and $91 \pm 15\%$ in people of ED ($p = 0.001$). In patients of AD, the slopes in the periods preceding (0.0% / day) and following (-0.07% / day) the pandemic were significantly different ($p < 0.001$). In patients of ED, the slopes in the periods preceding (0.01% / day) and following (-0.02% / day) the pandemic were similar ($p = 0.05$).

Conclusions: Medication adherence, a health behavior critical in the management of chronic diseases, was adversely affected by the COVID-19 pandemic in patients of African descent with glaucoma. The vulnerabilities exposed by the COVID-19 pandemic should be used to inform the development of interventions that will ensure continued use of medication during crisis periods, particularly in high-risk populations.

CONTROL ID: 3542618

SUBMITTER (NAME ONLY): Joanne Li

TITLE: Visualization of the human retinal pigment epithelial cell mosaic with and without adaptive optics using late phase indocyanine green imaging

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Li, T. Liu, J. Liu, A.J. Bower, J. Giannini, R. Lu, N. Aguilera, J. Tam, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: There are now a number of adaptive optics (AO) based approaches for assessing retinal pigment epithelial (RPE) cells in the living human eye. However, AO instruments are not yet widely accessible. Since the size of RPE cells is near the resolution capabilities of commercial instruments, we explore in this study whether RPE cells labeled using indocyanine green (ICG) can be visualized without AO.

Methods: Following intravenous injection of ICG dye, the RPE cells are labeled and can be imaged in the late phase (IOVS 57(10):4376-4384, 2016). ICG images of the RPE were acquired in 10 eyes from 10 healthy subjects using a custom-built AO instrument (AO-ICG) and a Heidelberg Spectralis with a 30° lens (Spectralis30). For 6 of the eyes, additional ICG images were obtained using a Heidelberg Spectralis outfitted with a high magnification module (HMM) 8° lens. The appearance of RPE cells was validated through direct comparison between images taken with and without AO in matching retinal locations within each eye. Both AO and non-AO images were analyzed using custom software to identify RPE cells from which cell density and spacing values were calculated.

Results: Across all three types of images (AO, Spectralis30, HMM), a heterogeneous pattern corresponding to RPE cells could be observed with sufficient contrast and resolution to identify RPE cells. The patterns observed in non-AO images matched those observed in AO images acquired at identical retinal locations (correlation coefficient: 0.7 ± 0.1). Although AO images had the highest contrast and resolution, followed by HMM, and then Spectralis30, there were no statistically significant differences between RPE cell measurements obtained with and without AO (AO vs. HMM, AO vs. Spectralis30, and HMM vs. Spectralis30; $p > 0.5$ for all comparisons; Kruskal-Wallis with Tukey's honest significance multiple comparison test). Measurements of cell density and spacing, obtained over a range of eccentricities out to 5.5 mm, were consistent with published normative data (BOE 8(10):4348-4360, 2017).

Conclusions: The heterogeneous late phase ICG pattern, which has previously been shown to enable RPE cell measurements from AO images, can also be observed without AO. This technique opens up the possibility of assessing and quantifying the RPE cell mosaic at the cellular level using conventional clinical imaging, even without AO.

CONTROL ID: 3542619

SUBMITTER (NAME ONLY): Hongli Yang

TITLE: Diagnostic accuracy of inner retinal layer thickness and reflectance intensity measurements assessed in posterior pole OCT scans of healthy and glaucomatous eyes

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine whether quantifying reflectance intensity in addition to layer thickness improves the ability to discriminate glaucomatous (GL) from healthy control (HC) eyes.

Methods: Posterior pole OCT scans (Spectralis, Heidelberg Engineering GmbH) were obtained in 188 GL and 360 HC eyes (61 B-scans, 768 A-lines each, spanning a 30°× 25° area). GL eyes were defined as having 24-2 visual field (VF) pattern standard deviation or glaucoma hemifield test outside normal limits on 2 consecutive tests. Automated segmentations within each B-scan were manually corrected when necessary. Mean thickness and intensity values for each A-line were measured for nerve fiber layer (NFL), ganglion cell layer (GCL), and inner plexiform layer (IPL). These intensity values were also normalized using the average value of the 7-pixels corresponding to the retinal pigmented epithelial (RPE) layer to generate axially (vertically) normalized (AN) intensity. Values were age-adjusted using the HC eyes. The average thickness, intensity and AN intensity values were calculated and used to create receiver operating characteristic (ROC) curves. Logistic regression models were used to assess whether intensity added additional diagnostic power.

Results: The median VF mean deviation in the GL eyes was -4.37 dB. The highest univariate areas under the ROC curve (AUROC) were for NFL thickness (NFLT: 0.916) and intensity (0.903, Table 1). The AUROC for GCL thickness (GCLT) was significantly smaller (0.882) than for NFLT ($p=0.04$), comparable to NFL intensity ($p=0.24$), but higher than all other parameters (all $p<0.001$). NFL intensity ($p<0.001$), NFLT ($p<0.001$) and GCLT ($p=0.01$) were significant predictors of the probability of having glaucoma. Addition of NFL intensity to thickness significantly improved this prediction ($p<0.001$). A model also including GCLT had higher AUROC (0.958) than any other combination (all $p < 0.02$, Figure 1).

Conclusions: In this group of mostly early GL eyes, the best diagnostic predictors were NFLT, NFL intensity, and GCLT. Current axial normalization of intensity values to RPE reflectance did not enhance diagnostic accuracy. Macular NFL reflectance intensity provides diagnostic information beyond thickness values alone and may have pathophysiological significance.

CONTROL ID: 3542620

SUBMITTER (NAME ONLY): Leo Thomas

TITLE: In vitro and in vivo studies of BI-X: A humanised Sema3A antibody

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Thomas, N. Zippel, H. Wu, M. Garneau, R. Bakker, Boehringer Ingelheim Pharma GmbH & Co. KG, GERMANY|C. Hess Kenny, Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: BI-X is an intravitreal anti-semaphorin 3A (Sema3A) agent under investigation in patients with laser-treated proliferative diabetic retinopathy and diabetic macular ischemia. We tested 4 hypotheses: H1) BI-X specifically binds to human Sema3A in an antibody-capture assay; in human retinal microvascular endothelial cell (HRMEC) assays, BI-X H2) prevents Sema3A- but not vascular endothelial growth factor-A (VEGF-A)-induced endothelial cell permeability and H3) prevents Sema3A-induced cytoskeletal collapse; H4) BI-X reduces ischemic avascular area and increases tip cell density in a mouse model of oxygen-induced retinopathy (OIR).

Methods: H1) Recombinant human, cynomolgus, mouse, rat and rabbit Sema3A were injected (40 µL/min for 600 s) over captured BI-X (0.5 µg/mL) and allowed to dissociate for 7200 s. H2) HRMECs were treated with either recombinant VEGF-A (100 ng/mL) or Sema3A (500 ng/mL), with and without BI-X (1 µg/mL) or anti-TNP (1 µg/mL) overnight. Permeability was determined based on the passage of FITC-coupled dextran through the endothelial cell layer. H3) Potency was determined with a concentration–response curve of recombinant human Sema3A. Cytoskeletal collapse was measured as reduction of cellular impedance. For specificity determination, HRMECs were stimulated with 0.5 µg/mL recombinant human Sema3A, 3C or 3E or 2 µg/mL recombinant mouse Sema3B or 3F with and without 2 µg/mL BI-X. H4) Newborn mice (n=23) were exposed to a 75% oxygen atmosphere from P7 to P12 and then returned to normoxia. The animals received a single 10 µg intravitreal injection of either BI-X or an IgG control antibody in each eye at P12. Tip cell density and avascular area were determined using retinal flatmounts prepared from eyes enucleated at P17.

Results: H1) BI-X binds to human, cynomolgus, mouse, rat and rabbit Sema3A with a K_D of 29 pM, 28 pM, 27 pM, 27 pM and 42 pM, respectively. H2) BI-X completely prevented the permeability induced by Sema3A, but not VEGF-A. H3) BI-X prevented cytoskeletal collapse induced by Sema3A (potency: 69 pM), but not Sema3B, 3C, 3E or 3F. H4) Tip cell density increased by 33% ($p<0.001$) and avascular area numerically decreased by 12% in BI-X-treated eyes compared with IgG control.

Conclusions: BI-X binds to human Sema3A with pM affinity, and specifically inhibits Sema3A function, preventing cytoskeletal collapse and endothelial cell permeability in vitro. BI-X also improved ischemia in a mouse model of OIR.

CONTROL ID: 3542623

SUBMITTER (NAME ONLY): Jillian Ziemanski

TITLE: Immortalized human conjunctival epithelial cells produce functional complement C3 and C4 proteins

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.F. Ziemanski, K.K. Nichols, Department of Optometry and Vision Science, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|A.J. Szalai, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: The complement cascade, best known for its role in host defense, has been shown to be strongly activated by immune complexes in many autoimmune diseases, suggesting that it may contribute to autoimmune dry eye disease (DED) such as Sjögren's syndrome (SS). The ocular surface is known to have a functional complement system, though the exact site(s) of complement-protein production remain unknown. As part of a larger project interrogating complement's role in SS-DED, we conducted a pilot study to assess whether complement proteins C3 and C4 were produced by immortalized human conjunctival epithelial cells (HCjE).

Methods: HCjE were maintained in a 6-well plate in KSFM + 5 ng/ml EGF + 50 µg/ml BPE for 2-4 days. Cell lysates were prepared, and total protein was quantitated (Pierce BCA kit). Samples of lysate (0.625-40 µg of total protein) were loaded in duplicate into 96-well plates, and the amounts of C3 and C4 were measured by Human Complement C3 and C4 ELISA kits (Abcam). To assess C3 and C4 function, we measured formation of soluble C5b-9 (sC5b-9) from HCjE lysates treated with heat-aggregated IgG, a known activator of the classical pathway of complement (CH50 EIA, Quidel). Briefly, 86 µl of IgG were added to 90 µg of HCjE total protein. The activated sample was diluted 1:2, 1:4, and 1:8 prior to performing an enzyme immunoassay targeting sC5b-9, a marker of the activated complement cascade.

Results: Across all HCjE lysates (n=12), the total protein concentration was 982.1 ± 115.19 µg/ml (mean \pm SD). Both C3 and C4 were detected in lysates with C3 being expressed at concentrations approximately 22-fold higher than C4. C3 was quantified at 0.152 ± 0.101 ng/µg of total protein and C4 at 0.007 ± 0.005 ng/µg of total protein. Upon activation by IgG, sC5b-9 was detected at dilutions of 1:2 (6.21 ± 1.20 CH50 U Eq/ml) and 1:4 (6.11 ± 0.45 CH50 U Eq/ml) but not at 1:8.

Conclusions: HCjE produce complement C3 and C4, suggesting that these proteins may be produced locally at the ocular surface. Supplementing HCjE lysates with IgG results in formation of sC5b-9, confirming that HCjE-derived C3 and C4 are functional and suggesting that HCjE likely produce all proteins (C1 through C9) required for the formation of sC5b-9 via the classical pathway. Further research is needed to confirm these findings in primary cells and to determine complement's role in SS-DE.

CONTROL ID: 3542624

SUBMITTER (NAME ONLY): Jinli Wang

TITLE: Impaired UPR^{ER} is associated with Chronic Endoplasmic Reticulum Stress in Aging Endothelial Cells

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, J.J. Wang, S.X. Zhang, Department of Ophthalmology and Ross Eye Institute, University at Buffalo, Buffalo, New York, UNITED STATES|S.X. Zhang, Department of Biochemistry, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related endothelial dysfunction is associated with multiple eye diseases. One potential mechanism is the disturbance of the endoplasmic reticulum environment (ER stress). In healthy cells, ER stress is constantly sensed and mitigated by a sophisticated adaptive mechanism namely the unfolded protein response of the ER (UPR^{ER}). In this study, we characterize the status of ER homeostasis and the UPR^{ER} in aging endothelial cells and elucidate a potential mechanism underlying vascular aging.

Methods: Brain microvascular endothelial cells (BMECs) were isolated from mice at ages of 2-24 months. To induce ER stress, BMECs were treated with either 0.5 μ M of thapsigargin (TG) or 0.5 μ g/ml of tunicamycin (TM) for 6 hours. Expression of UPR^{ER} genes was assessed by quantitative RT-PCR (qRT-PCR).

Results: Cell morphology and cell growth appeared to be similar among BMECs from different-age groups. In unstimulated cells, the basal levels of UPR^{ER}, indicative by the expression of X-box binding protein 1 (XBP1), activating transcription factor 4 (ATF4), activating transcription factor 6 (ATF6), binding-immunoglobulin protein (BiP, also known as GRP78), and protein disulfide isomerase (PDI), were significantly higher in aging BMECs (20-24 months) compared to the young group (2-4 months). In stress conditions, TG and TM treatment induced a robust increase of the UPR^{ER} in young BMECs, and this response was significantly decreased with age. Specifically, aging significantly reduced the expression of XBP1, ATF4, ATF6, and C/EBP-homologous protein (CHOP). Likewise, the expression levels of ER chaperons and foldases, such as BiP, DNAJC3/p58IPK, and PDI were markedly upregulated by TM and TG treatment in young BMECs, but to a significantly less extent in aging cells. Interestingly, TM, but not TG treatment, significantly upregulated NADPH oxidase 4 (NOX4) expression in young BMECs and the response was blunted in the aging group.

Conclusions: Our results suggest that there is a sustained ER stress in aging endothelial cells that may contribute to the increased endothelial dysfunction, inflammation, and apoptosis in aging vasculature. Moreover, the ability of activation of UPR^{ER} is drastically impaired in endothelial cells with age. The dysfunction of the adaptive response to stress conditions may lead to the accumulation of unfolded/misfolded proteins resulting in chronic ER stress in aging endothelial cells.

CONTROL ID: 3542625

SUBMITTER (NAME ONLY): Laura Magana Hernandez

TITLE: Connectomic reconstruction of synapses in the outer plexiform layer of a pure-rod retina

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Magana Hernandez, P.E. Perry, E. Hamada, I.A. Anastassov, Biology, San Francisco State University, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The elasmobranch little skate (*L. erinacea*) possesses a retina with only one type of photoreceptor, i.e. rods. A simplex retina like this allows for unique opportunities to study the vertebrate visual system. Unlike genetically modified rod-only models, this pure-rod retina has evolved naturally to the present state. Thus, we can study and describe the properties of rod circuitry within the context of a functional, evolutionarily optimized visual system, where all downstream components co-evolved to process signal from a single type of cell. Little is known about the wiring and synaptic architecture in the OPL of a pure-rod retina, where the first steps in visual information processing take place.

Methods: Eyes from little skate were hemisected and choroid-attached pieces of retina from the tapetal area were obtained. Retinal pieces were embedded in resin blocks and SB-3DEM was performed. The dataset analyzed here was from a region of interest in the OPL of the skate retina; width/height = 27.6µm, section thickness = 0.070µm, depth = 21.5µm. Voxel size was 4.5nmX4.5nmX70nm. 3D reconstructions and measurements of rod terminals with all invaginating and basal processes were done with Reconstruct and Amira software.

Results: There was great diversity in the types and # of invaginating and basal processes making contact with rods. ~12 anatomically distinct invaginating processes can be traced to one, or several different synaptic ribbons. These are presumed to belong to ON bipolar and horizontal cells. The full identity of each unique invaginating process could not be determined from this limited dataset. An additional ~3-4 processes made basal contacts outside of the invagination and are presumed to belong to OFF bipolar cells. The skate rod does not have an axonated terminal and ~4-6 filopodia of variable length can be traced to either neighboring rods, or yet unidentified cellular processes.

Conclusions: Skate rod terminal morphology suggests a hybrid rod-cone anatomy. The number of invaginating processes exceeds > 3-fold the usual number of four invaginating processes into a typical vertebrate mammalian rod. The multiple invaginating processes contacting skate rods are somewhat similar to the anatomical features typically observed in cone terminals.

CONTROL ID: 3542626

SUBMITTER (NAME ONLY): Marcus Mazzaferri

TITLE: The stellate varicose amacrine cell is positioned to provide a second layer of inhibition specific to the primate midget system

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Mazzaferri, A. Bordt, J. Kuchenbecker, D. Rezeanu, R. Barborek, M. Neitz, J. Neitz, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|S. Patterson, Center for Visual Science, University of Rochester, Rochester, New York, UNITED STATES|C. Puller, Department of Neuroscience, Carl von Ossietzky Universitat Oldenburg, Oldenburg, Niedersachsen, GERMANY|

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ABSTRACT BODY:

Purpose: Human vision served by the midget system evolved to deduce the reflectance properties of objects. To do this, the visual system separates information about reflectance from information about the properties of the illuminant. Some of this information is available at the edges of objects because illumination changes occur gradually across a scene while reflectance changes rapidly at the edges. Images processed through the primate midget system extract this reflectance information by being filtered through stages such that the color appearance of objects is determined solely by the contrast at their edges (Fig 1A). A first stage of this filtering process takes place in the outer retina by lateral inhibition from horizontal cells. We sought to characterize the circuitry of the inner retina specific to the midget system that might provide an additional stage of filtering.

Methods: We used serial block-face scanning electron microscopy in the macaque central retina (Patterson et al., 2019, Sci Rep) to reconstruct neurons in the inner retina that receive synaptic input from midget ON bipolar cells.

Results: We reconstructed a type of wide-field amacrine cell (n=2 for synaptic analysis, n=3 for morphology) that receives 97% of its input from and provides 98% of its output as reciprocal inhibitory feedback onto midget ON bipolar cells. Based on their stratification (78% IPL depth), the characteristic morphology of their dendritic trees and their dendritic varicosities, these were identified as ON stellate varicose cells. The dendritic trees of reconstructed cells overlapped extensively, forming dense coverage of the midget ON bipolar cell terminals (Fig 1B). We reconstructed 99 presynaptic midget ON bipolar cells and found that each made on average 2.3 ribbon synapses onto and received 1.5 reciprocal feedback synapses from an ON stellate varicose cell.

Conclusions: A dense network of ON stellate varicose amacrine cells specific to midget bipolar cells could provide a second layer of inhibition in the inner retina. By virtue of the delay of the inhibition from an additional synapse, the interaction between bipolar cell terminals and amacrine cells could act as a temporal filter contributing to the removal of signals other than those produced by contrast edges in a scene.

CONTROL ID: 3542628

SUBMITTER (NAME ONLY): Saaquib Bakhsh

TITLE: Patient preference regarding laser photocoagulation or cryoretinopexy for the treatment of retinal pathology

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bakhsh, R.A. Shields, M.A. Tahboub, A. Capone, Beaumont Health, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To date there has not been a study investigating patient preferences between laser photocoagulation or cryoretinopexy for the treatment of peripheral retinal pathology. We performed a retrospective single-center clinical survey study to assess patient preferences and investigate any underlying associations.

Methods: We performed a single-center, retrospective, twelve-question, patient-preference phone survey study of 100 qualifying patients (Figure 1). Details of the patients' age, gender, pathology location, laterality, laser type, laser spot size, power, number of spots, anesthesia type, number of cryopexy applications, same eye or fellow eye treatment, and time between treatments were also recorded. The primary outcome measure was the patient's preferred treatment with either laser, cryopexy, or no preference.

Results: Patients reported having experienced greater anxiety during the laser procedure (40%) (Figure 2A). 46% of patients reported experiencing more pain after treatment with cryopexy. Some patients had no pain during or after either procedure (Figure 2B). The incidence of adverse reactions after the procedure was higher for cryopexy. Slightly more patients (40%) perceived the laser to take longer than cryopexy (31%). The majority felt that it was easier to recover from laser (53%).

Patients who had undergone subconjunctival lidocaine for laser were more likely to prefer cryopexy ($p = 0.012$). There was a negative association between a patient's likelihood of preferring cryopexy and the number of applications ($p = 0.009$). Overall, 60% preferred laser, 25% preferred cryopexy, and 15% expressed no preference.

Conclusions: In conclusion, among patients who received both laser and cryopexy for the treatment of peripheral retinal pathology, the perception was that laser took longer than cryopexy but was easier to recover from. Overall, most patients (60%) preferred laser to cryopexy (25%). Subconjunctival anesthesia was less preferred to topical anesthesia for laser procedures. If cryopexy is to be performed, minimizing the number of freezes may improve the patient experience and recovery.

CONTROL ID: 3542635

SUBMITTER (NAME ONLY): San-San Cooley

TITLE: Evaluation of a New Device for Distance and Reading Tasks in Low Vision

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Cooley, R.A. Deffler, B.E. Dougherty, Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|J. Legerton, J. Marsh, Innovega Inc., San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The iOptik®/eMacula® uses spectacle-mounted micro-displays and specialty contact lenses to provide magnification and image modification, and may be useful for a range of tasks including reading, smart phone use and distance vision enhancement for the visually impaired. The purpose of this study was to evaluate this system's usefulness for near and distance visual tasks in people with low vision, as well as to assess users' opinions of it.

Methods: The system consists of a combination of two small micro-displays mounted for each eye in spectacle eyewear, a camera, and silicone elastomer contact lenses focused on a polarized display in the spectacle plane. The displays were connected to a computer which controlled the images on the screen. Visual acuity, contrast sensitivity, and reading testing were completed with habitual correction and low vision devices as well as with the iOptik/eMacula system, and a structured interview on device characteristics was completed following testing. Paired t-tests were used to compare vision and reading measurements between habitual correction and the iOptik/eMacula system.

Results: Nine participants with low vision were recruited from the low vision service at OSU. Mean±SD age was 53±17 and 77% were male. Mean better-eye baseline ETDRS VA with habitual correction was 50±7 (approximately 20/100), and mean contrast sensitivity was 1.56±0.20. Mean better-eye VA with the system was 86±5 (approximately 20/20), which was a significant improvement from habitual correction ($p<0.001$). Mean CS with the system was 1.60±.20, which was not significantly different from contrast sensitivity with habitual correction (1.56 ± 0.20 , $p=0.662$). All subjects were able to read 1M print with the system, and reading speeds were not significantly reduced compared to their habitual magnifiers ($p=0.436$). Subjects rated the comfort of the lens on each eye on a scale 1= poor and 10= excellent. The mean comfort score was 7.1 + 1.6. Three quarters of subjects responding felt the device would likely improve performance on tasks of daily living and increase independence.

Conclusions: An updated test version of the iOptik/eMacula system showed promise as an aid for distance and near tasks in people with low vision, and a majority of subjects thought the device would help with daily activities. Visual clarity and contrast sensitivity were improved from previous test versions.

CONTROL ID: 3542640

SUBMITTER (NAME ONLY): Christopher Sander

TITLE: Dissecting lipid contents in the distinct regions of native retinal rod disk membranes

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Sander, A. Sears, E.H. Choi, H.G. Jin, S. Suh, Pharmacology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|C. Sander, A. Sears, E.H. Choi, S. Kahremany, S. Suh, Z. Dong, D. Skowronska-Krawczyk, P.D. Kiser, K. Palczewski, Ophthalmology and Physiology and Biophysics, University of California Irvine, Irvine, California, UNITED STATES|A.F. Pinto, A. Saghatelian, Clayton Foundation for Peptide Biology, Salk Institute for Biological Studies, La Jolla, California, UNITED STATES|E. Pardon, J. Steyaert, Structural Biology Brussels, Vrije Universiteit Brussel, Brussels, BELGIUM|E. Pardon, J. Steyaert, Structural Biology Research Center, Brussels, BELGIUM|P.D. Kiser, Research Service, VA Healthcare Locations, Long Beach, California, UNITED STATES|K. Palczewski, Chemistry, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptors rely on distinct lipid domains to maintain their specialized features. Unlike protein localization, identification of critical differences in membrane content has not yet been expanded to lipids, due to the difficulty of isolating hyper-localized samples. We have overcome this by using styrene maleic acid (SMA) to co-immunopurify membrane proteins and their native lipids from two regions of rod outer segment (ROS) disks.

Methods: We developed a novel antibody against ABCA4 and nanobody against peripherin2/rod outer segment membrane protein 1 complex (per/ROM) to increase native tissue immunopurification efficiency. Isolated ABCA4, per/ROM and rhodopsin samples copurified with lipids and were extracted and subjected to untargeted lipidomic and fatty acid analysis. Relative abundance of lipid species was used to compare the environments of each protein sample. Principle component analysis (PCA) was used to group the samples by aggregate lipid profile and identify similar regions within the bilayer.

Results: Extensive differences between center (rhodopsin) and rim (ABCA4 and per/ROM) samples included a lower PC to PE ratio and increased LC- and VLC-PUFAs in the center relative to the rim region, which were enriched in shorter, saturated FAs. The comparatively few differences between the two rim samples likely reflect specific protein-lipid interactions. The rim region proteins grouped together in our PCA, separating from the rhodopsin samples.

Conclusions: The results of our PCA and more detailed analysis confirm that many of the diverse components found in this study are spread anisometrically across the continuous ROS disk membrane, favoring the center or rim region. Some of this systematic inhomogeneity is likely critical to the maintenance of healthy phototransduction and should be probed more deeply. Our high-resolution profiling of the ROS disk lipid composition provides a model for future studies of other complex cellular structures, enabling the explication of asymmetric lipid class distribution in continuous membranes.

CONTROL ID: 3542642

SUBMITTER (NAME ONLY): Lili Xie

TITLE: Chemokine CCL5 promotes robust optic nerve regeneration and mediates many of the effects of CNTF gene therapy

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Xie, Y. Yin, L. Benowitz, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ciliary neurotrophic factor (CNTF) is a therapeutic candidate for several ocular diseases and has been widely employed in studies of optic nerve regeneration. However, whereas recombinant CNTF (rCNTF) generally induces only low levels of optic nerve regeneration (unless SOCS3, suppressor of cytokine signaling-3) is deleted in retinal ganglion cells (RGCs), AAV-mediated CNTF expression in RGCs induces strong regeneration. Intravitreal virus injections induce moderate intraocular inflammation, and CNTF is a known immune modulator. We therefore tested whether the beneficial effects of AAV-mediated CNTF delivery are due to intraocular inflammation and elevation of pro-regenerative and neuroprotective factors.

Methods: rCNTF, AAV2-CNTF, AAV2-sh-CNTFR (targeting CNTFRa, the CNTF receptor) or control agents were injected intravitreally. Intravenous anti-Ly6G antibody (vs. isotype-matched IgG2a) was used to deplete neutrophils. C-C motif chemokine receptor 2 (CCR2) knockout mice were used to inhibit monocyte infiltration. Immunohistochemistry was used to identify various inflammatory cell types, inflammation-related growth factors (C-C motif chemokine ligand 5, CCL5, etc.) and relevant receptors. RT-PCR was used to quantify mRNA levels of these and other gene products. We also tested CCR5 general knockout, a receptor antagonist, and RGC-specific CCR5 knockdown.

Results: Whereas intravitreal rCNTF induced little axon regeneration, AAV2-CNTF had strong effects on RGC survival and axon regeneration. CNTFRa was expressed primarily in non-neuronal cells, and CNTFRa knockdown in RGCs did not alter AAV2-CNTF-induced regeneration. AAV2-CNTF attracted inflammatory cells, particularly in the optic nerve head, and increased mRNA levels for CCL5 9.5-fold. Either neutrophil depletion or blocking monocyte infiltration dramatically decreased AAV2-CNTF-induced RGC survival and axon regeneration. Administration of a CCR5 antagonist or RGC-specific CCR5 knockdown both reduced axon regeneration ~ 70%. In gain-of-function studies, intraocular rCCL5 stimulated considerable optic nerve regeneration in vivo

Conclusions: The beneficial effects of CNTF gene therapy after optic nerve injury are mediated through immune modulation and upregulation of CCL5. Our results also raise the possibility that other widely used gene therapies could act in an indirect manner via unanticipated indirect mechanisms

CONTROL ID: 3542646

SUBMITTER (NAME ONLY): Vincent Dong

TITLE: Evaluating the Utility of Deep Learning Using Ultra-widefield Fluorescein Angiography for Predicting Need for Anti-VEGF Therapy in Diabetic Eye Disease

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep learning (DL) is a class of machine learning that utilizes neural networks to generate representations that allow for distinguishing categories of interest. Being an unsupervised feature generation method, large training sets are typically needed to learn appropriate representations to discriminate the categories of interest. While DL has been extensively explored in ophthalmology for diagnostic applications, it has not been extensively evaluated for predicting need for future treatment, arguably a more challenging problem compared to disease diagnosis and one where large imaging datasets with accompanying treatment response and outcome information may not be available. The purpose of this study was to investigate the ability of DL to predict need for anti-VEGF from ultra-widefield angiograms (UWFA) in eyes with diabetic retinopathy (DR).

Methods: A retrospective image analysis study was conducted on eyes with DR that had UWFA imaging. DL was applied to the late phase UWFA images to classify eyes as needing anti-VEGF or not. In order to evaluate the impact of sample size on DL performance, the study set was sampled into five subsets of increasing size. For each subset experiment, a class activation map (CAM) was generated per sample to identify regions of interest (ROI) that the DL model places attention on, when making its predictions.

Results: Two-hundred seventeen eyes from 189 patients were included. 141 eyes required anti-VEGF treatment. Five subsets with balanced class distributions were generated from this dataset. Subsets increase by a factor of 28 in size from 28 to 140 eyes. The 3-fold cross-validated AUROC indicates minimal correlation between dataset size and model performance. The best performing model had an average AUROC of 0.628 ± 0.087 over the subsets. Resulting CAMs frequently demonstrated inconsistent identified ROI across subsets suggesting that DL tended to be sensitive to the choice of training cases across every fold.

Conclusions: In this study, regardless of sample size, DL was unable to consistently identify image representations from limited UWFA samples to predict need for anti-VEGF therapy. These findings suggest that other handcrafted radiomic approaches, multi-modal DL, and integration of multiple features might need to be considered for predicting need for treatment.

CONTROL ID: 3542652

SUBMITTER (NAME ONLY): Shinwu Jeong

TITLE: Matrix Metalloproteinase (MMP)-9 and Tissue Inhibitor of MMP (TIMP)-1 are Localized in Retinal Müller Glial Cell Cytoplasm and Nuclei and Their Expression Pattern is Modulated by Cytokines and Oxidative Stress

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Matrix metalloproteinases (MMPs) are involved in the inflammatory retinal degeneration and pathology of retinitis pigmentosa (RP). In rodent models, intravitreal injections with recombinant tissue inhibitor of MMP (TIMP)-1 reduces the progression of rod cell death, modifies cone cell distribution with Müller glial (MG) gliosis. To gain insights into the TIMP-1 cellular mechanisms, MMP-9 and TIMP-1 expression patterns in MG cells were investigated in vitro under proinflammatory or oxidative conditions.

Methods: Human MG cell line (MIO-M1 cells) were treated for 24 h with either IL-1 β (10ng/mL), TNF- α (10ng/mL), or H₂O₂ (0 μ M-600 μ M) to observe their effect on MMP-9 and TIMP-1 expression including viability, growth, secretion and subcellular compartmentalization. MTT and SRB assays measured cell viability; gelatin zymography, MMP-9 secretion; ELISA assays, TIMP-1; fluorescent immunocytochemistry, intracellular protein expression. Each treatment parameter was evaluated and compared with untreated controls.

Results: Viable cell densities are mildly increased by cytokines, particularly, by IL-1 β (20-30%, p<0.01). MMP-9 secretion is also increased by IL-1 β (200%, p>0.05) or TNF- α (300%, p<0.05); however, TIMP-1 secretion is decreased by IL-1 β (32%, p>0.05) or increased by TNF- α (24%, p>0.05). H₂O₂ treatments have minimal effect on cell viability or secretion of either protein. MMP-9 and TIMP-1 are both expressed, not only in the cytoplasm, but also inside the nucleus: the former is diffusely detected, but the latter, in speckles. Intracellular TIMP-1 aggregation is detected in the cytoplasmic area upon IL-1 β treatment. With H₂O₂ treatments, the cell morphology changes from cobble to spindle shapes, and the nuclei become enlarged, compared with untreated control, dose-dependently, [5% at 100 μ M (p>0.05), 35% at 300 μ M (p<0.001), and 62% at 600 μ M (p<0.0001)], with the nuclear TIMP-1 speckle numbers increasing concomitantly. H₂O₂ treatment does not alter the MMP-9 intracellular distribution pattern.

Conclusions: Cytokines alter disproportionately MMP-9 and TIMP-1 secretions. Intracellular and nuclear TIMP-1 is dynamically modulated in response to proinflammatory and oxidative insults in MG cells, implicating unrecognized functional roles in MGs in the retina.

CONTROL ID: 3542653

SUBMITTER (NAME ONLY): Rui Fan

TITLE: Deep learning for detecting glaucoma in the Ocular Hypertension Treatment Study: Implications for clinical trial endpoints

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To investigate the diagnostic accuracy of deep learning (DL) algorithms to detect primary open angle glaucoma (POAG) trained on fundus photographs from the Ocular Hypertension Treatment Study (OHTS).

Methods: 74,678 photographs from 3,272 eyes of 1,636 OHTS participants with a mean follow-up (range) of 10.7 (0.0, 14.3) years were used to train a ResNet-50 deep learning model to detect the OHTS I and II Endpoint Committee POAG determination based on optic disc (n=287 eyes, 3,502 photographs) and /or visual field (n=198 eyes, 2,300 visual fields) changes. OHTS training, validation and testing sets were randomly determined using an 85-5-10 percentage split by subject. Three independent test sets (1: UCSD Diagnostic Innovations in Glaucoma Study (DIGS), 2: ACRIMA (Spain) and 3: Large-scale Attention-based Glaucoma (LAG, China) were used to estimate the generalizability of the model. Areas under the receiver operating characteristic curve (AUROC) and sensitivities at fixed specificities were used to compare model performance. Evaluation of false positive rates at a fixed specificity of 90% was used to determine whether the DL model detected glaucoma before the Endpoint Committee determination.

Results: For the OHTS test set, the DL model achieved an AUROC (95% CI) of 0.87 (0.80, 0.91) for the overall OHTS POAG endpoint. For the OHTS endpoints based on optic disc changes or visual field changes, AUROCs were 0.90 (0.87, 0.93) and 0.87 (0.80, 0.91), respectively. False positive rates (at 90% specificity) were higher in earlier photographs of hypertensive eyes that later developed POAG by disc or visual field (19.1%), compared to hypertensive eyes that did not develop POAG (7.3%) during their OHTS follow-up. The diagnostic accuracy of the DL model developed based on the OHTS optic disc endpoint on the 3 independent datasets was lower with AUROC for DIGS of 0.74 (0.69, 0.79), ACRIMA of 0.74 (0.70, 0.77) and LAG of 0.79 (0.78, 0.81).

Conclusions: The high diagnostic accuracy of the current DL model suggests that DL can be used to automate the determination of POAG for clinical trials and management. In addition, the higher false positive rate in early photographs of eyes that later developed POAG suggests that DL models detected POAG in some eyes earlier than the OHTS POAG Endpoint Committee.

CONTROL ID: 3542654

SUBMITTER (NAME ONLY): Biraj Mahato

TITLE: Optical coherence tomography guided laser gene delivery in degenerated retina

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Photoreceptor loss is the final endpoint in nonexudative Age-Related Macular Degeneration (dry-AMD) and no curative treatments are available. Targeted optogene delivery to higher order neurons of retina in geographic atrophy (GA) regions in these patients is a promising approach to improve vision. Here, we report development of an optical coherence tomography (OCT) guided near-infrared laser irradiation platform combined with Surface Plasmon Resonance (SPR) of nanoparticles to deliver ambient-light activatable multi-characteristic opsin II (MCOII) plasmids into human cells and degenerated mouse retina (rd1) in a specially targeted manner. The method is based on nano-enhancement of near-infrared optical field by of bound to specific cells.

Methods: After pretreatment with functionalized gold nanorods (fGNRs) for 2 hrs, OCT guided laser (980 nm) delivery of MCOII-mCherry plasmids was performed in HEK cells to determine optimal laser parameter and plasmid concentration. Reporter expression was assessed after 48 hrs of laser delivery using confocal fluorescence microscopy. MTT assay was performed to check cytotoxicity after laser gene delivery in HEK cells. For in vivo OCT - guided laser gene delivery, 8-12 week-old rd1 mice were intravitreally injected with a 2µl mixture of fGNR (0.2 µg/µl) and MCOII plasmids (0.5 µg/µl) into each eye. 3-4 hrs post injection, laser delivery was performed in one eye and the contralateral eye was used as a control. The laser beam power, outside eye, was kept at 20 mW for targeted gene delivery. First, real time OCT imaging was used to locate optic nerve, and ~0.7 mm x 0.7 mm rectangular region was irradiated with the scanning laser beam for 400 secs. After 4 weeks of gene delivery, eyes were enucleated, retinal flat mount was prepared and immunostained with anti-mCherry and RBPMS antibody.

Results: MCOII-mCherry expression in HEK cells was found to vary based on laser beam power. MCOII delivery using optimal laser power (determined in HEK cells) led to mCherry expression in the RGC cells of rd1 mice. MTT assay and OCT measurement after laser delivery indicated minimal cytotoxic effects. Non-targeted regions did not show mCherry expression in either HEK cells or rd1 retina.

Conclusions: OCT guided laser delivery is an efficient and targeted method to deliver therapeutic genes into degenerated retina.

CONTROL ID: 3542663

SUBMITTER (NAME ONLY): Jingwen Cai

TITLE: Role for Arg1 and Arg2 in Age-related Intraocular Pressure Homeostasis

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is the major risk factor and treatment target of primary open-angle glaucoma (POAG). Exogenous nitric oxide (NO) increases outflow facility and lowers IOP. Since endogenous NO production is limited in part by altered activation of arginase with aging, we aimed to investigate the expression of arginases (Arg1 & Arg2) in the conventional outflow tissues and their potential role in IOP regulation over time.

Methods: Remnant human corneal rims after transplantation were fixed and embedded in paraffin for histological sections. Outflow tissues were incubated with antibodies against ARG1 or ARG2 followed by the secondary antibody for immunofluorescence-based protein expression analysis. The expression of ARG1 and ARG2 was also examined in primary human trabecular meshwork (TM) cells with or without cyclic stretch for 24 hours (n=5) using droplet digital PCR. IOP in three groups of littermate mice, wild type (C57BL6, n=40), Arg1^{+/-} (n=34), and Arg2^{-/-} (n=134) was measured using rebound tonometry once per week in both eyes from 24 weeks to death (up to 108 weeks). The IOPs of age-matched mice were compared using student t-test with a significance threshold of p<0.05. The images of anterior chamber and the iridocorneal angle were taken in mice older than one year using a Leica Envision SD-OCT R2200 system.

Results: ARG1 and ARG2 proteins are expressed in human conventional outflow tissues. In TM cells, the expression of ARG1/ARG2 did not change significantly in response to the mechanical stretch. In mice, the mean weekly IOP measurements were comparable among three groups until 45 weeks of age. While IOP levels of wild type mice progressively decreased from 13 mmHg to 12 mmHg at 50 weeks, and to 11 mmHg after 95 weeks, IOP of Arg1^{+/-} and Arg2^{-/-} mice was stable at 13 mmHg until up to 108 weeks. An open iridocorneal angle was confirmed in the old mice of all genotypes using SD-OCT imaging and histological morphological analysis.

Conclusions: ARG1 and ARG2 are expressed in the outflow tissues and cells. Partial loss of Arg1 or complete loss of Arg2 in mice abolished the age-related IOP decrease in aged wild type mice, suggesting their role in age-related IOP homeostasis.

CONTROL ID: 3542667

SUBMITTER (NAME ONLY): Jasmeen Randhawa

TITLE: The Effects of Breastfeeding on Retinoblastoma Development

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The protective effects of breastfeeding on various childhood malignancies have been established, but an association has not yet been determined for retinoblastoma (RB). We aimed to further investigate the role of breastfeeding in the development or severity of non-hereditary RB, specifically assessing its relationship to (1) age at presentation (2) ocular prognosis, and (3) extraocular involvement. We also assessed the role of socio-economic status (SES) in these outcomes.

Methods: A subgroup analysis was performed on a global dataset of 651 patients who received RB treatment and answered a neonatal questionnaire. 532 patients reported "breastfed" or "formula fed" feeding history and were included in the analyses. Patients noted to have a family history of RB (n=25) or sporadic bilateral RB (n=218) were excluded. Multiple regression was used to examine the predictive nature of breastfeeding status on age at presentation. Logistic regression was used to examine effects on enucleation status and lymph node involvement. Ordered logistic regression was used to examine the effects of breastfeeding on International Intraocular Retinoblastoma Classification System (IIRC) group, International Retinoblastoma Staging System (IRSS) stage, and distant metastases. Each model controlled for age, sex, SES and immunizations.

Results: Neither breastfeeding nor formula feeding was associated with differences in age (B = 0.66, 95% CI = -4.96, 6.27) or IIRC group (OR = 0.83, 95% CI = 0.41, 1.68) at presentation. In terms of clinical outcomes, neither breastfeeding nor formula feeding was associated with differences in enucleation (OR = 1.54, 95% CI = 0.80, 3.00), IRSS stage (OR = 1.37, 95% CI = 0.72, 2.60), lymph node involvement (OR = 0.51, 95% CI = .04, 6.73), or distant metastases (OR = 3.20, 95% CI = .40, 25.51). Consistent with previous studies, patients were significantly more likely to be diagnosed at a younger age if they reported higher SES (B=-5.62, 95%CI=-8.22, -3.01). Patients treated in high-income countries were more likely to present with a lower IRSS stage (OR = 9.67, 95% CI= 2.48, 37.69) and were less likely to necessitate enucleation (OR = 0.24, 95% CI= 0.06, 0.96).

Conclusions: This study suggests that breastfeeding neither impacts the sporadic development nor the severity of non-hereditary RB. As expected, children from higher SES countries have lower IRSS stage at presentation and lower overall risk of enucleation.

CONTROL ID: 3542668

SUBMITTER (NAME ONLY): Rita Flores

TITLE: IMPAIREMENT OF CHORIORETINAL VASCULATURE IN PATIENTS WITH INTERMEDIATE AGE-RELATED MACULAR DEGENERATION

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age related macular degeneration (AMD) is a multifactorial disease leading to loss of central vision; even though its complete pathogenesis is still unclear aging, genetics and smoking are the most important risk factors. Local hemodynamics may play a crucial role in the manifestation and progression of AMD pathologies.

Methods: A total of 179 eyes were recruited to this study, 149 eyes with intermediate AMD and 30 healthy controls. A total of 127 eyes were eligible for image binarization and included in the final analysis: Group 1: AMD eyes n=102 (80%) and Group 2: healthy controls n=25 (20%). 50 eyes presented soft or cuticular drusen (Group 1A), 35 eyes reticular pseudodrusen (Group 1B) and 17 eyes both types of drusens (Group 1C). Mean age in years in study sample was 77.9 ± 8.8 and the majority of the participants were women (70%).

Choroid and retinal vascular quantitative parameters were evaluated in an intermediate AMD population and compared with a control group. Spectral domain optic coherence tomography (SD-OCT) with enhanced depth imaging (EDI) and optic coherence tomography angiography (OCT-A), were acquired using OCT SPECTRALIS (Heidelberg Engineering, Heidelberg, Germany). Image binarization was used to obtain quantitative data of choroid and retinal capillary plexus evaluation.

Results: Considering choroid vascular parameters after binarization we found that Total subfoveal Choroidal Area (TCA) in Group 1 was $0.22 \pm 0.066 \text{ mm}^2$ and $0.29 \pm 0.083 \text{ mm}^2$ in Group 2. Luminal Area (LA) was also reduced in Group 1 ($0.1552 \pm 0.043 \text{ mm}^2$) compared with Group 2 ($0.203 \pm 0.053 \text{ mm}^2$) and those differences were statistically significant ($p < 0.05$). Regarding retinal capillary perfusion there was a trend to reduced vascular parameters in Group 1A in both superficial capillary plexus (LA: $9.44 \pm 1.1 \text{ mm}^2$) and in deep capillary plexus (LA: $9.80 \pm 0.89 \text{ mm}^2$) compared with Group 1B (LA: $10.13 \pm 1.3 \text{ mm}^2$ and $10.29 \pm 1.1 \text{ mm}^2$, respectively).

Conclusions: Our study corroborates that the chorioretinal vascular network are impaired in intermediate AMD patients. Retinal and choroidal vascular parameters could be attractive new prognostic markers for intermediate AMD. Future therapeutic approaches may target this vascular dysfunction and prevent disease progression in early and intermediate stages.

CONTROL ID: 3542683

SUBMITTER (NAME ONLY): Michelle Odonkor

TITLE: Effects of Image Quality on Grading Photographs of Trachoma

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Odonkor, F. Naufal, B. Munoz, S.K. West, Dana Center for Preventive Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Trachoma is the leading infectious cause of blindness worldwide. Prevalence can be assessed by field grading or grading photographs. We hypothesize that poor image quality may contribute to differential grading of trachomatous inflammation—follicular (TF) between field and photo graders.

Methods: Field grades for TF and tarsal conjunctival photographs were obtained by a field grader from one or both eyes in 3118 children from Kongwa District, Tanzania, 2 years post-MDA. 2 additional graders graded and adjudicated each photo. We identified the eyes where the field and photo TF grades did not match and assigned each eye an image quality score and a potential reason for mismatch (e.g., different interpretation of follicle number or size, field documentation error, or no obvious reason). We also assigned image quality scores to a random sample of 180 eyes with matching field and photo TF grades.

Results: 5220 eyes had matching field and photo TF grades while 177 eyes had mismatched field and photo TF grades (Fig 1). There was no difference in image quality between mismatch eyes where the field grader assigned a grade of TF and mismatch eyes where the photo graders assigned a grade of TF ($p=0.6209$), but there was a significant difference in image quality between eyes with matching field and photo grades and eyes with mismatched field and photo grades ($p=0.0186$). However, no image quality issue stood out as significantly different between eyes with matching vs. mismatched TF grades (Fig 2). Disagreement over follicle number (54.8% of mismatch eyes) or size (42.9%) were the most common potential reasons for grade mismatch.

Conclusions: Since there was a significant difference in image quality between eyes with matching vs. mismatched field and adjudicated photo grades, image quality seemed to contribute to grading disagreements between field and photo graders. Poor image quality may alter photo graders' view of the tarsal conjunctiva and affect their determination of follicle size or number. However, as there was no difference in image quality between mismatch eyes with a field vs. photo grade of TF, image quality did not seem to influence the direction of the mismatch (i.e., which graders assigned a grade of TF).

CONTROL ID: 3542691

SUBMITTER (NAME ONLY): Revathy Mani

TITLE: The impact of traumatic brain injury on delayed antisaccades and memory-guided pro- and antisaccades

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Traumatic brain injury(TBI) leads to cognitive, attentional and sensorimotor disturbances. Antisaccades and memory-guided saccades have been used to investigate inhibitory control and working memory respectively. However, no study has compared the extent of deficits across these tasks in TBI. In this study, we investigated the responses of delayed antisaccades and memory-guided pro- and antisaccades by systematically varying the delay in individuals with TBI and compared the performance across tasks.

Methods: Twenty-six subjects((mean age=22.4yr±6.6),12 males) with TBI participated. Subjects fixated on a central target and made either1)an antisaccade in response to a peripheral visible target for a delayed antisaccade task, 2)a prosaccade towards or 3)an antisaccade away from the remembered target cued for a memory-guided task. Saccades were made after a variable delay of 0,0.125,0.250,0.500 and 1s indicated by a visual cue. Saccadic latency, disinhibition errors (premature incorrect/correct saccades made before the cue) and directional errors(incorrect saccades made after the cue) were determined.

Results: A 5(delays)x3(tasks) repeated measures ANOVA with delays as within subject and tasks as between subject variables was conducted for latency, disinhibition and directional errors. There was a significant interaction effect between delays and tasks for latency ($F(8,281)=2.341$, $p=0.02$), directionally-correct ($F(6,204)=3.78$, $p=0.001$) and incorrect disinhibition errors ($F(6,244)=7.12$, $p<0.0001$) but not for directional errors ($p=0.62$). However, for directional errors, there was a significant main effect both for delay ($F(3.820,259.8)=15.08$, $p<0.0001$) and tasks ($F(2,75)=7.01$, $p=0.002$). The delayed antisaccade task demonstrated prolonged latency, increased directionally incorrect disinhibition and directional errors compared to memory-guided tasks while the memory-guided prosaccade task showed increased directionally correct disinhibition errors compared to antisaccade tasks.

Conclusions: Participants with TBI took longer time to generate delayed antisaccades and could not inhibit prosaccade responses towards the target during and after delay. For the memory-guided prosaccade task, the TBI participants could not inhibit premature prosaccades with longer delays. These deficits in voluntary saccades suggest impaired cognitive functions specific to response inhibitory control and impulsivity in TBI.

CONTROL ID: 3542694

SUBMITTER (NAME ONLY): Giovanni Montesano

TITLE: Do additional testing locations improve the detection of macular perimetric defects in glaucoma?

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the ability of additional central testing locations to improve detection of macular visual field defects in glaucoma.

Methods: 440 healthy people and 499 patients with Glaucomatous Optic Neuropathy (GON) from seven different clinical settings were tested with a fundus tracked perimeter (CMP, CenterVue, Italy) using a 24-2 grid with 12 additional macular locations (24-2+, Figure 1). GON was identified based on expert evaluation of optic nerve head photographs and optical coherence tomography scans, independently of the visual field (VF). We identified macular defects using locations with measurements outside the 5% and 2% normative limits on Total Deviation (TD) and Pattern Deviation (PD) maps within the VF central 10 degrees. Detection was based on the total amount of affected macular locations (overall detection) or on the largest number of affected macular points connected in a contiguous cluster (cluster detection). Number of locations and the cluster size to identify significant defects were used to obtain equivalent specificity between the 24-2 and the 24-2+, calculated using false detections in the healthy cohort. P-values for detection improvement were calculated via bootstrap and considered significant at $p < 0.05$.

Results: At matched specificity, the cluster detection identified significantly more macular defects with the 24-2+ compared to the 24-2 with all considered maps ($p < 0.001$). The increase in percentage of detection was 8% and 10% for TD-5% and PD-5% maps, respectively, and 5% and 6% for the TD-2% and PD-2% maps. For the overall detection, an improvement was only observed for the TD-2% and PD-2% maps (9% increase, $p < 0.001$). There was good but not perfect agreement between the two grids (Venn diagrams in Figure 2). The percentage of detected macular defects ranged from 30% to 50%, depending on the map and detection method used.

Conclusions: Additional macular locations can improve detection of macular defects without loss of specificity.

CONTROL ID: 3542698

SUBMITTER (NAME ONLY): Rajashekhar Gangaraju

TITLE: Mesenchymal stem cells induce Foxp3-Tregs to suppress effector T cells and protect against retinal ischemic injury

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mesenchymal stem/stromal cells (MSC) are well known for immunomodulation; however, the mechanisms involved in their benefits in the ischemic retina are unknown. In this study, we tested the hypothesis that MSC via upregulation of transcription factor forkhead box P3 (Foxp3) in T cells elicit immune modulation and thus protect against ischemic retinal damage

Methods: MSCs were generated from urine epithelial cells derived induced pluripotent stem cells (iPSC) through non-insertional reprogramming (iMSCs). Mitochondria transfer from MSC to immune cells was assessed by confocal microscopy, and oxygen consumption rates (OCR) were measured using Seahorse Flux Bioanalyzer. Activated splenocytes co-cultured with iMSC in differentiation medium were assessed with anti-Foxp3 antibody and analyzed by flow cytometry. Unilateral retinal ischemia reperfusion (I/R) were done in adult C57BL/6 mice by transiently elevating the intraocular pressure for 1 h. Uninjured eyes served as I/R controls. After 1 day of reperfusion, the animals were randomized to receive intravitreal iMSC (1000 cells/1mL) or saline (1mL). After 7 days, the retinal function was assessed by Electroretinogram (ERG). The retinal extracts were processed by qRT-PCR, and the retinal flat mounts were processed by confocal microscopy for Foxp3⁺ cells.

Results: In in-vitro cultures, iMSC transferred mitochondria to immune cells via F-actin nanotubes, significantly increased OCR for basal respiration and ATP production, suppressed effector T cells, and promoted differentiation of CD4⁺CD25⁺ Tregs in co-culture with mouse splenocytes. In in-vivo studies, iMSCs in I/R eye significantly increased Tregs in the retina compared to saline injected I/R eyes (63.4 ± 14.29 v/s 29.99 ± 6.69 cells/mm², p<0.05, anova). Furthermore, iMSC injected I/R eyes had decrease in retinal inflammation (IL1b: 6.09 ± 1.54 v/s 27.08 ± 8.69 fold p<0.01; Ccl2: 3.52 ± 0.96 v/s 13.6 ± 2.7 fold p<0.001,anova) and improved b-wave amplitudes compared to saline injected I/R eyes (at 1cd.s.m² 139 ± 48 v/s 48 ± 10 μ volt, p=0.05, t-test).

Conclusions: Our study demonstrates that iPSC derived MSCs can transfer mitochondria to T cells to enhance differentiation into Foxp3 Tregs. Additionally, our current data demonstrates that MSC can improve the retina's immune function through upregulation of Tregs to decrease inflammation to reduce I/R injury-induced retinal degeneration

CONTROL ID: 3542701

SUBMITTER (NAME ONLY): Qi Dong

TITLE: Evaluation of New Ophthalmology Curriculum for Medical Students

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Dong, S. Podila, L. Wolfel, G. Acosta, R.N. Mankad, A. Davis, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ophthalmology education is underrepresented in many medical school curricula which can lead to decreased physician competency in identifying and treating primary eye diseases. The University of New Mexico (UNM) introduced 6 additional hours of flipped classroom education as part of a new ophthalmology curriculum. We conducted a cross-sectional study to assess the efficacy of the new curriculum.

Methods: All medical students at UNM were invited to take part in the study, but only second-year students received the new curriculum. The study comprised an opinion survey and a 12-question knowledge assessment quiz based on objectives set by the American Academy of Ophthalmology. Mean quiz scores and survey outcomes were calculated for each class and the results were compared using a one-way analysis of variance (ANOVA).

Results: 72 participants completed the survey and 58 completed the quiz. The survey indicated that second-year students felt the most comfortable among all four classes answering ophthalmology questions on the USMLE Step 1 exam. Fifteen (57.7%) second-year participants felt somewhat or very comfortable, compared to just 4 (23.5%) third-year, 1 (6.3%) fourth-year, and 0 (0%) first-year students. Similarly, 23 (88.5%) second-year students felt that ophthalmology training was somewhat or very important. By comparison, only 13 (76.5%) third-year, 7 (53.9%) first-year, and 8 (50.0%) fourth-year students agreed. Additionally, 3 (11.5%) second-year students reported interest in ophthalmology as a specialty, compared to 4 (30.8%) first-year, 0 (0%) third-year, and 1 (6.3%) fourth-year students.

The quiz portion of the study revealed that third and second-year students performed comparably, with average scores of 68.8% (SD 15.8%) and 67.3% (SD 13.0%), respectively. Fourth and first-year students performed worse at 48.7% (SD 21.2%) and 31.8% (SD 17.3%), respectively.

Conclusions: The survey results demonstrate students that underwent the new curriculum felt more confident answering ophthalmology questions and were more likely to consider ophthalmology an important subject. Although the quiz results were comparable between second and third-year students, this may be the result of third-year students performing additional self-education to prepare for the recent USMLE Step 1 exam. Similarly, fourth-year students are farther removed from their Step 1 exam, which may explain the reduced knowledge retention reflected by the quiz.

CONTROL ID: 3542702

SUBMITTER (NAME ONLY): Natasha Kolomeyer

TITLE: Retrospective, multicenter, 12-month evaluation of ab-externo XEN Gel Stent placement: real-world data from the EXPAND Study Group

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The XEN gel stent was approved for ab-interno implantation and has been used for >10 years. Recently, surgeons worldwide have developed and adapted a novel approach, implanting the gel stent ab externo. This is the first evaluation of real-world data of the gel stent when placed ab externo.

Methods: In this multicenter, retrospective, chart review, consecutive ≥ 18 -year old patients with elevated intraocular pressure (IOP) requiring surgical intervention were included. Patients underwent ab-externo placement of gel stent alone or combined with phacoemulsification, with or without opening of the conjunctiva, ≥ 12 months before study inclusion. Mean IOP and number of topical IOP-lowering medications at baseline and 12 months were recorded, as well as ocular adverse events (AEs). Available preoperative, operative, and postoperative data were collected.

Results: The analysis included 472 eyes from 412 patients; 382 (80.9%) eyes received the gel stent alone. Mean age was 75.1 years (range, 21-98) and 54.7% of patients were female. Month-12 data was available for 193 eyes. Mean (standard deviation [SD]) IOP decreased from a medicated baseline of 20.8 (7.6) mmHg to 14.9 (5.1) mmHg at 12 months, a mean reduction of ~ 6 mmHg ($\sim 28\%$). 181 (93.8%) eyes required topical IOP-lowering medications at baseline vs 110 (57.0%) at 12 months, including 11 and 3 patients who also required oral therapy, respectively. The most frequent AEs were transient, self-resolving hypotony (< 6 mmHg – $n=66$, 22.8%), uncontrolled IOP requiring secondary surgical intervention ($n=39$, 13.5%), bleb leak ($n=37$, 12.8%), implant exposure/extrusion/conjunctival erosion ($n=20$, 6.9%) and choroidal effusion/hemorrhage/mixed effusion hemorrhage ($n=24$, 5.9%).

Conclusions: When placed via the novel ab-externo technique, the gel stent effectively lowered IOP and the IOP-lowering medication count, with a predictable and acceptable safety profile.

CONTROL ID: 3542703

SUBMITTER (NAME ONLY): Rayne Lim

TITLE: A novel CFH mutation affects FHL-1 expression and metabolism in EOMD patient derived iPSC-RPE.

SESSION TITLE: Retinal diseases: molecular and biochemical disease mechanisms

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Early onset macular drusen (EOMD) is a rare inherited retinal degeneration with similar clinical features to AMD. EOMD patients express high penetrance genetic variants in the complement factor H (CFH) gene that affect expression of the truncated isoform, factor H-like protein 1 (FHL-1). FHL-1 is highly localized to Bruch's membrane where it functions as an alternative pathway inhibitor of the complement system. However, little is known about the role of FHL-1 in the retinal pigmented epithelium (RPE). In this study, we generated and characterized EOMD-patient derived iPSC-RPE cells, and hypothesized that reduced FHL-1 expression results in the formation of basal deposits and reprogramming of RPE metabolism.

Methods: PBMCs isolated from EOMD patients were reprogrammed into iPSCs and differentiated into RPE using standard protocols. Sanger sequencing was performed to identify the novel CFH gene mutation. Minigene assays in HEK293T transfected cells were used to evaluate mutant FHL-1 expression. iPSC-RPE cultured on Matrigel-coated filters for 4-weeks were examined for ultrastructural differences using TEM. RPE cells cultured on flat bottom dishes were also harvested for WB, qPCR and immunocytochemistry of RPE markers, and targeted metabolomics was performed using LCMS/GCMS. iPSC-RPE from healthy age-matched donors were used as controls.

Results: EOMD patients expressed a novel c.351-2A>G mutation in the conserved AG dinucleotide at the 3' splice site of exon 4 in the CFH gene, resulting in exon 4 skipping and no expression of mutant FHL-1 protein in the minigene assay. iPSC-RPE generated from EOMD patients heterozygous for the mutation exhibited typical RPE morphology, pigmentation, and RPE marker expression, but had a 50% reduction in FHL-1 secretion. EOMD iPSC RPE cells formed large multilaminar crystalline-like deposits, consistent with the appearance of calcium oxalate. In addition, numerous electron lucent vesicles were noted in the basal deposits, and Oil Red O staining confirmed the presence of basal lipid deposits. Metabolite analysis revealed increased glucose consumption and lipid accumulation in the iPSC-RPE derived from EOMD patients.

Conclusions: EOMD iPSC-RPE have decreased FHL-1 expression, form basal laminar calcium and lipid deposits, and have increased glucose consumption and lipid accumulation, suggesting a crucial role for FHL-1 in the maintenance of RPE homeostasis.

CONTROL ID: 3542706

SUBMITTER (NAME ONLY): Victor Rodríguez-Lopez

TITLE: Fast subjective estimation of astigmatism with the Direct Subjective Refraction

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Rodríguez-Lopez, E. Esteban-Ibañez, Consejo Superior de Investigaciones Científicas, Madrid, Madrid, SPAIN|C. Dorronsoro, 2EyesVision, SPAIN|

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ABSTRACT BODY:

Purpose: The subjective estimation of astigmatism, part of the subjective refraction, is a tiresome procedure. Here we extend the Direct Subjective Refraction (DSR), a technology to obtain fast and unsupervised subjective measurements of the refractive error, to estimate astigmatism

Methods: In the DSR method, a temporal defocus wave (TDW; fast and periodic changes in defocus induced by a tunable lens projected onto the eye) interacts with the longitudinal chromatic aberration of the eye. The flicker and color artifacts that appear on a stimulus, are minimum when TDW matches the retinal plane, so the patients can find subjectively their refractive error, unsupervised, with a staircase procedure. The stimulus for astigmatism is a set of magenta, red and blue lines, tested parallel and perpendicular to the axis of astigmatism reported by an autorefractometer (ARK1 Nidek). The TDW was produced by a visual simulator (SimVisGekko 2EyesVision) with frequency 15Hz and amplitude 0.5D. 4 subjects (25-49yo) performed the DSR with free accommodation in both eyes, 4 repetitions, 2 axes. The mean difference between axes provided the amount of astigmatism (J0, J45). DSR was compared with traditional subjective refraction (TSR) performed by an optometrist. Visual function with the DSR and the TSR corrections were evaluated with VisualAcuity (VA), StereoAcuity (SA), and direct comparison of perceived visual quality

Results: DSR was able to measure small astigmatism with high repeatability (SD average across repetitions and subjects ± 0.13 D). Comparing DSR with TSR, M, J0 and J45 components showed high correlation ($p=5e-16$, $5e-12$, $9e-12$; $r=0.98$, 0.98 , 0.94). The mean difference in astigmatism (J0: 0.08 ± 0.11 D, J45: 0.01 ± 0.06 D) and the 95%CI Limits of Agreement (J0: $[-0.14$ to $0.30]$, J45: $[-0.11$ to $0.14]$ D) have subclinical importance. Both final refractions produce similar VA (mean difference -0.1 ± 0.01 logMAR; paired t-test $p=0.35$) and SA ($29 \pm 8''$; $p=0.4$). On average, TSR takes 4.9 ± 1.5 min while each repetition of DSR takes 47 seconds (per eye, including sphere). In direct comparisons, 50% of subjects preferred the final correction with DSR over with TSR

Conclusions: Using temporal defocus waves, DSR is able to measure astigmatism, providing similar values than the TSR, but more repeatable. Each unsupervised DSR measurement (sphere and astigmatism) takes less than one minute, allowing clinicians to spend more time evaluating other visual aspects

CONTROL ID: 3542708

SUBMITTER (NAME ONLY): Ting Su

TITLE: OCT4 and YY1 transcription factors regulate gene expression of an adenoviral ocular pathogen

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There are about 20 million ocular adenoviral cases per year in the United States. Epidemic keratoconjunctivitis (EKC) is the most highly contagious and most severe of these. EKC manifests with acute membranous keratoconjunctivitis and delayed-onset of corneal stromal infiltrates. Transcription factors (TFs) are sequence-specific DNA binding proteins. As intracellular parasites, viruses hijack host cellular proteins, including TFs, to control their gene expression and replication. We investigated the role of host TFs in the transcriptional regulation of a major EKC pathogen - human adenovirus species D type 37 (HAdV-D37).

Methods: We first performed in silico TRANSFAC database analysis to identify TF candidates for binding to the HAdV-D37 genome. Next, chromatin immunoprecipitation and high-throughput sequencing (ChIP-Seq) were performed in virus-infected A549 cells, including the TF YY1, previously reported to bind E1A. From the high-throughput sequencing reads (HiSeq 2500 system, illumina), motif analysis was performed, and the specific TF-viral DNA binding sites were validated by electrophoretic mobility shift assays (EMSA). Gene expression was studied in the setting of both TF-siRNA knockdown and overexpression, using RT-qPCR for viral transcripts spanning the whole genome.

Results: In silico analysis showed OCT4 as the TF with greatest binding affinity for the HAdV-D37 genome. By ChIP-Seq analysis, OCT4 and YY1 were shown to directly bind the viral DNA motifs, ATTTGCAT and CGCCATCTT, respectively, present in the non-coding regions of the inverted terminal repeat (ITR) and adjacent to E4 target genes. Both OCT4 and YY1 were shown to repress E3 (immune evasion genes) expression. Additionally, YY1 knockdown upregulated viral early gene expression, including E1B, E2A, and E2B.

Conclusions: OCT4 and YY1 directly bind to HAdV-D37 and downregulate E3 gene expression, potentially modulating host immune responses to infection. Our findings provide novel functions for non-coding viral DNA; in depth understanding of viral gene expression offers a unique perspective to treatment of ocular viral disease.

CONTROL ID: 3542718

SUBMITTER (NAME ONLY): Eric Enyong

TITLE: Compositional analysis of non-caveolar Caveolin-1-containing domains in Müller glia

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Caveolae, flask-shaped plasma membrane containing caveolin-1 (Cav1) and Cavin1/PTRF, are thought to play important roles in several ocular diseases. Cav1 and Cavin1/PTRF are co-expressed in many tissues, and deletion of one significantly downregulates expression of the other, resulting in loss of caveolae. Cavin1/PTRF is required to sequester Cav1 into caveolae and is the only protein reported to have a stabilizing effect on Cav1. However, our data suggest that in Müller glia, Cav1 protein is stable without Cavin1/PTRF and exists preferentially outside caveolae (non-caveolar Cav1). Our goal is to identify the mechanism of Cav1 stabilization and define the protein components of non-caveolar Cav1 domains in Müller glia. Herein, we present proteomic data on Cav1-containing domains in the presence and absence of Cavin1/PTRF

Methods: We used quantitative mass spectrometry (MS), to assess the protein composition of non-caveolar Cav1 immunoprecipitates (IPs) from immortalized Müller glia (MIO-M1) cells and compared this composition to Cav1 IPs from cells transduced with adenovirus driving expression of Cavin1/PTRF. The Core Laboratory for Molecular and Cytometry Research at the University of Oklahoma Health Sciences Center performed MS analysis using the Thermo Lumos Fusion tribrid Orbitrap mass spectrometer. We used STRING database to predict protein interaction networks and molecular pathways.

Results: We have previously identified that Cav1 protein is stable in MIO-M1 cells without Cavin1/PTRF and are devoid of morphologically-identifiable caveolae. Expression of recombinant Cavin1/PTRF in MIO-M1 cells resulted in dramatic increases in caveolae as determined by transmission electron microscopy. Mass spectrometric analysis of Cav1 immunoprecipitates from Cavin1/PTRF-transduced and control cells revealed 175 proteins differentially-associated with Cav1 when Cavin1/PTRF is expressed (40 with increased association, including the expressed Cavin1/PTRF; 135 with decreased association). Proteins with significantly increased association included actin cytoskeletal components. Intriguingly, a number of ribosomal proteins showed significantly decreased association with Cav1 when Cavin1/PTRF was expressed

Conclusions: Cavin1/PTRF expression in MIO-M1 significantly increases actin cytoskeleton interaction with caveolae and reduces ribosomal association with non-caveolar domains

CONTROL ID: 3542724

SUBMITTER (NAME ONLY): Cayla Ontko

TITLE: Cannabinoid Receptor 2 Agonist HU-308 Demonstrates Therapeutic Potential in Inflammatory Diabetic Retinopathy Models

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ontko, Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|M.J. Kim, T.E. Smith, G.W. McCollum, R. Yang, J. Penn, Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Increased retinal and vitreous levels of inflammatory cytokines are observed in early diabetic retinopathy (DR) progression and are experimentally linked to several hallmark DR features, including leukostasis and vascular hyperpermeability. Cannabinoid (CB) receptor 2 agonism has been shown to decrease inflammatory cytokine production and leukocyte recruitment in various non-ocular inflammation models, suggesting that CB2 agonism could have similar therapeutic potential in DR-related inflammation. This study tested the potential of CB2-selective agonist, HU-308, to attenuate DR pathologies in response to diabetes-relevant inflammatory stimuli (DRS), including increased inflammatory cytokine expression, adhesion molecule expression, leukostasis, and vascular hyperpermeability.

Methods: Primary human Müller cells (hMC) were treated with IL-1 β (1ng/ml) for 8hrs, and HU-308 (0.1uM) was added at the onset of treatment and again 4hrs later. Human retinal microvascular endothelial cells (HRMEC) were pre-treated with HU-308 (1uM) for 2hrs and TNF α (0.1ng/ml) was added for an additional 2hrs. Relative expression of inflammatory mediators and leukocyte adhesion molecules was analyzed via qRT-PCR. To investigate vascular responses in vivo, C57BL/6 mice received daily IP injections of HU-308 (5.0mg/kg) for 1wk prior to receiving an intravitreal injection of TNF α (25ng/ml). Quantitative fluorescein angiography (qFA) and leukostasis analyses were performed 6 and 12hrs later, respectively.

Results: HU-308 significantly decreased IL-1 β -induced expression of IL-1 β by 29.5% ($p=0.0295$) in hMC. HU-308 significantly decreased TNF α -induced expression of leukocyte adhesion molecules ICAM-1 by 26.8% ($p=0.0380$) and E-selectin by 21.7% ($p=0.0141$) in hRMEC. In vivo, systemic HU-308 significantly decreased TNF α -induced leukostasis by 55.3% ($p=0.0401$) and TNF α -induced vascular hyperpermeability by 74.7% ($p=0.0039$).

Conclusions: Consistent with our hypothesis, CB2 agonism was found to decrease cellular cytokine expression and leukocyte adhesion molecule expression in response to DRS, as well as decrease leukostasis and vascular hyperpermeability in an in vivo model of acute retinal inflammation. These results demonstrate that CB2 agonism has significant therapeutic potential for preventing retinal inflammation characteristic of early DR.

CONTROL ID: 3542731

SUBMITTER (NAME ONLY): Alyra Shaw

TITLE: Conjunctival and Scleral Thicknesses with and without Conjunctival Ultraviolet Autofluorescence

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Shaw, P. Rajasingam, B.A. Davis, M.J. Collins, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Ultraviolet autofluorescence (UVAF) is a clinical technique used to visualise conjunctival changes thought to be due to excessive sunlight exposure and so is considered to be an outdoor sunlight biomarker with UV damage and myopia applications. We performed an experimental observation study aimed to measure the conjunctival and scleral thicknesses in participants with and without conjunctival UVAF to better understand the underlying tissues changes.

Methods: Conjunctival UVAF photographs (Nikon D90, 375 nm LEDs) and anterior OCT volume scans (Heidelberg, Spectralis) of the right eye were taken on 42 participants with healthy eyes aged between 19 and 43 years of age. The participants were classified according to the presence or absence of UVAF on the temporal and nasal conjunctivas of the right eye, resulting in 4 groups (Table 1).

The OCT images of the temporal conjunctiva were exported and analysed with a previously reported semi-automated procedure using custom written software. From these segmentations, tissue thicknesses were determined for the conjunctival epithelium, conjunctival stroma and sclera for the 21 horizontal line scans analysed between 0 to 4 mm from the scleral spur.

Results: Significant differences in thickness for all 3 tissues were observed with the presence of UVAF with a thinner conjunctival epithelium, thicker conjunctival stroma and thicker sclera (ANOVA $p < 0.001$). The UVAF area was located in the lower half of scans (lines 1 to 10) for the majority of the participants, where the greatest conjunctival stromal thickness changes occurred. Groups 3 and 4 (those with temporal UVAF) had the thickest conjunctival stromas (Figure 1). The temporal conjunctival stroma was thinner for group 1 (neither nasal or temporal UVAF) compared to group 2 (which also had no temporal UVAF, only nasal UVAF) (ANOVA posthoc analysis $p < 0.001$).

Conclusions: The conjunctival epithelium, conjunctival stroma and sclera all had significant changes in tissue thickness with the presence of UVAF. A significant difference in temporal conjunctival stromal thickness was observed when the presence of both nasal and temporal UVAF was considered, suggesting that the tissue may be thickening before UVAF is visible. This may help to further understand the sunlight-related damage to this tissue.

CONTROL ID: 3542732

SUBMITTER (NAME ONLY): Fabio Feroldi

TITLE: Optoretinography in the human retina using AOOCT and AOSLO-based eye tracking

SESSION TITLE: Advanced imaging technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Feroldi, S. Mozaffari, F. LaRocca, P.K. Tiruveedhula, A.J. Roorda, School of Optometry and Vision Science Graduate Group, University of California Berkeley, Berkeley, California, UNITED STATES|P. Gregory, B. Park, Department of Bioengineering, University of California Riverside, Riverside, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optoretinography is a novel technique that uses light-based measurements to reveal retinal activity. Adaptive optics optical coherence tomography (AOOCT) produces an optoretinogram by resolving individual photoreceptors and recording their physical/physiological responses to light stimuli. However, detecting the nanometer-scale changes measured by AOOCT to obtain optoretinograms is hampered by eye motion. In other laboratories, careful registration of a sequence of volume images is required. Here, we present a system whereby real time eye tracking based on adaptive optics scanning laser ophthalmoscopy (AOSLO) is used to correct the position of the AOOCT beam and compensate eye motion.

Methods: The custom AOOCT system is based on a swept source laser centered at 1040 nm with a sweep rate of 100 kHz and an axial resolution of 7 μm in tissue. A dichroic mirror combines the AOSLO and AOOCT beams, which share the AO correction but have independent scanning systems. AOSLO is used to visualize the photoreceptor layer in real time and report eye movement at a 960 Hz rate using strip-based registration. The AOOCT beam was stabilized on the retina by actuating a MEMS mirror in the beam path counter to the eye movement. A 100 ms long flash of narrowband light was deposited on a dark adapted retina to stimulate the photoreceptors. Nanometer-scale changes within a targeted set of cones were obtained by measuring the phase difference between the inner/outer segment junction and the cone outer segment tips as a function of time.

Results: The physiological response of the photoreceptors was revealed as an elongation of the cone outer segment in response to the stimulus. By quantifying the physiological changes, we were able to identify cones belonging to different spectral sub-classes, and we confirmed the result over datasets acquired in separate occasions.

Conclusions: We were able to successfully quantify the response of individual photoreceptors to light stimuli, paving the way to obtain optoretinograms for classifying the cones and measuring other neural activity in the human retina.

CONTROL ID: 3542735

SUBMITTER (NAME ONLY): Jonathan Zippin

TITLE: Inhibition of soluble adenylyl cyclase (sAC) rescues defective melanosomal pH and pigmentation in oculocutaneous albinism type 2 (OCA2).

SESSION TITLE: Advances in intra and extra ocular pathologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Zippin, M. Yusupova, D. Zhou, Weill Cornell Medicine, New York, New York, UNITED STATES|K. Wakamatsu, Fujita Health University, JAPAN|

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ABSTRACT BODY:

Purpose: OCA2 is caused by mutations in an ion channel critical for the maintenance of the pH set-point of the melanosome, the organelle that makes melanin. Melanosomal pH controls pigmentation because tyrosinase is pH sensitive. Currently, there are no treatment options for patients who suffer from OCA2. We discovered that the sAC cAMP pathway regulates melanosomal pH. We hypothesize that inhibition of sAC would correct melanosomal pH and pigmentation in OCA2 melanocytes and mice.

Methods: We measured melanosomal pH in wild type and OCA2 loss of function (LOF) melanocytes using the pH sensitive molecule DAMP and microscopy. We measured melanosomal pH on a per-organelle level and assessed changes across thousands of melanosomes and multiple cells (n=30). We measured tyrosinase activity in live melanocytes using ³H-tyrosine and detecting the accumulation of ³H-H₂O in the media (n=10). We generated a OCA2^{-/-}, sAC floxed (f/f), Tyr-CRE-ERT2 mouse model to study the effects of sAC LOF in tyrosinase expressing cells on an OCA2 LOF background. sAC LOF was induced on post-natal days 2-4 by topical application of 4-hydroxytamoxifen to the skin and eyes. Pharmacological inhibition of sAC was conducted by daily intraperitoneal (IP) injection of sAC inhibitors (36mg/kg) for one month.

Results: sAC inhibition restored melanosomal pH and tyrosinase activity to normal levels in OCA2 melanocytes. Oca2^{-/-};sAC^{-/-} (sACKO) mice (n=20) had darker hair color at P28 as compared to Oca2^{-/-};sAC^{f/f} (sACWT) littermates (n=9). HPLC analysis of hair showed a significant increase in total melanin in sACKO mice. In addition, iris and choroid pigmentation was significantly increased in sACKO mice as measured by slit lamp (n=23) and Fontana-Masson staining (n=5) as compared to sACWT mice (n=14 and n=4, respectively). Electromicroscopy of sACKO eyes (n=5) revealed an increase in mature melanosomes in both melanocytes and RPE cells as compared to sACWT littermates (n=4). Furthermore, IP injection of sAC inhibitors increased pigmentation of Oca2^{-/-} eyes as compared to vehicle (n=4).

Conclusions: Our data reveals that restoration of normal melanosomal pH by inhibition of sAC can improve the pigmentation of cells and mice with OCA2 LOF. We propose that therapeutics designed to restore melanosomal pH may provide treatment opportunities for patients with OCA2 and other forms of albinism.

CONTROL ID: 3542739

SUBMITTER (NAME ONLY): Stuart Gardiner

TITLE: Clinicians' Use of Quantitative Information when Assessing Structural Progression in Glaucoma

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.K. Gardiner, R. Kinast, S.L. Mansberger, Devers Eye Institute, Portland, Oregon, UNITED STATES|T.C. Chen, Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|T.C. Chen, Harvard Medical School, Boston, Massachusetts, UNITED STATES|N.G. Strouthidis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|N.G. Strouthidis, Discipline of Clinical Ophthalmology and Eye Health, University of Sydney, Sydney, New South Wales, AUSTRALIA|C. De Moraes, Columbia University Irving Medical Center, New York, New York, UNITED STATES|K. Nouri-Mahdavi, Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|J. Myers, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Jeoung, Seoul National University Hospital, Jongno-gu, Seoul, KOREA (THE REPUBLIC OF)|J. Lind, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|L.A. Rhodes, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|D.L. Budenz, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: OCT scans contain large amounts of information which clinicians must consider when assessing the rate of glaucomatous progression. Yet images of the scans are small, so clinicians rely heavily on quantitative information provided in the form of global and sectoral layer thicknesses. We investigated which of these quantitative measures are most closely related to the subjective assessment of glaucoma experts who had all the OCT information available.

Methods: Eleven glaucoma specialists independently assigned scores for the rate of structural progression based on series of 5 biannual Heidelberg Spectralis OCT printouts from 100 glaucoma or glaucoma suspect eyes, from 51 participants in the Portland Progression Project longitudinal study. They also reviewed 20 of the series twice to assess repeatability. Scores were on a scale from 1 (improvement) to 7 (very rapid progression), and were averaged among clinicians. Generalized estimating equation linear models, weighted by intra-eye inter-clinician score variability, were used to predict the mean clinician score from the rates of change of Retinal Nerve Fiber Layer Thickness (RNFLT) or Bruch's Membrane Opening Minimum Rim Width (MRW), either globally or in the most rapidly thinning of the six sectors presented by the instrument's software.

Results: The average global RNFLT within the series was 79.3 μ m (range 41.4 to 126.6); average global MRW was 214.4 μ m. Of individual clinician scores, 95% varied by ≤ 1 point when repeated. The average mean clinician score was 2.6 (standard deviation 0.7, range 1.5 to 4.8). This score was more strongly correlated with the rate of change of RNFLT in the most rapidly changing sector ($R^2=0.657$ when expressed in %/y, or $R^2=0.582$ using μ m/y) than with the global RNFLT rate ($R^2=0.372$ and 0.305 respectively); see Figure 1. These comparisons persisted, albeit with smaller differences in R^2 , when the three outliers with apparent thickening of the RNFLT were excluded. Correlations with the rate of MRW thinning were consistently weaker (maximum $R^2=0.149$ for the most rapidly changing sector in %/y) than those for RNFLT for both global and sectoral analyses; see Figure 2.

Conclusions: The percentage rate of change of RNFLT in the most rapidly changing sector predicted experts' assessment of the rate of structural progression better than global rates. Sectoral RNFLT rates may be a useful addition to current clinical printouts.

CONTROL ID: 3542743

SUBMITTER (NAME ONLY): Sarah John

TITLE: Developing a deep learning classifier for uveitis scoring on mouse OCT images

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. John, J.J. Na, S. Swaminathan, L. Wilson, Y. Wu, K. Pepple, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop and validate an automated approach to scoring OCT images of ocular inflammation in experimental animals using deep learning.

Methods: Ocular inflammation was generated using the primed mycobacterial uveitis (PMU) model. Anterior chamber and posterior chamber optical coherence tomography (OCT) images were obtained using the Envisu R2300. On each image, degree of inflammation was classified using a 6 step categorical system with scores ranging from 0-4+ by three masked graders (A). Training set images were labeled with the score assigned by at least 2 out of the 3 graders. Images were divided into a training, validation and test set in a 80:10:10 ratio and a Deep Learning classifier algorithm based on a modified ResNet50 but allowing higher resolution images, was developed. Accuracy of the classifier compared to the human score was determined for anterior and posterior chamber images separately. Agreement between the classifier and the human graders was determined using Cohen's linear weighted Kappa. Comparison between human and classifier scores was performed using a confusion matrix on the test set.

Results: 1115 images (575 anterior chamber, 540 posterior chamber) were scored by human graders. Agreement between human graders was 0.87 and 0.83 on AC and PC images respectively. Agreement between the automated classifier and the human graders was 0.56 and 0.68 for AC and PC respectively. Absolute accuracy of the automated classifier was 56% for AC images and 57% for posterior images. The confusion matrix analysis (B) determined that accuracy was highest for scores of 0 which was also the most frequent score in the training set.

Conclusions: In this study, we found that human graders demonstrated strong agreement if one step differences inscore were accounted for with a weighted kappa. This is consistent with prior studies of inter-human agreement scoring in uveitis. Automated classification did not perform as well as human graders. Better performance and agreement between the automated and human graders was identified for posterior chamber images than on anterior chamber images. Performance was likely limited by the disproportionate number of score 0 images in the training set. Additional images at each score level will be required to improve classification accuracy.

CONTROL ID: 3542745

SUBMITTER (NAME ONLY): Kai Kang

TITLE: Diet-induced gut dysbiosis alters corneal immune cell distribution and gene expression in response to wounding

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kang, Q. Zhou, L. McGinn, Y. Luo, D. Skondra, A.R. Djalilian, M. Rosenblatt, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies have shown that commensal microbiome secretes various metabolites that can exert important effects on the host immunity, control inflammation and alter cellular biological functions. The gut microbiome is strongly altered by diets. However, little is known regarding the effect of microbiome on corneal immunity and corneal genetic expression. The purpose of this study is to describe the effect of diet-induced gut dysbiosis on corneal immunity and corneal gene expression after wounding.

Methods: This study is approved by the Animal Care and Use of the University of Illinois at Chicago. Five-week-old female C57BL6 mice were fed on a normal chow diet (ND), isocaloric low fat control diet (LD) or a 21% milk fat diet (simulating a Western Style, WD) for six weeks. A 2mm corneal epithelial debridement was performed(n=10). Cecal samples from mice were used for microbial diversity analysis(n>3). Immunofluorescence staining of corneal wholemount tissue at time 0 and 18 hours of debridement was used to visualize immune cell distribution, including anti-CD45, anti-LY6G, anti-TCR delta gamma, etc. RNA Seq using Illumina NovaSeq 6000 was performed from corneas 18 hours post debridement. RNA STAR was used to align transcripts to mm10 mouse genome. DESeq2 was used to perform differential gene analysis.

Results: Mice fed different diets had significant alterations in gut microbial alpha and beta diversities. After corneal debridement, increased TCR was observed in LD group, and decreased LY6G was observed in HFD group ($p<0.05$). 3158 genes were differentially expressed with 225 genes with greater than two-fold change. Go terms of differentially expressed genes included responses to external stimulus, cell proliferation, migration, adhesion, defense response, immune system process, leukocyte migration, etc. Top over-represented KEGG pathways included ECM-receptor interaction, Cytokine-cytokine receptor interaction, Focal adhesion, Hematopoietic cell lineage, Leukocyte transendothelial migration, etc.

Conclusions: Gut microbial dysbiosis may alter corneal immune cell distribution and genes related to epithelial function and corneal immunity.

CONTROL ID: 3542746

SUBMITTER (NAME ONLY): Jeffry Hogg

TITLE: The prevalence and impact of treatment delays in exudative age-related macular degeneration

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Hogg, O. Gkorou, H.J. Duncan, L.G. Stone, M. Blyth, L. Brandes, A. Devenport, L. Timms, J.S. Talks, Newcastle Eye Centre, Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|J. Hogg, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: There is a growing imbalance between clinical demand and capacity for exudative age-related macular degeneration (exAMD) in the UK National Health Service (NHS), but the degree of consequential sight loss remains unclear. This retrospective, observational clinical study aimed to quantify the delays to treatment which patients experience in a representative NHS centre, and to describe the associated visual outcomes.

Methods: The electronic medical record of a large provincial UK ophthalmology centre was interrogated for eyes diagnosed with exAMD in 2016 and treated with intravitreal injections (IVI) of aflibercept over a minimum of 3 years. The difference between all clinic appointments' planned and observed dates were calculated and totalled separately for each of the first 3 years of treatment. As a pragmatic observational study visual acuity (VA) was recorded as the best of unaided, spectacle corrected or pinhole corrected VA in early treatment of diabetic retinopathy (ETDRS) letters at the end of each year of treatment as well as the number of IVIs received. Descriptive and comparative statistics were performed with SPSS v.24 and unpaired t-tests were used to compare means.

Results: 175 eyes (89 left, 87 pseudophakic) from 175 patients (109 female, mean age 79.1 years) were identified. Mean VA change over a year of treatment was 5.3, -2.3 and -0.8 ETDRS letters with a mean of 1.8, 3.6 and 2.7 weeks of cumulative treatment delay in the first, second and third years of treatment respectively. 24 (14%), 49 (28%) and 42 (24%) eyes experienced a cumulative delay to planned treatment of 4 weeks or more in the first, second and third years of treatment respectively. VA change over a year of treatment was worse for patients experiencing 4 weeks or more of cumulative delay compared to those that did not, with mean changes of -0.6 (95%CI -6.0,4.8) versus 6.3 (4.1,8.4), -3.9 (-6.5,-1.2) versus -1.7 (-3.2,-0.1) and -3.7 (-6.3,-1.2) versus 0.1 (-1.4,1.6) over the first (p=0.02), second (p=0.15) and third (p=0.01) years of treatment respectively.

Conclusions: It is common for NHS exAMD patients to experience significant delays in their treatment, either due to service capacity or patient factors. These delays compromise visual outcomes, particularly within the first year. These data evidence the need for increasing care capacity and improving patient adherence to treatment for exAMD within NHS services.

CONTROL ID: 3542747

SUBMITTER (NAME ONLY): David Myung

TITLE: Bio-orthogonally Crosslinked Matrix Therapies for Corneal Defect Repair

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Myung, F. Chen, G. Fernandes-Cunha, P. Le, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|D. Myung, F. Chen, Ophthalmology, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|S. Hull, Chemical Engineering, Stanford University, Stanford, California, UNITED STATES|S. Heilshorn, Materials Science & Engineering, Stanford University, Stanford, California, UNITED STATES|
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ABSTRACT BODY:

Purpose: There remains a major clinical need for ways to overcome the shortage of cadaveric donor tissue needed to surgically treat corneal blindness worldwide. Our goal is to engineer matrix therapy that stabilizes deep corneal wounds and promotes epithelial regeneration and stromal remodeling without the need for a catalyst, light-activation, sutures, or donor tissue.

Methods: We have developed crosslinked matrices of collagen as well as collagen and hyaluronic acid that form under ambient conditions through strain promoted azide-alkyne cycloaddition (SPAAC), a bio-orthogonal form of copper-free click chemistry, after being applied to deep corneal wounds without the need for a catalyst or light energy source. In vitro cell culture, ex vivo organ culture, and in vivo rabbit corneal keratectomy models were used to evaluate the biologic activity of the gel constructs out to 2 months post-operatively. Slit lamp exam, fluorescein staining, anterior segment optical coherence tomography, pachymetry, tonometry, and immunohistochemistry were used to evaluate the corneas post-treatment.

Results: Collagen and collagen-hyaluronic acid gels crosslinked by SPAAC form in situ within minutes when applied to deep keratectomy wounds under ambient conditions without the need for a catalyst or light energy. We found that the hydrogels could be cured under an air interface or under a bandage contact lens, and could restore the smooth outer curvature of a keratectomized cornea. SPAAC crosslinking yielded gels that support multi-layered surface epithelialization, tight junction formation, new basement membrane deposition, and normal IOP and corneal thickness, and complete matrix remodeling at 2 months.

Conclusions: Bio-orthogonally crosslinked gels form in situ on corneal wounds under ambient conditions through copper-free click chemistry without the need for an external catalyst or light energy source. The gels support surface epithelialization and stromal remodeling out to 2 months, which suggests their promise as a therapeutic matrix for suture-free reconstruction of deep corneal wounds.

CONTROL ID: 3542750

SUBMITTER (NAME ONLY): Hailey Mair

TITLE: Rare case of Wolfram-like Syndrome case due to a missense WFS1 mutation

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Mair, N. Fowler, P. Sudhakar, R. Maldonado, University of Kentucky College of Medicine, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: In contrast to the classic autosomal recessive Wolfram syndrome, Wolfram-like Syndrome (WLS) is a rare, autosomal dominant disease caused by mutations in the WFS1 gene. It presents with optic atrophy, sensorineural hearing loss and diabetes mellitus. Here, we present a case of WLS without endocrine manifestations caused by a heterozygous missense WFS1 variant (c.2508G>T, p. Lys826Asn).

Methods: Single case with a heterozygous WFS1 variant (c.2508G>T, p.Lys836Asn), ophthalmic examination, multimodal imaging and genetic testing will be discussed.

Results: A 28-year-old Greek male was referred to our clinic for evaluation of bilateral optic nerve atrophy of unknown cause. Review of systems revealed bilateral sensorineural hearing loss for which he requires hearing aids. Family history was significant for early-onset severe hearing loss in his mother. The patient had best corrected visual acuity of 20/30 and 20/40 in the right and left eye, respectively. Pupillary responses, intraocular pressures and anterior segment exam were unremarkable. Fundus exam revealed normal appearance of the retina and bilateral tilted and pale optic nerves. Testing showed reduced contrast, color and depth perception. Visual fields showed supero-temporal and infero-nasal defects in both eyes. Optical coherence tomography revealed retinal nerve fiber layer global thinning in both eyes measuring 49 and 46 microns in the right and left eye, respectively. In addition, ganglion cell layer thickness was significantly reduced OU. MRI of the head and orbits was unremarkable. Blood work for toxic, infectious and nutritional causes of optic neuropathy were normal. Genetic testing was negative for mutations in OPA1, OPA3 and LHON panel; however, it revealed a heterozygous missense variant in WFS1 gene (c.2508G>T, p.Lys836Asn). To date, this variant is not present in gnomAd database and predicted to be pathogenic by in silico tools. His fasting blood glucose was 96mL/dL and hemoglobin A1C was 4.9%.

Conclusions: We present deep phenotyping of a previously described WFS1 variant (c.2508G>T, p. Lys836Asn) (Hogewind B. F., Pennings R. J., Hol F. A., et al. Autosomal dominant optic neuropathy and sensorineural hearing loss associated with a novel mutation of WFS1. Molecular Vision. 2010;16:26–35.). Our findings confirm this heterozygous variant in WFS1 as a cause of optic atrophy and hearing loss without neurologic, cardiac or endocrine problems.

CONTROL ID: 3542751

SUBMITTER (NAME ONLY): Shaohua Pi

TITLE: Characterization of retinal structural and vascular pathologies in Royal College of Surgeons rat using visible-light OCT

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Pi, B. Wang, R.C. Ryals, Y. Jia, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Royal College of Surgeons (RCS) rat is a prominent photoreceptor degeneration model that is often used to determine the safety and efficacy of prospective age-related macular degeneration and retinitis pigmentosa therapies. We aim to characterize retinal structural and vascular pathologies in RCS rat using visible-light optical coherence tomography (vis-OCT).

Methods: The retinas of pigmented RCS rats (9 animals) were scanned by a fiber-based vis-OCT system with a 1.7 μm axial resolution, 70 kHz A-scan rate, 100 nm-bandwidth wavelengths centered at 560 nm. The animals were anesthetized with ketamine (80 mg/kg) / xylazine (5 mg/kg) cocktail. Volumetric raster scans were acquired near optic disc at the age of 1 month, 3 months, and 8 months. Each scan contains 256 A-lines in each B-scan, 2 repeated B-scans at each Y-location, and 256 Y-locations in 2×2-mm or 1×1-mm regions. Retinal layers were segmented, and the retinal thickness maps and en face angiograms of inner retina were generated.

Results: At the age of 1 month, the RCS rats demonstrated normal retinal structure and vasculature. The outer plexiform layer (OPL) and outer nuclear layer (ONL) are clearly visualized from the OCT B-scans (Fig. 1). Nerve fiber bundles and inner retinal vessels with normal densities are demonstrated by their en face images. At the age of 3 months, the ONL disappears indicating the photoreceptor loss. However, the retinal vasculature and nerve fiber bundles appear not be affected by the thinning of retinal tissue. At the age of 8 months, the pathologies progress more dramatically - inner nuclear layer (INL) and OPL also vanish. At this stage, we can see damaged nerve fiber bundles and poor retinal perfusion.

Conclusions: High resolution OCT and OCTA at visible light band can be used to characterize retinal dystrophy in RCS rats. This preliminary study suggests retinal vasculature could be impaired as a consequence of neuronal cell death.

CONTROL ID: 3542753

SUBMITTER (NAME ONLY): Kenneth Kenyon

TITLE: Efficacy and Safety of the Melanocortin Agonist PL9643 in a Phase 2 Study of Subjects With Dry Eye Disease

SESSION TITLE: Dry eye clinical treatments

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Dry eye disease is a multifactorial inflammatory and aqueous tear deficiency characterized by ocular irritation and potential visual impairment. As melanocortin agonists may represent a novel therapeutic avenue to treat inflammatory ocular diseases, this phase 2 study evaluated efficacy and tolerability of the melanocortin receptor pan-agonist PL9643 in adults with dry eye disease.

Methods: This randomized, placebo-controlled, double-masked study enrolled subjects with mild, moderate, or severe dry eye disease. All subjects received placebo solution (vehicle diluent) during a 2-week run-in period; selected subjects were then randomized 1:1 to receive either placebo or PL9643 topical ophthalmic solution bilaterally 3 times daily for 12 weeks. Co-primary endpoints were changes in inferior corneal fluorescein staining and ocular discomfort (Ora Calibra[®] scale) after 12 weeks. Secondary endpoints were changes in additional signs and symptoms of dry eye after 2 and 12 weeks, as well as the occurrence of adverse events (AEs) throughout the study. Efficacy endpoints were evaluated in the intent-to-treat (ITT) population and in the subset of subjects with moderate or severe dry eye disease.

Results: In the overall ITT population (N=160), significant improvements in corneal staining or ocular discomfort were not observed after 12 weeks. However, in the subset of subjects with moderate or severe disease (n=61), significant improvements were observed in the primary sign endpoint, inferior corneal fluorescein staining (LS mean difference [SEM], -0.5 [0.2], P<0.05), as well as in multiple other signs (superior and total corneal staining; temporal and total conjunctival staining) and symptoms (ocular discomfort) after 2 or 12 weeks. No treatment-related serious or ocular

AEs were observed, and no subjects receiving PL9643 reported ocular instillation pain. Fewer AEs occurred among subjects receiving PL9643 compared with placebo.

Conclusions: In subjects with moderate or severe dry eye disease, ophthalmic PL9643 solution led to significant subjective and objective benefits by the first evaluation at 2 weeks and maintained for 12 weeks. PL9643 was well tolerated, with a safety profile comparable to placebo. Positive results across multiple signs and symptoms support the continued development of PL9643 as a novel therapeutic method for treating dry eye disease.

CONTROL ID: 3542756

SUBMITTER (NAME ONLY): Sara Beqiri

TITLE: Investigating the impact of saliency maps on clinician's confidence in model predictions

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Saliency maps have gained popularity in medical artificial intelligence (AI) studies due to their ability to highlight significant regions for model prediction, allowing greater interpretability of models and raising the prospects of their integration in clinical practice. This study explores whether saliency maps increase clinician confidence in diagnosis via an AI supported workflow.

Methods: 60,133 retinal fundus photography images and labels were gathered from public datasets. These were used to train a classification model on the Google AutoML platform to detect referable and non-referable diabetic retinopathy. Saliency maps were produced using the XRAI algorithm supported by the same platform, providing region-based attribution, suitable for fundus images.

A survey was sent to 6 participants, including 4 ophthalmologists with fellowship-level subspecialty training in retinal disease, and two ophthalmology trainees. They were shown 50 randomly selected images, each repeated 3 times. The image was first presented with the predicted class, secondly by class and Softmax score, thirdly by including a heatmap. After each assistance level, the readers rated their confidence in the prediction via a 5-point Likert scale.

Results: Paired tests showed a significant difference in confidence rating between all assistance types, with saliency maps performing the poorest (3.12 ± 1.28 , $P < 0.001$). On a second analysis, we separated predictions into correct and incorrect groups. The unpaired test results show that heatmaps accompanying incorrect labels were associated with a lower confidence than correct ones (incorrect: 2.14 ± 1.15 , correct: 3.23 ± 1.25 , $P < 0.001$). Similarly, we considered the impact of referable and non-referable cases separately. Results showed no significant difference in confidence from heatmaps between the categories ($P = 0.097$).

Conclusions: Our results show that XRAI heatmaps are associated with lower confidence in model predictions compared to the other two strategies. We emphasize the importance of considering their impact specifically for incorrect predictions and non-referable DR. For the prior, saliency could cause confirmation bias, whereas for the latter, it may mislead if there are no positive findings. Whilst saliency may be of at least some value in model interpretability, for its implementation as diagnostic assistance, higher standards of localisation and meaningful rationale are required.

CONTROL ID: 3542758

SUBMITTER (NAME ONLY): Qingying Jin

TITLE: Association of patient race and Hispanic ethnicity with age and severity of glaucomatous vision loss at first visit

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate associations of patient race and Hispanic ethnicity with age and severity of visual field loss in glaucoma patients at first visit.

Methods: All patients from Mass. Eye and Ear glaucoma service with Humphrey visual field (VF) measurements (SITA Standard or Fast 24-2) and an electronically available, questionnaire based self-reported race as either African, Asian, or European were selected. Hispanic ethnicity was represented as a questionnaire item separate from race. Age at the time of the first visual field measurement was associated with race as well as self-reported Hispanic ethnicity. Among all reliable (false positive/negative rate $\leq 20\%$, fixation losses $\leq 33\%$) first VF measurements of each patient, analogous race and ethnicity associations with VF mean deviation (MD) as a measure of glaucoma severity were determined.

Results: Among the 17,275 selected patients (56.5% female), 2,746 identified their race as African, 1,443 as Asian, and 13,086 as European; 869 did not respond to the Hispanic ethnicity item, while 427 identified as Hispanic (70 African, 6 Asian, 351 European). There was a significant (ANOVA, $p < 0.001$) main association between race and age at first visit (Fig. 1), with Asian being youngest patients (56.2 years), followed by Africans (57.7 years) and Europeans (62.2 years). Patients with Hispanic ethnicity were on average 6.3 years younger (54.8 years) at first visit (t-test, $p < 0.001$). Among the 17,275 first VFs of each patient, 13,918 met the reliability criteria. There was a significant race association with MD ($p < 0.001$; Fig. 2), with patients of African race having the most severe VF loss at first visit (-6.5 dB), followed by Asian (-4.4 dB) and European race (-3.6 dB). Hispanic patients had lower MD (-6.1 dB) than patients of non-Hispanic ethnicity (-4.0 dB) ($p < 0.001$). While Hispanic ethnicity among patients of African race was not associated with MD, among patients of European race, Hispanics had 2.2 dB lower MD at first visit ($p < 0.001$).

Conclusions: Patients of African and Asian race present younger at glaucoma service but still have more severe vision loss at first visit compared to European race patients. While Hispanic ethnicity among patients of African race was not associated with glaucoma severity, Hispanics or European race had significantly lower MD than patients of non-Hispanic European race.

CONTROL ID: 3542760

SUBMITTER (NAME ONLY): Alan Labrum

TITLE: Six Feet of Separation: Physical Distancing Impacts on Blind and Low Vision During COVID-19 Pandemic

SESSION TITLE: Visual Impairment during a pandemic

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Labrum, K. Marxen-Simonson, T. Zaback, A. Rule, J. Boyer, M. Brinks, Ophthalmology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Individuals with vision loss are experiencing new and unique challenges due to physical distancing during the COVID-19 pandemic. We conducted a cross sectional study to understand challenges and to learn about adaptive strategies employed.

Methods: The Casey Eye Institute EHR (EPIC) was queried for patients meeting the following criteria: best corrected visual acuity of 20/70 or worse in the better seeing eye; age 18-100, and active email address. 762 requests for participation in completing a 23-question survey were emailed via REDcap and responses were received from 46 patients; 19 male and 27 female. The data was analyzed using SPSS statistical software. Comparisons were made between age, duration of visual impairment, severity of visual impairment to effects of physical distancing and adaptive strategies. Comparisons were made using the chi-squared test.

Results: 44% of participants reported that physical distancing impacted their willingness to run essential errands and 52% agree or strongly agree that they have difficulty maintaining physical distancing due to their visual impairment. 65% agree or strongly agree that changes to the layout of familiar places, to encourage physical distancing, makes navigating more difficult. There is an association between age and this difficulty with navigating due to changes to the layout ($p<0.01$). Younger participants rated navigating as more difficult with changes to the layout, not older participants. 72% agree or strongly agree that visual markers used to indicate 6 feet physical distance are helpful in public places. 39% of participants reported that they use strategies to maintain physical distancing when in public. The most common strategies included Sighted Guide or avoiding situations where others may be present. Individuals with vision loss for >10 years, but not since birth, are most likely to report using strategies to maintain physical distancing.

Conclusions: The need to physically distance during a pandemic poses unique challenges for individuals with vision loss. Policies for physical distancing should consider this population. Visual markers on the ground to indicate 6 feet of separation can be helpful and it is important to be mindful when making changes to the environmental layout. Further research to learn more about the strategies utilized by this population to adapt to these challenges is needed.

CONTROL ID: 3542761

SUBMITTER (NAME ONLY): Pauline Khoo

TITLE: Signs and symptoms of dry eye in aromatase inhibitor therapy versus healthy control patients

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Khoo, T. Groeneveld, S.L. Watson, Save Sight Institute, The University of Sydney, Sydney, New South Wales, AUSTRALIA|F. Boyle, B. Forster, Mater Sydney, North Sydney, New South Wales, AUSTRALIA|S. O'Neill, Prince of Wales Hospital Nelune Comprehensive Cancer Centre, Randwick, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: In women receiving aromatase inhibitor (AI) therapy for breast cancer, dry eye is a significant cause of distress and treatment non-compliance. However, little is known of its effect on the ocular surface. This study aimed to compare dry eye clinical features in aromatase inhibitor (AI) therapy patients versus healthy postmenopausal women.

Methods: A comparative observational study of postmenopausal women treated with AI therapy versus healthy controls was conducted. Symptoms were assessed using a validated questionnaire (Ocular surface disease index [OSDI]). Dry eye clinical assessments and investigations (i.e. visual acuity, Schirmer's test II, non-invasive tear break up time [NIBUT], meibomigraphy) were performed. The primary outcome measure was dry eye symptoms measured via the OSDI and secondary outcome measures signs of dry eye disease.

Results: A total of 65 women were recruited, 25 AI and 40 healthy control patients. The mean age in the AI and healthy control group was 62 ± 10 and 60 ± 8 years ($p=0.132$), respectively. The mean OSDI score in the AI group was 24 ± 18 and controls 22 ± 24 ($p=0.174$). In the AI group, 16 patients were considered symptomatic ($OSDI \leq 13$) and 9 were asymptomatic. In the controls, 20 were symptomatic and 20 were asymptomatic for dry eye. Comparative analysis of the AI and control group found no significant difference between visual acuity ($p=0.728$) or Schirmer score ($p=0.108$). NIBUT was significantly longer in the AI group compared to controls ($p<0.001$) (11 ± 6 vs 3 ± 2 , respectively). Increased loss of meibomian gland was also observed ($p=0.022$) in the AI group (3 [IQR 2- 4]) compared to the controls (2 [IQR 1 – 3]).

Conclusions: Aromatase inhibitor therapy was associated with increased NIBUT and meibomian gland drop out. Increased NIBUT maybe due to tear film instability due to the higher meibomian gland drop. Meibography assessments could be used to screen women on AI therapy at risk of developing evaporative dry eye.

CONTROL ID: 3542763

SUBMITTER (NAME ONLY): Shi Song Rong

TITLE: Lack of association of primary open angle glaucoma with expansion of the ATXN2 trinucleotide repeat involved in spinocerebellar ataxia 2 and amyotrophic lateral sclerosis

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Rong, J.L. Wiggs, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|R. Igo, J. Cooke Bailey, Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|J. Cooke Bailey, Cleveland Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genome-wide association studies (GWAS) have identified significant association of SNPs located in the ATXN2 genomic region with primary open angle glaucoma (POAG) and intraocular pressure (IOP). The ATXN2 coding sequence includes a CAG repeat that when fully expanded (>34 repeats) causes spinocerebellar ataxia 2, and intermediate expansions (24-34 repeats) contribute to risk of amyotrophic lateral sclerosis (ALS) and other neurodegenerative disorders. In this study, we investigated this ATXN2 CAG repeat in POAG.

Methods: Fragment analysis was used to size the CAG repeat in 229 POAG cases and 213 controls selected from the NEIGHBORHOOD cohort. The entire repeat genomic region was sequenced using Haloplex next-generation sequencing (NGS) for the 229 POAG cases and 30 controls. SNPs in high LD (linkage disequilibrium) ($r^2 > 0.95$) with CAG repeats were used to test for association with POAG in the overall NEIGHBORHOOD case control cohort, and for association with POAG and related ocular traits in other published GWAS summary data.

Results: The CAG repeat size ranged from 19 to 27 in POAG cases and from 17 to 27 in controls. Both groups had a mean repeat size of 22, which is the average repeat size in normal populations. Among the 19 different repeat sequences identified by NGS, the most common sequence >22 was a 27 repeat ((CAG)₈(CAA)(CAG)₄(CAA)(CAG)₄(CAA)(CAG)₈) with a frequency of 2% in both cases and controls. All other repeats >22 had frequencies of <0.2% in the sequenced individuals. A SNP in high LD ($r^2 > 0.95$) with the 27 repeat (rs117129118) was not significantly associated with POAG (N=2606 cases, 2606 controls), or high-tension (N=1298) or low-tension glaucoma (N=561) in the NEIGHBORHOOD dataset (P>0.05). In published GWAS summary data, rs117129118 was also not associated with POAG, IOP, CDR, or CCT.

Conclusions: Expansion of the ATXN2 CAG repeat was not associated with POAG in a large case/control cohort suggesting that expansion of the ATXN2 CAG repeat does not alter glaucoma risk. These results suggest that other genetic variants in the ATXN2 locus contribute to POAG risk.

CONTROL ID: 3542770

SUBMITTER (NAME ONLY): Corinna Cozzitorto

TITLE: Col4a1 mutations alter neural crest cell migration that may contribute to anterior segment dysgenesis in mice.

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Cozzitorto, Z. Peltz, M. Mao, L. Della Santina, D.B. Gould, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in collagen type IV alpha 1 (COL4A1) and alpha 2 (COL4A2) cause a multisystem disorder characterized by variable cerebrovascular, ocular, renal and neuromuscular manifestations. The affected tissues are mainly derived from two distinct embryonic origins: the neural crest cells (NCCs) and the mesoderm germ layer. Approximately one-third of patients with COL4A1 and COL4A2 mutations have ocular anterior segment dysgenesis (ASD), including congenital glaucoma resulting from dysgenesis of structures derived from the periocular mesenchyme. Defects in NCC biology have long been proposed to contribute to ASD. Because vascular defects are common in patients with COL4A1 and COL4A2 mutations and can influence NCC survival and migration, we hypothesize that primary vascular defects may alter NCC biology underlying ASD.

Methods: Whole-mount immunofluorescence, confocal microscopy, and 3D reconstruction were performed on control and Col4a1 mutant mouse embryos at embryonic day (E) 9.5 and E10.5 using antibodies against CD31 to label vascular endothelial cells, and SOX10 to label migratory NCCs.

Results: Gross morphology and quantitative analysis of E9.5 Col4a1 mutant embryos showed abnormal cerebral vasculature remodeling compared to controls, revealing an early onset of cerebral angiogenesis defects. SOX10 and cleaved Caspase 3 labeling, respectively, revealed that Col4a1 mutant and control embryos had similar numbers of migrating cranial NCCs and a similar degree of cell death at both E9.5 and E10.5. However, compared to control littermates, cranial NCCs moving towards the eye region in E9.5 mutants showed abnormal migration, forming a less cohesive migratory stream. On the other hand, within the periocular mesenchyme of E9.5 and E10.5 Col4a1 mutant embryos, NCCs clustered more together and interacted more closely with the vasculature.

Conclusions: In agreement with our hypothesis, our results show for the first time that Col4a1 mutations lead to cranial NCC migratory defects in the context of early-onset defective angiogenesis. However, NCC number and survival are not affected by Col4a1 mutations. Further examinations are needed to understand both the molecular causes and consequences of the uncovered NCC migratory phenotype. Future work will also analyze the mesodermal contribution to ASD in Col4a1 mutants.

CONTROL ID: 3542772

SUBMITTER (NAME ONLY): Sunidhi Ramesh

TITLE: Evaluation of the Hypertensive Phase after Ahmed Glaucoma Valve Implantation in Neovascular Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the short- and intermediate-term outcomes of the Ahmed glaucoma valve (AGV) in neovascular glaucoma (NVG), comparing eyes with and without a hypertensive phase (HP).

Methods: This was a single-center retrospective case series of consecutive NVG eyes that underwent AGV implantation with ≥ 6 -month follow-up. HP was defined as intraocular pressure (IOP) >21 mmHg at ≥ 2 visits within the first 3 months following surgery. Reported outcomes included failure at month 6 and at the most recent visit. Failure was defined as IOP >21 mmHg, progression to no light perception (NLP) vision, or glaucoma reoperations (all with IOP-lowering medications). Other secondary outcomes included IOP and number of glaucoma medications.

Results: 76 eyes of 74 patients (37 without HP and 39 with HP) with follow-up duration of 28.9 ± 25.7 months ($P=0.602$) were included. Patient demographics, visual acuity (VA), number of medications, NVG etiology, and perioperative retina treatment were similar in both groups. Baseline IOP was higher in the HP group ($P=0.001$). At month 6, 13 HP (33.3%) eyes vs. 3 non-HP (8.1%) eyes met the failure criteria ($P=0.01$). However, at the most recent visit, failure was higher in the HP group; the difference did not reach statistical significance (53.8% vs 35.1%; $P=0.113$). Kaplan-Meier analysis showed similar cumulative failure in both groups ($P=0.180$) (Figure 1). Reasons for failure were similar between groups ($P=0.237$): high IOP in 9 (26.5%) eyes, progression to NLP in 10 (29.4%) eyes, glaucoma reoperation in 14 (41.2%) eyes, and tube removal in 1 (2.9%) eye.

With the exception of post-operative day 1, IOP during the first 6 postoperative months was significantly higher in the HP group ($P<0.05$ for all). At the most recent visit, IOP was similar in both groups ($P=0.211$) (Figure 2A), but number of medications was higher in the HP group ($P=0.023$) (Figure 2B). Postoperative complications were similar and infrequent in both groups.

Conclusions: HP eyes had higher preoperative IOP and more commonly failed in the first 6 months following AGV implantation in NVG compared to non-HP eyes. This study did not detect a significant difference in surgical failure at the most recent visit between the two groups, but HP eyes required a significantly higher number of medications.

CONTROL ID: 3542780

SUBMITTER (NAME ONLY): Joby Tsai

TITLE: Foveolar Avascular Zone Area Mediates the Effects of Retinal Ganglion Cells Dysfunction on Optic Nerve Rim Area in Glaucoma Suspects with Obstructive Sleep Apnea

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tsai, A. Tirsi, V. Gliagias, S. Park, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|P.H. Derr, Diopsys, Inc, New Jersey, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|D. Kacaj, John F Kennedy High School, Bellmore, New York, UNITED STATES|H. Sheha, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Tirsi, S. Park, S.A. Obstbaum, C. Tello, Ophthalmology, Manhattan Eye Ear and Throat Hospital, New York City, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent research suggests that normal tension glaucoma is a chronic progressive ischemic process in the optic nerve. This cross-sectional prospective study looked at the relationship among foveolar avascular zone (FAZ) area, a biomarker for retinal microvascular integrity, retinal ganglion cell (RGC) function assessed by pattern electroretinogram (PERG), and optic nerve head (ONH) rim area (RA) in glaucoma suspects (GS) with obstructive sleep apnea (OSA).

Methods: Nine consecutive GS participants (18 eyes) with normal visual fields tests and suspicious glaucomatous ONH appearance were enrolled and underwent a complete ophthalmologic examination, optical coherence tomography-angiography (OCTA), OCT, and pattern electroretinogram (PERG). FAZ area was measured using ImageJ software. Mediation Analysis Process by Andrew Hayes was tested. PERG parameters consisted of Magnitude (Mag, μV), Magnitude (MagD, μV), and MagD/Mag ratio. OCT RA was also used.

Results: Multiple linear regressions were calculated to predict RA (mm^2) based on age (years) and Mag (μV). A significant regression equation was found ($F(2,14)=6.234$, $p=0.012$) with an R^2 of 0.471. Predicted RA was equal to $1.245 + 0.102(\text{Mag}) - 0.006(\text{age})$. RA decreased by 0.006mm^2 for each year of age and decreased by 0.102mm^2 for every unit decrease in Mag. Only Mag was a significant predictor of RA ($p=0.037$). An identical regression model was found to be significant in predicting RA based on age and MagD ($F(2,14)=6.036$, $p=0.013$) with an R^2 of 0.463. Predicted RA was $1.275 + 0.100(\text{MagD}) - 0.006(\text{age})$. RA decreased by 0.006mm^2 for each year of age and decreased by 0.100mm^2 for every unit decrease in MagD. Only MagD was a significant predictor of RA ($p=0.042$). Mediation analysis revealed that FAZ area was a significant partial mediator in the relationship between MagD and RA. Both the direct (effect= 0.179 , $p=0.002$, 95% CI [0.073 , 0.286]) and indirect (effect= -0.055 , 95% CI [-0.137 , -0.006]) effects of MagD on RA remained significant, demonstrating that FAZ area is a partial mediator in this relationship.

Conclusions: We report PERG abnormalities in asymptomatic GS with OSA. Our data suggests early optic nerve and RA defects are mediated by chronic progressive microvascular abnormalities, possibly occurring simultaneously with vascular changes in optic nerve.

CONTROL ID: 3542787

SUBMITTER (NAME ONLY): Laura Downie

TITLE: A multicenter, double-masked, vehicle-controlled, randomized, parallel group clinical trial of AZR-MD-001 (AZR) in individuals with meibomian gland dysfunction

SESSION TITLE: Dry eye clinical treatments

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.E. Downie, Department of Optometry and Vision Sciences, The University of Melbourne, Parkville, Victoria, AUSTRALIA|S.L. Watson, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|J. Tan, F. Stapleton, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|C. Bosworth, Azura Ophthalmics, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) is characterized by terminal duct obstruction and/or changes to meibomian gland (MG) secretion. Pharmacological therapies for terminal duct obstruction in MGD are lacking. This clinical trial evaluated the safety and efficacy of AZR ointment/semi-solid drug, a novel MGD treatment.

Methods: A pre-planned interim-analysis (IA) of data from this multicenter, double-masked, vehicle-controlled, randomized, parallel group clinical trial (clinicaltrials.gov NCT03652051) was undertaken. Key participant inclusion criteria were an Ocular Surface Disease Index (OSDI) score of 13 to 33 and Meibomian Gland Score (MGS) <12. The IA involved participant groups that received sequentially higher concentrations of AZR (0.1% (n = 9), 0.5% (n = 7), or 1.0% (n = 7)) compared to vehicle (n = 9), in a 4:1 ratio within each group, over 3 months. Pre-specified efficacy measures included OSDI score, MGS and Meibomian Gland Yielding Liquid Secretion (MGYLS). Safety was evaluated using the adverse event (AE) rate.

Results: The mean (SD) age of each study group was similar (overall: 44.6 (19.7) years, n=33), and 52% of participants were female. At Month 3, a minimal clinically important improvement in dry eye symptoms (change in OSDI score ≥ 4.5 units) was observed in 22.2% (Vehicle), 22.2% (AZR 0.1%), 57.1% (AZR 0.5%) and 85.7% (AZR 1.0%) of participants. The difference between Vehicle and AZR 1.0% was significant ($p=0.03$). Least square mean change from baseline (higher scores indicate improvement) for MGS at Month 3 were: 4.5 ± 2.0 (Vehicle), 1.2 ± 2.0 (AZR 0.1%), 4.9 ± 2.1 (AZR 0.5%), and 12.2 ± 2.4 (AZR 1.0%). The difference between Vehicle and AZR 1.0% was significant ($p=0.03$). Results for MGYLS mirrored MGS. The percentage of participants with at least one ocular treatment-emergent AE was 44% (Vehicle), 44% (AZR 0.1%), 71% (AZR 0.5%), and 86% (AZR 1.0%). AEs were transient and did not impact willingness to continue study participation.

Conclusions: Clinically meaningful improvements in signs and symptoms were observed in individuals with MGD with AZR, with an acceptable safety profile. AZR-MD-001 has potential to be the first effective pharmacotherapy specifically for MGD.

CONTROL ID: 3542791

SUBMITTER (NAME ONLY): Abhi Wagh

TITLE: Ultrastructural features of rod synaptic terminals in the simplex retina of skate

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Wagh, J.G. Fathi, A. Baatar, I.A. Anastassov, Biology, San Francisco State University, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In duplex retinæ, the processing of visual information under scotopic and photopic light conditions is separated between the rod and cone photoreceptor systems. However, the elasmobranch little skate (*L. erinacea*) has a simplex retina, which contains only rods. This pure-rod retina can perform under scotopic and photopic light conditions with one complement of photoreceptors. We have little knowledge about the anatomical basis of this functional plasticity in skate rods.

Methods: Eyes from little skate were hemisected and choroid-attached pieces of retina from the tapetal area were obtained. Retinal pieces were embedded in resin blocks and SB-3DEM was performed. The dataset analyzed here was from a region of interest in the OPL of the skate retina with width/height = 34.4µm, section thickness = 0.075µm, and depth = 15µm. Voxel size was 4.5nmX4.5nmX75nm. 3D reconstructions and measurements of rod terminal features were done with Reconstruct and Amira software.

Results: The outer segments of skate rods display typical “stacked-disk” internal membrane morphology with the outer membrane separated in space from the disc membranes. A very short connecting cilium (CC) is present between the OS and the IS: d~250nm, length~400nm. Inner segments have multiple mitochondria and terminals have multiple synaptic ribbons. The majority of terminals have 2-3 synaptic ribbons. On rare occasions, terminals possessed 4 synaptic ribbons. Multiple invaginating processes can be identified (~12) and multiple filopodia of varying length extend from the periphery of each terminal.

Conclusions: Skate rods have a typical vertebrate rod OS morphology, but display hybrid characteristics in their inner segments and terminals. CCs are much shorter than in typical rods and resemble those of cones. The presence of multiple ribbons as organizing centers for transmitter release is an unusual characteristic for rods, but can be clearly seen in skate rods, suggesting the evolution of a hybrid morphology to accommodate functional plasticity.

CONTROL ID: 3542794

SUBMITTER (NAME ONLY): Winston Kung

TITLE: Fundus photography technique, clinical site experience, and the ability to acquire interpretable diabetic retinopathy fundus photos in a telemedicine program

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Kung, A. Hang, A. Husain, J. Jia, S. McMurtry, L. Cheng, J. Grachevskaya, J.D. Henderer, Y. Zhang, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|P. Kung, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In preparation for an artificial intelligence diabetic retinopathy initiative at Temple University Hospital, we changed our fundus photography screening protocol from a single fundus image per eye to two fundus images per eye. We also expanded the screening program from one primary care office to eight. We wished to determine whether these changes resulted in a significant difference in acquiring interpretable photographs and if there was a learning curve for new fundus photographers when expanding clinical sites.

Methods: The one-image protocol required a single macula-centered fundus photograph while the two-image protocol required both a macula-centered and an optic-nerve centered fundus photograph. The one-image protocol was in use at one site from 2016-2017 and the two-image protocol was in use at eight sites (including the original site and seven new sites) from 2018-2020. The percentage of interpretable photographs for each protocol and for each clinical site was measured and compared.

Results: 1377 photographs were taken using the one-image protocol and 928 (67.4%) were deemed interpretable. 3804 photographs were taken using the two-image protocol and 3009 (79.1%) were deemed interpretable (Figure 1). This was a statistically significant improvement ($X^2 = 237.29$, p-value < 0.001). When the 2018-2020 retinal screening exams were compared between the original site and new sites, there was no statistical difference in percentage of interpretable photos ($X^2 = 2.46$, p-value = 0.11), (Table 1).

Conclusions: Adding a second field of view yielded a greater percentage of interpretable photographs, which suggests that the two-image protocol may have helped minimize the impacts resulting from multiple additional clinical sites and varying photographer experience.

CONTROL ID: 3542799

SUBMITTER (NAME ONLY): Alfred Stett

TITLE: Transcorneal electrical stimulation slows down visual field decline in retinitis pigmentosa in a current-strength-dependent manner

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Stett, Okuvision GmbH, Reutlingen, GERMANY|J. Franklin, Institute of Medical Statistics and Computational Biology, University of Cologne, Koeln, GERMANY|F. Gekeler, Department of Ophthalmology, Klinikum Stuttgart Katharinenhospital, Stuttgart, Baden-Württemberg, GERMANY|A. Schatz, Centre for Ophthalmology, University Eye Hospital, Eberhard Karls Universität Tübingen, Tübingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Transcorneal electrical stimulation (TcES) is a clinically available method to slow down disease progression in retinitis pigmentosa (RP). We hypothesize that the effect of TcES on the rate of visual field loss obeys a dose-response relationship with current strength.

Methods: In a prospective, randomized study (clinicaltrials.gov: NCT01837901), one eye of each of 52 subjects with RP was transcorneally stimulated weekly for 30 minutes over a period of 52 weeks with biphasic current pulses (OkuStim, maximum 1.2 mA, 5 ms each phase, 20 Hz). The visual field areas (VFA) were repeatedly assessed in both eyes (Octopus 900, Goldman targets III4e, V4e). Stimulation current strength was 0% (sham), 150% and 200% of the patient's electrical phosphene threshold in 3 randomized groups of patients, respectively. In addition to the primary analysis, where the effect of TcES on the stimulated eyes was analyzed in relation to randomized group (Schatz et al., IOVS, 2017, 58:1), in the now presented secondary analysis, the percentage reductions of the VFA of the stimulated (R_1) and non-stimulated eyes (R_0) after 52 weeks of stimulation were analyzed in relation to the actual current strength. Mean current strength over 52 weeks stimulation was analyzed both as a continuous variable (linear regression) and an ordinal variable (5 classes, Jonckheere-Terpstra test).

Results: As the current strength increased, the VFA (V4e) decreased more slowly, whereby there was a significant linear relationship ($p = 0.049$) and a significant ordinal relationship ($p = 0.011$) between the differences in percentage reduction, ($R_1 - R_0$), and the current strength. In the eyes stimulated with more than 0.8 mA ($n = 9$), R_1 was $0.7\% \pm 7.2\%$ (mean \pm SD) compared with R_0 of $8.8\% \pm 9.1\%$ in the non-stimulated fellow eyes (difference between both eyes: $p = 0.098$, Wilcoxon signed rank test). In the sham group ($n = 20$) the mean percentage reductions R_1 and R_0 were $7.0\% \pm 11.1\%$ and $7.0\% \pm 16.1\%$. Analysis of VFA III4e yielded in no significant effect of TcES.

Conclusions: Our results are consistent with the hypothesis that by TcES the decline in VFA in patients with RP can be slowed significantly in a current-strength-dependent manner. Furthermore, they provide additional evidence that TcES is an efficient method that can stop or delay the disease progression in RP.

CONTROL ID: 3542801

SUBMITTER (NAME ONLY): Judith Flanagan

TITLE: Transdermal application of glycerol monolaurate ointment improves signs and symptoms of dry eye disease

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Flanagan, J. Diec, N. Yeotikar, D. Tilia, BHVI, Sydney, New South Wales, AUSTRALIA|J. Flanagan, D. Tilia, University of New South Wales School of Optometry and Vision Science, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To determine efficacy of transdermal glycerol monolaurate (GML) on signs and symptoms of dry eye disease (DED)

Methods: Participants (55; 78% female) with ≥ 1 expressible meibomian gland, and DED symptoms score >12 (OSDI) were randomly assigned to GML ointment (Lactic Acid 2%, GML 1% in petrolatum) or Control (White Petrolatum). Ointment was applied around the eye twice daily for 6 weeks. OSDI, blepharitis, meibum quality (MQ), meibomian gland expressibility (GE) were graded. Subjects were monitored at Wk1, 3 and 6 for changes relative to baseline (BL). Data were summarised as means \pm SD for variables on interval scales. Categorical variables were summarised as percentages. Subjective ratings and clinical grades were analysed using linear mixed models. Trial group differences were analysed at each visit if there was a significant interaction. Post hoc multiple comparisons were adjusted using Bonferroni's correction.

Results: There was no significant difference at BL between groups for any demographic, or physiological variable (all $p>0.05$). Significant reduction in OSDI was observed at Wk1 for both GML ointment and Control ($p=0.001$). Relative to Wk1, by Wk6 GML ointment showed further improvement in OSDI ($>65\%$, $p=0.003$) and GE ($p=0.003$) and approached significance in improvement in blepharitis ($p=0.051$) with no such improvements in Control. GML ointment showed greater improvement in OSDI at all visits compared to Control ($p\leq 0.038$). For subjects presenting with severe disease (≥ 4 out of 5 clinical signs) there was significant improvement in OSDI from BL over 6 weeks with GML ($p=0.009$) with $>72\%$ improvement relative to BL, and worsening with Control ($p=0.048$). Compared to Control, OSDI items relating to increased evaporation were significantly improved with GML ointment: windy conditions ($p=0.035$), low humidity ($p=0.030$), air conditioning ($p=0.022$). By Wk6, $>93\%$ subjects showed improvement with GML ointment for those subjects with worse BL GE (>1) ($p=0.001$) and >4 clinical signs ($p=0.003$) with no such improvement in Control.

Conclusions: Despite $>84\%$ of subjects presenting with only mild DED, the GML group achieved a minimal clinically important difference over 6 weeks, effecting improvement in signs and symptoms relative to degree of DED at BL suggesting greater benefits relative to worse dry eye at presentation.

CONTROL ID: 3542802

SUBMITTER (NAME ONLY): Hannah Whitmore

TITLE: TNF α -RUNX1 Pathway Regulates Retinal Endothelial Cell Survival and Response to Oxidative Stress

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Whitmore, D.Y. Shu, M. Saint-Geniez, L.A. Kim, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|H. Whitmore, D.Y. Shu, M. Saint-Geniez, L.A. Kim, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pro-inflammatory cytokine TNF α is increased in several angiogenic retinal diseases, including proliferative diabetic retinopathy (PDR). Our research on human micro-vascular retinal endothelial cells (HMRECs) has shown that high glucose and TNF α stimulation cause an additive effect on Runt-related transcription factor 1 (RUNX1) expression. This study aims to determine the role of RUNX1 in the modulation of the TNF α -stimulated oxidative stress response.

Methods: HMRECs were treated in supplemental growth factor free media for between 1 and 72 hours with D-glucose (30 mM), TNF α (5 ng/ml), RUNX1 inhibitors and combinations of these. Effects on gene expression were assessed by qRT-PCR. The Seahorse XF24 Mito Stress Test was used to determine the effects of these treatment conditions on mitochondrial respiration. One-way ANOVA was used for statistical analysis.

Results: TNF α +glucose significantly reduced both the spare ($p < 0.0001$) and maximal ($p < 0.01$) respiration capacity while increasing oxygen consumption ($p < 0.05$) in the Mito Stress Test. Additionally, after 48 hours TNF α significantly increased the expression of TNF-R1 (1.3 ± 0.1 fold, $p < 0.05$), while co-treatment of TNF α and RUNX1 inhibitor brought RUNX1 and TNF-R1 to basal levels (1.2 ± 0.2 fold, ns; and 0.9 ± 0.1 fold, ns; respectively). Superoxide dismutase 2 (SOD2) mRNA expression is significantly increased by TNF α +glucose stimulation (6.1 ± 0.1 fold, $p < 0.0001$, 48h). SOD2 expression is also increased by TNF α alone over a 1 - 72h timecourse analysis (5.7 ± 0.2 fold, $p < 0.0001$, 48h) and significantly reduced by RUNX1 inhibition (0.79 ± 0.1 fold, $p < 0.05$, 48h). In contrast, BCL-2 mRNA is upregulated with RUNX1 inhibition (1.4 ± 0.2 fold, $p < 0.005$, 48h).

Conclusions: These results suggest that while TNF α and glucose reduce mitochondrial respiratory capacity, inducing oxidative stress, SOD2 is significantly upregulated by TNF α -RUNX1 signaling and downregulated via RUNX1 inhibition. This indicates that SOD2 is acting as a protective factor to remove toxic superoxide in the presence of pro-inflammatory TNF α . Moreover, further pro-survival compensatory mechanisms appear to counter the decrease in SOD2 expression due to RUNX1 inhibition, via upregulation of anti-apoptotic BCL-2. This results in greater cell survival capability, even in a high oxidative stress environment.

CONTROL ID: 3542806

SUBMITTER (NAME ONLY): HENRY ZAPATA GALARZA

TITLE: Translational Read-through of a KCNJ13 nonsense mutation with ELX-01 and ELX-03 results in functional Kir7.1 channels

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. ZAPATA GALARZA, P.K. Shahi, B.R. Pattnaik, Department of Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|P.K. Shahi, B.R. Pattnaik, McPherson Eye Research Institute and Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|D.W. McMillin, D.K. Crawford, Eloxx Pharmaceuticals, Waltham, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The KCNJ13 gene encodes the inwardly rectifying potassium channel Kir7.1. Nonsense mutations in this gene are known to cause Leber Congenital Amaurosis 16 (LCA 16), leading to early-onset vision loss. This form of autosomal recessive blindness is characterized by severe vision impairment, nystagmus, and photophobia in the pediatric population. We previously demonstrated a readthrough of the Kir7.1 restored the channel function. In this study, we tested the effect of treating the KCNJ13 nonsense mutation W53X with the novel eukaryotic ribosome selective glycoside compounds ELX-01 and ELX-03.

Methods: Human Embryonic Kidney (HEK293T) cells were plated on a 35mm culture dish until 60-70% confluence. Cells were then transfected with a plasmid carrying KCNJ13 nonsense mutation at 53rd amino acid (c.158G>A, W53X) and fused with Green Fluorescent Protein (GFP). After 24 hours of transfection, the cells were incubated with readthrough compounds ELX-01 and ELX-03 at 1mM for additional 24 hours. The cells were transferred to glass coverslips for whole-cell patch-clamp electrophysiology. Ringer's solution was continuously perfused as an external solution. Rubidium (Rb+) -Ringer's solution was used to test the Kir7.1 channel function.

Results: Detection of GFP fluorescence in GFP tagged W53X transfected HEK293T cell membranes confirmed Kir7.1 protein expression. Previously demonstrated, W53X transfection resulted in non-measurable Kir7.1 current because of the truncated protein product. After we treated these cells with ELX-01 and ELX-03 at 1 mM concentration, the current-voltage curve showed inward rectifying Kir7.1 current. The maximum inward current measured at -160 mV was -90.63 ± 8.23 pA and -68.66 ± 30.56 pA, respectively, compared to only -18.61 ± 7.23 pA without the drug treatment. Upon substitution with Rb-Ringer, the maximum current amplitude did not change in non-treated cell measuring -18.92 ± 5.18 pA but increased to -502.93 ± 50.65 pA, a ~5.64-fold increase with ELX-01 treatment. Similarly, ELX-03 increased the maximum current to -768.02 ± 137.84 pA, representing a ~7.1-fold increase.

Conclusions: Both ELX-01 and ELX-03 are able to restore the translation of full-length and functional Kir7.1 channels in HEK cells. Further evaluation of these compounds will ensure readthrough effects on LCA16 patient-derived iPSC-RPE and mouse models for preclinical validation.

CONTROL ID: 3542809

SUBMITTER (NAME ONLY): Jack Greiner

TITLE: Association of Punctocanthal Epitheliopathy in Dry Eye Syndrome Secondary to Meibomian Gland Dysfunction

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.V. Greiner, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J.V. Greiner, P. Oliver, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|P. Oliver, Clinical Eye Research of Boston, Winchester, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jack Greiner: Commercial Relationship: Code N (No Commercial Relationship) | Paula Oliver: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study extends our preliminary report describing an epitheliopathy of the often overlooked punctocanthal region (PCR) of the eyelid margins and further establishes its association with dry eye syndrome (DES) secondary to meibomian gland dysfunction (MGD). The PCR of the eyelid margins extends from the puncta to the nasal canthus.

Methods: Symptomatic dry eye patients (Group 1;n=100] had SPEED symptom scores of ≥ 6 and meibomian gland assessment (MGA) scores ≤ 12 . The degree of MGD was measured according to methods previously described using a Meibomian Gland Evaluator to determine the secretory status of 15 meibomian glands of the lower eyelid (Greiner: Cur Eye Res 2012;37:272). Asymptomatic patients (Group 2;n=100) had SPEED scores < 6 and MGA scores ≥ 20 . Lid margins were stained with lissamine green (LG) and graded after 90s on a scale of 0-3. A grade of 0 indicated staining of the Line of Marx (LM) only and 3 indicated severe staining extending from the LM posteriorly in the sagittal plane up to > 1.25 mm. Comparative grading was made on the temporal, central, and nasal lid margin over the tarsal plate as well as the lid margin over the PCR. Statistical analyses included Student's t-test with $P < 0.05$ as significant.

Results: The PCR occupies up to 1/5 of the length of the lid margin and is slightly larger in the upper lid (UL) [$P < 0.05$]. Punctocanthal epitheliopathy (PCE) was greater than the lid wiper epitheliopathy (LWE) over the temporal, central, and nasal tarsal regions in the UL and lower eyelids (LL) in both Groups 1 and 2 ($P < 0.001$). The PCE staining was greater in the LL than in the UL in both Groups 1 and 2 ($P < 0.001$) and there was greater staining in Group 1 ($P < 0.001$).

Conclusions: PCE was greater in symptomatic dry eye patients with MGD than in asymptomatic patients with minimally detectable MGD. Although the PCE staining pattern resembles that of LWE, LG staining was greater in PCE. The PCR experiences inherently different lid mechanics than that of the conventional lid wiping action. The location and minimal motion of the PCR preclude PCE resulting from mechanical wiping of the lid margin as in LWE. PCE more likely results as a consequence of evaporation since this portion of the UL and LL margins may not undergo complete closure with blinking or sleeping. These observations support the hypothesis that PCE is a clinically relevant and readily observable marker of DES.

CONTROL ID: 3542810

SUBMITTER (NAME ONLY): Kimberly Gokoffski

TITLE: A Minimally Invasive Approach to Electrically Stimulating the Optic Nerve to Direct Retinal Ganglion Cell Axon Regeneration

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Gokoffski, J. Paknahad, G. Lazzi, Electrical Engineering, University of Southern California, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kimberly Gokoffski: Commercial Relationship: Code N (No Commercial Relationship) | Javad Paknahad: Commercial Relationship: Code N (No Commercial Relationship) | Gianluca Lazzi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A critical barrier to regenerating the optic nerve is directing long distance growth of damaged retinal ganglion cell (RGC) axons. We have generated significant evidence that suggests that the application of electric fields (EFs) may be a viable approach for promoting optic nerve regeneration. Here, we present an approach involving computational modeling paired with ex vivo and in vivo experiments to develop minimally invasive approaches to improve the voltage gradient along the electrically stimulated optic nerve.

Methods: We employed our AM/NEURON computational modeling tool to test different electrical stimulation strategies for improving the voltage gradient along the optic nerve. Ex vivo experiments with Long Evan rats were then performed for verification of computational predictions. Finally, we tested our best model in vivo using the optic nerve crush model. Electrodes were implanted and optic nerves were crushed. One week after crush, optic nerves were exposed to an asymmetric charge-balanced biphasic waveform for 5 hours daily x 10 days. Regenerative response past the crush site in stimulated animals was assessed by quantifying the number of axons at various distances past the injury site and compared to controls.

Results: Computational modeling showed the largest and most linear voltage gradient with the proposed stimulation setup. Ex vivo experiments showed that this setup generated an EF nearly 1.5X higher in amplitude compared to the intra-orbital/cranial electrodes (Voltage gradients: 176.5 ± 10.7 vs 102.7 ± 15.9 mV/mm (cathode); 80.7 ± 7.6 vs 35.6 ± 5.2 mV/mm (anode); $p < 0.0002$ and $p < 0.003$ respectively, $n=3$). Preliminary in vivo experiments showed that the minimally invasive set up was able to direct 3-fold more regeneration over controls, similar to rates directed by intra-orbital/cranial electrodes ($n=1$).

Conclusions: Here, we show that minimally invasive electrodes are more effective at generating an EF along the optic nerve compared to intra-orbital/cranial electrodes. Moreover, these electrodes are able to direct RGC axon regeneration after degeneration from crush injury has set in. This has important implications as there may be a delay between when patients develop optic neuropathies and their ability to receive care.

CONTROL ID: 3542818

SUBMITTER (NAME ONLY): Jennyffer Smith

TITLE: The relationship between Multifocal Electroretinogram Implicit Times, Blood Glucose and Blood insulin in Patients with Diabetes and Prediabetes

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Smith, C. Chao, K. Richdale, W.W. Harrison, University of Houston College of Optometry, Houston, Texas, UNITED STATES|T. Zderic, M. Hamilton, Health and Human Performance, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blood glucose (Bgl) concentration is known to have effects on retinal function testing, such as the multifocal electroretinogram (mfERG). Insulin is also known to impact pathophysiological processes in diabetes. However, there are no studies showing the relationship between insulin and retinal function at the time of testing. The purpose of this study is to assess the relationship between endogenous insulin and Bgl levels on mfERGs implicit times (IT) and amplitudes (Amp) in controls and subjects with pre-diabetes and diabetes (DM).

Methods: Forty-nine subjects participated in this cross-sectional study; 15 controls (HbA1c under 5.7%), 21 with pre-diabetes (HbA1c 5.7-6.4% with no DM medications), and 13 with type 2DM (HbA1c over 6.4% or on DM medications; average HbA1c 7.3%). Testing included endogenous insulin, Bgl, and HbA1c, all gathered within 15 minutes of mfERG testing. The last meal and time were surveyed. MfERG (VERIS) was completed on the right eye with 103 hexagons at near 100% contrast with a 4-minute m-sequence and a Burian-Allen electrode. MfERGs were evaluated for IT and Amp over the entire eye and at the fovea. Regression analyses, controlled for age, were used to determine associations between mfERG and blood analyses.

Results: There were significant associations between longer whole eye and foveal mfERG IT and higher Bgl ($r^2 = 0.17$ $p=0.012$; $r^2 = 0.11$ $p=0.05$). There was no relationship between insulin level and mfERG IT or Amp, but insulin was a confounder of the relationship between Bgl and IT. Including insulin in the model strengthens the relationship ($r^2 = 0.18$ $p=0.010$; $r^2 = 0.14$ $p=0.03$) for the whole eye and fovea, respectively. If Bgl and insulin are considered as a ratio (bgl/insulin) rather than independent factors, its relationship to IT is significant for the fovea ($r^2 = 0.18$ $p=0.045$), but not the whole eye ($p=0.42$). There was no relationship with mfERG Amp in any of these comparisons.

Conclusions: This study indicates that while Bgl is the most powerful influencer of retinal function in diabetes and prediabetes, insulin dysfunction may play a role. Insufficient insulin may be an important consideration for foveal health. Further studies with fasted participants and a wider range of HbA1c values are needed to determine insulin's implications in diabetic retinal neuropathy and retinopathy prevention.

CONTROL ID: 3542821

SUBMITTER (NAME ONLY): Hailey Holck

TITLE: Success of lower eyelid involutional entropion repair using fornix sutures and horizontal eyelid tightening

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Holck, Davidson College, Davidson, North Carolina, UNITED STATES|W. brundridge, San Antonio Military Medical Center, Fort Sam Houston, Texas, UNITED STATES|J. Buttram, William Beaumont Army Medical Center, El Paso, Texas, UNITED STATES|C. DeBacker, Ophthalmology, The University of Texas Health Science Center at San Antonio Department of Medicine, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effectiveness of horizontal eyelid tightening and fornix suture placement in the surgical management of lower eyelid involutional entropion.

Methods: This retrospective study reviewed 602 lower eyelids (484 patients) with involutional lower eyelid entropion who underwent surgical repair between August 2010 through September 2020 in a community subspecialty oculoplastics practice. All patients were followed for greater than three months postoperatively. Exclusion criteria included inadequate follow up or multi component lower eyelid entropion. ICD 9 code 374.01 and ICD 10 codes H02.032 and H02.035 were used to identify charts for review.

Results: 658 patient charts were reviewed with a diagnosis of lower eyelid involutional entropion. Of these, 602 eyelids of 484 patients (56% male, 44% female; age range 50-100 years old, 98% >60 years of age; 52% left lower eyelid, 48% right lower eyelid) underwent entropion repair combining horizontal eyelid tightening with full thickness forniceal (Quickert) sutures. With at least three months follow up (range 3-60 months), the recurrence rate of lower eyelid entropion was 1.2% (7/602 eyelids). Of these recurrences four out of the seven were noted to have significant enophthalmos preoperatively. Another 1.2% (7/602 eyelids) developed sequential ectropion, which required surgical correction between one and twelve months following the original surgery. Suture abscesses, while uncommon, were present in 1.8% (11/602 eyelids) and managed with oral and/or topical antibiotics. Four of those patients underwent removal of the Quickert sutures. None of these cases resulted in recurrent entropion.

Conclusions: Horizontal lower eyelid tightening and Quickert (fornix) sutures are a reliable and effective management of lower eyelid involutional entropion with low recurrence and complication rates. We believe this is the largest known review of the success of this procedure to date.

CONTROL ID: 3542827

SUBMITTER (NAME ONLY): Michael Langue

TITLE: Impact of Revised Phone Triage System on Clinician Callback Rate and Call Resolution Time in an Ophthalmology Resident-Run Urgent Care Clinic

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Langue, D. Cui, S. Athukorala, N. Kansara, M.L. Camacci, I.U. Scott, E.M. Bowie, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of a revised phone triage system on clinician callback rate and call resolution time in an ophthalmology resident-run urgent care clinic.

Methods: The Penn State College of Medicine Institutional Review Board deemed this study exempt from review. The data intake form utilized by staff answering patient phone calls into the Penn State Eye Center urgent care clinic was revised to include more detailed information regarding patients' symptoms, and staff training regarding each item on the form was provided by a senior ophthalmology resident. Proportion of calls that required clinician callback to clarify patient concerns and median time for call resolution were compared between patient phone calls immediately prior to (n=360) and immediately following (n=360) implementation of the revised phone triage system.

Results: Proportion of calls that required clinician callback to clarify patient concerns was 55% prior to and 36% following implementation of the revised phone triage system ($p<0.001$), and median call resolution time decreased from 174 to 136 minutes ($p=0.435$).

Conclusions: Implementation of a revised phone triage system, including staff training and a more detailed data intake form, was associated with a significant decrease in the proportion of patient calls that required clinician callback to gather additional information and a substantial decrease in median call resolution time.

CONTROL ID: 3542835

SUBMITTER (NAME ONLY): Shinri Sato

TITLE: Gut microbiota promotes chronic ocular graft-versus-host disease (cGVHD) through cellular senescence.

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sato, E. Shimizu, Y. Ogawa, K. Tsubota, Department of Ophthalmology, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Tokyo, JAPAN|S. Fukuda, Institute for Advanced Bioscience, Keio Gijuku Daigaku, Tsuruoka-shi, Yamagata, JAPAN|

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ABSTRACT BODY:

Purpose: Devastated gut microbiota is reported to be the substantial cause of GVHD. We previously reported the positive effect of gut decontamination using oral gentamicin (GM) administration in cGVHD model. As the molecular mechanism, we focused on cellular senescence and senescence-associated secretory phenotype (SASP) which promoted cGVHD in our previous report. Deoxycholic acid (DCA) and lipoteichoic acid (LTA); gram-positive gut bacterial metabolite and component each are known to promote cellular senescence and ursodeoxycholic acid (UDCA) is conversely known to suppress cellular senescence through the microbiome. The purpose of this study is to pursue the mechanism of relationship between cGVHD and microbiome by comparing cGVHD magnification and cellular senescence among cGVHD mice models treated with GM, UDCA, or GM+DCA+LTA.

Methods: Allogeneic BMT was performed to produce cGVHD mice by the bone marrow transplantation (BMT) from B10.D2. to BALB/c mice after the irradiation (7Gy). The cGVHD mice were treated per orally with GM, UDCA, GM+DCA+LTA or the solvent vehicle which was set to be the control. We performed 16S rRNA gene sequencing analysis of the gut microbiota, ocular examinations, histological investigations, immunohistochemical examinations, flow cytometry analysis and quantitative PCR at 4-week timepoints after BMT.

Results: Compared with cGVHD targeted organs (lacrimal glands, lungs, livers, large intestines) in vehicle-treated cGVHD mice, those in GM-treated cGVHD mice had fewer expression of DNA damage marker, senescent markers, SASP factors, and accumulation of LTA. 16S rRNA gene sequencing analysis of the gut microbiota revealed that the percentage of gram-positive bacterial strains was significantly decreased with GM treatment. Ocular examination, body weight reduction, and histological investigation of LGs were significantly improved in UDCA-treated cGVHD mice but these examinations in GM+LTA+DCA-treated cGVHD mice were worse than in cGVHD mice treated with GM only. The expressions of senescent markers and SASP factors in UDCA-treated LGs were suppressed compared with those in vehicle-treated LGs but cellular senescence was promoted in GM+DCA+LTA-treated LGs than in LGs treated with GM only.

Conclusions: Our results suggest that there could be an association between the gram-positive gut microbiome and development of cGVHD through cellular senescence.

CONTROL ID: 3542836

SUBMITTER (NAME ONLY): André Ferreira

TITLE: Optical Coherence Tomography Biomarkers - Vitreous Status Influence in Outcomes for Diabetic Macular Edema Therapy with 0.19 mg Fluocinolone Acetonide Implant

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ferreira, J.M. Leite, J. Melo-Beirão, A. Meireles, B. Pessoa, Service of Ophthalmology, Centro Hospitalar Universitario do Porto EPE, Porto, Porto, PORTUGAL|A. Ferreira, Department of Biomedicine - unit of Anatomy, Universidade do Porto Faculdade de Medicina, Porto, Porto, PORTUGAL|J. Melo-Beirão, A. Meireles, B. Pessoa, Department of Ophthalmology, Universidade do Porto Instituto de Ciencias Biomedicas Abel Salazar, Porto, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: To quantitatively assess functional and structural features in non-vitrectomized and vitrectomized DME patients after being treated with a FAc implant and to evaluate their influence in DME treatment response.

Methods: A retrospective review was conducted involving patients with DME who received a single intravitreal injection of the FAc implant at the Centro Hospitalar Universitário do Porto, Portugal. The study was designed to analyze the presence of quantitative structural OCT biomarkers at baseline and 12 months after FAc therapy according to vitreous status: vitrectomized eyes (group 1) and non-vitrectomized eyes (group 2). The secondary objectives were to analyze differences in treatment response and the need for additional therapy as well as to correlate those biomarkers with response to therapy. A significant functional improvement was considered a gain of at least 5 ETDRS letters. DME resolution was defined by $CFT \leq 300 \mu m$. The type of response was classified as (1) good responder when at 12-months post-FAc implant there was DME resolution with a significant functional improvement without additional treatments; (2) non-responder, when there was a $CFT > 400 \mu m$ or $\leq 10\%$ of CFT reduction and BCVA decrease (or BCVA gain < 5 letters); (3) moderate responder - between good and non-responder criteria; (4) non-good responders include non-responders and moderate responders.

Results: A total of 41 eyes from 30 patients were included in this study. At 12 months post-injection, group 1 patients had a lower central foveal thickness (CFT, $p=0.017$) and fewer hyperreflective dots (HRD, $p=0.028$) compared with group 2. Concerning the response, 30 (73%) patients presented a significant functional improvement with 17 (42%) having an increase of at least 15 ETDRS letters. Lower baseline BCVA and baseline SRF ($p=0.036$) were associated with an increase of at least 15 ETDRS letters ($p=0.012$). Overall, 13 (32%) eyes were judged to be good responders and 3 (7%) bad responders; therefore, 61% of eyes had a moderate response. Patients who needed additional therapy had a higher prevalence of subretinal fluid (SRF, 42% vs 3% $p=0.005$) at baseline.

Conclusions: This study supports the effectiveness of the FAc implant in the treatment of persistent or recurrent DME and reports significant changes in several SD-OCT parameters at 12 months post-FAc injection.

CONTROL ID: 3542837

SUBMITTER (NAME ONLY): Jihong Xie

TITLE: Monofocal, Diffractive Trifocal and EDOF IOLs

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Xie, G. Lau, Surgical R&D, Bausch and Lomb, Clearwater, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jihong Xie: Commercial Relationship: Code N (No Commercial Relationship) | George Lau: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Using optical raytracing simulation method to model and compare the optical performance of intraocular lenses (IOLs) with three optical designs.

Methods: Different optical design technologies were adopted in creating three types of IOLs. The monofocal baseline model is designed with conventional aspherical surface which provides appropriate spherical aberration compensation for the cornea; the trifocal IOL is designed with diffractive trifocal structure added to the monofocal baseline which provides 1.65D (intermediate) and 3.3D (near) add power at the IOL plane; and the extended depth of focus (EDOF) IOL is designed with zonal modification of the baseline monofocal surface, which includes three concentric refractive zones with individually optimized power and spherical aberration combinations. The EDOF IOL targets to extend depth of focus to 1.65D (IOL plane) to match the intermediate focus of the trifocal model. The imaging property of three IOLs are modeled and compared in an optical model eye using optical raytracing, and optical through focus performance were analyzed in terms of MTF, Visual Acuity simulation and Point Spread functions (PSF).

Results: Figure 1 provides visual acuity simulation with incremental defocus introduced to the model eye, which indicates:

a) Monofocal baseline provides the highest image contrast (MTF) at distance focus, however diffractive trifocal and EDOF show good and comparable distance vision, e.g. VA 20/20 or better

b) Diffractive trifocal and EDOF have similar intermediate visual acuity performance, e.g., 0.2 LogMAR (20/30) or better at defocus ~1.25D/80cm, ~1.5D/66cm

Diffractive trifocal provides near vision up to 2.5D/40cm, however, due to the nature of diffractive design, the trifocal presents “gaps” (phase reversal) in the defocus curves, which may contribute to vision fluctuation. EDOF design does not show this side effect. Figure 2 further illustrates the mentioned point by PSF with incremental defocus (Top: EDOF, Bottom: D Trifocal). Star testing simulation also implies that “halo” is more visible for diffractive trifocal than for EDOF lens

Conclusions: Both EDOF and diffractive trifocal design can achieve high quality intermediate vision comparing to a baseline monofocal IOL, e.g., 0.2 LogMAR or better for defocus of ~1.25D/ 80cm ~1.5D/66cm. Between diffractive trifocal and EDOF, the EDOF provides superior image quality by greatly reducing the side effects of “halo” and focusing fluctuation.

CONTROL ID: 3542839

SUBMITTER (NAME ONLY): Amy Stark

TITLE: 5,6-epoxyeicosatrienoic acid ethanolamide endocannabinoid mitigates diabetes-induced retinal vascular inflammation

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Stark, J.S. Penn, Pharmacology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|M. Giblin, Cell and Developmental Biology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|M.J. Kim, R. Yang, G.W. McCollum, J.S. Penn, Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inflammation is an early pathogenic event in diabetic retinopathy (DR). Activation of the cannabinoid-2 (CB2) receptor by endocannabinoids (eCB) promotes anti-inflammatory effects, suggesting potential therapeutic relevance in DR. 5,6-epoxyeicosatrienoic acid ethanolamide (5,6-EET-EA) is an eCB thought to reduce inflammation via CB2 activation. We investigated the potential of 5,6-EET-EA to mitigate DR-relevant inflammation, including adhesion protein expression and vascular permeability, both in vitro and in vivo.

Methods: Human Müller cells (HMC) were treated with 1ng/ml IL-1 β +/- 0.5 μ M 5,6-EET-EA and proper control reagents for 2hrs, washed, and treated again with 5,6-EET-EA or vehicle only for 6hrs to generate conditioned media (CM). Human retinal microvascular endothelial cells (HRMEC) were treated with CM for 2hrs before lysis for qRT-PCR analysis of cell adhesion proteins E-selectin (SELE), VCAM, and ICAM. Transendothelial electrical resistance was measured in HRMEC treated with 1ng/ml TNF α +/- 0.5 μ M 5,6-EET-EA. In vivo, mice were intravitreally injected with 15ng/ml TNF α +/- 0.5 μ M 5,6-EET-EA. Retinal vascular permeability was measured by quantitative fluorescein angiography (qFA) 6hrs after treatment.

Results: CM from IL-1 β -treated HMC increased expression of SELE by 63-fold, VCAM by 90-fold, and ICAM by 3.8-fold in HRMEC ($p < 0.001$). When 5,6-EET-EA was present during IL-1 β treatment of HMC, the CM reduced these induction levels in HRMEC by 58% for SELE, 66% for VCAM, and 39% for ICAM ($p < 0.001$). TNF α decreased HRMEC monolayer resistance by 15% 4hrs after treatment ($p < 0.001$). 5,6-EET-EA restored 68% of the deficit after 12hrs of treatment ($p < 0.001$) to levels comparable with controls ($p = 0.881$). In vivo, TNF α caused a 4-fold increase in vessel leakage ($p = 0.009$), whereas 5,6-EET-EA rescued TNF α -induced leakage to near-control levels ($p = 0.029$ vs. TNF α , $p = 0.739$ vs. control).

Conclusions: Our results indicate that 5,6-EET-EA offers anti-inflammatory relief of DR-relevant damage at multiple endpoints. 5,6-EET-EA reduced expression of multiple adhesion proteins in HRMEC stimulated by DR-relevant inflammation, and it decreased vascular permeability in both HRMEC and an acute model of retinal inflammation in vivo. Administration of exogenous eCB and/or CB2 activation may serve as valuable anti-inflammatory therapies for early-stage DR treatment.

CONTROL ID: 3542841

SUBMITTER (NAME ONLY): Katharina Foote

TITLE: Slit-scanning ophthalmoscopy to measure ultra-widefield peripheral refraction along nasal/temporal and superior/inferior meridians

SESSION TITLE: Refractive control: Molecular and Anatomical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.G. Foote, C. Leahy, M. Everett, J. Straub, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Katharina Foote: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Conor Leahy: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Matt Everett: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment) | Jochen Straub: Commercial Relationship(s);Carl Zeiss Meditec, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Autorefractors typically measure over a limited range of visual field angles. Retinal imaging, particularly ultra-widefield (UWF) imaging, has demonstrated utility in visualizing the periphery. UWF slit-scanning ophthalmoscopes can measure peripheral refraction over a wider field of view (FOV) and are faster and easier to use than open-field autorefractors. A prospective study was performed to examine UWF imaging feasibility to extend peripheral refraction measurement range to a full 130°.

Methods: A modified widefield slit-scanning ophthalmoscope (CLARUS™ 500, ZEISS, Dublin, CA) with prototype software was used to test 5 subjects with spherical equivalent refractions ranging from -12.25D to 0.00D. In order to capture overlapping 90° fields, images were acquired with the internal fixation at central position, and then with $\pm 20^\circ$ offsets along each meridian. The vertical component of refraction over the full FOV was determined from the slit-scan data. Fundus features were used to co-register and merge the fields, resulting in a 130° peripheral refraction map.

Results: An extended view of UWF peripheral refraction was obtained for emmetropic and myopic subjects. In Fig 1, a sample UWF absolute peripheral refraction map is shown. In Fig 2, relative peripheral refraction along the full nasal/temporal and superior/inferior meridians is displayed. These measures were computed from an average of 1° strip for each subject. Most myopic subjects show characteristic relative peripheral hyperopia along the nasal/temporal meridian and relative myopia along the superior/inferior meridian. Lid/lash artifacts prevented a full range of measurements in superior/inferior regions.

Conclusions: This study demonstrated a capability of providing data on an unprecedented FOV. Peripheral refraction measurements acquired on myopic eyes followed established trends. Consistent with literature, this study showed hyperopia increases more in the nasal/temporal field than in the superior/inferior field. This measurement technique could be useful for enhancing research in the field of myopia.

CONTROL ID: 3542851

SUBMITTER (NAME ONLY): Preston Kung

TITLE: Analysis of Ungradable Images in a Diabetic Retinopathy Telemedicine Screening Study

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Telemedicine diabetic retinopathy (DR) screening has become increasingly valuable in underserved communities. Poor photo quality significantly hampers screening efforts and can occur due to technical error or pathologies such as cataract, small pupils, or even vitreous hemorrhage. We performed a retrospective study to determine the final diagnoses at an in-person dilated fundus exam of patients who had ungradable telemedicine screening exams. We then compared them to patients with gradable screening exams.

Methods: From March 2018 to March 2020, we evaluated 1902 adult patients with diabetes who presented to one of several primary clinics in North Philadelphia. Non-dilated fundus photos were taken by a trained technician and read remotely by an optometrist. Patients who screened positive for DR, or had ungradable images due to poor view of the fundus were referred to an ophthalmologist for a dilated fundus exam. Initial screening results were compared to final diagnoses, and statistical analyses were performed using Fisher's exact test.

Results:

133 patients attended a follow-up appointment, of which 48 (36%) were referred for DR and 85 (64%) for ungradable images (Table 1). 33/48 (69%) patients who had DR on screening had some degree of DR on the final exam, although only 17/48 (35%) received the same grading on both exams. In comparison, only 16/85 (19%) patients who had ungradable photos had DR on their final exam ($p < 0.001$).

Of those who had ungradable images who did have DR on final diagnosis, there was a significant difference in distribution of disease severity compared to those who had gradable images (Table 2; $p = 0.039$). In those with ungradable images, there was a higher percentage of patients that had proliferative DR (44% vs. 15%) and a lower percentage that had mild NPDR (19% vs. 52%). However, the result was only marginally significant due to small sample size when the 1 unspecified DR patient was removed ($p = 0.057$).

Conclusions: Telemedicine is less effective in identifying patients who have DR when the image is ungradable. However, these patients may present with more severe pathology that worsen image quality, highlighting the importance of follow-up in these patients.

CONTROL ID: 3542853

SUBMITTER (NAME ONLY): Brett Davis

TITLE: The impact on eye length and vision performance for a range of positive defocus levels in two-zone bifocal contact lens adaptive optics simulations

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate short term changes of axial length (AxL), visual acuity (VA), contrast sensitivity (CS) and halo size with simulated 2-zone centre distance bifocal contact lens designs, with positive (+ve) defocus of different magnitudes, produced with adaptive optics (AO).

Methods: An AO system allowed subjects to view a micro-display through the simulated optical designs while AxL and vision performance were measured. 16 young subjects had AxL measured by a Lenstar before and after 40 mins of watching a movie on the micro-display through five AO induced optical designs (control, +3 DS and three 2-zone bifocal designs) (Figure 1). 8 subjects participated in the VA study, 4 in the CS study and 5 in the halo study. For VA, CS and halo tests, a 2-zone bifocal was used with a central distance zone of 2.5 mm and peripheral plus ranging from +1 to +10 D. For VA, high-contrast tumbling E letters were displayed on the AO system micro-display. The E letter for CS tests had three sizes of 0.3, 0.4 and 0.65 logMAR. Halo size measurements for the bifocal designs were performed through a split channel setup in the AO system.

Results: Greatest AxL reductions occurred for +3 D defocus and the bifocal design with peripheral +6 D (both $p < 0.005$). The +6 D periphery design also produced greater shortening of AxL compared to the +3 D periphery ($p < 0.001$). Increasing +ve defocus in the periphery caused a loss of VA ($F = 14.11$, $p < 0.005$) (Figure 2). However, the peak loss of VA occurred at about +2 D peripheral defocus and improved slightly for higher levels of defocus. The effect of increasing peripheral defocus on CS varied with the size of the test letter ($F = 57.84$, $p < 0.005$). For the largest letter, the effect of increasing +ve defocus was minimal, whereas for smaller letters, increasing peripheral +ve defocus continued to decrease CS. When the clear central zone size was fixed, higher plus power in the periphery was found to produce a larger halo.

Conclusions: Increasing peripheral plus power in a 2-zone simulated bifocal caused a greater reduction in short-term AxL. The peak loss of high contrast VA occurred at relatively low levels of peripheral defocus, whereas the loss of CS increased for smaller letter targets, as the defocus increased. Halo size increased with increasing peripheral plus defocus.

CONTROL ID: 3542855

SUBMITTER (NAME ONLY): Vinay Nilagiri

TITLE: Subjective measurement of the foveal Stiles-Crawford effect with accommodation

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To measure the Stiles-Crawford effect (SCE) with innovative technology to evaluate the changes in the directionality and photoreceptor alignment with accommodation.

Methods: A uniaxial Maxwellian system (spot size in pupil 0.5 mm diameter) was employed incorporating a spatial light modulator (Kopin SLM KCM-SK01-AA CyberDisplay®) to flicker at 2 Hz between two 2.3° fields corresponding to test (peripheral pupil) and reference (pupil center) positions. The participant's task was to determine thresholds at 13 positions along the horizontal pupil meridian by indicating if the test field was brighter or dimmer than the reference field. Thresholds were determined by a simple staircase procedure after four reversals at each pupil location. After dilating right eyes with 2.5% phenylephrine, seven emmetropes were tested at 0 D to 6 D accommodation stimulus levels in 2 D intervals. The data were fit by the Gaussian function, both if the fits were unforced or forced to pass through the threshold expected for the reference point. The directionality (ρ) and peak location values (x_{\max}) were compared for unforced and forced fits.

Results: As there were only small differences between the two fitting approaches, only unforced fits are mentioned in the text. The regression slopes on accommodation stimulus were not significant ($-0.0001 \text{ mm}^{-2}/\text{D}$, $R^2=0.0002$, $p = 0.94$) (Fig 1). There was a tendency for (x_{\max}) to shift temporally with increasing accommodation across the 6 D stimulus range. While this was not significant for regression fitting ($-0.058 \text{ mm}/\text{D}$, $R^2 = 0.06$, $p = 0.20$) (Fig 2), a paired t-test for 0 and 6 D accommodation stimuli showed significant change of 0.62 mm ($t(6) = 2.50$, $p = 0.046$).

Conclusions: The directionality did not change with accommodation, but the pupil peak location showed a significant temporal shift of approximately 0.62 mm with 6 D accommodation stimulus. It is possible that substantial changes in the directionality and a shift in the direction of peak location might occur at very high levels of accommodation.

CONTROL ID: 3542858

SUBMITTER (NAME ONLY): Brandon Baksh

TITLE: Corneal mechanical sensitivity in individuals with chronic pain

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Baksh, University of Miami, Coral Gables, Florida, UNITED STATES|C. Lieux, A. Galor, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine corneal mechanical thresholds in individuals with chronic pain using a Belmonte aesthesiometer.

Methods: We performed a cross-sectional study of South Florida veterans with chronic pain conditions (>3 months duration) seen at an eye clinic. Individuals were split into two groups based on the location of their pain: Group 1 included individuals with chronic pain conditions that involved the trigeminal system (e.g. migraine, burning mouth syndrome, trigeminal neuralgia, and trigeminomandibular disorder) while Group 2 included individuals with chronic pain conditions that did not involve the trigeminal system (e.g. back pain, knee pain). Dry eye symptoms and signs, systemic co-morbidities, and quality of life indices were also assessed via standardized questionnaires. Corneal mechanical thresholds were assessed using a modified Belmonte aesthesiometer. Our main outcome measure was comparison of mean corneal mechanical thresholds between our two groups via the independent t-test. Multivariable linear regression analysis was also performed to evaluate predictors of corneal mechanical threshold (dependent variable) while considering multiple independent variables (e.g. demographics, pain location, dry eye symptoms, signs, co-morbidities, quality of life). All reported p-values are two-tailed and $p < 0.05$ was considered statistically significant.

Results: The mean age of the 577 individuals included in the study was 61 ± 10.5 years; 89% were male, 45% self-identified as white, and 25% as Hispanic. Mean corneal mechanical threshold was lower among individuals with chronic trigeminal pain ($n=123$) compared to those without ($n=454$), 75 ± 43 vs 86 ± 43 mL/min, $p=0.015$. Multivariable analysis on 320 individuals with data for all variables demonstrated quality of life questionnaire scores (standardized $\beta = -0.49$, $p=0.002$), dry eye symptoms ($\beta = -0.30$, $p=0.039$), and presence of chronic trigeminal pain ($\beta = -0.44$, $p=0.002$) remained significant predictors of corneal mechanical detection threshold, with an overall $R^2=0.34$ for the model.

Conclusions: Chronic trigeminal pain, worse quality of life, and dry eye symptoms predicted lower corneal mechanical thresholds (higher sensitivity). This suggests a link between chronic trigeminal pain, quality of life, and corneal sensitivity.

CONTROL ID: 3542860

SUBMITTER (NAME ONLY): Ping Wei

TITLE: OCT and OCT Angiography in Optic Neuropathies

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Wei, J. Falardeau, J. Wang, L. Liu, O. Tan, Y. Jia, D. Huang, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess OCT and OCT angiography (OCTA) features in optic neuropathic diseases.

Methods: OCTA macular 6x6-mm and peripapillary 4.5x4.5-mm scans were obtained from the diseased eye of each patient and one eye of each normal participant, which included both structural and angiographic images. The flow signal was calculated using the split-spectrum amplitude-decorrelation angiography algorithm. The capillary density (CD) of peripapillary nerve fiber layer plexus (ppNFLP), vessel density (VD) of macular ganglion cell layer plexus (mGCLP) and macular superficial vascular complex (mSVC) were analyzed using a custom software with shadow removal, reflectance compensation and projection-resolved algorithms. The thickness of the peripapillary retinal nerve fiber layer (ppRNFL) and macular ganglion cell complex (mGCC), ganglion cell-inner plexiform layer (mGCIPL) was measured on structural OCT images.

Results: Nine patients (13 eyes) with optic neuropathy, including 8 eyes/6 patients with nonarteritic anterior ischemic optic neuropathy, 1 eye with posterior ischemic optic neuropathy, and 4 eyes/2 patients with pituitary tumor, and 31 age-matched normal participants were included. The ppNFLP CD, mGCLP VD, mSVC VD, and thickness of ppRNFL, mGCC, and mGCIPL were all significantly reduced in eyes with optic neuropathies (Table 1). The OCTA diagnostic accuracy of optic neuropathic disease, measured by the area under the receiver operating curve (AROC), was 0.921 for ppNFLP CD, 0.868 for mGCLP VD, 0.841 for mSVC VD (sensitivity at 95% specificity was 84.6%, 69.2%, and 53.8%, respectively). For structural OCT parameters, the AROC was 0.809, 0.921, and 0.834 for ppRNFL, mGCIPL, and mGCC thickness, respectively (sensitivity at 95% specificity was 61.5%, 92.3%, and 61.5%, respectively). The patterns of loss on OCT and OCTA maps correlated well with visual field (VF) (Figure 1). The ppNFLP CD had the best correlation with VF mean deviation, then the thickness of ppRNFL, mGCIPL, mGCC, and the VD of mSVC, and mGCLP (Pearson's $r = 0.793, 0.737, 0.721, 0.689, 0.626, 0.589$, respectively, all $P < 0.001$).

Conclusions: OCT and OCTA provide detailed visualization of the peripapillary and macular retinal changes, which correlate well with visual field loss. The patterns of loss could be useful for the diagnosis and classification of optic neuropathies, while the quantification of thickness and perfusion parameters could be useful for assessing disease severity and progression.

CONTROL ID: 3542863

SUBMITTER (NAME ONLY): Catherine Ye

TITLE: Foveal Vessel Density on OCTA Compared to Foveal Avascular Zone in T1DM Vision Health over a 5 Year Period

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Type 1 Diabetes Mellitus (T1DM) is a lifelong autoimmune disease that places individuals at risk for macrovascular as well as microvascular complications such as diabetic retinopathy (DR) which may lead to vision loss. Foveal Density (FD), which takes into consideration vascular branching complexity, may be a better indication of retina health than Foveal Avascular Zone (FAZ), a standard currently used.

Methods: Data from 122 subjects (8-78 years, 33% male) (109 T1DM, 13 non-T1DM) collected over a period of up to 5 years (2015-19). Demographics included age, onset of DM, and self-reported HbA1c. Measurements of the FAZ and FD were calculated from 3mm x 3mm scans with the Optovue AngioVue HD on the RTVue XR Avanti OCTA (Fremont, CA). Statistical analyses included linear regression, multivariable linear regression, and paired T test, completed in SPSS.

Results: Significant negative correlation was found between duration of diabetes and FD OU ($p=.00039$) with no correlation found with FAZ OU ($p=.60$), insulin pump use, duration of pump use, or onset of T1DM. We noted significant negative correlation between average HbA1c and FD OU ($p=.010$) compared to FAZ OU ($p=.95$). Mean FAZ and FD for non T1DM subjects were .281 and 50.8, respectively, mean FAZ and FD for T1DM were .238 and 49.2. No significant difference was found in either FAZ or FD between T1DM/non-T1DM groups (FAZ $p=.129$, FD $p=.069$). In a subgroup of 12 (75% T1DM, age 17-72 years) subjects for which we had FAD and FZ measurements spanning 5 years, there was statistically significant decline found in FD OU over that period ($p=.006$) with no correlating statistically significant trend found in FAZ OU ($p=.06$).

Conclusions: While FD and FAZ have a close correlation, FD may be a more accurate representation of retinal health due to vascular branching complexity rather than measurement of the vascular margins. This demonstrates that FD is inversely proportional to HbA1c, suggesting vascular branching is more sensitive to tight glycemic control than expansion of the FAZ. Duration of diabetes was also identified as a possible influencer of declining FD in retinal health. Decline in FD has been reported in worsening retinal outcomes, making OCTA a valuable tool in assessing retinal health in both T1DM and non-T1DM populations. Baseline OCTA measurements at onset of T1DM management should be an integral part of routine ophthalmic care.

CONTROL ID: 3542872

SUBMITTER (NAME ONLY): Madhusudhanan Balasubramanian

TITLE: Optic Nerve Head Elastography (ONH) for Detecting Glaucoma Progression

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Balasubramanian, A. Salehi, The University of Memphis Herff College of Engineering, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Changes in stiffness of the micro-environment of the ONH region is a significant risk factor for onset and progression of glaucoma (Hopkins A, et al, Am J Physiol Cell Physiol 2020) . Deformation of the ONH or its strain is dependent on the elastic modulus of the constituent elements of the ONH. Therefore, ONH strain is a predictor of changes in the stiffness of its micro-environment or changes in the effective force acting in the ONH region. We present computational approaches for estimating ONH elastography measures from optical images of the retina.

Methods: Confocal microscopy images of a cow lamina cribrosa from an experimental glaucoma study were used (Balasubramanian M, et al, IOVS 2004). Cow eyes obtained fresh were cut equatorially and the posterior segments perfused in oxygenated Dulbecco's solution were positioned in a controlled pressure chamber specifically designed to clamp onto the focusing objective. Images of the lamina cribrosa were acquired 60 minutes after stabilizing the chamber pressure at 12 mmHg and 60 minutes after elevating the chamber pressure to 60 mmHg. Deformation field depicting structural changes in the lamina cribrosa was estimated from the successive confocal images using the equations governing patterns of brightness changes or optical flow. Specifically, the governing partial differential equations of optical flow (strong form) was solved using a multiscale finite element method with hierarchical basis functions. Several candidate descriptors of elastography namely a) absolute strain magnitude, b) maximum normal strain, c) maximum shear strain, d) Von Mises coefficient, e) vorticity (as a measure of rigidity), f) divergence (degree of expansion) and g) relative strain ratio were estimated.

Results: Figure 1 shows planar structural changes in the architecture of the lamina cribrosa estimated non-invasively using our computational approaches. Figure 2 shows elastography of the cow lamina cribrosa under experimental pressure elevations. From the elastography maps, it can be observed that the laminar beams are at elevated strain levels under pressure elevations.

Conclusions: Computational approaches are useful for non-invasively estimating ONH strain from optical images of the retina (elastography). These elastographic measures are likely to be useful for predicting onset and progression of glaucoma as well as for clinical management of glaucoma using standard optical scans of the retina.

CONTROL ID: 3542874

SUBMITTER (NAME ONLY): Akshaya Thananjeyan

TITLE: The effect of chronic neuroinflammation on retinal morphology and the impact of curcumin treatment

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Thananjeyan, F. Ullah, E. Gyengesi, G. Muench, M. Cameron, School of Medicine, Western Sydney University, Campbelltown, New South Wales, AUSTRALIA

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ABSTRACT BODY:

Purpose: The impact of chronic inflammation on the retina in the absence of inheritable/acquired disease or trauma has not been widely investigated. We have previously shown, in a mouse model of chronic neuroinflammation (GFAP-IL6), that the number of microglia found in the retina is increased in response to chronic inflammation. Here, we assessed the impact of chronic neuroinflammation on retinal neurons themselves. Further, we evaluated efficacy of oral Meriva curcumin as a potential neuroprotectant.

Methods: The impact of inflammation on the retina was assessed by determining the length of the photoreceptor outer segments, thickness of outer nuclear layer (ONL) and inner nuclear layer (INL), and the density of cones. Heterozygous GFAP-IL6 mice (n=4), a model of chronic neuroinflammation, aged ~4 months were compared to their wild-type littermates (n=4). A separate cohort of GFAP-IL6 animals aged 4 months was treated with oral curcumin (n=5 ;140mg/kg) for 1 month (fed from 3 to 4 months) as a potential therapy to alleviate neuroinflammation.

Results: Chronic IL6 expression was found to cause a significant decrease in ONL thickness when comparing WT to GFAP-IL6 retinal sections, suggesting a loss of photoreceptors. Indeed, a reduction in overall cone density (labelled with peanut agglutinin) was observed in GFAP-IL6 mice although M-cone density (labelled with M-opsin) was unchanged suggesting S-cones are preferentially affected by chronic neuroinflammation. While rod photoreceptors may have been lost, no significant differences were seen in rod outer segment length between genotypes. There was a trend of reduced INL thickness, but this was not statistically significant. No obvious GFAP expression was observed in Müller cells in any group. However, significant GFAP staining could be found in astrocytes residing outside the inner limiting membrane although no obvious difference could be seen between groups. In the Meriva curcumin treated animals, both cone density and ONL thickness were indistinguishable from wild-types suggesting a significant neuroprotective effect.

Conclusions: Chronic inflammation leads to a reduction in cell bodies in the ONL as well as a reduction in cone density. Our results indicate that curcumin supplementation can protect the retina from these harmful effects of chronic neuroinflammation and may be a candidate to improve outcomes in patients with degenerative retinal disease.

CONTROL ID: 3542876

SUBMITTER (NAME ONLY): Archana Nigalye

TITLE: Comparison of macular pigment optical density measured with dual wavelength autofluorescence between 6° and 9° plateau references in non-advanced age-related macular degeneration and control patients

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Macular Pigment Optical Density (MPOD) can be measured with Heidelberg Spectralis dual wavelength autofluorescence by setting the plateau reference at different perifoveal eccentricities, where the MPOD value is arbitrarily defined as zero. Previous studies have used different plateau references, and there is a lack of evidence whether the choice of plateau location affects MPOD measurements across various macular disorders. We compared the MPOD values obtained with 2 commonly used plateau references of 6° and 9° in non-advanced Age-Related Macular Degeneration (AMD) and control patients.

Methods: Cross-sectional study where we prospectively enrolled 295 eyes of 166 individuals; 210 with non-advanced AMD (19 early AMD, 191 intermediate AMD) and 85 controls (>50 years) after institutional IRB approval. Participants were imaged and classified with color fundus photographs for AMD (Age-Related Eye Disease Study classification). Imaging was performed using Heidelberg Spectralis dual wavelength autofluorescence. MPOD sum of volume at 2° (SoV-2°) values were calculated by setting plateau reference to 6° and 9°. A linear mixed-effects model was used to find association of the pairwise difference between SoV-2° values using 9° and 6° plateau references, with the various predictors of MPOD values, including age, presence of AMD, intra-ocular lens status, AREDS supplement use, and smoking history.

Results: On average, SoV-2° was 13% higher when calculated using the 9° reference plateau point (mean ± std. = 3227 ± 1172) instead of the 6° reference (mean ± std. = 2853 ± 1034), with 374 ± 315 as the mean ± std. within-eye pairwise difference between the two plateau references. The SoV-2° calculated for 9° and 6° references were highly correlated ($R = 0.96$, $p < 0.001$). The pairwise difference between SoV-2° calculated with the 9° and 6° reference was not associated with age, presence of AMD, intra-ocular lens status, AREDS supplement use, or smoking history.

Conclusions: The MPOD sum of volume measurements calculated using the 9° or 6° references appear to be equivalent in non-advanced AMD and control patients. This work will enable direct comparison of the findings between studies using different plateau references.

CONTROL ID: 3542885

SUBMITTER (NAME ONLY): Michelle Abou-Jaoude

TITLE: Post-operative regimens after vitreoretinal Surgery. Is there a difference?

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Traditional extended drop regimens after vitreoretinal surgery can be burdensome, and whether abbreviated ointment-based regimens are equally effective has not been addressed in literature. We performed a retrospective consecutive case series from a single surgeon before and after a regimen switch to assess rates of cystoid macular edema (CME) and endophthalmitis between patients who received an extended drop regimen versus short term ointment therapy for routine vitreoretinal cases.

Methods: A retrospective chart review of 245 eyes that underwent routine vitreoretinal surgery from a single surgeon at multiple sites was conducted with IRB approval. Data collected included patient age, diagnosis, lens status, type of surgery, use of subconjunctival medications, use of sub-tenon kenalog (STK), final ocular fill, and postoperative regimen (4 weeks of drops versus one week of ointment). Routine surgeries were defined as pars plana vitrectomy for vitreous opacities, non-diabetic vitreous hemorrhages, epiretinal membranes, full-thickness macular holes, and vitreomacular traction. Exclusion criteria included follow-up of less than two weeks, surgery for retinal detachment, history of significant diabetic retinopathy/edema, significant unrelated retinal disease, or uveitis. Statistical analysis was done with SPSS (IBM, 27e). Binary logistic regression was conducted using a p-value threshold of 0.05 for confounding variables, and odds ratios were calculated.

Results: Of 245 eyes, 111 received antibiotic/steroid ointment for one week and 131 received an extended steroid drop taper with one week of antibiotic drops. 1/111 in the ointment developed endophthalmitis, and no patients in the drop group. 35/111 eyes in the ointment group versus 48/131 eyes in the drops group developed CME requiring treatment, and statistically significant risk factors across groups included type of surgery, use of STK, and age. No statistically significant differences were found in development of CME between the two therapy groups (p-value: 0.94, OR CI: 0.54-1.78).

Conclusions: We found no difference in the development of CME between the two postoperative regimen cohorts. Only one case of endophthalmitis was found, so statistical analysis was not possible for this endpoint. Further validation is required, but shorter ointment regimens may be a more feasible and equally efficacious alternative to extended drop regimens for routine vitrectomy.

CONTROL ID: 3542886

SUBMITTER (NAME ONLY): Mary Kim

TITLE: Aqueous Humor as a Liquid Biopsy for Uveal Melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.E. Kim, L. Xu, C. Peng, J.L. Berry, The Vision Center, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|M.E. Kim, Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|L. Xu, C. Peng, P. Kuhn, J. Hicks, Department of Biological Sciences, University of Southern California Dana and David Dornsife College of Letters Arts and Sciences, Los Angeles, California, UNITED STATES|P. Kuhn, J. Hicks, J.L. Berry, Norris Comprehensive Cancer Center, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mary Kim: Commercial Relationship: Code N (No Commercial Relationship) | Liya Xu: Commercial Relationship(s);Aqueous Humor Cell Free DNA for Diagnostic and Prognostic Evaluation of Ophthalmic Disease:Code P (Patent) | Chen-Ching Peng: Commercial Relationship: Code N (No Commercial Relationship) | Peter Kuhn: Commercial Relationship: Code N (No Commercial Relationship) | James Hicks: Commercial Relationship(s);Aqueous Humor Cell Free DNA for Diagnostic and Prognostic Evaluation of Ophthalmic Disease:Code P (Patent) | Jesse Berry: Commercial Relationship(s);Aqueous Humor Cell Free DNA for Diagnostic and Prognostic Evaluation of Ophthalmic Disease:Code P (Patent)

ABSTRACT BODY:

Purpose: Metastatic Uveal Melanoma (UM) is usually fatal within one year of symptom onset. There are a variety of biomarkers that can stratify patients' metastatic risk, but identifying them requires intraocular tumor biopsy. Liquid biopsy offers a less invasive alternative without the risks of retinal detachment and intraocular hemorrhage. We investigated whether the aqueous humor (AH) has sufficient tumor-derived cell-free DNA (cfDNA) to function as a liquid biopsy for UM.

Methods: This case series includes 7 eyes of 7 UM patients from whom 12 AH samples were taken during routine brachytherapy plaque placement and/or removal. Double stranded DNA (dsDNA), single stranded DNA (ssDNA), RNA, and microRNA (miRNA) were quantified with respective Qubit High Sensitivity Assay Kits (Thermo Fischer) for each sample. CfDNA was then isolated and sequenced on an Illumina platform to assess genome-wide somatic copy number alterations (SCNAs).

Results: AH derived cfDNA was detected in all samples (dsDNA mean = 0.7 ng/μL, range 0.01-7.5 ng/μL; ssDNA mean = 2.0 ng/μL, range 0-21.3 ng/μL). RNA was detected in 2 of 12 samples (mean = 1.6 ng/μL, range = 0.7-2.5 ng/μL), and miRNA was detected in 11 of 12 samples (mean = 1.7 ng/μL, range = 0.094-16.2 ng/μL). There was a significantly higher concentration of all nucleic acids (dsDNA, ssDNA, RNA, and miRNA) in post-radiation samples than pre-radiation samples (median = 0.085 ng/μL in pre-radiation, 0.333 ng/μL in post-radiation, $W = 1$, $z = -3.46$, $p = 0.00027$, Wilcoxon Signed-rank test). Confirmed UM genomic alterations of 6p gain, 6q loss, and 8q gain were identified in one post-radiation AH sample from an eye with an iridociliary body tumor. These SCNAs are characteristic of UM. No SCNAs were found in the AH from the pre-radiation sample in the same eye, or any of the other AH samples sequenced to date.

Conclusions: The AH is a source of cfDNA in eyes with UM, with a higher yield of all nucleic acids detected after brachytherapy radiation treatment. UM associated SCNAs were identified in the AH of one eye with an iridociliary tumor after radiation only; we hypothesize this may be due to intratumoral necrosis from the radiation as well as the proximity of the primary tumor to the AH. These results represent the first time that UM SCNAs have been identified in cfDNA isolated from the AH, and this provides preliminary evidence that the AH can serve as a liquid biopsy for UM.

CONTROL ID: 3542887

SUBMITTER (NAME ONLY): Santiago Angaramo

TITLE: Impact of Hypertension severity on risk of Diabetic Macular Edema development.

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Angaramo, D.A. Padovani-Claudio, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|Y. Liu, Q. Chen, Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|Q. Chen, D.A. Padovani-Claudio, Department of Ophthalmology and Visual Sciences, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Santiago Angaramo: Commercial Relationship: Code N (No Commercial Relationship) | Yuhan Liu: Commercial Relationship: Code N (No Commercial Relationship) | Qingxia Chen: Commercial Relationship: Code N (No Commercial Relationship) | Dolly Padovani-Claudio: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is controversy regarding the importance of blood pressure (BP) in the development of Diabetic Macular Edema (DME). We performed a retrospective, observational study to determine the effect of BP prior to the diagnosis of diabetic retinopathy (DR) on the risk of developing DME.

Methods: We analyzed twenty years of data (2001-2020) from the Synthetic Derivative, Vanderbilt's electronic health record de-identified database. Patients with any DR aged 18 and above were included. Systolic and diastolic BP values two years before the diagnosis of DR were extracted and their average was termed "Historic BP" (Figure 1). Using severity classifiers from The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High BP, patients were stratified into four groups: Normotensive, Prehypertension, Stage 1 hypertension (HTN), and Stage 2 HTN. From that point forward, each record was reviewed for DME, defined by the presence of appropriate claims data and review of the primary notes. A Cox proportional hazard model tested the effect of Historic BP severity on the hazard of developing DME adjusting for age at DR diagnosis, sex, race, HbA1c, BMI, and diabetes mellitus type/duration. Vanderbilt's Institutional Review Board deemed use of this de-identified database to be exempt.

Results: Of 1,350 patients identified with DR, 285 (21%) developed DME. A likelihood ratio test showed that Historic BP severity was significantly associated with developing DME ($p=0.0069$). Compared to the Normotensive group, patients with Pre-HTN ($HR=1.8$; 95%CI 1.1-3.0; $p=0.0145$), Stage 1 HTN ($HR=2.0$; 95%CI 1.2-3.2; $p=0.0102$), and Stage 2 HTN ($HR=3.3$; 95%CI 1.6-6.7; $p=0.00087$) were associated with an increased DME risk, independent of covariates. Historic HbA1c levels were associated with increased risk of DME ($HR=1.2$; 95%CI 1.2-1.3; $p<0.001$). However, other covariates did not increase the risk of DME.

Conclusions: This data suggests an increased risk of developing DME for patients with progressively more severe HTN levels compared to Normotensive patients. Thus, historical elements beyond the acute presence of HTN, such as chronic degenerative changes in the walls of arteries may predispose individuals to the development of DME. Further investigation of these findings would offer a novel understanding regarding the significance of HTN in DME development.

CONTROL ID: 3542898

SUBMITTER (NAME ONLY): Pengxiao Zang

TITLE: Deep-learning-aided Detection of Referable and Vision Threatening Diabetic Retinopathy based on Structural and Angiographic Optical Coherence Tomography

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Zang, T.T. Hormel, Y. Guo, C.J. Flaxel, S. Bailey, T.S. Hwang, Y. Jia, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|P. Zang, Y. Jia, Department of Biomedical Engineering, Oregon Health & Science University, Portland, Oregon, UNITED STATES|X. Wang, Shanxi Eye Hospital, Taiyuan, Shanxi, CHINA|

Commercial Relationships Disclosure (Abstract): Pengxiao Zang: Commercial Relationship: Code N (No Commercial Relationship) | Tristan Hormel: Commercial Relationship: Code N (No Commercial Relationship) | Yukun Guo: Commercial Relationship: Code N (No Commercial Relationship) | Xiaogang Wang: Commercial Relationship: Code N (No Commercial Relationship) | Christina Flaxel: Commercial Relationship: Code N (No Commercial Relationship) | Steven Bailey: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Hwang: Commercial Relationship: Code N (No Commercial Relationship) | Yali Jia: Commercial Relationship(s);Optovue:Code F (Financial Support);Optovue:Code P (Patent)

ABSTRACT BODY:

Purpose: We propose two fully automated deep-learning-aided frameworks for detecting referable and vision threatening DR (rDR and vtDR) from volumetric and en face structural and angiographic optical coherence tomography (OCT) data.

Methods: 3×3-mm macular OCTA scans were acquired from the eyes of 50 healthy participants and 293 patients with diabetes (with or without DR) using a spectral-domain OCTA system (Avanti RTVue-XR, Optovue Inc). Masked trained retina specialists graded the disease severity based on the Early Treatment of Diabetic Retinopathy Study (ETDRS) scale using 7-field fundus photography. rDR was defined as level 35 or worse, or any level with diabetic macular edema (DME). vtDR was defined as level 53 or worse, or level with DME. A 3D (EfficientNet-3D-B0) and a 2D (DcardNet-36) frameworks were constructed. Each was trained separately for rDR and vtDR. The rDR/vtDR detection performance of 3D and 2D frameworks were respectively optimized using the area under the receiver operating characteristic curve (AUC) and specificity at sensitivity over 95%. Class activation maps (CAMs) were also generated from each framework. Performance was evaluated with 5-fold cross-validation, with 60%, 20%, and 20% of the data split for training, validation, and testing, respectively.

Results: The 3D framework achieved AUC of 0.89 ± 0.04 for rDR and 0.88 ± 0.02 for vtDR. The 2D framework superior AUC of 0.95 ± 0.02 for rDR ($p=0.0130$) and 0.94 ± 0.02 for vtDR ($p=0.0009$). 2D framework demonstrated higher overall diagnostic accuracy, sensitivity, and AUC (t-test on 5-fold cross-validation output) (Table 1). By overlaying CAM on OCTA three-dimensionally, we found the regions with higher values in the CAMs were mostly focused on the non-perfusion areas (NPA) and fluid areas (Fig. 1).

Conclusions: We demonstrated that a deep-learning based framework can detect rDR and vtDR based on OCTA volume and 2D framework shows superior diagnostic power than 3D framework as trained by the currently available dataset.

CONTROL ID: 3542903

SUBMITTER (NAME ONLY): Matthew Wieder

TITLE: Factors Associated with Higher Post-Residency Ophthalmology Research Output - A Five-Year Analysis

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. He, Internal Medicine, Mount Sinai West Medical Center, New York, New York, UNITED STATES|A. Parsikia, Research Services, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|J. Mbekeani, Surgery, Jacobi Medical Center, Bronx, New York, UNITED STATES|J. Mbekeani, Ophthalmology & Visual Sciences, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|M.S. Wieder, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Matthew Wieder: Commercial Relationship: Code N (No Commercial Relationship) | Catherine He: Commercial Relationship: Code N (No Commercial Relationship) | Afshin Parsikia: Commercial Relationship: Code N (No Commercial Relationship) | Joyce Mbekeani: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate factors associated with post-residency research productivity among graduates of US ophthalmology programs.

Methods: A retrospective review was conducted of publicly available information of residents from 30 US ophthalmology programs, randomly selected from the top 100 Doximity-ranked programs. Demographics, academic factors, fellowship, and career choices of all graduates between 2009 and 2014 were documented. The current H-index, a measure of scientific output and citations, was also recorded. Publications from pre-residency, residency, and post-residency, including fellowship, were enumerated. Differences in publications between the 5yrs post-residency and the pre-residency/residency period were used as metrics of productivity. Analysis was conducted using Student's T-test, Pearson correlation, multivariate logistic regression, and odds ratio (OR) calculations with STATA-14 software. Significance was set at $p < 0.05$. Residents with incomplete data were excluded.

Results: 758 out of 768 residents, 306 females (40.4%) and 452 males (59.6%), met inclusion criteria. The mean (SD) number of pre-residency/residency publications was 1.7(4.0) and post-residency was 4.0(7.3) with a mean (SD) H-index of 4.2(4.9). Top rank residency ($p = 0.0013$), Alpha Omega Alpha (AOA) medical honor status ($p = 0.0015$), US medical school graduates ($p < 0.001$) and academic career ($p < 0.001$) were all significantly associated with higher pre/post-residency mean publication difference. Pursuing fellowship training was associated with higher total publications ($p < 0.001$). Of all pre-residency degrees, PhD had the greatest odds of high post-graduate publications (defined as > 4). There was a positive correlation between pre/intra-residency and post-residency publications ($\text{Rho} = 0.441$; $p < 0.001$) and mean difference of pre/post-residency publications for residents at a program and that program's rank ($\text{Rho} = 0.497$; $p < 0.001$). Multivariate logistic regression revealed, in order, academic career ($\text{OR} = 3.38$; $p < 0.001$), Heed fellows ($\text{OR} = 3.12$; $p = 0.031$), > 2 residency publications ($\text{OR} = 2.89$; $p < 0.001$), AOA status ($\text{OR} = 2.0$; $p = 0.004$), and top-rank residency ($\text{OR} = 1.89$; $p = 0.007$), had greatest odds of > 4 post-graduation publications.

Conclusions: Higher post-residency productivity was associated with multiple factors with choice of an academic career, Heed fellowship and residency productivity playing key roles.

CONTROL ID: 3542904

SUBMITTER (NAME ONLY): Justin Riffel

TITLE: Rate of acute postoperative endophthalmitis after phacoemulsification using intracameral moxifloxacin

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Riffel, A. Quick, University of Kansas Medical Center, Kansas City, Kansas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Justin Riffel: Commercial Relationship: Code N (No Commercial Relationship) | Anjulie Quick: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ophthalmologists are increasingly utilizing intracameral (IC) antibiotics for prophylaxis during cataract surgery. We performed a retrospective chart review to evaluate the rate of acute postoperative endophthalmitis (POE) after cataract surgery using IC moxifloxacin at a tertiary academic center.

Methods: International Review Board approval was obtained from the University of Kansas Medical Center prior to the study. We conducted a retrospective chart review of phacoemulsification surgeries with or without intraocular lens placement. Surgeries were performed as either standalone procedures or in combination with other ophthalmic surgeries. The surgeries were performed by six cataract surgeons at a single institution between February 1, 2018 and August 10, 2020. All patients included in analysis received IC moxifloxacin during surgery. Patients who underwent combination surgeries received postoperative topical antibiotics in addition to IC moxifloxacin, while those who underwent standalone cataract surgery received IC moxifloxacin alone. Patients who did not receive IC moxifloxacin due to a preexisting fluoroquinolone allergy were excluded from analysis. Analysis included the rate of acute POE following all surgeries and the occurrence of any adverse reactions to IC moxifloxacin administration in those with a preexisting fluoroquinolone allergy.

Results: 2,359 eyes underwent cataract surgery (standalone and combination surgeries combined) over the study period. Zero cases of acute POE were observed after all 2,359 surgeries (0%). There were no reports of adverse reactions to IC moxifloxacin administration in the 43 patients identified as having a preexisting fluoroquinolone allergy (72 surgeries total), despite the most commonly listed preexisting allergic reaction to fluoroquinolones being "rash or itching."

Conclusions: Our academic center's rate of acute POE after cataract surgery using IC moxifloxacin is 0%. No adverse reactions to IC moxifloxacin administration were reported in patients with preexisting fluoroquinolone allergy. Importantly, no cases of acute POE were identified in patients who underwent standalone cataract surgery using IC moxifloxacin without the addition of postoperative topical antibiotics.

CONTROL ID: 3542906

SUBMITTER (NAME ONLY): Jack Quach

TITLE: Influence of Frailty on the Structure-Function Relationship in Glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Quach, J.R. Vianna, Ophthalmology, Dalhousie University, Halifax, Nova Scotia, CANADA|O. Theou, Medicine, Dalhousie University, Halifax, Nova Scotia, CANADA|J. Quach, O. Theou, Physiotherapy, Dalhousie University, Halifax, Nova Scotia, CANADA|

Commercial Relationships Disclosure (Abstract): Jack Quach: Commercial Relationship: Code N (No Commercial Relationship) | Olga Theou: Commercial Relationship: Code N (No Commercial Relationship) | Jayme Vianna: Commercial Relationship(s);EadieTech:Code C (Consultant)

ABSTRACT BODY:

Purpose: Frailty is defined as a state of increased vulnerability to adverse health outcomes among people of the same chronological age. The purpose of this study was to evaluate the role of frailty on the structure-function relationship in glaucoma.

Methods: In this cross-sectional study, we consecutively recruited patients who had diagnosis of open-angle glaucoma by a glaucoma specialist. On the same visit, global retinal nerve fibre layer thickness (RNFLT) was measured by optical coherence tomography (OCT; 3.5 mm diameter peripapillary scan) and mean deviation (MD) was measured by 24-2 visual field (VF) examinations. We selected data from one random eye per patient for analysis. Frailty was measured by a questionnaire via phone call within 4 months of the OCT and VF examination. The questionnaire included 34 questions generating a frailty index (FI) score from 0 (healthy) to 1 (severely frail). This FI was based on a previously validated 36-item FI, with exclusion of 2 items related to glaucoma (cataract surgery and self-reported vision). The measured RNFLT values were adjusted for age and Bruch's membrane opening area. We created a multivariable linear regression model with MD as the dependent variable and RNFLT and FI as predictor variables. Furthermore, the interaction between RNFLT and FI was tested in a second model to explore whether frailty moderates the structure-function relationship. All regression models were adjusted for age and sex.

Results: We included 55 individuals (55% male) with mean (standard deviation; range) age of 70.3 (8.2; 45.0-89.0) years, mean adjusted RNFLT of 76.4 (14.1; 42.9-115.0) μm , mean MD of -2.99 (3.93; -17.94-1.34) dB, and mean FI score of 0.12 (0.08; 0.00-0.42). The multivariable linear regression model showed a significant association between adjusted RNFLT and MD (coefficient: 0.17 dB/ μm , p-value < 0.01) but not between FI score and MD (coefficient: 0.02 dB/FI*100, p-value = 0.87). There were no significant interactions between FI score and adjusted global RNFLT thickness (p-value = 0.93). The effect of frailty on the structure-function relationship is visualized in Figure 1.

Conclusions: In this relatively non-frail sample, FI score does not predict MD and is not a significant moderator of the structure-function relationship in glaucoma.

CONTROL ID: 3542907

SUBMITTER (NAME ONLY): Josiah To

TITLE: Low-Cost Photogrammetric Technique for Ophthalmic and Adnexal Volumetric Analysis

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.K. To, A.N. Vu, A.W. Browne, L.S. Ediriwickrema, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|A.W. Browne, Institute of Clinical and Translational Science, Department of Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Standardized tools do not exist to monitor volumetric or morphological changes in the periorbital region and ocular adnexa due to pathology such as oculofacial trauma, thyroid eye disease, and the natural aging process. We, therefore, developed a low-cost, 3D printed hybrid device and technique to quantifiably evaluate 3-dimensional oculofacial volumetric changes.

Methods: Images were taken using two Google Pixel 3 smartphones, which were attached to automatic rotating platforms using 3D printed mounts. The platforms were attached to height-adjustable poles with an 18 in and 10 in ring light. Cameras were centered 1.5 ft from the face at eye-level and their rotating axes angled at 12.5 degrees from center (Fig 1A). Subjects placed their faces through a foam backdrop with checkered squares, which were used as image registration landmarks (Fig. 1B). Subjects were instructed to remain motionless during the 60 seconds of image acquisition. Images with and without 3D printed phantom lesions (black domes) affixed above the brow were acquired. Images were processed in Metashape (Agisoft, St. Petersburg, Russia), a 3D reconstruction software. 3D rendered objects were then imported into Autodesk's Meshmixer where 3D facial renders were registered to each other (Fig. 1C-E). Digitally reconstructed 3D dome volumes were then measured within Meshmixer and compared to their respective calculated volumes. Calculations were based on dome diameters measured with a micrometer.

Results: 3D renderings of the ocular adnexa for 3 subjects were achieved using 60 photos acquired on our custom designed hardware. Differences between calculated and digitally analyzed volumes of 3D printed phantom lesions showed a percent difference of $2.33 \pm 2\%$ for 2060 μL , $4.79 \pm 2\%$ for 244 μL , and $25 \pm 17\%$ for 27.5 μL . Digitally measured phantom lesion volumes were accurate to within 6.8% of the calculated volumes as small as approximately 250 μL ; small dome volumes were digitally undermeasured about 25%.

Conclusions: We demonstrated a technique using a 3D printed hybrid device to analyze and quantify oculofacial volumetric changes with a resolution of approximately 250 μL .

CONTROL ID: 3542909

SUBMITTER (NAME ONLY): Rebecca Soares

TITLE: Geographic access disparities to clinical trials in retinopathy of prematurity in the United States

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.R. Soares, Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Rebecca Soares: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To identify geographic and socioeconomic variables predictive of residential proximity to retinopathy of prematurity (ROP) clinical trial locations.

Methods: This was a cross-sectional, retrospective study. Deidentified census-tract level data from public datasets and trial-level data from ClinicalTrials.gov were analyzed. We used an origin-destination cost-matrix to calculate the driving distance and travel time from the population-weighted United States (US) census tract centroid to the nearest clinical trial site. We then used data from the U.S. Census Bureau's American Community Survey and the Centers for Disease Control and Prevention to identify census-tract level socioeconomic factors predictive of driving distance and time. The primary outcomes were time traveled >60 minutes and distance traveled >60 miles from population-weighted census tract centroid to the nearest ROP clinical trial site.

Results: In a multivariable model, driving time >60 minutes had a significant association with rural vs. urban location [1.19 (1.17-1.22), adjusted odds ratio (aOR) (95% confidence interval), $p < 0.0001$], percentage of population <200% of federal poverty level (FPL) compared to the first quartile [second quartile 1.04 (1.03-1.05), third quartile 1.07 (1.06-1.08), fourth quartile 1.17 (1.16-1.19), $p < 0.0001$], and South [1.06 (1.05-1.07)] and West [1.24 (1.22-1.26), $p < 0.0001$] region as compared to Northeast. Driving time was inversely associated with county-level number of births < 1500g per 1000 people 0.98 (0.98-0.98), $p < 0.0001$. Similar predictors were found in distanced traveled >60 miles.

Conclusions: Conclusions: There are geographic maldistributions of clinical trial sites for ROP in the United States. Those with higher travel burden are more likely to reside in a census tract that is rural, low-income, and from areas outside the Northeast. Conversely, patients from counties with higher rates of very-low birth weight infants are less likely to live further from clinical trial sites.

CONTROL ID: 3542912

SUBMITTER (NAME ONLY): Luis Knight

TITLE: Detection of reduced mitochondrial ROS production but increased ROS levels and oxidative damage in the young xCT knockout mouse retina

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.J. Knight, R.M. Martis, J.C. Lim, Department of Physiology, The University of Auckland, Auckland, Auckland, NEW ZEALAND|M.L. Acosta, School of Optometry and Vision Science, The University of Auckland, Auckland, Auckland, NEW ZEALAND|P.J. Donaldson, School of Medical Sciences, The University of Auckland, Auckland, Auckland, NEW ZEALAND|

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ABSTRACT BODY:

Purpose: The cystine/glutamate antiporter (system xc-) mediates exchange of extracellular cystine for intracellular glutamate. The xCT knockout mouse (KO), in which the light chain subunit (xCT) of system xc- is removed, results in accelerated retinal aging relative to age matched wild-type (WT) mice due to alterations in glutamate and anti-oxidative mechanisms. We have previously shown that lack of xCT alters the glutamate/glutamine cycle and glycolytic metabolism. In this study, we extended our investigation to examine the effect of xCT removal on mitochondrial activity, reactive oxygen species (ROS) production, and oxidative damage.

Methods: Retinas from C57BL/6J and xCT KO mice were collected at 6 weeks (6W) and 9 months (9M). Mitochondrial activity and ROS production were measured via high-resolution respirometry using the Oroboros Oxygraph-2K system (n=6). Succinate, glutathione (GSH) levels and protein carbonyl and lipid peroxidation were measured in whole retinas using biochemical assays (n=6). GSH distribution in the retinal layers was quantified after silver-intensified immunogold labelling (n=6).

Results: High-resolution respirometry revealed 2-fold higher baseline ROS levels in the 6W KO retina compared to WT (ANOVA, $p < 0.05$), but levels were similar in the 9M mice. While whole retina GSH levels did not change between strains or age groups, GSH was significantly decreased in KO photoreceptors nuclear layer compared to WT at 6W. In addition, there were increased levels of protein carbonyls ($p < 0.05$) and 4-HNE ($p < 0.01$) in the 6W KO retina compared to WT. Succinate levels were similar at either age and in both strains of mice. However, high-resolution respirometry revealed increased respiratory complex I activity ($p < 0.01$), a trend for decreased respiratory complex II activity, and decreased mitochondrial ROS production in 6W KO retinas compared to WT ($p < 0.05$).

Conclusions: Loss of xCT function results in reduced photoreceptor GSH levels, increased baseline ROS, increased oxidative stress but decreased mitochondrial ROS production which may alter ROS signalling pathways important for normal retinal function. These early changes are back to normal in the 9M xCT KO which may suggest early metabolic and mitochondrial changes due to xc- pre-conditions the retina to accelerated aging.

CONTROL ID: 3542919

SUBMITTER (NAME ONLY): Wendy Linderman

TITLE: Peri-procedural risk of retinal artery occlusion in patients undergoing transcatheter cardiac interventions in the United States

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.L. Linderman, J. Chow, J.C. Wang, Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|G.C. Linderman, M. Mori, K. Schuster, Surgery, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Wendy Linderman: Commercial Relationship: Code N (No Commercial Relationship) | George Linderman: Commercial Relationship: Code N (No Commercial Relationship) | Jessica Chow: Commercial Relationship: Code N (No Commercial Relationship) | Makoto Mori: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Schuster: Commercial Relationship: Code N (No Commercial Relationship) | Jay Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Transcatheter procedures are increasingly used to treat a variety of cardiac conditions, but the risk of clinically significant peri-procedural retinal artery occlusion (RAO) has not been well characterized. In this study, we use the National Inpatient Sample (NIS) to determine the risk of peri-procedural RAO in transcatheter aortic valve replacement (TAVR) and percutaneous coronary intervention (PCI).

Methods: Patients who underwent TAVR and PCI were identified in years 2006 to 2017 of the NIS. NIS is a large, nationally representative sample of hospitalizations, which allows for characterization of rare events like RAO. Rates of transient, branch, central, and peripheral RAO were computed based on non-primary ICD-9/10 diagnosis codes assigned at discharge. The rate of peri-procedural stroke was also calculated for these procedures as a positive control, as these rates are well-characterized in the literature. Because NIS lacks present-on-admission flags to exclude pre-existing RAO, we report the rate of RAO as an upper bound of the true periprocedural rate. Sample weights published by the NIS were used to produce nationally representative estimates. To determine the significance of differences between rates, p-values were calculated by z-test.

Results: 161,829 patients underwent TAVR and 6,970,152 patients underwent PCI. The rate of all RAO in patients undergoing TAVR was 6.4/10,000 (95% CI 3.7 to 9.2), and non-transient RAO was 4.3/10,000 (95% CI 2.1 to 6.6). In patients undergoing PCI, the rate of all RAO was 2.0/10,000 (95% CI 1.7 to 2.2), and non-transient RAO was 6.0/100,000 (95% CI 4.9 to 7.6). The rate of stroke in patients undergoing TAVR and PCI was 2.1% (95% CI 1.9 to 2.2%) and 0.58% (95% CI 0.56 to 0.60%), respectively, consistent with previously published rates. The rate of peri-procedural RAO was higher in TAVR than in PCI (p-value < 0.001). The rate of peri-procedural stroke was higher than peri-procedural RAO in both TAVR and PCI (p-values < 0.001).

Conclusions: Peri-procedural RAO as a complication of TAVR and PCI is rare, with true rates likely to be less than 9/10,000 and 2/100,000, respectively. Peri-procedural RAO is significantly more common in TAVR than in PCI and less common than stroke in both procedures.

CONTROL ID: 3542920

SUBMITTER (NAME ONLY): Guanzheng Wang

TITLE: Prospective Validation of a Bi-modal Retinal Image Intelligent Analysis System at a District Hospital

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We have developed a bi-modal artificial intelligence(AI) system with deep learning algorithms to comprehensively identify pathological retinal features based on optical coherence tomography(OCT) and fundus photography(FP). Here, we designed a prospective experiment to validate its real-world clinical performance at a district hospital.

Methods: The AI system can identify 14 pathological and anomalous features from OCT(including drusen, macular hole and so on) and 12 pathological and anomalous features from FP(including diabetic retinopathy, pathological myopia and so on). To evaluate the performance of AI and the value of the system in clinical assistant diagnosis, we deployed the system to the Baoshan Branch of Shanghai Renji Hospital for a three-month(from August 2020 to October 2020) clinical validation. Topcon Maestro 3D OCT-1 in Radial scanning mode was used for data capturing which can obtain 12 radial 6mm macular OCT images and a 45-degree FP of the macula in a single acquisition. A total of 667 eyes from 363 patients(Female 186, 51.2%; Mean age 54.3, SD 11.0) where both OCT and FP were good quality were included in this validation. The OCT and FP reports generated by AI were independently reviewed by a senior ophthalmologist. The reviewer's judgement was considered as the gold standard.

Results: Table 1 shows the AI performance of OCT and FP on 667 eyes. For the 14 OCT features, the average sensitivity, specificity and accuracy were 97.2%, 98.7% and 98.6%, and for the 12 FP features were 94.9%, 99.2% and 98.9%, respectively. Since both OCT and corresponding FP were collected, different, complementary features in OCT and FP were found when judging retinopathy. There were 292 (43.7%) abnormal eyes recognized by OCT, 354(53.0%) by FP and 439(65.8%) by combining OCT and FP(Figure 1).

Conclusions: We examined the AI performance for detecting pathological and anomalous features in OCT and FP. For the features validated, AI performance can meet the requirements for community screening applications and primary hospital auxiliary diagnostic scenarios. Furthermore, the combination of OCT and FP can significantly improve the disease recognition performance of AI, because of the complementary information in simultaneously acquired OCT and FP.

CONTROL ID: 3542921

SUBMITTER (NAME ONLY): Eun Young Choi

TITLE: Spatial Patterns of Preclinical Visual Fields in Glaucoma

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate spatial patterns of preclinical visual fields and their association with future development of glaucoma.

Methods: We selected reliable 24-2 preclinical VFs for each eye from a multi-center dataset. Preclinical VFs were defined as mean deviation (MD) ≥ -1 dB, glaucoma hemifield test (GHT) within normal limits and pattern standard deviation (PSD) probability $> 5\%$. An unsupervised artificial intelligence method termed archetypal analysis was applied to determine the preclinical VF patterns from total deviation values. The VF patterns and global indices (age, MD, PSD) of the baseline VF were associated with the incidence of subsequent glaucoma diagnosis (defined by MD ≤ -3 dB and abnormal GHT and PSD probabilities on VFs measured at least 3 months from the baseline) using Cox survival regression with mixed effects addressing the issue of inter-eye correlations. Model selection was performed using Bayesian information criterion (BIC).

Results: We determined 10 preclinical VF archetypal patterns from 44,410 VFs including two variants of normal VF archetypes (ATs 1 and 5), superior and inferior loss (ATs 4 and 9), superior and inferior peripheral loss (ATs 10 and 8), nasal and temporal loss (ATs 3 and 7), nasal-temporal peripheral loss (AT 6) and central scotoma (AT 2). Among the 17,192 eyes with follow-up tests, 7.1% of the eyes were subsequently diagnosed with glaucoma at an average of 4.3 years with a standard deviation of 2.9 years. From univariable regressions, subsequent glaucoma diagnoses were positively associated ($p < 0.001$) with age, PSD, and ATs 3, 4, 6, 7, and negatively associated ($p < 0.001$) with MD and ATs 1, 2 and 5. From multivariable regressions with AT features, glaucoma diagnoses were positively associated ($p < 0.001$) with ATs 3, 4, 6, 7 and 9 after feature selection. When combining ATs with global indices, glaucoma diagnoses were positively correlated ($p < 0.001$) with age, PSD, and AT 3, and negatively correlated ($p < 0.04$) with ATs 1 and 8. AT 10 remained in the optimal model with an insignificant p value. The model combining the VF patterns with global indices strongly outperformed the model using global indices alone (BIC value lowering of 160; BIC lowering of > 6 indicates strong model improvement).

Conclusions: Preclinical VF patterns were assessed and quantified for the first time to our knowledge. These VF patterns can be used to improve prediction of future glaucoma diagnoses.

CONTROL ID: 3542924

SUBMITTER (NAME ONLY): Jeff Rabin

TITLE: ERG and VEP Metrics of Melanopsin Sensitive Ganglion Cells

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.C. Rabin, J. Lovell, N. Tahvilian, A. Ku, T. Contreras, J. Carachure, L. Geabou, J. Sies, D. Nguyen, University of the Incarnate Word Rosenberg School of Optometry, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intrinsically photosensitive retinal ganglion cells (ipRGCs) absorb short wavelength light via melanopsin mediating circadian photoentrainment, pupil responses, alertness & cognition, functions which persist despite blindness. Giant ipRGCs, which send signals to LGN/visual cortex implying a role in visual perception, show an inhibitory opponent S cone off response. Human long-latency ipRGC ERGs elicited with silent substitution utilize high contrasts which can lessen ipRGC isolation. We used selective chromatic adaptation to stimulate ipRGCs & S cones to reveal ipRGC ERGs & VEPs (Rabin et al. Eye 2020). Our purpose was to extend this effort & develop new metrics to quantify ipRGCs.

Methods: 20 adults (mean age 25 ± 3 , 14 females) participated after informed consent. A Ganzfeld (Diagnosys, LLC) was used to present 200-msec. blue flashes (448 nm) on a rod & LM cone saturating amber background (590 nm, 560 cd/m^2) to stimulate S cones (426 nm peak) & ipRGCs (480 nm). Simultaneous flash ERGs and VEPs were recorded in 1000 msec epochs after 30 sec. of adaptation to the amber background over a 4-log unit range (16.7 to .0167 cd/m^2). Digital values (μV vs. msec.) were averaged to compute mean ERGs ($n=20$) & VEPs ($n=14$). Control ERGs on the amber background showed no ERG to the ISCEV scotopic flash (0.01 $\text{cd/m}^2/\text{sec.}$) & a small S cone ERG to the 300X brighter standard flash indicating no recordable input from rods, M & L cones.

Results: ERGs revealed a small amplitude S cone ERG followed by a wave of negativity derived from S cone inhibitory input to ipRGCs. Amplitudes were quantified as this negative trough to the first positive peak (ipRGC on response). Log amplitude increased with log luminance ($F=13,787$, $P<.0001$, $r^2=1$). ipRGC latency was quantified as the difference between negative trough & positive peak latencies which was highly correlated with amplitude ($P<.0001$, $r^2=0.76$). The ratio of ipRGC amplitude/latency (throughput) provides a new metric which combines the two variables & is highly dependent on luminance ($P<.02$, $r^2=0.76$). The flash VEP 1st positive peak (decreased in glaucoma), increased exponentially with ipRGC amplitude ($r^2=0.91$), a potential visual perceptual metric of ipRGCs.

Conclusions: Selective chromatic adaptation reveals retinal & cortical function of ipRGCs, including unique inhibitory input from S cones & putative metrics of visual perception. Planned research will examine pupils using the same visual stimulus.

CONTROL ID: 3542927

SUBMITTER (NAME ONLY): Robin Kuriakose

TITLE: Comparative Outcomes of Intravitreal Triamcinolone Acetonide-Moxifloxacin with Intracameral Dexamethasone-Moxifloxacin-Ketorolac in Cataract Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Kuriakose, S. Cho, S. Nassiri, F. Hwang, Eye Institute, Loma Linda University, Loma Linda, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal or intracameral antibiotic-steroid formulations are effective in preventing infection and controlling postoperative intraocular inflammation in cataract surgery. This study sought to compare the effectiveness of intravitreal triamcinolone acetonide-moxifloxacin versus intracameral dexamethasone-moxifloxacin-ketorolac in cataract surgery.

Methods: A retrospective longitudinal comparative study among 401 consecutive eyes receiving either intraoperative triamcinolone acetonide-moxifloxacin or dexamethasone-moxifloxacin-ketorolac was performed between November 2016 and January 2020. Primary endpoints at postoperative day one (POD1), week one (POW1), and month one (POM1) included corneal edema, anterior chamber inflammation (ACI), and intraocular pressure (IOP).

Results: On POD1, there was no statistically significant difference between the two groups (OR: 1.11 [0.66-1.86]; $p=0.69$) but at POW1, dexamethasone-moxifloxacin-ketorolac had significantly more ACI compared to triamcinolone acetonide-moxifloxacin (OR: 2.11 [1.22-3.66]; $p=0.008$). By POM1, there was no significant difference ($p=0.98$). At all time points, corneal edema severity was not significantly different. IOP was found to be significantly elevated in the triamcinolone acetonide-moxifloxacin group compared to the dexamethasone-moxifloxacin-ketorolac group by POM1 (15.64mmHg versus 13.16 mmHg, $p=0.001$). There was no statistical difference in rates of CME (OR: 0.13 [0.01-1.51]; $p=0.06$) and there were no cases of endophthalmitis.

Conclusions: While triamcinolone acetonide-moxifloxacin demonstrates earlier postoperative inflammatory control compared to dexamethasone-moxifloxacin-ketorolac, both are effective in the postoperative recovery of cataract surgery. Additionally, intravitreal triamcinolone acetonide-moxifloxacin causes a slightly higher but significant IOP compared to intracameral dexamethasone-moxifloxacin-ketorolac. This study reinforces them as viable alternatives to traditional postoperative drops.

CONTROL ID: 3542940

SUBMITTER (NAME ONLY): Jacinta Walz

TITLE: Visuospatial attention allocation as an indicator of cognitive deficit in traumatic brain injury: a systematic review and meta-analysis

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Walz, R. Mani, S. Khuu, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA]

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ABSTRACT BODY:

Purpose: Traumatic brain injury (TBI) is characterised by a host of physiological and cognitive deficits such as attention problems. In the present study, we systematically reviewed previous literature that investigated whether and how TBI affects the ability to allocate visuospatial attention i.e., the ability to use and respond to endogenous and exogenous visual cues.

Methods: A literature search using keywords such as “traumatic brain injury” and “visual attention” found 50 papers. Of these, 18 met our inclusion criteria and a systematic review was conducted. 16 studies met the criteria for inclusion in our meta-analysis and 80 effect size estimates of various visual search and attention allocation tasks were obtained. These effect sizes were computed from 459 TBI cases and 458 matched controls using the random effect model.

Results: The systematic review indicated a large degree of variability in task design and a lack of consensus for assessing attention allocation between endogenous and exogenous attention tasks. The combined effect size of the impact of TBI on visuospatial attention allocation was large ($g=0.79$, $p<0.0001$) with medium heterogeneity ($I^2=68.39\%$). Subgroup analyses revealed an increase in deficit for moderate-to-severe and severe TBI compared to mild TBI ($F(2,76)=24.14$, $p<0.0001$, $g(\text{mild})=0.32$, $g(\text{moderate-to-severe})=0.95$, $g(\text{severe})=1.27$). Task type (no cue, endogenous or exogenous cue) had a significant impact on effect size ($g(\text{no cue})=0.98$, $g(\text{endogenous cue})=0.70$, $g(\text{exogenous cue})=0.45$, $p=0.0051$) indicating that higher order processes were affected to a greater degree than bottom-up processes. Meta-regression analyses revealed significant improvement in visual attention deficit with time ($p(\text{mild})=0.031$, $p(\text{moderate-to-severe})=0.002$, $p(\text{severe})<0.0001$) with recovery from mild injury occurring after approximately 460 days.

Conclusions: Visual attention is largely in deficit as a result of TBI. However, injury severity and the type of visual attention allocation (endogenous vs. exogenous) are significant factors in indicating the degree of deficit. Assessment of visual attention, using a systematic attention allocation task, may provide a useful clinical measure of cognitive impairment after TBI and could be used to detect and monitor TBI, indicate recovery over time or be used to assess the effectiveness of treatment and rehabilitation programs.

CONTROL ID: 3542941

SUBMITTER (NAME ONLY): Moosa Zaidi

TITLE: Inferring retinal ganglion cell light response properties from intrinsic electrical feature

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: An ideal epiretinal implant for treating vision loss would stimulate each retinal ganglion cell (RGC) of each distinct type according to its natural function, to reproduce the neural code of the retina. However, no methods exist to determine the normal, healthy light response properties of each RGC of each type in a region of retina that is no longer light-responsive. This study presents a method to infer a model of RGC light responses using only intrinsic features of recorded electrical activity.

Methods: Analysis was performed on 283 recordings from populations of ON and OFF parasol RGCs in isolated macaque retina using 512-electrode arrays. The type of each recorded RGC was determined from its light responses. To emulate interfacing to a blind retina, a classifier was used to infer the type (ON or OFF) of each cell using two features of recorded electrical activity, without reference to the light stimulus: the average electrical image (EI) of a spike over the electrode array, and the autocorrelation function (ACF) of spike times. EIs were also used to infer receptive field locations. A linear-nonlinear Poisson (LNP) light response model was then inferred for each cell using its true cell label, its estimated location, and the average spatiotemporal filter and nonlinearity in the population. The prediction accuracy of inferred models and models fitted to measured responses was compared, for white noise and natural scenes stimuli (Fig. 1).

Results: K-means (k=2) clustering of the top 2 principal components of ACFs reliably separated ON and OFF parasol cells in individual retinas. However, cluster labels (ON, OFF) could not be reliably determined from ACFs, due to inter-retina variability. Instead, ACF clusters were labeled using "votes" from a cell-by-cell linear classifier of selected EI features. This approach achieved 94% mean accuracy on 25 test retinas. Across six retinas, the RGC light response models produced a mean correlation between inferred models and data of 0.48 and 0.51, and between fitted models and data of 0.63 and 0.57 (an upper bound), for white noise and natural scenes stimuli respectively.

Conclusions: Intrinsic features of electrical activity can be used to infer RGC light response models.

CONTROL ID: 3542942

SUBMITTER (NAME ONLY): songyi seo

TITLE: A Fully Human Monoclonal Antibody Targeting c-KIT is a Potent Inhibitor of Choroidal Neovascularization in Murine Model of Neovascular Age-Related Macular Degeneration

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In our previous study, stem cell factor (SCF) and its receptor, cKIT, are identified as novel regulators of angiogenesis at hypoxia and pathological neovascularization in the eye, which suggests that suppression of SCF/cKIT signaling would be a new pharmacological strategy for the treatment of ocular vascular diseases such as neovascular age-related macular degeneration (nAMD). In this regard, the present study aims to determine the efficacy and safety of newly developed fully human monoclonal IgG targeting cKIT (NN2101) in the murine model of nAMD.

Methods: Inhibitory effect of NN2101 on SCF-induced angiogenesis was evaluated by western blotting and in vitro angiogenesis assays. Efficacy of intravitreal injection of NN2101 alone and its combination with aflibercept was determined using mice with laser injury-induced choroidal neovascularization (CNV). One week later, choroidal tissues were harvested for further analysis. Ocular toxicity and pharmacokinetics of intravitreal injection of NN2101 were assessed in mice and rabbits, respectively. All data were analyzed for normality, followed by an unpaired Student's t-test, one-way ANOVA with Bonferroni's test, or Kruskal-Wallis test.

Results: In hypoxic human vascular endothelial cells, NN2101 completely blocked the SCF-induced activation of cKIT/ β -catenin signaling pathways and increase in cell migration, tube formation, and proliferation. In mice with laser-induced CNV, an intravitreal injection of NN2101 (1.0 μ g) significantly alleviated CNV formation with a comparable efficacy of aflibercept (2.5 μ g) (Kruskal-Wallis test, $*p < 0.01$, $n > 6$ mice). Combined intravitreal injection of suboptimal doses of NN2101 and aflibercept substantially enhanced anti-angiogenic efficacy (Kruskal-Wallis test, $*p < 0.05$, $n > 7$ mice). In addition, NN2101 neither caused ocular toxicity nor interfered early retinal vascular development in mice. Ocular Pharmacokinetic analysis of the rabbits after intravitreal injection administration of NN2101 showed that NN2101 rapidly distributed and remained in retinal and choroidal tissues even after 30 days or more.

Conclusions: NN2101, a fully human monoclonal antibody targeting cKIT, may be a novel promising therapeutic and can enhance the potency of existing anti-vascular endothelial growth factor agents for the treatment of nAMD.

CONTROL ID: 3542948

SUBMITTER (NAME ONLY): Ting-I Sung

TITLE: COVID 19 and use of an iphone retinal camera

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sung, Neurobiology, University of California San Diego, La Jolla, California, UNITED STATES|G. Wu, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|B. Nguyen, Pacific Union College, Angwin, California, UNITED STATES|D. Chien, University of California Los Angeles, Los Angeles, California, UNITED STATES|J. Huynh, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Use of the D Eye attachment for the iphone as an optic nerve imaging option in patients in the COVID19 pandemic

Methods: Inclusion criteria: 20/20-20/50 vision, informed consent was obtained. D-Eye digital retinal camera (Padova, Italy) was used on the dilated and undilated eyes of patients. The camera was attached to an iphone 6 (Apple, Cupertino CA), video mode was used to attain an image of the optic nerve and internally timed on the iphone 6). Optos California model (Dunfermline, Scotland) was then used to take optic nerve images of both dilated and undilated eyes of patients for comparison. The start time and end time was recorded from the timestamp of the first and last image taken on Optos, then the difference between both timestamps was calculated to obtain time spent on OPTOS.

Results: For dilated patients (n=14, 26 eyes), the average time taken to obtain a clear video of both eyes using D-Eye was 28.5 seconds. The average time to take images of both eyes using OPTOS was 1.71 minutes. The p-value of the average time is 0.000373.

For undilated patients (n=10, 20 eyes), the average time of a clear video of both eyes using D-Eye was 29.8 seconds. The average time to take clear images of both eyes using OPTOS was 1.2 minutes. The p-value of the average time is 0.000213.

Conclusions: The D-Eye smartphone device and its short image acquisition time may be useful with wheelchair patients or with patients who want to be seen quickly in the COVID setting indoors or outdoors. We look forward to future studies of the D-Eye in the COVID era and ophthalmology.

CONTROL ID: 3542953

SUBMITTER (NAME ONLY): Jimmy Mailloux

TITLE: Retinal detachment caused by endophthalmitis: a retrospective case series study

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mailloux, A. Lachance, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Faculté de médecine, Université Laval, Québec, Québec, CANADA | A. Lachance, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Département d'ophtalmologie et d'oto-rhino-laryngologie – chirurgie cervico-faciale, Centre Universitaire d'Ophtalmologie, Hôpital du Saint-Sacrement, CHU de Québec-Université Laval, Québec, Québec, CANADA |

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ABSTRACT BODY:

Purpose: The present study reports patients with endophthalmitis-related retinal detachment (RD) managed with vitrectomy.

Methods: The present study included consecutive eyes who had surgery for endophthalmitis-related RD at CHU de Québec – Université Laval (Canada) between April 2009 and November 2019. The data were collected retrospectively. The main variables were: etiology of endophthalmitis, classified into endogenous and exogenous (posttraumatic, corneal ulcer, post cataract surgery and post intraocular injection), causing microorganisms found in the intraocular fluid (IOF), type and description of RD, best corrected visual acuity (BCVA) after vitrectomy, and retina status at final follow up. The main outcomes were the final visual acuity and retina status at final follow up.

Results: 17 eyes (14 males and 3 females) were included in this study. The mean age was 59 ± 20 (17-97) years. We identified many types of RD (8 tractional RD, 6 total RD, 2 rhegmatogenous RD, and 1 serous RD). Microorganisms were detected in 14 cases out of 17 (82.4%): Staphylococcus epidermidis in 3 cases, Staphylococcus lugdunensis in 1 case, Propionibacterium acnes in 2 cases and Streptococcus spp. in 3 cases (viridans, salivarius and pneumoniae). Concomitant microorganisms were found in 5 cases (Strep. B-hemolytic group G + Staphylococcus epidermidis, Propionibacterium acnes + Staphylococcus epidermidis + mycogenous elements, Streptococcus pyogenes + Staphylococcus epidermidis + Propionibacterium acnes, Streptococcus oralis + Streptococcus mitis and Staphylococcus saprophyticus + Staphylococcus warneri). The mean follow up duration was 13 months. The BCVA at last follow up was variable: 1 patient (5.9%) had a BCVA $\geq 20/40$, 6 patients (35.3%) had a BCVA between 20/40 and 20/400, 3 patients (17.6%) had a BCVA of counting fingers (CF), 4 patients (23.5%) had a BCVA of hand motions (HM), 2 patients (11.8%) had a BCVA of light perception (LP), and 1 patient (5.9%) had no light perception (NLP). 9 of 17 retina (52.9%) were successfully reattached, 5 of 17 retina (29.4%) were reattached with silicone oil, 1 retina was reattached with macular atrophy and 1 retina was reattached with macular fibrosis. One patient had evisceration of the eye.

Conclusions: Endophthalmitis-related RD is associated with poor visual acuity outcome (11 patients (64.7%) had CF, HM, LP or NLP as visual outcome) and microorganisms were frequently found in the IOF (71%).

CONTROL ID: 3542954

SUBMITTER (NAME ONLY): Vasanth Muthusamy

TITLE: What do healthcare consumers think about visual field tests: present and future

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To administer an on-line questionnaire in Australia to understand healthcare consumers experience with current visual field (VF) tests, and opinions regarding future improvements to VF tests.

Methods: A Qualtrics survey was distributed via Glaucoma Australia (support group for people with glaucoma), and to people with glaucoma who had previously participated in our research. The survey assessed three domains: 1) demographics and experience with visual field tests; 2) opinions regarding test duration and frequency; and 3) perspectives on future developments. Surveys with 100% question completion were analysed, resulting in a total of 152 responses. Median (IQR) is given for non-categorical data.

Results: Respondent demographics were: age 66 (60 - 72) years; most (70%) had experience of more than 11 visual field tests, with 37% having experience of more than 20 tests. Participants estimated that they completed visual field tests in 6 (5 - 8) minutes. The reported VF visit frequency was: once a year (29%), twice a year (57%), thrice a year (9%), every two years (3%), with others being less often. Opinions regarding test duration and frequency were as follows: participants were willing to accept an addition of 5 (3 - 6) minutes for a single VF test if more information about their VF could be obtained. We asked how many total tests per visit they would be prepared to undergo if evidence emerges that more than 1 test per appointment is useful: 1 test (7%), 2 tests (55%), 3 tests (18%), and >3 tests (20%). More respondents were prepared to increase tests per visit than increase visits per year. Table 1 describes participant responses regarding future VF developments.

Conclusions: Healthcare consumers prioritise information over test duration and are willing to undertake more or longer tests to obtain more information. This study provides valuable information on healthcare consumer preferences for VF tests, and may help scientists and industry design and understand healthcare consumer preparedness for new VF methods.

CONTROL ID: 3542955

SUBMITTER (NAME ONLY): David Ramsey

TITLE: Investigating the Arden hypothesis: a one-year trial investigating the prevention of dark adaptation as complementary therapy for diabetic macular edema

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Ramsey, G.R. Blaha, J. Chang, F.C. Barouch, J.L. Marx, Ophthalmology, Beth Israel Lahey Health, Burlington, Massachusetts, UNITED STATES|D.J. Ramsey, G.R. Blaha, J. Chang, F.C. Barouch, J.L. Marx, Ophthalmology, Tufts University School of Medicine, Peabody, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Light-at-night is an effective method to arrest the dark adaptation of rod photoreceptors and thereby reduce the metabolic activity of the retina, with the aim of reducing oxygen consumption associated with hypoxia that is present in the retina of patients with diabetic retinopathy. The present study evaluated the feasibility of wearing an illuminated sleep mask in patients with diabetes treated for clinically-significant macular edema (CSME) with intravitreal injections.

Methods: Patients with diabetic retinopathy initiating monthly injections of bevacizumab or ranibizumab for CSME were enrolled in a pilot study that used light masks to deliver light-at-night. Patients were randomized to one of two different light regimens in order to differentiate the tolerability of the device from that of the light-at-night treatment. One group received masks equipped with green LEDs (520nm) with an intensity chosen to inactivate the dark current (100 LUX). The other set of masks were configured with red LEDs (670nm) below the threshold necessary to prevent dark adaptation (<5 LUX). Primary outcome was the ability to use the device continuously over the 12-month trial. Secondary outcome was the number of anti-vascular endothelial growth factor (VEGF) injections.

Results: Out of 30 patients consented, 11 participants (37%) failed to adopt the light mask, returning the device within the first week. Five out of nine participants (56%) assigned to masks with red LEDs withdrew or failed to complete the 12 monthly study visits, while two out of ten participants (20%) assigned to the masks equipped with green LEDs did not complete the trial (OR 0.10 CI 0.01 to 0.95, P = 0.046). Using an intention-to-treat analysis found no difference in the number of intravitreal injections administered to participants with red versus green masks (12.3 versus 10.8, P = 0.122). Self-reported compliance with nightly use of the sleep mask was poor. Only an average of 63% of logs documenting nightly battery changes were returned by participants who completed the trial (range 19% to 100%).

Conclusions: Use of a lighted sleep mask poses a challenge for a majority of patients treated for CSME with anti-VEGF injections. There is insufficient evidence to evaluate the effectiveness of light-at-night delivered by this means as a complementary therapy for diabetic retinopathy.

CONTROL ID: 3542958

SUBMITTER (NAME ONLY): Koosha Ramezani

TITLE: Longitudinal Follow-up of Vascularized Drusen

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To Evaluate the correlation of baseline characteristics of vascularized drusen with the risk of progression to choroidal neovascularization (CNV) using optical coherence tomography angiography (OCTA).

Methods: This was a post-hoc longitudinal analysis of eyes from the PROCON study, a 24-month masked controlled study evaluating intravitreal quarterly aflibercept for prophylaxis against conversion to exudative disease in 128 patients with intermediate non-exudative AMD in the study eye and exudative AMD in the fellow eye. OCTA B-scans were analyzed at baseline to detect eyes with vascularized drusen (presence of flow within the drusen). Eyes were graded for conversion to exudation using fluorescein angiography and structural OCT. Characteristics of vascularized drusen were evaluated at baseline and the last available visit in eyes with no conversion, or the visit immediately prior to conversion in eyes that converted.

Results: Eight vascularized drusen in 6 eyes identified by OCTA were included. Two eyes developed CNV after 15 and 9 months. In the 4 eyes with no CNV development, the mean [SD] baseline height, width, and area at the maximum height of vascularized drusen were 75.667 [11.96], 196.833 [57.41], and 0.012 [0.005] microns, respectively. In the two eyes with CNV development, the mean [SD] baseline height, width, and area at the maximum height were 88.5 [19.09], 265 [25.46], and 0.015 [0.001] microns, respectively (P-values > 0.05 for differences between two groups).

In 1 non-converted eye the vascularized druse was not detected on the follow up visit. The mean [SD] of the vascularized drusen height, width, and area at the maximum height at the 24-month follow-up in eyes with no conversion were 69.800 [8.07], 234.00 [86.28], and 0.012 [0.005] microns, respectively. These values were 90.5 [7.78], 256 [45.25], and 0.020 [0.005] microns for the two eyes with conversion (P-value = 0.03 for differences in druse height and >0.05 for width and area between two groups at follow up). No overlying retinal pigment epithelium disruption was noted over vascularized drusen on either baseline or follow up. Two drusen in eyes with conversion and three drusen from two non-converted eyes showed ellipsoid zone line disruption.

Conclusions: In this study, the 2 eyes with conversion had larger vascularized drusen at baseline. Larger studies are required to explore the association of vascularized drusen characteristics and CNV development.

CONTROL ID: 3542959

SUBMITTER (NAME ONLY): Sonali Nashine

TITLE: ROLE OF INFLAMMATION MARKERS AND EFFECTS OF HUMANIN G IN AMD

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.R. Nashine, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|M. Kenney, Pathology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inflammation is a critical player in the etiology and pathogenesis of Age-related Macular Degeneration (AMD). Humanin G (HNG) is a Mitochondrial Derived Peptide (MDP) that is cytoprotective in AMD. The goal of this study was to test our hypothesis that the inflammation markers- CD62P i.e., P Selectin and CD62E i.e., E Selectin proteins, are increased in AMD and HNG treatment in vitro leads to reduction in their protein levels.

Methods: In this study, we used: 1) blood plasma isolated from AMD patients and age-matched control subjects, and 2) AMD and control transmitochondrial RPE cybrid cell lines. HNG was exogenously added to AMD cybrids, which have identical nuclei from the mitochondria-deficient ARPE-19 cells but differed in mitochondrial DNA (mtDNA) content derived from clinically characterized AMD patients and control subjects. Cell lysates were extracted from untreated and HNG-treated AMD and control cybrids, and then analyzed using the Luminex multiplex assay to determine the protein levels of CD62P and CD62E.

Results: The CD62P protein levels were 152% higher in AMD plasma samples (2.52 ± 0.41 , $n=3$) vs. Controls (1 ± 0.2 , $n=3$) ($p=0.03$). Treatment with HNG led to a 37% decrease in CD62P protein levels in control cybrid cell lysates (Untreated: 1 ± 0.34 ; HNG-treated: 0.63 ± 0.04) and a 21% decrease in CD62P protein levels in AMD cybrid cell lysates (Untreated: 1 ± 0.24 ; HNG-treated: 0.79 ± 0.09). Furthermore, CD62E protein levels were 176% higher in AMD plasma samples (2.76 ± 0.48 , $n=3$) vs. Controls (1 ± 0.28 , $n=3$) ($p=0.03$). Treatment with HNG led to 18% decrease in CD62E protein levels in AMD cell lysates (Untreated: 1 ± 0.02 ; HNG-treated: 0.82 ± 0.02). No difference was found in CD62E protein levels between untreated vs. HNG-treated control cell lysates.

Conclusions: In summary, we observed: 1) significantly higher levels of CD62P and CD62E proteins in AMD plasma samples compared with control plasma samples, and 2) HNG reduced the CD62P and CD62E protein levels in cell lysates, thereby suggesting that HNG may rescue the mtDNA-mediated inflammation in AMD cybrids. In conclusion, this study presents novel findings that suggest the role of 1) CD62P and CD62E in AMD pathogenesis and 2) HNG as a potential target for reducing Selectins-associated inflammation in AMD. Further studies are required to establish the role of HNG in reducing inflammation by decreasing the protein levels of Selectins in AMD.

CONTROL ID: 3542962

SUBMITTER (NAME ONLY): Seyed Omid Mohammadi

TITLE: Toxicity of p(g3T2) Polymer on Human Retinal Pigment Epithelium Cells

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To analyze the effects of the conjugated p(g3T2) polymer, a rapidly expanding material that can increase its volume by a factor of 100, on human retinal pigment epithelium cell proliferation in vitro.

Methods: Human retinal pigment epithelium cells (ARPE-19) were plated for 24 hours on p(g3T2)-coated well plates. The polymer has a polythiophene backbone with ethylene glycol side chains. To coat the plates, 20µL per well of a 1mg/mL polymer/DMSO solution was applied. The plates were shaken gently until the solution was dry. Non-polymer-coated plates were plated with ARPE-19 cells in the same culture media; this was used as the control for this study. Using the label-free confluence measurement of Incucyte® system over a 132-hour time period, both plates were analyzed for percent cell confluency by analyzing the occupied area of the wells, and then a two-way repeated-measures (RM) ANOVA was performed.

Results: The p(g3T2)-coated plate showed an increase in overall percent confluency from 35.5% to 79.7% over 132 hours (Figure 1). When compared to the control, the confluency of the p(g3T2)-coated plate became significantly lower after 56 hours and remained lower throughout the rest of the study (p=0.0002). In addition, the overall confluency rate of the p(g3T2)-coated polymer was lower than that of the control visualized in the differing slopes in Figure 1.

Conclusions: The increase in ARPE-19 cell proliferation when plated on the p(g3T2)-coated plate suggests the p(g3T2) polymer did not cause any severe toxic effects. The polymer did produce a lower percentage of confluency when compared to the control. This may be due to the polymer physically hindering the cells from adhering to the surface of the plate. This pilot study suggested that p(g3T2) had a mild effect on ARPE-19 cell proliferation, but no apparent widespread cell death was observed. Further studies using different cell lines and ex vivo tissues treated with p(g3T2) are underway to establish a preclinical safety profile of this polymer with many potential therapeutic applications.

CONTROL ID: 3542966

SUBMITTER (NAME ONLY): Rui Ma

TITLE: Synthetic retinal ganglion cell image generation for deep-learning-based neuronal tracing

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ma, L. Hao, X. Mendoza, M. Khodeiry, Y. LIU, R.K. Lee, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|R. Ma, Y. Tao, M. Shyu, Department of Electrical and Computer Engineering, University of Miami School of Engineering, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: While most deep learning-based retinal ganglion cell (RGC) neuronal axon and dendritic tracing algorithms have superior performance over conventional ones, they usually require a large amount of manually annotated training data and do not generalize well when the types of neurons in training and testing datasets are significantly different. We developed and tested an automated deep learning-based neuronal tracing approach that can be applied to trace the axons and dendrites in different types of retinal ganglion cell images that does not require manually traced neuronal images for training.

Methods: A data mining algorithm is proposed to learn the noise patterns from raw retinal ganglion cell images. These noise patterns were incorporated into 2,400 digitally reconstructed neuron images downloaded from open source databases of neuronal morphologies to obtain a training dataset of synthetic neuron images. A deep learning-based image segmentation model, ResUNet, was then employed to trace the axons and dendrites in neuronal images. This deep learning model was trained using our synthetic dataset and evaluated on two different testing datasets, including a different synthetic neuron dataset with 300 images and an RGC neuron dataset with 52 images. For the synthetic testing dataset, the digitally reconstructed neurons were utilized as the ground truth images for tracing, while manual tracing results from human experts were considered as the gold standard for the RGC datasets.

Results: Our neuron tracing model can effectively trace the axons and dendrites in both synthetic and RGC neuron images. Quantitatively, our model achieves average foreground, background and overall accuracy of 0.880, 0.994 and 0.993 on the synthetic dataset, 0.757, 0.990 and 0.990 on the RGC dataset, respectively.

Conclusions: The tracing results demonstrate that our neuronal image generation algorithm can accurately produce training data. More importantly, unlike all the other deep-learning-based neuron tracing algorithms, our approach does not require manually traced neuronal image during training and significantly improves raw data analysis times.

CONTROL ID: 3542967

SUBMITTER (NAME ONLY): Jessica Liu

TITLE: Consequences of Treatment Lapse in Retinal Vein Occlusion Patients Receiving Anti-Vascular Endothelial Growth Factors Injections

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Liu, P. Alsaloum, R.P. Singh, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|A. Iyer, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|P. Kaiser, Dartmouth College, Hanover, New Hampshire, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-vascular endothelial growth factor (VEGF) injections are first-line therapy for retinal vein occlusion (RVO). However, it is challenging for patients to maintain appropriate care due to the high frequency of injections required for anti-VEGF therapy. This study examines the response of retinal biomarkers to lapses in anti-VEGF treatment in RVO patients.

Methods: A retrospective chart review evaluated patients with branched retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO) at the Cleveland Clinic from January 2012 to June 2020. Patients 18 or older were divided into two cohorts: RVO patients with no lapse in anti-VEGF treatment (control group) and RVO patients with a lapse ≥ 3 months (lapse group). Notably, patients on treat-and-extend or pro re nata protocols were excluded. Central subfield thickness (CST) and visual acuity (VA) were collected at baseline, the first appointment post-lapse, and at 3, 6, and 12 month follow up appointments. Relationships between continuous variables were assessed using t-tests while relationships between categorical variables were assessed using Pearson Chi-Square or Fisher Exact tests.

Results: Lapse patients (n=69) and control patients (n=69) had similar baseline CST ($347.7 \pm 127.8 \mu\text{m}$ vs $365.6 \pm 139.4 \mu\text{m}$, $p=0.436$) and VA (64.1 ± 20.6 ETDRS vs 58.9 ± 20.2 ETDRS, $p=0.588$). Lapse patients experienced a significant increase in CST after discontinuing anti-VEGF therapy (lapse: $398.7 \pm 191.3 \mu\text{m}$, control $338.9 \pm 119.9 \mu\text{m}$, $p=0.034$). This persisted 12 months post-lapse and after re-initiation of anti-VEGF agents (lapse: $381.6 \pm 161.1 \mu\text{m}$, control: $307.5 \pm 95.4 \mu\text{m}$, $p=0.017$). Lapse patients also experienced a decrease in VA after lapse (lapse: 54.5 ± 25.0 ETDRS, control: 64.7 ± 17.5 ETDRS, $p<0.001$) that recovered after 6 months.

Conclusions: Patients with BRVO or CRVO with any lapse in treatment are at risk for poorer outcomes. Though VA normalizes upon treatment resumption, patients experience a statistically and clinically significant increase in CST that does not recover. Further analysis may focus on the impact of persistent anatomic change present 1 year after anti-VEGF resumption.

CONTROL ID: 3542974

SUBMITTER (NAME ONLY): Roger Beuerman

TITLE: Non-contact device for the rapid identification of fungal and bacterial pathogens in the living cornea

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.W. Beuerman, Hamilton Eye institute, Univ TN Health Science Center, Memphis, Tennessee, UNITED STATES|R.W. Beuerman, T. Aung, Anti-infectives, Singapore Eye Research Institute, Singapore, --Please select a state--, SINGAPORE|E. Tan, Tan-Technospex Pte, SINGAPORE|

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ABSTRACT BODY:

Purpose: Optimal treatment of anterior segment bacterial or fungal infections is compromised by the restrictions on obtaining adequate microbial samples from the living eye resulting in identification in only about 50% of cases. The goal of this study has been to test a new instrument designed as a noncontact, safe and accurate in experimental infections of the rabbit cornea. Corneal scanning required 10-20 sec. Both genus and species data was obtained for most organisms.

Methods: Sterile miniblade (Beaver-Visitec International, MA, USA) was used to make corneal scratches and ten microliters of a bacterial suspension containing 1×10^5 colony forming units (CFU) per microliter *P. aeruginosa* or *Staphylococcus aureus*, MRSA was topically applied to the scratched cornea. Raman spectrum imaging was carried out at day 1 and day 3 post infection. The custom-built Raman spectroscopy system consist of a near-infrared laser (785nm) as the excitation source. To image the mouse cornea, a special holder was built and integrated into a XYZ motorized stage. The light collected was focused onto the slit of a spectrometer (Andor, Kymera 328i). A back-illuminated deep-depleting thermoelectrically cooled 1024×127 pixel CCD (Andor, iDus 401) was used for the acquisition of Raman spectra. Additional rabbit corneas were infected with *C. albicans* (ATCC 2091), *A.fumigatus* (ATCC 3626) , or *F. solani* (ATCC 46492) and imaged at three days post-infection. Principal component analysis was the primary method of analysis.

Results: Our modified Raman Spectroscopy system analyzes the interaction of light with materials and living cells and tissues providing information about the structure of the scanned substance. As a non-destructive technique it reflects protein structure.

The spectrum for *S. aureus* (ATCC 29213) and *P. aeruginosa* (ATCC 9027) revealed peaks such as uracil, phenylalanine, amide I and amide III. However, the amplitudes of these spectra peaks varied according to the organism making the organisms readily differentiated. Spectra for the three fungi were individually differentiated. Principal component analysis confirmed the raw data results.

Conclusions: The new method presented here has advantages over competing techniques of conventional pathogen identification or confocal, MALDI or immunological methods as it is rapid, non-damaging and gives both genus and species information.

CONTROL ID: 3542980

SUBMITTER (NAME ONLY): Yudong Tao

TITLE: Deep reinforcement learning for optimized visual field analysis

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Existing visual field testing algorithms rely on manually crafted rules to determine the contrast sensitivity of a light stimulus at each step as well as the stopping criterion, which is suboptimal in terms of testing accuracy and speed. We developed and tested a deep reinforcement learning (DRL)-based visual field testing algorithm that achieves greater performance gain in terms of testing accuracy, speed, and robustness than the Zippy Estimation by Sequential Testing (ZEST) algorithm.

Methods: Our algorithm formulates the procedure of white-on-white static automated perimetry (SAP) as a reinforcement learning problem, with the perimeter modeled as an intelligent agent that could interact with the patient. At each step, the agent can choose to present a stimulus with a specific intensity to the patient or activate a stop signal to end the test and predict the sensitivity. By training the agent on our visual field dataset with 275 normal and 433 glaucomatous visual fields, a new rule is learned by the agent. This rule can guide the agent to perform a series of optimized actions in each test, which leads to the highest testing accuracy with the fewest number of stimuli presentations.

Results: The proposed algorithm was evaluated on both synthetic datasets and our patient visual field dataset under different prior distributions. Experimental results show that our algorithm is 9.4% faster and 5.6% more accurate than ZEST ($p = 0.025$). Meanwhile, our algorithm can generalize better than ZEST when the distribution of testing data is different from the initial distribution.

Conclusions: Our results demonstrate that our DRL-based visual field testing algorithm performs better than ZEST. By maintaining higher accuracy with reduced testing time, our algorithm increases clinic efficiency, improves patient satisfaction, and improves testing results with less patient fatigue. Moreover, the improved generalization ability our algorithm ensures test reliability and robustness of our algorithm.

CONTROL ID: 3542986

SUBMITTER (NAME ONLY): Marium Sohail

TITLE: FREE DOWNLOADABLE APP TRACKS FUNCTIONAL GLAUCOMATOUS LOSS

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sohail, S.H. Hirji, J.M. Liebmann, G.A. Cioffi, D. Blumberg, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the covid crisis and beyond, it is critical that we find home-based monitoring tools to measure progressive glaucomatous damage. The primary purpose of this study is to examine the correlation between glaucomatous visual field loss and contrast sensitivity (CS) measured using a home based app.

Methods: 30 patients across the glaucomatous disease spectrum and with good central visual acuity tested a home based app, the Berkeley Contrast Squares (BCSA), that measures CS. The BCSA is a free-downloadable tool that records users' binocular contrast sensitivity and is valid for varying degrees of visual acuity. Patients were sent a video (4min 46s) via email that contained detailed instructions on how to download and use the BCSA at home. The test-retest window was 15 weeks. Validity analyses was calculated using a mixed effects linear regression with log contrast sensitivity as the predictor and visual field as the outcome.

Results: In glaucoma patients the overall correlation for test-retest reliability was 0.94. Validity analyses showed high correlations between home-based contrast testing and 10-2 VF ($p=0.002$) and 24-2 VF ($p=0.05$). A change in 0.1 Log Weber corresponded to a 0.8 dB decline in 24-2 VF MD (95%CI [0.24 to 18.0])) and a 1.3 dB decline in 10-2 VF MD (95% CI [5.2 to 21.0]).

Conclusions: A free downloadable app provides a highly repeatable measure of CS. These results significantly correlate with functional visual field loss. This study suggests that the Berkeley Contrast Squares App has potential to be adopted as a home monitoring tool to track the progression of glaucoma between regular office visits.

CONTROL ID: 3542990

SUBMITTER (NAME ONLY): Nita Valikodath

TITLE: Longitudinal OCTA changes in non-proliferative diabetic retinopathy

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Valikodath, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|D. Le, X. Li, X. Yao, J.I. Lim, Department of Ophthalmology and Visual Sciences, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate optical coherence tomography angiography (OCTA) changes in patients with non-proliferative diabetic retinopathy (NPDR)

Methods: This is a preliminary study to explore early vessel parameter changes after an anti-VEGF intravitreal injection in eyes with macular edema and NPDR. The electronic medical record was reviewed to obtain information regarding disease severity, presence of diabetic macular edema and treatment. OCTA information was reviewed and six quantitative OCTA features including VCI (vessel complexity index), VAD (vessel area density), VSD (vessel skeleton density), BVT (blood vessel tortuosity), VDI (vessel diameter index), and VPI (vessel perimeter index) were recorded. Statistical analyses were performed using MATLAB (Mathworks, Natick, MA, USA).

Results: A total of 23 eyes of 19 patients were evaluated across three visits. Mean visual acuity was 20/40 at visit 1, 20/50 at visit 2 and 20/50 at visit 3. From visit 1 to visit 2, 21 eyes remained stable, 3 eyes improved, and 6 eyes worsened in severity. From visit 2 to visit 3, 20 eyes remained stable, 7 eyes improved and 2 eyes worsened.

VCI was 0.37 ± 0.23 at visit 1, 0.46 ± 0.32 at visit 2, and 0.39 ± 0.32 at visit 3 (visit 1 and 2, $p=0.09$). VAD was 0.43 ± 0.27 at visit 1, 0.54 ± 0.31 at visit 2, and 0.48 ± 0.33 at visit 3 (visit 1 and 2, $p=0.01$). VSD was 0.45 ± 0.28 at visit 1, 0.54 ± 0.31 at visit 2, and 0.45 ± 0.32 at visit 3 (visit 1 and 2, $p=0.03$ and visit 2 and visit 3, $p=0.08$). BVT was 0.56 ± 0.22 at visit 1, 0.41 ± 0.27 at visit 2 and 0.44 ± 0.26 at visit 3 (visit 1 and 2, $p=0.01$ and visit 1 and visit 3, $p=0.04$). VDI was 0.25 ± 0.33 at visit 1, 0.18 ± 0.26 at visit 2, and 0.22 ± 0.25 at visit 3 (visit 2 and 3, $p=0.006$). VPI was 0.58 ± 0.29 at visit 1, 0.44 ± 0.26 at visit 2, and 0.61 ± 0.31 at visit 3 (visit 1 and 2, $p<0.001$, visit 2 and 3, $p=0.001$). See Figure 1 for an example of a patient with NPDR and OCTA changes.

Conclusions: Quantitative OCTA features including VAD, VSD, VPI, and BVT changed significantly between visits and can detect early changes in NPDR.

CONTROL ID: 3542991

SUBMITTER (NAME ONLY): Negin Nadvar

TITLE: A Novel Index for Quantification of Cross-modal Plasticity in Sight Restoration

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Nadvar, L. HERNANDEZ-GARCIA, J. Weiland, Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|J. Jonides, Department of Psychology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|J. Weiland, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have implied that sight restoration may result in reduction in (tactile-visual) cross-modal plasticity in primary visual cortex (V1), a potential impediment to recovery. However, using tactile-evoked V1 responses has not been shown to be an effective biomarker for plasticity, due to the extensive inter-subject variability reported in absolute activation baseline. In this work, we propose a novel index for measuring the tactile-visual plasticity in sight restoration that may more effectively quantify cross-modal plastic changes.

Methods: We recruited 2 blind retinitis pigmentosa subjects, implanted with Argus II retinal prosthesis per an approved IRB at the University of Michigan: P1 (male) and P2 (female), both implanted in the left eye and right-handed while received the implant 4 and 5 years ago, respectively. We collected functional MRI data from the subjects during right-hand tactile tasks. Activations were calculated in each subject's native space in the identified regions of interest (ROIs) for V1 and left primary somatosensory cortex (S1) in terms of strength (mean z statistics) and extent (%activated voxels in the ROI, FDR<0.05). Our proposed indices were calculated as the ratio of the strength of activation in S1 to V1 (S1 strength:V1 strength) and the ratio of extent of activation in S1 to V1 (S1 extent:V1 extent).

Results: Our results indicated that the S1 strength:V1 strength and S1 extent:V1 extent were higher in P1 (2.7 ± 0.8 and $9.7\% \pm 12.5\%$) with larger average device usage (1 hour/day) compared with P2 (2.1 ± 0.7 and $2.5\% \pm 1.2\%$) with less usage (2 hours/week). This cross-modal effect could not be uncovered by merely relying on the absolute strength/extent of activation in V1 for P1 (1.4 ± 0.4 and $22.5\% \pm 17.6\%$) compared with P2 (1.7 ± 0.3 and $40.0\% \pm 18.5\%$).

Conclusions: We hypothesize that our proposed S1:V1 index more accurately quantifies differences in strength and extent of activation by taking into account the relative contribution of V1 and S1 in processing a tactile task in each subject. We also propose that the extent of device usage, and not necessarily the time-since-implantation, cited in prior studies, is an effective factor for reversing cross-modal changes. Data from larger numbers of subjects with this rare condition are needed to further investigate our proposition.

CONTROL ID: 3542992

SUBMITTER (NAME ONLY): Jason Fan

TITLE: Visual Acuity Outcomes in Patients with Post-Surgical Suprachoroidal Hemorrhage

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fan, K. Fan, J.L. Hudson, H. Al-khersan, T. Lazzarini, H.W. Flynn, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate recent visual acuity (VA) outcomes in patients with suprachoroidal hemorrhage (SCH) after surgery, and to identify clinical features associated with visual prognosis.

Methods: A retrospective case series of 20 eyes from 20 patients diagnosed with SCH after cataract or glaucoma surgery between Jan. 2014 and Oct. 2020. Tabulated variables included age, sex, hypertension, diabetes, anticoagulation status, lens status, previous ocular surgery, surgery type causing SCH, presenting VA, presenting intraocular pressure (IOP), concurrent pathology on presentation (including flat anterior chamber, vitreous hemorrhage, retinal detachment), duration of apposition, management of SCH (observation, primary drainage, or delayed vitrectomy (PPV)), and post-operative outcomes (VA and IOP). The following LogMAR assignments were utilized: counting fingers = 1.9, hand motion = 2.3, light perception = 2.7, and no light perception = 3. OLS and logistic regression analyses were used for continuous and binary variables, respectively.

Results: The mean patient age was 81 years (SD 13.9), and 14 of 20 eyes were pseudophakic. In the series: 9 cases were post-glaucoma surgery, 7 post-cataract surgery, 4 post-corneal surgery (DSEK or PKP), and 2 from perforated corneal ulcers. SCH developed intraoperatively in 3 cases and post-operatively in 17 cases. The average VA on presentation was 2.45 LogMAR (SD 0.625), and average IOP was 20.1 mmHg (SD 16.9). 10 cases were managed with observation, 9 with delayed PPV, and 1 with delayed drainage. The average post-operative VA was 2.26 LogMAR (SD 0.66) on POD1, and 1.81 LogMAR (SD 0.94) on POM1. Presenting VA was predictive of POD1 ($b=0.563$, $p=0.013$) and POM1 VA ($b=0.74$, $p=0.022$).

Conclusions: Findings from this case series suggest that advances in the management of post-operative SCH have led to improved visual outcomes. A similar study performed at our institution 20 years prior showed that only 8/51 (16%) patients achieved 20/200 vision or better, and 14/51 (27.5%) patients had NLP vision after SCH. In this current series, 6/20 (30%) achieved 20/200 vision or better, and only 3/20 patients (15%) had NLP vision after SCH. Although no specific intervention was found to be predictive of better outcomes, further study of additional cases is required for a comprehensive comparison.

CONTROL ID: 3542998

SUBMITTER (NAME ONLY): Natalia Binczyk

TITLE: Frequency of anti-VEGF intravitreal injections (IVI) after post-injection endophthalmitis in patients with neovascular age related macular degeneration (nvAMD)

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.M. Binczyk, D. Plemel, M. Tennant, Ophthalmology, University of Alberta, Edmonton, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: Controversy exists regarding the impact of post injection endophthalmitis on IVI frequency in patients with nvAMD. We performed a retrospective chart review to assess the effect of anti-VEGF related endophthalmitis on injection frequency in patients with nvAMD.

Methods: All cases of post-IVI endophthalmitis occurring in Edmonton, Alberta, Canada between 2012-2019 were reviewed. Electronic records were analyzed for frequency of IVI, visual acuity (VA), central foveal thickness (CFT), intraretinal fluid (IRF) and subretinal fluid (SRF) height in endophthalmitis eyes and fellow unaffected control eyes. Microsoft Excel was used for data analysis.

Results: Out of 23 eyes with endophthalmitis, 21 (91%) maintained follow up for at least 12 months post endophthalmitis. 16 out of 23 fellow unaffected eyes required IVI and were used as controls. There was a statistically significant reduction in IVI frequency and VA in the first year post as compared to pre endophthalmitis (Tables 1 and 2). No significant reduction in IVI frequency was observed in the second-year post endophthalmitis for case eyes, nor at any time in the control eyes. There was no significant change in CFT, IRF/SRF, or percentages of dry retinas in either cases or controls.

Conclusions: In patients with nvAMD, eyes with post injection endophthalmitis receive fewer IVIs in the first year post endophthalmitis. Control eyes continue to receive intravitreal anti-VEGF at a statistically unchanged frequency over the same time period. Markers including CFT, IRF/SRF, and percentage dry retinas remain statistically unchanged, suggesting disease stability despite a decrease in injection frequency. Larger studies are needed to further clarify the impact of endophthalmitis on the frequency of IVI.

CONTROL ID: 3542999

SUBMITTER (NAME ONLY): David Cui

TITLE: Disparities in Dry Eye Severity and Access to Dry Eye Care in Racial and Ethnic Minorities

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Cui, P. Mathews, G. Li, L. Guo, S. Van Court, E. Akpek, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess dry eye severity and access to dry eye care in racial and ethnic minorities.

Methods: Patients with dry eye seen at a tertiary academic medical center, evaluated between 2003 to 2020 were identified using international classification of disease codes M35.0, H16.222, H04.123, 710.2, 375.15. According to self-identified demographics for race and ethnicity, four cohorts of patients were created: Asian, Black, Hispanic, and White. Retrospective review of electronic health records was performed to collect demographics, socioeconomic factors, prior access to dry eye care, and clinical dry eye parameters at baseline as well as last visit.

Results: A total of 464 patients were included (156 White, 85 Asian, 157 Black, and 66 Hispanic). Compared to White patients (3.2%), a greater proportion of minorities lacked health insurance or were on Medicaid (Asians 10.6%, $p=.019$; Blacks 8.3%, $p=.054$, Hispanics 18.2%, $p<.001$). Blacks and Hispanics had a lower estimated median household income than Whites (Whites \$98,260; Blacks \$75,554, $p<.001$; Hispanics \$86,839, $p=.0331$). At baseline visit, lower proportion of minorities had received prescription treatment or in office dry eye procedure (Whites 61.5%; Asians 43.5%, $p=.007$; Blacks 30.57%, $p<.001$; Hispanics 43.9%, $p=.016$). There was no difference with regard to autoimmune disease prevalence at final visit, or diagnosis during follow-up ($P > .05$). In addition, at baseline visit, minorities (compared to Whites) had worse clinical dry eye parameters for mean conjunctival lissamine green staining score (Whites 1.69; Asians 2.44, $p=.032$; Hispanics 2.60, $p=.012$), corneal fluorescein staining score (Whites 1.56; Asians 2.25, $p=.005$; Blacks 2.47, $p<.001$; Hispanics 2.42, $p=.001$), and tear osmolarity (Whites 299.54 vs Blacks 307.98, $p=.001$). Following appropriate treatment, patients with a minimum of 18 months of follow up had no statistically significant differences for any clinical dry eye measurements at final visit.

Conclusions: Our findings demonstrate that racial and ethnic minorities present with worse dry eye parameters. This might be due to disproportionate access to dry eye care, potentially secondary to socioeconomic barriers as well as underappreciation of dry eye among minorities leading to differential treatment by providers.

CONTROL ID: 3543000

SUBMITTER (NAME ONLY): Noam Rudnick

TITLE: Characterizing collateral vessels in patients with branch retinal vein occlusions using wide-field swept-source OCT angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Rudnick, J. Wang, F. Vingopoulos, I. Garg, Y. Cui, Y. Zhu, R. Le, R. Katz, Y. Lu, J. Miller, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|J. Wang, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|Y. Zhu, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|R. Le, Wenzhou Medical University Eye Hospital, Wenzhou, Zhejiang, CHINA|

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ABSTRACT BODY:

Purpose: To date, optical coherence tomography angiography (OCTA) studies in retinal vein occlusions have primarily characterized collateral vessels (CVs) in the macula. The goal of this study was to use wide-field swept-source OCT angiography (WF SS OCTA) to characterize the morphology and functional significance of both macular and extramacular CVs in patients with a history of branch retinal vein occlusion (BRVO).

Methods: Twenty-eight eyes with a history BRVO were imaged using 12x12mm WF SS OCTA. CVs and non-perfusion area (NPA) were identified by two independent reviewers using ImageJ. Mixed effects multivariate regression analyses of factors associated with NPA and visual acuity were performed. Region of interest analysis of individual CVs was performed to identify correlations between CV size, depth and retinal location.

Results: Overall, 43% of eyes with BRVO showed evidence of collateral vessels on WF SS OCTA. Of these CVs, 55% were found in the macular region and 45% were extramacular. Analysis of collateral depth revealed that 87.3% of CVs coursed at least partly through the deep capillary plexus (DCP), while the remaining 12.7% of CVs were found to be strictly superficial. No CVs confined only to the DCP were identified. Pearson's correlation analysis of individual collateral vessels revealed that CV depth increased with distance from the optic disc ($r = 0.36$, $p = 0.007$) and CV size increased with distance from the fovea ($r = 0.38$, $p = 0.005$). Multivariate regression analysis did not reveal statistically significant associations between CVs and NPA, or between CVs and visual acuity. Worse visual acuity (higher logMAR score) was associated with greater NPA ($p < 0.001$). NPA was in turn associated with greater central subfield thickness, a marker of macular edema ($p = 0.022$).

Conclusions: A large fraction of CVs that form after BRVO are extramacular, and the morphology of CVs varies as a function of retinal location. These results illustrate the importance of WF SS OCTA in BRVO, as heterogeneity in CV structure may correlate with distinct functional roles.

CONTROL ID: 3543001

SUBMITTER (NAME ONLY): Sumaiya Karim

TITLE: Copolymer surface modification for the modulation of lens epithelial cell behaviour

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Karim, L.A. Wells, Chemical Engineering, Queen's University, Kingston, Ontario, CANADA|

Commercial Relationships Disclosure (Abstract): Sumaiya Karim: Commercial Relationship: Code N (No Commercial Relationship) | Laura Wells: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Responsive surfaces can be created by modifying materials with switchable molecules to optimize the properties at the surface for modulating cell behaviour. Azobenzene can reversibly switch from the trans- to the cis-conformation with 365 nm light. Photo-responsive surfaces can reversibly influence protein adsorption and cellular interactions. Evidence suggests the design and material of intraocular lenses (IOLs) influence lens epithelial cell (LECs) behaviour to propagate complications post-lens replacement surgeries. This research develops photo-switchable surfaces for IOLs using azobenzene to modulate LEC behaviour.

Methods: Circular glass coverslips were coated in 35% methacrylic acid (MAA) with isodecyl acrylate (IDA), which has shown to improve healing responses (Wells and Sefton, 2014). These coatings were grafted with 4-(phenylazo)benzoic acid with an amine-terminated triblock copolymer as a spacer using carbodiimide chemistry. Azobenzene changes using UV (ultraviolet) light exposures, followed by observing 325 nm peaks to identify the trans-conformation with UV-VIS (ultraviolet-visible) light spectroscopy. Human LECs (B3-LECs) were incubated on modified coatings and with or without UV light to measure their viability using the alamarBlue and LIVE/DEAD assays.

Results: MAAcoIDA coatings were grafted with $7.4 \pm 2.2 \text{ nmol/cm}^2$ of azobenzene. UV-VIS spectroscopy confirmed that grafted azobenzene on the surface retained the ability to photoisomerize shown through reductions in absorbance at 325 nm (Fig. 1). Current work shows a red-shifted absorbance maximum as trans-azobenzene complexes with β -cyclodextrin and still undergo photoisomerization with the cis-conformation unable to bind with β -cyclodextrin.

B3-LECs incubated with unmodified MAAcoIDA and azo-functionalized coatings had no changes in viability over 48 hours ($p > 0.05$) (Fig. 2). There were no changes in viability when B3-LECs were exposed to low-power (2.5 mW/cm^2 , 45 minutes) ($p > 0.05$) and high-power UV light (18 mW/cm^2 , 45 minutes[SK1]) ($p > 0.05$). Cells grown with azobenzene-grafted copolymers under UV light are expected to have changes in behaviour.

Conclusions: These studies modified regenerative copolymers with azobenzene, which can reversibly bind with β -cyclodextrin. The resulting coatings show low toxicity and are expected to modulate LEC behaviour upon UV exposures with intensities demonstrated not to effect LEC viability.

CONTROL ID: 3543002

SUBMITTER (NAME ONLY): Julia Fu

TITLE: Removal of retinal neovascularization in DL-AAA rabbit model using concurrently applied ultrasound bursts and nanosecond laser pulses

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fu, Y. Yu, Y.M. Paulus, Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|Y. Yu, Department of Ophthalmology, Xiangya Hospital, Central South University, Changsha, Hunan, CHINA|Y. Qin, X. Wang, Y.M. Paulus, Department of Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|Y. Qin, X. Wang, Institute of Acoustics, School of Physics Science and Engineering, Tongji University, Shanghai, P. R., CHINA|X. Yang, Institute for Bioengineering Research and Department of Mechanical Engineering, University of Kansas School of Engineering, Lawrence, Kansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal neovascularization (RNV) is critical to the pathogenesis of many eye diseases, including diabetic retinopathy, a leading cause of vision loss among working-age adults. A novel, controllable photo-mediated ultrasound therapy (PUT) is demonstrated to treat RNV in an in vivo rabbit model. PUT selectively removes angiogenesis by combining low intensity nanosecond pulse duration laser and ultrasound without damaging surrounding tissue.

Methods: An integrated therapeutic ultrasound (0.5 MHz bursts, 10% duty cycle, 10 Hz), laser treatment system, and CCD camera system was devised. An Nd:YAG laser produced 1064 nm laser pulses with 5-ns pulse duration and 10-Hz pulse repetition rate. Laser treatment was initiated at the beginning of each ultrasound burst with a spot size of 5 mm. An in vivo rabbit model of RNV was developed in 6 Dutch Belted pigmented rabbits with intravitreal injection of DL-alpha-aminoadipic acid (AAA) to induce stable, long-term RNV. Eight weeks after injection, RNV rabbits were treated with PUT and serially monitored for up to 4 weeks after treatment with fundus photography, fluorescein angiography (FA), OCT, and indocyanine green angiography (ICGA).

Results: In the PUT treatment group, RNV in the treatment area was effectively removed with minimal damage to the surrounding retinal and choroidal structures. Rapid regression of RNV was shown within 1-day following treatment, and vessel blockage within the treatment area remained stable for at least 4 weeks with persistent regression of RNV (Fig 1). A significant average reduction in RNV of $58.4\% \pm 1.9\%$ was observed 21 days after PUT treatment. In the control group, where no treatment was used, persistent RNV remained stable for up to 52 weeks.

Conclusions: The experimental results demonstrate that a single treatment of PUT can rapidly and effectively remove RNV in this rabbit model with effects that persist for at least 1 month. Minimal treatment side effects are observed.

CONTROL ID: 3543003

SUBMITTER (NAME ONLY): Clement Chan

TITLE: A Randomized Clinical Trial of Pneumatic Vitreolysis with C_3F_8 for Vitreomacular Traction and A Single-Arm Study of Pneumatic Vitreolysis with C_3F_8 for Macular Hole: DRCR Retina Network Protocols AG and AH

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate pneumatic vitreolysis (PVL) as treatment for vitreomacular traction (VMT) in eyes with and without full-thickness macular hole (FTMH)

Methods: Two multi-center studies conducted across 28 sites in the US. Protocol AG was a randomized clinical trial comparing PVL using C_3F_8 gas with observation (sham injection) in eyes with VMT less than 3000 μm in adhesion length and no FTMH. Protocol AH was a single-arm study assessing PVL using C_3F_8 gas for closure of FTMH no more than 250 μm wide at the narrowest point (AH). Baseline standardized visual acuity (VA) was required to be between 20/32 and 20/400 in AG, and between 20/25 and 20/400 in AH. PVL (AG and AH) or sham injection (AG only) was given at baseline; rescue vitrectomy could be performed if prespecified criteria were met. Primary outcome of AG was central VMT release without rescue at 24 weeks. Primary outcome of AH was FTMH closure without rescue at 8 weeks; central VMT release without rescue at 24 weeks was a secondary outcome. Change in VA from baseline, receipt of rescue vitrectomy, and ellipsoid zone integrity were secondary outcomes in both studies. Shape discrimination hyperacuity was tracked for AG. Rates of retinal tears and detachment were key safety outcomes.

Results: Protocol AG enrolled 46 participants with VMT; at baseline, mean age was 72 years, 67% were female, mean VA was 68.5 letters (Snellen equivalent 20/50), 7% had an epiretinal membrane in the central subfield, and median length of vitreomacular adhesion in the central subfield was 495 μm . Protocol AH enrolled 35 participants with VMT and FTMH; mean age was 69 years, 69% were female, mean VA was 55.8 letters (Snellen equivalent 20/80), 3% had an epiretinal membrane in the central subfield, and mean MH width at the narrowest point was 82 μm . Results have been analyzed and reviewed by the Data and Safety Monitoring Committee, but per National Eye Institute requirements for NIH-funded clinical trials, primary results cannot be made publicly available before publication. Submission and publication of the manuscript are anticipated before presentation of the results at the 2021 ARVO annual meeting.

Conclusions: Conclusions will follow from the results presented.

CONTROL ID: 3543005

SUBMITTER (NAME ONLY): Rishi Gupta

TITLE: A comparison of perception of pain in patients receiving neurolept anesthesia at 2 different time points for refractive laser assisted cataract surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.B. Gupta, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|E. Tam, H. Chiu, R. Maini, I. Gold, S. Somani, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The purpose of this study is to assess the impact of neurolept anesthesia administration timing on the perception of pain in patients undergoing refractive laser-assisted cataract surgery (ReLACS).

Methods: This is a prospective REB randomized control trial at an ambulatory surgical center in Toronto, Ontario, Canada. Patients undergoing cataract surgery were selected in a consecutive manner. Patients were randomized to either receiving neurolept anesthesia following completion of the ReLACS procedure and just prior to draping the eye (standard, n = 38), or, prior to the initiation of the ReLACS procedure (early, n = 35). Primary outcome metrics included pain scores on the visual analogue scale (VAS) from zero (no pain) to ten (unbearable pain) at post-operative day zero (POD0) and post-operative week one (POW1). Secondary outcome measures included a State-Trait Anxiety Inventory (STAI) pre-operative anxiety questionnaire (measured on a scale of 20-80), surgeon and anesthesiologist patient cooperation scores measured on a scale of zero (no event) to three (marked eye and head movement and lid squeezing), ocular metrics (anterior chamber depth, intraocular pressure, surgical time, phacoemulsification energy), and perioperative vitals.

Results: Mean pain scores of early and standard groups at POD0 were 0.59 and 0.79 (p = 0.38), respectively, and at POW1 were 0.76 and 0.87 (p = 0.71), respectively. Linear regression analysis of pain scores incorporating all independent variables (ocular metrics and perioperative vitals) between both groups were also not statistically significant at POD0 (p = 0.40) and POW1 (p = 0.17). In all patients, each 1 mm increase of anterior chamber depth caused an increase of 1.23 pain units (p = 0.02) at POW1. For pain scores at POW1 in all patients, the second eye had an increase of 0.70 pain units (p = 0.02) relative to the first eye.

Conclusions: In patients undergoing refractive laser assisted cataract surgery, there was no difference in pain scores between early and standard timing of neurolept anesthesia administration at both POD0 and POW1. Patients perceived increased levels of pain in the second eye at POW1 relative to their first eye. Furthermore, an increase in ACD was also strongly correlated with an increase in pain scores at POW1.

CONTROL ID: 3543007

SUBMITTER (NAME ONLY): Priya Gupta

TITLE: A complex retinal dystrophy-obesity phenotype is associated with compound heterozygous loss-of-function TUB gene mutations

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Schoch, V. Shashi, Dept. Pediatrics/Medical Genetics, Duke University, Durham, North Carolina, UNITED STATES|Y. Jiang, Dept. Genetics, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|P. Gupta, A. Iannaccone, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The tub^{-/-} (tubby) mouse (rd5) has long been known to express a complex retinal dystrophy-obesity phenotype with features abridging the Bardet-Biedl (BBS) and Alström (ALMS) syndromes, but to date there is only 1 report of a human counterpart (Borman et al. Hum. Mutat. 2014). Here we report the second ever family presenting with a tubby-like phenotype in association with TUB mutations in 2 affected Caucasian brothers, PT1 and PT2 (49 and 46 yo)

Methods: Testing included visual acuity, semi-automated kinetic perimetries (SKPs), flash electroretinograms (ERGs), macular and retinal nerve fiber layer (RNFL) ocular coherence tomography (OCT), fundus autofluorescence, photos, and fluorescein angiography (FA). Smell function was also assessed (UPSIT scratch-and-sniff test). Whole exome sequencing genotyping was conducted within the Undiagnosed Disease Network project

Results: Both patients exhibited photoreceptor degeneration with disseminated chorioretinal atrophic nummular lesions peripherally and at the arcades, bilateral bull's eye maculopathy with partial foveal residue, and moderately to severely reduced acuity. SKPs were markedly constricted, and ERGs markedly reduced. In both patients a disproportionate vision loss compared to the retinal phenotype led to the identification of RNFL thickening and disc inflammation on FA, which were found to be linked to a secondary autoimmune involvement that responded in part to periocular/intravitreal steroids and oral immunosuppressives. Both patients had BMI>36, borderline cognition, decreased smell, and no dystrophic extremities. PT2 had dilated cardiomyopathy and hypertension. PT1 had sensorineural hearing loss. Both patients shared the c.1359_1360delAG, p.R453Sfs*10, and the splice site c.1380+1G>A TUB mutations. Heterozygous changes in other genes were also identified in both patients, and a novel change in the RP1L1 gene in PT2

Conclusions: We provide further evidence that human TUB mutations are associated with a complex tubby-like syndromic retinal ciliopathy abridging the BBS and ALMS spectrum. The cause for the systemic phenotypic variability remains to be elucidated. Vision loss was augmented by secondary autoimmune phenomena that may be linked to the known role of TUB in regulating microglial phagocytosis through MERTK, a gene known to be associated with pathogenic secondary autoimmunity in both RCS rats and Mertk^{-/-} mice

CONTROL ID: 3543014

SUBMITTER (NAME ONLY): Asad Durrani

TITLE: Rate of endophthalmitis and associated risk factors following open globe injuries: A 17-year analysis

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.F. Durrani, P.Y. Zhao, Y. Zhou, S.T. Armenti, D.C. Musch, D.N. Zacks, Department of Ophthalmology and Visual Sciences, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|M.J. Huvard, Department of Ophthalmology, University of Colorado Health, Aurora, Colorado, UNITED STATES|L. Azzouz, J.M. Keil, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|V.S. Dedania, Department of Ophthalmology, New York University School of Medicine, New York, New York, UNITED STATES|D.C. Musch, Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess risk factors for development of endophthalmitis following open globe injury.

Methods: A retrospective chart review of all patients treated for open globe injury at the University of Michigan from January 2000 through July 2017 was conducted. Exclusion criteria included intravitreal injection or intraocular surgery in the 30 days prior to injury or less than 30 days of follow-up. A total of 586 out of 993 eyes were included in the study. The main outcome measure was the rate of endophthalmitis in these eyes.

Results: 25/586 eyes (4.3%) presented with endophthalmitis, or developed endophthalmitis following globe closure. Of these, 12/25 eyes (48.0%) presented with endophthalmitis and 13/25 eyes (52.0%) developed endophthalmitis after globe closure. Multivariate logistic regression analysis identified time to globe repair (OR 4.5, CI 1.9-10.7, p = 0.0008), zone I injury (OR 3.6, CI 1.1-11.0, p = 0.0282), and need for additional surgery (OR 5.5, CI 1.5-19.7, p = 0.0092) as factors associated with increased risk of developing endophthalmitis. Subconjunctival antibiotics (OR 0.3, CI 0.1-0.7, p = 0.0036) were associated with decreased risk of developing endophthalmitis.

Conclusions: Prompt closure of the globe and use of subconjunctival antibiotics may reduce the risk of endophthalmitis in open globe injuries. Furthermore, a one-time dose of prophylactic antibiotics with same day discharge and delayed IOFB removal with intravitreal injection of antibiotics did not increase the rate of endophthalmitis. Open globe injuries can be visually devastating and understanding what factors predict and protect against endophthalmitis is paramount to achieving the best possible visual outcomes.

CONTROL ID: 3543018

SUBMITTER (NAME ONLY): Salvador Garza

TITLE: Evaluation of meibography scores as age increases in Hispanic patients

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Garza, M. Herrera-Rodriguez, M.A. Hernandez-Delgado, M. Salan-Gomez, S. Guevara-Quintanilla, J.E. Valdez, Ophthalmology Institute Hospital Zambrano Hellion, Tecnologico de Monterrey, Instituto Tecnologico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To describe the meibography scores according to age in Hispanic population

Methods: Retrospective observational case series. A sample of 192 records from patients referred to the Cornea and Refractive Surgery Service from Ophthalmology Institute Hospital Zambrano Hellion, Tecnologico de Monterrey from January 2020 to December 2020. Patients diagnosed with dry eye were included in the study. Meibography was performed using the OCULUS Keratograph 5M. The meibography scale used measured the percentage of gland dropout from a score of 0 (No gland dropout) to 3 (more than 66% gland dropout). A statistical analysis between the score and the patients age followed.

Results: From the entire study sample, a random sample of 40 patients (80 eyes) was included. 26 (65%) were female and 14 (35%) were male. The age range was from 14-87 years with an average of 45.3 years. The lowest meibography score reported was 0 and the highest 3. The mean of both eyes was calculated for each patient and then compared to their age. An average of 1.47 ± 0.72 was calculated in those younger than 65 years and an average of 2.9 ± 0.22 in those 65 years or older. A statistically significant ($p < 0.05$) moderate positive correlation ($r = 0.39$) between age and a worse score in the meibography was found.

Conclusions: We found that meibography scores tend to get worse with the passage of time. Such a different mean meibography score between those younger than 65 years and those older, may suggest that changes may also accelerate after certain age. A larger sample size could increase the Pearson coefficient.

CONTROL ID: 3543019

SUBMITTER (NAME ONLY): Andrew Feola

TITLE: Effects of Multiple Pathological Stimuli on Optic Nerve Head Deformation

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Feola, Center for Visual and Neurocognitive Rehabilitation, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|A. Feola, C.R. Ethier, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|B.C. Samuels, Ophthalmology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Computational modeling has been used to better understand how intraocular pressure (IOP), intracranial pressure (ICP), and choroidal swelling influence deformation of the human optic nerve head (ONH). Here, we expand on these models to investigate how pathophysiological levels of choroidal swelling occurring during spaceflight (Laurie+, IOVS 2018) compare to the effects of other pathological conditions, e.g. glaucoma (elevated IOP) and idiopathic intracranial hypertension (elevated ICP).

Methods: We used our established computational model of the posterior eye (Feola+, IOVS, 2018), which included the choroid and Bruch's membrane to examine choroidal changes over a cardiac cycle. Our baseline condition represented an individual in the upright position: IOP=15 mmHg, ICP=0 mmHg, mean arterial pressure=57 mmHg, and no choroidal swelling (0 uL). We then applied supra-physiologic or "pathologic", loading conditions including choroidal swelling (50 uL of swelling), elevated IOP (30 mmHg), and elevated ICP (20 mmHg), and then calculated the peak first and third principal strains in the prelaminar neural tissue (PLNT), lamina cribrosa (LC), and retrolaminar neural tissue (RLNT) relative to our baseline condition.

Results: Variation in material properties resulted in a wide range of predicted strains under supra-physiological loading (Figure). In the PLNT, increasing choroidal swelling affected the magnitude and range of peak strains. Within the lamina cribrosa, elevated IOP caused the highest peak compressive strains. Elevated ICP resulted in the largest strains in the RLNT.

Conclusions: Computational modeling indicates that pathologic choroidal swelling places biomechanical strain on tissues of the ONH that are similar or larger than the peak strains associated with elevated IOP and ICP. Changes in the choroid likely play a larger role in ophthalmic pathologies, such as spaceflight-associated neuro-ophthalmic syndrome (SANS) than previously recognized.

CONTROL ID: 3543020

SUBMITTER (NAME ONLY): Tomohiro Niizawa

TITLE: Topical Ketotifen fumarate inhibits mast cell degranulation and loss of retinal pigment epithelial cells in rat model for geographic atrophy

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Niizawa, I.A. Bhutto, A. Tiwari, R.R. Grebe, M.M. Edwards, G.A. Lutty, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|J. Alt, R. Rais, Johns Hopkins University Brain Science Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have reported that subconjunctival slow-released 48/80 stimulated continuous degranulation of choroidal Mast cells (MCs) and resulted in loss of retinal pigment epithelium (RPE), reduced electroretinogram (ERG) and thinning of retina and choroid, i.e. a geographic atrophy (GA)-like phenotypes in the rat. Moreover, quiescing MCs with oral administration of the MC stabilizer, ketotifen fumarate (KTF), prevented these changes. We herein evaluated whether topical administration of KTF has the potential to prevent these GA-like changes.

Methods: First, we analyzed the levels of KTF in plasma, RPE/choroid/sclera, retina and brain, administered orally and topically twice daily for 5 days, in the eye tissues of normal Sprague Dawley rats. Second, the rats were divided into three groups: group 1, the rats were implanted 48/80 in a hydrogel in the superior subconjunctival space and treated with 1% (10mg/ml) of KTF eye drops; group 2, rats were implanted with 48/80 hydrogel and treated with phosphate buffer saline (PBS); and group 3, rats were implanted with an empty hydrogel only and treated with 1% KTF eye drops. KTF and PBS was topically administered twice daily for 8 weeks. Rats were sacrificed 1, 2, 4 and 8 weeks (w) after implantation. MCs were stained with nonspecific esterase (NSE), RPE labeled with RPE65 in whole mount choroids, and retinal and choroidal area determined in cryosections stained with picosirius red. Dark-adapted ERG was also performed to evaluate retinal function.

Results: We found the highest level of KTF (average 5.6 nM/mg) in the RPE/choroid/sclera of the rats given topical administration in the pharmacokinetic study. At 1w and 2w after implantation, daily treatment with KTF prevented MC from degranulation (38 % reduction at 1w and 38.5 % at 2w of PBS treated, n=6 and n=3, p<0.001 and p<0.01, respectively). The RPE loss with 48/80 was significantly prevented by KTF treatment at 2w and 4w compared to PBS treatment (59.8 % and 34.8 %, n=3 and n=6, both p<0.001). There was a significant difference for preventing the ERG amplitude declining in KTF treated rat at 8w (n=6 per group).

Conclusions: Topical KTF eye drops had efficacy in preventing MCs degranulation and loss of RPE in our GA-like rat model. These data suggest that topical KTF eye drops might be a new therapeutic drug for treating GA.

CONTROL ID: 3543027

SUBMITTER (NAME ONLY): Monika Fleckenstein

TITLE: Disease Progression in Individuals with Age-related Macular Degeneration and Homozygous Risk at the CFH-CFHR5 or ARMS2/HTRA1 Loci

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To characterize the independent contributions of the two most common age-related macular degeneration (AMD) loci (the CFH-CFHR5 locus on chromosome 1 [Chr1] and the ARMS2/HTRA1 locus on chromosome 10 [Chr10]) to (1.) risk of conversion to late-stage disease and (2.) to atrophy enlargement once converted into non-exudative late AMD.

Methods: Individuals with AMD and homozygous for risk variants at Chr1 ('Chr1-risk') or at Chr10 ('Chr10-risk'), respectively, recruited at the John A. Moran Eye Center and its ancillary satellite locations, were analyzed. Multimodal imaging data was reviewed to confirm and expand AMD grading, including incomplete and complete retinal pigment epithelium and outer retinal atrophy (iRORA and cRORA), respectively. Total atrophy lesion size was quantified from fundus autofluorescence images using semi-automated software or by manually outlining lesion boundaries on serial, near infrared reflectance images combined with optical coherence tomography volume scans. Survival analyses were performed using Cox proportional hazard models. Associations between genetic group and square-root transformed atrophic area were assessed using multivariable mixed-effect regression models.

Results: Subjects from the Chr10-risk group (n = 92) were more likely (factor of 2.6 [1.3;5.5]) to convert to a late stage phenotype, as compared to the Chr1-risk group (n = 309) (p = 0.01), after adjusting for age and AMD severity at first

visit. The difference was primarily driven by conversion to macular neovascularization, which occurred earlier in the Chr10-risk group as compared to conversion to atrophy. Evaluation of 108 subjects (150 eyes) with manifest cRORA showed that eyes of the Chr10-risk group ($n = 39$) exhibited a significantly more rapid square-root atrophy enlargement rate, as compared to eyes from the Chr1-risk group (111 eyes) (estimated difference 0.14 mm/year [0.11;0.17], $p < 0.001$).

Conclusions: These findings reveal distinct differences in the contribution of the two major AMD genetic loci to late stage AMD phenotypes, which are likely caused by distinct biology associated with Chr1- and Chr10-directed disease. It will be prudent to consider the impact of these two loci in the design and interpretation of results in future AMD clinical trials.

CONTROL ID: 3543032

SUBMITTER (NAME ONLY): Yang Pan

TITLE: The ARMS2 insertion/deletion leads to systemic upregulation of secreted HTRA1 levels in the blood in AMD patients

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: AMD is a multi-factorial retinal disease, which affects millions of elderly people worldwide. We have previously demonstrated that the in/del sequence along with its downstream promoter region can significantly induce HTRA1 transcription in the transfected cell line 661W. Furthermore, our previous study of Htra1 transgenic mice driven by a CAG promoter showed a CNV-like phenotype after 12 months, while the use of a retinal pigment epithelial cell specific promoter by others has demonstrated polypoidal choroidal vasculopathy (PCV)-like phenotypes but not CNV. Therefore, we hypothesize that CNV is triggered by overexpression of HTRA1 in tissues outside of the eye. Here, we analyze the HTRA1 concentration in blood to correlate secretion of HTRA1 with the in/del in AMD.

Methods: Quantitative RT-PCR was performed to identify the HTRA1/Htra1 mRNA level across different human and mouse tissues, respectively. PCR and direct sequencing were performed to identify indel genotype in human samples from Japan, India, Australia, and the USA. To compare allelic or genotypic frequencies, the Chi-square test was used in additive models of each case group with controls. To identify the HTRA1 concentration in these blood samples (including serum and plasma), the ELISA was performed. The expression vector with the indel-HTRA1 was transfected into 661W, COS-7, and HEK-293 cells to observe HTRA1 secretion by ELISA. Moreover, ELISA was also performed in iPSCs derived from AMD patients.

Results: HTRA1/Htra1 was ubiquitously expressed across different tissues in both human and mice. Overexpression of Htra1 in mice demonstrated increased Htra1 protein serum concentration. Comparison of AMD patients with controls showed a significantly increased HTRA1 concentration in blood of AMD patients. Moreover, the increased secretion of HTRA1 protein was observed in the in/del-HTRA1 transfected cells and iPSCs derived from AMD patients. Furthermore, the HTRA1 protein blood level rises progressively with age in controls but remains high in AMD patients.

Conclusions: The in/del genotype is associated with AMD leading to an increase of HTRA1 secretion. The HTRA1 blood level is significantly higher in AMD patients with GA or CNV than age-matched controls, strongly suggesting that AMD is triggered by systemic increases of HTRA1 reaching the retinal choroidal capillaries through the bloodstream.

CONTROL ID: 3543035

SUBMITTER (NAME ONLY): Keshav Patel

TITLE: Sociodemographic factors and follow-up for intravitreal injections during the COVID-19 pandemic

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Patel, K. Astafurov, Rutgers Robert Wood Johnson Medical School, Piscataway, New Jersey, UNITED STATES|A. Port, NJ Retina, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic significantly disrupted outpatient ophthalmologic care. Factors such as income, race, language and age may contribute to healthcare barriers which were exacerbated by the pandemic. Patients requiring ophthalmologic care, especially those on a regimen of anti-VEGF intravitreal injections, faced challenges in receiving routine treatment. Patients treated for diseases such as age-related macular degeneration (AMD) risk permanent vision loss if treatment is delayed. This study seeks to explore the sociodemographic factors that influenced patient follow-up during the COVID-19 pandemic.

Methods: The electronic medical record for the NJ Retina group was searched for subjects that had intravitreal injections with any anti-VEGF medication to treat AMD, using CPT and ICD-10 codes respectively, in January-February of 2020. These patients were divided based on if they attended the follow-up injection appointment within 2 weeks past the recommended interval. Information from their charts was used including age, sex, marital status, race, ethnicity, language, insurance type, time as a patient and zip code. Median household income data by zip code in New Jersey, from the US Census Bureau, were used to estimate average household income. Statistical analysis of factors was performed using SPSS v26 software.

Results: 4242 patients had intravitreal injections during the chosen timeframe. 3527 of them attended their follow-up appointment and 715 did not. Those who followed up tended to be younger and patients of the practice for longer than those who did not. Those who followed up had a higher percentage of people who were white, married and insured (table A). A logistic regression was performed to ascertain the effects of age, sex, marital status, language, insurance and income on the likelihood of follow up (table B). This model was statistically significant and demonstrated that decreased age, being married, speaking English and having Medicare or a Group Policy as primary insurance were independent predictors of follow-up.

Conclusions: Sociodemographic factors, including age, marital status, race, language and insurance status were associated with significant differences in patient follow-up for intravitreal injections to treat AMD during the COVID-19 pandemic.

CONTROL ID: 3543038

SUBMITTER (NAME ONLY): Renick Lee

TITLE: Microscopic Regional Changes in the Elastic Properties of Myopic Guinea Pig Choroid

SESSION TITLE: Role of choroid and sclera in myopia development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.D. Lee, K. Ito, J. Liqin, D.G. Yu, Q. Hoang, Ocular Imaging, Singapore Eye Research Institute, Singapore, SINGAPORE|R.D. Lee, Health, Torrens University Australia - Sydney Campus The Rocks, Sydney, New South Wales, AUSTRALIA|Q. Hoang, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J. Mamou, F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|S.A. McFadden, Vision Sciences, Hunter Medical Research Institute and School of Psychology, College of Science, Engineering and Environment, The University of Newcastle, Callaghan, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: In myopia development, the choroid provides an essential interface to translate retinal signals into scleral remodelling, but the mechanisms remain elusive. Using scanning acoustic microscopy (SAM) with 7- μ m lateral resolution, we studied the dependency of the choroidal biomechanical properties in myopic guinea pigs (GP) eyes.

Methods: Thirteen 1-week old GPs were form-deprived for 1 week in the right eye to induce myopia while the left eyes were untreated. GPs were then euthanized and both eyes enucleated, flash-frozen and 12- μ m thick serial cryosections were obtained in either a vertical (superior/inferior) or horizontal (nasal/temporal) orientation across the posterior pole. Specimens were scanned with a custom-made SAM with a 250-MHz transducer. Bulk modulus (K) and mass density (ρ) 2-dimensional maps were calculated from the SAM data via a frequency-domain approach. SAM maps were manually segmented to isolate choroidal stroma. To assess the biomechanical properties locally, the choroid was divided into adjacent regions of interest (ROIs) sized 0.2 mm laterally and 0.65 mm in anterior-posterior direction. Within each ROI, the mean and standard deviation of each parameter were calculated. The association between biomechanical parameters and region, myopia status and eccentricity relative to the optic nerve was assessed with linear regression analysis.

Results: Relative myopia ranged from -3 to -9.3D. Among control eyes, mean K in the temporal region was greater than the nasal (containing the central axis, +448 MPa, $p < 0.001$). Per 1 mm in increased eccentricity, nasal K increased by 70 MPa in control eyes ($p = 0.046$). Temporal K decreased by 100 MPa in myopic eyes ($p = 0.015$). Among myopic eyes, ρ was 0.03 g/cm^3 greater in the superior vs. nasal region ($p = 0.04$). In the nasal region, ρ was 0.03 g/cm^3 greater in control vs. myopic eyes ($p < 0.01$). Per 1 mm in increased eccentricity, superior ρ increased by 0.01 ($p = 0.003$) and nasal ρ by 0.01 g/cm^3 in control eyes ($p = 0.02$), whereas in myopic eyes, nasal ρ decreased by 0.03 g/cm^3 ($p = 0.04$) and temporal ρ by 0.04 g/cm^3 ($p < 0.001$).

Conclusions: Choroidal stroma biomechanical properties display myopia-, eccentricity- and region-dependent differences. Our results support the idea that myopia development and possibly scleral remodelling depends on microstructural and biomechanical alterations in the choroidal stroma.

CONTROL ID: 3543040

SUBMITTER (NAME ONLY): Wei Kong

TITLE: Reflection ratio of the retinal nerve fiber layer changes in glaucoma eyes

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Kong, X. Liu, M. Shi, G. Li, W. Yao, L. Liu, Eye School of Chengdu University of TCM, Chengdu, Sichuan, CHINA|W. Kong, W. Yao, L. Liu, Ineye Hospital of Chengdu University of TCM, Chengdu, Sichuan, CHINA|

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ABSTRACT BODY:

Purpose: Glaucoma damages the retinal nerve fiber layer (RNFL). Animal models show that the ratio of RNFL reflection at 488 nm and 820 nm provides sensitive detection of optic neuropathy. This study investigated RNFL reflection ratio in normal and glaucoma patients.

Methods: Tomography imaging mode of the Heidelberg Retinal Angiography (HRA) was used to take fundus images with filters set to BP (500 – 560 nm) and IR (820 nm). For each wavelength, a series of 64 images scanning through the retina was obtained (Fig. 1c). A circle with radius of 3.2 mm was defined (Fig. 1a). Reflection profile around the circle was calculated for each image. For each wavelength, the maximum reflection profile (R_{BP} and R_{IR}) was identified. The profiles before and after (thin arrows in Fig. 1c) the maximum reflection at distance of $\pm 2/3$ times of the average RNFL thickness measured by OCT were also obtained. To remove the contribution of the deep layers' reflection, $R_{BP0} = R_{BP} - R_{BP_After}$ and $R_{IR0} = R_{IR} - R_{IR_After}$ were calculated. Reflection ratio $r_0 = R_{BP0}/R_{IR0}$ was then calculated. To eliminate the effects of the optical properties of the anterior chamber, the ratio, $r_{before} = R_{BP_before}/R_{IR_before}$, was calculated. The relative reflection ratio of the RNFL was then calculated as $r = r_0/r_{before}$ and used in this study.

Results: Four normal and four glaucoma eyes were studied. In normal eyes, r varied little around the optic nerve head (ONH) with the value ranging from 0.95 to 1.18 (Fig. 1d). In contrast, r of glaucoma eyes varied greatly around the ONH and significantly lower than the normal (Fig. 1e).

Conclusions: Findings were consistent with the animal experiments (Huang et al. ARVO E-abstract 4780, 2020). Because RNFL reflection at different wavelengths were associated with different axonal ultrastructure, changes of the reflection ratio may provide a complimentary assessment of the RNFL damage in glaucoma eyes.

CONTROL ID: 3543042

SUBMITTER (NAME ONLY): Ashton Perlroth

TITLE: The Impact of the COVID-19 Pandemic on Intravitreal Bevacizumab Use

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Perlroth, K. Mishra, D.V. Do, Byers Eye Institute, Stanford Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has led to stay-at-home orders which may lead to fewer medical and ophthalmology visits. Efficacy of treatments for retinal vascular diseases such as wet age-related macular degeneration (wet AMD) depend on strict adherence to regimens of anti-vascular endothelial growth factor (VEGF) injections. The purpose of this study is to describe and compare the number of bevacizumab injections administered in 2019 and 2020 to determine if the COVID-19 pandemic may have affected usage.

Methods: We conducted a single-center, retrospective observational study which compared the number of bevacizumab injections in January through November 2020 with the number of bevacizumab injections in 2019. The total number of injections for each month and year were compared.

Results: The total number of bevacizumab injections in 2020 (Jan-Nov) was 683 compared to 801 in 2019 (Jan-Nov), a 14.7% reduction ($p = 0.02$). Significantly fewer injections were administered in March, April, and May 2020 ($p < 0.01$), and from August to November ($p < 0.01$). The fewest number of injections for 2020 were administered in April ($n = 45$) and May ($n = 45$).

Conclusions: In this patient population, a significant reduction in bevacizumab injections occurred during the COVID pandemic, and the drop in injections was first seen in March 2020 which coincided with stay-at-home orders within the catchment area. These data suggest that the Covid-19 pandemic likely affected the number of patients coming to the retina clinic. Additional data is needed to determine if other factors may have contributed to this decline, and if these missed visits has adversely affected visual acuity outcomes.

CONTROL ID: 3543051

SUBMITTER (NAME ONLY): Jennifer Craig

TITLE: Randomized controlled trial evaluating novel keratolytic for MGD treatment

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.P. Craig, K. Nel, Department of Ophthalmology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|F. Stapleton, J. Tan, School of Optometry and Vision Science, UNSW Sydney, New South Wales, AUSTRALIA|S. Thackwray, USC Clinical Trials, University of the Sunshine Coast, Sunshine Coast, Queensland, AUSTRALIA|J. Lallu, School of Optometry and Vision Science, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|S.A. Read, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|C. Bosworth, Azura Ophthalmics, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Ductal epithelial hyperkeratinization is believed to play a key role in the loss of gland function in the development of meibomian gland dysfunction (MGD). This study evaluates a novel topical keratolytic therapy (selenium disulphide) for MGD and associated evaporative dry eye disease (DED).

Methods: Participants with MGD were randomly assigned (1:1) twice weekly, evening application of either AZR-MD-001 0.5% ointment (Azura Ophthalmics) or AZR-MD-001 vehicle, in a multicenter, investigator-masked, vehicle-controlled, randomized, parallel group study (trial registration # NCT04391959). The main outcome measures compared between the active compound and vehicle, include Meibomian Gland Score (MGS), the number of meibomian glands yielding lipid secretion under application of 1.25g/mm² pressure (Meibomian Gland Evaluator, J&J Vision), and Ocular Surface Disease Index (OSDI) symptom score.

Results: Between July and October 2020, 30 participants (50% female) were enrolled. Mean (SD) participant age on enrolment was 58 (17) years and 64% had been diagnosed with MGD at least 5 years previously. Baseline MGS was 6.34 (3.92) and OSDI score was 38.2 (10.8). Seven patients discontinued; 1 for tolerability issues (burning on application) and 6 for protocol violations. All other participants completed the Month 1.5 visit. Data unmasking to allow full analysis follows the final Month 3 visit for the last participant in early January 2021.

Conclusions: Uniquely targeting hyperkeratinisation as a root cause of MGD, this novel topical pharmacotherapy demonstrates potential to alter meibomian gland function and symptoms associated with DED secondary to MGD. Reported ocular surface outcomes of this trial, revealed following unmasking, represent the first level 1 scientific evidence to consider the efficacy of AZR-MD-001 0.5% in treating MGD.

CONTROL ID: 3543053

SUBMITTER (NAME ONLY): PremNandhini Satgunam

TITLE: Children with amblyopia have deficiency in searching real world images

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Satgunam, K. Nagarajan, Brien Holden Institute of Optometry and Vision Science, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|G. Luo, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Based on poor conjunction search performance in individuals with amblyopia, it is speculated that these individuals would have difficulties in their day-to-day activities. We investigated visual search performance in this cohort with real world images.

Methods: A real world image was displayed on a computer screen along with a search target. Participant was asked to find the search target within the displayed image and click on it. Two groups of children participated: controls (monocular visual acuity 20/25 or better) and patients having anisometropic amblyopia (anisometropia ≥ 1.5 D and interocular visual acuity difference ≥ 2 lines). Three viewing conditions (binocular, dominant eye, and non-dominant (or amblyopic) eye) were tested in a random order. In each of these conditions 30 images were presented. Dominant eye in the control group was determined using the Porta test. Search performance was assessed using integrated performance (IP) that accounts for both accuracy and time taken. Eye movements were tracked with Eyelink1000. Saccade count, run count (number of repeated viewing) and average fixation duration were analysed.

Results: 23 patients (mean age: 10 ± 0.6 years) and 13 controls (10 ± 0.9 years) participated. Dominant eye visual acuity was comparable between the two groups ($p=0.54$). The mean interocular-visual acuity difference in patients was $\log\text{MAR } 0.35 \pm 0.03$. As expected, patients had the worst search performance [$\text{IP}=0.14 \pm 0.01$] in the amblyopic eye. However, their performance was also significantly ($p<0.03$) poor in both binocular [$\text{IP}=0.19 \pm 0.01$] and dominant eye [$\text{IP}=0.18 \pm 0.02$] when compared to the controls' binocular [$\text{IP}=0.26 \pm 0.02$] and dominant eye $\text{IP}=0.25 \pm 0.03$] viewing conditions. While the average fixation duration between patients and controls were comparable ($p=0.9$), the saccade (patients= 20.1 ± 1.5 , controls= 15 ± 1.1 , $p=0.03$) and run counts (patients= 8.2 ± 0.77 , controls= 6.1 ± 0.4 , $p=0.03$) were significantly more in patients.

Conclusions: Despite having normal acuity in the dominant eye, children with anisometropic amblyopia show a visual search deficiency for real world images. This is similar to the performance observed in conjunction search, which requires feature binding. The poor visual search performance could be due to deficiencies in higher cortical functions rather than low-level visual functions. More run counts to revisit the same image areas suggests deficiency in visual coding.

CONTROL ID: 3543055

SUBMITTER (NAME ONLY): Stephanie Chen

TITLE: Resident-driven telehealth visits after cataract surgery: Minimizing exposures during COVID-19

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Chen, T.A. Chen, T. Ahmad, C. Sun, N. Parikh, S. Ramanathan, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: During the coronavirus (COVID-19) pandemic, reducing unnecessary clinic visits is critical to limit risk of exposure for patients and providers. We hypothesized that final visual outcomes and postoperative complication rates in patients with postoperative week 1 (POW1) telehealth visits would be similar to patients with in-person POW1 visits in this retrospective cohort study.

Methods: All uncomplicated cataract surgeries performed by senior residents with routine postoperative day 1 (POD1) exams and POW1 telehealth visits conducted from July 1, 2020 to December 31, 2020 at a single academic institution were reviewed. Controls were drawn from uncomplicated surgeries performed by senior residents with in-office POW1 visits during the same period the year prior (7/1/19 – 12/31/19). Visual outcomes, including final corrected distance visual acuity (CDVA) and deviation of manifest refraction from the target refraction, were compared between the two groups, along with rates of significant postoperative complications.

Results: Thirty-eight patients (51 eyes) with POW1 telehealth visits and 44 patients (57 eyes) with POW1 in-office visits were included in the study. There were no statistically significant differences in baseline demographics or preoperative CDVA and biometry measurements between the two groups. The average final postoperative month 1 (POM1) logMAR CDVA was 0.030 and 0.021 ($p=0.284$) in the telehealth and in-office groups, respectively, with 44 (86%) telehealth eyes and 51 (90%) in-office eyes within 0.50 D of the target refraction ($p=0.610$). Six eyes (12%) in the telehealth group and 3 eyes (5%) in the in-office group developed complications noted at the POM1 visit ($p=0.222$), comprised of pseudophakic cystoid macular edema (CME) or mild persistent/recurrent postoperative iritis. In all instances, the CME and iritis resolved with topical steroids and/or NSAIDs, with final CDVA 20/30 or better.

Conclusions: There was no statistically significant difference in final CDVA, refractive outcomes, or postoperative complication rates in eyes undergoing POW1 telehealth as compared to in-office visits. In uncomplicated cataract surgeries, POW1 telehealth visits can be a safe and effective alternative to in-office visits to minimize exposure risks during the COVID-19 pandemic.

CONTROL ID: 3543058

SUBMITTER (NAME ONLY): Alexander Pinhas

TITLE: Fixed-Volume Gas Fill Technique Following Pars Plana Vitrectomy in Retinal Re-Attachment Surgery

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Pinhas, V. Sun, C.S. Wilkins, M.S. Wieder, M. Labowsky, G. Landa, T.O. Muldoon, R.B. Rosen, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|R.B. Rosen, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The commonly used fixed-concentration technique of gas fill, following retinal re-attachment by pars plana vitrectomy (PPV), fluid-air exchange (FAX) and endolaser (EL), involves an approximately 30-50cc lavage with iso-expansile or slightly expansile concentrations of either C3F8 or SF6 gas. This retrospective case series evaluated the efficacy and safety of a gas-sparing fixed-volume technique to achieve extended tamponade.

Methods: Following FAX and EL, trocars were removed and sclerotomies were closed with trans-conjunctival vicryl suture, leaving the retina temporarily under air. Using a 30-gauge needle on a 3cc syringe, 1.0cc of 100% C3F8 or SF6 was injected into the vitreous cavity through the pars plana. Using the same syringe, gas volume was then removed as needed while palpating the globe, ensuring that the eye was left at physiological intraocular pressure (IOP). The main outcome measures included post-operative ocular hypertension (OHTN, defined as IOP>24mmHg) rate, gas bubble duration, anatomical retinal re-attachment rate, and occurrence of endophthalmitis.

Results: The fixed-volume gas fill technique was used on 13 eyes of 13 patients (9 males, 4 females) with an average age of 51 years (range 39-67 years) (Table 1). Ten patients had rhegmatogenous RDs (RRDs), two had diabetic tractional RDs (TRDs) and one had combined diabetic TRD with RRD. Post-operative OHTN rate for C3F8 was 45% (5 out of 11 patients) within the first week (Table 2). Two of these patients had pre-existing glaucoma, one had history of ocular trauma, and two were diabetics. The post-operative OHTN was responsive to medical therapy. Neither of the 2 SF6 patients had post-operative OHTN. The average gas bubble duration for C3F8 was 8 weeks (range 6-12 weeks), and that for SF6 was 2 weeks. Anatomical retinal re-attachment rate was 92% (12 out of 13 patients). There were no cases of post-operative endophthalmitis.

Conclusions: The fixed-volume gas fill technique in this case series had similar post-operative OHTN rates compared to the fixed-concentration technique reported in the literature (6-67% of eyes with SF6, and 18-59% of eyes with C3F8), with similar gas duration and retinal re-attachment rates. The fixed-volume technique may have a few advantages, including gas conservation; and, avoiding hypotony during sclerotomy closure, especially with larger gauge sclerotomies.

CONTROL ID: 3543068

SUBMITTER (NAME ONLY): Zhuo Shao

TITLE: The Role of Extended Phenotyping and Functional Testing in Variant Interpretation of a Complex Patient with Overlapping Traits

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Biallelic pathogenic variants in G protein subunit beta 5 (GNB5) gene causes developmental delay, seizures, hypotonia, sinus node dysfunction and retinal defects featuring bradyopsia and rod ON-bipolar dysfunction. This study investigated the pathogenicity of a homozygous variant of uncertain significance in GNB5 annotated as GNB5L: c.920T>G (p.L307R); GNB5S: c.794T>G (p.L265R) identified in a patient through Whole Exome Sequencing who was newborn screening positive for 3-methylcrotonyl-CoA carboxylase (3-MCC) deficiency with clinical features unexplained by 3-MCC.

Methods: Various clinical signs were ascertained by chart review. Detailed eye exams and extended electroretinogram (ERG) were performed. Fibroblast cell line was derived from patient's skin biopsy for gene expression and protein localization using digital PCR, Western Blot and Immunohistochemistry (IHC). Bioluminescence Resonance Energy Transfer (BRET) – based signaling assay and measuring stability of Regulator G-protein signaling (RGS) complexes in expression assays were used to investigate the impact of the variant on the function of Gβ5-s.

Results: The ocular features of the 9 year-old proband included high myopia, normal fundus and a subtle cone photo-transduction recovery deficit. Her extra-ocular features included severe intellectual disability (ID) and repeated cardiac arrests. The 3-MCC deficiency was confirmed with molecular finding of homozygous MCCC1 (c.1394C>T p.T465I) variant and decreased enzyme activity. The severity of her ID was atypical for 3-MCC deficiency and more in keeping with GNB5-disorder. Cardiac arrest is only known to GNB5-related disorder. In vitro study showed severe loss of function of abolishing the ability of Gβ5-s containing RGS complexes to deactivate signaling via D2 dopamine receptor due to destabilization of RGS complexes. Fibroblast culture demonstrated minimal change in GNB5 expression and translation by digital PCR and Western blots. Differences in subcellular co-localization of Gβ5 and its binding partners were seen with IHC.

Conclusions: Proband's ERG phenotype is consistent with defective function of GNB5L whereas her cardiac and neurodevelopmental phenotype together with the in vitro functional analysis indicates defective GNB5S function. This study highlights the importance of detailed phenotyping and need of functional assays to aid variant classification.

CONTROL ID: 3543070

SUBMITTER (NAME ONLY): Jochen Straub

TITLE: Clinical use of fully remote-controlled retinal optical coherence tomography (OCT) during the COVID-19 pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Straub, T. Callan, K. Makedonsky, P. Sha, P. Malvania, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Physical separation is the most effective means of protecting patients and clinical staff from the spread of the coronavirus. In order to be able to continue clinical studies in a safe environment, we have developed an imaging workflow that uses fully remote-controlled diagnostic OCT devices in clinical studies.

Methods: Retinal OCT imaging was performed using commercially available OCT devices, remote desktop access software and consumer video conferencing technology on mobile phones and tablets. This method completely separates the patient from the operator and creates the safest condition during the COVID-19 pandemic. We have used CIRRUSTM HD-OCT 5000 (ZEISS, Dublin, CA), CIRRUSTM 6000 (ZEISS, Dublin, CA), and PLEX® Elite 9000 (ZEISS, Dublin, CA). We have used Facetime, Zoom, and Microsoft Teams video conferencing software and TeamViewer remote desktop software.

Results: From March to November 2020, we have conducted 12 remote clinical studies. Imaging was performed by 4 different operators. We have imaged 158 eyes of 79 healthy volunteers aged from 30-65 years old. During each imaging session we captured between 4 and 10 OCT scans per eye. Every imaging session was performed entirely remotely with the volunteer in the office and the operator controlling the device from their home. Figure 1 shows the setup of a remote-controlled imaging setup illustrating the remote desktop software shown on a laptop computer as well as the Facetime video conferencing setup.

Conclusions: We have demonstrated that during pandemics like COVID-19, OCT retinal imaging studies can be performed in a safe environment by completely separating patient and operator and using video conferencing and remote desktop software. We were able to complete all OCT scan acquisitions requested in the clinical studies. The exam time did not appear to be longer than during in-person exams.

CONTROL ID: 3543071

SUBMITTER (NAME ONLY): Guan Xu

TITLE: Resolving the complex anatomy of aqueous veins and perilimbal sclera using multispectral photoacoustic imaging

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The lack of risk factors and biomarkers to predict the outcome in lowering intraocular pressure (IOP) is a critical barrier to provide safe and effective surgical interventions for patients with glaucoma. Beyond the trabecular meshwork, which represents the proximal tissue for aqueous humor drainage, there is limited knowledge on the resistance mechanisms of distal drainage including Schlemm's canal, collector channels, and downstream aqueous and intrascleral veins in the perilimbal sclera. The purpose of this study is to resolve the complex anatomy in the aqueous vein-sclera tissue complex.

Methods: Aimed at differentiating between the aqueous veins and intrascleral veins, we perfused enucleated porcine eyes with optical contrast agent in red. A multispectral photoacoustic microscopy system with laser illuminations at 532 nm and 1200 nm was fabricated targeting the contrast agents in aqueous veins, and the collagen and lipid content in the perilimbal sclera. The laser beams are collimated to 3 mm in diameter in separate light paths, merged by a dichroic mirror, and focused at the tissue sample surface by an objective lens with a focal length of 30 mm. A galvanometer orients the laser beams in 2-dimension before the objective lens, forming a 10 mm x 10 mm field of view. The thermoelastic effect of the illumination generates acoustic waves in the targeted tissue components, which are captured by an ultrasound transducer. The temporal resolution of the transducer, in addition to the 2-dimension optical scanning, forms a 3 dimensional representation of the anatomies in the tissue sample.

Results: The system was examined with optical phantoms. Images at the two optical wavelengths show the capability to distinguish the aqueous veins and the scleral tissue. Fig. 1 shows a representative image of aqueous veins in a porcine eye by assembling images acquired at multiple locations. Details of the aqueous veins anatomies are shown in the subpanels.

Conclusions: Photoacoustic imaging demonstrates proof-of-concept for the ability to distinguish and resolve anatomy of the aqueous veins and perilimbal sclera. Coupled with tools for manipulating and monitoring IOP, this technology can advance knowledge of the aqueous humor dynamics and the biomechanics of the aqueous vein and perilimbal sclera tissue complex.

CONTROL ID: 3543072

SUBMITTER (NAME ONLY): Diane Sayah

TITLE: Association between beta peripapillary atrophy area and ocular rigidity, choroidal thickness and choroidal pulsatility in open-angle glaucoma

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Beta peripapillary atrophy (β PPA) has been shown to be associated with open-angle glaucoma (OAG), its severity and risk of progression. The pathophysiological mechanism leading to β PPA development remains uncertain. Scleral stiffness is thought to be a major determining factor for strain at the optic nerve head. Hence we hypothesize that ocular rigidity (OR), an important biomechanical parameter of the eye which accounts primarily for the stiffness of the sclera, may be involved. The purpose of this study is to evaluate the relationship between OR and the extent of β PPA in eyes with OAG.

Methods: OR was measured using an optical method developed by our group (Beaton et al., 2015; Sayah et al., 2020). Time-lapse optical coherence tomography (OCT) imaging and automated choroidal segmentation was used to measure the average submacular choroidal thickness (CT) and the pulsatile choroidal volume change (Δ CT). By deriving the pulsatile ocular volume change and measuring the pulsatile pressure change by dynamic contour tonometry, OR was estimated using Friedenwald's equation. The total β PPA area was quantified using the calipers provided by the Spectralis Heidelberg software. OR differences in OAG subjects with and without β PPA, as well as correlations of OR, CT and Δ CT with β PPA area were assessed using SPSS.

Results: Sixty-seven eyes of 63 subjects with OAG were considered in the study. No significant difference in OR was found in eyes with and without β PPA ($p=0.806$). β PPA area and OR were both correlated with ocular axial length (AL) ($r_s=0.314$, $p=0.01$ and $r_s=-0.401$, $p=0.001$ respectively), whereas β PPA area and age were not ($p=0.811$). OR and β PPA area were not significantly correlated ($p=0.601$), even after controlling for AL ($p=0.857$). β PPA area was inversely correlated with CT ($r_s=-0.392$, $p=0.001$) and Δ CT ($r_s=-0.275$, $p=0.024$). Gamma peripapillary atrophy was significantly correlated with AL ($r_s=0.369$, $p=0.002$) and CT ($r_s=-0.314$, $p=0.010$), but not with Δ CT ($p=0.146$) and OR ($p=0.691$).

Conclusions: Interestingly, although OR and β PPA area were both correlated with AL, OR and β PPA area were not significantly correlated in our cohort. However, we did find an inverse correlation between β PPA and both CT and Δ CT in eyes with OAG. This data suggests that reduced choroidal thickness and reduced choroidal pulsatility are associated with the presence of β PPA in OAG.

CONTROL ID: 3543081

SUBMITTER (NAME ONLY): Bingjie Wang

TITLE: Predictive model for visual acuity in diabetic retinopathy using OCT and OCTA parameters

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Wang, Q. You, S. Pi, Y. Guo, T.S. Hwang, Y. Jia, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|Y. Jia, Department of Biomedical Engineering, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To propose a predictive model for visual acuity (VA) in eyes with diabetic retinopathy (DR) using optical coherence tomography (OCT) and OCT angiography (OCTA) scans.

Methods: We acquired 3×3-mm central scans with a commercial OCT system (Avanti RTVue-XR, Optovue, Inc.). Two OCTA parameters, 3-dimensional para-FAZ vessel density (3D-PFVD) and fractal dimension of deep capillary plexus (DCP), and two OCT parameters, central 1-mm fluid volume and ellipsoid zone (EZ) defect area, were derived from the scans (Figure 1). The central macular thickness (CMT) and foveal avascular zone (FAZ) area, available from the commercial software, were also recorded. We applied a linear multivariate regression to correlate macular parameters with VA at baseline and at 12 months. The Mann-Whitney U test evaluated the VA prediction errors ($VA_{predicted} - VA_{actual}$) of the model created from baseline visits as applied to the baseline vs. 12-month follow up visits.

Results: This study included 234 eyes with DR of varying severity (Early Treatment of Diabetic Retinopathy Study (ETDRS) letter score range: 40-93), 81 eyes of them had 12-month follow up visits (ETDRS letter score range: 51-92). 3D-PFVD ($r=0.610$, $P<0.001$), DCP fractal dimension ($r=0.606$, $P<0.001$), EZ defect area ($r=-0.574$, $P<0.001$) and central fluid volume ($r=-0.536$, $P<0.001$) all achieved better correlations than CMT ($r=-0.464$, $P<0.001$) or FAZ area ($r=-0.117$, $P=0.075$). The regression model combining both OCTA and OCT parameters had significantly ($P<0.001$) better VA prediction performance ($r=0.75$) than that including OCTA parameters only ($r=0.65$). The model created from baseline visit achieved comparable performance when applied to 12-month follow up visits ($P=0.18$).

Conclusions: We have demonstrated OCT- and OCTA-derived parameters that correlate better with VA than CMT and FAZ area. A multivariate regression model combining the parameters created from the baseline visit achieved excellent correlation with VA for both baseline and 12-month follow up visits.

CONTROL ID: 3543085

SUBMITTER (NAME ONLY): Satish Panda

TITLE: Use of Artificial Intelligence to Describe the Structural Signature of the Glaucomatous Optic Nerve Head

SESSION TITLE: Deep learning for classification and segmentation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.K. Panda, Biomedical Engineering, National University of Singapore, Singapore, SINGAPORE|S.K. Panda, M.J. Girard, Ophthalmic Engineering & Innovation Laboratory (OEIL), Singapore Eye Research Institute, Singapore, SINGAPORE|T.A. Tun, S. Perera, C. Cheng, T. Aung, Singapore Eye Research Institute, Singapore, SINGAPORE|C. Cheng, T. Aung, M.J. Girard, Duke-NUS Medical School, Singapore, SINGAPORE|A. Thiéry, Department of Statistics and Applied Probability, National University of Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate the complex structural changes in the optic nerve head (ONH) with the development of glaucoma and to find novel biomarkers to describe the structural phenotype of the glaucomatous ONH.

Methods: We recruited 3,782 subjects (2233 glaucoma, 1549 non-glaucoma) and imaged the ONH of each subject using optical coherence tomography (OCT). Using a deep learning network, we automatically segmented seven neural and connective tissue layers of the ONH. The segmented OCT images were then reduced to a few latent features (LFs) and reconstructed using an autoencoder. A network with MLP layers was used concurrently to classify the images as glaucoma or non-glaucoma from the LFs. We then performed a principal component analysis (PCA) on LFs and identified the principal components (PCs). Subsequently, we altered the magnitude of each PC in steps and reported how it impacted the morphology of the ONH. To facilitate visualization, we used Uniform Manifold Approximation and Projection (UMAP) to further reduce the LFs to a 2D space.

Results: The image reconstruction quality and diagnostic accuracy increased with the numbers of LFs; with 54 LFs, the Dice coefficient for the reconstructed images was 0.86 ± 0.04 , and the accuracy was $92.0 \pm 2.3\%$. Using UMAP, we were able to dissociate non-glaucoma eyes from glaucoma eyes into two distinct clusters (Fig. 1; AUC = 0.96). The PC1 values for non-glaucoma and glaucoma eyes were significantly different ($p < 10^{-9}$), and by varying it from a high value (non-glaucoma eye) to a low value (glaucoma eye), we observed thinning of neural and connective tissue layers, decrease in minimum rim width, and increase in prelaminar depth. When PC1 was changed incrementally, we observed ONH structural changes (non-glaucoma to glaucoma zone) that may reflect progression.

Conclusions: Our network identified novel biomarkers and revealed the structural changes in the glaucomatous ONH. PC1 summarized multiple and simultaneous structural variations into a single number, and by changing its magnitude, the ONHs transitioned from a non-glaucoma to a glaucoma zone. The paradigm introduced herein may help us describe the structural phenotype of the glaucomatous ONH.

CONTROL ID: 3543087

SUBMITTER (NAME ONLY): Konstantin Astafurov

TITLE: Long-term outcomes of a surgical technique for scleral suture fixation of a posteriorly dislocated lens-bag complex without conjunctival opening (Hoffman pockets)

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Astafurov, J. Prenner, H. Fine, M. Wheatley, Ophthalmology, Rutgers—Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To present long-term outcomes of a surgical technique for rescuing and sclerally fixating a posteriorly dislocated lens-bag complex without the need for conjunctival incision.

Methods: A retrospective chart review of 17 patients (19 eyes) who underwent posterior chamber intraocular lens (IOL) rescue using Hoffman pocket technique was performed. Data were collected on patients with greater than 1 year follow up after surgery. Out of 19 surgical eyes, 6 had greater than 5 year follow up.

Results: The average follow up for all surgical eyes was 37 months (3.2 years). For all eyes with greater than 12 month follow up, the average preoperative vision was 20/343, and the final average vision was 20/46. In the group of surgical eyes with greater than 5 year follow up, the average follow up time was 69 months (5.8 years) with the average preoperative vision 20/305, and the final average vision 20/34.

Four out of 19 eyes had decentration of the sutured intraocular lens, 3 of which required additional surgical repair: two early – less than 6 months after the initial surgery, and one late – 5 years after the initial surgery. In one of those eyes the lens-bag complex was repositioned using the same surgical technique, and in two eyes an IOL exchange for anterior chamber IOL was performed.

Conclusions: Outcome data at greater than 1 year follow up support Hoffman pocket technique as a valuable surgical approach for the rescue of a dislocated lens-capsular bag complex. The rate of recurrent IOL malposition with this technique is relatively low, with most of those events occurring early after the surgery.

CONTROL ID: 3543093

SUBMITTER (NAME ONLY): Lan Li

TITLE: Efficacy of the Diquafosol Sodium and Tocopherol Acetate (Vitamin E) Mixture Eye Drops in Murine Dry Eye

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Li, R. Jin, Y. Li, H. Yoon, J. Kim, H. Yoon, K. Yoon, Ophthalmology, Chonnam National University Medical School and Hospital, Gwangju, KOREA (THE REPUBLIC OF)|L. Li, H. Yoon, Biomedical Sciences and Center for Creative Biomedical Scientists, Chonnam National University, Gwangju, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To investigate the therapeutic effects of diquafosol sodium (DQS) and tocopherol acetate (TCP) mixture in a mouse model of experimental dry eye (EDE).

Methods: After being exposed to desiccating stress for 5 days, mice were treated with eye drops consisting of 3% DQS alone or mixed with 0.005% or 0.01% TCP. Tear volume, tear film break-up time (TBUT), corneal fluorescein staining scores (CFSS), and tear film lipid layer grades (TFLLG) were measured at 0, 5 and 10 days after treatment. Ten days after treatment, the ROS production, MDA levels, and CD4+interferon (IFN)- γ T cells were measured in the cornea and conjunctiva, and the levels of tumor necrosis factor (TNF)- α , interleukin (IL)-1 β , IL-6, and chemokine CC motif ligand 4 (CCL4), and counts of goblet cells were measured in the conjunctiva.

Results: TBUT of the DQS and 0.005% or 0.01% TCP mixture group showed significant increases at 10 days after treatment, compared with the EDE and DQS alone groups ($P < 0.05$). CFSS significantly decreased in the DQS and 0.01% TCP mixture group when compared with EDE and DQS alone groups at 5 and 10 days after treatment ($P < 0.05$). The DQS and 0.01% TCP mixture group showed a significant increase in TFLLG compared with the EDE and DQS alone groups at 10 days after treatment ($P < 0.05$). DQS mixed with 0.005% or 0.01% TCP group showed lower ROS production and MDA levels than in the EDE and DQS alone groups ($P < 0.05$). Furthermore, the DQS and 0.01% TCP mixture group also showed higher conjunctival goblet cell density, and lower CD4+ IFN- γ T cells, and levels of TNF- α , IL-1 β , and CCL4 than in the EDE and DQS alone groups ($P < 0.05$).

Conclusions: The DQS and TCP mixture eye drops had a beneficial effect on the tear films and ocular surface of murine dry eye. When compared to DQS eye drops, the application of DQS and TCP mixture eye drops can be more effective by improving clinical parameters including TFLLG, TBUT, and CFSS, reducing ROS, inflammatory molecules, and T cells, and increasing conjunctival goblet cell density for EDE.

CONTROL ID: 3543095

SUBMITTER (NAME ONLY): Dagny Zhu

TITLE: Ophthalmology Inquiries on Reddit: What Should Physicians Know?

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Zhu, NVISION Eye Centers, Rowland Heights, California, UNITED STATES|A. Dave, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients are increasingly turning to social media to discuss personal medical questions. Despite being a popular social media site, Reddit has often been overlooked as a source of data on patient perspectives and concerns in the field of ophthalmology. We analyzed posts in the Ophthalmology subreddit, r/Ophthalmology, to better understand what conditions patients are talking about online and how often those who make posts are referred to different forms of medical care by commenters.

Methods: This cross-sectional study analyzed posts and their comments from March 18, 2018 to November 9, 2020. All posts and comments on r/Ophthalmology are public and were accessed using the Python Reddit API Wrapper. Posts and comments that were deleted or removed on or prior to November 9, 2020 were not included. The text of posts and comments were analyzed for unique references to ophthalmic conditions from the American Academy of Ophthalmology's Eye Health A-Z through a keyword search. Additionally, this text was analyzed for mentions and recommendations to different types of medical care.

Results: A total of 919 posts were collected from the timeframe above. An auto-moderator makes a comment on every post to discourage patients from asking personal medical questions. Despite this, over two-thirds (612/919) of posts mentioned medical treatment for eye conditions in either a post, comment, or both. Within posts, flashes and floaters are the most common condition with 48/312 (15%) unique mentions followed by glaucoma (7.4%) and retinal detachment (6.7%) (Figure 1). Within comments, cataracts are the most common condition with 71/586 (12%) unique mentions followed by glaucoma (8.9%) (Figure 2). Almost half of all posts mention ophthalmology and 9% go as far as to recommend the poster seek ophthalmic care. One-third of posts have no mention or recommendation of any type of medical care (Figure 3).

Conclusions: These findings show that patients are seeking information about their eye health on the r/Ophthalmology subreddit and that Reddit users are engaging with these types of posts. It is important for the vision community to understand what conditions patients are asking about online and how commenting patients respond to these posts to better educate all patients in the office.

CONTROL ID: 3543096

SUBMITTER (NAME ONLY): Youngyoon Amy Seo

TITLE: Collagen gels crosslinked by photoactivation of riboflavin for corneal defect repair

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Seo, G. Fernandes-Cunha, F. Chen, P. Le, C. Logan, D.C. Mundy, D. Myung, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|D. Myung, Ophthalmology, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal disease and injuries resulting in stromal defects put the cornea at risk of perforation and/or permanent scarring leading to blindness. A biomaterial that not only occupies a defect but also supports epithelialization may improve clinical outcomes and has the potential to reduce the need for further surgical intervention and the cadaveric donor corneal tissue it typically requires. Light activation of riboflavin is being used to crosslink and strengthen stromal collagen in cases of corneal ectasia. Here, we evaluate the use of this modality to also crosslink exogenously supplied collagen in situ at corneal wound sites.

Methods: Riboflavin was mixed with native, unconjugated collagen type I of varying concentrations and exposed to blue and UV light at increasing time intervals. Mechanical properties of the resulting collagen gels, including both storage and loss moduli as a function of exposure time, were studied using a rheometer. Collagen gels photoactivated with riboflavin were then evaluated in an in vivo deep keratectomy model in rabbits, where a 3.5 mm diameter and ~50% depth stromal defect was filled with the gel which was light-cured in situ. The treated eyes were clinically examined and excised after 1 week for immunohistochemical evaluation.

Results: Rheological experiments demonstrated successful gelation of collagen with increasing stiffness as a function of light exposure time using both blue light and UV light. The gels formed in situ by photoactivation of riboflavin were clinically well-tolerated and supported corneal epithelialization after 1 week in vivo. Immunohistochemical analysis exhibited expression of 4-hydroxynonenal (4-HNE) within the epithelium and alpha-smooth muscle actin within the surrounding stroma.

Conclusions: Our study suggests that riboflavin-mediated crosslinked of exogenous collagen type I has the potential to fill and stabilize corneal defects with a matrix that can support epithelialization. Further work to characterize the biological response of the cornea to this modality is merited.

CONTROL ID: 3543097

SUBMITTER (NAME ONLY): Ai Ping Yow

TITLE: Diagnostic performance of automated circumpapillary retinal nerve fiber layer (RNFL) segmentation with high-resolution swept-source optical coherence tomography in Glaucoma

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Yow, D. Wong, B. Tan, L. Schmetterer, SCBE, Nanyang Technological University, Singapore, Singapore, SINGAPORE|A. Yow, D. Wong, B. Tan, J. Chua, L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|R. Husain, Singapore National Eye Centre Glaucoma Department, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Glaucoma is a progressive optic neuropathy that leads to loss of retinal ganglion cells and thinning of retinal nerve fiber layer (RNFL), causes visual field loss and ultimately irreversible blindness. Thinning of RNFL can be quantified by performing objective thickness measurement along circumpapillary RNFL using optical coherence tomography (OCT), for glaucoma diagnostic and monitoring purposes. However, manual measurement is tedious. We evaluate the diagnostic performance of automated circumpapillary RNFL segmentation in swept-source OCT (SS-OCT) images.

Methods: SS-OCT volumes of the optic nerve head (ONH) comprising 250 glaucomatous and 75 normal eyes were collected using a Plex Elite 9000 (Carl Zeiss Meditec, USA) OCT system. Each acquired volumetric scan was processed to reconstruct a single circumpapillary cross-sectional image along a 3.46mm diameter circle centred at the ONH. A trained deep convolutional neural network using a U-Net architecture was then used to segment the circumpapillary RNFL from the cross-sectional images. A global RNFL thickness value was tabulated for each eye by averaging the obtained RNFL profile. Receiver operating characteristic (ROC) analysis was used to assess the overall diagnostic performance.

Results: Mean severity of the glaucoma eyes in our study was -3.64 ± 0.20 dB. For the glaucoma eyes, the mean thickness of the segmented RNFL was 84.97 ± 0.74 μ m, which was significantly different ($P < .001$) from that of the normal eyes (104.24 ± 1.21 μ m). As shown in Fig 1, our automated RNFL segmentation achieved an area under the ROC curve (AUC) of 0.91 (95% CI: 0.86 to 0.94). Example segmentation results are shown in Fig 2.

Conclusions: The results show a high diagnostic accuracy for circumpapillary RNFL segmentation for glaucoma detection, indicating the potentiality of automatic segmentation of circumpapillary RNFL in both healthy and glaucoma cases for detecting glaucoma.

CONTROL ID: 3543099

SUBMITTER (NAME ONLY): Hassanain Qambari

TITLE: Longitudinal analysis of retinal microvascular changes and its association with diabetic retinopathy

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Qambari, S. Saha, S. Seal, C. Dehghani, S. Frost, CSIRO Health and Biosecurity, Canberra, Australian Capital Territory, AUSTRALIA|C. Dehghani, University of Canberra, Canberra, Australian Capital Territory, AUSTRALIA|K. Edwards, N. Pritchard, N. Efron, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|A. Russell, The University of Queensland, Saint Lucia, Queensland, AUSTRALIA|Y. Kanagasingam, The University of Notre Dame Australia, Fremantle, Western Australia, AUSTRALIA|H. Qambari, M. Tennant, The University of Western Australia, Perth, Western Australia, AUSTRALIA|R. Malik, The University of Manchester, Manchester, Manchester, UNITED KINGDOM|R. Malik, Weill Cornell Medicine-Qatar, QATAR|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is the leading cause of blindness in the working-age population. Identifying early retinal microvascular changes relevant to DR has the potential to detect DR prior to physical manifestations in the eye. This study aims to determine a set of microvascular biomarkers that are responsible for the development and progression of DR.

Methods: A retrospective study cohort consisting of baseline and follow-up images of 30 healthy and 30 diabetic participants randomly chosen from the LANDMark study. Diagnosis of DR was based on Early Treatment of Diabetic Retinopathy Study scale. A set of 84 geometric microvascular parameters (GMP) were generated from macular centred images using a semi-automated, multi-step web-based Vascular AnalySis Program (VASP). VASP automatically identified vessel boundaries, categorized vessels into arteries or veins, and divided the fundus into multiple zones. An experienced grader confirmed and adjusted the outputs produced by VASP (when necessary), and GMPs were then generated. We analysed the four evolution of all 84 GMPs returned by VASP and compared each parameter between the two groups. Demographic comparisons were performed using a Chi χ^2 test and parameter analysis was performed using a Generalised Linear Model to correct for confounders.

Results: The mean age of diabetic cohort was 57 ± 11 years, with their average BMI significantly greater than the healthy cohort ($28 \pm 6 \text{ kg/m}^2$, $p=0.03$). Supine systolic and diastolic blood pressure were significantly higher ($p<0.001$ & 0.03) in diabetes. From the 84 generated GMPs, five were significantly different between the two groups. In relation to the diabetic cohort, these topographic differences can be summarised as: increased tortuosity for all vessels in Zone C ($p=0.002$), increased tortuosity thickness for arteries and veins in Zone B,C ($p=0.02$ & 0.03), increased asymmetric width ratio for vessel branches in Zone C ($p=0.01$), and the combined width of 2 major vein trees in Zone C increased ($p=0.04$).

Conclusions: Our study found a significant increase in five novel GMPs exclusive to diabetes. Following further research, these objective measurements could be used as biomarkers to identify patients at risk of developing referable DR and enable timely treatment, thus reducing the risk of blindness.

CONTROL ID: 3543102

SUBMITTER (NAME ONLY): Eric Van Meter

TITLE: Comparing fixational stability of D1 baseball players as measured by Tracking Scanning Laser Ophthalmoscopy to healthy controls

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare Tracking Scanning Laser Ophthalmoscopy (TSLO) measurements of eye fixation in elite D1 baseball players against a control group of healthy, non-baseball players as a preliminary investigation into the mechanism of Quiet Eye.

Methods: Thirty-four young, healthy control subjects (CS) (19F, 15M) aged 13-27 and 26 male D1 baseball players (BP) aged 18-22 participated in the study. For the CS analysis, two 30-second videos were split into three, separate 10-second recordings. Subjects were instructed to fixate on the upper right corner of a 5°x 5° 840nm imaging raster. For the BP, at least three 10-second videos were recorded per eye utilizing the same fixation stimuli and instructions as the CS. Offline, custom MATLAB software was used to stabilize the videos, extract eye motion at 480Hz, and compute microsaccade amplitude, peak velocity, peak acceleration, drift proportion, and drift amplitude. The bivariate contour ellipse area (BCEA) was calculated for each participant.

Results: A mixed effects model was conducted for each fixation measure to see if there was a difference in means (SD) between BP versus CS. Microsaccade mean amplitude was 0.30° (0.15) vs 0.46° (0.21) for BP vs CS ($p < 0.005$). Microsaccade mean peak velocity was 38.99°/sec (24.85) vs 79.68°/sec (49.13) for BP and CS ($p < 0.0005$). Microsaccade peak acceleration was 10510.05°/sec² (9742.58) vs 30997.33°/sec² (22431.55) for BP vs CS ($p < 0.0001$). Drift proportion was 0.88 (0.09) vs 0.84 (0.08) for BP vs CS ($p < 0.05$). BCEA of the drift was 0.10°² (0.13) vs 0.22°² (0.21) for BP vs CS ($p < 0.005$). There was no statistically significant difference in drift amplitude between BP and CS.

Conclusions: D1 baseball players exhibited more stable fixations in performing the given fixation task on TSLO as demonstrated by smaller mean microsaccade amplitudes, velocity, acceleration, and greater drift proportion. Whether this increased fixational stability is the result of an innate ability or is the result of the visual training required to play the visually demanding sport of baseball is still undetermined and warrants further investigation. Additional evaluation of eye motion with TSLO may provide promising insight into the mechanisms of Quiet Eye and on-field performance for baseball players in sports vision.

CONTROL ID: 3543107

SUBMITTER (NAME ONLY): Helen Makarenkova

TITLE: Single cell RNA sequencing reveals cellular and molecular complexity of adult lacrimal gland

SESSION TITLE: Lacrimal gland and Meibomian gland

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.P. Makarenkova, V. Delcroix, O. Mauduit, T. Umazume, Molecular Medicine, The Scripps Research Institute, La Jolla, California, UNITED STATES|C.S. De Paiva, Ocular Surface Center, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Single-cell RNA sequencing using 10X Genomics platforms is an effective way to reveal the heterogeneity of the lacrimal gland, define specific cell lineages, and to identify novel or poorly studied cell types.

Methods: We used unbiased high-throughput single-cell RNA sequencing (scRNA-seq) to identify the transcriptional profiles of adult lacrimal glands and analyzed the transcriptomes of lacrimal gland cells obtained from 3 adult mice. Transcriptionally similar cells were aggregated and analyzed using R Studio, Seurat, and the recently developed Rosalind software. Validation of each cluster has been done by genetic cell lineage labeling combined with analysis of label retaining cells and immunostaining.

Results: Unsupervised clustering resulted in the identification of 21 cell clusters. We have identified 8 epithelial cell clusters: basal ductal contractile cells, expressing several actins, keratins (Krts) and Btg2 (with anti-proliferative properties); basal ductal cells of the progenitor type, expressing Krts, KIT, Wfdc2, and Cnnd, luminal ductal cells, expressing a specific marker of luminal cells Krt19, intercalated duct cells with progenitor cell properties, three different types of acinar cells, expressing Aqp5, and myoepithelial cells, expressing smooth muscle actin (Acta2) and other contractile genes. Stromal and immune cells were identified based on the expression of vimentin (Vim), Ptprc (CD45), Pecame1, and Acta2. We identified 13 types of stromal cells, including two populations of endothelial cells, pericytes - smooth muscle cells of endodermal origin, expressing Acta2 and desmin (Des), two populations of fibroblasts: matrix producing fibroblasts and growth factor expressing fibroblasts. We also identified several clusters of immune cells, such as natural killer cells, tissue specific macrophages, small clusters of cytokines producing macrophages, antigen presenting cells, mast cells, and tissue resident T cells: CD4⁺ T cells, CD8⁺ T cells and Tregs. Analysis of label retaining cells combined with lineage tracing, immunostaining and image analysis confirmed classification of lacrimal gland epithelial cells. Thus, similar to scRNA-seq data, progenitor cells have been found within the basal layer of ducts and within intercalated ducts.

Conclusions: Single cell RNA-sequencing uncovered discrete transcriptional signatures of specific cell types within poorly identified cell populations.

CONTROL ID: 3543112

SUBMITTER (NAME ONLY): Isabella Loh

TITLE: Effect of Axial Length on the Difference Between SS-OCT and SD-OCT Retinal Nerve Fiber Layer Thickness Measurements in Highly Myopic Eyes

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Recent studies have suggested the superior diagnostic ability of swept-source optical coherence tomography (SSOCT), versus spectral-domain OCT (SDOCT), in localizing glaucomatous defects in eyes with low to moderate myopia. Here, we compare SSOCT and SDOCT retinal nerve fiber layer thickness (RNFL) measurements in highly myopic (HM) eyes, to determine if the difference in SSOCT and SDOCT RNFL (diffRNFL) is correlated with axial length (AL).

Methods: 43 eyes from 34 HM patients (AL 28.0 ± 1.6 , 24.0 to 31.6mm) were scanned with SSOCT (PLEX Elite) and SDOCT (Cirrus). RNFL was measured and segmented into 4 quadrants and 12 clock-hour segments. Linear regression analysis was performed to evaluate the association between diffRNFL and potential baseline predictor variables (AL, age, gender, laterality, lens status, glaucoma diagnosis [GLC], myopic macular degeneration [MMD] severity, peripapillary atrophy [PPA] severity, disc tilt severity, and presence of intrachoroidal cavitation [ICC]).

Results: In univariate regression analysis, AL was significantly associated with diffRNFL in the inferior quadrant ($\beta=13.50\mu\text{m}$, $p<0.001$), but not in the overall mean, nasal, superior or temporal quadrants (all $p>0.05$). After adjusting for potential confounding variables (MMD, tilt, ICC, GLC and PPA), multivariate analysis demonstrated that every 1mm increase in AL was associated with a $9.33\mu\text{m}$ increase in inferior quadrant diffRNFL ($p=0.03$). When holding potential confounders (including AL) constant, there was a $12.29\mu\text{m}$ greater inferior quadrant diffRNFL per unit increase in PPA severity ($p=0.046$).

In multivariate analysis of SDOCT RNFL values, after adjusting for potential confounders (MMD, tilt, ICC, GLC and PPA), every 1mm increase in AL was associated with a $7.47\mu\text{m}$ decrease in inferior quadrant RNFL ($p=0.001$). In contrast, multivariate analysis of SSOCT RNFL, after adjusting for potential confounders (MMD, tilt, ICC, GLC and PPA), showed that inferior quadrant RNFL was not significantly associated with AL ($p=0.64$).

Conclusions: The difference in SSOCT and SDOCT measurements of inferior quadrant RNFL was shown to increase with longer AL. Moreover, inferior quadrant RNFL was unaffected by AL on SSOCT, but decreased with longer AL on SDOCT. Taken together, this suggests SSOCT may provide more robust RNFL measurements in HM eyes in which there is suspicion for myopic glaucoma.

CONTROL ID: 3543115

SUBMITTER (NAME ONLY): Zirong Li

TITLE: Low-Cost Raspberry Pi Stereoscopic Fundus Imaging System

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Li, J.K. To, A.N. Vu, A.W. Browne, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|A.W. Browne, Institute of Clinical and Translational Science, Department of Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fundoscopic examination clinical ophthalmology provides a sense of depth for ophthalmologists to better evaluate ocular health and disease progression. Optical coherence tomography can capture three-dimensional anatomy, but is not routinely available in the developing world. Therefore, we designed a cost-effective stereoscopic camera system able to produce optically registered photos of the fundus, which can be used for ophthalmic diagnosis and management in low resource settings.

Methods: Fundoscopic images were taken using the Raspberry Pi (RPI) compute module 3+, RPi stereo camera module, and two 5-megapixel RPi camera modules. Each RPi camera module was encased in a 3D printed custom adapter allowing 6 degrees of freedom (forward/backward, left/right, up/down), attached to a Zeiss 6x18 T monocular, and then connected to a custom 3D printed binocular indirect ophthalmoscope case for the Heine Omega 180 (Fig 1B). The RPi camera modules' central axes were manually aligned using text and a grid on a sample paper. The fundus was visualized through a Volk Digital Clear Field indirect ophthalmic lens that fit into a custom 3D printed focusing track. Light from the Heine Omega 180 was used for transpupillary illumination of the fundus for image acquisition. The entire image capture system was attached to an existing slit lamp for ease of test administration. All custom 3D printed parts were constructed using Polylactic Acid on the Fused Deposition Modeling 3D printer Prusa MK3. Both video capture and image acquisition were controlled by an in-house graphical user interface written in Python using the OpenCV library.

Results: The tonal quality (brightness, contrast, color balance) of the color retinal photographs demonstrate adequate image quality for use in diagnostic evaluation. The optic nerve, macula, and retinal blood vasculature can be clearly visualized.

Conclusions: We built an economic stereoscopic camera system that can capture clear images of the fundus, which can also be remotely accessed for teleophthalmology. Moreover, the high image quality-to-price ratio, stereoscopic function, and remote access make our camera system sustainable in developing countries.

CONTROL ID: 3543119

SUBMITTER (NAME ONLY): Nihal Kaplan

TITLE: The battle of the Ephs in regulating miRNA boundaries in ocular anterior segmental epithelia

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is a strict boundary within the anterior segmental epithelium where more differentiated corneal epithelial cells are clearly segregated from their limbal epithelial counterparts. Expression patterns of Eph/Ephrins as well as miRNAs show compartmentalization at the limbal/corneal junction. We have shown that reciprocal expression patterns of EphA2 and Ephrin-A1 are likely to contribute to normal limbal-corneal epithelial compartmentalization. Moreover, miRNA (miR)-184 is prominently expressed in corneal epithelial cells, and acts as a negative regulator of corneal angiogenesis. Therefore, we investigated whether Eph/Ephrin signaling is responsible for the miR-184 expression pattern in cornea.

Methods: RNA-seq analysis was performed on human limbal and corneal epithelial cells (HLEC and HCEC) treated with antagomirs or Ephrin-A3 overexpression, and validated by real time qPCR and western blotting. Retroviral transduction was used to manipulate Ephrin-A levels. Antagomirs and siRNA knock-down were used to study changes in miR-184 levels by Taqman PCR.

Results: We show that similar to miR-184, miR-210 is prominently expressed in corneal epithelial cells while expression of its well-known target, Ephrin-A3, is restricted to limbal basal cells. Interestingly, antago-210 markedly decreased miR-184 levels, suggesting that miR-210 positively regulates miR-184. Ephrin-A3 overexpression reduced miR-184 levels in HLECs, while Ephrin-A3 knocked down in antago-210 treated cells reversed the reduction seen in miR-184 levels. A transcription factor with a putative binding site on the miR-184 regulatory region was increased both with Ephrin-A3 and antago-210 treatment. Knock-down to reduce ATF3 levels showed increased miR-184 levels, suggesting a role for ATF3. Although antago-210 treatment resulted in increased EphA2 and reduced Ephrin-A1 levels, manipulation of EphA2/Ephrin-A1 expression had no effect on miR-184 levels. However, EphA1, a close relative of EphA2, is enriched in limbal epithelium and siRNA depletion of EphA1 in limbal epithelial cells enhances miR-184 levels and prevents inhibition of miR-184 expression by Ephrin-A3.

Conclusions: Our data clearly demonstrate a link between miR-210 and EphA1/Ephrin-A3 signaling in restricting miR-184 expression within corneal epithelial cells. The functional significance of such regulation insures proper limbal vascularity while keeping the cornea avascular.

CONTROL ID: 3543122

SUBMITTER (NAME ONLY): Caitlin Logan

TITLE: Supramolecular host-guest hyaluronic acid hydrogels for corneal endothelial cell delivery and epithelial wound healing

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Corneal disease and scarring are major causes of blindness, with a need for improved treatment approaches. Hyaluronic acid (HA), a naturally occurring, biocompatible glycosaminoglycan with known corneal wound healing effects, is rapidly cleared from the eye. Supramolecular, non-covalent crosslinking modalities, including host-guest interactions, have been developed as ways to create biomaterial polymer networks with dynamic, reversible crosslinks. Here, supramolecular HA (s-HA) hydrogels were formed by cyclodextrin (CD) and adamantine (Ad) host-guest interaction to serve both as a potential vehicle for endothelial cells and as a possible promoter of epithelial wound healing.

Methods: S-HA hydrogels were synthesized by host-guest interaction between HA-CD and HA-Ad or HA-Ad-FITC. Primary corneal endothelial cells (CECs) were grown in culture and either covered with or encapsulated in s-HA hydrogel and evaluated using a live/dead assay at Time 0, Day 1, 2, and 3. To study epithelial healing, a total corneal epithelial debridement was performed, followed by application of s-HA, linear HA, or saline, with fluorescein examination on Day 1, 2, and 3 to determine wound size, and enucleated and fixed in paraformaldehyde for cryosectioning and immunohistochemical analysis on Day 3. Cryosections were stained for actin or nuclei, or immunostained for CD45 or vimentin and analyzed by confocal microscopy.

Results: Following encapsulation and needle injection, CECs showed greater than 90% viability, demonstrating the s-HA hydrogel to be a suitable vehicle. On Day 1, CECs remained dispersed within the hydrogel, but by Day 3, a subset of cells were seen to adhere to the tissue culture plate. In rats, all injured corneas were healed by Day 3. Animals treated with s-HA exhibited less corneal edema, fewer activated cells in the subepithelial stroma following wound closure, and reduced stromal expression of both CD45 and vimentin, with thickness and staining patterns more similar to normal controls than the linear HA or saline-treated eyes. Additionally, linear HA and saline treated eyes showed increased actin filament formation within stromal keratocytes compared to s-HA treated eyes and normal controls.

Conclusions: Supramolecular HA hydrogels have potential for corneal endothelial cell encapsulation as a delivery vehicle, as well as enhanced epithelial wound healing.

CONTROL ID: 3543124

SUBMITTER (NAME ONLY): Mélanie Hébert

TITLE: Outcomes in primary uncomplicated rhegmatogenous retinal detachment repair: a propensity-matched cohort analysis

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hébert, E. You, S.R. Qi, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Hopital du Saint-Sacrement, Quebec, Quebec, CANADA|J. Garneau, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The optimal procedure to manage simple rhegmatogenous retinal detachment (RRD) is still debated. We performed a retrospective, propensity-matched cohort analysis to compare primary repair failure and final visual acuity (VA) following rhegmatogenous retinal detachment (RRD) repair using pars plana vitrectomy (PPV) only or PPV with scleral buckle (PPV-SB).

Methods: Chart review was done of all 1516 consecutive patients operated for uncomplicated RRD repair using PPV (n=816) or PPV-SB (n=700) and sulfur hexafluoride gas (SF_6) or perfluoropropane gas (C_3F_8) at a tertiary care center between 2014 and 2018. Patients with other etiologies of RD were excluded. Choice of procedure was at the discretion of the treating surgeon. We used a propensity score to obtain a 1:1 nearest-neighbor matching with a caliper of 0.2 accounting for age, sex, laterality, lens status, myopia, macula status, number of detached quadrants and tears, presence of inferior RD and tears, symptoms duration, visual acuity (VA) at baseline, and tamponade agent. Patients with missing data were excluded.

Results: After matching, both groups (n=368 in each group) were well balanced for baseline characteristics, tamponade agent used, and follow-up durations. At presentation, patients had symptoms for 12.2 ± 14.8 days and 2.6 ± 0.8 quadrants were affected with 2.1 ± 1.5 retinal tears. Most patients were macula-off (n=443, 60%) and baseline VA in logMAR was 0.99 ± 1.09 . Treatment mostly used SF_6 (n=581, 79%).

Mean follow-up was 15.6 months. There were less recurrences of RRD in the PPV group (PPV: n=18, 5% vs. PPV-SB: n=41, 11%; $p=0.002$). More surgeries per patient were required to correct these recurrences in the PPV-SB group (PPV: 1.06 ± 0.28 surgeries vs. PPV-SB: 1.14 ± 0.42 ; $p=0.002$). Proliferative vitreoretinopathy and/or epiretinal membrane as a cause of recurrence was higher in the PPV-SB group (PPV: n=10, 3% vs. PPV-SB: n=26, 7%; $p=0.006$). VA in the PPV group was better at 3 months (PPV: 0.38 ± 0.47 vs. PPV-SB: 0.47 ± 0.50 ; $p<0.001$) and final follow-up (PPV: 0.27 ± 0.33 vs. PPV-SB: 0.35 ± 0.49 ; $p=0.009$).

Conclusions: Following uncomplicated primary RRD repair, there were less recurrences and better VA at follow-up in patients who underwent PPV only compared to PPV-SB.

CONTROL ID: 3543128

SUBMITTER (NAME ONLY): Sara Aurora Garcia y Otero Sánchez

TITLE: Angle-Closure Glaucoma Treated with Selective Laser Trabeculoplasty. Report of Efficacy and Safety after One-Year.

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Garcia y Otero Sánchez, J.A. Paczka, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|F. Garcia-y-Otero, departamento de oftalmología, ISSSTE Hospital Regional Valentín Gomez Farías, Guadalajara, Jalisco, MEXICO|J. Moreno- Nava, Oftalmología Torre A, Centro Medico Puerta de Hierro Especialidades, Guadalajara, Jalisco, MEXICO|S. Garcia y Otero Sánchez, J.A. Paczka, L.A. Paczka-Giorgi, Research department, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|L.A. Paczka-Giorgi, Research department, Asistencia e Investigación en Glaucoma, Guadal, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Selective laser trabeculoplasty (SLT) enhances outflow facility but depends on angle openness to be performed. Any angle-closure glaucoma (ACG) is not a good candidate for SLT, although if angle shallowness is reversed by any means, laser energy can be applied in the trabecular tissue and have a therapeutic effect. The aim of this retrospective study was to investigate the results of SLT in patients with angle-closure glaucoma with accessible angle view after a procedure to deepen the anterior chamber.

Methods: A retrospective assessment of the medical records of consecutive angle-closure glaucoma cases treated with SLT was performed in a specialized center in western Mexico. Forty-five cases from 26 patients were selected; using the data of one eye per patient, selected in at random. Baseline data and information from the follow-up visits for one year were analyzed. The studied variables were best-corrected visual acuity (BCVA), Goldmann IOP, number of antiglaucoma medications, collateral procedures (surgery/laser), visual field indexes, cup to disc (CD) ratio, thickness of retinal nerve fiber layer (RNFL), thickness of the ganglion cell layer, success procedural rate (pre-established criteria) and presence of complications.

Results:

Patients included in the study (14 females, 12 males) had a mean age of 63.0 ± 10.1 years. Mean time from prior anterior chamber deepening procedure[1] (8, iridotomy; 6, iridoplasty; 5, phaco+IOL, 5, iridotomy+ iridoplasty; 2, iridotomy+phaco+IOL) and SLT was 12.8 ± 10.0 months. Baseline IOP (19.1, S.E. 0.38 mmHg) was significantly less ($p=0.001$) than all five post-SLT timepoints (table 1). No significant changes in the BCVA ($p=0.18$), VFI (0.11), RNFL (0.13), and CD ratio (0.40) were found before and after the laser procedure. Baseline number of glaucoma medications (median, 2; range, 1-4) was significantly greater as compared to the last visit (median, 2 ; range 1-3; $p=0.0001$). Success rate at one year was 65.4%. A transient IOP spike occurred in only 2 cases and was solved with a conservative approach. No other complications were recorded.

Conclusions: According to the current results, SLT could be offered as a good additive treatment for angle-closure glaucoma when the irido-corneal angle can be adequately viewed after an anterior chamber deepening procedure is performed.

CONTROL ID: 3543129

SUBMITTER (NAME ONLY): Gunay Uludag

TITLE: Efficacy and safety of tocilizumab in the management of non-infectious retinal vasculitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Uludag, M. Halim, A. Akhavanrezayat, W. Matsumiya, C. Yasar, B. Pham, J.J. Hwang, S. Lajevardi, B.C. Lam, I. Karaca, A. Mobasserian, J. Regenold, D.V. Do, Y.J. Sepah, Q.D. Nguyen, Byers Eye Institute, Stanford University, Palo Alto, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center, Sunnyvale, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the efficacy and safety of intravenous (IV) tocilizumab (TCZ) in patients with non-infectious retinal vasculitis who failed conventional immunomodulatory therapy (IMT) and anti-tumor necrosis factor-alpha (anti-TNFa) therapy.

Methods: Medical records of seven patients with retinal vasculitis treated with monthly or biweekly IV TCZ (8 mg/kg) at a university uveitis clinic were reviewed to include demographics, ocular findings, previous treatment modalities, optical coherence tomography, and wide-angle fluorescein angiography (WAFA). Patients included in this index study were refractory to at least one IMT and anti-TNFa agent. Outcome measures were changes in visual acuity (VA), central macular thickness (CMT), and WAFA score. The Angiographic Scoring for the Uveitis Working Group (ASUWOG) system was utilized for FA scoring.

Results: Ten eyes of seven patients received TCZ therapy for a diagnosis of retinal vasculitis. The median age of patients was 14 years (range, 7-24). 57% of subjects were female. Clinical diagnosis of patients was chronic juvenile idiopathic uveitis (n:4), idiopathic retinal vasculitis (n:2), and HLA-B27-associated uveitis (n:1). Previous treatments of patients include methotrexate (n: 6), adalimumab (n:4), infliximab (n:6), and golimumab (n:2). The mean duration of TCZ therapy, up to most recent visit, was 7.1±3.5 months. The mean VA improvement was +4.0±5.6 ETDRS letters. None of the patients showed worsening in the VA. The mean CMT reduced from 373 ± 100mm to 298 ± 40mm (p>0.05), and the mean FA score reduced from 12.7 ± 4.8 to 4.2 ± 3.7 (p<0.001). Repeated infusions of TCZ were well tolerated by all subjects. One patient developed mildly elevated liver transaminases, which subsequently normalized. Figure demonstrates WAFA and OCT findings in a representative patient.

Conclusions: IV TCZ is a potentially effective and safe therapeutic option for the management of retinal vasculitis refractory to conventional IMT and anti-TNFa therapy.

CONTROL ID: 3543133

SUBMITTER (NAME ONLY): Kei Furushima

TITLE: Increased expression of regulator of G-protein signaling 5 (RGS5) in proliferative diabetic retinopathy

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Regulator of G-protein signaling 5 (RGS5) is a responsible molecule for pathological tumor neovascularization and has been reported to be involved in cancer, wound healing, and fibrosis. In this study, we investigated the expression of RGS5 in proliferative diabetic retinopathy (PDR).

Methods: Thirty vitreous humor and six fibrovascular membrane (FVM) samples were collected during vitrectomy in patients with PDR. Thirty vitreous humor and six FVM samples were collected during vitrectomy in patients with epiretinal membrane as controls. The expression of RGS5 in FVM was identified by immunostaining. The mRNA expression level of RGS5 was detected by quantitative RT-PCR, and the concentration of RGS5 in vitreous humor was detected by ELISA.

Results: Immunostaining showed co-staining of RGS5 and α SMA in FVMs from PDR patients. The mRNA expression levels of RGS5 were significantly higher in PDR patients compared with controls ($P<0.01$). RGS5 levels in the vitreous humor were significantly higher in PDR patients compared with controls ($P<0.001$). Among PDR patients, mean RGS5 level in the vitreous humor were significantly higher in eyes with FVM than in eyes without FVM ($P<0.02$).

Conclusions: Our results suggest that RGS5 may be involved in the development of FVM associated with PDR.

CONTROL ID: 3543135

SUBMITTER (NAME ONLY): Jin A Choi

TITLE: Vasin, an antagonist of TGF- β is decreased in glaucoma patients

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Choi, S. Karnam, N. Skiba, R. Maddala, P. Challa, R. Vann, V. Rao, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|J. Choi, Ophthalmology, Catholic University of Korea School of Medicine, Seoul, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To explore the role of vasin, a common constituent of human aqueous humor, and a known regulator of TGF- β activity in the etiology of glaucoma and trabecular meshwork physiology.

Methods: Vasin levels in the aqueous humor of glaucoma patients (POAG and Uveitis) were determined by mass spectrometry and ELISA. The effects of vasin on TGF- β 2 induced activation of SMAD signaling, and the effects of ADAM17 on vasin secretion in human TM, were evaluated by immunoblot analyses.

Results: Aqueous humor derived from both primary open-angle glaucoma (POAG, n=20)) and uveitis glaucoma (n=12) patients showed a significant but moderate decrease in vasin levels compared to age and gender matched non-glaucoma (cataract) patients. Recombinant vasin significantly suppressed TGF- β 2-induced SMAD 2/3 phosphorylation and α -smooth muscle actin, in human TM cells compared to control TM cells. The profile of extracellular vasin of human TM cells was found to be different with treatment of ADAM17 inhibitor. Although vasin has been reported to be anti-apoptotic and localized to the mitochondria in mouse embryonic fibroblasts, the protein exhibited vesicular distribution in human TM cells.

Conclusions: These results reveal that levels of the active form of vasin (secreted extracellular domain of the transmembrane form of vasin) are decreased in the aqueous humor of POAG and uveitis glaucoma patients. Vasin is known to antagonize TGF- β 2 signaling in human TM cells. Taken together, these findings suggest a crucial role for vasin in the etiology of glaucoma, and support the potential therapeutic significance of vasin in treatment of glaucoma.

CONTROL ID: 3543137

SUBMITTER (NAME ONLY): Darren Knight

TITLE: Anatomic and Visual Outcomes in Recurrent and Chronic Macular Hole Surgery

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although infrequent, reoperations for recurrent or persistent full thickness macular holes have been shown to have a lower success rate based on anatomic and functional outcomes. The optimal approach to these recurrent or persistent macular hole cases who have already undergone removal of the posterior hyaloid and primary ILM removal remains under active investigation. Given the variety of surgical approaches utilized around the world, there is a need for a relatively large series to demonstrate real world visual compared to anatomic outcomes after surgery for recurrent macular holes alone. Based on the multitude of published and successful surgical techniques, a direct comparison of approaches was undertaken.

Methods: Clinical charts of all patients who underwent recurrent macular hole surgery between 2010 and 2020 were reviewed to identify appropriate patients. Operative notes were reviewed for secondary vitrectomy procedures and the surgical technique was recorded. Particular attention was paid to phakic status and whether the internal limiting membrane was removed at the time of primary macular hole repair. Best corrected visual acuity (BCVA) was obtained at 3 months and 6 months post operatively. OCT measurements were reviewed to obtain average macular hole thickness. Eyes were excluded who carried a diagnosis of pathologic myopia (spherical equivalent greater than -8), central retinal vein occlusion, or a history of ocular trauma. All eyes in whom a macula hole was identified along with a retinal detachment were excluded for concurrent cases.

Results: 29 patients were identified to have undergone surgery for recurrent macular hole with complete followup. Patient demographics included a mean age 66.3 ± 17 . 16 patients received ILM flap, 4 patients underwent macular amniotic membrane graft, 2 macular redetachment, 7 use of silicone oil tamponade, and 5 a combination of these techniques. Mean BCVA at baseline was 20/125 and remained at 20/125 equivalent at 3 months. At 6 months the vision had declined to 20/160. The closure rate with all techniques was 81.8% after repeat surgery.

Conclusions: Although anatomic success was achieved in the majority of cases, visual improvement did not always correlate. Additional work is needed to identify better vision salvaging techniques in surgery for recurrent or persistent macular holes.

CONTROL ID: 3543138

SUBMITTER (NAME ONLY): YINGLUO XIONG

TITLE: bFGF alleviated dry eye disease by modulating inflammatory response and promoting healing process both in vitro and in vivo

SESSION TITLE: Cytokines, growth factors, anti-inflammatory

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Dry eye disease is a multifactorial disease accompanied by ocular damage. Basic fibroblast growth factor (bFGF) plays an essential role in wound healing, however, its role in dry eye induced ocular damage remains controversial. In this study, we elucidated cellular and molecular major markers of eye inflammation after the use of bFGF in preclinical settings.

Methods: We established in vitro inflammatory model by stimulation of IFN- γ and TNF- α in human corneal epithelial cell (HCEC) and conjunctival epithelial cell (HconEpic). We observed cellular responses, including cell viability, migration, and secretion of cytokines w/o bFGF. In vivo model was established by scopolamine-stimulation in C57BL/6J mouse. bFGF was applied and sodium hyaluronate eye-drop was used as positive control. Corneal damage was evaluated by fluorescein staining. Cytokines and mucus were assayed with ELISA and IHC staining.

Results: bFGF promotes proliferation and migration of HCEC and HconEpic. Under low-dose IFN- γ and TNF- α induced inflammation, bFGF effectively protected cells from death. We have noticed that IL-1 α , IL-1 β , IL-6 and MMP9 by HCEC, IL-6 and MMP9 by HconEpic were upregulated upon IFN- γ and TNF- α stimulation. bFGF downregulated the level of IL-1 α , IL-1 β , IL-6 and MMP9 in HCEC. A slight inhibitory effect on the expression of IL-6 by bFGF was observed in HconEpic. Regarding results from cytokine studies, we obtained consistent results from in vivo study. bFGF also showed therapeutic effect on dry eye as evidenced by increased tear secretion, attenuated fluorescein staining of corneas, decreased corneal matrix swelling and fewer number of vessels around conjunctiva. Interestingly, sodium hyaluronate showed no effect on mucus secretion, while bFGF obviously improved the mucus to a normal level.

Conclusions: bFGF showed protective effects on ocular surface epithelial cells in moderate inflammation by promoting cell proliferation, migration and regulating cytokine production. bFGF attenuated mouse dry eye induced ocular damage and increased mucus secretion. All evidence indicated that bFGF could be a prospective approach for the treatment of dry eye, at least in non-severe dry eye disease.

CONTROL ID: 3543139

SUBMITTER (NAME ONLY): Jeffrey Eng

TITLE: Vertical Transect Analysis of Optical Coherence Tomography Images in Patients Treated for Diabetic Macular Edema

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is a common cause of vision loss among diabetics. Optical coherence tomography (OCT) remains a vital component in the evaluation and management of diabetic macular edema. We sought to evaluate whether Draper's novel vertical transect analysis (VTA), when applied to OCT images in eyes with DME, might accurately predict treatment endpoints.

Methods: A post-hoc analysis was performed on OCT images and clinical data from the TYBEE clinical trial. TYBEE is a multicenter, randomized, masked clinical trial to evaluate the safety and efficacy of suprachoroidal triamcinolone acetonide along with intravitreal Eylea compared with Eylea monotherapy in patients with DME and without prior pharmacologic treatment. Best corrected visual acuity (BCVA) was determined at the clinical sites participating in the clinical trial. OCT central subfield thickness (CST) and Diabetic Retinopathy Severity Score (DRSS) were determined at a central Reading Center. OCT images were processed by automatic segmentation then manually adding a line for the fovea. The vertical transect analysis was then performed on baseline and post-treatment OCT images (both processed and unprocessed) with regression analysis.

Results: BCVA significantly correlated with VTA applied to processed baseline plus post-treatment OCT images ($P=0.044$) and with VTA applied to processed baseline OCT images ($P=0.038$). The change in visual acuity from baseline to post-treatment did not significantly correlate with VTA applied to unprocessed baseline OCT images ($P=0.086$) or with processed baseline OCT images ($P=0.300$). The CST significantly correlated with VTA applied to unprocessed ($P=0.048$) and processed ($P=1.87e-4$) baseline plus post-treatment OCT images and to processed ($P=0.007$) baseline OCT images. However, the change in CST from baseline to post-treatment did not significantly correlate with VTA applied to both unprocessed ($P=0.629$) and processed ($P=0.412$) baseline OCT images. The DRSS and change in DRSS from baseline to post-treatment did not significantly correlate with VTA applied to any OCT images.

Conclusions: There was correlation between BCVA/CST and VTA but no correlation between DRSS and VTA. With more study, VTA has the potential to be a powerful clinical and research tool to predict clinical endpoints in patients undergoing treatment for diabetic macular edema.

CONTROL ID: 3543141

SUBMITTER (NAME ONLY): Eisuke Shimizu

TITLE: Innovative artificial intelligence-based cataract diagnostic method uses a slit-lamp video recording device and multiple machine-learning

SESSION TITLE: Deep learning for classification and segmentation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The use of artificial intelligence (AI) remains limited in cataract imaging diagnosis because there is a lack of numerous standardized images and analysis models. An AI model for cataract diagnosis could potentially be created by slit-light images and machine-learning. We aimed to determine whether our machine-learning model based on images recorded with a slit-lamp device would have the comparable diagnostic performance to that of ophthalmologists.

Methods: A dataset comprising 18,596 frames collected retrospectively were used for training and cross-validation of a machine-learning algorithm. Cataract diagnosis, cataract severity grading, and surgical indication prediction between our model and evaluations performed by ophthalmologists were assessed the use of a slit-lamp device to record cataract video and machine-learning system. A sensitivity, specificity, positive predictive value, and negative predictive value for cataract diagnosis and surgical indication. The area under the receiver operating characteristic curve for each cataract grading. Weighted kappa statistics for cataract video analysis and cross-validation.

Results: Our model could diagnose cataract with sensitivity, 99.60% (95% confidence interval [CI], 99.40–99.70), and specificity, 96.00% (95% CI, 83.40–99.30), compared to the diagnostic performance of ophthalmologists. The results of cataract severity grading were nuclear cataract (NUC) 0: Area under curve (AUC), 0.987 (95% CI, 0.947–1.000); NUC1: AUC, 0.916 (95% CI, 0.888–0.945); NUC2: AUC, 0.862 (95% CI, 0.844–0.879); and NUC3: AUC, 0.943 (95% CI, 0.931–0.955). For overall cataract grading, the accuracy was 87.80% (kappa, 0.811 [95% CI, 0.791–0.831]). The surgical indication prediction with a sensitivity of 91.80% (95% CI, 82.00–95.10) and specificity of 92.30% (95% CI, 86.10–94.40). The cross-validation accuracy was 86.0% (kappa, 0.800 [95% CI, 0.780–0.820]).

Conclusions: We successfully created a high-performance cataract diagnostic AI using machine-learning from images recorded with a portable slit-lamp device, which can simplify the cataract diagnostic process and be of particular use in settings where access to ophthalmologic services is not available.

CONTROL ID: 3543152

SUBMITTER (NAME ONLY): Karine Bigot

TITLE: Human transferrin protects retinal ganglion cells in a rat model of ocular hypertension

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is a progressive optic neuropathy characterized by retinal ganglion cell (RGC) degeneration and visual field loss. Dysregulation of iron homeostasis and oxidative stress have been implicated in the pathogenesis of glaucoma. EYS611 is a novel non-viral gene therapy delivering sustained intraocular concentration of human transferrin (Tf), an endogenous iron chelator. We previously demonstrated that EYS611 slowed disease progression in acute and chronic rat models of retinal degeneration supporting its development for retinitis pigmentosa and dry age-related macular degeneration. To evaluate whether EYS611 could be protective in glaucoma, we evaluated the effect of Tf in a rat model of ocular hypertension (OHT).

Methods: OHT was induced by injection of magnetic microbeads into the anterior chamber of adult Brown Norway rats (n = 5/group). Animals then received four weekly intravitreal injections of Tf (240 µg/eye) or vehicle (BSS). Naïve rats served as normotensive internal controls and remained untreated. Intraocular pressure (IOP) was measured during the 4 week-experimental period. Pattern electroretinogram (pERG) was measured prior to OHT, then 2 and 4 weeks after OHT. RNA-binding protein with multiple splicing (RBPMS) immunolabeling of flat-mounted retinas was used for RGC quantification at 4 weeks.

Results: IOP in rats with OHT was significantly increased over naïve controls by 48h and remained elevated for the entire 4-week experimental period. Both treated groups had lower pERG amplitude compared to naïve controls on weeks 2 and 4. Significantly lower RGC density (-49.7%) was reported in BSS-treated animals at week 4 in comparison to naïve animals (958 ± 146 cells/mm² vs. 1927 ± 61 cells/mm², $p < 0.0001$) whereas RGC density in Tf-treated rats was not statistically different from RGC density of naïve animals ($p = 0.17$). Tf administration preserved RGC by about 70% compared to BSS-treated animals with OHT (1628 ± 92 and vs. 958 ± 146 cells/mm², $p 0.0013$).

Conclusions: These results demonstrate the ability of Tf to protect RGCs exposed to elevated IOP, suggesting that iron chelation could benefit glaucoma patients. These proof-of-concept findings and previous data demonstrating sustained intraocular production of Tf following non-viral gene transfer strongly support the evaluation of EYS611 for long-term and effective neuroprotection in glaucoma.

CONTROL ID: 3543154

SUBMITTER (NAME ONLY): Hui Wang

TITLE: Associating retinal layer thicknesses of the macula with cognitive speed and executive function

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To associate ten macular retinal layer thicknesses with cognitive speed and executive function.

Methods: From the age and sex stratified, population-based LIFE-Adult-Study, spectral domain optical coherence tomography (OCT) volume scans of the macula (97 horizontal B-scans, each consisting of 512 A-scans) were selected from participants with reliable measurements (quality ≥ 20 dB) who underwent cognitive assessment by both parts of the trail-making test (TMT; illustrated in Fig. 1A), with TMT Part A testing cognitive speed and Part B assessing executive function. On each B-scan, ten retinal layers were segmented (Fig. 1B). Separately for each of these layers, at each of the 49,664 A-scans, partial Pearson correlations between layer thickness and each TMT part adjusted for age were calculated. P-values were adjusted for multiple comparisons by the false-discovery method.

Results: 17,759 eyes of 8,958 subjects were included (4,670 female/4,288 male; age range: 20-79 years). Figure 2 shows the pointwise partial correlation maps for each layer and test. Inner retinal layers were stronger associated with both TMT subtests than outer layers. The largest percentage of significant retinal locations was found for the retinal nerve fiber layer (RNFL; TMT-A/B: 72%/68%), followed by the ganglion cell layer (GCL; TMT-A/B: 48%/26%). Generally, TMT-A (cognitive speed) was stronger associated with layer thicknesses than TMT-B (executive function), but amount and spatial arrangement of the associations are similar for both subtests, with the notable exception of the outer photoreceptor segment thickness, which is significantly correlated over 29% of the macula with TMT-A but entirely uncorrelated with TMT-B. Thinner inner layers over large macular areas are related to worse cognitive performance. Layer thinning spares areas nasal to the fovea for RNFL and is ring-shaped around the fovea for most other inner layers.

Conclusions: Previous dementia studies related cognitive decline to thinning of a single retinal layer (RNFL) and typically analyzed areas close to the optic disc. Here, we analyze ten retinal layers of the macula and demonstrate

associations between worse cognitive performance and reduced retinal layer thickness over large areas. This was most pronounced for RNFL and GCL, two layers that are also closely related to optic nerve damages, but selected effects also occurred in outer layers.

CONTROL ID: 3543170

SUBMITTER (NAME ONLY): Irmela Mantel

TITLE: Transscleral optical phase imaging revealing the choriocapillaris structure

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Transscleral optical phase imaging (TOPI) has been developed in order to visualize retinal pigment epithelium (RPE) cells in vivo. In addition, it reveals a background reflectance pattern which is investigated in this study as the choriocapillaris structure.

Methods: Healthy volunteers and participants with non-neovascular AMD were recruited for TOPI, associated with conventional imaging: spectral domain optical coherence tomography, autofluorescence, color and infrared fundus imaging. Six squares of 5.04x5.04 degrees were acquired with TOPI: one was foveal, four were localized in the macular quadrants with 3.8° eccentricity, and one to the investigators discretion. The resulting TOPI images were confronted with information from conventional multimodal imaging. The results are presented in a descriptive way.

Results: Included were 51 healthy eyes from 30 volunteers (mean age 35±11 years; 37% females), and 10 eyes of 8 AMD patients (mean age 75.5±5.5 years, 50% females). The RPE cells visualized in healthy participants showed a hexagonal pattern with a darker center and a lighter border. However, this pattern was seen on reticular pattern of linear zones with lighter and darker background grey, of 2 to 3 RPE cells width. This reticular background pattern was highly regular in healthy eyes. In AMD eyes with atrophic changes it became a dominant image feature due to high contrast, showing more irregularity. However, in deeper atrophy, the reticular pattern was lost and only larger choroidal vessels were visible. All observations suggested that the reticular pattern corresponds to the choriocapillaris.

Conclusions: TOPI reveals, in vivo, the human choriocapillaris structure in addition to the RPE cells. This novel imaging capacity may be of great value in order to study various pathologies involving the choriocapillaris.

CONTROL ID: 3543171

SUBMITTER (NAME ONLY): Zahra Tajbakhsh

TITLE: Minimal persistent inflammation during the silent phase of allergic conjunctivitis observed with in vivo confocal microscopy

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Minimal persistent inflammation at the conjunctival and nasal epithelium of asymptomatic rhinitis patients has been detected, revising therapeutic strategy to target the inflammatory response in preference to symptom-based therapy. We have previously shown increased density and morphology of dendritiform cells in the cornea and conjunctiva in active allergic conjunctivitis during the pollen season. This study aimed to assess whether the changes in dendritic cells persisted during the silent symptom-free phase of allergy.

Methods: Twenty allergic participants (mean age 43.3 ± 14.3 years, 55% female) were examined during active allergic conjunctivitis and when the allergy was in silent phase (at least 4 symptom-free weeks). In vivo confocal microscopy (HRTIII) was performed on the right eye in five locations (central cornea, inferior whorl, temporal corneal periphery (1mm inside limbus), temporal corneal limbus, and temporal bulbar conjunctiva (2-3 mm away from limbus)). Five best-focused, non-overlapping images from each location and one from the inferior whorl were analysed. Dendritiform cells (DC) were counted manually, and morphology of corneal cells was recorded using grading scales for cell body size, dendrite length, and dendrite shape. Differences between phases (Wilcoxon Signed Rank test) and between regions (Friedman with post-hoc tests) were examined.

Results: DC density in the conjunctiva was higher in the active phase than the silent ($p=0.001$) but was not significantly different between phases at any of the corneal regions (central $p=0.70$; periphery $p=0.32$; limbus $p=0.14$; inferior whorl $p=0.84$). DC density was higher at the limbus than all other locations ($p \leq 0.001$) during both phases, and the fewest DC were observed at the inferior whorl. During the active phase, DC cell body size at all corneal locations was larger ($p \leq 0.03$), and dendrites were longer at the corneal periphery and limbus ($p < 0.01$), than in the silent phase. Conjunctival DC morphology was assessed qualitatively and observed in both phases to have long thin dendrites and in some participants a wire-netting pattern.

Conclusions: This study demonstrated the persistence of dendritiform immune cells in the cornea, but not in the conjunctiva, in the absence of symptoms in patients with allergic conjunctivitis. These cells were observed to have a lower morphology grade suggesting a less activated state.

CONTROL ID: 3543180

SUBMITTER (NAME ONLY): Shahzan Anjum

TITLE: VEGF-A in Lacrimal gland Adenoid Cystic Carcinoma

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Anjum, S. Sen, S. Bakhshi, S. Kashyap, K. chosdol, N. Pushker, M.S. Bajaj, M.C. Sharma, R. Meel, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: To evaluate the status of Vascular Endothelial Growth Factor-A (VEGF-A) in lacrimal gland Adenoid cystic carcinoma (ACC) and to correlate with high risk clinicopathological features.

Methods: A retrospective analysis of 30 histopathologically proven ACC patients was undertaken. Clinicopathological features were recorded & 1-55 months follow up was available. TNM staging was done (AJCC, 8th edition). VEGF-A expression was evaluated by immunohistochemistry (IHC) (clone VG1). The association between VEGF-A and clinicopathological variables was analysed using Fisher's exact test; survival by Kaplan-Meier and statistical analysis using log-rank test. Cox regression was performed to determine its prognostic significance.

Results: Of the 30 ACC cases, there were 15 females and males respectively with a mean age of 38 ± 25.8 years. Large tumor size (>2 cm) was found in 86.6% (26/30) cases. The growth pattern was cribriform (n=16), solid (n=9) and mixed (n=5). Perineural invasion was present in 33.3% (10/30), intracranial extension in 16.6% (5/30) & bone erosion in 33.3% (10/30) cases. Exenteration was performed in 23.3% (7/30). Recurrence developed in 60% (18/30), systemic metastasis and death both in 20% (6/30) cases. VEGF-A overexpression was seen in 46.6% (14/30) cases. Clinicopathological correlation revealed VEGF-A to be significantly associated with solid histologic pattern ($p=0.04$) and intracranial extension ($p=0.01$). On Kaplan-Meier analysis, expression of VEGF-A ($p=0.002$), solid histologic pattern ($p=0.004$), perineural invasion ($p=0.003$), bone erosion ($p=0.000$), T3-T4 stage ($p=0.004$), intracranial extension ($p=0.01$) and exenteration ($p=0.01$) significantly correlated with reduced disease free survival. Univariate analysis showed significant correlation of VEGF-A overexpression, solid histologic pattern, perineural invasion, bone erosion, T3-T4 stage, intracranial extension, exenteration and metastasis. On multivariate analysis VEGF-A (HR: 15.2, 95% CI: 1.9-119.4, $p=0.010$) and bone erosion (HR: 21.0, 95% CI: 1.7-247.8, $p=0.015$) were found significant prognostic factors along with metastasis (HR: 5.3, 95% CI: 1.0-26.8, $p=0.04$).

Conclusions: Overexpression of VEGF-A along with bone erosion and metastasis are all important poor prognostic factors in the outcome of lacrimal gland ACC. Studies on a larger cohort is necessary to further validate VEGF-A as a potential therapeutic target in the management of lacrimal gland ACC.

CONTROL ID: 3543185

SUBMITTER (NAME ONLY): Einat Shneor

TITLE: A novel diagnostic tool for Keratoconus and its severity

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shneor, A. Gordon-Shaag, A. Gedeon Abou Said, Dept. of Optometry, Hadassah Academic College, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: An arc shaped black shadow ("black sign") has been observed when using ophthalmoscopy on keratoconus patients (fig. A). We aimed to develop and validate a novel method (Patent pending) for detection of clinical and subclinical keratoconus (KC and KCS) based on the presence of this black sign.

Methods: A device was designed to enable to the clinician to hold the ophthalmoscope at an appropriate angle and distance and attach it to a smartphone (iPhone XS Max) to take a picture of the eye. The clinician using the device was masked to the KC status of the subjects. A masked observer determined the presence of the black sign in the downloaded images. AutoCAD software was used to measure the sign's width. KC, KCS and healthy subjects were included in this study. A diagnosis of KC was based on abnormal tomography and at least one clinical sign of KC. KCS had only abnormal topography. Both eyes were included in the analysis for KC and KCS, while only the right eye for controls. Subjects underwent corneal tomography (Sirius, CSO) and a full ocular exam. KC severity was graded based on Belin ABCD Criteria. Sex, age and tomography parameter differences between groups were evaluated by Chi square and Mann Whitney tests. Spearman correlations were performed between the width of the black sign and ABCD Criteria.

Results: Twenty KC and KCS subjects (24 eyes with KC and 12 eyes with KCS, 10 males, mean age 28.2 ± 9.1 , range 20-56 years) and 35 healthy controls (19 males, mean age 25.1 ± 6.7 , range 20-52 years) participated in this study. Groups were similar in age ($U=246.5$, $p=0.07$) and sex ($\chi^2=0.09$, $p=0.76$) but different in spherical equivalent ($p<0.01$), anterior and posterior keratometry ($p<0.001$), thinnest and central corneal thickness ($p<0.0001$) and front and back apex curves ($p<0.0001$).

The black sign was observed in all KC and KCS images but in none of the controls. The width of the black sign was negatively correlated to Belin Criteria (A, Anterior Elevation: $r=-0.74$, $p<0.0001$; B, Back Elevation: $r=-0.79$, $p<0.0001$; C, Thinnest Corneal Thickness: $r=-0.58$, $p<0.0001$; D, Distance Visual Acuity: $r=-0.36$, $p=0.03$).

Conclusions: This novel method may differentiate between KC and KCS and healthy controls based on the presence of the black sign. The thickness of the black sign is negatively correlated to KC severity. Therefore, this method can be used for screening population and following the progression of the diseases.

CONTROL ID: 3543193

SUBMITTER (NAME ONLY): Sylvain Fisson

TITLE: Systemic anti-transgene T-cell immune response induced by subretinal AAV gene transfer can be inhibited by a simultaneous co-injection of peptides from the transgene product

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Fisson, G.A. Chauveau, J. Vendomele, A. Galy, Genethon, Inserm UMR_S951, University of Evry, University Paris Saclay, Evry, FRANCE|S. Fisson, G.A. Chauveau, D. Dalkara, Institut de la Vision, Inserm UMR_S968, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: While subretinal injection of adeno-associated virus (AAV) gene therapy vectors can successfully treat several inherited retinal diseases, some patients display inflammatory events. The eye is known as an immune-privileged site but anti-capsid and anti-transgene immune responses have been reported in some patients, possibly contributing to the loss of transduced cells. We previously reported that a subretinal injection of AAV8 triggers a systemic anti-transgene T-cell response in a dose-dependent manner, and that an antigen introduced into the subretinal space can provide a systemic antigen-specific immunosuppression referred to as subretinal-associated immune inhibition (SRAII). Here, we hypothesize that peptides from the transgene product, have utility as SRAII inducers when introduced simultaneously with the AAV.

Methods: A single subretinal injection of AAV8 with peptides from the transgene product was performed. The transgene cassette encoding GFP and HY male antigen, containing MHC class I- and MHC class II-restricted T cell epitopes (UTY and DBY peptides immunodominant in H-2b female mice), was packaged into AAV8 under the ubiquitous PGK promoter and injected subretinally with or without HY peptides at day 0 in female wild type C57BL/6 and pathophysiological rd10 mice. ELISpot and multiplex assays were done 3 to 14 days post injection for systemic anti-transgene specific primary T-cell response evaluation, or at day 21 (following a subcutaneous challenge at day 14 with HY peptides adjuvanted in CFA) for memory T-cell response analysis.

Results: We found in both models that: (i) subretinal injection of 2.10e9 or 5.10e10 vg of AAV8-PGK-GFP-HY triggered a dose-dependent systemic primary and memory anti-transgene Th1/Tc1 responses, (ii) the simultaneous co-injection of AAV8 and of HY peptides inhibited both CD8+ and CD4+ T-cell specific primary and memory responses against HY even at high dose (5.10e10 vg) of AAV.

Conclusions: SRAII phenomenon seems to be a powerful systemic immunosuppressive mechanism specific to a transgene expressed in an eye. Since we have confirmed these results in the rd10 pathophysiological context, co-injection of the transgene product and the therapeutic vector may be considered as a new immunomodulatory strategy to control inflammatory reactions in the context of ocular gene therapy.

CONTROL ID: 3543194

SUBMITTER (NAME ONLY): Mark Jenkins Sanchez

TITLE: Machine learning classification of visual acuity curves for spectacle independence prediction

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. Jenkins Sanchez, M. Faria-Ribeiro, P. Piers, Research and Development, Johnson and Johnson Surgical Vision, Groningen, Groningen, NETHERLANDS|L. Tsai, S. Bentow, Clinical Science, Johnson and Johnson Surgical Vision, Santa Ana, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: For patients that undergo cataract surgery, Spectacle Independence (SI) is one of the desired clinical outcomes, especially when implanted with presbyopia correcting intraocular lenses (IOLs). Although Through Focus Visual Acuity (TFVA) can be accurately predicted based on preclinical simulations and measurements [1], there is a need for a robust model to allow predictions of SI ahead of clinical trials.

Methods: It is expected that the TFVA curve measured on an implanted subject is related to the SI outcome. However, establishing a direct correlation between TFVA and SI is challenging. In this work, we build on previous work and further characterize the link between observed TFVA curves and the SI outcome. We use a Machine Learning (ML) approach to train several different algorithms to classify TFVA curves into SI and non-SI. These include LR, LDA/QDA, KNN, NB, SVM. The training data used for these classification algorithms are binocular TFVA curves (from -3D to 0D, 0.5D steps) and answers to questionnaires related to the subjects SI compiled from multiple clinical studies with a variety of implanted lens models. We use a subset of this full clinical set as a validation check on the different algorithms and compare the results to those obtained with the model developed previously. Additionally, we compare the performance impact of also including each subject's manifest refraction in the training data.

Results: Results show an improvement with respect to the accuracy (at least 10%) of our previous model when classifying curves from the validation dataset. We also find that the strongest predictors of SI in this context are the VA scores in the near range (-3 to -2D) consistent with previous findings. We also compare the predictions of SI for average clinical and preclinical curves with the observed SI in the clinical datasets showing good correlation between them. Including manifest refraction in the training data did not noticeably improve prediction accuracy.

Conclusions: We conclude that the tested ML models, TFVA can be used to predict the SI outcome with a reasonable degree of accuracy and can already give directional information when used with preclinical data. They give improved accuracy as compared to the previous model. However, the attained accuracy (above 70%) may indicate that other factors could also play a role in the SI and could be used to improve predictions further.

CONTROL ID: 3543218

SUBMITTER (NAME ONLY): Alberto de Castro

TITLE: Effect of axial and lateral fixational eye movements in corneal topography measurement with OCT

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. de Castro, E. Martinez-Enriquez, P. Urizar, A. Curatolo, S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: The topography of the cornea can be quantified three-dimensionally with Anterior Segment Optical Coherence Tomography (OCT) systems. However, the measurement is not instantaneous and during the scan, fixational eye movements may influence the results. We used simulations to model the influence of axial and lateral eye movements in the variability of repeated corneal topography measurements.

Methods: We used experimental data from two custom-built Fourier domain anterior segment OCT systems collected in 28 participants. The first system was a spectral OCT (OCT1), with a repetition rate of 25K A-scans/s and 10x10mm (300x50 A-scans) lateral range, and the second a swept source OCT (OCT2), 200K A-scans/s, scanned 15x15mm (300x150 A-scans). The measurement time was 0.6 and 0.41 s respectively. Simulations of the acquisition in both systems were performed assuming lateral and axial eye movements using the MATLAB Image System Engineering Toolbox for Biology (ISETBIO). On each OCT scanner position, eye shifts were applied in the x y and z directions and the sag calculated. To simulate higher eye movements a factor F of 1.5 was applied. The central 3 mm of the data were fitted by a sphere (radius R) and the residuals were fitted by Zernike polynomials (6th order coefficients, zC). The standard deviation (std) of the fittings to simulated data and experimental results were compared.

Results: The maximum shift from the fixation point simulated by the eye movement model was 40 μm . OCT1/OCT2 average std across subjects was 0.18/0.17 mm for R, 3.96/3.46 for the 3rd and 3.33/1.65 μm for the 4th order zC. Simulations std for F=1 and 1.5 was 0.15/0.07 and 0.18/0.13 mm for R, 2.35/1.15 and 2.99/1.84 for the 3rd and 1.47/1.16 and 2.19/1.76 μm for the 4th order zC, respectively. When only lateral movements were considered, the simulations predicted 50% lower std values.

Conclusions: The simulations of the raster scan acquisition of corneal topographies including fixational eye movements modeled with the ISETBIO Toolbox predict with high accuracy the experimental variability in the fitting parameters when axial movements are included. While the statistics of the axial eye movements may be different than those in the lateral direction, these simulations can serve to understand the sources of variability in topography measurements and to evaluate different scanning patterns.

CONTROL ID: 3543219

SUBMITTER (NAME ONLY): Mengyuan Ke

TITLE: Melanin accumulation in choroid observed with the calibrated degree of depolarization in PS-OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Melanin naturally presents in the eye including the iris, retinal pigment epithelium, and choroid. The concentration of the melanin changes with aging¹. Polarization-sensitive OCT (PS-OCT) enables the measurement of the degree of depolarization (DOP) of the eye. Recent studies have shown that DOP is a feasible way to measure the melanin in animals² and human³. However, the DOP signal is highly correlated with the light intensity⁴. In this study, we developed an ad-hoc calibration method to decouple the DOP and intensity in a customized PS-OCT. In a guinea pig model, we longitudinally measured the DOP and estimated the melanin distribution in a guinea pig model for 8 weeks in vivo.

Methods: To mitigate the correlation between image intensity and DOP, we fitted an empirical function between SNR and DOP with measured data from an Albino eye (Fig. 1a), assuming no physical depolarization induced by pigmentation. The calibrated DOP was obtained by subtracting the original DOP from the reference DOP in the SNR-DOP function. A total of 10 eyes from 5 guinea pigs (4 pigmented; 1 albino) were imaged weekly with a PS-OCT for 8 weeks. We evaluated the difference of DOP signals associating with pigmentation, ages, and individuals.

Results: We found that the SNR-DOP empirical function was consistent in different datasets from different albino animals (Fig. 1a). After applying the calibration, the DOP contrast was better in agreement with the distribution of melanin, mainly concentrated in the choroid, (Fig. 1b 1c). We quantified calibrated DOP in retinal volume scans (Fig. 2i 2ii) and found it was increasing in pigmented eyes with age (Fig. 2iii).

Conclusions: In this study, we demonstrated that the DOP from a PS-OCT could be calibrated to present better contrast of pigmentation in the eye. We observed the DOP was increasing with age in young pigmented guinea pigs, revealing that melanin accumulated in the choroid.

CONTROL ID: 3543226

SUBMITTER (NAME ONLY): Sarah Hull

TITLE: Phenotypic variability of WFS1 related eye disease

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Wolfram syndrome characterised by diabetes mellitus (DM), sensorineural hearing loss (SNHL), optic atrophy and diabetes insipidus arises from bi-allelic variants in WFS1. Less commonly, heterozygous variants are associated with a similar phenotype. In this retrospective, observational study, a group of patients with variants in WFS1 underwent detailed phenotypic analysis.

Methods: A series of 8 patients from 6 families were ascertained from the New Zealand Database of Inherited Retinal and Optic Nerve Disease. Targeted Sanger sequencing or next generation sequencing using an ocular gene panel were performed. Detailed phenotyping included retinal imaging, electrophysiology, neuroimaging and endocrine investigations.

Results: 8 patients (5 female, 3 male) from 6 families (2 Māori, 2 Asian, 1 Pasifika, 1 NZ European) were ascertained. Four families (6 patients) had likely pathogenic variants in WFS1 consistent with recessive disease in 3 and possible dominant disease in one. All 6 patients had optic atrophy with temporal>nasal disc pallor and marked nerve fibre layer thinning on optical coherence tomography. DM was identified in 5 of 6 patients (average age of onset 9 ± 4 years), 2 had SNHL, 2 had reduced fertility and one had diabetes insipidus. The patient with a heterozygous variant found by Sanger sequencing, had optic atrophy, DM, congenital SNHL, DM and premature ovarian insufficiency. Her initial presentation was with optic atrophy with very high blood sugars were identified as part of subsequent systemic investigations. She also had cortical blue dot cataract and persistent bilateral microcystic macular edema despite optimised glycemic control. It is possible that she has a second large copy number variant not identified by Sanger sequencing.

Two further probands had an identical variant (p.Val606Gly) of uncertain significance predicted to be damaging by multiple in silico tools, and with an allele frequency of 3.54×10^{-5} on gnomAD. This was homozygous in one patient with isolated extensive posterior chorioretinal atrophy onset in her 5th decade and heterozygous in a patient with optic atrophy, SNHL and impaired glucose tolerance onset in his 6th decade.

Conclusions: The phenotypic spectrum related to WFS1 variants is highly variable with only one patient in this series representing the full Wolfram spectrum. For patients presenting with optic atrophy, DM investigations are warranted.

CONTROL ID: 3543230

SUBMITTER (NAME ONLY): Philipp Matten

TITLE: Determination of the protective properties of Ophthalmic Viscosurgical Devices through an automatic segmentation pipeline of the anterior segment in porcine eyes using OCT

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Matten, M. Wuest, R.A. Leitgeb, W. Drexler, CMPBME, Medizinische Universität Wien, Wien, Wien, AUSTRIA|M. Wuest, Hochschule Aalen, Aalen, Baden-Württemberg, GERMANY|O. Findl, Department of Ophthalmology, Hanusch-Krankenhaus, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: During cataract surgery the lens is destroyed with ultrasound and its fragments become projectiles that may cause irreversible damage to the corneal endothelium. To increase the stability of the surgical environment and to coat the endothelium with a protection layer, Ophthalmic Viscosurgical Devices (OVDs) are injected into the anterior chamber. We present a method to quantitatively evaluate the still poorly understood protective properties and distribution of OVDs.

Methods: For this work we imaged 100 porcine eyes. Each eye was imaged twice, resulting in 200 Optical Coherence Tomography (OCT) volume scans which stretched over $6 \times 6 \times 2.9 \text{ mm}^3$ (X x Y x Z) sampled at $512 \times 128 \times 1024$ pixels. All images were acquired with a ZEISS LUMERA® 700 with ZEISS RESCAN® 700. Simulated cataract surgery was performed using a BSS-milk-solution (100:1) to create a high-contrast layer beneath the OVD (fig.1 A-C). Through the first part of the here presented pipeline we manually segmented the cornea (epithelium and endothelium) and the OVD BSS-solution boundary layer of approx. 3000 b-Scans. In the second part of the pipeline, a UNet based convolutional neural network (CNN) was trained to automatically segment the cornea (fig.1 (i)), BSS-milky emulsion (fig.1 (ii)) and background (fig.1 (iii)).

Results: We measured for the first time the thickness of the OVD protection layer over a field of view of 6 by 6 mm. We accurately segmented a large data base of 200 OCT volumes and could quantitatively determine the protective properties of OVDs via thickness maps (fig.2 B). From these thickness maps we were able to derive the spatial distributions of every measurement (fig.2 B). We also found that there are notable differences between the layer thicknesses of the different kinds of OVDs.

Conclusions: We presented a method to evaluate for the first time the thickness and homogeneity of protection layers formed by OVDs over a wide field of view, using OCT. This method will in a next step be utilized to investigate the minimal required OVD layer thickness to effectively protect the corneal endothelium.

CONTROL ID: 3543235

SUBMITTER (NAME ONLY): Brian Dang

TITLE: Optically-triggered oxidative stress in mouse RPE as a model of geographic atrophy in AMD

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.Q. Dang, I. Mollhoff, E.V. Tieu, S. Chung, R.J. Zawadzki, G. Yiu, Department of Ophthalmology & Vision Science, University of California Davis, Davis, California, UNITED STATES|R. Meleppat, P. Zhang, R.J. Zawadzki, UC Davis Eyepod Department of Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Efforts to develop novel therapies for geographic atrophy (GA) in age-related macular degeneration (AMD) are limited by the paucity of preclinical animal models. Here, we developed a model of GA using viral transduction of retinal pigment epithelium (RPE) with fluorescent reactive oxygen species-generating proteins (RGPs) in mouse eyes to enable focal, titratable acceleration of oxidative stress in RPE mitochondria.

Methods: We performed subretinal injections of an AAV8 vector expressing KillerRed, mCherry, or control GFP under an RPE-specific Bestrophin (VMD2) promoter and a mitochondrial targeting sequence into the eyes of wild-type C57BL/6J mice. At 3 weeks after viral transduction, we focally exposed a $500 \times 500 \mu\text{m}^2$ square region of the retina to 300-700 μW of 561nm light over 20 minutes using a custom scanning-laser ophthalmoscopy (SLO) system to activate the fluorescent RGPs and induce RPE oxidative stress. Structural changes in the retina over 4 weeks were measured in vivo using optical coherence tomography (OCT) and ex vivo by immunostaining with antibodies to rhodopsin to assess rod outer-segments and cone arrestin to assess cone density on histological sections, and ZO-1 to assess the RPE mosaic on RPE flatmounts.

Results: AAV8-mediated expression of KillerRed in RPE resulted in global outer retinal and RPE disruption prior to light exposure, while expression of mCherry and GFP showed intact retinal architecture at baseline. Optical activation of AAV8-mCherry triggered a focal area of outer retinal and RPE atrophy resembling GA, with $12 \pm 4\%$ loss in outer nuclear layer (ONL) thickness, $32 \pm 9\%$ loss in photoreceptor outer segment (OS) length, and $15 \pm 7\%$ loss in RPE thickness, while focal activation of AAV8-GFP did not produce any detectable retinal damage. Immunohistochemistry revealed focal atrophy, with $29 \pm 4\%$ reduction in rod outer segments and $17 \pm 6\%$ reduction in cone density, and RPE disruption and loss within the area of light exposure.

Conclusions: Optogenetic activation of AAV8-mediated mCherry expression in RPE using SLO generates focal outer retinal and RPE atrophy in mouse eyes, and may serve as an inducible model of oxidative stress and GA. This model could be adapted to nonhuman primates for preclinical testing of novel therapies for atrophic AMD.

CONTROL ID: 3543236

SUBMITTER (NAME ONLY): Christina Kiel

TITLE: Allele-specific influence of seed polymorphism rs2168518 in hsa-miR-4513 on expression of neovascularization-associated genes

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Kiel, T. Strunz, F. Grassmann, B.H. Weber, Institute of Human Genetics, Universitat Regensburg, Regensburg, Bayern, GERMANY|D. Hasler, G. Meister, Regensburg Center for Biochemistry (RCB), Universitat Regensburg, Regensburg, Bayern, GERMANY|F. Grassmann, Institute of Medical Sciences, University of Aberdeen, Aberdeen, Aberdeen, UNITED KINGDOM|B.H. Weber, Insitute of Clinical Human Genetics, Universitätsklinikum Regensburg, Regensburg, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: MicroRNAs (miRNAs) are small post-transcriptional regulators offering promising molecules as biomarkers or targets for innovative approaches to treat complex diseases such as age-related macular degeneration (AMD). Hsa-miR-4513 appears an excellent candidate as it contains a seed polymorphism (rs2168518) which is specifically associated with the neovascular (NV) form of AMD. So far, little is known about the biological mechanisms underlying this association. We therefore aimed to identify allele-specific target genes of hsa-miR-4513 to clarify its contribution to NV.

Methods: We performed high-throughput RNA sequencing (RNA-Seq) in a miRNA overexpression model in human umbilical vein endothelial cells transfected with hsa-miR-4513, separated by the rs2168518 alleles. Promising allele-specific target genes were independently verified by quantitative reverse transcription PCR (qRT-PCR) and further validated via protein expression. Allele-specific miRNA binding was analyzed with a luciferase reporter assay. Further, publicly available databases were utilized to link target genes to phenotypes previously described to be associated with hsa-miR-4513.

Results: Overall, we identified 23 allele-specific target genes of hsa-miR-4513 by RNA-Seq and independently replicated 19 of these via qRT-PCR. Western Blot analysis and luciferase reporter assays conducted for five to six exemplary genes further confirmed the allele-specific regulation of these genes by hsa-miR-4513. Remarkably, multiple allele-specific target genes of hsa-miR-4513 are linked to various phenotypes while two genes, namely CDKN2A and TBC1D5, have been reported before to be related to eye phenotypes.

Conclusions: Our study revealed multiple promising allele-specific target genes of hsa-miR-4513, which offer the unique opportunity to elucidate the association of this miRNA with NV. Especially CDKN2A and TBC1D5 are highlighted as interesting allele-specific target genes and provide a basis for further follow-up studies.

CONTROL ID: 3543240

SUBMITTER (NAME ONLY): AMITHAVIKRAM HATHIBELAGAL

TITLE:

Effects of chromatic saturation on visual search performance in individuals with congenital colour vision deficiency

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.R. HATHIBELAGAL, Brien Holden Institute of Optometry and Vision Science, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

Commercial Relationships Disclosure (Abstract): AMITHAVIKRAM HATHIBELAGAL: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Individuals with congenital Colour Vision Deficiency (CVD) tend to have lower accuracy and longer reaction times in search-based colour tasks. This study investigated the effects of chromatic saturation on visual search performance in individuals with colour vision deficiency.

Methods: Seven individuals with CVD (3 protans and 4 deuterans; all males; average age: 30 ± 2 years) participated in this study. The colour vision defect was identified by HRR plates. Four images (depicting natural sceneries or flowers/fruits or birds/animals or everyday task) for each of the 15 colour combinations (red/green, red/white, red/grey, red/purple, red/orange, red/brown, red/black, green/grey, green/white, green/yellow, green/brown, green/blue, orange/yellow, brown/orange and black/brown) were manipulated into two categories namely 'low' (-75 %) and 'high' saturation (+75 %) using the GIMP software (Version 2). The altered image sets (low and high) along with 'original' set (unaltered) were presented on a colour-calibrated monitor using the Psychopy program (Version 2.7). The CIE 1931 (x, y) co-ordinates for each colour were obtained based on the tristimulus measured using an XRite Colorimeter. The participants viewed the screen binocularly from a test distance of 1m. The instructions for identifying the specific-coloured target in each presentation preceded the image by three seconds. The participants had to respond within 3 seconds following the image presentation by clicking on the target in the image. The display monitor was screen-recorded throughout the test which was later manually analyzed to derive the correctness of the response. The visual performance was computed as a product of accuracy percentage and reciprocal of the reaction time (s).

Results: Overall the improvement in visual performance (≥ 10 % than original) in 'high' saturation conditions was observed for green/blue, brown/black and red/green combinations. On the other hand, increasing saturation for combinations such as orange/brown and green/yellow deteriorated the visual performance (≥ 10 % poorer than original) in both the groups.

Conclusions: The improvement/worsening of visual search performance on increasing the saturation of the images depends on specific colour combinations. Therefore, specific recommendations for increase in colour saturation for improvement in visual performance can potentially be developed.

CONTROL ID: 3543248

SUBMITTER (NAME ONLY): Hadas Ketter-Katz

TITLE: Housing RCS rats under SPF conditions alters intestine microbiota and ameliorates retinal degeneration

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Ketter-Katz, R. Saeed, I. Sher, Y. Rotenstreich, Sheba Medical Center The Goldschleger Eye Institute, Tel Hashomer, Ramat Gan, ISRAEL|H. Ketter-Katz, R. Saeed, I. Sher, Y. Haberman, Y. Rotenstreich, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, Tel Aviv, ISRAEL|R. Hadar, G. Efroni, T. Braun, A. Amir, Y. Haberman, Sheba Medical Center, The Pediatric Gastroenterology Unit, Tel Hashomer, Ramat Gan, ISRAEL|

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ABSTRACT BODY:

Purpose: To investigate the association between gut microbiome composition and retinal degeneration rate in RCS rats raised in specific pathogen free (SPF) and non-SPF conditions.

Methods: RCS rats were born and raised in Sheba Medical Center animal facility under SPF (n=69) and non-SPF conditions (n=48). Fecal samples were individually collected every two weeks for microbiome analysis and the rats were examined for retinal structure by Spectral Domain Optical Coherence Tomography (SD-OCT), blue light autofluorescence fundus (BL-FAF) imaging and histopathology. Retinal function was assessed by Electroretinogram.

Results: Gut microbiome significantly differed between rats that were raised in non-SPF vs. SPF conditions. 90 different bacterial amplicon sequence variant (ASVs) were increased in non-SPF and other 34 bacterial ASVs were increased in SPF raised rats. Specific bacterial ASVs showed increased abundance with increasing rat age, and those were observed in earlier ages in rats raised in non-SPF conditions compared to rats raised in SPF conditions (p=0.002).

BL-FAF imaging revealed significantly smaller hypofluorescent lesions in rats raised in SPF conditions. This was more specifically noted at the age of 12 weeks, where the hypofluorescent lesion area was 6.8 fold higher non-SPF rats vs. rats raised in SPF conditions (p=0.003). Significantly shorter latencies were recorded for scotopic a- and b-waves and photopic b-waves in rats raised in SPF conditions as early as 4 weeks of age compared to rats raised in non-SPF conditions (p=0.02, p<0.001, p<0.001 respectively). At age of 8 weeks, the scotopic a-wave latency recorded in rats raised in non-SPF conditions was 1.7 fold longer (57.69 ± 11.57 ms) compared to rats raised in SPF conditions (33.11 ± 2.93 ms, p=0.04). SD-OCT total retinal thickness was higher in the superior part of the retina in rats raised in SPF conditions (294.83 ± 12.64 mm) compared with rats raised in non-SPF conditions (260.327 ± 10.76 mm, p=0.05).

Conclusions: Microbial diversity and age-related microbial dynamics were observed in non-SPF vs. SPF rats, in parallel to more rapid and severe retinal degeneration, and may present potential intervention strategy for slowing disease progression.

CONTROL ID: 3543259

SUBMITTER (NAME ONLY): Ya Xing Wang

TITLE: 10-year Incidence of Open-Angle Glaucoma in Highly Myopic Eyes as Compared with Non-highly Myopic Eyes in the Beijing Eye Study

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Wang, C. Wei, J. Xu, L. Xu, J. Jonas, Beijing Institute of Ophthalmology, Beijing Tongren Hospital, CHINA|J. Jonas, Medical Faculty Mannheim of the Ruprecht-Karls-University of Heidelberg, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the 10-year incidence of open-angle glaucoma (OAG) in highly myopic eyes as compared with non-highly myopic eyes in the population-based longitudinal Beijing Eye Study (BES).

Methods: Out of 4439 participants aged 40+ years who took part in the BES in 2001, 2695 participants (60.7%) were re-examined in 2011, while 397 (8.5%) individuals had died. The study population was into a highly myopic group (refractive error ≤ -6 diopters [D]), moderately myopic group (-3 to -6 D), low myopic group (-1 to -3 D), and emmetropic/hyperopic group (> -1 D). Incident glaucoma was defined as new development of glaucomatous optic neuropathy in 2011. A flicker method was used to compare aligned photographs of the optic nerve head and retinal nerve fiber layers, taken at baseline and after 10 years. The anterior angle was evaluated with anterior segment optical coherence tomography.

Results: Incident OAG was found in 74 participants among 2492 participants free of glaucoma at baseline, with the 10-year incidence of $3.0 \pm 0.3\%$ (95% confidence interval (CI): 2.4 to 3.7%). The incidence was highest in the high myopia group ($12.3 \pm 3.2\%$, odds ratio (OR): 6.5, 95% confidence interval of OR: 2.8, 15.1), followed by the moderately myopic group ($8.2 \pm 1.9\%$, OR: 4.1, 95% CI: 2.0, 8.7) and the low myopic group ($5.8 \pm 1.2\%$, OR: 2.8, 95% CI: 1.5, 5.3), as compared with the emmetropic group ($2.1 \pm 0.3\%$). OAG incidence was higher in participants with older age, higher intraocular pressure, thinner cornea, and with a larger cup-disc diameter ratio (all $P \leq 0.01$) in the emmetropic eyes. In the highly myopic group, OAG incidence was associated with male sex ($P=0.03$) and marginally associated with a thinner cornea ($P=0.06$), but not with age ($P=0.27$).

Conclusions: In a 10-year follow-up, high myopia was a major risk factor for the development of OAG with a 6.5-fold risk increase as compared with emmetropic eyes in an adult Chinese population recruited by a population-based manner.

CONTROL ID: 3543267

SUBMITTER (NAME ONLY): Juana Gallar

TITLE: Influence of tear volume on corneal surface temperature values measured by infrared thermography

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Gallar, C. Luna, S. Quirce, M. Acosta, Instituto de Neurociencias UMH-CSIC, Universidad Miguel Hernandez de Elche - Campus San Juan de Alicante, San Juan de Alicante, SPAIN|J. Gallar, Instituto de Investigacion Sanitaria y Biomedica de Alicante, San Juan de Alicante, SPAIN|

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ABSTRACT BODY:

Purpose: To analyze whether tear volume changes induced by ocular inflammation or instillation of warm saline solution affect corneal surface temperature (CST) values in guinea pigs.

Methods: Young guinea pig eyes of both sexes were used in the study. Tear volume was measured as the mm of wet phenol red threads applied on the lower lid for 30s. CST was measured from infrared video images taken with an infrared video camera. Temperature value immediately after eye opening and its change during the following 10 seconds were analyzed using dedicated software. In a group of guinea pigs previously sensitized to ovalbumin, experimental parameters were obtained at basal condition and after inducing allergic keratoconjunctivitis (AK) by ocular application of ovalbumin. In a separate group of naïve animals, measures were performed in basal conditions and after increasing the aqueous component of the tear film by topical application of different volumes (5-10 µl drops) of saline solution warmed up to 37°C avoid changing the temperature of the cornea (mean basal value: 36.5±0.1°C).

Results: During AK, all the animals presented conjunctival hyperemia, and significant increase in tear volume (+10.3±3.8 mm, n=6; p<0.05) and CST values (+0.25±0.12°C; p<0.01). When the aqueous component of the tear film was artificially increased in naïve guinea pigs by instillation of warm saline tear volume increased significantly (+14.8±1.9 mm and +21.0±2.1 mm, for of drops of 5 and 10 µl, respectively; p<0.001), and CST values decreased between 0.14°C and 0.96°C, proportionally to the drop volume (r=-0.405, Pearson correlation coefficient, p<0.05).

Conclusions: Corneal surface temperature increases during ocular allergic keratoconjunctivitis, probably due to the conjunctival and limbal hyperemia induced by inflammation. The corneal surface temperature values obtained by infrared thermography in this condition may be underestimated because surface temperature values seem to be affected by the amount of liquid over the cornea. The influence of tear volume on corneal surface temperature values should be considered when using infrared thermography as a complementary tool in ocular surface disorders diagnosis.

CONTROL ID: 3543270

SUBMITTER (NAME ONLY): Manuel Gonzalez de la Rosa

TITLE: Fully automated Deep Learning analysis of hemoglobin images of the optic nerve associated with perimetry for the study of glaucoma

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gonzalez de la Rosa, D. Gonzalez-Hernandez, D. Perez-Barbudo, Instrumentacion y Oftalmologia INSOFT SL, SPAIN|M. Gonzalez-Hernandez, Ophthalmology, Hospital Universitario de Canarias, La Laguna, Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: Colorimetric analysis of optic nerve images for assessing their hemoglobin distribution (Laguna ONhE) (1-4) is tested in combination with perimetry.

Methods: Deep learning training was used to identify nerve edges, laterality of the eye, image quality, vessel segmentation and classification (normal vs glaucoma). Data was compiled into a "Globin Distribution Function" (GDF), which was also associated with visual field irregularity indices: Pattern Standard Deviation (PSD), square root of loss variance (sLV), and threshold coefficient of variation (TCV) (5).

477 normal eyes and 333 confirmed and suspected glaucoma eyes, which were examined with three fundus cameras, two perimeters and two visual field strategies. The results were compared with Cirrus OCT.

Results: GDF sensitivity identifying glaucoma was 75.7% for a specificity of 99.0%. The most sensitive OCT index was the Rim Area (sensitivity 67.0%, $P=0.0131$). Its association with visual field irregularity produced the following AUC's: GDF&PSD-sLV = 0.963-0.986 and GDF&TCV = 0.965-0.987, while Rim Area&PSD = 0.927-0.960, Vertical Cup/Disc&PSD = 0.929-0.961 and RNFLT&PSD = 0.894-0.933 ($P<0.0001$ in all cases). For 99% specificity, GDF&TCV achieved 80.8% sensitivity and RNFLT&PSD 72.4%.

In cases where the morphological or functional indices had an unusual level in regard to 95% of normal subjects, the GDF&TCV achieved AUC's of 0.99-1.00 and sensitivities of 87.3-96.0% for 99% specificity.

Conclusions: Laguna ONhE associated to perimetry offers relevant diagnostic results in glaucoma, although new studies might be necessary to consolidate such results.

References:

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CONTROL ID: 3543273

SUBMITTER (NAME ONLY): Jinu Han

TITLE: Highly sensitive and specific in silico program to detect RP1 Alu insertion from short-read sequencing data

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate mobile element insertions (MEIs) in exon 4 of RP1 and develop a simple approach to detect RP1 MEIs by searching unprocessed short reads.

Methods: A total of 494 unrelated patients with inherited retinal diseases were genotyped. Proband-only whole-genome sequencing (WGS) or trio WGS was performed in 16 unsolved families after targeted or whole exome sequencing. WGS revealed an RP1 Alu insertion in exon 4 in 2 families. The Linux program grep was developed to search for common MEIs in RP1 exon 4. A 26-bp “probe” sequence containing the known junction sequence of the MEI and corresponding wild-type 26bp sequence was used (See https://github.com/jin0008/RP1_aluinsertion). Additional screening for this mutation was performed in 273 unrelated patients.

Results: Among the 273 patients, 5 families had a heterozygous RP1 Alu insertion. In patients with heterozygous RP1 Alu insertion, 3 patients with the compound heterozygous c.5797C>T:p.(Arg1933*) variant had macular dystrophy and 2 patients with more proximal truncating variants (c.4196del and c.4582_4584del) had early-onset cone-rod dystrophy. The AluY insertion resulted in c.4052_4053ins:p.(Tyr352Alafs*9), which was confirmed by polymerase chain reaction and gel electrophoresis. No homozygous RP1 Alu insertion was found in our cohort. A simplified grep search code revealed a variant allele frequency of 0.282 (interquartile range, 0.232–0.383), with no false-positive results in 120 control samples.

Conclusions: The MEI in RP1 exon 4 is common founder mutation in Korean, occurring in 1.8% of our cohort. The RP1 Alu grep program detected AluY insertion in RP1 efficiently without preprocessing of raw data or complex installation processes.

CONTROL ID: 3543276

SUBMITTER (NAME ONLY): Meha Kabra

TITLE: CRISPR base editing as a potential therapeutic approach for Kir7.1 channelopathy

SESSION TITLE: Gene therapy in ocular diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Leber Congenital Amaurosis 16 (LCA16) is a severe form of inherited ocular channelopathy caused by point mutations in KCNJ13, which affect the retinal pigment epithelial (RPE). AAV-gene therapy related immune responses, CRISPR/Cas9 gene editing associated off-targets, and unintended indels pose some challenges in clinical use of such treatments. We used Adenosine and Cytosine CRISPR base editors (ABE and CBE) for proof-of-concept correction of KCNJ13 point mutations (c.158G>A [p.W53X] and c.431T> C [p.L144P]) using nanoparticle-mediated delivery to induced pluripotent stem cell-derived RPE (iPSC-RPE).

Methods: Base editing was carried out using either ABE or CBE mRNA with a guide RNAs specific to the W53X or L144P mutant allele. A HEK293-FRT stable cell line expressing Kir7.1-L144P and Kir7.1- W53X were base edited via electroporation using CBE and ABE mRNA respectively. LCA16-W53X patient-specific fibroblasts and iPS-RPE cells were also targeted with ABE mRNA delivered using nanoparticles. Base editing efficiency, protein expression, localization, and channel function were assessed in edited cells and were compared with non-edited mutant and WT cells. Potential off-targets were screened to evaluate the accuracy and efficacy of CRISPR BEs.

Results: CBE mRNA for L144P correction in HEK cells resulted in 66% editing. The degenerate nature of codons for provides additional flexibility to correct L144P point mutation. Higher rate (~24%) were observed in treated L144P-cells due to multiple bystander cytosines at the targeted locus.

ABE mRNA for W53X (TaG>TgG) correction in HEK stable cells showed 50% editing efficiency than RNP approaches (25% efficiency). Nanoparticle-mediated delivery of ABE-mRNA and sgRNA in fibroblasts (47% editing) and iPSC-RPE (20% editing) established its use for in vivo BE delivery. Control fibroblast cells lacking the mutant allele showed about 1% indels. On target indel mutagenesis (<3%) and deep sequencing of potential off-target sites (<1%) indicated

high accuracy of the ABEs. Electrophysiology assays demonstrated robust rescue of channel function in the edited iPSC-RPE cells.

Conclusions: Our results show application of CRISPR base editing for precise correction of point mutations with reduced off-targets compared to CRISPR/Cas9-mediated gene editing. Restoration of channel function in edited iPSC-RPE cells suggests potential of CRISPR BE as a treatment for childhood blindness.

CONTROL ID: 3543277

SUBMITTER (NAME ONLY): Max Brinkmann

TITLE: Histology and clinical lifecycle of acquired vitelliform lesion, a pathway to atrophy in age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.P. Brinkmann, J. Messinger, D. Kar, K.R. Sloan, L. Chen, C.A. Curcio, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|M.P. Brinkmann, T. Hamann, M. Wiest, S.A. Zweifel, Department of Ophthalmology, University of Zurich, Universitat Zurich, Zurich, ZH, CH, academic, Zurich, Zurich, SWITZERLAND|T. Bacci, K. Freund, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|T. Bacci, K. Freund, LuEsther T. Mertz Retinal Research Center, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|L. Chen, State Key Laboratory of Ophthalmology, Sun Yat-Sen University, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Acquired vitelliform lesions (AVL) are a CAM5 optical coherence tomography (OCT) feature in age-related macular degeneration (AMD; PMID 33348085) and may be a distinct pathway leading to complete retinal pigment epithelium (RPE) and outer retinal atrophy (cRORA; PMID 29103793). This study aimed to correlate OCT to histology in eyes with AMD, evaluate AVL content, identify clinical and diagnostic biomarkers, and to generate hypotheses about the AVL lifecycle.

Methods: Donor eyes (n=2) underwent multimodal ex vivo imaging prior to histologic processing. Light microscopy was corresponded to OCT B-scans. Transmission electron microscopy was used for qualitative and quantitative analysis of AVL content via point-counting stereology. AMD eyes exhibiting AVL by OCT (and if available, color fundus photography and fundus autofluorescence) were selected retrospectively from two 3°clinics. In vivo OCT from 41 eyes followed up to 12 years was evaluated.

Results: Histology confirmed characteristic AMD deposits, photoreceptor (PR) degeneration, and AVL material located foveally between the PR and RPE. Light and transmission electron microscopy revealed an inhomogeneous AVL composition including RPE organelles (3–22 % of volume), outer segments (OS, 2–10 %), lipid droplets (0.2–12 %), and a flocculent material (57–59 %). Clinical cases showed high prevalence of subretinal drusenoid deposit (SDD), subfoveal predilection and AVL growth / regression phases. Most resorbing / collapsing AVL disappeared within 1 year after maximum AVL expansion (max. exp.). Hyperreflective foci and ellipsoid zone dis-integrity were rarely observed before AVL formation and frequently at max. exp. Hyperreflective thickening of the RPE-basal lamina-Bruch's membrane (RPE-BL-BrM) band was always observed at max. exp. and not before AVL formation.

Conclusions: AVL includes an extracellular deposit with varying amounts of RPE granules, some OS, and a major component remaining to be identified. Histologic composition and clinical appearance of AVL content and adjacent RPE-BL-BrM band indicate that RPE granules translocate from the RPE layer and are a transitory part of the AVL. Subfoveal predilection, autofluorescence, association with SDD, and growth / regression phases raise the possibility that AVL formation includes dysregulation of PR-specific molecular pathways, as suggested for SDD and drusen (PMID 23266879).

CONTROL ID: 3543283

SUBMITTER (NAME ONLY): Juan Tabernero

TITLE: Effects of peripheral refractive errors when negotiating steps

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the impact of different types of peripheral refractive errors (positive, negative and cylindrical) when subjects perform a functional test of ascending and descending steps.

Methods: A circular hole subtending 32-degree over the retina was practiced on the surface of four types of ophthalmic lenses: i) plano lenses (null dioptric power), ii) positive and negative lenses (± 2 D and ± 4 D) and iii) oblique cylindrical lenses ($+2$ D and $+3$ D) oriented at 45-degree. The lenses were mounted over standard frames with the hole aligned to the particular line of sight of six subjects, allowing intact vision across the 32-degree central field and inducing a variety of refractive errors in the rest of the peripheral visual field. The task for the subjects was to negotiate a floor obstacle consisting of two ascending steps (13 cm high each), an elevated platform (1 m long) and two descending steps (equal high as the ascending steps). Each subject performed four trials with each spectacle. A camera equipped with a fish-eye lens captured the movement (at 110 Hz) of the subjects' feet navigating the obstacle. Two LEDs were attached to subjects' shoes to mark the feet trajectories. Kinovea software was used to track the LED trajectories that were exported and analysed using Mathematica software.

Results: Average navigation times through the obstacle (with respect to the case of plano lenses) were a 15% (SD $\pm 13\%$) and a 5% (SD $\pm 10\%$) slower when subjects wore the $+4$ D and $+2$ D lenses respectively. Similarly, with the cylindrical lenses, navigation times were $18 \pm 19\%$ ($+3$ D) and $6 \pm 9\%$ ($+2$ D) slower than with plano lenses. However, with the -2 D negative lenses, navigation times did not increase with respect to plano lenses ($-1 \pm 9\%$) and they barely increased with the stronger -4 D negative lenses ($6 \pm 11\%$). Kinematic analysis of the trajectories showed a more cautious gait approach (more steps, slower gait) and more foot misplacements when wearing the positive and cylindrical lenses than with negative lenses.

Conclusions: Superimposed positive and cylindrical peripheral refractive errors had instantaneous effects on functional vision when negotiating steps. These data may be relevant when considering the potential effect in daily activities of increased peripheral refractive errors in cataract patients after implantation of standard intraocular lenses.

CONTROL ID: 3543286

SUBMITTER (NAME ONLY): Michel Giunta

TITLE: Treatment switch from aflibercept to ranibizumab pre-filled syringe in Canadian DME patients in a real-world setting: The PRECISE study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Giunta, A. Kalevar, Universite de Sherbrooke, Sherbrooke, Quebec, CANADA|P. Trottier, LASIK MD, Quebec, CANADA|L. Caron, Universite Laval, Quebec, Quebec, CANADA|S. Somani, University of Toronto, Ontario, CANADA|R. Tuli, University of Ottawa, Ottawa, Ontario, CANADA|R. Tuli, The Retina Centre of Ottawa, Ottawa, Ontario, CANADA|G. Cordahi, Universite de Montreal, Montreal, Quebec, CANADA|J. Gavalakis, E. Adiguzel, Novartis Pharma Canada Inc, Dorval, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: PRECISE is the first study to evaluate treatment outcomes in patients having neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME) with an inadequate response to aflibercept (AFL) who were switched to ranibizumab pre-filled syringe (RBZ-PFS) in a routine clinical setting. There are limited data from real-world on treatment switch in patients showing inadequate response to ongoing AFL and thus far, there is no report on treatment switch exclusively to RBZ-PFS. Here, data of currently enrolled patients with DME are presented.

Methods: PRECISE is an observational, multicenter, real-world switch study in prior AFL-treated Canadian patients with nAMD and DME. Eligible patients, aged ≥ 18 years, who received ≥ 3 AFL injections, were switched to RBZ-PFS based on clinician's discretion and treated as per the product label. Primary endpoint is the mean change in central retinal thickness from baseline to Day 90. Secondary endpoints include best-corrected visual acuity change, treatment regimen and safety. The study aims to enroll ~396 eyes (nAMD/DME=320/76) from 15 clinical centers across Canada.

Results: Amongst patients with DME, 8.6% and 91.4% had Type 1 and Type 2 diabetes, respectively, with 91.4% on medication. Median time since diagnosis to treatment switch to RBZ-PFS was 2.8 years in DME cohorts. Prior to study entry, median number of treatments with any anti-VEGF were 21/13 and AFL injections were 18/10 in the DME cohort. Key reasons for treatment switch in the DME patients were (i) lack of response to treatment (persistent fluid: 80.0%, loss of vision: 2.9%, unsatisfactory vision gains: 2.9%); (ii) unable to extend dosing (2.9%); (iii) safety concerns (ocular: 2.9%; systemic: 0%), and (iv) other (5.7%). Other baseline characteristics of switched patients and preliminary treatment outcomes will be presented.

Conclusions: Real-world evidence from the PRECISE study provides useful information that the key reason for treatment switch was lack of response to AFL treatment, primarily due to presence of fluid in the macula. Results from our study will further our current understanding and enhance routine clinical care of these patients.

CONTROL ID: 3543291

SUBMITTER (NAME ONLY): Anna-Kaisa Rimpelä

TITLE: Predicting intravitreal clearance of small-molecule drugs using Caco-2 permeability as a surrogate for ocular tissue permeability

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rimpelä, Y. Cui, A. Sauer, Drug Discovery Sciences, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: The discovery of small-molecule drugs for intravitreal administration would benefit of simple methods to evaluate vitreal clearance for the screening of new drug candidates. The current methods available have limitations in their applicability to small-molecule drugs and suitability to predict vitreal clearance in human. Permeability of posterior eye tissues is often described as the rate-limiting step for small-molecule clearance and a suitable permeability assay would ease clearance prediction. Therefore, we evaluated the use of Caco-2 cell intrinsic permeability as a surrogate for the permeability of posterior ocular tissues to predict vitreal clearance.

Methods: We measured Caco-2 permeability of a set of small-molecule drugs and predicted their vitreal clearance calculated from diffusion and permeability clearances for the rabbit eye. We used the geometric mean of the directional permeabilities as an estimate of intrinsic permeability to avoid the effect of transporters expressed in Caco-2 cells. We then compared the predicted clearances to rabbit vitreal clearances available in literature and in-house at Boehringer Ingelheim.

Results: Most of the predicted clearances were within a two-fold range of the measured values. For low permeability compounds ($<5 \times 10^{-6}$ cm/s), diffusion to the aqueous humor was predicted as the major route of elimination in the rabbit. For high permeability compounds ($>30 \times 10^{-6}$ cm/s), diffusion to the posterior segment was predicted to be the rate-limiting step, suggesting that diffusion rate determines the upper limit of vitreal clearance for any compound when not considering possible degradation within the vitreous.

Conclusions: Caco-2 intrinsic permeability is a suitable surrogate for posterior segment tissue permeability to predict vitreal clearance of small molecules in rabbits. For an accurate prediction, the effect of diffusion rates on the clearance should also be considered. The prediction can be applied to human by using human eye dimensions in the calculation.

CONTROL ID: 3543292

SUBMITTER (NAME ONLY): Milagros Mateos

TITLE: Long-term Topical Anti-glaucoma Therapy Impairs the Outcome of Non-Penetrating Deep Sclerectomy

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The failure of trabeculectomy has been related to the chronic ocular surface inflammation produced by the long-term use of topical anti-glaucoma medications. Our aim was to find out whether previous topical hypotensive therapy also influences the outcome of another type of glaucoma surgery, non-penetrating deep sclerectomy (NPDS).

Methods: This is a retrospective study of patients diagnosed of open-angle glaucoma who underwent NPDS at the Glaucoma Unit, Valladolid Clinic Hospital, Spain in the last 5 years. Eyes were divided into two groups based on intraocular pressure (IOP) values at 12 months after NPDS: success group (IOP<21 mmHg) and failure group (IOP>21 mmHg). All patients were under topical hypotensive therapy with up to 3 active substances in commercialized topical formulations, either separately or in combination. Normal distribution of variables was determined with Shapiro-Wilks test. The relationship between both groups was statistically analyzed in 5 variables by Mann-Whitney test: number of active substances used, drops per day, benzalkonium chloride (BAK)-containing drops per day, polyquad-containing drops per day, and duration of pharmacological treatment.

Results: We included 48 eyes from 34 patients (16 females, 18 males; mean age 72.5±13 years). Previous mean IOP was 22.2±6.4 mmHg. Patients had been using topical anti-glaucoma therapy for 5.4±6.8 years before surgery. NPDS surgical success rate was 87.5%, meaning that there were 42 patients in the success group and 6 in the failure group. Change in IOP 12 months after NPDS was -7.9±6.8 mmHg in the success group and +1.3±11.8 in the failure group, respectively. The number of drops per day was significantly ($p=0.037$) greater in the failure group (3.2 ± 0.4) than in the success group (2.5 ± 0.8). There were not significant differences between groups in the other 4 variables analyzed, although the number of BAK-containing drops per day and the duration of pharmacological treatment were higher in the failure group.

Conclusions: The negative impact of long-term hypotensive topical treatment in NPDS outcome seems to be related with the amount of eyedrops instilled per day. Consequently, medical treatment should be minimized as much as possible before opting for this surgical anti-glaucoma therapy.

CONTROL ID: 3543294

SUBMITTER (NAME ONLY): Agnieszka Zielinska

TITLE: The influence of stimulus defocus on two-photon visibility thresholds

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Zielinska, M. Szkulmowski, K. Komar, Institute of Physics, Faculty of Physics, Astronomy and Informatics, Nicolaus Copernicus University in Torun, Torun, POLAND|P. Ciacka, K. Komar, Institute of Physical Chemistry Polish Academy of Sciences, Warsaw, POLAND|

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ABSTRACT BODY:

Purpose: In the two-photon vision, a non-linear optical effect in the visual pigments, namely the two-photon absorption, causes the human eye to perceive pulsed infrared light as visible light with approximately halved wavelength. The phenomenon is characterized by highly localized stimulation of the retina with no glare, which can be a very useful feature in developing novel devices for ophthalmic diagnostics. In this work, we focus on longitudinal spatial properties of two-photon stimuli and study the influence of beam defocus on visibility thresholds upon two-photon excitation with infrared light (1040 nm) compared with visible light at 520 nm. The findings may be useful for the interpretation of two-photon perimetry results as well as for the design considerations of future two-photon ophthalmological devices.

Methods: We employed a custom-build, dual-wavelength (1040 nm and its second harmonic at 520 nm) microperimeter to measure visual thresholds (in two-photon and one-photon vision, respectively) by using the 4-2-1 staircase strategy. We tested 3 healthy dark-adapted volunteers with dilated pupils and accommodation blocked by administration of 1% Tropicamide drops. The stimuli were scanned circumferences of 1.0 deg diameter presented with varying degrees of defocus (-5 D to +5 D). The diameters of both beams at the pupil plane were equal to 1.1 mm. Experiments were conducted in scotopic and photopic (4.28 log phot Td) conditions obtained by Maxwellian view illumination of the retina with 520 nm light. The study was approved by the Ethics Committee of the Collegium Medicum, NCU.

Results: We observed no changes in the effect of defocus on normalized visibility threshold in the range (-1 D to +1 D) for both wavelengths. For larger values of beam's defocus (> 4 D and < -4 D), there are differences between 520 nm and 1040 nm beams (more pronounced increase in IR thresholds). The observed differences are statistically significant for scotopic case.

Conclusions: The results are consistent with the phenomena resulting from diffraction. For a given numerical aperture, the effect of two-photon excitation is similar to the one-photon case, as the properties of nonlinear excitation (quadratic dependence of the signal on intensity) are largely compensated by diffraction (i.e., twice longer Rayleigh range). The results highlight the leading role of optical, rather than neuronal or physiological factors in two-photon infrared vision.

CONTROL ID: 3543295

SUBMITTER (NAME ONLY): Shailja Tibrewal

TITLE: Evaluation of dry eye in pediatric vernal-keratoconjunctivitis (VKC) using clinical tests and non-invasive ocular surface analyser (OSA)

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Presence of dry eyes in children with VKC is often under recognised and clinical tests like tear-film break up time test using fluorescein dye (TBUT) and Schirmer's are difficult to perform. The aim of the study was to compare dry eye in children with VKC as compared to normal children using dry eye symptom score, clinical tests and OSA (SBM, sistemi).

Methods: This case control study was conducted between May 2019 to Nov 2019. Children with VKC were recruited as cases and those with only refractive errors as controls. The clinical parameters recorded in VKC children were type and extent of VKC, Bonini's grading and corneal fluorescein staining. Both cases and controls underwent TBUT, schirmer's II test and OSA. The OSA parameters recorded were non-invasive TBUT (NiBUT), meibomian gland (MG) loss, tear meniscus height and lipid layer type. The OSA and clinical parameters were compared between the cases and controls and were correlated with the modified ocular surface disease index (OSDI) symptom scores.

Results: 83 children with VKC (9 ± 1 years) and 30 controls (11 ± 1 years) were enrolled. Seasonal disease was seen in 63% and perennial form was seen in 37%. The proportion of limbal, palpebral and mixed type of VKC was 5%, 40% and 55%. The proportion of male patients was more in the VKC group (83% vs 27%, $p=0.0$). TBUT was found to be lower in VKC children (8.8 ± 4.5 secs) as compared to the controls (10.8 ± 5.5 secs); $p=0.04$. Dry eyes (TBUT <10 secs) was seen in 59% in VKC and 30% in control group ($p=0.015$). OSDI scores were significantly higher in the VKC group (32 ± 18 vs 15 ± 11 ; $p=0.0$). Among the OSA parameters only the pattern of lipid layer was found to be different among the two groups, the open meshwork being more common in the VKC group (70% vs 47%; $p=0.01$). The NiBUT was lower in the VKC group but did not achieve statistical significance (7 ± 3 secs vs 8 ± 2 secs, $p=0.05$). The corneal fluorescein staining positively correlated with limbal papillae ($r=0.334$, $p=0.00$) and negatively with TBUT ($r=-0.384$, $p=0$). None of the clinical or OSA parameters correlated with the OSDI scores except the lipid layer morphology.

Conclusions: Children with VKC had higher prevalence of dry eyes, lower TBUT and higher OSDI scores as compared to children without it. The tear film morphology seen in OSA could be an indicator of dry eyes in children.

CONTROL ID: 3543299

SUBMITTER (NAME ONLY): Carla Sanjurjo Soriano

TITLE: Functional validation of a CRISPR/Cas9 strategy correction of the two most prevalent USH2A mutations in iPSC-derived retinal organoids

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Sanjurjo Soriano, A. Roux, I. Meunier, V. Kalatzis, Institute of Neuroscience Montpellier (INM)-INSERM U1298-Université de Montpellier, FRANCE|

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ABSTRACT BODY:

Purpose: Mutations in USH2A are the most frequent cause of the syndromic IRD Usher syndrome type 2 (USH2), and the non-syndromic autosomal recessive retinitis pigmentosa (arRP). There are two recurrent USH2A mutations (c.2276G>T and c.2299delG), which account for approximately half the patient cohorts. Currently, there is no available treatment and disease models for these mutations are not available. We previously reported successful CRISPR/Cas9 correction of these two recurrent mutations in patient iPSC. Here, we differentiated isogenic corrected and non-corrected iPSC lines onto retinal organoids to functionally validate the strategy and to obtain a disease model of these two recurrent mutations.

Methods: Isogenic corrected and non-corrected iPSC lines together with a wild-type (WT) iPSC line were differentiated onto retinal organoids using a combinatory two-dimensional (2D) and 3D protocol. iPSC-derived retinal organoids were maintained as floating cultures until processing of the sample. Four different time points (56, 100, 150, 225 days) were analyzed by qPCR and immunofluorescence studies for the expression of common photoreceptor markers. Photoreceptor ultrastructure was also investigated using electron microscopy (EM).

Results: The generated iPSC-derived retinal organoids express common photoreceptor markers such as CRX, Recoverin, Rhodopsin, Rhodopsin-kinase, Opsins, Cone-arrestin. In addition, they express outer segments (OS) photoreceptor markers such as ABCA4, PDE6B and PRPH2. The photoreceptors within the retinal organoids present key features of photoreceptor maturation, such as a connecting cilium and OS, as observed by EM. Characterization of corrected and non-corrected retinal organoids show a clear reversion of the aberrant phenotype in the CRISPR-corrected organoids compared to the USH2A mutant organoids, functionally validating our CRISPR strategy.

Conclusions: The results presented here provide hope for a future therapy applicable to a large number of patients carrying USH2A mutations. The functional validation of the CRISPR strategy in retinal organoids, brings this therapy one step closer to clinical translation. In addition, insights into the differential pathophysiology of USH2 and arRP have been obtained.

CONTROL ID: 3543300

SUBMITTER (NAME ONLY): Hannah Dunbar

TITLE: MACUSTAR cross-sectional data: Repeatability and discriminatory power of visual function tests

SESSION TITLE: AMD: Clinical and translational research I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.M. Dunbar, A. Abdirahman, G.S. Rubin, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|H.M. Dunbar, G.S. Rubin, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|C. Behning, M. Schmid, Institute of Biomedical Statistics, Computer Science and Epidemiology, Bonn, GERMANY|D.J. Taylor, B.E. Higgins, G. Montesano, A. Binns, D. Crabb, City University of London, London, London, UNITED KINGDOM|J.H. Terheyden, Department of Ophthalmology, University Hospital Bonn, Bonn, GERMANY|N. Zakaria, S. Poor, Novartis Institute for Biomedical Research, Massachusetts, UNITED STATES|U.F. Luhmann, Roche Pharma Research and Early Development, F. Hoffmann-La Roche Ltd, Basel, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To examine the repeatability of a visual function (VF) test battery and its power to discriminate between structurally defined age-related macular degeneration (AMD) stages.

Methods: Subjects with no AMD and Beckman defined early(e), intermediate(i) and late(l) AMD were recruited across 18 European study sites. All subjects performed a VF battery at day 0 and 14 ± 7 comprising chart-based [Best-Corrected Visual Acuity (BCVA), Low Luminance Visual Acuity (LLVA), Moorfields Acuity Test (MAT), Pelli Robson Contrast Sensitivity (CS) and International Reading Speed Test (IReST); and novel tests [Mesopic (MesAT) and Scotopic (ScoAT) average thresholds by S-MAIA microperimetry and AdaptDx Rod Intercept Time (RIT)]. Repeatability of all measures was assessed by Intraclass Correlation Coefficients (ICC). Discriminant ability to distinguish between those with and without AMD and between neighbouring disease severity states was evaluated using Receiver Operator Characteristic (ROC) analyses, reporting Area Under the Curve (AUC) and partial (pAUC) at 80% specificity. Here we report the ability to distinguish between no AMD and iAMD.

Results: 301 subjects were recruited. 290 completed both visits [eAMD (n=28), iAMD (n = 167), lAMD (n=41) and no AMD (n=54)]. The cohort was roughly 2/3rd female (62.1%) with a mean age of 71. Repeatability was higher for chart-based than novel tests, with chart-based ICCs ranging from 0.88 (CS) to 0.96 (BCVA), whereas novel test ICCs ranged between 0.27 (RIT) and 0.93 (ScoAT) when all cases were considered and 0.73 (RIT) and 0.93 (ScoAT) when 3 extrapolated RIT values were removed. Discriminatory power of chart-based tests between no AMD and iAMD was moderate with AUCs of between 0.57 (IReST, pAUC = 0.04) and 0.77 (CS, pAUC = 0.08). Considering novel tests, discriminatory ability of microperimetry between no AMD and iAMD was moderate, and higher for scotopic testing (MesAT: AUC = 0.67; pAUC = 0.05; ScoAT: AUC = 0.70; pAUC = 0.06), whereas RIT values were slightly better, particularly when pAUCs were considered (RIT: AUC = 0.71; pAUC = 0.09).

Conclusions: Though CS, MesAT, ScoAT and RIT demonstrate moderate discriminatory power between no AMD and iAMD, a sizable proportion of iAMD subjects had normal VF. Given the substantial phenotypic variation in structurally defined iAMD, subgroup analyses are required to identify those with poorest VF and potential structural correlates.

CONTROL ID: 3543316

SUBMITTER (NAME ONLY): Nisamar Betancor Caro

TITLE: GLAUCOMA SCREENING IN 285,320 OPTIC DISC COLOR IMAGES USING LAGUNA ONhE HEMOGLOBIN DISTRIBUTION ANALYSIS

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess a mass screening in general population, mainly European, using the Laguna ONhE system to detect glaucoma.

Methods: 285,320 retinographies obtained in numerous locations with various fundus cameras were analyzed fully automatically and unsupervised via Internet, between January 2019 and December 2020. Deep Learning was used for identifying the eye (left or right), segmenting the disc and vessels, detecting image quality and generating a glaucoma classifier. A multi-factor index called Globin Distribution Factor (GDF) described in previous publications (1-9) was used. The amount of hemoglobin, the cup/disc ratios and the areas of the rim sectors were also estimated.

Results: 6.1% of cases were discarded because the system detected poor image quality, or absent or sectioned optic disc. 4.9% of the cases that could be analysed showed GDF below -15 (percentile 1% of the normal population) and 87.6% above 0 (percentile 5% of the normal population) (Figure). Cases with low GDF showed abnormal data in areas and indices associated with glaucoma (Table).

Conclusions: Although the data collection model did not allow individual diagnostic confirmation, GDF scores were consistent with the expected prevalence of glaucoma in the general population (10). Data and rates among such cases differ from normality as might be expected in glaucoma.

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CONTROL ID: 3543318

SUBMITTER (NAME ONLY): Chloe Thomas

TITLE: Delivering topical IL-33 with a cell penetrating peptide to treat neovascular age-related macular degeneration.

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the most common cause of central vision loss globally. Neovascular AMD (nAMD) is currently treated with regular intraocular injections of anti-VEGF therapies, to which some patients are unresponsive, while multiple injections are not well-tolerated and can cause complications including infection. We previously demonstrated intraocular delivery of recombinant interleukin-33 (IL-33) reduced laser-induced choroidal neovascularisation (CNV) pathology in a mouse model, offering a promising new treatment. Additionally, an eyedrop of bevacizumab complexed to a cell penetrating peptide (CPP) reduced lesion size equivalent to intravitreal injection delivery in a mouse CNV model. Thus, we propose combining IL-33 immunotherapy and our delivery agent, IL-33+CPP6, to be developed as a topical formulation.

Methods: Human recombinant IL-33 was complexed with the CPP to assess cell toxicity, MTT and LDH assays for 48h over a dose range of 0.2–200pg/ul in cultured human RPE (ARPE-19) and human ocular choroidal fibroblasts (HOCFs). HOCF scratch assay was performed and cells treated with media, vehicle, CPP, IL-33 (200pg/ul) or IL-33+CPP and imaged over 48h. The percentage wound closure (end vs start width) was measured using Cell IQ software. N=3, repeated on 3 independent occasions.

Results: IL-33+CPP complexes were non-toxic to ARPE-19 or HOCFs across a dose range (0.2–200pg/ul). In ARPE-19 cells and HOCFs, there were no differences after treatment in total viable cell number (total cell LDH; P=0.8306, P=0.9641, ANOVA) or significant changes in cellular viability (MTT assay; P=0.9772, P=0.2910, ANOVA). Importantly IL-33+CPP had equivalent significant biological effects to IL-33 alone, reducing wound healing (~15% less wound closure at 48h vs media/vehicle/CPP6). Across groups in scratch assay, there was a significant effect on percentage wound closure (P=0.0430, ANOVA), with borderline significance in post-hoc analysis (Tukey) between media and IL-33 (P=0.0529) and IL-33+CPP (P=0.0639) treatments.

Conclusions: IL-33+CPP is a promising treatment in a formulation of a drop for nAMD. IL-33+CPP demonstrates non-toxicity and has preserved biological effect as direct IL-33 administration. Further experiments will assess ocular penetration and in vivo efficacy of our topical administration.

CONTROL ID: 3543319

SUBMITTER (NAME ONLY): Haris Cheong

TITLE: Image Restoration Algorithms for OCT Images of the Optic Nerve Head: Performance comparison between OCT-GAN and Compensation

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To perform both qualitative and quantitative analysis of OCT-GAN and Compensation algorithms for shadow removal from Single-frame optical coherence tomography (OCT) B-scans.

Methods: 2,328 OCT B-scans (75x averaging) and 2,328 single-frame B-scans were acquired through the center of the optic nerve head (ONH) using Spectralis OCT (Heidelberg Engineering, Germany) for both eyes of 13 subjects. Extracted features from three perceptual loss networks pre-trained on Imagenet datasets were used with manual segmentations of retinal shadows (where 1 represented a shadow pixel and 0 represented a lack thereof) to train a generative adversarial network (referred to as OCT-GAN) to simultaneously remove retinal shadows and speckle noise. OCT-GAN and OCT compensation were then used on 97 single-frame OCT B-scans from one OCT volume and results were compared qualitatively (for shadow removal and speckle noise) and quantitatively using layerwise pixel intensities (LPI), an indicator for brightness of a specific retinal layer, and the intralayer contrast (ILC), a measure of shadow visibility ranging from 0 (shadow-free) to 1 (strong shadow). ILC was computed in the Retinal Pigment Epithelium (RPE) layer and LPI was computed for the Retinal Nerve Fiber Layer (RNFL), the Ganglion Cell Layer (GCL) + Inner Plexiform Layer (IPL), the Inner Nuclear Layer (INL), and the Outer Plexiform Layer (OPL).

Results: The mean ILC decreased from 0.40 ± 0.087 to 0.10 ± 0.074 ($74.3 \pm 19.2\%$) vs 0.21 ± 0.17 ($51.0 \pm 36.1\%$) for OCT-GAN and OCT compensation respectively, indicating shadow removal for both techniques. LPI increased by $4.34 \pm 3.66\%$, $4.58 \pm 4.36\%$, $8.29 \pm 6.91\%$, $0.4 \pm 3.80\%$ for OCT-GAN but decreased by $56.0 \pm 12.9\%$, $70.0 \pm 7.70\%$, $74.3 \pm 7.30\%$, $69.7 \pm 15.6\%$ for compensation for the RNFL, GCL+IPL, INL, and OPL layers, respectively. OCT-GAN images had visibly less speckle than compensated images and lacked artifacts commonly found in compensated images (inverted shadows, hyper-reflective spots, noise over-amplification at high depth). Both OCT-GAN and compensation were unable to completely remove large retinal shadows.

Conclusions: OCT-GAN had better shadow removal in the RPE layer and did not suffer from layer dimming commonly observed with compensation. Both algorithms could be considered as pre-processing steps to improve the diagnosis and prognosis of glaucoma from OCT images.

CONTROL ID: 3543321

SUBMITTER (NAME ONLY): Mario Romano

TITLE: Evaluation of retinal viability after simulation of vitreoretinal surgery in porcine eyes ex vivo

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate retinal viability in porcine eyes ex-vivo after simulation of vitreoretinal surgery by combined use of medical devices including BSS, vitreal staining, ILM staining, perfluorooctane and silicone oil endotamponade with minimal and with residues removal.

Methods: 25 porcine eyes were obtained from local slaughterhouse, disinfected with povidone iodide 5% and vitreoretinal surgery was simulated according to the following conditions: A) No surgery control: eye bulbs were kept for 30 min at room temperature (RT); B) Sham Surgery: vitreoretinal surgery with the sole use of BSS, 30 min at RT; C) Cytotoxic control: vitreoretinal surgery with BSS, injection of 1-H-perfluorooctane on retina, contact time 30 min at RT; D) Surgery with residues: vitreoretinal surgery with the use of BSS, vitreal staining, ILM staining, perfluorooctane and silicone oil endotamponade, leaving high residues of all materials; E) Surgery with removal of residues: vitreoretinal surgery with the use of BSS, vitreal staining, ILM staining, perfluorooctane and silicone oil endotamponade with careful removal of the residues. Each simulated condition was tested at least in quadruplicate by two technicians. Immediately after surgery, the retina was extracted from each eye bulb and at least 16 samples with 3 mm diameter were prepared. Retinal cells viability was determined after extraction, using TOX-1 In Vitro Toxicology Assay Kit, MTT based (Sigma-Aldrich, Italy). A viability < 70% is the cytotoxicity threshold.

Results: Retina extracted from eye globes subjected to no surgery (A) and sham surgery (B) showed optimal cell viability (96 to 100%). Retina extracted after the surgery with residues removal (E) showed good cell viability (average 86%), while retina from eye bulbs after surgery with high residues (D) and cytotoxic control (C) resulted in high retinal cytotoxicity corresponding to low average cell viability of 40% and 29%, respectively.

Conclusions: The tested conditions indicated that vitreoretinal surgery performed with the combined use of the medical devices (vitreal stain, ILM stain, perfluorooctane and silicone oil endotamponade) do not affect retinal viability if the residues of used medical devices are properly removed. The presence and accumulation of high residues derived from the medical devices used during vitreoretinal surgery could negatively impact retinal viability.

CONTROL ID: 3543322

SUBMITTER (NAME ONLY): Xinwen Yao

TITLE: Full Circumferential 3D Reconstruction of Schlemm's Canal in Living Human Using Megahertz Swept Source OCT

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Schlemm's canal (SC), a ring-shaped structure encircling the cornea, is responsible for intraocular pressure regulation and plays an important role in the onset and progression of glaucoma. This study explores the possibility of full circumferential three-dimensional (3D) reconstruction of SC in living human by using a megahertz (MHz) swept-source optical coherence tomography (OCT) prototype at 1060nm for motion-free SC imaging and a semi-automatic algorithm for SC segmentation from the OCT intensity images.

Methods: Eight volumetric scans were acquired around the limbus of both eyes of one healthy volunteer. Each scan was located at one of the cardinal and intercardinal positions to fully cover the SC. An external fixation target was introduced to ensure normal incidence at the corneal surface at each position. The fast scan was along the longitudinal direction of the SC at each of the cardinal positions, while kept in horizontal direction at the intercardinal position. Each volume took less than one second to complete. The OCT B-scans that contain SC were selected and processed for segmentation. A semi-automatic active contour segmentation algorithm was implemented and the segmented 3D SC mask from each volume was stitched. Quantitative metrics derived from the 3D segmentation were presented and analyzed.

Results: Figure 1 shows the rendering of the stitched SC segmentation for both eyes. The rapidly changing size as well as the branching of collector channels was faithfully depicted in the 3D reconstruction. Table 1 summarizes the quantitative metrics. The mean cross-sectional area (CSA) as well as the maximum opening of SC was highest in the superior position in the right eye, while temporal-superior in the left. The tendency of increased collector channels in the inferior quadrant compared to the superior was noticed as well.

Conclusions: We demonstrated full circumferential SC imaging using 1060 nm MHz SS-OCT in living human eyes without motion artifacts. The semi-automatic active contour segmentation algorithm was applied in the B-scans along the longitudinal direction of the SC, which yielded reliable 3D SC segmentation results. The full circumferential imaging and segmentation of SC enabled more sophisticated analysis of SC morphology, offering a new way for examination of the aqueous outflow pathway.

CONTROL ID: 3543324

SUBMITTER (NAME ONLY): Li Dong

TITLE: In Vivo Imaging of the Sclera in Guinea Pigs

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Dong, W. Wei, Beijing Tongren Hospital, Beijing, Beijing, CHINA|J. Jonas, Ruprecht-Karls-Universität Heidelberg Philosophische Fakultät, Heidelberg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To evaluate the feasibility of in vivo imaging of the sclera using spectral-domain optical coherence tomography (SD-OCT) in normal guinea pigs.

Methods: Nineteen pigmented guinea pigs with an age of 3-4 weeks were included in the study. Under general anesthesia, all animals underwent sonographic measurements of the axial length using an A/B scan and OCT imaging of the posterior ocular segment. At study end, the animals were sacrificed and the eyes of 10 animals were histopathologically examined. We measured the scleral thickness on the OCT images and upon histomorphometry. The reproducibility of the measurements was additionally assessed.

Results: On the OCT images, the sclera was presented as hyperreflective signals beneath the choroid. The scleral thickness measured near the optic nerve head (mean: $105.7 \pm 23.1 \mu\text{m}$) was not significantly correlated with axial length (Pearson correlation coefficient $r=0.02$, $P=0.40$). A high correlation was found for the comparison of intra-observer measurements of scleral thickness (intraclass correlation coefficient (ICC)=0.92, 95% CI: 0.86-0.96; $P<0.001$), and a high agreement was present for the inter-observer reproducibility ($r=0.99$; $P<0.001$). The Bland-Altman plots showed that 7.9% (3/38) of the points were located outside of the 95% limits of agreement. The scleral thickness as measured on the OCT images was significantly higher than that the values obtained by histomorphometry ($116.0 \pm 26.0 \mu\text{m}$ versus $77.6 \pm 13.4 \mu\text{m}$; $P=0.002$), with a low correlation coefficient ($r=0.07$).

Conclusions: Our study shows the feasibility of SD-OCT for in vivo imaging of sclera in guinea pigs with an acceptable intra-observer repeatability and inter-observer reproducibility. This technique provides support for examining the role of the sclera in ocular disorders in studies involving guinea pigs.

CONTROL ID: 3543325

SUBMITTER (NAME ONLY): samar Yahya

TITLE: A founder allele deleting CRX causes late-onset macular disease by haploinsufficiency

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To characterise the phenotype in eight cases with macular disease and determine the cause and molecular mechanism underpinning their condition.

Methods: Patients underwent ophthalmic examination and probands from each family were subject to exome or genome sequencing, and PCR amplification of the breakpoint followed by cloning and Sanger sequencing or direct Sanger sequencing. Microsatellites in or near the CRX locus were genotyped for haplotype analysis.

Results: All eight cases carry the same heterozygous 126 kb deletion encompassing TPRX1, CRX and SULT2A1. 294 base pairs of sequence at each end of the deletion is 78% identical, corresponding to Alu repeats, suggesting these have driven non-allelic homologous recombination (NAHR) to create this deletion. The deletion was absent from 382 controls screened by breakpoint PCR and 13,096 Clinical Genetics patients with a range of inherited conditions screened by array CGH. The Database of Genomic Variants highlights two potentially similar deletions in a study of 29,084 patients with developmental disorders, though precise breakpoints are unclear. Microsatellite genotypes suggest that the seven families studied herein are not closely related, but SNP genotypes immediately adjacent to the breakpoints point to a distant ancestral founder.

Conclusions: Previous reports found that heterozygous putative CRX null alleles were associated with a normal ocular phenotype, implying loss of function of one copy of CRX is tolerated. However, we now show that CRX whole-gene deletion causes a dominant macular disease with late onset, proving that CRX haploinsufficiency causes retinal dystrophy. Previous reports of haploinsufficiency in asymptomatic carriers could be the result of variable expressivity, non-penetrance in younger carriers, or a relatively mild phenotype that was overlooked. Since heterozygous deletions of this size may be difficult to detect, and given the previous published suggestion that heterozygous CRX null alleles do not cause retinal disease, this variant may have been overlooked in previous genetic screens.

CONTROL ID: 3543330

SUBMITTER (NAME ONLY): Karen Beets

TITLE: The Mouse Sodium Iodate Model Exhibits Acute Retinal Inflammation

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Beets, M. Porcu, T. Hu, J. Feyen, Oxurion NV, Leuven, BELGIUM|

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ABSTRACT BODY:

Purpose: Sodium iodate (NaIO_3)-induced retinal degeneration is a widely used model to investigate late stage dry age-related macular degeneration (AMD), a multifactorial disease characterized by retinal degeneration, retinal pigment epithelium (RPE) damage, oxidative stress and inflammation that ultimately leads to blindness and for which no therapy is currently available. The aim of this study was to characterize expression of inflammatory markers in the mouse NaIO_3 model.

Methods: Male C57BL/6J mice (7- to 8-week-old) were intraperitoneally injected with 50mg/kg NaIO_3 or phosphate buffered saline. One or three days later, protein lysates were prepared from retina and RPE/choroid tissues. The expression of ten different cytokines (IFN γ , IL1 β , IL2, IL4, IL5, IL6, CXCL1, IL10, IL12p70 and TNF α) were analyzed using the mouse proinflammatory panel 1 (Mesoscale).

Results: In the retina, NaIO_3 treatment significantly increased IL1 β , IL6, CXCL1 and TNF α levels at both day one and three. Interestingly, these protein levels decreased from day one to day three. In the RPE/choroid, NaIO_3 treatment significantly increased IL1 β and CXCL1 levels at day three. In contrast to the retina, IL1 β and CXCL1 levels increased from day one to day three. Other cytokine levels were unaffected or below the lower limit of detection.

Conclusions: In conclusion, NaIO_3 treatment results in acute increase of specific inflammatory proteins in the retina and RPE/choroid. The data suggests that, after the NaIO_3 insult, the inflammatory marker levels first peak in the retina, followed by the RPE/choroid. Overall, the mouse NaIO_3 model is an attractive tool to investigate AMD hallmarks, including inflammation.

CONTROL ID: 3543339

SUBMITTER (NAME ONLY): Lena Zobel

TITLE: Gene Therapy Successfully Restores Retinal Function and Delays Degeneration in a Mouse Model of CNGB1-linked Retinitis Pigmentosa

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zobel, S. Michalakis, Department of Ophthalmology, Ludwig-Maximilians-Universitat Munchen, Munchen, Bayern, GERMANY|L. Zobel, J.E. Wagner, M. Biel, S. Michalakis, Department of Pharmacy - Center for Integrated Protein Science Munich (CIPSM), Ludwig-Maximilians-Universitat Munchen, Munchen, Bayern, GERMANY|C.R. O'Riordan, A.M. Frederick, Gene Therapy, Sanofi SA, Framingham, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa type 45 (RP45) is an autosomal-recessively inherited blinding disease caused by mutations in the cyclic nucleotide gated channel subunit beta 1 (CNGB1) gene. The disease leads to progressive retinal degeneration affecting rod photoreceptors and subsequently cone photoreceptors. Gene augmentation therapy using recombinant adeno-associated virus (rAAV) vectors poses a tangible and potentially curative therapeutic option. In this study, we developed a novel gene augmentation therapy for rod-targeted delivery of human CNGB1 using an rAAV5 (rAAV5.hCNGB1) and evaluated its efficacy in the Cngb1 knockout (Cngb1^{-/-}) mouse model of RP45.

Methods: We designed a novel rAAV vector optimized for specific and efficient expression of full-length human CNGB1 in rods under the control of a short human rhodopsin promoter (hRHO194), and packaged it with AAV serotype 5. Increasing doses of rAAV5.hCNGB1 were delivered subretinally in 4-week-old Cngb1^{-/-} mice and the therapeutic effect was assessed short-, mid- and long-term. Transgene expression and retinal morphology were investigated via immunohistochemistry. Visual recovery was analyzed in vivo by electroretinography (ERG) while morphological preservation was monitored via spectral-domain optical coherence tomography (SD-OCT). Additionally, spatial navigation was tested by a visual Water Maze to evaluate the processing of visual information in treated mice.

Results: Treatment with rAAV5.hCNGB1 achieved substantial preservation of rod and cone photoreceptors in Cngb1^{-/-} mice. Furthermore, we show that the supplemented hCNGB1 was capable of forming functional heteromeric rod CNG channels with the endogenous mouse CNGA1 subunit leading to recovery of rod photoreceptor function. CNGB1 expression increased dose-dependently and resulted in increased ERG-b-wave amplitudes and therefore in enhanced visual acuity in Cngb1^{-/-} mice. Moreover, Cngb1^{-/-} mice were able to process the gained retinal function and showed significant improvement when navigating in the dark. This rescue effect persisted for at least 9 months post injection.

Conclusions: The novel rAAV5.CNGB1 vector supports efficient and specific human CNGB1 protein expression in affected murine rod photoreceptors resulting in recovered rod function and deceleration of retinal degeneration in the Cngb1^{-/-} mouse model of RP45.

CONTROL ID: 3543342

SUBMITTER (NAME ONLY): Vincent Garmo

TITLE: 5-year treatment patterns in patients with DME following intravitreal (IVT) anti-VEGF therapy

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Garmo, A. Menezes, Genentech Inc, South San Francisco, California, UNITED STATES|P. Emami-Naeini, UC Davis Eye Center, Sacramento, California, UNITED STATES|N. Boucher, R. Fernando, Vestrum Health, Ottawa, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: To describe the long-term impact of treatment (tx) regimens on vision outcomes in patients (pts) with diabetic macular edema (DME) who received IVT anti-vascular endothelial growth factor (VEGF) therapy from a large US electronic health record (EHR) database.

Methods: EHR data (Vestrum Health; 01-01-2014 to 06-30-2020) were analyzed. Tx naïve pts were followed for 5 yrs from first tx (i.e. index) with IVT anti-VEGF. Pts were stratified by baseline visual acuity (VA) and also evaluated for other DME-related tx, including IVT steroids, focal laser, and pan-retinal photocoagulation (PRP).

Results: 1657 eyes were stratified and analyzed by index VA. On average, pts received 6.8 anti-VEGF injections in yr 1, and ~4 injections per yr in following yrs. Overall, pts gained 4.0 Early Treatment Diabetic Retinopathy Study (ETDRS) letters from baseline to 5 yrs (65.6 vs 69.6 letters; ~ 20/40 Snellen), though pts lost roughly 3 letters from their peak of 72.5 letters at yr 1. 80% of pts with $\geq 20/40$ index VA were able to maintain VA of $\geq 20/40$ at 5 yrs, while only 58%, 31%, and 30% of pts with 20/40–20/100, 20/100–20/200 and $< 20/200$ index VA, respectively, were able to reach $\geq 20/40$ at 5 yrs (Fig 1). At the end of yr 1, pts who received 1–4 (28%), 5–6 (17%), 7–8 (20%), and ≥ 9 (35%) injections in the first yr gained 2.9, 7.6, 7.9, and 9.4 letters, respectively. Pts receiving 1–4 injections in yr 1 had the highest baseline VA (67.0 vs. 64.3 letters in ≥ 9 group), but had the lowest VA at yr 5 (68.1 vs. 70.7 letters in 9+ group) (Fig 2). More injections correlated with improved VA ($P < 0.001$). In subsequent yrs, VA was mostly lost or unchanged (–1.2, –0.9, 1.1, and –0.8 letters at yr 3; –1.7, –0.5, –0.4, and 0.2 at yr 5). 33% of pts received laser tx (focal or PRP) in yr 1, dropping to 16%, 11%, 7% and 5% in yrs 2, 3, 4 and 5, respectively.

Conclusions: Overall, pts with DME gained vision through 5 yrs, but were not able to maintain peak vision following yr 1 of tx. More injections were associated with improved VA gains at yr 1 and beyond, suggesting increased injections could result in lasting improved vision. Pts with $\geq 20/40$ index vision, and pts receiving more injections at baseline maintained better overall vision throughout the study, suggesting that early and frequent tx is likely to result in optimal long-term vision.

CONTROL ID: 3543346

SUBMITTER (NAME ONLY): POONAM NAIK

TITLE: Differential Transcriptome and modulated gene profile associated with Multi-Drug Resistant (MDR) *Pseudomonas aeruginosa* endophthalmitis in a mouse model

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. NAIK, S. Pandey, D. Rudraparsad, J. Joseph Ruben, Jhaveri Microbiology, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|P. NAIK, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|M. Naik, D. Mishra, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Increasing incidences of multidrug-resistant infections in endophthalmitis threaten our ability to treat and manage this condition. Host immunity is often-overlooked in the clearance of these infections. We aimed to study the differential host immune response observed during Multidrug-resistant- *Pseudomonas aeruginosa* (MDR-PA) endophthalmitis by studying their gene expression in a murine model.

Methods: Exogenous *P. aeruginosa* endophthalmitis was induced in C57BL/6 mice using clinical isolates of MDR-PA and drug-susceptible *Pseudomonas aeruginosa* (S-PA). Disease progression was monitored by slit-lamp examination and assigning clinical scores at 6hr and 24hr p.i., following which eyes were enucleated and bacterial burden was estimated. The extent of retinal damage was assessed by H&E and GFAP staining. PMN influx was determined by CD45 and Myeloperoxidase (MPO) staining. Microarray analysis was performed using SuperPrint G3 Mouse Gene Expression v2 chip, and data was analysed using Genespring GX 11.5 software.

Results: Intravitreal injection of MDR-PA and S-PA at 10,000 cfu, resulted in non-resolving ocular inflammation as evidenced by increased corneal haze, diminished vitreous clarity and red reflex. Higher bacterial load was observed in MDR-PA infected mice at 24h Vs S-PA infected eyes (5.6×10^5 CFU/eye vs 4.2×10^5 CFU/eye), correlating with increased clinical severity in MDR-PA infected eyes ($p=0.003$). Histological analysis revealed higher CD45-positive cells ($p=0.01$), GFAP positive cells ($p=0.05$), and MPO-positive cells ($p=0.02$) in the retinal layers of the MDR-PA infected mice. Temporal microarray analysis identified 5674 genes that were differentially upregulated in MDR-PA mice and included; IL-6, IL-15, IL-7, IL-1 β , NCF-1 and 2, Complement factor B and Pyruvate kinase while IL-9, PDGF- β , Anocatmin-6 and ATP-binding cassette were downregulated. Gene ontology and pathway analysis revealed the involvement of immune cells trafficking, apoptosis, tissue destruction markers, production of reactive oxygen species, and regulation of lipid metabolism.

Conclusions: Our study demonstrates, for the first time a differential host immune response by MDR-PA compared to S-PA in a mice model of endophthalmitis, and this can be used to identify anti-inflammatory targets for MDR-PA endophthalmitis.

CONTROL ID: 3543347

SUBMITTER (NAME ONLY): eleonora borda

TITLE: Three-dimensional concentric bipolar electrodes for high resolution optic nerve stimulation

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. borda, V. Gaillet, M. Airaghi Leccardi, D. Ghezzi, Medtronic Chair in Neuroengineering, Center for Neuroprosthetics and Institute of Bioengineering, Ecole Polytechnique Federale de Lausanne, Lausanne, VD, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa is a leading cause of blindness in industrialized countries, for which there is still no established prevention, treatment or cure. In the past decade, retinal prostheses emerged as promising technology to restore vision. On the other hand, optic nerve stimulation was proposed as an attractive alternative to retinal prostheses, by acting directly on the axons of the ganglion cells and avoid exclusion criteria of retinal implants. Our goal is to develop a novel self-opening intraneural electrode array (OpticSELINE) based on a 3D concentric bipolar configuration, where a local return electrode surrounds each stimulating electrode. This solution was chosen to achieve higher stimulation resolution by confining the electrical stimulation.

Methods: Intraneural electrode arrays were manufactured using wafer-scale processes. Sixteen concentric bipolar electrodes were fabricated with a 3D multilayer process in platinum / platinum black over a polyimide flexible substrate. Electrochemical characterization was performed before and after platinum black coating. In parallel, a hybrid FEM / NEURON simulation of the optic nerve was performed to evaluate the performance of the concentric bipolar electrode configuration. To performFor in-vivo experimentsvalidation, the OpticSELINE was implanted in the optic nerve of anesthetized rabbits, while the electrical activity of the contra-lateral visual cortex was recorded.

Results: The electrochemical study showed that platinum black reduces the impedance module below 10 kOhm and the charge storage capacity was nearly 5 times higher compared to bare platinum for actives sites of 0.0013 mm^2 . The hybrid simulation showed that the area of the optic nerve activated by a current pulse is greatly reduced using concentric bipolar electrodes compared to standard monopolar configuration. Preliminary in-vivo results show that the amplitude of electrical evoked-potentials is lower when stimulation is applied with the local return configuration with respect to the monopolar one.

Conclusions: This technology has the potential to allow stable and selective stimulation of the optic nerve during chronic implantations. The advancement will improve the use of the OpticSELINE as visual prosthesis for blind patients and as tool to further investigate the effect of the electrical stimulation in the visual system.

CONTROL ID: 3543351

SUBMITTER (NAME ONLY): Quan Hoang

TITLE: Ultrasonic Assessment of Gaze-Induced Deformation of Posterior Staphyloma in Highly Myopic Eyes by Means of a Semi-Automated Assessment of Local Radius of Curvature

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q.V. Hoang, D.G. Yu, Y. Dan, I. Loh, K. Tey, K. Ito, Singapore Eye Research Institute, Singapore National Eye Centre, Duke-NUS, SINGAPORE|Q.V. Hoang, R.H. Silverman, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|T.H. Lye, J. Mamou, F. L. Lizzi Center for Biomedical Engineering, Riverside Research, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ultrasound is a commonly available tool to assess the properties of the posterior eye, allowing us to characterize morphological changes and mechanical properties with kinetic exam. Here, we determine if the stress and strain of eye movements result in gaze-induced deformation of posterior staphyloma in highly myopic (HM) eyes.

Methods: A prospective imaging study was performed on 101 HM eyes (axial length range: 27.0 to 39.3 mm) of 52 patients with a clinical diagnosis of posterior staphyloma. 10 MHz B-scan ultrasound images oriented along the visual axis were acquired while subjects fixated in 5 directions (primary, nasal, temporal, down and up gaze). An algorithm was used to assess the local radius of curvature (K in mm^{-1}). Specifically, an intensity-based segmentation algorithm tracked the vitreoretinal boundary and calculated K using differential calculus applied to the traced boundary. Positive K implies anterior convexity, whereas negative K implies posterior convexity. Larger K value implies a greater spatial change. The standard deviation (std) of K represents the level of non-uniformity along the curve of the entire posterior wall. One static frame for each scan direction was chosen to calculate the average and std of K in each direction. The Kruskal-Wallis test with the Tukey-Kramer method (as post hoc multiple comparisons) was performed to assess statistical significance between groups.

Results: Overall, we found significant gaze-induced posterior eye shape changes among the different gazes when grouped together ($p < 0.001$). Specifically, among the vertical scans, the average K in upgaze was 0.019 mm^{-1} greater than in primary gaze ($p < 0.001$). Also, the average K in upgaze was 0.021 mm^{-1} greater than in downgaze ($p < 0.001$). Std of K in upgaze was 0.081 mm^{-1} greater than in primary gaze ($p < 0.001$). Also, std of K in upgaze was 0.058 mm^{-1} greater than in downgaze ($p < 0.001$). There were no significant gaze-induced posterior eye shape changes with horizontal eye movements (all $p > 0.05$).

Conclusions: Significant gaze-induced staphyloma deformation was confirmed by ultrasound B-scan-based assessment, which is consistent with studies suggesting the association of environmental factors, such as excessive nearwork, with myopia development and progression.

CONTROL ID: 3543352

SUBMITTER (NAME ONLY): Justyna Furso

TITLE: Complexation of A2E with a model protein increases photoreactivity of the bis-retinoid in selected model systems

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Furso, A. Zadlo, G. Szewczyk, T. Sarna, Department of Biophysics, Jagiellonian University Faculty of Biochemistry Biophysics and Biotechnology, Uniwersytet Jagiellonski w Krakowie Wydział Biochemii Biofizyki i Biotechnologii, Krakow, PL, academic/biosci, Krakow, POLAND|

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ABSTRACT BODY:

Purpose: It has been postulated that the age pigment lipofuscin mediates photochemical reactions, which can contribute to oxidative stress in the outer retina. Chronic oxidative stress may lead to the onset of age-related macular degeneration (AMD). Lipofuscin is a composite granule with several chromophores, including a pyridinium bis-retinoid A2E, which according to the common belief, is responsible for photoreactivity and phototoxicity of this age pigment. Even though in simple model systems the photochemical reactivity of A2E was shown to be moderate or even low, it exhibited significant phototoxicity in retinal pigment epithelium cells in vitro. This vitamin A-derivative accumulates with senescence in retinal tissues and by forming adducts with biomolecules, may induce potential phototoxicity. In this study, we examined if the complexation of A2E with a model protein affected photoreactivity of this bis-retinoid.

Methods: The formation of non-covalent complexes of A2E with bovine serum albumin (BSA) was determined by UV-Vis absorption and emission spectrophotometry. The photochemical reactivity of bis-retinoid A2E and its complex with BSA was analyzed by time-resolved singlet oxygen phosphorescence, electron paramagnetic resonance (EPR)-spin trapping, and EPR-oximetry, using an appropriated spin trap and spin probe, respectively, and oxidation of the fluorogenic coumarin boronic acid probe.

Results: The obtained data indicate that A2E after complexation with the model protein exhibited enhanced photoreactivity generating, upon irradiation with blue light, reactive oxygen species, particularly singlet oxygen. Aerobic photoexcitation of A2E-BSA complexes resulted in the formation of protein hydroperoxides suggesting that A2E was able to oxidize this model protein in vitro.

Conclusions: The ability of A2E to oxidize model protein upon excitation with blue light suggests that the pyridinium bis-retinoid may also oxidatively modify cellular proteins and change their key properties.

CONTROL ID: 3543354

SUBMITTER (NAME ONLY): Matt Trinh

TITLE: Location-specific patterns of inner retinal thinning in intermediate Age-related Macular Degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Trinh, M. Kalloniatis, L. Nivison-Smith, Centre for Eye Health Ltd, Kensington, New South Wales, AUSTRALIA|M. Trinh, M. Kalloniatis, L. Nivison-Smith, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To examine inner retinal thickness changes of intermediate age-related macular degeneration (iAMD) eyes using grid-wise cluster analysis for macular optical coherence tomography (OCT) volume scans.

Methods: OCT macular cube scans ($30^\circ \times 25^\circ$) were acquired for 91 eyes with iAMD from 91 participants, and 91 sex- and age-similar normal eyes from 91 participants. Thicknesses of the retinal nerve fibre layer (RNFL), ganglion cell layer (GCL), and inner plexiform layer (IPL) were defined at 60-64 locations across an 8×8 grid ($3^\circ \times 3^\circ$ per grid) centred on the fovea. Previously developed topographical clusters, i.e. locations of isometric normative thicknesses, were used to define location-specific comparisons between iAMD and normal eyes.

Results: Location-specific analysis of iAMD versus normal eyes demonstrated various patterns of thickness changes in each inner retinal layer. The RNFL displayed no significant differences across the macula; the GCL displayed thinning towards the fovea (mean difference \pm SEM: $-1.63 \pm 0.5\%$ to $-5.07 \pm 1.07\%$, $P < 0.01$ to < 0.0001) and borderline thickening towards the peripheral macula ($1.26 \pm 0.48\%$, $P < 0.01$); the IPL displayed diffuse thinning ($-2.23 \pm 0.53\%$ to $-4.1 \pm 0.74\%$, $P < 0.001$ to < 0.0001).

Conclusions: Location-specific thickness changes in the GCL and IPL support potential anterograde trans-synaptic degeneration in intermediate AMD, with sparing of the RNFL. These data may better guide clinical diagnosis and monitoring of intermediate AMD to include inner retinal measures.

CONTROL ID: 3543356

SUBMITTER (NAME ONLY): Takao Hirano

TITLE: Evaluation of the vitreoretinal interface in eyes with diabetic retinopathy using a 23 mm wide-field OCT

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Hirano, Y. Chiku, K. Hoshiyama, T. Murata, Shinshu Daigaku, Matsumoto, Nagano, JAPAN|

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ABSTRACT BODY:

Purpose: It is well known that there is a high prevalence of vitreoretinal interface abnormalities, such as epiretinal membrane and incomplete vitreoretinal separation, in patients with diabetic retinopathy (DR). Xephilio OCT-S1 (Canon) can capture a swept source OCT image up to 23 mm with a single acquisition and is expected to provide detailed evaluation of the vitreoretinal interface over a wide field. We aimed to evaluate the vitreoretinal interface with wide-field OCT in eyes with DR.

Methods: This cross-sectional study included 193 eyes of 112 patients (mean [SD] age, 63[12] years; 41 females, 71 males) with DR. All patients underwent 23 mm OCT imaging using OCT-S1 through the fovea, with the focus placed at -3.0 diopter to the vitreous cavity, to visualize the vitreoretinal interface in more detail. All eyes staged by diabetic retinopathy severity were classified into posterior vitreous detachment (PVD) stages and categorized by the presence or absence of vitreoretinal interface abnormalities.

Results: The cohort of eyes with no DR (16 eyes; mean age: 68[14] years) consisted included seven eyes with stage 2 PVD, nine eyes with stage 4 PVD, and no eyes with vitreoretinal interface abnormalities. The eyes with non-proliferative diabetic retinopathy (NPDR; 81eyes; mean age: 65[11] years) included eight eyes with stage 0 PVD, 11 eyes with stage 1 PVD, 13 eyes with stage 2 PVD, six eyes with stage 3 PVD, and 43 eyes with stage 4 PVD. Of these, 23% had vitreoretinal interface abnormalities. The eyes with PDR (96 eyes; mean age: 59[11] years) included eight eyes with stage 0 PVD, seven eyes with stage 1 PVD, 21 eyes with stage 2 PVD, 24 eyes with stage 3, and 36 eyes with stage 4 PVD, of which 43% had vitreoretinal interface abnormalities.

Conclusions: Although there was no significant difference in the composition of the PVD stage according to DR severity, the proportion of vitreoretinal interface abnormalities increased with severity.

CONTROL ID: 3543357

SUBMITTER (NAME ONLY): Paloma Rodríguez-Esteve

TITLE: NON INVASIVE EVALUATION OF THE AGING OF THE CRISTALINE LENS IN NORMALS AND DIABETICS

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gonzalez-Hernandez, A. Pareja-Rios, Ophthalmology, Hospital Universitario de Canarias, La Laguna, Canarias, SPAIN|M. Gonzalez de la Rosa, Instrumentacion y Oftalmologia INSOFT SL, Santa Cruz de Tenerife, Santa Cruz de Tenerife, SPAIN|P. Rodríguez-Esteve, A. Pareja-Rios, Escuela de Doctorado, Universidad de la Laguna Facultad de Ciencias, La Laguna, Islas Canarias, SPAIN|

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ABSTRACT BODY:

Purpose: The color of the optic nerve's central vessels, visible over the white myelin background, may serve as a reference to evaluate the increase in lens absorption to short wavelength radiation. It would allow observing premature lens aging in diabetic patients.

Methods: Fundus images were obtained from 354 normal and 307 diabetic eyes with a Topcon TRC-NW300 fundus camera (Topcon, Japan). Image quality, laterality of the eye, nerve position and nerve and vessel segmentation were automatically assessed by using the Deep Learning training for the Laguna ONhE program which is mainly used for glaucoma (1-4). A multiple regression equation was calculated based on the RGB components of the vessels so as to deduce the biological age of normal subjects. This equation was also used for the diabetic population.

Results: The biological age of normal subjects was estimated with a standard error (SE) of 5.93 years. Estimated age = $27.25 + (-0.366 \cdot R) + (1.556 \cdot G) + (-1.59 \cdot B)$ ($r = 0.911$, $p < 0.0001$). Much more aging was observed in diabetic patients $SE = 10.556$ ($r = 0.614$, $p < 0.0001$), as well as a greater dispersion (Figure).

Conclusions: Crystalline lens aging can be estimated by observing the changes in color of the retinal central vessels as they pass through the optic disc. These data confirm previous normal results obtained with the fundus camera DEC-200 (MiiS, Taiwan)(5). At the moment we have not been able to reproduce these results, with equal precision, in all the fundus cameras. We have the hypothesis that some more modern or more sophisticated fundus cameras may have an intense filtering of ultraviolet radiation.

CONTROL ID: 3543359

SUBMITTER (NAME ONLY): Bing Dai

TITLE: Velocity discrimination in infantile nystagmus syndrome (INS)

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Dai, K.M. Cham, L.A. Abel, Optometry & Vision Sciences, The University of Melbourne, Melbourne, Victoria, AUSTRALIA

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ABSTRACT BODY:

Purpose: Research on infantile nystagmus syndrome (INS) and velocity discrimination is limited, and no research has examined velocity discrimination in subjects with INS at their null position and away from it. This study aims to investigate how individuals with INS perform, compared with controls, when carrying out velocity discrimination tasks. Particularly, the study aims to assess how the null position affects their performance.

Methods: INS subjects (N=21) and controls (N=16) aged 12 and above were recruited. They were required to perform horizontal and vertical velocity discrimination tasks at two gaze positions. For INS subjects, testing was done at the null position and 15° away from the null. If there was no null, testing was done at primary gaze position (straight-ahead) and 15° away from primary. For controls, testing was done at primary gaze position (straight-ahead) and 20° away from primary. Horizontal and vertical velocity discrimination thresholds were determined by a Weber fraction ($\Delta V/V$). Two-way ANOVAs were used for statistical analysis.

Results: INS subjects showed significantly higher horizontal ($37.59 \pm 18.56\%$) and vertical ($28.12 \pm 12.40\%$) velocity discrimination thresholds compared with controls (horizontal: $19.85 \pm 10.06\%$, vertical: $19.75 \pm 9.39\%$) at both gaze positions ($P < 0.001$). Within the INS group, 12 INS subjects who had an identified null position showed significantly lower horizontal ($27.00 \pm 7.90\%$) and vertical ($23.08 \pm 8.58\%$) thresholds at the null than at 15° away from it (horizontal: $37.61 \pm 18.08\%$, vertical: $28.89 \pm 9.23\%$, $P < 0.05$).

Conclusions: Velocity discrimination was impaired in INS subjects, with better performance at the null. These findings could assist us in understanding of how INS actually affects the daily activities of patients, and aid us in developing new clinical visual function assessment for INS.

CONTROL ID: 3543362

SUBMITTER (NAME ONLY): Doreen Schmidl

TITLE: Shear-stress dependent viscous properties of hyaluronic-based lubricants

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Schmidl, G. Garhofer, L. Schmetterer, Department of Clinical Pharmacology, Medizinische Universität Wien, Wien, Wien, AUSTRIA|L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|

Commercial Relationships Disclosure (Abstract): Doreen Schmidl: Commercial Relationship(s);Thea Pharma:Code C (Consultant) | Gerhard Garhofer: Commercial Relationship(s);Thea Pharma:Code C (Consultant) | Leopold Schmetterer: Commercial Relationship(s);Thea Pharma:Code C (Consultant)

ABSTRACT BODY:

Purpose: The viscous properties of topical eye drops play an important role in the lubrication of the ocular surface. In the present study, we compared the shear-stress dependent viscous properties of high-molecular weight hyaluronic acid (HMWHA) versus low molecular-weight hyaluronic acid (LMWHA) combined with trehalose using a novel optical rheometer for accurate viscosity analysis of liquid samples. In addition, the viscosity of natural tears was studied.

Methods: The measurements of viscosity were done using the Fluidicam RHEO technology (FORMULACTION, Toulouse France), a fully automated rheometer combining microfluidic and imaging technologies. Measurements were done at a shear rate range between 3000 s^{-1} to $30\,000 \text{ s}^{-1}$ in order to mimic the shear stress during eye blinking on the ocular surface. A HMWHA lubricant product (0.18% HA) was compared to a product containing LMWHA (0.15% HA) combined with trehalose (Thealoz Duo, Thea Pharma, Clermont Ferrand, France). In addition, natural tears as obtained from healthy subjects were used as comparator.

Results: As expected for a non-Newtonian liquid, the natural tears showed almost no change in viscosity in response to changes in shear stress (natural tear viscosity was $0.91 \text{ mPa}\cdot\text{s}$ at 3000 s^{-1} , and $0.80 \text{ mPa}\cdot\text{s}$ at $30\,000 \text{ s}^{-1}$). The hyaluronic-acid based eye drops had a higher viscosity compared to natural tears ($p < 0.001$). The LMWHA product containing trehalose showed a viscosity of $2.26 \text{ mPa}\cdot\text{s}$ at 3000 s^{-1} that decreased to $1.77 \text{ mPa}\cdot\text{s}$ at $30\,000 \text{ s}^{-1}$. The HMWHA product had the highest viscosity ($p < 0.001$ versus LMWHA product containing trehalose) of $4.73 \text{ mPa}\cdot\text{s}$ at 3000 s^{-1} decreasing to $2.44 \text{ mPa}\cdot\text{s}$ at $30\,000 \text{ s}^{-1}$. The decrease of viscosity with increasing shear rate was more pronounced for the HMWHA product (-48%) than for the LMWHA product containing trehalose (-20%).

Conclusions: The present study confirms that neither natural tears nor the hyaluronic acid-based lubricants are Newtonian liquids. Combination of LMWHA with trehalose demonstrated a rheological behaviour closer to natural tears than the HMWHA product.

CONTROL ID: 3543363

SUBMITTER (NAME ONLY): Kilian Schmidt

TITLE: Effect of increased vascular endothelial growth factor on fluorescence lifetime of human retinal microvascular endothelial cells in vitro

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Schmidt, K. Kern, Y. Miura, Institute of Biomedical Optics, University of Lübeck, Lübeck, GERMANY|Y. Miura, Department of Ophthalmology, University of Lübeck, Lübeck, GERMANY|

Commercial Relationships Disclosure (Abstract): Kilian Schmidt: Commercial Relationship: Code N (No Commercial Relationship) | Katharina Kern: Commercial Relationship: Code N (No Commercial Relationship) | Yoko Miura: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Vascular endothelial growth factor (VEGF) is known to disrupt tight junction of vascular endothelial cells and induce their proliferation, leading to vascular leakage and neovascularization as seen in diabetic retinopathy. The aim of this study is to investigate the effect of VEGF on cell metabolism and the fluorescence lifetime of retinal microvascular endothelial cells using fluorescence lifetime imaging microscopy (FLIM).

Methods: An immortalized cell line of the human retinal microvascular endothelial cells (HRMEC) were treated either with 10 ng/ml VEGF₁₂₁, only with the vehicle (400 nM hydrogen chloride), or without any addition (control) for 48 hours. Cell metabolic activity and mitochondrial membrane potential were assessed using MTT and JC-10 assays. Mean fluorescence lifetime (t_m) was measured using two-photon microscopy combined with FLIM (excitation at 740 nm, detection with a single channel for 380 nm to 680 nm). t_m of cell nuclei and mitochondria were analyzed separately with SPCImage software.

Results: The MTT assay showed an increase in cellular metabolic activity, and the JC-10 assay detected a significant increase in mitochondrial membrane potential in cells treated with 10 ng/ml VEGF. In FLIM, t_m of the mitochondria was significantly longer than in the nuclei of the same cells under all three conditions. FLIM further revealed that the cells treated with 10 ng/ml VEGF showed longer t_m in mitochondria than control and vehicle-treated cells, where the difference was on the verge of statistical significance ($p = 0.08$). Comparing the ratios between t_m of mitochondria and cell nuclei, VEGF-treated cells showed a significantly higher ratio ($p < 0.05$).

Conclusions: The results of the MTT and the JC-10 assays suggested that VEGF may increase mitochondrial activity of HRMEC, and FLIM could indicate these changes in a label-free live cell imaging. Elongation of t_m in mitochondria of VEGF-treated cells may suggest the increase of protein-bound nicotinamide adenine dinucleotide (NADH), further indicating the increased function of mitochondrial respiration. VEGF-induced changes in FLIM on retinal cells may provide insight into the clinical application of fluorescence sensing in different chorioretinal pathological conditions, where VEGF plays a significant role.

CONTROL ID: 3543368

SUBMITTER (NAME ONLY): Shaun Leo

TITLE: The Heritability of Different Photopic Negative Response Components Explored in a Twin Study

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The photopic negative response (PhNR) is a late component of the light-adapted full-field electroretinogram (ERG) that reflects the function of retinal ganglion cells. In response to standard stimuli, a positive component, the i-wave, is superimposed on this response, creating a pre- and post-i-wave trough, termed PhNR1 and PhNR2. We explored relative contributions of genetic and environmental factors to variance in these PhNR components using a classic twin study.

Methods: As part of a larger study, 210 largely healthy adult twins from the TwinsUK cohort underwent full-field electroretinography incorporating standards set by the International Society for Clinical Electrophysiology of Vision (ISCEV). Responses were recorded using conductive fibre electrodes in the lower conjunctival fornix and averaged from both eyes. PhNR parameters were derived from the standard LA 3.0 response (amplitudes measured from baseline and peak times measured from the time of flash delivery). Coefficients for intra-pair correlation were calculated for monozygotic (MZ) and dizygotic (DZ) pairs (Pearson coefficients unless the parameter deviated from a normal distribution in which case Spearman coefficient was calculated).

Results: Full-field ERGs (including PhNRs) and zygosity data were available for 206 twins in total (59 MZ and 44 DZ pairs), 94% were female. The mean (SD) age for the cohort was 63 (11) years. Mean (SD) amplitudes were 11.1 (4.9) and 17.1 (5.7) microvolts for PhNR1 and PhNR2 respectively; mean (SD) peak times were 42.8 (2.5) and 63.3 (4.4) ms respectively. Correlation coefficients for MZ pairs were 0.74 and 0.61 for amplitudes, and 0.50 and 0.36 for peak times. Respective DZ coefficients were 0.38 and 0.39 for amplitudes, and 0.24 and 0.29 for peak times. The peak time distribution for PhNR2 deviated significantly from normal.

Conclusions: This is the first twin study to explore both PhNR components. Coefficients of intra-pair correlation were consistently higher for MZ than DZ twins for all parameters, indicating that genetic factors are likely to be important in shaping these responses. The differences between MZ and DZ correlations appeared more marked for the PhNR1 component, suggesting this may be relatively less affected by environmental factors.

CONTROL ID: 3543375

SUBMITTER (NAME ONLY): Conceição Lobo

TITLE: Characterization of risk phenotypes of type 2 diabetes nonproliferative retinopathy

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Phenotypes of diabetic retinopathy, particularly B and C, have been shown previously to be associated with risk of progression and development of sight-threatening complications (macular edema and proliferative retinopathy). In this work, we have further characterized these type 2 diabetes (T2D) retinopathy phenotypes, in terms of systemic and ocular features.

Methods: Patients with T2D and nonproliferative retinopathy (NPDR) were examined using 7-fields color fundus photography (CFP) and optical coherence tomography (OCT and OCTA). Phenotype classification was performed based on microaneurysm turnover (MAT, on CFP) and central retinal thickness (CRT, on OCT). Phenotype B was identified by low MAT (< 6) and increased CRT and Phenotype C by higher MAT (≥ 6) with or without increased CRT. ETDRS grading of seven fields CFP was performed. The following systemic factors were also evaluated: age, sex, diabetes duration, lipidic profile, inflammatory cytokines and hemoglobin A1c (HbA1c).

Results: 141 eyes with NPDR, one eye per patient, 81 with phenotype B and 60 with phenotype C were included in the analysis. The patients presenting phenotype C had higher HbA_{1c} levels ($p=0.048$) and patients with phenotype B had higher values of HDL cholesterol ($p=0.036$) and interleukin-8 ($p=0.027$). Phenotype C was characterized by lower macular vessel density ($p\leq 0.012$) and thinning of the ganglion cell layer (GCL; $p=0.006$). As expected by the initial phenotype characterization, phenotype C showed higher MAT ($p<0.001$) and phenotype B higher values of retinal thickness (CRT, $p<0.001$). Phenotype C was also identified in eyes with more severe ETDRS level (50%, ETDRS 43-47) than phenotype B (17% ETDRS 43-37).

Conclusions: Of the two phenotypes of NPDR in T2D associated with risk of developing sight-threatening complications, phenotype C is characterized by microvascular alterations represented by higher MAT and increased capillary closure on OCTA and by neurodegenerative changes, represented by GCL thinning, whereas phenotype B is characterized locally by increased CRT and systemically by increased levels of inflammatory markers.

CONTROL ID: 3543382

SUBMITTER (NAME ONLY): Shachi Saluja

TITLE: Intra-Vitreous Delivery of Interferon Gamma Using Porous Silicon for Treatment of Age-Related Macular Degeneration (AMD).

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Sub-retinal fibrosis remains a challenge to vision even after administering optimal treatments for AMD. Here, we propose porous silicon microparticles (pSiMPs) as reservoir of interferon gamma (IFN γ)-an antifibrotic cytokine, that allow slow release for >30 days minimising rapid clearance and low bioavailability in the eye. Using experimental models, we show that single injection of pSiMPs loaded with IFN γ (pSiMPs- IFN γ) into the vitreous may suffice to adequately treat AMD.

Methods: The pSiMPs were prepared from standard silicon wafer etching using electrochemical anodization in HF/ ethanol mixtures, followed by ultrasonic fracturing. Microparticles were size excluded and characterised using scanning electron microscopy (SEM).

The pSiMP surface was subjected to 1-allyl-2,3-isopropylidene glycerol hydrosilylation to add an active aldehyde moiety to enhance protein binding. WST cell proliferation assay was used to establish the biocompatibility of these pSiMPs.

Transforming growth factor-beta (TGF- β) was used to induce fibrosis in ARPE 19 cells. After 14 days of TGF- β exposure, the cells were treated with pSiMPs- IFN γ . Cell extracts were collected at 7-day interval up to four weeks and their collagen content (indicator of fibrosis) was evaluated using western blot and Sirius red-fast green (RG) staining. Further, we are evaluating our reservoir system in retinal mimics developed using human mesenchymal stem cells and CNV rat model to explore its preclinical potential.

Results: The average particle size characterized by SEM imaging was 20.5 \pm 7 μ m. FTIR-ATR confirmed the addition of aldehyde group to the pSiMPs. The WST assay confirmed that the cells were viable on incubation with pSiMPs up to 96 hours.

The collagen content increased on addition of TGF- β . On addition of pSiMPs- IFN γ , the collagen content decreased steadily over four weeks. Polarised microscopy imaging of RG staining of cells confirmed these results. Total collagen content evaluation reassured a similar pattern indicating that IFN γ is continually released from the pSiMPs.

Conclusions: Through this study, we have demonstrated that the pSiMPs can be used as a reservoir system for sustained intravitreal delivery of IFN γ to reduce fibrosis in AMD. This system can be extended to other eye conditions where posterior segment delivery of therapeutics is limited.

CONTROL ID: 3543383

SUBMITTER (NAME ONLY): Coen de Vente

TITLE: Making AI Transferable Across OCT Scanners from Different Vendors

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep neural networks (DNNs) for optical coherence tomography (OCT) classification have been proven to work well on images from scanners that were used during training. However, since the appearance of OCT scans can differ greatly between vendors, these DNNs often fail when they are applied to scans from different manufacturers. We propose a DNN architecture for age-related macular degeneration (AMD) grading that maintains performance on OCTs from vendors not included during training.

Methods: 2,598 and 680 Heidelberg Spectralis OCT scans from the European Genetic Database were used for development and testing, respectively. We tested transferability with 339 AMD-enriched Topcon OCTs from the Rotterdam Study.

AMD severity classification was determined manually in accordance with the Cologne Image Reading Center and Laboratory and Rotterdam Classification, respectively. Classifications were harmonized for the evaluation of the DNNs.

The proposed DNN considers each B-scan separately using a 2D ResNet-18, and internally combines the intermediate outputs related to each B-scan using a multiple instance learning approach. Even though the proposed DNN provides both B-scan level and OCT-volume level decisions, the architecture is trained end-to-end using only full volume gradings. This specific architecture makes our method robust to the variability of scanning protocols across vendors, as it is invariant to B-scan spacing.

We compare this approach to a baseline that classifies the full OCT scan directly using a 3D ResNet-18.

Results: The quadratic weighted kappa (QWK) for the baseline method dropped from 0.852 on the Heidelberg Spectralis dataset to 0.523 on the Topcon dataset. This QWK drop was smaller ($p = 0.001$) for our approach, which dropped from 0.849 to 0.717. The difference in area under the Receiver Operating Characteristic (AUC) drop was also smaller ($p < 0.001$) for our approach (0.969 to 0.906, -6.5%) than for the baseline method (0.971 to 0.806, -17.0%).

Conclusions: We present a DNN for AMD classification on OCT scans that transfers well to scans from vendors that were not used for development. This alleviates the need for retraining on data from these scanner types, which is an expensive process in terms of data acquisition, model development, and human annotation time. Furthermore, this increases the applicability of AI for OCT classification in broader scopes than the settings in which they were developed.

CONTROL ID: 3543384

SUBMITTER (NAME ONLY): Apoorv Chebolu

TITLE: The Transition from PRN to Treat and Extend: Do Patients See the Difference?

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chebolu, J. Walsh, Ophthalmology, Albany Medical Center, Albany, New York, UNITED STATES|J. Busingye, Ophthalmology, Albany VA Hospital, Albany, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate patients with choroidal neovascularization (CNV), retinal vein occlusion (RVO), or diabetic macular edema (DME) transitioned from a pro re nata (PRN) to a treat-and-extend (TAE) protocol.

Methods: Retrospective chart review of patients treated with intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections initially on a PRN protocol transitioned to a TAE protocol for at least 6 months of follow-up. Best corrected visual acuity (BCVA) and central foveal thickness (CFT) on optical coherence tomography were collected.

Results: Eighty-one eyes from 74 patients treated for 211.5 ± 43.7 and 43.5 ± 1.3 weeks on PRN and TAE protocols, respectively. Overall, BCVA improved from 0.61 ± 0.07 to 0.57 ± 0.06 logMAR following this transition ($p=0.22$). Eyes with a worse BCVA at initiation of the TAE protocol ($<20/70$; $n=32$) were noted to have a significant improvement from 1.17 ± 0.11 to 0.92 ± 0.10 logMAR ($p < 0.01$). Among different disease cohorts, the RVO eyes ($n=17$) experienced the greatest improvement in visual acuity 0.84 ± 0.16 to 0.67 ± 0.13 logMAR ($p=0.18$). A significant improvement in CFT was noted following the transition, 341.2 ± 13.6 to 261.0 ± 8.3 μm ($p < 0.001$). The number of anti-VEGF injections per year increased from 3.2 ± 0.3 to 9.5 ± 0.3 following the transition from the PRN to TAE protocol ($p < 0.001$). Six patients were lost to follow-up due to frustration with the TAE protocol and 2 patients elected to restart a PRN protocol after attempting the TAE protocol.

Conclusions: Transitioning from a PRN to a TAE protocol offers most patients significant anatomic benefits with less robust functional benefits. Interestingly, in a small sample size the RVO eyes experienced the most substantial BCVA improvement. An important consideration in this transition is the increased annual injection burden, which may be met with objection by certain patients who prefer the PRN protocol.

CONTROL ID: 3543385

SUBMITTER (NAME ONLY): Marion Schroeder

TITLE: M-CHARTS evaluation and comparison of two Aflibercept regimens for neovascular age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schroeder, M. Loevestam-Adrian, Lunds Universitet, Lund, SWEDEN|

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ABSTRACT BODY:

Purpose: To compare multiple functional and physiological outcomes with M-CHARTS values in patients treated with aflibercept for neovascular age-related macular degeneration (nAMD) in two arms, label vs treat-and-extend (TAE).

Methods: This prospective study randomized 41 eyes of 41 treatment-naïve patients with nAMD to two regimens. Arm 1 was treated with aflibercept according to label with three monthly injections, followed by bimonthly injections to the end of year one, thereafter the regimen changed to TAE. Arm 2 received the TAE regimen over the total study period of 18 months. Number of injections, best-corrected visual acuity (VA), near visual acuity (NVA), full-field and multifocal electroretinography (ffERG, mERG), optical coherence tomography (OCT) had been presented in a previous report. The present study evaluated M-CHARTS variables, including a questionnaire, horizontal metamorphopsia (MH), vertical metamorphopsia (MV), and vision-related quality of life (QoL) with the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25).

Results: In arm 1, 19 eyes presented with available baseline and follow-up data for M-CHARTS values, 18 eyes in arm 2. From baseline to the final follow-up, the MV score improved significantly in arm 1 from $.65 \pm .53$ to $.44 \pm .53$; $p=.029$, and in arm 2 from $.49 \pm .48$ to $.20 \pm .29$; $p=.007$. The MH score showed significant improvements in arm 1 from $.74 \pm .55$ to $.41 \pm .51$; $p=.028$, but no significant changes in arm 2 from $.64 \pm .63$ to $.33 \pm .48$; $p=.075$. The M-CHARTS questionnaire score showed decreased subjective perception of metamorphopsia in arm 1 from $1.79 \pm .85$ to $1.58 \pm .69$; $p=.331$; in arm 2 from $2.17 \pm .78$ to $1.56 \pm .784$; $p=.022$. During the 18 months, we found no significant correlation between changes of MV, MH or M-CHARTS questionnaire results and changes of VA, NVA, ffERG, mERG, and QoL composite score. When comparing the mean change of variables over time and between regimens, we only found a statistically significant difference between the two arms in two vision-related subgroups of the NEI-VFQ-25, general vision; $p=.001$, and near activities; $p=.012$.

Conclusions: MV emerged as statistically significant variable to follow-up and quantify metamorphopsia. As earlier described, M-CHARTS variables presented as independent parameters. The outcomes of the two aflibercept regimens showed no significant differences, besides two vision-related items of the NEI-VFQ-25.

CONTROL ID: 3543386

SUBMITTER (NAME ONLY): Ylenia Giarratano

TITLE: Long-term risk assessment of living kidney donors: a retinal study

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Living kidney donors are typically considered to have normal kidney function. Recently, concerns have been raised on the long-term risk of both cardiovascular and chronic kidney disease (CKD) following kidney donation. However, quantitative risk assessment tools are lacking. We propose a retinal imaging approach to gain insights into the timing of vascular changes in kidney donors.

Methods: We prospectively recruited three groups: 30 healthy subjects, 30 patients with stable CKD, and 30 kidney donors. Optical coherence tomography angiography images of one eye per participant were acquired. Image processing was performed using a U-Net neural network to segment the vasculature. The binarised image was converted into a vascular network object (graph) from which vessel characteristics were extracted. We obtained retinal measurements (e.g., nodes in the graph, size and shape of intercapillary space) from each region of interest in the retina, up to a total of 593 phenotypes. Multivariate models, corrected for age and gender, assessed statistically significant retinal characteristics that discriminated CKD from health.

Correlated vascular measures were removed and the remaining measures used to perform principal component analysis (PCA) to visualise patient distributions in a 2-dimensional (2D) space. Finally, clustering analysis was performed to investigate the separability between these two groups. Using the same PCA transformation, we projected kidney donors in our 2D space to observe their distribution in the healthy-CKD plane. Also, we investigated if donor PCA projection was associated with estimated glomerular filtration rate (eGFR), a routine clinical measure of kidney function.

Results: Our results show that PCA separates healthy subjects from those with CKD (accuracy=0.82). When we projected kidney donors into the same 2D space, they distributed across the two previous clusters, suggesting that some donors have similar retinal vascular characteristics to CKD whilst others resemble health. These differences were not associated with eGFR.

Conclusions: Our data suggest that retinal imaging may be used to discriminate those with normal kidney function from those with CKD. Whether these differences might link to patient outcomes remains unclear. Retinal imaging may identify living kidney donors at risk of future CKD and cardiovascular disease.

CONTROL ID: 3543397

SUBMITTER (NAME ONLY): Julia Mai

TITLE: SD-OCT based analysis of treatment effects on Geographic Atrophy secondary to AMD in the FILLY trial of Pegcetacoplan

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Mai, S. Riedl, G.S. Reiter, D. Lachinov, W. Vogl, H. Bogunovic, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To perform OCT-based analysis of RPE and photoreceptor atrophy progression in patients enrolled in the FILLY trial.

Methods: SD-OCT (Spectralis) images from the FILLY trial, a sham controlled phase 2 clinical study of geographic atrophy (GA) with intravitreal pegcetacoplan, an investigational therapy targeting complement C3, were analyzed. A-scan based manual annotation of the absence of the following bands was performed on baseline and year one SD-OCT volumes: retinal pigment epithelium (RPE), ellipsoid zone (EZ) and external limiting membrane (ELM). These manual annotations were also used to develop and validate an algorithm to automatically delineate GA areas. The growth rate of the resulting areas was calculated using the square root transformation. The difference in growth between treatment regimens (monthly injection (AM), injection every other month (AEOM), and sham (SM)) was calculated using the Kruskal-Wallis-test. Post-hoc pairwise testing was performed using Bonferroni correction for multiple testing.

Results: 145 OCT images were annotated from baseline and 115 from year 1. In total, 113 matched (38 AM, 36 AEOM, 39 SM) OCT volumes were included for analysis. Results are presented as mm change and interquartile range (IQR). Median growth of RPE-loss was 0,158 [0,057 – 0,296] in the AM group, 0,190 [0,106 – 0,336] in the AEOM group and 0,255 [0,188 – 0,359] in the SM group. The difference between AM and SM was statistically significant ($p = 0,014$).

Median growth of EZ-loss was 0,127 [0,041 – 0,247] in the AM group, 0,179 [0,101 – 0,293] in the AEOM group and 0,232 [0,130 – 0,349] in the SM group. Likewise to RPE-loss, the difference between AM and SM was statistically significant ($p = 0,017$).

There was no significant difference in ELM-loss growth between the treatment groups ($p = 0,114$).

Conclusions: Analysis of SD-OCT imaging provided consistent results in the measurement of GA lesion growth compared to FAF. In addition to significantly slower growth of RPE atrophy, SD-OCT data showed significant reduction in EZ impairment, indicative of slowed disease progression in patients treated with pegcetacoplan monthly. Therefore, a combination of SD-OCT imaging and advanced analysis may be the optimal methodology for measuring disease activity and potential therapeutic efficacy in GA.

CONTROL ID: 3543398

SUBMITTER (NAME ONLY): Ahmed Amayem

TITLE: A Non-Contact Corneal Aesthesiometer (NCCA) Validation Study in Normal Eyes

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Validation of a modified version of an NCCA (NCCAm) and comparison with the Cochet Bonnet Aesthesiometer (CBA) in subjects with normal corneas.

Methods: The NCCA device described by Murphy et al (1996, 1998) to measure corneal sensitivity was modified as follows: The air reservoir was placed outside the enclosure and the fan inside, and a 3-way solenoid valve was used to save space. An adapter for the Goldmann tonometer was designed to hold the nozzle to ease accessibility at a standard slit lamp. A 250 µm filter was added to the patient line as a precaution against dust and contaminants. A user-friendly calibration feature was implemented while a manual valve was added to the exhaust line to ensure equalization of pressure in the exhaust and patient lines. The device allows for fine pressure adjustments down to 0.02 mbars. The configuration chosen was a 0.5 mm nozzle diameter, 0.9 second puff duration and 1 cm distance to cornea.

The left eye central corneal sensitivity of 21 subjects (12 females) was tested using the NCCAm and the CBA gold standard was used for comparison. The NCCAm pressure started at 0.01 mbar (subthreshold) and increased in 0.02 mbar intervals until the participant felt the stimulus (ascending threshold). Then the pressure was decreased until the patient no longer felt a stimulus and the last felt pressure was recorded (descending threshold). The mean of the two measurements was their NCCAm result. This was repeated for 3 rounds at 5 minute intervals.

Results: All CBA measurements were normal (6.0 cm). The NCCAm ascending threshold was repeatedly higher (mean 0.06 mbars; $p < 0.001$) than the descending threshold, but this difference was stable (linear mixed-effect model: $F = 0.5$, $df = 2$, $p = 0.62$). Furthermore, an intra-class analysis (ICC) showed an excellent agreement between the three rounds ($\rho_{ICC} = 0.90$ [95% CI: 0.83-0.95]). NCCAm mean (\pm SD) threshold values of 0.177 ± 0.045 mbar ranging from 0.085 to 0.532 mbar were obtained. Consistent with Murphy 1996, the NCCAm allows corneal sensitivity measurement below the detection threshold of CBA.

Conclusions: The NCCAm is a compact user-friendly device enabling reliable corneal sensitivity measurements. It also allows the detection of inter-subject differences that are not detected with the traditional CBA.

CONTROL ID: 3543400

SUBMITTER (NAME ONLY): Hwee Tay

TITLE: Retina Specific Laminin 523 Drives Differentiation of Pluripotent Human Stem Cells to Photoreceptor Progenitors Promoting Retina Function

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Tay, V. Chrysostomou, S. Adusumalli, J. Guo, W. Tan, Z. Cai, L. Chong, E. Petretto, K. Tryggvason, Duke-NUS, Duke-NUS Medical School, Singapore, SG, academic/medsch, SINGAPORE|H. Andre, A. Kvanta, St. Erik Eye Hospital, SWEDEN|S. Tun, V.A. Barathi, G. Tan, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Advanced stages of macular degeneration are the main causes of blindness that involve irreversible photoreceptor loss. Visual cycle is dependent on the photosensitive photoreceptors and retinal pigmented epithelium (RPE). Provision of RPE alone is insufficient and existing methods to generate photoreceptors are not reproducible and inefficient. Therefore, our aim is to develop an alternative method that generates clinically safe and functional photoreceptors to treat vision loss. Our hypothesis is that transplantable competent photoreceptor progenitors are able to engraft and mature in vivo, thereby promoting visual response.

Methods: We have generated a previously unavailable human recombinant retina-specific laminin isoform LN523 that recapitulates the inter-photoreceptor matrix. Human pluripotent stem cells are efficiently differentiated towards photoreceptor progenitors after 32 days in a two steps method, with the support of this analogous retina matrix. This method is chemically defined and xenogen-free which does not involve re-plating and manual dissections. Day 32 photoreceptor progenitors co-expressing CRX and RCVRN were transplanted in the sub-retinal space of rabbit and rd10 mice model. Electroretinogram (ERG) was performed to test the functional visual response in the post-transplanted mice model.

Results: This method is highly reproducible based on the single cell transcriptomic and immunohistochemical analyses tested on four different human pluripotent stem cell lines. The differentiated photoreceptor progenitors were found to engraft and express mature photoreceptor markers in the retina in vivo where they also present promising evidence of synaptic connectivity with degenerated rabbit host retina. Additionally, the transplanted photoreceptor progenitors preserve the host photoreceptor outer nuclear layer and also exhibited statistically significant improved photoreceptor a-wave response based on ERG analysis in nine P30 rodent rd10 model.

Conclusions: We found an alternative photoreceptor differentiation platform using our novel retina specific laminins. This method potentially promotes retina function and may constitute an important step towards the future use of hESC-derived photoreceptors to treat vision loss.

CONTROL ID: 3543401

SUBMITTER (NAME ONLY): Junwoo Lee

TITLE: Long-term changes of fundus autofluorescence in chronic central serous chorioretinopathy

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, K. Kim, E. Kim, S. Yu, Kyunghee university medical center, KOREA (THE REPUBLIC OF)

Commercial Relationships Disclosure (Abstract): Junwoo Lee: Commercial Relationship: Code N (No Commercial Relationship) | Kiyoun Kim: Commercial Relationship: Code N (No Commercial Relationship) | Eung Suk Kim: Commercial Relationship: Code N (No Commercial Relationship) | Seung-Young Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate long-term clinical outcomes and fundus autofluorescence (FAF) changes in patients with chronic central serous chorioretinopathy (CSC) according to different FAF patterns.

Methods: This retrospective study included 22 eyes of 20 patients from 5 years follow-up diagnosed with central serous chorioretinopathy. Best corrected visual acuity, subfoveal choroidal thickness, fundus autofluorescence (FAF) patterns with spectral domain optical coherence tomography, the number of intravitreal anti-VEGF injection and the number of PDT were examined.

Results: Initial fundus autofluorescence patterns of 22 eyes were grouped as blocked (9, 40.91%), mottled (1, 4.55%), hyper (6, 27.27%), hyper/hypo (5, 22.73%), or descending tract (1, 4.55%). Average onset age was 49.77 ± 8.19 . After 5 years, FAF pattern progression showed total 12 eyes (54.55%), blocked (100.0%), mottled (0.0%), hyper (33.3%), hyper/hypo (20.0%), descending tract (0.0%). Mean fundus hypofluorescence change was $0.42 \pm 0.67 \text{ mm}^2$. Visual prognosis was associated with changes of hyper/hypofluorescence area in fundus autofluorescence image.

Conclusions: Progression of FAF was observed in eyes with more progressive patterns. Visual prognosis with chronic central serous chorioretinopathy more correlate with hyper/hypofluorescence change.

CONTROL ID: 3543403

SUBMITTER (NAME ONLY): Kim Kyung Woo

TITLE: Changes in Gene Expression Profiling and Phenotype in Aged Multidrug Resistance Protein 4-Deficient Mouse Retina

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kyung Woo, S. Kusuhara, A. Katsuyama-Yoshikawa, S. Nobuyoshi, M. Kitamura, S. Mori, N. Sotani, K. Ueda, W. Matsumiya, A. Miki, T. Kurimoto, H. Imai, M. Nakamura, Department of Surgery, Division of Ophthalmology, Kobe University Graduate School of Medicine, JAPAN|

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ABSTRACT BODY:

Purpose: Multidrug resistance protein 4 (MRP4) is an energy-dependent membrane transporter responsible for cellular efflux of a broad range of xenobiotics and physiological substrates. Here, we aimed to investigate the effects of ageing and MRP4 deficiency using gene expression microarray and morphological and electrophysiological analyses of the mouse retina.

Methods: Mrp4-knockout (null) mice and wild-type (WT) mice were reared in the same condition to 8-12 weeks (young) or 45-55 weeks (aged). RNA was extracted from 6 retinas for each mouse genotype (WT and Mrp4-null), and RNA microarray using Agilent SurePrint G3 Mouse Gene Expression Arrays 8x60K Ver. 2.0 and the following KEGG pathway analyses were performed. Then, retinal wholemount immunostaining, immunohistochemical and H&E staining of tissue sections were conducted to assess changes in retinal layers and retinal cell types among 4 age/genotype categories (young/aged WT mice and young/aged Mrp4-null mice). Finally, electroretinogram was recorded to detect the difference in retinal function between aged WT and aged Mrp4-null mice.

Results: Microarray analysis identified 186 differentially expressed genes from the retinas of aged Mrp4-null mice compared with aged WT mice, and subsequent gene ontology and KEGG pathway analyses showed that differently expressed genes were related to lens, eye development, vision, and transcellular barrier function which are involved in metabolic pathways or viral infection pathways. No significant change in thickness was observed for each retinal layer among 4 age/genotype categories. In addition, immunohistochemical analyses of retinal cell type did not exhibit an overt change in cellular morphology or distribution among 4 age/genotype categories, either. Electroretinogram responses showed no significant differences in the amplitude or the latency between aged WT mice and aged Mrp4-null mice.

Conclusions: Although it affects gene expression profile in the mouse retina, ageing would be an insufficient stress to cause some damage to the retina in the condition of MRP4 deficiency.

CONTROL ID: 3543405

SUBMITTER (NAME ONLY): Gregor Reiter

TITLE: Identification of initial events leading to outer retinal atrophy in age-related macular degeneration using deep learning quantifications

SESSION TITLE: AI in the retina: Clinical Applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G.S. Reiter, S. Riedl, A. Rivail, J. Mai, W. Vogl, C. Grechenig, H. Bogunovic, U. Schmidt-Erfurth, Christian Doppler Laboratory for Ophthalmic Image Analysis, Department of Ophthalmology and Optometry, Medical University of Vienna, AUSTRIA|Z. Wu, R.H. Guymer, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|Z. Wu, R.H. Guymer, Ophthalmology, Department of Surgery, The University of Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To investigate temporal changes of deep learning quantified imaging biomarkers in intermediate age-related macular degeneration (iAMD) in eyes developing initial outer retinal atrophy associated with incipient macular atrophy (iMA).

Methods: Eyes with iAMD from the sham treatment cohort of a prospective randomized clinical trial (LEAD study) were included. SD-OCT scans were acquired every 6 months for a follow up of 3 years. All eyes were re-graded for the development of iMA (choroidal hypertransmission (HT) > 125µm + evidence of RPE irregularities) on OCT in the absence of signs of exudation (IRF, SRF). Inner nuclear layer/outer plexiform layer (INL/OPL) subsidence (with at least subsidence of the INL-OPL and OPL-ONL junctions) was also annotated in all time-points for all iMA cases. Photoreceptor (PR) thickness, ONL thickness, drusen thickness (DT) and HT were measured using AI algorithms. Morphological changes before and after INL/OPL subsidence, as well as differences between areas of pathological and intact outer retina (subsidence/drusen/non-drusen area) were assessed using mixed effect models considering both eyes and multiple lesions per eye.

Results: Out of 280 eyes, 54 eyes developed iMA, of which 52 eyes presented with INL/OPL subsidence prior to iMA. Progressive PR thinning was present as the first sign of outer retinal changes with a mean thinning of -0.34 µm/month; 95% CI: -0.36,-0.33). ONL thinning was present after PR thinning (mean: -0.47 µm/months; 95% CI: -0.51,-0.44). DT decreased and HT appeared after the last visit before INL/OPL subsidence (Figure 1). A significant difference between INL/OPL subsidence area, drusen area and non-drusen area was identified for longitudinal PR thinning, ONL thinning, DT and HT (all p<0.001, except DT: p=0.047).

Conclusions: PR thinning on in-vivo OCT is an initiating sign of developing outer retinal atrophy in non-neovascular AMD. Subsequently, ONL thinning becomes apparent, DT declines and HT appears, leading to iMA in the vast majority of cases. Precise assessment of deep learning quantified retinal biomarkers using longitudinal in-vivo OCT volumes allows accurate identification and evaluation of early morphological alterations. These findings give new insight into the pathomechanism of atrophy development in AMD and provide novel possibilities in disease monitoring.

CONTROL ID: 3543409

SUBMITTER (NAME ONLY): Niccolo Dosto

TITLE: Electronically Monitored Steroid Eye Drop Adherence After Trabeculectomy Compared to Short-Term Surgical Success

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Dosto, T.V. Johnson, E. McGlumphy, H.A. Quigley, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure adherence with steroid eye drops after trabeculectomy with an electronic monitoring device compared to short-term achievement of target IOP.

Methods: Open angle glaucoma patients who underwent trabeculectomy were instructed on use of an electronic monitor attached to a topical steroid drop bottle that recorded drop use in real time through wireless technology. Patients were prescribed only 1% prednisolone acetate every 2 hours while awake for 1 week, then 4 times a day for 1 week tapered by 1 drop/week until week 6. Postop visits were at 1, 3 and 6 weeks, 3 and 6 months, and 1 year. Primary outcome was percent adherence compared to achievement of IOP target. Secondary outcomes were comparison of adherence to a questionnaire estimating adherence to daily glaucoma drops, grading of bleb morphology, reported pain, and anterior chamber inflammation grade.

Results: Data were available for 60 subjects at 6 weeks, 24 at 6 months and 10 at 1 year postop. Devices recorded drop use in 82 of 85 subjects. Total adherence was $90 \pm 14\%$ with q2h frequency at $79 \pm 18\%$. Total adherence did not significantly differ by age, race or sex, nor was it related to inflammation or pain for 6 weeks. 82% achieved target IOP at 6 weeks (49/57, 3 incomplete). Adherence was $78 \pm 18\%$ for eyes \leq target IOP at 6 weeks and $86 \pm 16\%$ for those $>$ target ($p=0.27$). 15/49 subjects \leq target and 7/8 $>$ target at 6 weeks were women ($p=0.0043$). Eyes with 6-week IOP < 6 mm Hg had lower adherence than those ≥ 6 mmHg (ratio taken/ideal drop adherence: 84% vs 0.92%, $p=0.07$). Predicted adherence from a daily glaucoma drop questionnaire did not correlate with steroid drop adherence. At 6 months, 16/24 reached IOP target, while 10/10 eyes were below target at 1 year. Those achieving target IOP without further glaucoma surgery were not more adherent than those who were over target (74% vs. 80%, $p=0.50$).

Conclusions: Detailed eye drop adherence data can be obtained electronically in real time, showing substantial adherence with postop steroid drops after glaucoma surgery. With the protocol of steroid drops used here, the observed adherence was not related to success of IOP control at 6 weeks or 6 months after surgery. Low postop IOP at 6 weeks was potentially related to poorer adherence.

CONTROL ID: 3543410

SUBMITTER (NAME ONLY): Joëlle Vergroesen

TITLE: From gut to glaucoma: translating the microbiome to the eye

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.C. Klaver, Ophthalmology/Epidemiology, Erasmus MC, Rotterdam, NETHERLANDS| J. Vergroesen, W.D. Ramdas, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Vergroesen, Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Institute of Molecular and Clinical Ophthalmology, Basel, SWITZERLAND|R. Kraaij, Internal Medicine, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C. van Duijn, University of Oxford Nuffield Department of Population Health, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Several studies provided compelling evidence that the immune system is involved in the pathogenesis of open-angle glaucoma (OAG). Reactive oxygen species and cytokines produced by the gut microbiome may play a role in this process, traveling from the gut mucosa to the eye. Therefore it is of interest to find changes in the microbiome of patients with OAG.

Methods: Population-based cohort study. All participants underwent extensive ophthalmic examinations, including intra-ocular pressure (IOP), retinal nerve fiber layer (RNFL), and vertical cup-to-disc ratio (VCDR) measurements, and provided a stool sample. A 16S rRNA gene profile dataset was generated and PICRUST tool was used to obtain predicted bacterial functions. Beta-diversity was calculated and compared using Bray-Curtis dissimilarity matrices. The relationship between alpha-diversity and OAG and OAG-associated parameters was assessed by logistic and linear regression analyses, respectively, adjusted for age, sex, body-mass index, and medication use. The same analyses were performed to assess these relationships at taxa level.

Results: When comparing OAG cases with controls, no differences in alpha- and beta diversity were observed. On taxa level, a higher abundance of the family Rikenellaceae, more specifically the genus Alistipes (OR [95% CI]=1.69 [1.17-2.54]), was associated with higher OAG risk (OR [95% CI]=1.60 [1.11-2.38]). The family Clostridiaceae1 was associated with a lower IOP (estimate=-0.121; p-value=0.001) and smaller VCDR (estimate=-0.024; p-value=0.002). At genus level, Clostridiumsensustricto1 showed the same effects (estimate=-0.120; p-value=0.002 and estimate=-0.023; p-value=0.003, respectively). Predicted functional metagenome analysis showed an association between the lysosome and OAG (OR [95% CI]=2.50 [1.18-4.68]) and RNFL (estimate=-5.273; p-value=0.007).

Conclusions: This study showed associations between the gut microbiome and OAG, as well as with OAG-associated parameters. Predicted functional metagenome analysis revealed the lysosome as potentially interesting for the development of glaucoma. Although replication studies are necessary, our findings display a new pathway in the pathogenesis of glaucoma.

CONTROL ID: 3543415

SUBMITTER (NAME ONLY): Husvinee Sundaramurthi

TITLE: Evaluation of Anti-Cancer Properties of Selective Histone Deacetylase 6 Inhibitors in Uveal Melanoma

SESSION TITLE: Advances in Diagnosis and Treatment of Uveal Melanoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Sundaramurthi, B.N. Kennedy, Conway Institute, University College Dublin, Dublin, IRELAND|H. Sundaramurthi, B.N. Kennedy, School of Biomolecular and Biomedical Science, University College Dublin, Dublin, IRELAND|S.G. Mulero, Unit of Biomarkers and Susceptibility, Oncology Data Analytics Program (ODAP), Catalan Institute of Oncology (ICO), Oncobell Program, Catalan Institute of Oncology (ICO), Oncobell Program, Bellvitge Biomedical Research Institute (IDIBELL) and CIBERESP, L'Hospitalet de Llobregat, Barcelona, SPAIN|S.G. Mulero, Department of Clinical Sciences, Universitat de Barcelona Facultat de Medicina i Ciències de la Salut, Barcelona, Catalunya, SPAIN|M. Buckley, Ireland Ocular Melanoma Group, Dublin, IRELAND|J.M. Piulats, Medical Oncology Department, Catalan Institute of Cancer (ICO), IDIBELL-OncoBell, Hospitalet de Llobregat, Barcelona, SPAIN|J.M. Piulats, Clinical Research in Solid Tumors Group (CREST), Bellvitge Biomedical Research Institute IDIBELL-OncoBell, CIBERONC, Hospitalet de Llobregat, Barcelona, SPAIN|

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ABSTRACT BODY:

Purpose: Approximately 50% of patients diagnosed with uveal melanoma (UM) develop metastatic disease, with a median overall survival of 4 to 15 months. Current treatment options display limited benefit, hence, the need to identify novel drugs to treat primary and metastatic UM. Histone deacetylase 6 inhibitors (HDAC6i) show promise as anti-cancer agents and are under clinical trial investigation for several cancers. The goal of this study is to: 1) uncover the ability of select HDAC6i to prevent primary and metastatic UM cell growth in vitro and 2) to understand how HDAC6i prevent UM cancer hallmarks.

Methods: Correlation between HDAC6 expression and patient survival was determined in UM patient samples from The Cancer Genome Atlas (TCGA) database (n = 80). Survival of UM cells derived from primary (Mel285 and Mel270) and metastatic (OMM2.5) tumours was evaluated following selective inhibition of HDAC6, using clonogenic cell survival assays. Cells were treated with 10, 20 or 50 µM of three selective HDAC6i (Tubastatin A, ACY-1215 and Tubacin; N = 3) for 96 hours and cultured for an additional 10 days. Apoptotic populations were detected in ACY-1215 treated OMM2.5 cells (24 or 96 hours) by YOPRO-1/propidium iodide staining using flow cytometry. To uncover the mechanism of action of HDAC6i, mass spectrometry analysis was performed on whole proteome of OMM2.5 cells treated with 20 µM ACY-1215 for 24 hours (N = 4).

Results: HDAC6 expression in UM patient samples from TCGA database revealed that low levels of HDAC6 expression correlated to a statistically significant reduction in overall survival (p = 0.0033) and progression free survival (p = 0.024) probabilities. A dose dependent reduction in cell survival was observed across all three UM cell lines treated with HDAC6i. OMM2.5 cells treated with 50 µM ACY-1215 for 96 hours resulted in extensive apoptosis with <2% of cell populations surviving compared to vehicle controls (>90% survival). Whole proteome profiling of ACY-1215 treated OMM2.5 cells identified 4423 proteins with 352 significantly altered compared to vehicle control treated cells.

Conclusions: Our findings suggest that HDAC6i are efficacious as anti-UM agents. Further investigations will utilise in vivo zebrafish xenograft models and validation of mechanism of action.

CONTROL ID: 3543419

SUBMITTER (NAME ONLY): Jong Beom Park

TITLE: Clinical Outcome of Anti-VEGF in type 1 Choroidal Neovascularization secondary to Central Serous Chorioretinopathy

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Park, K. Kim, E. Kim, S. Yu, Kyung Hee Medical Center, KOREA (THE REPUBLIC OF)|

Commercial Relationships Disclosure (Abstract): Jong Beom Park: Commercial Relationship: Code N (No Commercial Relationship) | Kiyoun Kim: Commercial Relationship: Code N (No Commercial Relationship) | Eung Suk Kim: Commercial Relationship: Code N (No Commercial Relationship) | Seung-Young Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To analyze the type 1 choroidal neovascularization (CNV) patients with central serous chorioretinopathy (CSC) patterns of fundus autofluorescence (FAF) abnormalities

Methods: This retrospective study included 19 eyes of 19 patients who were diagnosed with type 1 choroidal neovascularization with central serous chorioretinopathy (CSC) patterns of fundus autofluorescence abnormalities and characteristics of pachychoroid spectrum. Fundus autofluorescence patterns with spectral domain optical coherence tomography, best corrected visual acuity, subfoveal choroidal thickness and patterns of intravitreal anti-VEGF injection in type 1 choroidal neovascularization patients were analyzed.

Results: A total of 19 patients were consisted of 12 males and 7 females. The mean patients age was 68.79 ± 7.55 years and the mean subfoveal choroidal thickness was 301.79 ± 96.35 micron. Central serous chorioretinopathy (CSC) pattern of fundus autofluorescence abnormalities of type 1 choroidal neovascularization patients were grouped as mottled (36.8%), hyper (26.3%), hyper/hypo(36.8%). The mean number of intravitreal anti-VEGF injection per year was significantly lower in the hyper/hypo group than in the hyper group ($p=0.046$). Also there was a significant positive correlation between the subfoveal choroidal thickness and the interval of loading phase to maintenance phase of intravitreal anti-VEGF injection ($r=0.458$, $p=0.049$).

Conclusions: The central serous chorioretinopathy (CSC) patterns of fundus autofluorescence (FAF) abnormalities in type 1 choroidal neovascularization patients are helpful when predicting the number of intravitreal anti-VEGF injection per year. Additionally the interval of loading phase to maintenance phase of intravitreal anti-VEGF injection can be considering by the subfoveal choroidal thickness of type 1 choroidal neovascularization patients.

CONTROL ID: 3543422

SUBMITTER (NAME ONLY): Victor Perez

TITLE: Variant in the TNFRI gene associated with response to topical anti-TNF α antibody fragment OCS-02 in patients with dry eye disease

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.L. Perez, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Victor Perez: Commercial Relationship(s);Oculis:Code C (Consultant)

ABSTRACT BODY:

Purpose: In a Phase 2 study, a novel topical ocular anti-TNF α antibody fragment, OCS-02, was found to be significantly more effective than vehicle in relieving ocular discomfort associated with severe dry eye disease (DED). An exploratory pharmacogenetics analysis identified genetic factors that may influence the response to OCS-02 in patients with DED.

Methods: Genomic DNA from consenting patients was extracted from blood samples. Genotyping data were generated using TaqMan[®] technology. Candidate genes and single nucleotide polymorphisms (SNPs) were selected for pharmacogenomic analysis based on the drug target (TNF- α) or its receptor (TNFRI), or association with Sjogren's syndrome. A total of 8 SNPs were analyzed. A mixed model repeated measures analysis with Bonferroni correction was used to test the association between genotype and the primary efficacy outcome measure (change from baseline in global ocular discomfort score at Day 29). To test the interaction between genotype and treatment, an ANCOVA model was used with baseline global discomfort score, age and race included as covariates. For SNPs found to be associated with the primary endpoint, the percentage of patients with improvement in global ocular discomfort score > 20 (i.e. high responders) was analyzed by genotype using Fisher's exact test.

Results: Samples from 86 patients in the per protocol population treated (OCS-02, n = 43, vehicle, n = 43) were utilized for pharmacogenomic analysis. Among the 8 SNPs tested, only one showed a significant effect on the response to OCS-02 after Bonferroni correction ($p < 0.0001$). This effect was only present in patients treated with OCS-02. Genotype-treatment interaction analysis using ANCOVA also found that the identified SNP was significantly associated with response. The proportion of OCS-02 patients with high responder status was significantly greater for the CC genotype ($P < 0.05$, Fisher's exact test); no significant effect was observed in patients treated with vehicle.

Conclusions: This pharmacogenetic analysis demonstrated a statistically significant association between response to OCS-02 in patients with DED and a SNP biomarker. The CC genotype was significantly associated with high response to OCS-02. Additional studies are needed to better understand the role of unique SNPs in dry eye disease and susceptibility to anti TNF α therapies.

CONTROL ID: 3543428

SUBMITTER (NAME ONLY): Ravid Doron

TITLE: Contrast sensitivity and Higher-Order Aberrations in Keratoconus subjects

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Doron, E. Shneor, Dept. Optometry, Hadassah Academic College, Jerusalem, Jerusalem, ISRAEL|D.P. Pinero, Dept. Optics, Pharmacology and Anatomy, Universitat d'Alacant, Alicante, SPAIN|

Commercial Relationships Disclosure (Abstract): Ravid Doron: Commercial Relationship: Code N (No Commercial Relationship) | David Pinero: Commercial Relationship: Code N (No Commercial Relationship) | Einat Shneor: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Keratoconus (KC) has negative impact on visual quality that is commonly explained by contrast sensitivity reduction. Ocular higher-order aberrations (HOA) are significantly increased in Keratoconus subjects and has been shown to correlate with a decrease in contrast sensitivity. However, the link between contrast sensitivity and HOA in the early stages of the disease is unclear. This study aim was to evaluate contrast sensitivity and HOA in mild KC and subclinical Keratoconus (KCS) subjects.

Methods: Subjects underwent a complete ocular exam including autokeratometry, corneal tomography (Sirius, CSO), autorefraction and ocular HOA (L-80 wave+, Luneau). Diagnosis of KC was based on abnormal topography/tomography and at least one standard KC clinical sign. The criteria for KCS was abnormal/topography and or tomography but without clinical signs. Contrast sensitivity was tested using a psychophysical two-alternative forced-choice Gabor patches in three spatial frequency (6, 9 and 12 cycles/degree). Analysis included both eyes for KC and KCS subjects, but only one eye (randomly assigned) for healthy controls. Data were compared between controls and KC and KCS group and between KC and KCS group with VA of 0.00LogMar using Mann Whitney test and Fisher's exact test. Friedman and Wilcoxon signed-rank tests compared contrast sensitivity for different frequencies. Spearman correlation test was done to analyze the correlation between ocular HOA and contrast sensitivity.

Results: Twenty-two KC and KCS subjects (38 eyes: 28 KC, 10 KCS, mean age 25.6 ± 5.0 years, VA 0.08 ± 0.12 LogMar, 20 had VA of 0.00 LogMar) and 35 healthy control subjects (35 eyes, mean age 25.0 ± 2.6 years, VA 0.00 ± 0.00 LogMar) were included in the study. The control group showed lower ocular HOA ($p < 0.000$) and higher contrast sensitivity for 6, 9 and 12 cpd ($p < 0.001$) compared to KC and KCS group and compared to KC and KCS group with 0.00VA. Most ocular HOA were negatively correlated to contrast sensitivity in all three frequencies for KC and KCS group and for 9 and 12 cpd for KC and KCS with 0.00VA.

Conclusions: KC and KCS subjects with normal VA showed reduction in contrast sensitivity and higher ocular HOA compared to controls. In addition, ocular HOA were negatively correlated to contrast sensitivity for 9 and 12 cpd. This suggests that HOA underlies the poor vision quality of KC subjects.

CONTROL ID: 3543430

SUBMITTER (NAME ONLY): Anil Upreti

TITLE: Transcriptome analysis of lens epithelial explants upon vitreous-induced fiber cell differentiation

SESSION TITLE: Lens Development and Differentiation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Lens epithelial explants provide a useful tool for studying lens cell proliferation and fiber cell differentiation in vitro. Vitreous humor can induce both epithelial cell proliferation and characteristics of fiber cell differentiation including the accumulation of b- and g-crystallins and cell elongation in explants. Here we performed an analysis of transcriptional changes induced by both explanting and by the addition of vitreous. We sought to determine how closely the transcriptome of vitreous-induced fiber cells in explants mirrors that of endogenous lens fiber cells.

Methods: Lens epithelial explants were prepared from 8-day old FVB/N mice. RNA was extracted from fresh lens epithelium, from lens explants after 1 day in culture without vitreous, and from lens explants after 1, 5, and 10 days of treatment with 50% vitreous and sent for RNA-sequencing. Raw sequence reads were aligned to the mouse transcriptome and gene counts were summarized for differentially expressed genes (DEGs), then used for downstream evaluation such as clustering and gene ontology analysis. The DEG criteria was $\log_2FC > 1.5$ and $p < 0.05$. Explant RNA-Seq data was compared to that of endogenous FVB/N newborn lens epithelial cells and lens fiber cells.

Results: Gene expression analysis showed that the explants upregulated genes related to immune response and inflammation. Vitreous induced a short-term increase in Cdk1 and reduction in the expression of many crystallin transcripts. However, during the 10 days of vitreous exposure, the explants exhibited an overall loss of transcripts normally enriched in lens epithelial cells (e.g. Sulf1, Flt1, Cdh1, and Gja1) and a gain of transcripts characteristic of fiber cell identity (e.g. Cryba4, Cryg1, Crybb1, Dnase2b, Mip, and Lim2). Gene ontology analysis of the upregulated genes in vitreous-treated explants revealed enrichment for terms relating to developmental process, anatomical structure development, regulation of ERK1 and ERK2 cascade, positive regulation of MAPK cascade.

Conclusions: RNA-Seq analysis revealed that in contrast to endogenous fiber cells, vitreous-exposed explants induced expression of genes related to injury response. However, after 10 days of vitreous exposure, the overall transcriptome of lens epithelial explants matched that of newborn lens fiber cells far more closely than that of endogenous lens epithelium.

CONTROL ID: 3543435

SUBMITTER (NAME ONLY): Sheela Evangeline Kumaran

TITLE: Application of Rasch model to score the SF-36 instrument administered to a sample with acanthamoeba keratitis

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kumaran, N.A. Carnt, S. Yeo, K. Pesudovs, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA]

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ABSTRACT BODY:

Purpose: The medical outcomes short form (SF-36) survey is widely used to measure generic health related quality of life (QoL). The survey covers eight key health concepts and is traditionally scored using summative scoring technique. The aim of this study was to apply Rasch analysis, a modern probabilistic measurement model to score the SF-36 survey that was administered to a clinical sample of contact lens wearers with acanthamoeba keratitis (AK).

Methods: The SF-36 survey was completed by 77 AK patients from Moorfields Eye Hospital, UK. Ordinal responses to the SF-36 items were coded such that higher value indicate better QoL. The Andrich rating scale Rasch model was applied using the Winsteps program (version 4.4.8). The psychometric properties (category functioning, measurement precision, fit statistics, and dimensionality) of the original SF-36 subscales and Rasch-derived subscales were explored and person measures (scores) corresponding to valid subscales were obtained.

Results: The median age (range) of the participants was 33.6 years (19.9 –76.5) and 42 (54.5%) were female. Of the eight original subscales, three, namely the physical functioning (PF), role limitations due to physical health (RLPH) and role limitations due to emotional problems (RLEM) did not form valid scales due to low measurement precision (person separation index <1). Re-analysis starting with all 36 items in the model and testing for principal components yielded five valid scales consistent with the original design: role limitations (9 items), general health (5 items), pain (2 items), emotional well-being (5 items) and energy/fatigue (4 items). A newly organized “role limitations” scale encompassed items from the original SF-36 subscales of RLPH, RLEM and social functioning. The physical functioning items did not form a valid scale and were eliminated. The final Rasch-derived scales exhibited optimal category functioning, unidimensionality and excellent reliability (Wright’s sample independent person /test reliability > 0.85). These psychometrically valid, interval scales were able to generate meaningful person measures.

Conclusions: Five psychometrically valid SF-36 scales were derived using Rasch analysis for this sample with AK. These could be used to assess the burden of AK disease in contact lens wearers and potentially in other eye conditions.

CONTROL ID: 3543438

SUBMITTER (NAME ONLY): Georges Nassrallah

TITLE: Objective Analysis of Capsulorhexis factors and Posterior Capsular Opacification in 246 Post-Mortem Eyes

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Nassrallah, C. Mastromonaco, R. Denis, A.B. Dias, N. Saheb, M.N. Burnier, McGill University, Montreal, Quebec, CANADA]

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ABSTRACT BODY:

Purpose: Meticulous construction of an adequate capsulorhexis is the cornerstone of successful cataract surgery. The rate of development of posterior capsular opacification (PCO) has been found to be reduced when capsulorhexis are made smaller, centrally and overlapping the optic. However, there have not been recent studies assessing for the capsulorhexis factors contributing to PCO in post mortem eyes with intraocular lenses (IOL) and operated using newest phacoemulsification machines. This study aims to evaluate the capsulorhexis structure in post-mortem eyes and determine factors associated with PCO.

Methods: A total of 246 post-mortem pseudophakic human eyes were obtained from the Minnesota Eye Bank and examined at the MUHC-McGill University Ocular Pathology & Translational Research Laboratory. Microscope photographs were taken of the eyes in Miyake view and of the extracted lens-capsule complex. PCO and Soemmering's Ring (SR) density, were quantified using Automated Detector Opacification Software (ADOS) as a factor of intensity and area. Miyake views and graphical analysis software were used to assess capsulorhexis area, area of non-overlap of the anterior capsule with the IOL, size of the shortest anterior capsular leaflet, and area of anterior capsule coverage on the IOL. Linear regression analysis was used to determine the relationship of these factors with PCO and SR formation as well as statistical significance.

Results: Capsulorhexis area showed a weak negative correlation ($R^2 = 0.06$) with PCO formation ($P < 0.0001$), although with only a modest effect (slope = -0.019). Anterior capsular coverage area was positively correlated with both PCO ($R^2 = 0.10$, slope = 0.027, $P < 0.0001$) and SR ($R^2 = 0.02$, slope = 0.213, $P = 0.011$), but again with only weak association. Area of non-overlap of the anterior capsule with the IOL and size of the shortest anterior capsular leaflet were not significantly associated with PCO or SR formation.

Conclusions: The pathogenesis of PCO development after cataract surgery is multifactorial. This study shows that with modern operating technology, rhexis factors have at best a modest influence on PCO formation. Factors such as time from surgery to death and intra-operative capsular polishing technique likely play a more significant role.

CONTROL ID: 3543445

SUBMITTER (NAME ONLY): Alejandra Tamayo Duran

TITLE: Development of in vitro and ex vivo tools for functional characterization of variants of uncertain significance in aniridia

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tamayo Duran, M. Tarilonte Misas, J. Moya, P. Ramos, S. Swafiri, F. Blanco, C. Ayuso, M. Cortón, Genetics and Genomics, Instituto de Investigacion Sanitaria de la Fundacion Jimenez Diaz, Madrid, Madrid, SPAIN|A. Tamayo Duran, S. Swafiri, F. Blanco, C. Ayuso, M. Cortón, Centro de Investigacion Biomedica en Red de Enfermedades Raras, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: PAX6 mutations lead to aniridia, a panocular disorder that usually involves iris and foveal hypoplasia, cataract, corneal dystrophy, as well as abnormalities of the optic nerve.

Here, we describe the development of two molecular approaches for the functional characterization of coding and non-coding variants with uncertain significance (VUS) and their impact on the canonical PAX6 splicing in aniridia patients.

Methods: For in vitro splice assays, a genomic segment encompassing the region of interest of PAX6 along with flanking sequences was amplified by PCR from genomic DNA and was cloned into an expression vector. VUS were introduced in the wild-type minigene constructs by site-directed mutagenesis. The minigene assays were performed by transient transfection into kidney HEK-293 and/or retinal ARPE-19 cell lines.

For ex vivo splice assays, lymphoblastoid cell lines (LCL) were established by Epstein Barr virus transformation of blood lymphocytes from patients carrying VUS and control healthy individuals.

Both HEK-293 transfected cells and lymphoblastoid cells were harvested and total RNA was extracted and reverse transcribed. The splicing patterns of mRNA transcripts were compared by semiquantitative PCR and sequencing.

Results: We have developed four minigene wild-type constructs involving the full exonic and intronic sequences of PAX6: i) the 5'UTR region (exons 1 to 4), ii) exons 5a and 6, iii) exons 5 to 7 and iv) exons 8 to 11, respectively. To date, a total of 13 variants have been assayed. 11 out 13 showed aberrant splicing patterns that include different mechanisms such as single or multiple exon skipping, exon elongations, intron retentions and new pseudoexon inclusions by the alternative use of cryptic splicing sites.

Ex-vivo expression analysis in LCL from 5 carrier patients showed alterations on splicing patterns. Two out five were also tested by in vitro splice assays and the findings on splicing patterns correlate with those observed in minigene assays.

Conclusions: Minigene PAX6 assays carrying multiple exons and LCL studies are useful strategies to gain insight into the pathogenicity of the poorly explored non-canonical splice PAX6 variants. These methods along with in silico analysis are easy-to-carry approaches for robust splice variant analysis and to help bring molecular diagnosis to aniridia patients.

CONTROL ID: 3543446

SUBMITTER (NAME ONLY): Katie Curran

TITLE: Treating sight-threatening diabetic retinopathy in Vietnam using laser or anti-VEGF injections: Patients' perspectives

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of this study was to understand patients' knowledge and attitudes towards laser versus anti-vascular endothelial growth factor (VEGF) injections used to treat sight-threatening DR in a low-middle income country, Vietnam. The main purpose was to provide data to help the Ministry of Health make evidence-based decisions that can improve DR management in Vietnam.

Methods: This is a descriptive qualitative study. Participants provided information about four topics: their knowledge of diabetes and DR, views on their treatment, perceived barriers to treatment and suggestions on how to improve care. Semi-structured interviews were conducted with 12 patients with DR from Ho Chi Minh City and six from Hanoi, Vietnam. Data were analysed using thematic framework analysis.

Results: The average age of participants was 53.7 years (SD±11.6 years), and 7/18 (38.9%) were female. Among the 18 participants interviewed, five (27.8%) accepted laser treatment and four accepted anti-VEGF injections (22.2%), with the remainder refusing treatment. Patients reported that it is the doctors who select the most appropriate DR treatment for their patients in Vietnam, and they often explain the benefits and risks of the chosen treatment. Patients accept that treatment clinics are busy, but regardless, they would like to receive more information on treatment schedules and likely prognosis and potential visual outcomes they can hope for. Pain was reported as a side effect of laser by two patients, with one patient reporting pain after anti-VEGF injections. The main barriers to treatment were the high cost of treatment and other out-of-pocket costs (e.g. related to travel). Patients wanted to have fewer treatment and monitoring appointments and attend clinics that are nearby in order to minimise the impact on their daily life.

Conclusions: The current study has identified themes patients reported on their treatments with laser and anti-VEGF injections for DR. Reducing treatment costs, optimising treatment protocols so fewer in-person attendances are required to complete a course of treatment, and expanding the network of clinics offering treatment outside urban areas have been the lead topics for discussion. These findings are crucial to inform policy changes in Vietnam and might be generalisable to other low-resource settings.

CONTROL ID: 3543455

SUBMITTER (NAME ONLY): Amy Leung

TITLE: Investigation of Ataluren (PTC124) as a potential therapeutic for LCA4 in a patient-derived iPS-retinal organoid model

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Leber congenital amaurosis type 4 (LCA4), a severe form of inherited retinal dystrophy, is an autosomal recessive disorder caused by mutations in aryl hydrocarbon receptor interacting protein-like 1 (AIPL1). AIPL1 is a photoreceptor-specific co-chaperone that is crucial for the correct folding and assembly of the cGMP phosphodiesterase PDE6 complex. AIPL1 is highly heterogeneous, but W278X -which encodes a premature stop codon in the last exon of the AIPL1 transcript- is the most common (50-65% frequency) LCA4 pathogenic allele. The position of the W278X mutation renders it potentially amenable to translation readthrough inducing drug (TRID) therapy, which aims to override the premature stop codon with the incorporation of near-cognate tRNA amino acids.

Methods: In order to test TRID therapy as a potential treatment for LCA4, induced pluripotent stem cells (iPSC) were derived from 4 different LCA4 patients, comprising one W278X homozygote and 3 W278X compound heterozygotes. Retinal organoids (ROs) were differentiated and extensively characterised. 10ug/ml PTC124 was tested on patient ROs from D120 onwards, when AIPL1 expression is observed in developing photoreceptor cells.

Results: LCA4-ROs were indistinguishable from control in terms of organoid structure, retinal cell development and differentiation kinetics. Both control and LCA4-ROs generated the full complement of retinal cell types, with an outer nuclear layer (ONL) comprised of photoreceptors with presumptive inner/outer segment structures. However, LCA4-ROs lack detectable AIPL1 protein in the ONL, and PDE6A and PDE6B are absent, recapitulating key aspects of LCA4. PTC124-treated W278X+/+ and +/- LCA4-ROs displayed partial rescue of AIPL1 protein, proving that PTC124 is indeed able to drive readthrough of the W278X allele. Moreover, low-level restoration of PDE6B was seen in W278X+/+ LCA4-ROs.

Conclusions: Patient-derived LCA4 ROs recapitulate the key molecular features of LCA4, validating it as a useful in vitro system in which to interrogate novel therapies. Excitingly, PTC124 was able to partially restore AIPL1 protein in W278X-/+ and +/- LCA4-RO photoreceptors with limited rescue of PDE6B in W279X+/+ RO, potentially due to the increased amount of W278X transcript in these ROs. These results demonstrate that translational readthrough therapy might be a promising approach to LCA4 treatment.

CONTROL ID: 3543457

SUBMITTER (NAME ONLY): Langis Michaud

TITLE: THE MONTREAL EXPERIENCE : PART I- BASICS AND TREATMENT ALGORITHM

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Michaud, P. Simard, R. Marcotte-Collard, Optometry, Universite de Montreal, Montreal, Quebec, CANADA|M. Ouzzani, Optometry, Universite d'Oran 1 Ahmed Ben Bella, Oran, ALGERIA|

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ABSTRACT BODY:

Purpose: Over the past 10 years, authors refined myopia control strategies (MCS) after following 800 children at the Montreal School of Optometry Clinic (EOUM).

Methods: EOUM approach is based on 3 pillars: normal binocular function (BV), control of the central and peripheral blur, and of the environment. A dose-response approach is applied. This means to use/design optical devices bringing the highest convex power in the pupil area, without inducing blur at distance, with no impact on BV. MCS are selected on : rate of progression, age of myopia onset, corneal parameters, pupil area, risk factor for ocular pathology, patient's lifestyle, compliance. Goal is to generate a customized approach for each patient. In this poster, treatment algorithm is explained. For this study, data are extracted from the file of each patient who: consulted between Jan 2017-Dec 2018 and were kept under the same design/concentration. Clinical population is composed of 310 patients (35% Cauc.-45% Asian), median age of 11 (range 5-18). The treatment options were orthokeratology (4 designs; N=140), multifocal soft contact lenses (SMCL; 5 designs; N=128), and low dose atropine (LDA 0.01%-0.05%; N=42).

Results: Results are analyzed through sophisticated statistical models. The goal of modeling was to assess whether myopia control type had a statistically significant effect on AL progression over time, and, if so, to estimate the 12-24 month progression differences between MCS. Models were fit that accounted for within-subject correlation. Overall results indicate that AL growth, at 1-2 years, was the lowest when using OK lenses (0.13/0.29um [95%CI 0.100-0.158/0.26-0.34] vs SMCL (0.18/0.36um [95%CI 0.14-0.21/0.30-0.41) or LDA (0.19/0.37um [95%CI 0.14-0.25/ 0.29-0.46). OK advantage was statistically significant at 1 year vs SMCL(p=0.03) or LDA(0.034), but not significant at 2 years (SMCL p=0.055; LDA p=0.10). SMCL was comparable to LDA at 1(p=0.54) and 2 years (p=0.77). Detailed results will be presented in part 2.

Conclusions: Montreal experience reveals that customized approach is effective. This means that it brings AL evolution close to non-myopic kids when MCS is properly selected. OK gives better results at 1 year but the 3 methods become similar at 24 months.

CONTROL ID: 3543458

SUBMITTER (NAME ONLY): Nigus Asefa

TITLE: Development and validation of myopia proxy using self-reported refractive error-related questions: the Lifelines cohort

SESSION TITLE: Refractive Error and Myopia

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.G. Asefa, I. Nolte, H. Snieder, Epidemiology, Universiteit Groningen Faculteit Medische Wetenschappen, Groningen, Groningen, NETHERLANDS|A. Neustaeter, J. Vehof, N.M. Jansonius, Ophthalmology, Universiteit Groningen Faculteit Medische Wetenschappen, Groningen, Groningen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Ophthalmic examination in large population-based cohorts is challenging and time-consuming. To address this, (1) we built a myopia proxy that can be applied in large population-based studies and (2) validated the proxy by confirming its association with educational attainment and a polygenic risk score (PRS) for myopia.

Methods: Data were collected between 2014-2017 from 88,646 Dutch adults from the Lifelines cohort. We did a three-step analysis. In Step 1, we performed principal component analysis (PCA) to responses of five refraction-status questions posed to Lifelines participants. In Step 2, we measured the refractive state in a subset of Lifelines participants (n=209) and performed logistic regression using myopia (mean spherical equivalent [MSE] < -0.5 D) as dependent and the principal components (PCs) (with an eigenvalue ≥ 1) as independent variables. We used ROC curve analyses to identify specificity, sensitivity, and the classification threshold. In Step 3, the classification equation was applied to the remaining Lifelines participants from Step 1. The value of the proxy was then explored by determining the prevalence of myopia and calculating its association with educational attainment and a PRS of myopia. Analyses were adjusted for age and sex.

Results: 77,213 participants (58.1% females) were eligible for the PCA. Of these, about three-quarters (73.4%) were wearing either glasses or contact lenses. Using measured MSE as a gold standard, the first two PCs had a specificity (95% CI) of 92.4% (87.3-96.6%), and sensitivity (95% CI) of 89.1% (80.0-96.4%) for myopia. The area under the ROC curve (95% CI) was 94.5% (90.6-98.4%). The age-standardized prevalence (95% CI) of myopia was 34.7% (34.3-35.1%). Compared to low education level, the odds ratios (95% CI) of myopia were 1.60 (1.53-1.70, $P = 4.04 \times 10^{-82}$) and 2.40 (2.30-2.54, $P = 2.19 \times 10^{-252}$) for medium and high education levels, respectively (Figure A). Similarly, PRS analysis showed a dose-response relationship with myopia (Figure B). Compared to the lowest decile of the PRS, the highest decile had an OR (95% CI) of 4.24 (3.68-4.91, $P = 5.27 \times 10^{-86}$) for myopia.

Conclusions: Self-administered refractive error questions are effective in capturing myopic cases in a population-based setting.

CONTROL ID: 3543462

SUBMITTER (NAME ONLY): kimberley delaunay

TITLE:

Role of light in the regulation of ocular corticosteroids and its involvement in myopic staphyloma

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) might be an important target cell type in the development of posterior staphyloma as the mutation of megalin (a multiligand receptor) in RPE cells induces high myopia (HM) and staphyloma. Staphyloma results from elongation of the eye, thinning of the choroid, and a posterior protrusion that stretches the retina and the RPE/choroid/sclera complex. In addition to genetic factors, environmental factors and particularly light exposure is recognized as a major factor for HM development. There is an interaction between light exposure, circadian cycle and the concentration of hormones, such as corticosteroids but the exact role of light and corticoids on the expression of genes involved in HM and staphyloma has not been analyzed in RPE cells. The aim of this work was to analyze the expression of genes involved in HM and staphyloma in human RPE cells derived from iPSc in response to light or corticoids exposure.

Methods: Human iPSC-derived RPE (iRPE) cells were treated with aldosterone, cortisol and cortisol + RU-486 for RNA-Seq transcriptome analysis. In a second experiment, iRPE cells were exposed at 180j/cm² light dose at 8:00 a.m. during 5 consecutive days to white light (2700K), blue (454nm) or red (631nm) light. On day 5, iRPE cells were collected for RNA extraction at 9:00 a.m., 12:00 p.m. and 8:00 p.m. Circadian clock (PER1, PER2, PER3, CLOCK, BMAL1, CRY1, CRY2), tissue remodeling- (MMP2, TIMP2, ABCA4, COL1A1) corticosteroids- (NR3C2, NR3C1, HSD11B2) and connexin-related (GJD2) genes expression were assessed by RT-qPCR.

Results: Treatment of iRPE cells with corticosteroids induced changes in gene expression of PER1, ABCA4, COL1A1, GJD2 and DKK1. These genes have been found to be associated with the development of HP. Moreover, only exposure to blue light induced in iRPE cells an overexpression of the glucocorticoid receptor (NR3C1) and a decrease in GJD2 transcripts, while the expression of most of genes of interest was differentially regulated in all lighting conditions when compared to unexposed control cells.

Conclusions: Data suggest a biological crosstalk between corticosteroids mechanisms of action and detrimental alteration of the circadian rhythm by inappropriate light exposure, resulting in the activation of molecular events implicated in posterior staphyloma pathogenesis in highly myopic individuals.

CONTROL ID: 3543469

SUBMITTER (NAME ONLY): JOHN HINKLE

TITLE: Outcomes In Eyes Lost to Follow-up After Treatment with Steroid Injections for Retinal Pathology

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the effect of loss to follow-up (LTFU) on eyes treated with intraocular and periocular steroid injections.

Methods: Patients receiving intraocular or periocular steroid injections for retinal diseases and who were subsequently LTFU for at least 180 days after injection were included. Charts were reviewed for visual acuity (VA), intraocular pressure (IOP), and central foveal thickness (CFT) at the treatment visit before LTFU, the first return visit, and visits 3, 6, and 12 months later.

Results: Fifty-three eyes of 47 patients were identified. Mean age was 62.3 years, mean LTFU duration was 295 days, and mean follow-up period after returning was 392 days. Indications for steroid injections were: uveitis-associated cystoid macular edema (CME) 23/53 (43.5%), diabetic macular edema (DME) 13/53 (24.5%), post-surgical CME 13/53 (24.5%), and retinal vein occlusion (RVO) 4/53 (7.5%). The injection preceding LTFU was periocular triamcinolone in 31/53 (58%) eyes and intravitreal steroid in 22 of 53 eyes (42%) (dexamethasone intravitreal implant in 15/53 (28%) and triamcinolone in 7/53 (14%)). Compared to mean VA prior to LTFU [0.59, Snellen ~20/77], the mean VA was not significantly different at each time point after return (first return visit [0.62, Snellen ~20/83, p=0.6], month 3 [0.55, Snellen ~20/70, p=0.6], month 6 [0.55, Snellen ~20/70, p=0.5], month 12 [0.64, Snellen ~20/87, p=0.6]).

Overall, at all return visits, there was a slight increase in IOP. At the first return visit, 8/53 (15%) had IOP \geq 21 mmHg (range= 8-31) but only 2 patients required treatment with a single new anti-hypertensive medication. No patient required glaucoma surgery. The DME group showed greater mean IOP at first return visit [17.45 mmHg, p=0.04] and at 12 month after return [20.25 (5.2), p=0.02] compared to before LTFU (13.76 mmHg). CFT increased after return visit (392 mm) compared to prior to LTFU (369 mm, p=0.35). The mean CFT declined significantly by month 6 [294 mm, p=0.005] and month 12 [269 mm, p<0.001].

Conclusions: Eyes LTFU after receiving steroid injections did not experience significant morbidity. Mean VA, IOP, and CFT were not significantly worse immediately after LTFU and 12 months later, though patients with DME did experience a more significant increase in IOP.

CONTROL ID: 3543471

SUBMITTER (NAME ONLY): Mike Wels

TITLE: Photoporation of the corneal epithelium with biocompatible poly-dopamine nanoparticles for the delivery of biologics

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wels, F. Sauvage, K. Raemdonck, K. Braeckmans, S. De Smedt, Laboratory of General Biochemistry and Physical Pharmacy, Universiteit Gent, Gent, BELGIUM|D. Roels, Department of Ophthalmology, Universitair Ziekenhuis Gent, Gent, BELGIUM|

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ABSTRACT BODY:

Purpose: Treatment of rare corneal diseases besides transplantation are sparse. Delivery of biologics such as siRNA and mRNA could provide effective treatments however it still remains challenging due to the numerous ocular barriers.

Irradiation of light absorbing nanoparticles (NPs) leads to an ultrafast heating causing evaporation of the surrounding medium and the formation of vapor nanobubbles (VNB) which when collapsed porate cell membranes allowing intracellular delivery of macromolecules. This method, photoporation, has been studied in the past years to deliver different cargos. In this project we investigate bioinspired poly-dopamine (PDA) NPs to improve biologics delivery in the corneal epithelium.

Methods: Freshly enucleated bovine eyes were used to isolate and culture primary bovine corneal epithelial cells (pBCEC) or used intact as an ex vivo model to test different PDA NP sizes (90 nm vs. 260 nm) and concentrations ($8.0\text{-}160 \times 10^7$ nps/ml). These NPs were irradiated by a nanosecond pulsed laser (3 ns at 532 nm with fluences of $0.9\text{-}2.7 \text{ J/cm}^2$) to allow VNB formation. These NPs were investigated on their ability to form pores after laser treatment allowing to transfect pBCEC with FITC-dextran of different molecular weights (10 kDa, 150 kDa and 500 kDa).

Results: We observed 10 kDa dextran were more efficiently delivered than 500 kDa dextran (80% vs 40% respectively) likely due to their smaller molecular weight. Comparing 90 nm and 260 nm sized NPs in optimized conditions did not show a difference in delivery yield and only a slight change in relative mean fluorescent intensity (up to 1.3 times higher for 500 kDa dextran). The 260 nm NPs did however show an increased toxicity at equal concentrations.

Intact bovine eyes were treated with 90 nm PDA NPs and 10 kDa dextran. Optimal concentrations determined in vitro however did not show increased uptake compared to dextran alone. Increasing the PDA concentration (500 fold) however showed clearly increased uptake as visualized through full cornea microscopy and corneal sections.

Conclusions: In this work we have successfully synthesized 90 and 260 nm biocompatible PDA NPs. We have shown these NPs were able to create VNB and porate the cell membrane as observed with the increase in delivery efficiency in vitro. In an intact bovine eye, we have been able to efficiently deliver dextran to the corneal epithelial layer.

CONTROL ID: 3543475

SUBMITTER (NAME ONLY): Lies De Groef

TITLE: Comparative retinal imaging in mouse models of proteinopathies identifies disease-specific biomarkers

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. De Groef, L. Veys, M. Vandenabeele, L.K. Moons, Department of Biology, Katholieke Universiteit Leuven, Leuven, Flanders, BELGIUM|X. Hadoux, P. van Wijngaarden, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|S. Lemmens, I. Stalmans, Katholieke Universiteit Leuven Universitaire Ziekenhuizen Leuven Campus Gasthuisberg Dienst Ophthalmology, Leuven, Flanders, BELGIUM|L. Serneels, B. De Strooper, Katholieke Universiteit Leuven Groep Biomedische Wetenschappen, Leuven, Flanders, BELGIUM|J. Theunis, VITO NV, Mol, Antwerpen, BELGIUM|

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ABSTRACT BODY:

Purpose: In previous research we have shown that the App^{NL-G-F} mouse retina mimics the early, preclinical stages of Alzheimer's disease, and that retinal imaging offers unique opportunities for research and drug discovery [1] . In this follow-up study, we have used in vivo and ex vivo retinal imaging in conjunction with immunohistochemistry and molecular assays, in a range of mouse models of neurodegenerative diseases characterized by protein aggregation, to identify the pathological correlates of imaging biomarkers.

Methods: Mouse models of alpha-synuclein, tau, and amyloid overexpression/aggregation underwent a battery of retinal examinations, including in vivo optical coherence tomography and electroretinography as well as ex vivo hyperspectral imaging (HSI; Snapscan, Imec). HSI spectra were analyzed as previously described [1]. Retinal samples were collected for immunohistochemistry and molecular studies of protein aggregation.

Results: Diverging patterns of retinal dysfunction and/or degeneration were observed in the different mouse models, illustrating the varied impacts of these protein aggregates on retinal structure and function. Moreover, while all protein aggregates led to HSI changes in the 450-600 nm range, distinct signatures were observed. Immunohistochemical and molecular studies revealed that the observed HSI changes correlated both with levels of the protein aggregates that are the hallmarks of these diseases, and with levels of soluble oligomers.

Conclusions: HSI can be used to quantify retinal amyloid beta, underscoring its potential as a biomarker for Alzheimer's diagnosis and disease monitoring. Moreover, our research indicates that the HSI signatures of alpha-synuclein, tau, and amyloid aggregates are distinct. These findings add further evidence to suggest that retinal HSI may have utility in the diagnosis and stratification of proteinopathies associated with the most common forms of human neurodegenerative diseases.

[1] Vandenabeele et al. (2021) Acta Neuropathologica Communications [<https://rdcu.be/cdbmS>]

CONTROL ID: 3543477

SUBMITTER (NAME ONLY): Guorong Li

TITLE: Effects of phenylephrine on proximal and distal conventional outflow vessels in living animals

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Li, K. Choy, K. Hake, S. Farsiu, D.W. Stamer, Duke University, Durham, North Carolina, UNITED STATES|C.R. Ethier, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Increased resistance to aqueous humor outflow through conventional outflow tissues is a primary risk factor for glaucoma, however, underlying mechanisms are not fully understood. The majority of outflow resistance occurs where the trabecular meshwork (TM) and inner wall of Schlemm's canal (SC) interact. Yet, 25-40% of outflow resistance is generated by vessels distal to SC. Phenylephrine (PE), a mydriatic eye drop, is a vasoconstrictor that reduces rabbit conjunctival venous diameter and velocity, and induces IOP fluctuations in humans. The aim of this study was to investigate the effects of PE on outflow tissue morphology and IOP in living mice.

Methods: Both genders of Balb/c and C57BL/6 mice were used (Duke animal protocol A001-19-01). Anterior ocular tissue behaviors were visualized in living animals by SD-OCT (Bioptigen) in response to topical 1.25% PE alone or with 0.5% tropicamide (trop). Red blood cells (RBCs) in Schlemm's canal (SC) were visualized in Balb/c mice using bright field microscopy of anterior segment flat mounts. IOP was measured by tonometry (TonoLab). Aqueous humor flow patterns were observed using 0.1µm green fluorescent beads perfused into living eyes and quantified using custom software.

Results: Average IOP increased post drug treatment (40-120 min) with either topical PE (2.05 ± 0.85 mmHg, n=3) or PE+trop (2.88 ± 0.20 mmHg, n=6). Treatment with either PE or PE+trop appears to cause elevated episcleral venous pressure as indicated by RBC accumulation in SC over 2 quadrants from ~5 to 120 min post drug treatment. Cross-sectional area of SC lumen became smaller ~20 min post PE+trop treatment by $32.2 \pm 6.2\%$ (n=3). Meanwhile, a decreased amount of fluorescent beads appeared in outflow tissues 40 min post PE+trop treatment compared to PBS-treated controls. Finally, PE had similar effects in mice to those known to occur in human eyes: a decrease of anterior segment depth, anterior ciliary body motion, and pupillary dilation.

Conclusions: Phenylephrine induced RBCs accumulation in SC and decreased amount of tracer accumulation in TM, which could be due to PE constricting distal outflow vessels. Interestingly, PE decreased SC lumen area indicating that PE effects on ciliary body and iris may also be involved in the changes of outflow function as pilocarpine does. PE effects on outflow function may be via both conventional and uveal outflow pathways and should be further investigated.

CONTROL ID: 3543481

SUBMITTER (NAME ONLY): Manon Veldman

TITLE: Usability and feasibility study of a vision-specific E-health intervention to reduce fatigue in adults with visual impairment.

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Veldman, H.P. van der Aa, G. van Rens, R.M. Van Nispen, Ophthalmology, Amsterdam Universitair Medische Centra, Amsterdam, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Former research shows that 57% of the adults with visual impairment experience symptoms of severe fatigue. As there is no evidence based treatment, we developed a blended vision-specific cognitive behavioral and self-management based E-health intervention, called E-nergEYEze, to reduce fatigue in visually impaired adults. The intervention is (digitally) guided by social workers and digital features are explained by computer trainers. The purpose was to investigate the usability and feasibility regarding accessibility of the prototype.

Methods: E-nergEYEze has been developed based on evidence-based practice by a design team, who provided input for relevant themes and content based on new and existing modules. A usability study was conducted among 5 adults (mean age 54y, 80% male) with different eye conditions and severity of vision loss. Participants were asked to test E-nergEYEze while applying the think-aloud method, followed by a semi-structured interview. A thematic approach was used to analyze the data, after which the prototype was modified. A feasibility study was performed among 10 adults (mean age 50y, 60% male) with visual impairment and severe fatigue. The primary outcome was the Checklist Individual Strength subscale fatigue severity measured before and 3 months after baseline measurement.

Results: The prototype required substantive adjustments, lay-out changes and additional guidance by professionals. Participants of the usability study were interested to follow the intervention themselves. The feasibility study showed a significant reduction of severe fatigue (Wilcoxon Matched-Pairs test; z-score -2.652, p-value 0.008, SD 3.03-8.20). All participants recommended the intervention to others and gave E-nergEYEze a median score of 8.0 (range 7-10). One participant was lost to follow-up due to personal circumstances and two because of different expectations of the intervention.

Conclusions: Results of the E-nergEYEze prototype pilot study are promising in reducing fatigue in adults with visual impairment. As the design, severity of the visual impairment and skills on assistive technology determine the ability to access E-health for people with visual impairment, we carefully considered accessibility for users with visual impairment in the development of E-nergEYEze. Cost-effectiveness of E-nergEYEze is currently investigated in a randomized controlled trial.

CONTROL ID: 3543483

SUBMITTER (NAME ONLY): Andrew Antoszyk

TITLE: Initial Aflibercept Versus Vitrectomy with Panretinal Photocoagulation for Vitreous Hemorrhage (VH) From Proliferative Diabetic Retinopathy (PDR): A DRCR Retina Network Randomized Clinical Trial

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.N. Antoszyk, Ophthalmology, Charlotte Eye Ear Nose and Throat Associates, CHARLOTTE, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Andrew Antoszyk: Commercial Relationship(s);JAEB:Code C (Consultant);Roche:Code F (Financial Support);Regeneron:Code F (Financial Support);Genentech:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Vitreous hemorrhage (VH) from PDR is a frequent cause of visual acuity (VA) loss in diabetics, but the optimal management strategy is unclear. We compared the effect of initial treatment with intravitreal aflibercept vs vitrectomy with panretinal photocoagulation (PRP) on VA and the ability to perform regular activities

Methods: Adults at 39 sites in US and Canada, with VA loss due to VH from PDR, were randomly assigned to initial treatment with aflibercept (N=100) or vitrectomy with PRP (N=105) and followed for 2 years. Aflibercept treatment began with 4 monthly injections. All eyes could receive aflibercept or vitrectomy during follow-up per prespecified criteria. The primary outcome was mean VA over 24 weeks (area under the curve)adjusted for baseline VA. Secondary outcomes included VA at 4 weeks and 2 years and the percentage of activity impairment due to VA on the Workplace Productivity and Impairment Questionnaire (100%=completely prevented regular activities; 0%=no effect).

Results: At baseline, mean age was 57 years, 115 (56%) were male, and mean VA was 34.5 letters (Snellen equivalent (SE) 20/200). Over 2 years, 33 aflibercept group eyes (33%) received vitrectomy and 34 vitrectomy group eyes (32%) received aflibercept. Excluding deaths, 90% completed the 2-year visit. Mean VA over 24 weeks was 59.3 vs 63.0 letters (SE 20/63 vs 20/63) with aflibercept vs vitrectomy (adjusted difference=-5.0, 95% CI, -10.2 to 0.3; P=.06), respectively. At 4 weeks, mean VA was 52.6 letters vs 62.3 letters (SE 20/100 vs 20/63) with aflibercept vs vitrectomy (adjusted difference=-11.2 [95% CI, -18.5 to -3.9] P = .003) and at 2 years, 73.7 vs 71.0 (SE 20/40 vs 20/40) (adjusted difference=2.7 [95% CI, -3.1 to 8.4], P= .36) letters, respectively. The mean reduction in activity impairment due to VA over 24 weeks with aflibercept was 21% versus 27% with vitrectomy (adjusted difference=7% [95% CI, 1% to 13%], P=.02); at 2 years, the difference was 3% (P=.31).

Conclusions: Among eyes with vitreous hemorrhage due to PDR, there was no significant difference in mean VA over 24 weeks after initiating treatment with aflibercept vs vitrectomy with PRP. Initial vitrectomy improved participants' VA and ability to perform daily activities faster than aflibercept.

CONTROL ID: 3543487

SUBMITTER (NAME ONLY): Hrvoje Bogunovic

TITLE: Predictive Identification of the Fastest Progressing Geographic Atrophy Lesions based on Deep Learning in the Phase 2 FILLY clinical trial of Pegcetacoplan

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Bogunovic, D. Lachinov, J. Mai, G.S. Reiter, S. Riedl, W. Vogl, U. Schmidt-Erfurth, Medizinische Universitat Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: In patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD), the speed of progression is highly variable. To evaluate the potential of artificial intelligence (AI) for therapeutic dosing frequency, we trained a deep learning-based algorithm to predict the growth of GA lesions and to identify patients with the fastest growing lesions ("fast progressors").

Methods: OCT scans (512x49x496 voxels, Heidelberg Engineering) of study eyes of patients with GA; that were enrolled in FILLY phase II clinical trial to study the effect of pegcetacoplan (APL-2), and investigational therapy targeting complement C3. GA lesion size at baseline and year 1 was manually annotated on fundus autofluorescence (FAF) by a reading center using RegionFinder and on OCT by an expert reader. Fast progressors were defined as the top 20% of the lesion size growth distribution. A deep learning method was then trained to predict the one year GA growth from a baseline OCT scan. Predictive performance was evaluated using a five-fold cross-validation.

Results: 155 study eyes were included in the analysis that completed the one-year follow-up and had a sufficient image quality to allow for the training and evaluation. Patients from each study arm were considered and fast progressors were identified independent of treatment. Of the top 20% of patients (n =31), 15 were in the sham treatment arm, 11 were treated with APL-2 every other month, and 5 were treated with APL-2 monthly. Atrophy measured on FAF and on OCT showed a concordance of $R^2=0.9$. The evaluation showed that the growth was predicted with a correlation of $R=0.57$, $R^2=0.32$, and the detection of fast progressors achieved an area under the curve AUC of 0.83 (CI: 0.75-0.90) corresponding to a sensitivity of 0.78 and specificity of 0.70.

Conclusions: Fully automated prediction of GA lesion growth from OCT scans is possible, and it allows identification of fast progressors, who may need more intensive treatment. FAF atrophy measurements were consistent with the OCT-based ones. The results of this pilot study are a promising step toward clinical decision support tools for therapeutic dosing and guidance of patient management on a large scale, once such treatments become available.

CONTROL ID: 3543497

SUBMITTER (NAME ONLY): Anneli Savinainen

TITLE: Ocular distribution and exposure of AU-011 after suprachoroidal or intravitreal administration in an orthotopic rabbit model of human uveal melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Savinainen, C.C. Rich, Aura Biosciences, Cambridge, Massachusetts, UNITED STATES|H.E. Grossniklaus, S. King, Emory Eye Care Center, Atlanta, Georgia, UNITED STATES|J. Wicks, Stage Bio, Mt Jackson, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Anneli Savinainen: Commercial Relationship(s);Aura Biosciences:Code E (Employment) | Hans Grossniklaus: Commercial Relationship: Code N (No Commercial Relationship) | Shin King: Commercial Relationship: Code N (No Commercial Relationship) | Joan Wicks: Commercial Relationship: Code N (No Commercial Relationship) | Cadmus Rich: Commercial Relationship(s);Aura Biosciences:Code E (Employment)

ABSTRACT BODY:

Purpose: The aim of this study was to compare the ocular distribution and exposure, after suprachoroidal (SC) and intravitreal (IVT) administration of AU-011 in a rabbit model of human uveal melanoma. AU-011 (belzupacap sarotalocan) is designed to be a highly tumor targeted treatment for uveal melanoma that causes acute cellular necrosis with pro-immunogenic cell death, which triggers a secondary immune response. AU-011 has shown promising preliminary results in a Phase 1b/2 clinical trial for primary choroidal melanoma delivered by IVT administration. A Phase 2 clinical trial is ongoing to evaluate SC administration.

Methods: Human uveal melanoma 92.1 cells were implanted in the choroid of rabbit eyes. Once tumors reached ~5mm in basal diameter, AU-011 was administered by SC or IVT injection. Ocular tissues including tumor samples were taken at multiple time points up to 48 hours post injection. The bioanalytical method for exposure in vitreous, choroid/retina and tumor were based on an electrochemiluminescence immunoassay. Distribution of AU-011 in the tumor was evaluated by immunohistochemical staining using a monoclonal rat antibody against the virus-like particle component of AU-011.

Results: After SC administration, we observed negligible levels of AU-011 in the vitreous and high exposure levels in the tumor and choroid/retina. The exposure remained high in the tumor up to 48 hours post injection for both routes of administration. The exposure of AU-011 in the tumor was approximately 5x higher when AU-011 was administered by SC injection compared to IVT injection. Mean concentrations were 12459 +/- 5190 and 1996 +/- 421 ng/mL, respectively. Positive IHC staining support that AU-011 was present in the tumor after both SC and IVT administration. AU-011 staining was observed penetrating throughout the tumor in the SC injected group whereas AU-011 staining in the IVT injected eyes demonstrated that AU-011 was mostly localized on the apex or vitreal surface of the tumor.

Conclusions: These data suggest that SC administration is superior to IVT administration with an improved tumor distribution, higher tumor bioavailability and less unintended exposure in the vitreous and other key ocular structures, which may result in an improved therapeutic index. AU-011 is currently being evaluated in two clinical trials, one with SC and one with IVT administration.

CONTROL ID: 3543498

SUBMITTER (NAME ONLY): Eirini Chatziralli

TITLE: Optical coherence angiography changes in macular area in patients with proliferative diabetic retinopathy treated with panretinal photocoagulation: Preliminary results of a prospective study

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Chatziralli, E. Dimitriou, D. Kazantzis, G. Theodossiadis, P. Theodossiadis, 2nd Department of Ophthalmology, National and Kapodistrian University of Athens, GREECE|

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ABSTRACT BODY:

Purpose: Controversy exists regarding the impact of panretinal photocoagulation (PRP) in retinal perfusion in patients with proliferative diabetic retinopathy (PDR). The purpose of this prospective study was to evaluate the changes of foveal avascular zone (FAZ) area and vessel density (VD) in superficial (SCP) and deep capillary plexus (DCP) in association with functional changes in patients with PDR treated with PRP.

Methods: Participants in this study were 16 patients with PDR and no macular edema, who were eligible for PRP. All participants underwent best-corrected visual acuity (BCVA) measurement, optical coherence tomography (OCT) and OCT angiography (OCTA) at baseline (before treatment) and at months 1 and 3 after completion of PRP treatment. Comparison of OCTA parameters and BCVA between baseline and months 1 and 3 after PRP was performed. Correlation of OCTA parameters and BCVA was also done.

Results: 22 eyes of 16 patients with PDR were included in the study. There was a statistically significant decrease in FAZ area at month 3 of the follow-up period compared to baseline ($p < 0.001$), while no difference was noted at month 1 of the follow-up period ($p > 0.05$). Of note, FAZ became significantly more circular 3 months after PRP ($p = 0.022$). There was no statistically significant difference in VD in both SCP and DCP at month 1 and 3 of the follow-up period ($p > 0.05$ in all comparisons). The FAZ area was associated with BCVA during the whole follow-up period ($p < 0.001$, $p = 0.014$ and $p < 0.001$ for baseline and months 1 and 3 respectively).

Conclusions: Although VD was not significantly affected by PRP at the short-term follow-up of 3 months in patients with PDR, the FAZ area became significantly more circular and decreased significantly at month 3 of the follow-up period, suggesting that re-distribution of blood flow may occur in hypo-perfused foveal capillary plexus after PRP in patients with PDR.

CONTROL ID: 3543500

SUBMITTER (NAME ONLY): Shin Kadomoto

TITLE: Ultrastructural Changes of Hard Exudates in Retinal Vein Occlusion Examined by Offset Pinhole Adaptive Optics Scanning Light Ophthalmoscope

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kadomoto, Y. Muraoka, A. Uji, M. Ishikura, N. Nishigori, A. Tsujikawa, Kyoto University, Kyoto City, JAPAN|

Commercial Relationships Disclosure (Abstract): Shin Kadomoto: Commercial Relationship(s);Canon:Code R (Recipient);Santen:Code R (Recipient);Nidek:Code R (Recipient) | Yuki Muraoka: Commercial Relationship(s);Novartis Farma K.K.:Code R (Recipient);Nidek:Code R (Recipient);Canon:Code R (Recipient) | Akihito Uji: Commercial Relationship(s);Canon:Code R (Recipient);Santen:Code R (Recipient);Nidek:Code R (Recipient) | Masaharu Ishikura: Commercial Relationship: Code N (No Commercial Relationship) | Naomi Nishigori: Commercial Relationship: Code N (No Commercial Relationship) | Akitaka Tsujikawa: Commercial Relationship(s);Nidek:Code F (Financial Support);Santen:Code F (Financial Support);Canon:Code F (Financial Support);Novartis Farma K.K.:Code F (Financial Support);Bayer:Code F (Financial Support);Alcon:Code R (Recipient)

ABSTRACT BODY:

Purpose: Adaptive optics scanning light ophthalmoscope (AOSLO) is considered to be well-positioned to detect early manifestations of retinal pathology. Additionally, offsetting the confocal aperture in the AOSLO enables the blocking of specular reflection from the inner retina and the enhancement of the image contrast of the retinal structures. Our purpose was to investigate the ultrastructure of hard exudates (HEs) in patients with retinal vein occlusion (RVO) using offset pinhole AOSLO.

Methods: Six eyes of 6 patients (2 men and 4 women; mean age, 67 years) with RVO were studied. The prototype offset pinhole AOSLO (Canon Inc., Tokyo, Japan) used in this study is capable of real-time correction of ocular aberrations during imaging, which allows a transverse resolution of approximately 3 μm (beam diameter: 6.7 mm) with pupil dilation. The pinholes were offset by 180 μm (3.75 airy disk diameter) in opposite directions in the plane horizontal to the retina. The HEs were examined by color fundus photography (CFP), and the offset pinhole AOSLO at 6 and 12 months after the onsets.

Results: On CFP, the HEs associated with RVO were seen as yellowish cylindrical structures, which were considered to be obliquely oriented in the Henle's fiber (Fig. 1). In contrast, the offset pinhole AOSLO resolved homogeneously hyperreflective crystalline units inside the cylindrical structure of the HEs (Fig. 1). The mean size of the crystalline units was $32.7 \pm 2.8 \mu\text{m}$ at 6 months. Parts of the crystalline units of the HEs were longitudinally disrupted, and the unit formations of the HEs were obscured at 12 months (Fig. 1).

Conclusions: Using offset pinhole AOSLO for eyes with RVO, the crystalline units of HEs and the longitudinal changes were observed with high contrast, which could not be elucidated by CFP.

CONTROL ID: 3543503

SUBMITTER (NAME ONLY): Conrad Merkle

TITLE: Melanin identification using spectroscopic OCT and clinical feasibility evaluation

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Melanin content in the retina can be identified non-invasively by polarization-sensitive optical coherence tomography (PS-OCT), however few clinical OCT systems have the hardware required to perform this analysis. Here, we propose to use traditional OCT at the clinical 840 nm wavelength range to obtain similar identification of melanin content through spectroscopic analysis to make this biomarker available to more clinical systems.

Methods: In this study, a custom PS-OCT ophthalmoscope for rodent retinal imaging was used to acquire PS-OCT and traditional OCT data simultaneously. Retinal data was acquired from a very-low-density lipoprotein receptor (VLDLR) mouse model using a traditional volumetric angiogram scan profile with 5 B-scan repeats at each slow-axis position. The VLDLR model presents with substantial retinal lesions and migration of melanin into the inner retina. Spectroscopic processing split the OCT spectrum into 20 channels across an 85 nm band from 803 to 888 nm (Figure 1). Clinical feasibility testing used the central 10 channels for a narrower 40 nm bandwidth from 825 to 865 nm. A spectroscopic filter was developed to highlight positive spectral slopes associated with melanin and was compared against PS-OCT and traditional OCT in the VLDLR model.

Results: Images of melanin using the spectral filter method produced similar features to those obtained from PS-OCT including melanin migration and disruption of layers containing melanin in the VLDLR model. It was noted that the spectral filter was in general noisier than the PS-OCT signal and presented artefactual signals below large vessels. While the spectral filter images were further noisier using the 40 nm clinical bandwidth rather than the full 85 nm bandwidth, key features could still be distinguished. Intensity images were not able to specifically distinguish the above features.

Conclusions: The presented spectral filter for melanin identification was able to show similar information to PS-OCT. While the spectral filter did not provide as robust of a signal as PS-OCT, it did not require PS-OCT hardware, which few clinical OCT systems possess. For this reason, this spectroscopic approach may allow more rapid enhancement of clinical OCT by using existing clinical systems with spectroscopic post-processing.

CONTROL ID: 3543504

SUBMITTER (NAME ONLY): Takahiko Hayashi

TITLE: Descemet Membrane Endothelial Keratoplasty (DMEK) in vascularized high-risk eyes

SESSION TITLE: Corneal transplantation and surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Hayashi, Ophthalmology, Nihon Daigaku Igakubu Daigakuin Igaku Kenkyuka, Itabashi-ku, Tokyo, JAPAN|W. Zhang, D. Hos, S. Schrittenlocher, S. Siebelmann, M. Matthaei, B. Bachmann, F. Bock, C. Cursiefen, Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|V.N. Le, Ophthalmology, Hue College of Medicine and Pharmacy, Hue University, VIET NAM|

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ABSTRACT BODY:

Purpose: Although DMEK has lower rates of immune reaction in non-vascularized low-risk eyes, the outcome of DMEK in vascularized eyes, has been unknown. Therefore, the aim of this study was to analyze the clinical outcome of DMEK in vascularized high-risk eyes.

Methods: This retrospective single-center consecutive study included the patients after DMEK which were selected from the prospective Cologne DMEK Database between 2012 and 2017 at University of Cologne, Germany. This study was performed in accordance with the tenets of the Declaration of Helsinki, and the protocol was approved by the local ethical review committee (14-373). The clinical outcomes were evaluated from the medical record.; best corrected visual acuity (BCVA; converted to logarithm of the minimum angle of resolution [logMAR]), central corneal thickness (CCT), endothelial cell density (ECD), rebubbling, cystoid macular edema (CME), immune reactions, and graft failure are evaluated. In addition to the standard ophthalmic examinations, neovascularization (NV) was graded from the slit-lamp pictures in a standardized fashion, as previously described.

Results: In this study, 24 eyes of 24 patients were selected (mean age, 65.0 years; mean follow-up duration, 14.8 months [6–36 months]), which included 14 vascularized eyes after failed PK, nine vascularized eyes with long-standing bullous keratopathy, and one vascularized eye with chemical burn. There was no primary graft failure in any case. The BCVA improved from 1.60 ± 1.02 logMAR, preoperatively, to 0.47 ± 0.37 logMAR, 12 months postoperatively ($p < 0.001$). The CCT decreased from 824 ± 193 μ m, preoperatively, to 544 ± 48 μ m, 12 months postoperatively ($p = 0.001$). The donor corneal endothelial cell density (ECD) decreased from $2,272 \pm 723$ cells/mm², preoperatively, to $1,570 \pm 279$ cells/mm², 12 months postoperatively. The total loss of ECD after the surgery was $40.7\% \pm 13.0\%$. Eight of 24 eyes (33.3 %) required rebubbling. There was no cystoid macular edema during the follow-up in this case series. Immune reactions occurred in one of 24 eyes (4.2 %) after DMEK. Interestingly, the NV score significantly improved from 2.00 ± 0.49 quadrants to 1.53 ± 0.50 quadrants ($p = 0.014$, Wilcoxon test). The representative picture is shown in Figure 1.

Conclusions: DMEK could be a good option to treat endothelial dysfunction with vascularized high-risk eyes successfully.

CONTROL ID: 3543507

SUBMITTER (NAME ONLY): Patrícia Ottaiano

TITLE: Comparison of self-confidence between glaucoma and age-related macular degeneration patients who live in a developing country.

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Ottaiano, C.S. Germano, K.S. Tomishige, R.M. Maccione, N. Kasahara, Ophthalmology, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, BRAZIL

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ABSTRACT BODY:

Purpose: The correct performance of daily life activities, e.g. walking and manipulating objects, requires good postural control. Self-confidence to perform daily activities is a function decreased in the elderly. Age-related macular degeneration (AMD) patients report decreased level of confidence in performing specific activities without losing balance or becoming unsteady. This topic, however, has not been extensively studied in patients with eye diseases especially in low-middle income countries. This cross-sectional, case-control study aimed to compare the self-confidence between primary open-angle glaucoma (POAG) and AMD Brazilian patients.

Methods: Patients with AMD, POAG, and normal controls underwent a complete eye examination including measurement of best-corrected visual acuity, biomicroscopy, tonometry, eye fundus evaluation, and all participants answered the Brazilian-Portuguese version of the Activities-specific Balance Confidence (ABC) scale. The ABC scale is a 16-item questionnaire with 11-point subscales. Each individual item measures the level of confidence in performing a specific task without losing balance or becoming unsteady by asking participants to assign scores ranging from 0 (no confidence) to 100% (totally confident). A 50-80% score indicates a moderate level of physical functioning. Scores were compared among groups with the ANOVA test.

Results: The sample comprised 48 patients with AMD, 56 with POAG, and 53 controls. All groups were matched for age, gender, ethnic distribution, and comorbidities. The ABC scale score was lower for both POAG (63.5 ± 25.7) and AMD (69.9 ± 24.9) as compared to controls (95.3 ± 9.1 , $P < 0.000$); POAG patients scored lower than AMD ($P = 0.026$, Tukey HSD).

Conclusions: In this cohort of Brazilian subjects, POAG patients reported lower self-confidence performing daily activities without losing balance more than AMD patients and are at higher risk of falling. This observation might be related to loss of peripheral vision.

CONTROL ID: 3543508

SUBMITTER (NAME ONLY): Caroline Germano

TITLE: Comparison of the illness perception between age-related macular degeneration and glaucoma patients living in a middle-income country

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.S. Germano, P.A. Ottaiano, R.M. Maccione, K.S. Tomishige, N. Kasahara, Ophthalmology, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: Once diagnosed with a disease, patients develop organized patterns of beliefs about their condition. Negative illness perceptions can lead to poor recovery and increased healthcare use regardless of objective measures of disease severity. This topic has not been extensively studied in patients with eye diseases especially in low-middle income countries. Individuals' perceptions vary across different populations and affect coping styles. This cross-sectional, case-control study aimed to compare the illness perception between primary open-angle glaucoma (POAG) and age-related macular degeneration (AMD) Brazilian patients.

Methods: Patients with AMD, POAG, and normal controls underwent a complete eye examination including measurement of best-corrected visual acuity, biomicroscopy, tonometry, eye fundus evaluation, and all participants answered the Brief Illness Perception Questionnaire (Brief IPQ) to assess mental defeat. The Brief IPQ has 9 items rated using a 0-to-10 response scale. Five of the items assess cognitive illness representations: consequences, timeline, personal control, treatment control, and identity. Two of the items assess emotional representations: concern and emotions. One item assesses illness comprehensibility. The summed score was compared among the groups with the ANOVA test.

Results: The sample comprised 48 patients with AMD, 56 with POAG, and 53 controls. All groups were matched for age, gender, ethnic distribution, and comorbidities. Both AMD and POAG patients scored higher than normal controls (50.4 ± 10.5 , 49.5 ± 14.4 , and 10.7 ± 17.6 , respectively, $P < 0.000$). The difference between AMD and POAG did not reach statistical significance (Tukey HSD $P = 0.978$).

Conclusions: Despite clinically and pathogenically different diseases, POAG and AMD patients had similar illness perceptions in a cohort of patients who live in a middle-income country. These results can help patients to take specific actions to regulate their emotions and improve the treatment outcome of their illness.

CONTROL ID: 3543509

SUBMITTER (NAME ONLY): Felix Goldbach

TITLE: Impact of baseline vitreomacular interface status on the treatment choice between aflibercept, bevacizumab or ranibizumab for diabetic macular edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Goldbach, G. Mylonas, B. Haj Najeeb, G. Deak, M. Michl, B. Gerendas, U. Schmidt-Erfurth, Department of Ophthalmology and Optometry, Medizinische Universität Wien, Wien, Wien, AUSTRIA|J. Brugger, Center for Medical Statistics, Informatics, and Intelligent Systems (CeMSIIS), Medizinische Universität Wien Universitätsklinik für Innere Medizin I, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To investigate the impact of baseline vitreomacular interface (VMI) status and anti-vascular endothelial growth factor (Anti-VEGF) therapy on treatment outcomes in patients with diabetic macular edema (DME) treated with aflibercept, bevacizumab or ranibizumab.

Methods: Post hoc analysis of prospective randomized 12-month multicenter clinical trial data from patients enrolled in the DRCR.net Protocol T study. The source of the data is the DRCR Retina Network, but the analyses, content and conclusions presented herein are solely the responsibility of the authors and have not been reviewed or approved by DRCR Retina Network. In this study, 660 patients with DME were randomly assigned to aflibercept, bevacizumab or ranibizumab. Optical coherence tomography images from patients who completed the month 12 visit of the study were analyzed at the baseline and at the last visit to identify the presence of total vitreomacular adhesion (VMA), partial vitreomacular adhesion, vitreomacular traction syndrome and total posterior vitreous detachment (PVD). Grading for all the above-mentioned variables were made by two trained and certified readers of the Vienna Reading Center.

Results: Six hundred sixty eyes (660 patients) were randomized in the Protocol T study. Six hundred twenty-nine were eligible for this post hoc analysis based on the study criteria. Total adhesion patient group gained 3.7 more ETDRS letters whereas patients with partial VMA gained 3.1 more ETDRS letters on average compared to the total PVD group at the end of the 12 months follow up ($p < 0.001$). Baseline VMI status had no significant influence on CST at the 12 months visit ($p = 0.144$). All three investigated agents used in the Protocol T study showed equal effectiveness on the improvement of VA and on the reduction of macular edema, independently of baseline VMI status.

Conclusions: This study adds evidence that the VMI status impacts functional outcomes in patients with DME treated with anti-VEGF agents. Patients with total or partial VMA at baseline may derive greater improvements in visual acuity after anti-VEGF treatment compared with those with total PVD.

CONTROL ID: 3543518

SUBMITTER (NAME ONLY): Imran Khatri

TITLE: Frequency and Type of Incidentally Found Pathology During Pars Plana Vitrectomy with Secondary Intraocular Lens Placement

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Khatri, M.D. Karl, M.P. Ohr, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a lack of literature describing the frequency of incidentally found pathology during pars plana vitrectomy (PPV) with insertion of a secondary intraocular lens (IOL). We performed a retrospective chart review to report on the frequency and type of pathology discovered during PPV with secondary IOL insertion.

Methods: Operative notes for surgeries performed by a single surgeon at an academic tertiary hospital between January 1, 2015 and January 1, 2020 were reviewed. A total of 208 PPV with insertion of secondary IOL surgeries were performed during this time. Eyes with a prior history of significant trauma (n=31), history of complicated cataract surgery at the time of initial IOL insertion (n=11), a history of prior PPV in the operative eye (n=16), or with inadequate data in patient chart (n=3), were excluded (n=61). Variables recorded from charts were age, gender, laterality, lens status, presence and type of peripheral retinal pathology on both pre-operative and intra-op scleral depressed exam, whether intra-operative intervention was performed for this pathology, and whether secondary IOL placement was deferred due to pathology discovered.

Results: Out of the initial 208 cases reviewed, 146 eyes from 140 patients (89 male, 51 female) met inclusion criteria. Of these 146 eyes, 30 (20.5%) had incidental pathology discovered intraoperatively where treatment was deemed necessary. The attached figure displays the type of pathology found. Unspecified retinal breaks were found in 10 out of 30 eyes, retinal holes in 5 out of 30, horseshoe tears in 2 out of 30, retinal tufts in 5 out of 30, lattice degeneration in 8 out of 30, retinal hemorrhage in 1 out of 30, and an ora bay in 1 out of 30.

Of the total 146 eyes, 18 (12.3%) were treated with laser, 14 (9.6%) were treated with cryotherapy, and 11 (8.2%) received gas (C3F8, n = 4 [2.7%]; SF6, n = 8 [5.5%]). Of the 146 eyes, 8 (5.48%) were discovered to have peripheral pathology that deferred secondary IOL placement and required a second surgery for lens placement, if the patient desired.

Conclusions: Incidentally discovered pathology is common during pars plana vitrectomy for placement of a secondary intraocular lens. Surgeons should proceed cautiously and perform careful scleral depressed exam intraoperatively to minimize risk of leaving untreated pathology in vitrectomized eyes.

CONTROL ID: 3543520

SUBMITTER (NAME ONLY): Anaïs Françon

TITLE: Evaluation of the Blue Light Hazard weighting in phototoxicity in a rat model

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Currently, the evaluation of the phototoxicity of light sources focuses on their blue component. Light spectra are weighted using the Blue Light Hazard (BLH) curve that peaks at 445nm. Thus, the blue component is considered as the only source of phototoxicity. The other wavelengths of the spectrum, such as green or red, are assumed to be non-toxic for the retina. In addition, the phototoxicity threshold for blue light at 445nm is used to define the limit exposure value (LEV) and corresponds to an energetic retinal dose of $11\text{J}/\text{cm}^2$ for rodents. Here, we aim to evaluate the state that only blue wavelengths are phototoxic and the pertinence of the current LEV.

Methods: Male Wistar rats were exposed to light-emitting diodes (LED) displaying different wavelengths and at various retinal doses. Damages induced by light exposure were evaluated by immunostaining and TUNEL staining on retina sections or flat mounts of the retinal pigmented epithelium (RPE).

Results: We show that at a retinal dose 20-fold lower than the phototoxicity threshold, blue and white LED induce a significant retinal degeneration characterized by rod demise. When analyzing cell death and oxidative stress after exposure to LED, BLH-weighted retinal doses of $0.2\text{J}/\text{cm}^2$ and $0.02\text{J}/\text{cm}^2$ for blue and white LED respectively constitute the thresholds at which almost no damage is observed. Moreover, addition of a red component, by simultaneous exposure of rats to white and red LED, significantly decreases photoreceptor cell death. LED-induced damages are also observed in the RPE with changes in the RPE cell structure and size, and patches accumulation of rhodopsin aggregates.

Conclusions: Taken together these results suggest that the phototoxicity threshold for rat could be overestimated by a factor of 50. Moreover, we note differences in the effects of blue and white LED at similar retinal doses, highlighting the negative impact of the other wavelengths contained in white light on phototoxicity. Also, the protective effect of the red component underlines the different effects of each part of the spectrum, indicating that the evaluation of phototoxicity should not be restricted to the blue part of the spectrum. Thus, the use of the BLH weighting to assess the LEV must be reconsidered.

CONTROL ID: 3543521

SUBMITTER (NAME ONLY): Friederike Kortuem

TITLE: Short term morphological rescue of the fovea after gene therapy with voretigene neparvovec

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.C. Kortuem, M. Kempf, R. Jung, C. Kortum, S. Ott, K. Stingl, K. Stingl, Ophthalmology, Eberhard Karls Universitat Tübingen, Tübingen, Baden-Württemberg, GERMANY|M. Kempf, K. Stingl, K. Stingl, Centre for Rare Eye Diseases, Eberhard Karls Universitat Tübingen, Tübingen, Baden-Württemberg, GERMANY|S. Kohl, Institute for Ophthalmic Research, Eberhard Karls Universitat Tübingen, Tübingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Leber congenital amaurosis type 2 (LCA2) and early-onset severe retinal dystrophy (EOSRD) are linked to visual impairment with nyctalopia and visual acuity reduction in early childhood. In 2017, the first gene therapy voretigene neparvovec (LuxturnaTM) for patients with LCA and EOSRD caused by bi-allelic mutations in the RPE65 gene has been approved. Here we report on an example of short-term change in the foveal morphology after functionally successful gene therapy with voretigene neparvovec in a 15-year old patient.

Methods: The clinical examinations included best corrected visual acuity (BCVA), spectral domain optical coherence tomography (OCT) and adaptive optics retinal imaging.

Results: During follow-up over a period of three months after the treatment an improvement of the photoreceptor structure could be observed in OCT, with a clear demarcation of the external limiting membrane and changes in the photoreceptor mosaic on adaptive optics retinal imaging. These morphological rescue parameters correlated in part with the improvement in foveal mediated vision after the treatment and adaptive optics imaging. Although the visual acuity improved only slightly at month 3, objective central cone evaluation with chromatic pupil campimetry showed an increase in the central function. In daily life, the patient reported her visual experience after the treatment as 'brighter'.

Conclusions: Rapid changes in the photoreceptor morphology after successful gene therapy in patients with LCA/EORD can be quantifiable on individual level.

CONTROL ID: 3543522

SUBMITTER (NAME ONLY): Antoine Rivail

TITLE: Topographic conversion model of outer retinal atrophy progression in intermediate age-related macular degeneration using deep learning

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Rivail, G.S. Reiter, S. Riedl, J. Mai, W. Vogl, C. Grechenig, U. Schmidt-Erfurth, H. Bogunovic, Department of Ophthalmology and Optometry, Medizinische Universität Wien, Wien, Wien, AUSTRIA|Z. Wu, R.H. Guymer, Centre for Eye Research Australia, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|Z. Wu, R.H. Guymer, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To investigate morphological risk factors and their precise quantification using deep learning algorithms for INL/OPL subsidence (at least subsidence of INL-OPL and OPL-ONL junctions) in patients with incipient macular atrophy (iMA) using a local survival model.

Methods: A series of anatomical features were extracted with deep learning methods in a cohort of eyes with bilateral large drusen at baseline: photoreceptor (PR) thickness, outer nuclear layer (ONL) thickness and drusen thickness (DT). Areas of INL/OPL subsidence were manually annotated in every eye which developed iMA during the 36-months follow-up. For each eye, the retina was divided in three zones at the visits preceding the first observed subsidence: zone of INL/OPL subsidence at first appearance, zone over drusen (>40µm height) and reference zone (rest of the 3mm circle, centered on fovea); an example is presented in figure 1. Average values for the anatomical features were computed for each zone. A mixed effects Cox survival model (one group per eye) was fitted to estimate the hazard ratio for each zone.

Results: Out of 280 eyes, 54 eyes developed iMA, of which 52 eyes, presented with INL/OPL subsidence prior to iMA, were selected. For each anatomical feature (PR, ONL and DT), the average zone values were normalized and fed to the survival model. The fitted model coefficients were -0.83 for PR ($p<0.001$), -0.56 for ONL ($p<0.01$) and -0.25 for DT ($p=0.15$). Negative values indicate higher risk for thinner PR, ONL and DT. Therefore, PR thinning and ONL thinning were found to be significant risk factors of INL/OPL subsidence development in iMA patients with a hazard ratio at one standard deviation under the mean of 2.86 and 2.13, respectively. However, drusen thickness was not found to be a significant factor.

Conclusions: Survival analysis of anatomical features in early INL/OPL subsidence eyes allowed us to identify PR thinning and ONL thinning as risk factors for the development of INL/OPL subsidence. This indicates that these subtle changes occur in the outer retina before becoming clinically apparent as macular atrophy. This highlights the importance of protecting PR integrity for potential early intervention in AMD. AI algorithms are essential to identify and precisely measure subclinical early morphological changes on OCT.

CONTROL ID: 3543523

SUBMITTER (NAME ONLY): Alessandra Carmichael-Martins

TITLE: Improved Adaptive Optics Scanning Laser Ophthalmoscope and lens for gonioscopic imaging

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Carmichael-Martins, T. Gast, B. King, S.A. Burns, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: To improve a gonioscopy lens (Goniolens) design coupled to a pupil-steerable Adaptive Optics Scanning Laser Ophthalmoscope (AOSLO) for high-resolution imaging of the iridocorneal angle (ICA). While glaucoma is a multifactorial disease, intraocular pressure (IOP) is the only modifiable risk factor and many treatments are aimed at the trabecular meshwork (TM). We recently reported using AO gonioscopy to image the TM at high resolution (King et al. 2019). However, the source of optical aberrations in normal gonioscopic imaging is unclear, and most Goniolenses are not optimized for this purpose. We propose a new Goniolens design to improve optical image quality and light coupling from an enhanced AOSLO to allow imaging of different regions of the TM.

Methods: The design of the Indiana University AOSLO was altered to 1) increase distance to the patient and 2) allow beam steering to image different regions of the ICA while maintaining optical quality. A Goniolens was designed using ray tracing software (Zemax®) to improve performance given manufacturing and operating constraints. Light coupling from the AOSLO was improved by steering the imaging beam as it enters the Goniolens, while maintaining optical performance. Optical aberrations induced at the surfaces of the lens and model eye, as well as image quality at different positions of the ICA were analyzed.

Results: The AOSLO design allows beam steering via a tiltable field mirror over an area of 45x70mm at the pupil plane within the diffraction limit, allowing rotation of the Goniolens on the eye to image different sectors of the ICA. An air-spaced doublet button lens design reduced spherical aberration and improved RMS from 0.4λ , with the original singlet, to 0.04λ . Beam steering in the button lens enables access to the anterior segment with precise localization from the iris surface to the corneal endothelium with spot sizes of $\sim 5\mu\text{m}$ with only defocus and astigmatism AO correction.

Conclusions: A novel Goniolens was designed to improve optical quality and coupling between a new AOSLO and the TM. Beam steering facilitates imaging as the lens is rotated to different sectors of the ICA, and the beam can be steered from the pupil plane to target different tissues within the angle. This technique may allow further structural characterization of the TM in patients, and to monitor changes in glaucoma and following treatment.

CONTROL ID: 3543524

SUBMITTER (NAME ONLY): Taiji Nagaoka

TITLE: Retinal Blood Flow Dysregulation Precedes Neural Retinal Dysfunction in Type 2 Diabetic Mice

SESSION TITLE: Blood flow, ischemia, reperfusion

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Nagaoka, J. Hanaguri, H. Yokota, M. Watanabe, S. Yamagami, Ophthalmology, Nihon University School of Medicine, Tokyo, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: We investigated the susceptibility of retinal neurovascular coupling and neural function to type 2 diabetes.

Methods: The longitudinal changes in retinal neuronal function and blood flow response to a 3-minute flicker light stimulation and a 10-minute systemic hyperoxia were evaluated every 2 weeks in diabetes db/db mice and their corresponding controls (db/m) from age 8 to 20 weeks. The retinal blood flow and neural activity were assessed using laser speckle flowgraphy and electroretinography (ERG), respectively.

Results: The body weight and blood glucose levels were significantly higher in db/db mice while systemic blood pressure and ocular perfusion pressure were unchanged with age. The resting retinal blood flow was comparable between two groups throughout the study. Flicker light and hyperoxia elicited a consistent increase and decrease in retinal blood flow, respectively, in db/m mice independent of age. However, these flow responses were significantly diminished in db/db mice at 8 weeks of age and then became unresponsive to stimulations at 12 weeks.

Subsequently, the ERG implicit times for oscillatory potential wave was significantly increased at 14 weeks of age while the amplitude of all waves and the implicit time of a-wave and b-wave remained unchanged.

Conclusions: The retinal blood flow responses to flicker light and hyperoxia are gradually diminished during the progression of diabetes and the ERG alteration occurs at the time corresponding to exhausted retinal blood flow regulation. The deficiency of neurovascular coupling and flow regulation in the retina appears to precede neural dysfunction in the mouse with type 2 diabetes.

CONTROL ID: 3543527

SUBMITTER (NAME ONLY): Annechien E.G. Haarman

TITLE: Variable threshold burden style rare-variant tests identify novel genes associated with refractive error in a large multi-ancestry cohort

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Myopia is a complex refractive error trait with a rapidly increasing prevalence and visual burden world-wide. GWA studies have currently identified >500 common variants for refractive error, but they have not yet dissected many rare variants with potentially large effects. This study aimed to identify these variants using exome chip screening in a large multi-ancestry cohort.

Methods: A total of 10 population-based cohorts from CREAM were included in the current study and grouped into Indo-Europeans and East Asians. Exome array genotypes (Illumina HumanExome-12) were jointly called to increase the number of rare (i.e. MAF<1%) variants. Three other CREAM studies, the Raine Eye Health Study, Beaver Dam Eye study and EPIC-Norfolk, were used as replication cohorts.

Different approaches to analyses are useful because they have different strengths in their ability to identify candidate genes. We analyzed spherical equivalent (SER in diopters (D)) using the EMMAX version of the variable threshold (VT) test, which increases power on rare variants (compared to single variant tests) by creating a new gene-based marker. We meta-analyzed the p-values of all datasets (discovery and replication) together using the method described by Fisher, implemented in the R package metap. We conducted an IPA pathway analysis to assess enriched pathways and to prioritize genes based on predefined criteria.

Results: The total discovery study included 17,904 (13,037 Indo-European and 4,867 East-Asian) individuals with a mean (SD) SER of 0.01 (2.30) D. In the meta-analysis, which combined the VT results across all cohorts, 43 genes were found to be genome-wide significant (defined as $\leq 1 \times 10^{-5}$). The most significant gene was GDF15 on chromosome 19 ($P = 5.12 \times 10^{-9}$). 40% of the identified genes showed an association with a human ocular disease, 21% evidence of human ocular expression and 12% demonstrated an ocular phenotype in knock-out mice. Cell cycle processes and embryonic development were implicated as important underlying pathways. Among the most biologically plausible gene hits were CHST6 and GRHL2 ($P=8.99 \times 10^{-7}$ and $P= 1.42 \times 10^{-6}$ respectively); both associated with corneal dystrophies.

Conclusions: Using exome chip, we identified rare variants for refractive error in 43 novel genes. Further validation studies are necessary to evaluate their role in refractive error development.

CONTROL ID: 3543528

SUBMITTER (NAME ONLY): Yoshiaki Yasuno

TITLE: Imaging quality of Lissajous scan OCT for in vivo retinal imaging

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Motion correction of retinal OCT imaging is required for accurate assessment of diseases. We have developed Lissajous scan OCT which enables motion correction while preserving global structure. This study aims at comparing the image quality of Lissajous scan OCT with those of the conventional raster scan.

Methods: The Lissajous and raster scan OCT have been obtained by a custom-made 1.0- μm swept-source OCT device with a scan speed of 100,000 A-line/s. The motion-corrected raster scan OCTA has been obtained with DRI OCT Triton (Topcon Corp., Tokyo, Japan). For Lissajous scan OCT, the eye movements are estimated by co-registering small portions of the Lissajous scan. And motion-free three-dimensional volumes and en face images of OCT and OCT angiography (OCTA) images are created by using the estimated motion amounts.

Fifty-two eyes of 62 patients with retinal abnormalities were scanned over a $3 \times 3 \text{ mm}^2$ area. The motion-corrected superficial retinal OCTA images of Lissajous scan and raster scan have been evaluated by an expert grader and scored with six levels (0: low to 5: high). In 21 eyes of 21 subjects, cross-sectional OCT B-scan of Lissajous scan and raster scan have been compared.

Results: Figure 1 shows motion-corrected en face superficial OCTA images of a representative case. The mean score of motion-corrected superficial OCTA images were 3.7 for raster and 3.4 for Lissajous. Although the score of raster scan is slightly high, the difference was not statistically significant ($p\text{-value}=0.067$, Wilcoxon's signed-rank test). Figure 2 shows representative OCT B-scans of the raster and Lissajous scan at the almost same location. In 19 out of 21 eyes, both raster and Lissajous scans showed the same score. In 2 out of 21 eyes, Lissajous-scan-based B-scans showed a better score.

Conclusions: Lissajous scan OCT achieves comparable image quality in en face OCTA and cross-sectional OCT imaging to those of raster scan OCT.

CONTROL ID: 3543532

SUBMITTER (NAME ONLY): Timothy Plageman

TITLE: Arvcf maintains lens transparency through the stability of the adherens junctional complex in lens fiber cells

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.F. Plageman, K. Herman, N. Houssin, J. Martin, College of Optometry, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of cell adhesion in lens transparency is difficult to assess because of the developmental and physiological roles known adhesion proteins play in this process. We have discovered that Arvcf, a member of the p120-catenin subfamily of catenins which binds to the juxtamembrane domain of cadherins and regulates GTPase signaling, is strongly expressed in lens fiber cells and is important for maintaining lens transparency with age. Arvcf knock-out (KO) mice develop cortical cataracts at approximately 6 months of age without other developmental anomalies. Because of its potential role in lens fiber cell adhesion, it is hypothesized that the loss of Arvcf promotes cortical opacities due to a reduction in the stability of the cadherin complex and adhesion junctions between lens fiber cells.

Methods: The role for Arvcf in the lens was tested through biochemical screening and histological analysis of lenses from control and knock-out mice. Additionally, high-resolution microscopy methods including super-resolution confocal and scanning electron microscopy were utilized to assess changes to fiber cell morphology and protein localization.

Results: Lens fiber cell lysates from control and Arvcf KO mice were analyzed via mass spectroscopy following immunoprecipitation with N-cadherin antibody in order to determine how protein interactions were affected by the loss of Arvcf. We found that several proteins with known roles in promoting the stability of adherens junctions to have a significantly reduced ability to associate with N-cadherin including b-catenin, a-N-catenin and actin. Confocal analysis and quantitative localization experiments confirmed a significant reduction of these proteins between the junctions of lens fiber cells. Super-resolution imaging also demonstrated that the localization of cadherin associated proteins is significantly attenuated within the normally Arvcf-rich interlocking protrusions that emanate from the tricellular junctions of lens fiber cells in the region of cortical transparency loss of the lens.

Conclusions: These data indicate that the Arvcf protein maintains cortical transparency through the stabilization of the cadherin complex within interlocking protrusions and bicellular junctions of lens fiber cells. In addition, these results suggest that cortical cataracts may be caused by a decrease in cell adhesion between lens fiber cells.

CONTROL ID: 3543536

SUBMITTER (NAME ONLY): Ilias Milionis

TITLE: Utilization of metal complexes in the tears biomarkers assay

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Milionis, C.N. Banti, K. Sarakinou, S. Hadjidakou, Department of Chemistry, University of Ioannina, GREECE|I. Milionis, Eye Clinic, University Hospital Ioannina, Ioannina, Epirus, GREECE|

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ABSTRACT BODY:

Purpose: Reduced urea concentration, could lead to disorganization and decompose of the tear film which is related with Ocular Surface Diseases (OSD). Moreover, urea is an indicator for OSD, such as Dry Eye Syndrome (DES). Recent epidemiological studies show that DES is a common disorder, which appears especially in the elderly population, affecting up to 20 % of adults. The lack of clinical symptoms makes the diagnosis of DES very difficult. Nowadays, a colorimetric enzymatic method for determining urea is used in cell and tissue culture supernatants, urine, plasma, serum, and other biological samples. Therefore the development of new urea assay is a matter of research interest.

Methods: Copper(II) - urea complexes $\text{Cu}_2(\text{CH}_3\text{COO})_4\text{U}_2$ (1) and $\text{Cu}(\text{NO}_3)_2\text{U}_4$ (2), (U= urea) have been synthesized and characterized. Compounds 1-2 were used for the qualitative and quantitative determination of urea by Thin Layer Chromatography (TLC) densitometry assay and Fluorescence Spectroscopy:.

Results: For the determination of urea in tears, the graphs of the TLC spots intensity vs the concentration of standard solutions of 1 and 2 are used. The concentrations of 1 and 2 vs spot's intensity (Int) are linearly fitted. Tears were collected using Whatman paper and they were added into DMSO solution which contain copper(II) salts. The content of urea in the sample is determined by the complex:Urea molar ratio in 1 and 2. The quenching (by 66 (1) or 48 (2) %) at the energy emitted when the tears/DMSO solution were incubated with copper acetate or nitrate is also correlated with DES diagnosis.

Conclusions: The concentration level of urea in the tear fluid is a diagnostic biomarker for the detection of the dry eye syndrome (DES). The complexes 1 and 2 are used for their chromatographic and spectroscopic characteristics which consequently lead to the identification and determination of urea in tears. Although more experiments should be carried out before a reliable method could be established, however, the importance of urea in eye disorders diagnosis makes TLC-densitometry and fluorescence spectroscopy a possible candidate for the development of a novel urea assay

CONTROL ID: 3543538

SUBMITTER (NAME ONLY): Laura Kowalczyk

TITLE: Transscleral Optical Phase Imaging of healthy human Retinal Pigment Epithelium

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Kowalczyk, C. Moser, Laboratory of Applied Photonic Devices (LAPD), Ecole Polytechnique Federale de Lausanne Faculte des Sciences et Techniques de l'Ingenieur, Lausanne, SWITZERLAND| L. Kowalczyk, I. Mantel, A. Iskandar, A. Gryczka, A. Navarro, F. Jeunet, Jules-Gonin Eye Hospital, Fondation Asile des aveugles, Universite de Lausanne Faculte de biologie et medecine, Lausanne, VD, SWITZERLAND|R. Dornier, M. Kunzi, T. Laforest, EarlySight SA, SWITZERLAND|F.F. Behar-Cohen, Centre de Recherche des Cordeliers, From physiopathology of ocular diseases to clinical developments, INSERM, Paris, Île-de-France, FRANCE|F.F. Behar-Cohen, Ophtalmopôle, Cochin Hospital, Assistance Publique - Hopitaux de Paris, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The retinal camera using Transscleral Optical Phase Imaging (TOPI) provides in vivo images of retinal pigment epithelium (RPE) cells. We performed a clinical study to characterize healthy RPE cells and to assess the repeatability and the safety of the RPE imaging.

Methods: Healthy volunteers were recruited. After a standard eye examination, spectral domain optical coherence tomography, infrared, autofluorescence and color fundus imaging, they underwent TOPI examination. Six 5.04x5.04°, high resolution, in vivo images of RPE cells at different locations, associated with 30x30° infrared reflectance images, were acquired per eye. The ophthalmic examination was repeated 1 to 3 weeks after TOPI. RPE images were analyzed with a custom automated software to extract cell features. The coefficient of variation (CoV) of three parameters was established on 31 areas, imaged 3 to 7 times and realigned.

Results: Included were 52 eyes (axial length 24.1±0.96 mm) of 31 participants (age 36.5±13.2 years, range 21-70; 20 males, 11 females). Multimodal imaging showed no difference before and after TOPI. The cell features extracted from the RPE images covering an eccentricity of 1.9° to 16.9° from the fovea were: RPE density 3610±321 cells/μm², cell area 238±23 μm², intercellular distance 14.3±1.1 μm, circularity 0.88±0.019, elongation 0.63±0.025, border distance CoV 0.16±0.013, solidity 0.95±0.001. The number of neighboring cells was close to 5.7±0.1 whatever the age, eccentricity and axial length. Cell density remained constant with age and eccentricity, while it decreased with axial length (R²0.62). Morphological features slightly varied with age, with reduced circularity (R²0.22), increased elongation (R²0.21) and border distance CoV (R²0.22). The CoV calculated for density, area and intercellular distance were 3.9±1.7%, 4.4±1.9% and 2.7±3.1.

Conclusions: The present study demonstrates that in vivo human RPE imaging using TOPI is safe and repeatable. The quantitative analysis provides the first and significant database of in vivo RPE cell features, consistent with the previous in-vivo studies on RPE cells, that can be used as normative database for future diagnostics of retinal diseases at the single cell level.

CONTROL ID: 3543539

SUBMITTER (NAME ONLY): Emily Witsberger

TITLE: Refractive Outcomes of Superficial Keratectomy for Salzmann Nodular Degeneration

SESSION TITLE: Corneal transplantation and surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Witsberger, L. Maguire, S.V. Patel, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Salzmann nodule degeneration is associated with induced cylinder and irregular astigmatism that improve after nodule excision. The purpose of this study was to quantify changes in manifest refractive error and corneal curvature at 1 month and ≥ 12 months after Salzmann nodule excision.

Methods: In a retrospective consecutive series, changes in manifest refractive error (spherical-equivalent), mean keratometric power (Km), and best-corrected visual acuity (BCVA) were compared for 73 eyes of 58 patients who underwent superficial keratectomy for Salzmann nodular degeneration by 2 surgeons at Mayo Clinic in Rochester, MN between 2014 and 2019. Eyes with ocular comorbidities that might affect visual acuity or keratometry were excluded. Comparisons between preoperative and postoperative measurements were made by using generalized estimating equation models.

Results: Mean patient age was 66 years, and 68 patients (93%) were female. Spherical-equivalent manifest refractive error was -0.27 ± 2.66 D before nodule excision and became more myopic (-1.10 ± 2.78 D) at 1 month after nodule excision ($n=69$, $p<0.01$) with no change at 12 months ($n=14$, $p=0.13$). A myopic shift ≥ 0.5 D occurred in 65% of eyes, and >1.0 D in 36% of eyes. K_m increased from 42.7 ± 2.1 D before nodule excision to 44.2 ± 1.8 D at 1 month after excision ($n=49$, $p<0.01$). BCVA improved from 0.18 ± 0.15 logMAR (Snellen equivalent 20/30) before nodule excision to 0.06 ± 0.15 logMAR (20/23, $n=69$, $p<0.001$) at 1 month after excision with no change at 12 months ($n=14$, $p=0.73$).

Conclusions: In addition to the known change in cylinder, Salzmann nodule excision is associated with a clinically important myopic shift in most eyes caused by corneal steepening. Patients should be counseled about the likelihood of a myopic shift after nodule excision, and cataract surgery should be deferred to at least one month after nodule excision for keratometric stability.

CONTROL ID: 3543540

SUBMITTER (NAME ONLY): Hang Nguyen

TITLE: Comparison of Therapist Ratings to Low Vision Patient Self-Reports

SESSION TITLE: Visual Impairment and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Nguyen, K. Fujiwara, C. Bradley, R.W. Massof, Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare occupational therapist (OT) Functional Independence Measure (FIM) ratings of functional abilities to low vision patient self-reports using the Activity Inventory (AI).

Methods: 136 low vision rehabilitation patients served by 10 different OTs rated the importance and difficulty of goals in the AI before and after rehabilitation. For each goal rated with nonzero importance and difficulty, the patient's OT also rated the patient's independence using the FIM.

Ratings were analyzed using a Rasch model: The Method of Successive Dichotomizations (MSD), in R with item measures anchored. This allowed us to compare person measures estimated from patient ratings and from therapist ratings on the same scale.

Results: Rater bias can be estimated from the intercepts of Deming regression lines fitted to the pre- and post-rehabilitation data. The intercept for pre-rehabilitation data was -1.48 logits (SE = 0.24), while for post-rehabilitation it was 0.09 logits (SE = 0.24). This shows that patients and OTs were in agreement post-rehabilitation, but that OTs underestimated patients' functional abilities at baseline. In both cases the slopes were not significantly different from 1. The average difference between person measures from pre to post was 1.60 logits for OTs and 0.28 logits for patients rating themselves.

Conclusions: Our findings indicate a strong bias leading to overestimation of improvement in functional ability measures based on OT ratings relative to outcome measures based on patient self-reports in low vision rehabilitation.

CONTROL ID: 3543546

SUBMITTER (NAME ONLY): Matthew Muller

TITLE: Enhanced visualization of hyperpigmentation using near infrared multiply scattered light imaging

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Muller, A.E. Elsner, J.A. Papay, Aeon Imaging, LLC, Bloomington, Indiana, UNITED STATES|A.E. Elsner, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: To enhance AMD screening by improving the visibility of hyperpigmentation (HP) using near infrared (NIR) multiply scattered light imaging.

Methods: We compared two datasets of non-mydratic confocal and multiply scattered light images taken with the Digital Light Ophthalmoscope (DLO) (Aeon Imaging, LLC) using red (630 nm) and NIR (860 nm) light. The red and NIR dataset consisted of 21 subjects aged 48.2 \pm 15.3 yr, and 20 subjects aged 53.1 \pm 13.7 yr, respectively.

The DLO is a confocal retinal camera that projects illumination lines onto the retina that are synchronized to the readout of a CMOS rolling shutter camera. Multiply scattered light imaging is performed in real-time by applying leading and lagging timing offsets between the center of the illumination lines and detection aperture. The offsets were set to 0.5x and 1x the aperture widths of 51 and 102 micron for the red and NIR images, respectively.

DLO image frames were automatically registered, manually reviewed, and averaged. The coefficient of variation (CV) of the retinal background temporal to the OD macula was calculated in the confocal red and NIR images. HP was identified in 5 of the 20 NIR subjects. The Michelson contrast of the HP regions was computed for the NIR confocal, both offsets, and the mean of each leading and lagging offset pair.

Results: Choroidal vessel contrast contributed to a higher mean CV using red vs. NIR light (0.14 \pm 0.05 vs. 0.07 \pm 0.03). In an example AMD subject, the max HP signal in red-light images was achieved with confocal imaging, at 4.2 standard deviations < the adjacent mean background. In the corresponding NIR images, the max HP signal occurred at a 102 micron offset, at 5.0 standard deviations < the mean. Averaging the NIR offset pairs suppressed shadowing caused by drusen, reducing the variation in the adjacent background and further increasing the HP signal to 11.1 standard deviations < the mean.

The Michelson contrast in the NIR images of the 5 HP subjects was 0.09 \pm 0.01, 0.07 \pm 0.01, 0.06 \pm 0.01, 0.10 \pm 0.01 and 0.10 \pm 0.01 in the confocal, 51 micron offset, mean 51 micron offset pair, 102 micron offset, and mean 102 micron offset pair, respectively.

Conclusions: Real-time visualization of HP in the presence of nearby drusen can be improved by averaging the leading and lagging offset images. Averaging reduced distracting intensity variation in the adjacent retina while maintaining the Michelson contrast.

CONTROL ID: 3543547

SUBMITTER (NAME ONLY): Sumeet Sarin

TITLE: AAVHSCs, a Nuclease-Independent Approach for Transduction in Non-human Primate Brain and Retina and Editing of Retinal Cells in Human Organotypic Explants

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sarin, H. Chen, T. Seabrook, R. Resendes, S. Venu, J. Ellsworth, J. Wright, S. Krupa, O. Francone, J. Gingras, A. Seymour, Homology Medicines, Bedford, Massachusetts, UNITED STATES|C. Bell, T. McGee, Y. Qiu, Novartis Institutes for Biomedical Research (NIBR), Massachusetts, UNITED STATES|D.A. Ammar, N. Sprehe, Lions Eye Institute for Transplant & Research (LEITR), Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously shown that a subset of AAVHSCs (AAVHSC7, 15 and 17) cross the non-human primate blood-retinal barrier (BRB) and blood-brain barrier (BBB) following a single intravenous dose. We have now extended this analysis to a panel of 11 AAVHSC capsids. AAVHSCs can be used to transduce various cell types in the central nervous system and edit the genome of dividing cells in a nuclease-free manner. Here we investigate the tropism of AAVHSCs, specifically to the visual pathways, and investigate whether AAVHSCs can induce genome editing in human disease relevant retinal cells using ex vivo (human retinal explant cultures) models.

Methods: We delivered AAVHSCs intravenously (IV) to juvenile Cynomolgus macaques (non-human primates; NHPs), negative for neutralizing Clade F antibodies, with either formulation buffer (FB) or one of a total of 11 variant AAVHSC (4-7E13 vgs/kg, n = 25 macaques) vectors that contain a gene transfer construct expressing CBA.eGFP. We harvested brains and eyes at 2 weeks post-dose and monitored vector genomes (vgs) by ddPCR and eGFP expression by immunohistochemistry. In addition, two NHPs were dosed subretinally (SR @ 1E12 vgs/eye) with AAVHSC15-CBA.eGFP or FB. Human retinal explants were incubated with FB, or with (2.5E11vgs/explant) AAVHSC15-CMV.eGFP (n = 6), or AAVHSC15.B2M (n=12), a construct that contains homologous arms to edit the human beta-2-microglobulin (B2M) genomic locus.

Results: All AAVHSCs cross the BRB and BBB following a single-IV delivery in NHPs. The majority of AAVHSC capsids transduce retinal cells and retinofugal pathways including the retinogeniculate and retinotectal nuclei. Following a single-SR dose, AAVHSC15 transduces photoreceptors (PRs) and retinal pigment epithelial cells (RPE) in NHPs. Similarly, PRs are transduced in human retinal explants. Using next-generation sequencing, we confirm AAVHSC15.B2M-mediated integration into the human B2M locus.

Conclusions: In NHPs, AAVHSCs exhibit capsid selectivity along key relay points of the visual pathways. AAVHSCs are capable of transduction and genome editing in therapeutically relevant retinal cells based on results obtained in vivo (NHPs) and ex vivo (human). In human organotypic retinal explants, we demonstrate transduction and nuclease-free genome editing in disease relevant cell types.

CONTROL ID: 3543548

SUBMITTER (NAME ONLY): Emiliano Teran

TITLE: Machine-Learning Predictor of Refractive Error from Foveal Pit Characteristics

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study aims to determine the patient's refractive error from the foveal pit's morphology using tridimensional modeling of the foveal pit and machine-learning algorithms.

Methods: Eighty-five subjects (47 males and 38 females) with ages ranging from 18 to 27 were evaluated. We divided the study into three stages: (1) clinical, (2) extraction of the foveal pit morphology, and (3) machine-learning models. (1) The axial length (AL) and spherical equivalent (SE) of each participant were obtained with an IOL Master 700 and an autorefractometer. The spherical equivalent was also verified through wet retinoscopy. We classified the groups in terms of their mean axial length and spherical equivalent. (2) A 3D foveal pit model of each participant was obtained from images obtained with a Spectralis OCT (Heidelberg Engineering). We obtained three areas along with the pit: the rim, the mid, and the flat. The volume of the pit, the macula, and the retina were also calculated. (3) Then, we trained seven machine learning models: Artificial Neural Network (ANN), Classification and Regression Trees (CART), k-Nearest Neighbors (kNN), Linear Discriminant Analysis (LDA), Ordinal Logistic Regression (OLR), Support Vector Machines (SVM), and Random Forest (RF).

Results: (1) The short-eye group has an average axial length of 22.5 mm (21.82/22.89 mm) and a spherical equivalent of +0.5 D (+0.25/+1.5 D), the emmetropic group has an average axial length of 23.62 mm (23.08/24.46 mm), and an average spherical equivalent of -0.25 D (-2.0/+1.25 D), and the long-eye group has 25.48 mm (24.7/26.60 mm) of axial length and -3.75 D (-6.0/+0.5 D) of spherical equivalent. (2) We found that the rim's area presents the highest correlation with the refractive error of the patient. Mid and the flat areas are also good predictors of the patient's refractive status. Pit volumes showed a strong association with participants' refractive status. (3) The random Forest model shows the best performance with a predictive power of 77%.

Conclusions: The random Forest model shows the best performance in predicting axial refractive errors. This model was able to properly classify 77% of the subjects in one of the three groups: short-eyes (21 mm axial length), normal-eyes (23 mm axial length), and long-eyes (25 mm axial length).

CONTROL ID: 3543549

SUBMITTER (NAME ONLY): William Wong

TITLE: The Anti-Scarring Role of Lycium Barbarum Polysaccharide on Cornea Epithelial-Stromal Injury

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wong, A.C. Lo, Y. Chan, K.C. Shih, Ophthalmology, The University of Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: The study is to assess whether Lycium barbarum polysaccharide (LBP) solution can be a novel therapy in modulating fibroblasts differentiation after corneal epithelial- stromal injury in a three-dimension model.

Methods: A 3D model made of PDMS elastomers is created to mimic the anatomy and physiology of the corneal stroma. The chip consists of a cell culture chamber and is connected to two channels where medium or LBP is supplied. Human fibroblasts are suspended in collagen to form a three-dimensional hydrogel construct. Cells are pre-treated with optimized 2 mg/mL LBP for 24 hours, followed by 10 ng/mL TGF-b1 for another 24 hours.

Results: Fibroblasts pre-treated with LBP showed a decreased expression of alpha-smooth muscle actin, which is a prominent marker of myofibroblasts. Pro-fibrotic proteins such as vimentin, collagen II and collagen III are as well reduced. Cell-laden hydrogel pre-treated with LBP revealed no significant contraction compared to that in control group ($p=0.29$) while group pre-treated with TGF-b1 showed increased contraction by 17.3% ($p<0.001$). The stiffness of the hydrogel treated with TGF-b1 alone had an increase by 3.55-fold ($p=0.02$) yet that in the LBP group showed no significant difference compared to that in control group ($p=0.9964$)

Conclusions: LBP can be a potential topical therapy to prevent corneal scarring prior to surgery. Optimized LBP concentration can potentially lead to fewer adverse effects compared to standard pharmacological treatments while minimizing fibroblast differentiation.

CONTROL ID: 3543551

SUBMITTER (NAME ONLY): Fernando Abib

TITLE: Differences of the Endothelial Mosaic of Fuchs Endothelial Dystrophy examined by Non-Contact and Contact Corneal Specular Microscopes

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.C. Abib, Anatomy, Universidade Federal do Parana, Curitiba, PR, BRAZIL|F.C. Abib, Cornea, Prof. Fernando Abib Eye Clinic, Curitiba, Paraná, BRAZIL|

Commercial Relationships Disclosure (Abstract): Fernando Abib: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The Descemet Membrane Excrescences (DME) characterizes Fuchs Endothelial Dystrophy (FED). The most severe affected areas of the Endothelial Mosaic (EM) are the central and paracentral, the most preserved is superior. Specular Microscopy is a non-invasive examination to access the EM. The selection of the best CSM, Non-Contact (NC) or Contact (C), it helps to understand the degree of EM involvement in the FED, as a whole. Purpose: To know the profile and the degree of impairment of the EM by DME in the central area (CA) and in the furthest areas from the CA possible to be evaluated in FED patients examined by NC CSM and C CSM.

Methods: Cross-sectional study: 34 eyes of 17 patients with FED diagnosis at the Clinica de Olhos Prof. Dr. Fernando Abib (Curitiba, Brazil).

NC CSM (Tomey EM4000, USA) and C CSM (BioOptics, USA) were used to score the damage of the EM by EMD (Figure 1) in examinations performed consecutively by the same examiner. The scored areas of the EM: CA and furthest areas from the CA at 4 hours (4h), 8 hours (8h), and 12 hours (12h). The mean score (MS) of the examined areas were presented by statistical descriptive. The comparison of the MS between the studied areas with NC and C CSM will be reported in percentage of total agreement and up to one degree of disagreement ($\Delta 1$). Comparisons of MS of NC CSM versus C CSM were made at CA, 4h, 8h, and 12h using the T-Test for 2 dependent means (level of significance <0.05).

Results: Percentage of agreement (Figure 2) - CA: total agree 44%, $\Delta 1$ Agree 85%; 4h: total agree 2.9%, $\Delta 1$ agree 20%; 8h: total agree 11.7%, $\Delta 1$ agree 14.7%; 12h: total agree 0%, $\Delta 1$ agree 14.7%.

Comparison between NC and C CSM at the studied areas (Figure 2): CA not significant ($p>.05$); 4h significant ($p<.05$); 8h significant ($p<.05$); 12h significant ($p<.05$).

Conclusions: Examinations performed on FED patients, by NC CSM and C CSM in the CA of the EM, show similar results; at the most distant EM areas possible to be examined from the center by these devices (4h, 8h, 12h) the results are totally different.

The endothelial mosaic least affected by EMD was found when the same eyes were examined by C CSM, which means that NC CSM acquire EM images closer of the central area and C CSM get images beyond of those acquired by NC CSM. It is confirmed that C CSM assess the periphery of EM, NC CSM does not.

CONTROL ID: 3543558

SUBMITTER (NAME ONLY): Kristy Lee

TITLE: Establishing Standardized Criteria to Improve the Interpretation of Genetic Testing for Ocular Disorders

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In 2014 the American Academy of Ophthalmology recommended patients receive genetic testing for inherited eye diseases. This recommendation, along with sponsored genetic testing programs, has greatly increased utilization of genetic testing. While genetic testing can inform a clinical diagnosis and determine the inheritance pattern, the genetic basis of ocular diseases is diverse, requiring large comprehensive gene panels. This it can also lead to many candidate variants per patient, increasing the risk of a genetic misdiagnosis. Differing standards on variant calls, especially around variants of uncertain significance (VUS), can lead to different genetic interpretations.

The Clinical Genome Resource (ClinGen) is an international consortium funded primarily by the National Human Genome Research Institute of NIH to promote the standardization of gene and variant interpretation to improve clinical care. The Ocular Clinical Domain Working Group (CDWG) within ClinGen was established in 2019 to address this need for inherited eye diseases.

Methods: The CDWG convened an executive committee of clinicians and researchers with expertise in retinal, glaucoma and neuro-ophthalmology disorders. Expert panels (EP) are being developed to tackle gene curation (GCEP) to assess the association between a particular gene and a disease phenotype and variant curation (VCEP) to assess the pathogenicity of variants within selected genes with respect to a specific phenotype. The variant curation process has been given US FDA recognition.

Results: We established 2 GCEP's (Retina and Glaucoma/Neuro) and 4 VCEP's (OPA1, Glaucoma, LCA, X-linked retinal dystrophy) with an additional ABCA4 VCEP in development. The membership, curation protocols and gene curation results are available on the ClinGen website (<https://clinicalgenome.org/>). Variant classifications and supporting data will be available in the NIH ClinVar database.

Conclusions: By assessing the strength of gene/disease associations, standardizing FDA recognized gene-specific variant curation guidelines, sharing genomic data amongst expert members and incorporating data from existing

disease databases, the number of VUS will decrease, improving the value of genetic testing as a diagnostic tool and guiding patient eligibility for the growing clinical pipeline of genetic therapies for inherited retinal diseases.

CONTROL ID: 3543560

SUBMITTER (NAME ONLY): K Varsha Mohan

TITLE: Development of retinitis pigmentosa patients derived retinal neural like cells (RNLCs) for disease modelling strategies.

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mohan, Product Development Cell, National Institute of Immunology, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: The multipotent progenitor monocyte population in PBMCs have been used to generate cell which can be reconditioned called Reconditioned Monocytes (RM). These RMs have been sourced to differentiate in Retinal Neuron like Cells (RNLCs) in our lab. The RNLCs have shown to be a viable alternate to conventional cell-based therapy. Therefore, we aimed to analyse the potential of patient derived RNLCs for in vitro disease modelling for Retinitis Pigmentosa and a mutation specific in vitro model.

Methods: Differentiating RP patient derived PBMCs into RNLCs was established by the two- step approach. Wherein, the PBMCs were isolated by density centrifugation method. The PBMC layer was collected and the adherent monocyte cells were supplemented with dedifferentiation media for 6 days. The reconditioned monocytes cells were then supplied with re-differentiation media until the cells attain the retinal phenotype at day 8. For the disease modelling study the cells were characterized by in vitro apoptosis profiling and compared with exome and clinical data.

Results: Figure 1: Cumulative assessment of 40 RP patients against 30 healthy donors indicated that at D1 the monocytes were equally viable however apoptosis rates varied in the RP RLNCs with diverse patterns due to individual mutations' appearance in the RLNCs and surmounting the effect. Thus, individual mutation specific patterns were studied. Figure 2: (A) RP1 displayed higher rate of apoptosis on day14 when compared to D6 and D10. (B) RP7 displayed higher rates of RNLC apoptosis on D6 while the RLNC were increasing viable at subsequent D10 and D14.

Conclusions: Thus, the source retinal gene mutation manifests in the peripheral monocyte derived RLNCs and shows patterned apoptosis due to the directional manifestation of the developmental genes. In vitro study of patient specific behaviour of retina towards degeneration can help understand the effect of any drug or cell-based therapy and mimic the patient condition to clinically characterize the rate of degeneration in a step towards targeted personalized medicine.

CONTROL ID: 3543566

SUBMITTER (NAME ONLY): Jeanette Du

TITLE: Ahmed vs. Baerveldt Implant Outcomes in Resident Performed Surgeries

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Du, T. Tai, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: As glaucoma drainage implants (GDI) are increasingly used to treat refractive glaucoma, numbers of these surgeries performed by trainees have also increased. The objective of this study is to assess the safety and success of GDI surgeries performed by residents as primary surgeon. Baerveldt surgeries and post-operative care may be more complex than Ahmed surgeries, and therefore may have different outcomes in the hands of residents than in the hands of more experienced surgeons. Efficacy and complications will be compared with those reported in the literature.

Methods: This is a retrospective study conducted at a single academic institution. Records of subjects who underwent either Baerveldt glaucoma implant (BGI) or Ahmed glaucoma valve (AGV) placement from 2011-2016 were reviewed. Patients with prior penetrating keratoplasty, GDI surgery, or combined GDI-cataract surgery were excluded. Baseline patient characteristic and clinical data up to 4 years after surgery were obtained. Surgical success rate was defined as IOP maintained ≤ 21 and ≥ 5 , without need for further glaucoma surgeries or NLP vision.

Results: A total of 121 subjects were included in the study. 44 eyes received the Ahmed FP7 implant and 77 eyes received the Baerveldt 250 mm or 350 mm implant. Average pre-operative IOP was 32.3 mmHg. At months 1, 3, 6, 12, and 24, overall average IOP was 18.7, 17.2, 15.9, 15.6 and 15.0 mmHg, respectively. Average IOP was significantly different between AGV and BGI eyes only at months 3 and 6. The average number of glaucoma medications pre-operatively and at last follow up was 3.9 and 2.7, respectively. Success rates were not significantly different between the two devices at 6, 12, or 24-months (Table). There was no significant difference between Kaplan-Meier survival curves for the two devices ($p=0.074$).

Conclusions: GDI surgery performed by residents was effective in lowering IOP and decreasing number of pressure-lowering drops in patients with refractory glaucoma for up to 24-months. IOP was significantly higher for AGV versus BGI surgeries at months 3 and 6, corresponding with the hypertensive phase associated with AGV implantation. There were no significant differences in success rates detected between the devices. Longer follow up time and assessment of complication rates may better characterize the safety and efficacy of tube surgeries performed by residents.

CONTROL ID: 3543569

SUBMITTER (NAME ONLY): Emily Liu

TITLE: Visual field and Visual Acuity changes in the Natural History of Choroideremia

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the natural history of visual acuity (VA) and visual field (VF) sensitivity in choroideremia (CHM). Choroideremia (CHM) is an X-linked degenerative retinal disease caused by deletions or mutations in the CHM gene which impacts the Rab escort protein-1 (REP-1). Study of the natural history of CHM may inform future therapeutic approaches.

Methods: A global retrospective chart review of anonymized patient records from 8 institutions. Eligibility criteria included male and born between 01Jan1930 to 31Dec2005, genetically confirmed CHM, and ≥ 2 clinic visits spanning ≥ 5 years. Data including VA and kinetic VF sensitivity (measured by sum total meridian degrees) were collected.

Results: Deidentified medical charts from 125 males (age at clinic visit ranged 2-82 years) were collected. All had recorded VAs that were converted to a LogMAR score. Age and VA demonstrated a non-linear relationship: VA remained fairly stable through the fourth decade of life then worsened by a rate of 0.026 LogMAR per year. Kinetic VF sensitivity was available for 107 eligible subjects (age 7-82 years) and decreased with age. There was a statistically significant age-effect interaction by VF test type for both the I4e and V4e stimuli for each of the left and right eyes ($p < 0.001$). A 1-year increase in age decreased the I4e visual field by approximately 10.4 sum total meridian degrees for the left and right eyes; the V4e visual field decreased by approximately 24.3 sum total meridian degrees for the left and right eyes.

Conclusions: In a cohort of genetically confirmed CHM patients, VF deterioration occurs at a higher rate than visual acuity early in the disease, whereas VA decreases are more profound in the later stages.

CONTROL ID: 3543570

SUBMITTER (NAME ONLY): David Liao

TITLE: Intravitreal Injection of Allogeneic Human Retinal Progenitor Cells (hRPC) for Treatment of Retinitis Pigmentosa: A Prospective Randomized Controlled Phase 2b Trial

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Liao, D.S. Boyer, Retina Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|B.D. Kuppermann, M. Mehta, R. Kammer, B. Mills, J. Yang, H. Klassen, University of California Irvine, Irvine, California, UNITED STATES|P. Kaiser, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|J. Heier, A. Joseph, OCB, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: hRPC secrete neurotrophic factors that promote photoreceptor cell survival and function. This paracrine mechanism has shown promise as a therapy for RP agnostic to genetic subtype. A phase 2b trial was conducted to evaluate intravitreal injection of allogeneic hRPC for treatment of RP.

Methods: Patients with RP and best-corrected visual acuity (BCVA) between 20/80 and 20/800 were randomized to two treatment groups (single injection of 3.0×10^6 or 6.0×10^6 hRPC) or sham. The primary efficacy endpoint was mean change in BCVA at month 12. Secondary endpoints included a low luminance mobility test (LLMT), contrast sensitivity (CS), kinetic visual fields (VF), and a visual function questionnaire VA LV VFQ-48 (VFQ). Analyses included a per protocol population and a post hoc analysis in a target subgroup meeting the following criteria: 1) study eye with baseline central fixation, 2) study eye without severely constricted field ($\geq 12^\circ$ diameter), and 3) study eye did not have significantly worse BCVA than fellow eye (≤ 15 letters).

Results: 84 total patients were randomized; 8 were excluded from the per protocol analysis for protocol violations and 2 were lost to follow up (N=74). Mean changes in BCVA from baseline to month 12 were +2.81, +2.96, and +7.43 letters in sham (N=26), 3.0×10^6 hRPC (N=25), and 6.0×10^6 hRPC (N=23) groups, respectively. In the post hoc analysis of the target subpopulation, mean changes in BCVA from baseline to month 12 were +1.85, -0.15, and +16.27 letters in sham (N=13), 3.0×10^6 hRPC (N=13), and 6.0×10^6 hRPC (N=11) groups, respectively (p=0.003 for 6.0×10^6 hRPC vs sham). Improvements in the 6.0×10^6 group were also observed in all other secondary endpoints. hRPC treatment was well tolerated with generally minor and transient adverse events; there was one treatment related serious adverse event in the 3.0×10^6 hRPC arm (ocular hypertension that resolved with treatment), but none in the higher dose arm of 6.0×10^6 hRPC.

Conclusions: Intravitreal injection of hRPC is a novel approach for treatment of RP, independent of the genetic subtype. This phase 2b study demonstrates a strong safety profile and encouraging biological activity, warranting progression to phase 3.

CONTROL ID: 3543572

SUBMITTER (NAME ONLY): Alex Nixon

TITLE: 'Physiologic' Eye Growth in Myopic Children

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nixon, X. Cheng, N.A. Brennan, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Alex Nixon: Commercial Relationship(s);Johnson and Johnson Vision:Code E (Employment) | Xu Cheng: Commercial Relationship(s);Johnson and Johnson Vision:Code E (Employment) | Noel Brennan: Commercial Relationship(s);Johnson and Johnson Vision:Code E (Employment)

ABSTRACT BODY:

Purpose: Emmetropic eyes show 'physiologic' eye growth, an ongoing elongation of the eye during childhood and teenage years in the absence of substantial refractive change, attributable to loss of crystalline lens power. It has been hypothesized that a proportion of growth in myopic eyes is also physiologic and not directly linked to refractive progression. However, Mutti et al (OVS, 2012;89:251) among others have reported that lens thinning ceases rather abruptly during myopia onset, raising the question of the existence of this component of growth in myopes in the absence of significant changes to corneal curvature.

Methods: Subject data were drawn from control groups described in Cheng et al (Acta Ophthalmol 2020;98:e346). Changes in spherical equivalent cycloplegic autorefraction (Δ SECAR; WAM-5500) and axial length (Δ AL; IOLMaster) were available for untreated right eyes of myopes aged 8 to 11 years at one (N= 151) and two (N= 99) years follow-up. Total least squares regression was performed across feasible values of λ (ratio of the measurement variance of Δ SECAR to that of Δ AL). The intercept of the regression line when Δ SECAR was equal to zero was taken to be physiological eye growth (figure 1). 95% CIs for this intercept were obtained by bootstrapping.

Results: The results were sensitive to λ , but even in the extreme case of $1/\lambda = 0$, the lower limit of the 95% CI was greater than zero, providing evidence for existence of physiologic growth in myopes (figure 2). No consistent change in physiological eye growth across age was detected within this group. Gradients relating Δ SECAR to Δ AL match expectations from optical calculations.

Conclusions: This analysis supports the existence of physiological eye growth in myopic children. Estimated size of physiological growth at 1- and 2- years seems to be less than that reported for emmetropes.

CONTROL ID: 3543575

SUBMITTER (NAME ONLY): Eduardo Martinez-Enriquez

TITLE: OCT-based anterior segment geometry changes with age and accommodation

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Martinez-Enriquez, M. Velasco-Ocana, S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To estimate anterior segment geometry upon accommodative demand for different ages, which will give insights on new strategies for presbyopia correction

Methods: 43 subjects participated in the study (ages 21 to 64; SE: +1.25 to 8.25D). Images of the eye's anterior segment were obtained while the subject viewed monocularly a Snellen E-letter, using custom 3-D spectral Optical Coherence Tomography (s-OCT, 840 nm, 25000 A-scans/s, axial range: 7 mm, axial pixel resolution: 3.4 μ m). 5 measurements (3-D images) were acquired (300 A-scans x 50 B-scans, 11-mm lateral range) for each of the different accommodative demands induced with a Badal optometer: 0-6 D (1 D-steps). Custom algorithms were used for geometrical quantification of Anterior Chamber Depth (ACD), Lens Thickness (LT), Anterior Lens Radius (RAL) and Posterior Lens Radius (RPL). Change of these geometrical parameters in the non-accommodative state (0D) with age, and change of the parameters per diopter of accommodative demand (acD) with age (i.e., how the geometry changes in response to an accommodation stimulus as a function of age) were evaluated in terms of linear correlations.

Equation of the best fitting line, Pearson correlation coefficient (r), and p -values for testing the hypothesis of no correlation were obtained

Results: For the non-accommodative state (0D), LT increased significantly with age ($p < 0.01$; $LT = 3.16 + 0.02 \cdot \text{age}$; $r = 0.76$), and the rest of parameters decreased significantly with age: ACD ($p < 0.01$; $ACD = 3.38 - 0.008 \cdot \text{age}$; $r = -0.37$), RAL ($p < 0.01$; $RAL = 13.07 - 0.06 \cdot \text{age}$; $r = -0.56$) and RPL ($p < 0.01$, $RPL = 6.79 - 0.012 \cdot \text{age}$; $r = -0.51$). Changes of the parameters per diopter (mm/D) with age were also obtained. $\Delta LT / \text{acD}$ decreased significantly with age ($p < 0.01$; $\Delta LT / \text{acD} = 0.11 - 0.0018 \cdot \text{age}$; $r = -0.84$), and the rest of parameters increased significantly with age: $\Delta ACD / \text{acD}$ ($p < 0.01$; $\Delta ACD / \text{acD} = -0.06 + 0.00096 \cdot \text{age}$; $r = 0.75$), $\Delta RAL / \text{acD}$ ($p < 0.01$; $\Delta RAL / \text{acD} = -1.14 + 0.02 \cdot \text{age}$; $r = 0.83$) and $\Delta RPL / \text{acD}$ ($p < 0.01$; $\Delta RPL / \text{acD} = -0.32 + 0.006 \cdot \text{age}$; $r = 0.71$). No parameter changed significantly with accommodative demand from around 55-60 y.o.

Conclusions: All the analyzed geometrical parameters decreased significantly with age in the non-accommodative state (0D) except for the LT, that increased, so that the lens becomes more rounded with age. Besides, changes of all the parameters in response to an accommodation stimulus are smaller in absolute value with age, leading to presbyopia around 55-60 y.o.

CONTROL ID: 3543581

SUBMITTER (NAME ONLY): David Birch

TITLE: Dark-adapted visual fields (DAVF) in patients with two disease-causing variants in USH2A

SESSION TITLE: Retinitis pigmentosa: clinical

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To identify and measure rod-mediated visual field thresholds using two-color dark-adapted chromatic (DAC) perimetry in a subset of participants in the RUSH2A study, determine the percentage of participants that retain rod function, and explore the relationship between dark adapted visual fields (DAVF) from DAC perimetry and parameters of rod function from electroretinogram (ERG) and full-field stimulus thresholds (FST).

Methods: At 6 sites, participants from the Rate of Progression of USH2A-related Retinal Degeneration (RUSH2A) 4-year natural history study of Usher syndrome type 2 (USH2) and non-syndromic autosomal recessive retinitis pigmentosa (ARRP) were invited to participate in the DAVF ancillary study. Dark-adapted retinal sensitivity was tested using cyan and red test protocols on the DAC perimeter (Medmont), and loci where cyan relative to red sensitivity was > 5 dB were considered rod mediated. Measures of full-field rod mean sensitivity, number of rod loci, maximum sensitivity, DAVF full-field hill of vision (DAVF V_{TOT}), and 30-degree hill of vision (DAVF V_{30}) were determined. Correlations between DAVF measures and standard clinical measures were estimated, as were kappa statistics (κ) for agreement between DAVF and other modalities regarding evidence of rod function.

Results: 49 participants (55% female, 95% white) were screened for DAVF rod function; 38/49 (78%) were found to have evidence of rod function. For comparison, 15/49 (31%) had measurable rod ERGs. For those 40 years of age or older, 7 with unmeasurable ERGs retained some rod visual field. DAVF maximum sensitivity was highly correlated with FST white thresholds ($\rho = -0.80$, $p \leq 0.001$). DAVF mean sensitivity, DAVF V_{TOT} , and DAVF V_{30} were more moderately correlated with FST white thresholds ($\rho = -0.71$, -0.72 , and -0.61 , respectively; all $p \leq 0.001$). Agreement regarding evidence of rod function with DAVF was relatively poor for both FST white ($\kappa = 0.35$, 95% CI = [0.14, 0.57]) and ERG Rod B-Wave ($\kappa = 0.16$, 95% CI = [0.004, 0.31]).

Conclusions: Our results suggest rod-mediated function is present in many patients with symptomatic USH2A-related retinal degeneration, including many without measurable rod ERGs. FST and DAVF represent two potential measures of rod function suitable for longitudinal measures in clinical trials for inherited retinal degenerations.

CONTROL ID: 3543586

SUBMITTER (NAME ONLY): Nicholas Kalafatis

TITLE: Gender and racial differences in ocular and systemic vascular biomarkers and contrast sensitivity of open-angle glaucoma patients

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate differences in the relationship between ocular and systemic vascular biomarkers in male and female open-angle glaucoma (OAG) patients of African (AD) and European (ED) descent.

Methods: This analysis included a total of 131 confirmed early to moderate OAG patients (99 ED, 32 AD) evaluated for: intraocular pressure (IOP) via Goldmann tonometry, systolic, diastolic, and mean arterial blood pressures (SBP/DBP/MAP) via automated ambulatory sensor, and ocular perfusion pressure (OPP=2/3MAP-IOP), systolic OPP (SOPP=SBP-IOP), diastolic OPP (DOPP=DBP-IOP), and mean OPP (MOPP=MAP-IOP) were calculated. In addition, visual contrast sensitivity (CS) detection via Vector Vision Systems was assessed. Measurements were evaluated between AD and ED and between male and female OAG patients using unpaired t-tests with $p < 0.05$ considered statistically significant.

Results: In the overall sample of all OAG patients (both AD and ED), biomarkers of systemic blood pressure and various calculations of OPP were significantly higher in males compared to females ($p = 0.000-0.032$). Additionally, OAG patients of AD had significantly higher systolic and diastolic blood pressures and corresponding OPP compared to those of ED ($p = 0.008-0.047$). In all OAG patients, male OAG subjects had higher CS detection compared to females, OAG patients of ED had higher CS detection than OAG patients of AD, and female OAG patients of ED had higher CS detection compared to female OAG patients of AD ($p < 0.05$, all comparisons).

Conclusions: In this cohort of OAG patients, biomarkers of systemic and ocular perfusion were significantly different between male and female OAG patients of AD and ED. Specifically, systemic blood pressure and calculations of OPP were significantly higher in male compared to female OAG patients as well as in OAG patients of AD compared to ED. Higher CS detection was found in male compared to female OAG patients and in OAG patients of ED compared to AD. Individualized approaches to glaucoma management that consider patient demographics including gender and race may improve the precision of patient care.

CONTROL ID: 3543590

SUBMITTER (NAME ONLY): Christopher Brady

TITLE: Crowdsourcing Can Match Field Grading Validity for Follicular Trachoma

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As trachoma is eliminated, field graders lose exposure to the disease and become less adept at identifying follicular trachoma (TF). New solutions to complete field surveys including photography and telemedicine may be needed to ensure elimination and accurately monitor for re-emergence. Expert grading of images is costly and time intensive. Our purpose was to validate crowdsourcing for follicular trachoma image interpretation.

Methods: Tarsal plate images acquired using a smartphone-based device during a 2019 field survey in Tanzania (n=1000) were posted to the Amazon Mechanical Turk (AMT) crowdsourcing marketplace for grading as "not-TF," "possible TF," "probable TF" or "definite TF." Each image was graded by 7 unique graders who received \$0.05 USD per image. The grades were summed to create a raw score (0-21) which was analyzed by receiver-operating characteristic (ROC) using images with concordant field and expert photo grades to determine the optimal diagnostic set-point. Kappa, sensitivity and specificity were then analyzed at various prevalences of disease.

Results: 7000 grades were rendered in 1 hour for \$420 USD. The raw score produced an area under the ROC of 0.940 (95% CI 0.902-0.977). Optimizing the setpoint to a raw score of 7 produced a kappa of 0.43, sensitivity of 84.8%, specificity of 90% and % correct (to master/field grade) of 89.3% in the full sample with a prevalence of 5.7% TF. When normal images were randomly removed from the sample to mimic the prevalences used to validate field graders (30% & 75% TF), the kappa ranged from 0.71-0.74 which is within the acceptable range per the World Health Organization. Images with discordant field and expert grades were more likely to receive a raw score in the middle of the range suggesting disagreement among crowdsourcers as well.

Conclusions: Crowdsourcing was able to rapidly and accurately identify TF on smartphone-acquired photographs with minimal training. Agreement with a reference standard is poor in a sample with low TF prevalence, but when held to the same standard as a skilled field grader in the current training paradigm, crowdsourcing may be acceptable. Further testing compared to field grading in low prevalence areas is needed.

CONTROL ID: 3543598

SUBMITTER (NAME ONLY): Marta Jiménez-García

TITLE: Keratoconus progression forecast by means of a time delay neural network

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Early detection of keratoconus (KC) progression is of utmost importance for the prudent and economical use of crosslinking. If KC progression could be accurately predicted, the timing of the follow-up visits could be customized to the patient's needs. The aim of this study was to verify whether the progressive trend of the ectasia can be forecasted based on two prior tomographies, and verify the accuracy of the predictive system when labelling eyes as stable or suspect progressive.

Methods: The observational multicenter REDCAKE study enrolled 906 KC patients measured at least twice. A time delay neural network was implemented. The network receives 6 features as input, measured in two consecutive examinations; all of them are potentially platform-independent (age, the mean keratometry in a 3mm area around the maximum curvature, the steepest radius and best fit sphere of the front surface, the mean radius of the back surface and LOGIK). Subsequently, the system predicts the values of the 2nd follow-up and determines its classification (stable or suspect progressive) based on the significance of the change from the baseline value (Figure 1). Different configurations and datasets were applied to evaluate robustness to errors and stability of the system. In the first dataset, 3 consecutive examinations of good quality were assembled to create each one of the triplets (N=811); in the second dataset, one examination was allowed to be of lower quality (marked in yellow by the tomographer software, N=1236). Data was divided as follows: 85% for training and 15% for external validation. Each configuration was trained/validated 10 times with random data splits.

Results: The results obtained were modest, with an average sensitivity $s=71\%$ and specificity $sp=81\%$ when classifying eyes as stable or suspect progressive (Table 1). On average, the positive and negative predictive values were $PPV=71\%$ and $NPV=80\%$, respectively. Also including time series with one error did not significantly worsen the results ($s=72\%$, $sp=78\%$, $PPV=72\%$, $NPV=78\%$).

Conclusions: The results obtained seem insufficient to decide on a surgical procedure such as crosslinking, however, they may be used to customize the timing for the next follow-up based on the predicted status. This predictive system constitutes another step towards a personalized management of KC disease.

CONTROL ID: 3543602

SUBMITTER (NAME ONLY): Sohani Amarasekera

TITLE: Predictive model for incomplete and complete retinal pigment epithelium and outer retinal atrophy in non-exudative age related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Non-exudative age related macular degeneration (NEAMD) is a significant cause of visual impairment and reduced quality of life worldwide. Prior studies examined associations between individual biomarkers on optical coherence tomography (OCT) and progression of disease. However, no comprehensive study has been undertaken to study the natural history of OCT biomarkers in NEAMD and to model their likelihood in predicting development of end-stage disease; namely incomplete retinal pigment epithelium and outer retinal atrophy (iRORA) and complete retinal pigment epithelium and outer retinal atrophy (cRORA).

Methods: Retrospective chart review at two academic practices. Patients diagnosed with NEAMD for whom yearly OCT scans were obtained for at least 4 consecutive years were included. Baseline demographic, visual acuity, Age-Related Eye Disease Study (AREDS) staging, and OCT data was collected. OCTs were assessed for presence or absence of 11 features individually associated with progression of NEAMD, both at baseline, and on all subsequent follow up scans. Likewise, charts were reviewed to assess visual acuity and staging of NEAMD at all follow up visits.

Results: 107 eyes of 88 patients met inclusion criteria. Patients had yearly OCTs for a median duration of 62 months (range: 48 months-132 months). During this time, of 107 eyes, 14 eyes (14%) progressed to exudative AMD, 17 eyes (16%) progressed to iRORA, 26 eyes (25%) progressed to cRORA, and 49 eyes (44%) did not progress to atrophy or exudative disease. Baseline OCT features associated with progression to iRORA and cRORA included hyporeflective intra-retinal spaces ($p<0.05$), drusen ooze ($p<0.01$) and drusen collapse ($p<0.05$). Features found in serial OCTs associated with progression to iRORA and cRORA included hyporeflect dots ($p<0.05$), hyporeflective foci ($p<0.01$), hyporeflective intra-retinal spaces ($p<0.01$), drusen ooze ($p<0.01$) and drusen collapse ($p<0.01$). In 72% of patients with bilateral involvement, OCT biomarkers of progression in one eye was predictive of progression to a similar extent of disease (exudative, iRORA, cRORA, or no atrophy) in the fellow eye.

Conclusions: This comprehensive study examines OCT biomarkers of NEAMD progression to iRORA and cRORA. These biomarkers can be used to predict progression of NEAMD disease, both in the affected eye, and in the fellow eye.

CONTROL ID: 3543603

SUBMITTER (NAME ONLY): Scott Lallier

TITLE: Resveratrol Attenuates Priming of the NLRP3 Inflammasome by Hydrogen Peroxide

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Lallier, N.A. Besley, P. Yang, G.J. Jaffe, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Scott Lallier: Commercial Relationship: Code N (No Commercial Relationship) | Nicholas Besley: Commercial Relationship: Code N (No Commercial Relationship) | Ping Yang: Commercial Relationship: Code N (No Commercial Relationship) | Glenn Jaffe: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The NLRP3 inflammasome has been implicated in the pathogenesis of age-related macular degeneration (AMD). It has been previously suggested that reactive oxygen species can prime the NLRP3 inflammasome and induce inflammatory cytokine expression. We and others have shown that resveratrol decreases oxidant injury in RPE cells. However, the effect of resveratrol on oxidant-induced inflammasome priming and inflammatory expression in RPE cells has not been well established. Here we test hydrogen peroxide's (H_2O_2) ability to prime the inflammasome and induce inflammatory gene expression in cultured human retinal pigment epithelial (RPE) cells. We hypothesized that H_2O_2 would prime the inflammasome, induce inflammatory gene expression, and that resveratrol would protect against these effects.

Methods: Cultured human RPE cells were treated with 30 μ M resveratrol for 2.5 hours, followed by treatment with 700 μ M hydrogen peroxide in the presence or absence of 30 μ M resveratrol for 2.5 or 4 hours as indicated.

Phosphorylation of Nuclear Factor Kappa B (NF- κ B) was evaluated using western blot. Inflammasome and classic inflammatory gene expression was measured with qPCR.

Results: H_2O_2 treatment resulted in a 4-fold increase ($p < .05$) in phosphorylation of NF- κ B as determined by western blot. H_2O_2 treatment resulted in an 18-fold increase in NLRP3 ($p < .05$), 1.8-fold increase in IL-1 β ($p < .05$), and 2.4-fold increase in IL-8 ($p < .05$) as determined by qPCR. Resveratrol protected against the upregulation of NLRP3 ($p < .05$) and IL-1 β ($p < .05$) by H_2O_2 . Resveratrol did not significantly reduce IL-8 expression. Under these experimental conditions, no increase was observed in IL-6, MCP-1, or CXCL1 gene expression.

Conclusions: H_2O_2 primes the human RPE cell NLRP3 inflammasome and upregulates inflammasome-associated cytokines. These effects were blocked by resveratrol. Further studies are needed to determine if other oxidants prime the RPE cell inflammasome, and the mechanism by which resveratrol exerts its inhibitory effect. These studies will add to our understanding of the pathogenesis of AMD and possible preventive strategies.

CONTROL ID: 3543606

SUBMITTER (NAME ONLY): Scott Greenwald

TITLE: Optic disc edema and chorioretinal folds develop during strict head-down tilt bedrest with and without artificial gravity

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.H. Greenwald, S. Laurie, K. Marshall-Goebel, PhD, L.P. Pardon, S.M. Lee, KBR, Houston, Texas, UNITED STATES|C. Stern, Deutsches Zentrum fur Luft- und Raumfahrt, Koln, Nordrhein-Westfalen, GERMANY|H. Sangi-Haghpeykar, E.M. Bershad, Baylor College of Medicine, Houston, Texas, UNITED STATES|B. Macias, NASA Johnson Space Center, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Spaceflight-associated neuro-ocular syndrome (SANS) is a condition that is hypothesized to develop as a consequence of the chronic headward fluid shift that occurs in sustained weightlessness. Here, we exposed healthy subjects to strict 6° head-down tilt bedrest (HDTBR) to generate a sustained headward fluid shift in the Artificial Gravity Bedrest with the European Space Agency (AGBRESA) study and assessed SANS-related ocular changes (e.g., optic disc edema, chorioretinal folds). A subset of these subjects were exposed to artificial gravity (AG) via centrifugation during HDTBR to investigate whether this intervention can attenuate fluid shift-induced ocular changes.

Methods: Data were collected in 24 healthy subjects during 60 days of strict 6° HDTBR, as well as during the pre- and post-HDTBR phases with the subjects in seated and supine postures. The cohort was divided into 3 groups (n=8/group), two of which received 30 minutes total per day of AG (0.3 g at the eyes) by either continuous (cAG) or intermittent (iAG) short-arm centrifugation. Optical coherence tomography images were acquired to quantify changes in peripapillary total retinal thickness (TRT), retinal nerve fiber layer thickness, and choroidal thickness, and to detect chorioretinal fold development. Intraocular pressure, standard automated perimetry, and optical biometry data were also collected.

Results: TRT increased from seated baseline as a function of HDTBR duration for each group. By HDTBR day 58, TRT was increased by 35.9 µm (95% CI, 19.9-51.9 µm, P < 0.0001), 36.5 µm (95% CI, 4.7-68.2 µm, P = 0.01), and 27.6 µm (95% CI, 8.8-46.3 µm, P = 0.0005) for the control, cAG, and iAG group, respectively. The cAG and iAG groups were not different from the control group for this measure during HDTBR (P > 0.6). Although not apparent at HDTBR day 30, chorioretinal folds were observed by HDTBR day 58 in 6 subjects (n≥1 per group).

Conclusions: The headward fluid shift generated by strict 6° HDTBR leads to the development of early optic disc edema, as detected by increased TRT, and chorioretinal folds in some subjects. Therefore, this spaceflight analog is an appropriate model for investigating the etiology of SANS and refining countermeasure strategies. 30 minutes of either cAG or iAG daily does not counter the effects of the headward fluid shift on the eye, suggesting that longer duration exposures are required.

CONTROL ID: 3543608

SUBMITTER (NAME ONLY): Chen Yu

TITLE: Markers of Protective Microglia in Mouse Models of Outer Retinal Degeneration Are Present in Human AMD

SESSION TITLE: Microglia and other Macrophages in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Yu, E.M. Lad, A.D. Proia, D.R. Saban, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|D.R. Saban, Immunology, Duke University, Durham, North Carolina, UNITED STATES|A.D. Proia, Pathology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many, if not most, forms of retinal degeneration, including age-related macular degeneration (AMD), involve the ectopic accumulation of subretinal macrophages, but their role in human diseases remains elusive. We recently described a unique subtype of bona fide microglia that are dominant in the subretinal space in the light damage (LD) paradigm and rhodopsin P23H mutant knockin mice. These subretinal microglia are transcriptionally reprogrammed and contribute to restricting disease progression, such as loss of structural integrity of the retinal pigment epithelium (RPE) and death of photoreceptors. However, whether this population of reprogrammed microglia is a general response across etiologically distinct forms of degeneration, including human AMD, is unknown.

Methods: To address this question, we utilized single cell RNA-sequencing, and compared our findings in LD model (O'Koren and Yu et al, 2019) with another three distinct disease models in mice. These include: an acute model in NaIO₃ mediated RPE injury; a chronic degeneration model of P23H mice; and advanced aging model of wildtype 2-year-old mice. Furthermore, selected markers were analyzed by immunolabeling and confocal microscopy in mouse models and also examined in human post-mortem macular sections from a total of 36 patients categorized by Sarks' grading system.

Results: We showed that transcriptional reprogrammed microglia are conserved among all mouse models studied. Moreover, confocal microscopy revealed that subretinal Iba1⁺ cells dominantly expressed markers of this reprogramming in all four mouse models. Likewise, in human postmortem retina we observed enriched subretinal staining of such markers in subjects with intermediate to advanced AMD (Sarks 3, 4, and 5), whereas few positive cells were found in control or early AMD subjects (Sarks 1 and 2).

Conclusions: Our findings demonstrate that transcriptionally programmed microglia in the subretinal space are present in the studied acute and progressive models of degeneration, as well as in advanced aging mice. Importantly, we show evidence that this unique population may also be relevant in forms of human AMD.

CONTROL ID: 3543609

SUBMITTER (NAME ONLY): Julius Mdzomba

TITLE: The role of Nogo-A in visual deficits induced by retinal injury

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.B. Mdzomba, S. Joly, L. Rodriguez, V. Pernet, Universite Laval, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The transmembrane protein Nogo-A is a potent inhibitor of neuronal plasticity and repair. After CNS injury, Nogo-A prevents the cytoskeleton rearrangements required for functional rewiring of neuronal circuits. Its neutralization can support axonal regeneration and neuronal recovery. The goal of this study was to investigate the role of Nogo-A in the visual impairments induced by N-Methyl-D-Aspartate-induced (NMDA) excitotoxicity in the adult mouse. Excitotoxic damage is thought to be a major pathological mechanism causing retinal dysfunction in ocular diseases. In addition, we evaluated Nogo-A expression changes in diabetic human retinæ.

Methods: Different levels of retinal injury were induced by intravitreal injection of 0.5-40 nmol of NMDA. Nogo-A's function was blocked by using either knock-out (KO) mice or by intravitreally injecting a highly specific monoclonal function-blocking antibody (11C7) two days after NMDA injection. Visual function was followed using the optokinetic response (OKR) and by electroretinogram (ERG) recordings. Visual cortex activity was monitored through local field potential (LFP) recording. Immunofluorescence on retinal flat-mounts and on retinal sections was used to observe neuronal survival and Nogo-A expression changes.

Results: Intravitreal administration of 0.5nmol of NMDA produced damage limited to the ganglion cell layer (GCL), consisting of a drop of ~20 % in OKR spatial sensitivity and a ~30-% reduction in the number of ganglion cells (GC). 5nmols of NMDA produced extended destruction in the inner retina, as shown by the loss of ~80% of GC, the decrease of OKR spatial sensitivity by ~80%, and the decrease of the ERG b-wave amplitude by ~50%. Nogo-A KO mice and animals intravitreally injected with 11C7 showed a marked OKR spatial sensitivity improvement after NMDA-induced injury. In the same experimental groups, reduced LFP latency suggested enhanced visual cortex activation in response to eye stimulation with light flashes. However, 11C7 did not significantly influence GC survival. In human diabetic eyes, Nogo-A was overexpressed, suggesting its possible contribution to visual deterioration in ocular diseases affecting GC.

Conclusions: Our data suggest that Nogo-A is implicated in the development of permanent visual deficits caused by retinal injury. Intravitreal administration of Nogo-A-neutralizing antibodies may promote visual recovery in retinal diseases such as diabetic retinopathy.

CONTROL ID: 3543610

SUBMITTER (NAME ONLY): Mario Matthaei

TITLE: Investigating the role of the fibrillar layer in Fuchs endothelial corneal dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Matthaei, T. Clahsen, S. Siebelmann, L.M. Heindl, B. Bachmann, C. Cursiefen, A. Hribek, Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|C. Büttner, Human Genetics, Universitätsklinikum Erlangen, Erlangen, Bayern, GERMANY|

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ABSTRACT BODY:

Purpose: Recent studies from our laboratory demonstrate that a fibrillar layer (FL) consisting of a collagen I (COL I)-, collagen III (COL III)- and collagen IV (COL IV)-rich matrix exists in the central endothelium of the majority of advanced Fuchs endothelial corneal dystrophy (FECD) patients and that there is a significant decrease in endothelial cell density in this FL region. The present study sought to investigate the role of the FL in advanced FECD in more detail.

Methods: Ingenuity pathway analysis (IPA) was performed in a previously generated data set after RNA sequencing in the corneal endothelium of advanced (modified Krachmer grade 5+6) FECD patients (n=14) and controls (n=10). Differential expression of selected genes was confirmed using quantitative real-time PCR and the expression of the proteins localized in explanted Descemet endothelium complexes (DEC) using immunofluorescence flatmount staining. Cell-culture experiments in a human corneal endothelium derived cell line (HCEC-12) investigated the influence of Transforming Growth Factor Beta (TGF- β) stimulation and altered growth on FL specific collagen coatings in vitro.

Results: IPA identified hepatic fibrosis/hepatic stellate cell activation as the most strongly affected signaling pathway and TGF- β as the top upstream regulator in the corneal endothelium of advanced FECD patients. QPCR and immunofluorescence confirmed differential expression of fibrosis/ TGF- β -related genes (including Collagen V (COL V), Secreted Protein Acidic And Cysteine Rich (SPARC), and Platelet Derived Growth Factor-C (PDGF-C)) and altered protein expression pattern in advanced FECD DECs compared to normal. TGF- β stimulation induced overexpression of fibrosis related targets whereas growth experiments showed decelerated growth on FL related collagens.

Conclusions: This study provides further evidence that activation of the TGF- β signaling cascade and a fibrotic response play a role in the development of the FL. Subendothelial deposits formed during this reaction may contribute to a concomitant toxic microenvironment.

CONTROL ID: 3543612

SUBMITTER (NAME ONLY): Ashay Bhatwadekar

TITLE: Dapagliflozin treatment protects from diabetic retinopathy

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Bhatwadekar, D. Mathew, H. Dhami, E. Bello, Q. Luo, Indiana University

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a chronic and progressive complication of diabetes. Dapagliflozin, a new class of anti-diabetic medication, is beneficial in reducing blood glucose; however, its role in DR remains unknown. Therefore, this study aims to investigate the protective effect of dapagliflozin on the development of DR.

Methods: The db/db mice were treated with dapagliflozin via diet for six months and the body weight, food consumption monitored every week. The blood glucose, HbA1c and electroretinogram (ERG) were assessed at 2 and 6 months. At study termination, the retinas were processed for trypsin digestions and real-time qPCR. In parallel, the human retinal endothelial cells (HRECs) were treated with dapagliflozin concentrations 0.1-100 μ M in a logarithmic range. The cell viability was assessed using Alamar Blue Assay, and the migration response was studied using a scratch wound-healing assay.

Results: The dapagliflozin treatment reduced blood glucose and HbA1C; however, there was no change in body weight or food intake. The db/db mice exhibited higher amplitude for ERG 'b' wave, which was decreased after dapagliflozin treatment. Dapagliflozin treatment resulted in downregulation of mRNA for pro-inflammatory markers along with a decrease in acellular capillary numbers in db/db mice. The HRECs were viable at all concentrations except for the 100 μ M dapagliflozin dose. The scratch wound assay demonstrated a significant reduction in wound closure and rate of migration after 4 and 8 hours of dapagliflozin treatment for the 50 and 100 μ M concentrations.

Conclusions: Overall, dapagliflozin treatment was successful in regulating photopic ERG 'b' wave amplitude, glycemic control and, decreasing acellular capillary numbers and inflammation in vivo, and decreasing the wound closure in in vitro assays. In conclusion, our studies suggest that dapagliflozin could be beneficial in the treatment of DR due to its effect on glycemic control and potential anti-inflammatory and anti-angiogenic action.

CONTROL ID: 3543613

SUBMITTER (NAME ONLY): Bomina Park

TITLE: Cell type specific expression of soluble epoxide hydrolase protein and mRNA in human AMD and murine eyes with choroidal neovascularization

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Park, T.W. Corson, Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|X. Qi, M.E. Boulton, Ophthalmology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|B. Park, T.W. Corson, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Soluble epoxide hydrolase (sEH) metabolizes pro-resolving epoxy fatty acids into diols. sEH is a potential therapeutic target for choroidal neovascularization (CNV) in wet age-related macular degeneration (AMD) and other eye diseases. Localization of sEH in the retina is contentious and cross-interpretation among different studies is complicated due to antibody limitations. This study aimed to define the localization of sEH through co-staining with retinal cell type markers and RNAscope in situ hybridization in human AMD and control eyes, and in mouse eyes with and without laser-induced CNV.

Methods: Paraffin sections of eyes from anonymized human wet AMD and control subjects were obtained from the National Disease Research Interchange. 7-week old C57BL/6J mice underwent laser-induced CNV and on day 3 post laser, enucleated eyes were fixed and cryosectioned. Coimmunostaining was done for sEH, retinal pigment epithelium (RPE), and photoreceptor markers. RNAscope was performed using target specific probes for EPHX2 (encoding sEH) and images were acquired by confocal microscopy.

Results: Costaining of sEH with cell type markers revealed that sEH is overexpressed in photoreceptors and RPE cells in areas with degenerative changes. By RNAscope, EPHX2 mRNA was also highly expressed in the pathological conditions compared to controls. EPHX2 mRNA was seen in the inner nuclear layer, outer nuclear layer and RPE of the normal and diseased human and mouse retina.

Conclusions: Previous data showed sEH expression in vasculature, Müller glia, and inner and outer segments of photoreceptors. Here, we also revealed sEH protein and mRNA expression in the RPE. Overexpression of sEH at the protein and mRNA level in CNV and disease-relevant cell types indicates a functional role of sEH in AMD pathophysiology and provides a context to target these cell types for developing pharmacotherapies.

CONTROL ID: 3543615

SUBMITTER (NAME ONLY): Sara Mayer

TITLE: BBS10 knockout mouse exhibits developmental lack of cone function and recapitulates retinal degeneration.

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mayer, J. Thomas, A. Mahoney, S. Bhattarai, Q. Zhang, E. Stalter, P. Datta, Y. Hsu, J. Garrison, C. Searby, S. Seo, V. Sheffield, A.V. Drack, Ophthalmology, The University of Iowa Hospitals and Clinics Department of Pathology, Iowa City, Iowa, UNITED STATES|S. Mayer, J. Thomas, A. Mahoney, S. Bhattarai, Q. Zhang, E. Stalter, P. Datta, Y. Hsu, J. Garrison, C. Searby, S. Seo, V. Sheffield, A.V. Drack, University of Iowa Institute for Vision Research, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the retinal phenotype in mice with knockout of the Bbs10 gene, a component of the BBS/CCT chaperonin complex, and compare with mutation of Bbs1, a component of the BBSome.

Methods: A mouse model of Bardet Biedl Syndrome type 10 (BBS10) was developed by knocking out the Bbs10 gene. ERG, OCT, and visually guided swim assay (VGSA) natural history data were collected and were compared to WT and Bbs1^{M390R/M390R}.

Results: Bbs10^{-/-} mice initially weigh less than littermates (KO 7.2 gms vs WT 13.2 at P19) and are viable only with special feeding and husbandry. By 3 months Bbs10^{-/-} are heavier (KO 32.1 gms vs WT 22.8, p=0.0149). ERG amplitudes are lower than WT by P19 (p=0.006) and VGSA is worse in the dark by 3.5 months (p= <0.0001), and in light by 9 months (p=<0.0001). At the earliest age tested, P21, there is no recordable 5 Hz flicker response in Bbs10^{-/-}. Bbs1^{M390R/M390R} are heavier than WT by 3 months (p=0.012) and have a recordable 5 Hz flicker until 6 months of age. At 6 months of age, Bbs10^{-/-} mice have significantly worse ERG than Bbs1^{M390R/M390R} in dark adapted 0.01 (p=0.0001), Standard Combined Response (p=<0.0001) and Light Adapted 5 Hz flicker (p=0.0476). In the VGSA, Bbs10^{-/-} had worse time to platform than Bbs1^{M390R/M390R} in the 4-6 month dark swim (p=<0.0001) and 9-11 month both light (p=0.0186) and dark (p=<0.0001). On OCT at 2 months old ONL is equal in WT and Bbs10^{-/-} (0.046 µm) but is 26% thinner in Bbs1^{M390R/M390R}. By 6 months Bbs1^{M390R/M390R} is 39% and Bbs10^{-/-} is 13% of WT. WT ONL remained stable to 9 months.

Conclusions: Bbs10^{-/-} mice eyes recapitulate retinal degeneration seen in human BBS10 and resemble retinal degeneration seen in Bbs1^{M390R/M390R} with important differences: Bbs10^{-/-} never develop a 5Hz flicker cone response, and have faster retinal degeneration overall. Our study correlates with recent human data suggesting BBS10 retinopathy is more severe and progresses faster than BBS1 (Heon et al.). Lack of 5 Hz flicker response in Bbs10^{-/-} suggests an early role in cone function for BBS10.

References:

Heon, E et al. Comparative natural history of visual function from patients with biallelic variants in BBS1 and BBS10. Submitted IOVS, ARVO 2021.

Tanimoto N, et al. ERG assessment of rod and cone mediated bipolar cell pathways using flicker stimuli in mice. *Scientific Reports* | 5:10731 | DOI: 10.1038/srep10731

CONTROL ID: 3543616

SUBMITTER (NAME ONLY): Charles Hennings

TITLE: Prognostic determinants of postoperative pseudophakic macular oedema in a tertiary hospital setting

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hennings, K. Alattar, M.B. Goncalves, S. Wagner, P. Keane, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|P. Keane, Biomedical Center, Moorfields Eye Hospital, National Institute for Health Research, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Post-operative pseudophakic cystoid macular oedema (PCMO) is a cause of impaired postoperative vision in modern cataract surgery. Known risk factors include intraoperative complications such as posterior capsule rupture and preoperative factors including diabetes mellitus, uveitis, vein occlusions and epiretinal membrane. A paucity in consistency of definition both clinically and with OCT imaging has led to a wide range of conclusions. Our aim is to report statistical baseline demographic and OCT characteristics in a patient cohort from a tertiary eye hospital setting

Methods: A data-warehouse query for all eyes receiving cataract surgery between January 2012 and December 2019 was performed. Inclusion criteria were age above 16, the presence of OCT imaging pre and postoperatively and at least 1 post-operative clinic letter. First and second eyes of patients were included but re-operations on the same eye were excluded. Datatables were merged and a Structured Query Language (SQL) fuzzy logic word search was performed on all electronic letters. Variations on PCMO nomenclature within these letters including, irvine-gass syndrome in both american and english spelling were identified. Sociodemographic (age, sex, ethnicity, socioeconomic deprivation index), presence of diabetes mellitus and OCT longitudinal data were auto extracted and analysed. For validation purposes a subanalysis of random generated patient numbers was performed by hand for comparison on 15% of the entire cohort.

Results: 6287 patients were identified with operations performed on 9126 eyes. 53% were female, 2033 of British descent, 3647 of ethnic background the rest not being stated on the records. The average age at the time of surgery was 68.0 (SD 13.0) and 1804 patients were diabetic. The rate of all complications in this select cohort was 6.5% with a posterior capsular rupture rate of 1.1%. 56.0% of eyes were found to have PCMO. There was no statistical difference in the mean index of multiple deprivation score between those that developed PCMO (mean 5.2, SD 2.5) and those that did not (mean 4.9, SD 2.4, $p = 0.16$).

Conclusions: PCMO remains a risk in modern day cataract surgery regardless of intraoperative complications. OCT post-operatively is useful in its diagnosis and it can manifest sub-clinically. The use of postoperative NSAIDs in those known or at risk of PCMO can reduce its occurrence.

CONTROL ID: 3543623

SUBMITTER (NAME ONLY): Thomas Carr

TITLE: Interpretable staged transfer learning improves OCT classification and clinical explanation of retinal diseases from small sample sizes

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Machine learning has a considerable data dependence that increases the resources required for its use. In addition, these algorithms are often black box systems, with unexplained behaviours.

The aim of this study was to develop a machine learning training methodology that is able to achieve accurate, explainable results to classify OCT scans using a small sample size of images, which we have termed interpretable staged transfer learning (iSTL) (Figure 1).

Methods: The iSTL classification algorithm was trained to identify normal, diabetic retinopathy (DR), central serous retinopathy (CSR) and macular hole (MH) OCT images from a target training dataset of 50 images per class. To achieve this the algorithm was initialised with source ImageNet pretrained weights and was then trained on a large bridge dataset of OCT images from a separate open source dataset. Bridge training reduces domain difference between source and target datasets. The algorithm was then trained on the target dataset, which was synthetically expanded using data augmentation at a ratio of 4:1. Data augmentation uses random image transformations to generate new disease appearances from existing data. iSTL was compared to algorithms trained using traditional direct transfer learning (DTL) initialising with ImageNet weights only against unseen target images. Attention maps were generated using SHapley Additive exPlanations (SHAP).

Results: Against unseen data the best iSTL model achieved greater overall accuracy (0.94), mean specificity (0.93), sensitivity (0.93) and f1-score (0.93) compared to DTL (0.86, 0.84, 0.80, 0.80) (Table 1).

Attention maps showed finer attention to pathologically important areas by iSTL. DTL exhibited wider attention across each image, frequently attributing importance to non-clinically significant areas (Figure 2).

Conclusions: Our results show that iSTL scores higher against unseen data compared to DTL, demonstrating the effectiveness of our performance-boosting methods with small sample sizes. To avoid a black-box system and to be able to action results, clinicians must be able to interpret its predictions. Attention maps show that iSTL uses clinical features to make predictions and not uninterpretable abstractions. The sample size used could be gathered in clinical outpatient settings allowing small-scale research to be carried out without significant resources.

CONTROL ID: 3543627

SUBMITTER (NAME ONLY): Hanna Dumanska

TITLE: Mechanisms of hypoxia-induced pathological synaptic plasticity in the visual retinocollicular pathway

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Dumanska, N. Veselovsky, Department of Neuronal Networks Physiology, Institut Fiziologii imeni O O Bogomolca Nacional'na akademii nauk Ukraini, Kiiv, Kiiv, UKRAINE]

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ABSTRACT BODY:

Purpose: Retinocollicular projections represent the first part of the extrageniculate visual pathway. Its lesion could lead to navigation, orientation and visual attention deficits. We focused on defining processes and mechanisms underlying the early stage of hypoxic injury of the neurotransmission in the originally-developed in vitro model of the retinocollicular pathway.

Methods: The in vitro model was a coculture of dissociated rat retinal cells and superficial superior colliculus (SSC) neurons. Using the paired patch-clamp technique, we recorded pharmacologically isolated NMDA-, AMPA- and GABA_A-mediated postsynaptic currents in SSC neurons by generation action potentials in presynaptic retinal ganglion cells. The local application of hypoxic solutions on pairs of neurons was used to mimic short-term hypoxic states.

Results: The hypoxia induces long-term depression (LTD) of GABA_A neurotransmission ($34 \pm 9\%$, $P < 0.001$, $n = 23$), temporary suppression of AMPA ($32 \pm 7\%$, $P < 0.01$, $n = 22$) and long-term potentiation (LTP) of NMDA transmission ($170 \pm 11\%$, $P < 0.01$, $n = 26$). Also, oxygen deprivation leads to a reduction of voltage-dependent magnesium blockade of evoked NMDA response. All NMDA currents were analyzed in terms of their kinetic characteristics. This analysis revealed that hypoxia-induced LTP and reduction were accompanied by a rapid and irreversible decrease of the decay time of the NMDA currents (from 37.2 ± 5.4 ms to 18.5 ± 7.2 ms, respectively).

Conclusions: The hypoxia-induced LTP of NMDA transmission mediates an increase of calcium ions influx and leads to apoptotic cell death. There are several protective mechanisms to prevent that. The first one belongs to the GABAergic retinocollicular projections. Their physiological role is in the regulation of the activation of NMDA transmission. The next one is the voltage-dependent magnesium blockade of NMDA receptors. Hypoxia impairs both protective mechanisms and enhances the pathological effect of LTP of NMDA transmission. Moreover, data strongly suggest that irreversible increase in NR2A-to-NR2B subunit ratio underlies the hypoxia-induced pathological LTP of retinocollicular NMDA neurotransmission. The results obtained reflect the electrophysiological basis and may serve to reveal new approaches for pharmacological and therapeutic interventions for a hypoxia-involved pathological lesion of the retinocollicular pathway.

CONTROL ID: 3543628

SUBMITTER (NAME ONLY): Keke Liu

TITLE: Regression-based strategies to reduce false-positive glaucoma diagnoses when using OCT and OCT angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To correct refractive error-associated bias in optical coherence tomography (OCT) and OCT angiography glaucoma diagnostic parameters.

Methods: OCT and OCT angiography imaging were obtained from participants selected from the Hong Kong FAMILY cohort, a population-based study. Only normal eyes were included in this study. Software on the Avanti AngioVue system were used to measure the peripapillary nerve fiber layer thickness (NFLT) and nerve fiber layer plexus capillary density (NFLP CD), and macular ganglion cell complex thickness (GCCT) and superficial vascular complex vascular density (SVC VD). The glaucoma diagnostic threshold was set at the 5th percentile of emmetropic (-1 to +1 D) eyes.

Results: A total of 1346 eyes from 792 participants were divided into four subgroups for data analysis (Table 1). After accounting for age, gender, and signal strength, multiple linear regression showed strong dependence for NFLT and GCCT on eye axial length (AL), spherical equivalent (SE) refraction, and apparent optic disc diameter (DD) on the OCT scans. Compared to structural parameters, NFLP CD had less dependence and SVC CD had no significant dependence on AL, SE, and DD. Compared to the emmetropic group, the false positive rate was significantly (Chi square test $p < 0.003$) elevated in both the high and low myopia groups for NFLT, NFLP CD, and GCCT (Table 2). Regression-based adjustment of diagnostic parameter with AL or SE significantly (McNemar test $p < 0.04$) reduced the elevated false positive rate. Adjustment using DD was ineffective.

Conclusions: Myopic eyes are biased to have lower NFLT, GCCT, and NFLP CD measurements, leading to elevated false positive rate of glaucoma diagnoses. Regression-based adjustment using AL and SE, but not DD, were effective in eliminating this bias. SVC CD was unbiased by refractive error even without compensation and may be more reliable for glaucoma assessment in high myopes.

CONTROL ID: 3543629

SUBMITTER (NAME ONLY): kangwei jiao

TITLE: Identification of Important Molecular Players in Photoreceptor Cell Death in Inherited Retinal Degeneration: An RNA-Seq- and Bioinformatics-Based Study

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. jiao, C. Wei, L. Xiao, Z. Hu, Ophthalmology, affiliated hospital of Yunnan university, Kunming, Yunnan, CHINA]

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ABSTRACT BODY:

Purpose: Here, changes in the gene expression, molecular mechanisms, and pathogenesis of inherited retinal degenerations (IRDs) were studied to identify predictive biomarkers for their varied phenotypes and provide a better scientific basis for their diagnosis, treatment, and prevention.

Methods: Differentially expressed genes (DEGs) between retinal tissue from retinitis pigmentosa (RP) mouse models obtained during the photoreceptor cell death peak period (Pde6b^{rd1} at PN11, Pde6b^{rd10} at PN18, Prph^{rd2} at PN21) and retinal tissue from C3H wild-type mice were identified using Illumina high-throughput RNA-sequencing. Co-expression gene modules were identified using a combination of GO and KEGG enrichment analyses and gene co-expression network analysis. CircRNA-miRNA-mRNA network interactions were studied by genome-wide circRNA screening.

Results: Ped6b^{rd1}, Ped6b^{rd10}, and Prph^{rd2} mice had 1,926, 3,096, and 375 DEGs, respectively. Mainly, genes related to ion channels, stress, inflammatory processes, tumor necrosis factor (TNF) production, and microglial cell activation were up-regulated, and genes related to endoplasmic reticulum regulation, metabolism, and homeostasis were down-regulated. Differential expression of transcription factors and non-coding RNAs generally implicated in other human diseases was detected. CircRNA-miRNA-mRNA network analysis confirmed that these factors may be involved in photoreceptor cell death. Moreover, excessive cGMP accumulation causes photoreceptor cell death, and cGMP-related genes were generally mutated.

Conclusions: We screened genes and pathways related to photoreceptor cell death. Additionally, up-stream regulatory factors, such as TFs and non-coding RNA and their interaction networks were analyzed. Furthermore, RNAs involved in IRDs were functionally annotated. Thus, this study lays a foundation for future studies on the photoreceptor cell death mechanism.

CONTROL ID: 3543630

SUBMITTER (NAME ONLY): Judith Birkenfeld

TITLE: Improved detection of corneal deformation asymmetries in keratoconus patients using multi-meridian deformation imaging

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate a recently developed multi-meridian air-puff deformation Optical Coherence Tomography (OCT) system (ImTopScanner) for improved early keratoconus (KC) detection in vivo. To investigate deformation asymmetries that are expected to occur due to biomechanical (bm) changes in KC corneas, on two meridians.

Methods: Multi-meridian air-puff OCT (Curatolo, BOE, 2020) was used to collect deformation images of three KC and two healthy corneas in vivo. The system allows deformation imaging along both, horizontal (H) and vertical (V) corneal meridian during a 20ms air-puff excitation. Custom image processing tools quantified (1) the deflection area (DeflArea) between undeformed and deformed cornea, (2) the Asymmetry in DeflArea (ADA), i.e. the difference between nasal/temporal and superior/inferior DeflArea. Eyes were also measured with a Pentacam®. Patient-specific finite element models were generated. In KC eyes, an algorithm detected the cone area and allocated it a separate material. Through an inverse analysis procedure and simulation of air-puff pressure, corneal material stiffness for second-order Ogden material model was estimated.

Results: KC eyes were classified into two mild and one moderate KC eyes, using the Pentacam Topographic Keratoconus Classification (Chen, JCRS, 2019). The mean DeflArea (H and V) at maximum deformation was $2.79 \pm 0.04 \text{ mm}^2$, $3.12 \pm 0.27 \text{ mm}^2$, and $2.88 \pm 0.17 \text{ mm}^2$, from the lowest to highest disease severity, respectively. In the same order, the absolute value of ADA at maximum deformation was $0.02 \pm 0.06 \text{ mm}^2$, $0.14 \pm 0.12 \text{ mm}^2$, $0.18 \pm 0.04 \text{ mm}^2$ (H), and $0.21 \pm 0.08 \text{ mm}^2$, $0.23 \pm 0.02 \text{ mm}^2$, and $0.3 \pm 0.02 \text{ mm}^2$ (V), revealing a lower ADA, but a more pronounced (up to a factor of 3) relative difference between H and V ADA for mild KC eyes. For healthy eyes, ADA remained $< 0.2 \text{ mm}^2$. Simulations estimated a $35.5\% \pm 10.0\%$ stiffness reduction in the cone area of KC eyes in comparison to outside the cone at 4% strain.

Conclusions: Initial results show that multi-meridian deformation imaging can aid in early detection of corneal bm changes taking place in KC. Differences in deformation asymmetries between orthogonal meridians may be more pronounced in early disease stages, where corneal geometry has not been significantly altered. Consideration of two meridians and identification of KC cone location are important for simulating realistic corneal material behavior in KC eyes.

CONTROL ID: 3543631

SUBMITTER (NAME ONLY): Noorjahan Panjwani

TITLE: Galectin 8 impairs TLR4 signaling and dampens innate immune response to *P. aeruginosa* infection in mouse corneas

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.A. Panjwani, Z. Cao, A. Ramadan, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The current study was designed to examine the role of a carbohydrate-binding protein, galectin 8, (Gal-8) in *P. aeruginosa* (PA) keratitis pathogenesis, and to characterize the mechanism by which Gal-8 modulates innate immune response in PA keratitis.

Methods: Two approaches were used. In the first, corneas of C57BL/6 wild-type (WT) or Gal-8 knockout (Gal-8 KO) mice were infected with PA. The severity of bacterial keratitis was graded on day 1 and day 3 post-infection (p.i.) by slit lamp using a scoring system ranging from 0 to 4, and then corneas were harvested for bacterial enumeration. In the second approach, to study the mechanism by which Gal-8 modulates the innate immune response: (i) affinity chromatography experiments were conducted to determine whether specific molecules of the TLR-4 complex bind to Gal-8, and (ii) in vitro experiments were performed to determine whether the addition of exogenous Gal-8 influences the activation of TLR-4 pathway in bone marrow-derived macrophages (BMDMs) stimulated with LPS.

Results: Gal-8 KO mice exhibited less severe infection in comparison to WT mice as indicated by lower opacity scores and reduced bacterial load. In vitro studies showed that: (i) Gal-8 binds to CD14 but not to TLR4 in a carbohydrate-dependent manner, (ii) the addition of exogenous rGal-8 significantly inhibits the delivery of LPS from CD14 to MD2/TLR4 and impairs activation of TLR4 pathway in BMDMs stimulated with LPS as indicated by a decrease in TNF α , IL-6, MD-2 and MyD88 expression and I κ B phosphorylation.

Conclusions: Gal-8 modulates the pathogenesis of PA keratitis by inhibiting the activation of TLR4 pathway.

CONTROL ID: 3543632

SUBMITTER (NAME ONLY): Chelsey Doyle

TITLE: The TGFβ2 induced microRNAome of the trabecular meshwork

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Transforming growth factor beta 2 (TGFβ2) plays an important role in the pathogenesis of primary open angle glaucoma (POAG). TGFβ2 induces pathological changes in the trabecular meshwork (TM) and dysregulates microRNA (miRNA) expression. MiRNAs are cell and context specific epigenetic regulators of cellular functions and signalling pathways. Small RNA-sequencing was performed using cultured normal human TM cells treated with TGFβ2 to identify the TGFβ2 miRNAome.

Methods: Primary normal human TM cell cultures (n=5) were treated with TGFβ2 (5ng/mL) for 24 hours. RNA was extracted using Qiagen AllPrep kit and small RNA-sequencing was performed at the Genomics Core Facility in Queen's University Belfast following QIAseq miRNA library prep with sequencing on the Illumina platform. Bioconductor was used for primary miRNA mapping and secondary differential expression. MiRNAs were analysed using miRTargetLink, TargetScan and miRTarBase to detect strong experimentally validated gene targets, and miRNAs with strong targets were run through KEGG analysis using DIANA mirPath v.3 software and miRPathDB to identify enriched pathways. MiRNA qPCR was performed to validate and replicate the small RNA-sequencing data in four independent biological samples for 10 miRNAs of interest.

Results: Significant (p<0.01) differential miRNA expression was seen for twenty-two miRNAs including miR-503, miR-145 and miR-143. At a significance level of p<0.05, seventy-two miRNAs were significantly altered of which five are implicated in the regulation of TGFβ signalling. qPCR confirmed significant differential miRNA expression in five miRNAs of interest. Enriched pathways regulated by these miRNAs included modulation of TGFβ signalling and the Hippo, MAPK and TNF signalling pathways. The identified SMAD-regulated miRNAs play roles in senescence, inflammation, and fibrosis.

Conclusions: Understanding the role of the TGFβ2 miRNAome in the TM will improve our understanding of physiological and pathological states in the TM. MiRNAs are epigenetic regulators of signalling pathways and the ability to therapeutically manipulate miRNAs with inhibitors or mimics may be an efficient therapeutic approach in POAG.

CONTROL ID: 3543634

SUBMITTER (NAME ONLY): Justine O'Brien

TITLE: Uncovering novel drugs that restore vision by combining biological and computational drug discovery processes

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. O'Brien, A. Cerquone Perpetuini, B.N. Kennedy, University College Dublin Conway Institute of Biomolecular and Biomedical Research, Dublin, IRELAND|R. Scoffin, Cresset BioMolecular Discovery Ltd, Cambridge, Cambridgeshire, UNITED KINGDOM|J. O'Brien, A. Cerquone Perpetuini, B.N. Kennedy, University College Dublin School of Biomolecular and Biomedical Science, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRD) are a group of conditions with progressive photoreceptor or RPE dysfunction resulting in blindness. Most IRDs lack effective treatments and novel therapies are needed to preserve vision. Phenotype-based screening of randomised compound libraries enables unbiased identification of first-in-class drugs. Here, we combine biological and virtual screening processes to identify novel compounds which rescue vision in a zebrafish model of IRD.

Methods: Phenotype-based drug discovery was performed on the atp6v0e1^{UCD6} zebrafish model of impaired vision screening a DIVERSet-Exp MF6 randomised compound library. 80 drug compounds were combined into 18 orthogonal drug pools for each plate testing. Visual behaviour was analysed at 5 days post-fertilisation by optokinetic response. Identified hits undergo iterative rounds of ligand-based computational screening to identify 3D analogues. A proof-of-concept virtual screen to identify mimetics of known neuroprotectant 7,8-dihydroxyflavone (7,8-DHF) was performed using Cresset Blaze™ software. Additional triaging was performed using Cresset Forge™ and KNIME.

Results: The orthogonal pooling protocol successfully detected visual rescue of atp6v0e1^{UCD6} in tubastatin A spiked pools (positive control) with 3-fold visual improvement and no toxicity in 10 µM pools of each drug. Orthogonal drug pooling is ongoing with 480 compounds tested to date. 7.4% of drug pools display a visual improvement of ≥4 fold with a toxicity level of 3.7%. An initial raw list of 2,000 molecules from a database of 16 million compounds was obtained from the Blaze™ screen. Manual analysis by 2D similarity calculations and murcko clustering shortlisted a final 25 compounds for biological validation.

Conclusions: We present a bespoke drug discovery workflow combining in vivo phenotype-based screening of visual behaviour cross informed with computational methods. This process successfully detects pools and single drugs restoring vision in atp6v0e1^{UCD6}. Drugs identified will undergo iterative rounds of computational/ biological refinement to provide further insights into IRD mechanisms and therapeutic development.

CONTROL ID: 3543637

SUBMITTER (NAME ONLY): BOWEN WANG

TITLE: RIP3-Mediated Necroptosis Triggers the Activation of NLRP3 Inflammasome in Dry Eye

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. WANG, X. Zuo, J. Yuan, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: To explore the role of necroptosis in dry eye disease(DED), and reveal its underlying mechanisms upon inflammatory initiation.

Methods: C57BL/6 wild-type(WT), RIP3^{-/-}, and NLRP3^{-/-} mice were exposed to desiccating stress (subcutaneous scopolamine [0.5 mg/0.2 mL] 3 times a day, humidity < 30%) for 7 days to establish experimental dry eye model. Cornea fluorescein staining, tear secretion, numbers of conjunctival goblet cells were assessed. Ultrastructural features of cell death were examined by transmission electron microscope(TEM). Western blot assays and immunofluorescence staining were used to measure the changes of RIPK3, MLKL, NLRP3, IL-1b, etc. mRNA expression was analyzed by RNA –sequencing(RNA-seq) and quantitative PCR.

Results: We observed extensively swollen and necrotic form of death of corneal epithelium detected by TEM in dry eye mouse model. Moreover, RNA-seq and GO analysis showed that both necroptosis and inflammation-related pathway were significantly sensitized. Western blot and immunofluorescence assay showed that an remarkably increase of RIP3, MLKL and NLRP3, IL1β in WT(DED) mice. Interestingly, we discovered that specific suppression of necroptosis in RIP3^{-/-}(DED) mice was able to alleviate the clinical parameters and abolished the activation of NLRP3, IL1β. However, although NLRP3^{-/-}(DED) mice also had obviously reduced corneal defects compared to WT(DED) mice, insignificant changes of necroptosis markers were detected. Accordingly, our data suggested that subconjunctival injection of NEC-1, a necroptosis inhibitor showed remarkable treatment effect in DED mice and inhibited NLRP3-related inflammation activation.

Conclusions: RIP3-mediated necroptosis in corneal epithelium activates the NLRP3 inflammatory pathway and promotes the development of DED.

CONTROL ID: 3543642

SUBMITTER (NAME ONLY): Tiarnan Keenan

TITLE: Cluster analysis and phenotype-genotype assessment of geographic atrophy secondary to age-related macular degeneration in the Age-Related Eye Disease Study 2

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.D. Keenan, E. Agron, E.Y. Chew, Department of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|N.L. Oden, T.E. Clemons, A. Henning, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|L. Fritsche, University of Michigan, Ann Arbor, Michigan, UNITED STATES|W.T. Wong, Janssen Research and Development LLC, Raritan, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore whether geographic atrophy (GA) in age-related macular degeneration (AMD) consists of two or more partially distinct phenotypic subtypes and to test genetic associations. This is important since GA subtypes driven by different genetic factors might require customized therapeutic approaches.

Methods: AREDS2 participants with incident GA were eligible (one eye per participant). Phenotypic features from reading center grading of fundus photographs were subjected to cluster analysis (Table), by both k-means and hierarchical methods. In pre-specified hypothesis tests, identified clusters were compared by four pathway-based genetic risk scores: complement (19 SNPs/6 loci), extracellular matrix (6 SNPs/5 loci), lipid (7 SNPs/4 loci), and ARMS2 (1 SNP/locus).

Results: The cohort comprised 598 individuals (mean age 74y). In cross-sectional phenotypic analyses, k-means identified two clusters: A and B (367/231 members, respectively), while hierarchical clustering identified four (Figure): C-F (451/112/12/5). In longitudinal phenotypic analyses, k-means identified two: G and H (310/288); hierarchical clustering identified none. The groups of clusters were not correlated with one other by membership (Pearson's $r \leq 0.20$). In cross-sectional analyses, GA configuration was the predominant factor for A-E membership. In longitudinal analyses, smoking status determined G vs H. Despite adequate power, pairwise cluster comparison by the four genetic risk scores demonstrated no significant differences ($p > 0.05$ for all).

Conclusions: In this large study, cross-sectional cluster analyses revealed GA subtypes defined principally by GA configuration. However, these subdivisions were not replicated in longitudinal analyses. Given the absence of significant cluster-genotype associations, for any eye with GA, physicians are unlikely to infer the main genetic driver of GA from phenotype alone. The inconsistencies in optimal cluster numbers and characteristics suggest that GA may show continuous phenotypic variation across a spectrum, rather than consisting of phenotypic subtypes that remain partially distinct over time, with separate genetic etiologies.

CONTROL ID: 3543645

SUBMITTER (NAME ONLY): Miin Roh

TITLE: Progression of Diabetic Retinopathy in Presence of Age-related Macular Degeneration

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Roh, M. Gilbert, M.A. Elmasry, J. Rhee, A. Rageh, P.S. Silva, J.K. Sun, L.P. Aiello, Ophthalmology, Harvard Medical School, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|M. Gilbert, Northwest Vision Institute, Bellevue, Washington, UNITED STATES|M.A. Elmasry, Ophthalmology, Alexandria University, Alexandria, EGYPT|

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ABSTRACT BODY:

Purpose: To evaluate the association between the presence of age-related macular degeneration (AMD) and progression of diabetic retinopathy (DR).

Methods: We retrospectively identified patients with at least mild nonproliferative diabetic retinopathy (NPDR), with or without AMD at the Joslin Diabetes Center. Inclusion criteria were age >50yrs, baseline visit between 2007-2014, >3 years of follow-up, and ICD-9/10 diagnosis code of mild to severe nonproliferative diabetic retinopathy (NPDR) with or without AMD. Patients were excluded if they had received prior anti-vascular endothelial growth factor (VEGF) injections or had proliferative DR (PDR) or neovascular AMD at baseline. AMD grading used the Age-Related Eye Disease Study classification system. DR progression was defined as >2-step progression in clinical grade or progression to PDR. Multivariable Cox regression analysis and Cox proportional hazards regression model were used to assess factors associated with progression of DR. Mediation analysis was performed in patients who had both baseline hemoglobin A1c (HbA1c) and average HbA1c values to investigate whether average HbA1c mediates the association between the presence of AMD and progression of DR.

Results: After exclusion, there were 223 eyes (138 patients) with DR with AMD and 476 eyes (260 patients) with DR without AMD included in the analysis. A total of 61 eyes (9.87%) had either ≥2-step progression of DR or progression to PDR during the follow up period (50 eyes (7.5%) had ≥2-step progression of DR and 46 eyes (6.6%) progressed to PDR). The rates of ≥ 2-step DR progression (HR 0.34, 95% CI 0.12~0.97, p=0.044) and progression to PDR (HR 0.34, 95% CI 0.13~0.90, p=0.0304) were lower in eyes with AMD compared to eyes without AMD in multivariable Cox regression analysis. Mediation analysis revealed that the association between the presence of AMD and decreased progression of DR was not affected by diabetic control measured by average HbA1c. Subgroup analysis revealed that there is a possible protective effect against ≥2-step DR progression and/or progression to PDR with lower HbA1c at baseline and current smoking status.

Conclusions: There is a lower rate of DR progression in patients with mild to severe NPDR when AMD coexists at baseline compared to those without AMD. The presence of AMD may have a protective effect against DR progression independent of diabetic control measured by HbA1c.

CONTROL ID: 3543647

SUBMITTER (NAME ONLY): Garrett Oberst

TITLE: Analgesic Efficacy for anti-VEGF Intravitreal Injections

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Oberst, C. Fraser, Ophthalmology, University of Kentucky Medical Center, Lexington, Kentucky, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Garrett Oberst: Commercial Relationship: Code N (No Commercial Relationship) | Claire Fraser: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal specialists continue to debate the best method for achieving adequate analgesia prior to intravitreal injections. This was an observational study at a large academic center to assess whether differences in analgesic procedure resulted in differences in pain levels.

Methods: Observational study of patients receiving intravitreal anti-VEGF injections at a university medical center. Inclusion criteria included any patient receiving anti-VEGF injections. Data including age, race, gender, diagnosis, number of injections at given visit, speculum use, and anti-VEGF medication administered were collected. Data regarding the numbing procedure were recorded including all times relative to injection and number of separate administrations of proparacaine, betadine, and akten gel. Patients were asked to rate their pain at the time of injection on a scale of 1-10 using a visual analog pain scale.

Results: 85 patients and 103 total eyes were injected. Those who received more than one drop of proparacaine perceived less pain than those receiving one or zero drops (2.13 vs. 3.27, $p=0.019$). Pain scores decreased with longer intervals from last akten gel administration to time of injection (3.33 for under 5 minutes vs. 2.86 for 6-10 minutes vs. 2.08 for over 11 minutes, $p=0.08$). While not statistically significant, patients who received injections from residents or fellows perceived higher pain scores than those from attending physicians (3.47 vs. 2.64, $p=0.10$). No statistically significant difference in pain perception was found based on demographic differences, medication injected, or speculum use. No difference was found regarding number of administrations or timing of proparacaine or betadine. Additionally, there was no statistically significant difference in pain scores regarding number of administrations of akten gel.

Conclusions: Only those who received more than one proparacaine drop were found to have statistically significant lower scores than those who received one or zero drops. Most variables measured in this study led to no difference in pain score. The data from this study can be used to improve the analgesia and overall patient experience prior to receiving intravitreal injections.

CONTROL ID: 3543648

SUBMITTER (NAME ONLY): Yinga Wu

TITLE: MiRNA-24 represses TGF- β 2 induced epithelial-mesenchymal transition (EMT) and fibrosis in RPE cells

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wu, K. Brynn, J. Ma, S. Wang, Tulane University, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yinga Wu: Commercial Relationship: Code N (No Commercial Relationship) | Katherine Brynn: Commercial Relationship: Code N (No Commercial Relationship) | Jing Ma: Commercial Relationship: Code N (No Commercial Relationship) | Shusheng Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ocular fibrosis can cause vision loss without treatment available. Subretinal fibrosis occurs in response to choroidal neovascularization (CNV) in wet Age-related macular degeneration (AMD), which is not treatable by anti-VEGF therapy. We have reported that miR-24 inhibits CNV in mice by regulating actin cytoskeleton remodeling. The purpose of the project is to define the function of miR-24 in subretinal fibrosis. We hypothesize that miR-24 overexpression can repress RPE-derived epithelial-mesenchymal transition (EMT) and subretinal fibrosis in AMD disease.

Methods: ARPE-19 cells or primary human RPE (hRPE) cells were treated with pre-miR-24 or adenovirus expressing miR-24 (Ad-miR-24). miR-24 overexpression was quantified by qRT-qPCR. EMT-associated gene expression in TGF- β 2 treated RPE cells was measured by Western blot and immunostaining. The expression of potential miR-24 target genes, SMAD3, LIMK2 and PAK4, were measured by Western Blot after miR-24 overexpression with or without TGF- β 2 treatment. Novel miR-24 target gene, SMAD3, was confirmed by luciferase assays. Lentivirus-mediated overexpression of target genes were used to rescue miR-24 overexpression phenotype. Stress fiber formation was visualized by Phalloidin staining and quantified by measuring the ratio of G-actin/F-actin. Student's t-test was used for statistical analysis.

Results: MiR-24 was significantly increased in APRE-19 or hRPE cells using Ad-miR24 or pre-miR-24. Markers of myofibroblast and fibrosis, including α -SMA, Fibronectin, Collagen III and Collagen I, were induced an in vitro EMT and fibrosis model. Overexpression of miR-24 repressed expression of these proteins as shown by Western blot analyses and immunostaining. SMAD3, a major protein critical for fibrosis by mediating TGF- β signaling, was identified as a miR-24 target gene, and was downregulated by miR-24 overexpression. Overexpression of miR-24 target genes SMAD3 or LIMK2 partially rescued miR-24 overexpression phenotype. miR-24 also repressed stress fiber formation and increased ratio of G-actin/F-actin, consistent with downregulation of its verified target protein LIMK2 and PAK4.

Conclusions: MiR24 overexpression prevents EMT and fibrosis and actin cytoskeleton dynamics through targeting SMAD3, LIMK2 and PAK4 in RPE cells. MiR-24 can be investigated as a therapeutic target for subretinal fibrosis in vivo.

CONTROL ID: 3543650

SUBMITTER (NAME ONLY): Jana Sajovic

TITLE: Characterisation of Stargardt disease pathogenesis associated with the frequent ABCA4 mutation c.5714+5G>A

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sajovic, A. Meglič, M. Jarc-Vidmar, M. Hawlina, A. Fakin, Department of Ophthalmology, Univerzitetni kliničny Center Ljubljana, Ljubljana, SLOVENIA|F.P. Cremers, M. Khan, Z. Corradi, C. Dhaenens, Radboudumc Department of Human Genetics, Nijmegen, Gelderland, NETHERLANDS|F.P. Cremers, Z. Corradi, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|M. Khan, Universitair Medisch Centrum Groningen Pathologie en Medische Biologie, Groningen, NETHERLANDS|C. Dhaenens, Centre Hospitalier Regional Universitaire de Lille Pole de Biologie Pathologie Genetique, Lille, Hauts-de-France, FRANCE|D. Glavač, Univerza v Ljubljani Institut za patologijo, Ljubljana, Ljubljana, SLOVENIA|A. Maver, M. Volk, B. Peterlin, Clinical institute of genomic medicine, Univerzitetni kliničny Center Ljubljana, Ljubljana, SLOVENIA|

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ABSTRACT BODY:

Purpose: To study the effect of ABCA4 mutation c.5714+5G>A on retinal structure and mRNA.

Methods: Sixteen patients were divided into two groups: group 1 harboured splicing mutation c.5714+5G>A in trans with a null mutation (6 patients); group 2 had two null mutations (10 patients). Visual acuity, autofluorescence and optical coherence tomography of the right eyes were analysed. Areas of definitely decreased autofluorescence (DDAF) and thickness of the outer nuclear layer (ONL) in the macula were measured. Correlation between the degree of retinal pigment epithelium (RPE) atrophy (DDAF area) and loss of photoreceptors (ONL thickness) was compared between groups using multiple linear regression. Mann-Whitney U Test was used for comparing sets of data. The effect of c.5714+5G>A on RNA splicing was analysed using reverse transcription (RT)-PCR of mRNA isolated from patient-derived photoreceptor progenitor cells (PPCs).

Results: Age at the exam did not differ significantly between the two groups (33.5 vs 20.5 yrs; $p>0.05$). However, group 1 patients had significantly later median age of onset (17.5 vs 8.0 yrs; $p<0.01$) and significantly better visual acuity (0.2 vs 0.02; $p<0.05$). Median ONL thickness was significantly higher in group 1 (15.9 μm vs 0.5 μm ; $p<0.01$), whereas median DDAF area was comparable between the groups (12.7 mm^2 vs 15.1 mm^2 ; $p>0.05$). Multiple linear regression showed a significant correlation between ONL thickness and DDAF area within each genotype group. For a similar RPE atrophy area, patients in group 1 have much better photoreceptor preservation ($p<0.01$). RT-PCR of mRNA from PPCs from a patient carrying c.4539+1G>T and c.5714+5G>A using primers in exons 38 and 44 showed a major normal product and minor exon 40 and exon 39/40 deletion products.

Conclusions: Patients harbouring ABCA4 mutation c.5714+5G>A displayed significantly milder phenotypes for all parameters, which is in accordance with our RNA results in PPCs and previous in vitro splice assays, suggesting that this is a moderately severe variant. Thicker ONL layer when compared to double null patients with DDAF of similar size suggests different disease pathogenesis characterised by predominant RPE loss and relative photoreceptor sparing in association with c.5714+5G>A allele.

CONTROL ID: 3543654

SUBMITTER (NAME ONLY): Preethi Ganapathy

TITLE: Mechanosensitive channel inhibition attenuates TGF β 2-induced actin cytoskeletal remodeling in optic nerve head astrocytes.

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.S. Ganapathy, A.C. Kirschner, J. Yablonski, A.N. Strat, T. Bague, H. Li, S. Herberg, Ophthalmology & Visual Sciences, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|A. Patteson, Physics, Syracuse University, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Astrocytes within the optic nerve head undergo actin cytoskeletal rearrangement early in glaucoma, prior to the development of tissue stiffening. Elevated transforming growth factor (TGF) β 2 levels within astrocytes have been described in glaucoma, and TGF β signaling induces actin cytoskeletal remodeling and extracellular matrix (ECM) stiffening in many tissues. A key mechanism by which astrocytes sense and respond to external stimuli is via mechanosensitive ion channels. Here, we tested the hypothesis that inhibition of mechanosensitive channels will attenuate TGF β 2-mediated optic nerve head astrocyte actin cytoskeletal remodeling and ECM stiffening.

Methods: Primary optic nerve head astrocytes were isolated from C57BL/6J mice and cell purity was confirmed by immunostaining. Astrocytes were treated with control medium, 5 ng/ml TGF β 2, 500 nM GsMTx4 (a mechanosensitive channel inhibitor), or 5 ng/ml TGF β 2 + 500 nM GsMTx4 for 48 h. FITC-phalloidin staining was used to assess the formation of f-actin stress fibers and to quantify the presence of crosslinked actin networks (CLANs). Cell reactivity was determined by immunostaining for GFAP. 3D hydrogels were made by mixing primary astrocytes with functionalized ECM components, UV-crosslinked using a photoinitiator, and subjected to the above treatments for 7 d. Live/dead staining was used to confirm astrocyte viability and hydrogel stiffness was measured using rheometry.

Results: Primary optic nerve head astrocytes were positive for the astrocyte marker GFAP and negative for markers for microglia (Iba1) and oligodendrocytes (OSP1). Increased %CLAN-positive cells were observed after 48-h treatment with TGF β 2 vs. control (23.8% vs 5.3%, $p < 0.0001$). Co-treatment with GsMTx4 decreased %CLAN-positive cells vs. TGF β 2 treatment (12.4% vs 23.8%, $p < 0.0001$) and decreased the presence of f-actin stress fibers. TGF β 2 treatment increased GFAP fluorescence intensity, which was decreased when co-treated with GsMTx4 ($p < 0.05$). Cells within hydrogels maintained $>90\%$ viability after 7 d. Hydrogels treated with GsMTx4 were less stiff when compared to control and TGF β 2-treated hydrogels ($p < 0.01$).

Conclusions: Our data suggest inhibition of mechanosensitive channel activity as a potential therapeutic target to prevent actin cytoskeletal remodeling and tissue stiffening within the optic nerve head in glaucoma.

CONTROL ID: 3543655

SUBMITTER (NAME ONLY): Ryan Zukerman

TITLE: Diurnal optic nerve head blood flow biomarker differences between male and female subjects with and without glaucoma measured by optical coherence tomography angiography

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zukerman, A. Harris, B.A. Siesky, A. Verticchio Vercellin, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|R. Zukerman, University of Miami School of Medicine, Miami, Florida, UNITED STATES|F. Oddone, IRCSS Fondazione G B Bietti per lo Studio e la Ricerca in Oftalmologia ONLUS, Roma, Lazio, ITALY|R.B. Rosen, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|L.W. Rowe, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|A. Verticchio Vercellin, Università degli Studi di Pavia, Pavia, Lombardia, ITALY|G. Eckert, Department of Biostatistics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the differences in diurnal optic nerve head (ONH) blood flow biomarkers between male and female subjects with and without open-angle glaucoma (OAG) as measured by optical coherence tomography angiography (OCT-A).

Methods: 34 subjects (21 OAG: 7 male, 14 female; and 13 healthy: 6 male, 7 female) were assessed for ONH and radial peripapillary capillary layer (RPC) flow area (mm^2), vessel density percentage (NH VD%, RPC VD%), and flow index (NH index, RPC index) using OCT-A (RTVue XR Avanti SD-OCT with AngioVue® software, Optovue, Fremont, CA, USA) at 9:00, 11:00, 14:00, 16:00, and 18:00 during a single day. Results were analyzed using two-sample t-tests assuming unequal variances to analyze the differences between genders. P-value<0.05 was considered statistically significant.

Results: The OCT-A blood flow parameters were significantly lower in male OAG patients compared to female OAG patients at 18:00 (ONH flow area: $2.33 < 2.84 \text{mm}^2$, $p=0.012$; RPC flow area $1.25 < 1.66 \text{mm}^2$, $p=0.016$; NH VD% $66.55 < 75.67$, $p=0.041$; NH index $0.07 < 0.08$, $p=0.05$). There were no statistical significant differences between OAG male and female in RPC VD% ($p=0.075$) or RPC index at 18:00 ($p=0.16$). No other statistically significant differences were found at 9:00, 11:00, 14:00 or 16:00 time points between male and female OAG patients, or between healthy male and female subjects at any time point ($p>0.05$).

Conclusions: Our findings highlight possible diurnal gender-based variance in OCT-A ocular blood flow biomarkers of OAG patients, warranting further study to confirm our results.

CONTROL ID: 3543659

SUBMITTER (NAME ONLY): Yoko Miura

TITLE: Fluorescence Lifetime Imaging Ophthalmoscopy of mouse models of age-related macular degeneration

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Miura, B. Lewke, E. Ishizuka, R. Brinkmann, Institute of Biomedical Optics, University of Lübeck, Lübeck, GERMANY|Y. Miura, S.R. Sonntag, S. Grisanti, Department of Ophthalmology, University of Lübeck, Lübeck, GERMANY|E. Seifert, R. Brinkmann, Medical Laser Center Lübeck, GERMANY|

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ABSTRACT BODY:

Purpose: Fluorescence lifetime (FLT) is a fluorophore-specific property and cellular FLT may be influenced by cell metabolic states. Fluorescence lifetime imaging ophthalmoscopy (FLIO) is a new method that enabled the measurement of FLT of ocular fundus. The purpose of this study was to investigate the fundus FLT of mouse models of retinal degeneration with FLIO.

Methods: Two mouse models of age-related macular degeneration (AMD), apolipoprotein E (ApoE) deficient mice (ApoE^{-/-}) and nuclear factor erythroid 2-related factor 2 (NRF2) deficient mice (Nrf2^{-/-}), and wild type mice (control; C57BL/6J) were investigated monthly from 3 months old (24 mice per strain). Under general anesthesia, slit lamp Ophthalmoscopy, FLIO, optical coherence tomography (OCT) and fundus photography were conducted. The mice were euthanized either at 6 months old or 11 months old. The blood plasma was collected to examine the level of total antioxidant capacity (TAC). The frozen sections of the enucleated eyes were assessed with lipid stainings (Oil Red O).

Results: AMD-like pathological findings (e.g. drusen) were observed after 7 months old in some mice of AMD models. The mean FLT (τ_m) was generally shortened with age in all groups. Both AMD models showed significantly shorter τ_m than the control at 4 months old. After that, τ_m of ApoE^{-/-} mice was further shortened to a larger extent than the control until 11 months old in both spectral channels, whereas Nrf2^{-/-} mice showed an apparently prolonged τ_m in the long spectrum channel. The strongest lipid staining of the Bruch's membrane was observed in ApoE^{-/-} mice at 11 months old. The blood TAC of ApoE^{-/-} mice was significantly higher than the control at 6 and 11 months. Nrf2^{-/-} mice showed higher TAC at 6 months old than control, but then decreased and no more difference was found from the control group at 11 months old.

Conclusions: Both mouse models of AMD showed a temporarily shorter fundus FLT than the wild type at a very early time point, presumably owing to the metabolic activation due to stress. After that, however, the fundus FLT of these two strains progressed totally differently over time. The systemic antioxidant capacity could be associated with this difference. These results strongly suggest that FLIO may indicate early changes of metabolic and redox states of the retina prior to the onset of degenerative retinal disorders.

CONTROL ID: 3543661

SUBMITTER (NAME ONLY): Jacob Nilles

TITLE: Immunomodulatory gene therapy for treatment of ocular graft vs host disease

SESSION TITLE: Corneal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Nilles, D. Roberts, B. Salmon, B.C. Gilger, North Carolina State University, Raleigh, North Carolina, UNITED STATES|M. Hirsch, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular graft versus host disease (OGvHD) is a common complication of allogeneic hematopoietic stem cell transplantation (HSCT) and frequently manifests as keratoconjunctivitis sicca (KCS). The aim of this study was to evaluate the efficacy of a single subconjunctival (SC) dose of adeno-associated virus (AAV) gene therapy encoding human leukocyte antigen G (HLA-G) to induce ocular immune tolerance and inhibit clinical signs of OGvHD.

Methods: The major histocompatibility mismatch chronic OGvHD murine model was created, as described by Perez (2016; doi:10.1016/j.bbmt.2016.07.012). Animal use was approved by the NC State University IACUC (protocol #20-122-B). To create the murine OGvHD model, bone marrow (BM) and splenocytes were collected from male C57BL/6 (n=4) mice 6-8 weeks of age. Female BALB/c mice (n=12), aged 6-8 weeks, were administered 700cGy total body X-ray irradiation, as optimized in our preliminary studies. Two hours after irradiation, mice were injected into a lateral tail vein with 1×10^7 BM cells and 1×10^6 splenocytes. Following injection, body weights and tear production (phenol red test) were recorded, and scores (0-4) (observer blinded to treatment groups) of the eyelid margins, corneal opacity, and corneal fluorescein were collected through day 44 after HSCT. At 7 days following HSCT, mice received in both eyes either a single SC injection of AAV8-HLA-G1&5 (1×10^9 vg/eye), no treatment (n=4), or 2µL of CsA 1% solution twice daily (n=4).

Results: Eyelid scores of eyes dosed with AAV-HLA-G were significantly lower than untreated or CsA treated eyes from 24-44 days after HSCT ($p < 0.03$ Wilcoxon). Cornea scores of eyes dosed with AAV-HLA-G were significantly lower than untreated or CsA treated eyes from 27-44 days after HSCT ($p < 0.01$, Wilcoxon). Fluorescein scores of eyes dosed with AAV-HLA-G and CsA were significantly lower than untreated eyes from 30-44 days after HSCT ($p < 0.02$, Wilcoxon). No statistically significant difference in weight or tear production was observed between any of the three treatment groups.

Conclusions: These results further validate the function of HLA-G in the murine model, indicate that the SC therapeutic route targets relevant ocular tissues, and provides strong support that HLA-G-based gene therapy will be an effective single vector treatment for OGvHD. Further evaluation of AAV-HLA-G based therapeutics are warranted for ocular surface and intraocular immune-mediated diseases.

CONTROL ID: 3543662

SUBMITTER (NAME ONLY): Henk Weeber

TITLE: Light intensity distribution of presbyopia-correcting intraocular lenses

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.A. Weeber, F. Gounou, P. Piers, R&D, AMO Groningen b.v., NETHERLANDS|

Commercial Relationships Disclosure (Abstract): Henk Weeber: Commercial Relationship(s);AMO Groningen b.v.:Code E (Employment) | Franck Gounou: Commercial Relationship(s);AMO Groningen b.v.:Code E (Employment) | Patricia Piers: Commercial Relationship(s);AMO Groningen b.v.:Code E (Employment)

ABSTRACT BODY:

Purpose: The diffractive efficiency is traditionally defined as the ratio of usable energy relative to total incident energy for individual diffraction orders of a diffractive optical element. For many of the current presbyopia-correcting intraocular lenses the traditional methods for determining light distribution are not suitable, because of overlapping foci or even lack of discrete foci. The goal of this study was to develop a new method of determining the image (light) intensity produced by diffractive ophthalmic lenses over the visual defocus range from far to near.

Methods: As in our previous study, light intensities were measured in an optical setup consisting of a white light source, slit target, collimator, cornea, liquid cell, relay lens and imaging camera. Care was taken that the incoming light intensity was kept at a constant level for all measurements. The image (line spread function, LSF) was recorded over a range of defocus positions.

Light intensity was evaluated over the central part of the LSF up to the first minimum of the image of a diffraction limited system (Airy disk for white light).

Design features measured included diffractive multifocal and extended depth of focus IOLs. An aspherical refractive monofocal lens which fully corrects the corneal monochromatic aberrations was used as a reference lens.

Results: With the new method, 41 LSF images were recorded for each lens, over a defocus range from -4 to +1 diopter. Considering the linear relationship between the logarithm of the light intensity and visual acuity (Sheedy 1984), the measurement results are evaluated as $\log(\text{intensity})$. The relative light intensity (RLI) is defined as $\log(\text{intensity})$ of the study IOL divided by the $\log(\text{intensity})$ of the monofocal reference IOL. For the distance focus, LRI is 0.93, 0.94 and 0.95 for the multifocal IOL, the extended depth of focus IOL, and the hybrid IOL, respectively.

At defocus levels exceeding -1 diopter, LRI was larger than 1.0 for all study lenses, which can be attributed to their presbyopia correcting nature, i.e. being multifocal or having an extended depth of focus.

Conclusions: Measurements of through focus light intensity can be used to assess the light distribution and present the results in a clinically relevant metric, here called the relative light intensity (LRI).

CONTROL ID: 3543663

SUBMITTER (NAME ONLY): Kishan Pithadia

TITLE: The association between systemic disease and affliction with both glaucoma and macular degeneration

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Pithadia, Augusta University, Augusta, Georgia, UNITED STATES|B. Strelow, A.Y. Zhang, D. Fleischman, Ophthalmology, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|Z. Zhang, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) and glaucoma are both leading causes of vision loss. Glaucoma affects the optic nerve while AMD affects the macular retinal pigment epithelium. Both result in vision impairment, with AMD primarily affecting central vision and glaucoma typically affecting peripheral vision. Each condition has been associated with increased systemic comorbidities compared to control populations. However, no literature discusses comorbidities seen in patients simultaneously affected with glaucoma and AMD. We investigate whether there is an increased association with other systemic conditions in these patients, as presenting with both ophthalmologic conditions may provide greater insight into a patient's overall health or response to stress.

Methods: The i2b2 interface was used to access the Carolina Data Warehouse, which contains clinical data for patients seen in the University of North Carolina Health System. Datasets of patients seen from April 2004 to June 2018 were created by searching ICD codes, yielding a set comprised of patients with each of the following diagnoses: glaucoma only, AMD only, glaucoma and AMD, and cataracts. Within each group, prevalence of systemic diseases was searched, and a Friedman's two-way analysis of variance compared prevalence between groups. Groups were further compared on race, age, and sex distributions to rule out confounders.

Results: The i2b2 database identified 5243 patients with glaucoma only, 6726 with AMD only, 402 with combined disease, and 25450 with cataracts only. Patients with both glaucoma and AMD compared to groups with glaucoma alone and cataracts alone were more likely to have heart failure ($p=.036$, $.036$, respectively) and dementia ($p=.023$, $.00349$). Demographic analysis indicated a statistically significantly older population with both glaucoma and AMD compared to glaucoma alone, but no other differences were seen between group demographics.

Conclusions: The significantly increased prevalence in heart failure and dementia in the group with both glaucoma and AMD may suggest an increased propensity to developing these diseases in patients with both ophthalmologic conditions. These associations and underlying pathologic mechanisms may provide insight into health management and prognostication for these individuals.

CONTROL ID: 3543666

SUBMITTER (NAME ONLY): Henar Albertos-Arranz

TITLE: Phenotypic differences in the PRPH2 mutation in members of the same family assessed with OCT and OCTA

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Albertos-Arranz, X. Sánchez-Sáez, N. Martínez-Gil, M. Ruiz-Pastor, P. Lax, N. Cuenca, Physiology, Genetics and Microbiology, University of Alicante, Alicante, Comunidad Valenciana, SPAIN|J. Delgado, Asociación Retina Asturias/Cantabria, SPAIN|I. Pinilla, Ophthalmology, Hospital Clinico Universitario Lozano Blesa, Zaragoza, Aragón, SPAIN|I. Pinilla, Instituto de Investigacion Sanitaria Aragon, Zaragoza, SPAIN|R. Coco-Martín, Universidad de Valladolid, Instituto de Oftalmobiología Aplicada, Valladolid, Castilla y León, SPAIN|R. Coco-Martín, OFTARED, Instituto de Salud Carlos III, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Central choroidal dystrophies comprise degenerative diseases of the retina where choroid is also affected. The main cause of these dystrophies is related to mutations in the PRPH2 gene involved in the formation and maintenance of outer segments discs of photoreceptors. This study analyzes the structural changes of the retina and the vascular network in some members of a Spanish family with different choroidal dystrophies.

Methods: Cross-sectional and comparative study of 4 family members. OCT images in the macula were analyzed quantitative and qualitatively. Outer and inner retina measurements were done in the fovea and parafovea. Slabs of superficial vascular plexus, intermediate and deep capillary plexuses and choriocapillaris and choroid vessels were obtained to study their morphology and possible degeneration signs. Alterations in the foveal avascular zone (FAZ) were also described.

Results: Different clinical findings were present among family members with the same PRPH2 mutation: half were diagnosed with central areolar choroidal dystrophy (CACD) while the rest showed extensive chorioretinal atrophy (ECA). Retinal degeneration was mainly located at fovea and parafovea in CACD patients and the outer nuclear layer thickness in the FAZ was considerably reduced. ECA patients showed a more general degeneration that spread out through the central retina. The third outer hyperreflective band in OCT, considered as outer segments phagocytosed by the retinal pigment epithelium, was the first one disrupted of the four outer bands. Vascular degeneration was similar among them. Capillary drop out areas were larger in the deep capillary plexus. Microaneurysms were mainly detected in the superficial vascular plexus and were more easily found at early stages. Intraretinal microvascular abnormalities and vascular loops were observed in retinal plexuses. Extensive degeneration areas of choriocapillaris were seen in OCTA images which allowed to visualize the structure of choroid vessels.

Conclusions: Same PRPH2 mutation among different family members can cause phenotypic variations since youth. Clinical diagnosis and stage disease can be more easily defined in chorioretinal dystrophies using OCT and OCTA. Support. FEDER-PID2019-106230RB-I00. FPU16/04114, FPU18/02964. RETICS-FEDER RD16/0008/0016. Retina Asturias/Cantabria. FARPE-FUNDALUCE. IDIFEDER/2017/064, ACIF/2020/203. RD16/0008/0001.

CONTROL ID: 3543669

SUBMITTER (NAME ONLY): Stefano Barabino

TITLE: Efficacy of a New Tear Substitute Containing Hyaluronic Acid and a Low Dose of Hydrocortisone in Dry Eye Disease

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Barabino, Ophthalmology, Ocular Surface & Dry Eye Center, ASST Fatebenefratelli SACCO-University of Milan, Milan, ITALY|E. Vilella, S. Marini, Ophthalmology, ASST Fatebenefratelli SACCO-University of Milan, Milan, ITALY|L. Loreggian, C. Loretelli, P. Fiorina, Dipartimento di Scienze Biomediche e Cliniche "L. Sacco", University of Milan, International Center for T1D, Pediatric Clinical Research Center "Romeo ed Enrica Invernizzi", Milan, ITALY|P. Fiorina, Nephrology Division, Boston Children's Hospital, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G. Spedicato, Università Cattolica del Sacro Cuore di Milano, Milan, ITALY|M. Rolando, Ocular Surface Center, Is.Pre Oftalmica, Genoa, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the effect of a new tear substitute containing hyaluronic acid (HA) and a low dose (0.001%) of hydrocortisone in patients with dry eye disease in a randomized, double-masked pilot study.

Methods: Dry eye and treatment outcomes were assessed by SANDE questionnaire, Schirmer I test, tear BUT, conjunctival staining by using a new formulation of liquid lissamine green, and fluorescein corneal staining (baseline, day 7 and 28). Immune cells (CD45⁺, CD14⁺, CD4⁺, CD8⁺) were detected by impression cytology and flow cytometry at baseline and day 28. All patients (n=40) received fluorometholone eye drops bid for one week. The study group used the new tear substitute (Idroflog, Alfa Intes, Italy) bid for one week and qid for three weeks; the control group used HA alone with the same regimen. Intraocular pressure (IOP) was recorded at baseline, day 7 and 28.

Results: Severity and frequency of symptoms were improved in both groups at day 7 and 28. Fluorescein and liquid lissamine green staining were significantly decreased at day 30 in the study group respect to the control ($p \leq 0.05$). No significant changes were recorded for Schirmer test and BUT. While CD45⁺ cells were decreased in both groups, CD14⁺ cells and the CD4/CD8 ratio significantly decreased in the study group only ($p \leq 0.05$). None of the treated eyes showed significant increase in IOP at day 28.

Conclusions: The results show the efficacy of a new a tear substitute to improve signs of dry eye, and to control inflammation over time. Further results are expected at a longer follow up (6 months), but the importance of chronic use of tear substitutes containing low percentage of steroids in dry eye seems to be demonstrated.

CONTROL ID: 3543671

SUBMITTER (NAME ONLY): Elton Zhou

TITLE: The Natural History of Choroidal Melanoma: A Systematic Review and Meta-analysis

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.K. Zhou, L.L. Shen, A. Ahluwalia, R. Pointdujour-Lim, L.V. Del Priore, Ophthalmology, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|S. Khetpal, M. Sun, R. Yusuf, H. Grossetta Nardini, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveal melanoma is the most common primary intraocular tumor in adults with over 5 million cases per year worldwide. Choroidal melanoma accounts for 90% of these tumors. Due to the high risk of metastasis, choroidal melanoma is almost always treated and therefore the natural growth of untreated choroidal melanoma is unknown. In this study, we attempted to model the growth pattern of untreated choroidal melanoma and analyze the natural progression of the disease.

Methods: We conducted a systematic search of Clinicaltrials.gov, Ovid MEDLINE, PubMed for unindexed materials, Ovid Embase, Science Citation Index Expanded, and the Cochrane Library for publications involving untreated choroidal melanoma tumor size published prior to April 30, 2019. An exponential model of tumor growth was developed using tumor height over time from individual subjects. To correct for differences in the time of enrollment for subjects, a temporal translation factor was applied to convert "time after enrollment" to "inferred age of tumor." Regression analysis was used to find optimal tumor doubling time and initial tumor height. The relationship between tumor volume and tumor height was modeled as a cubic function using a subset of the data. From this relationship, tumor volume and volume doubling time were estimated from tumor height and height doubling time, respectively.

Results: Forty-four patients from three studies were identified that met our inclusion criteria. The tumor height data were well described by our exponential model which estimated a tumor height doubling time of 27.2 months and initial tumor height of 1.05mm ($R^2 = 0.77$). Our model of tumor volume as a cubic function of tumor height found that volume = $2.07 \times \text{height}^3$ ($R^2 = 0.86$). This suggests that the tumor volume doubling time is one-third of tumor height doubling time, thus predicting a tumor volume doubling time of 9.05 months.

Conclusions: From our analysis, untreated choroidal melanoma tumors appear to grow exponentially with a volume doubling time that matches the current literature (5.1-17.0 months). Additionally, our model predicted the height at which the tumors begin to grow exponentially. This value corresponded to an initial tumor volume of 2.40mm^3 . This model of choroidal melanoma growth patterns may help to understand treatment efficacy compared to the natural progression of the disease as well the transition from benign nevus to malignant tumor.

CONTROL ID: 3543672

SUBMITTER (NAME ONLY): Rakin Muhtadi

TITLE: Premature infants born less than 25 weeks need more ophthalmology exams and treatment for ROP than older premature infants

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Muhtadi, V.S. Hawn, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|P.D. Suman, U. Mian, Montefiore Medical Center, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of Prematurity (ROP) is a sight threatening disease that can affect preterm infants. It is unclear how low gestational age affects ophthalmologic screening and treatment rates. This study evaluates the examination and treatment rates of infants born less than 25 weeks gestational age (GA) compared to those born 25 weeks or greater requiring screening for ROP.

Methods: This is a retrospective, cross sectional study of infants who met institutional ROP screening criteria and were admitted to two Montefiore Medical Center (Bronx, NY) NICUs from January 2017 to June 2020. Data was collected using EMR (Epic Systems Corporation, Verona, Wisconsin). Patients were excluded if they were transferred to another facility before screening was completed.

Variables analyzed were GA, birth weight, number of ophthalmology exams (inpatient/outpatient), worst stage of ROP, type I disease or APROP in either eye.

Infants were divided into two groups: Group "GA<25" were those with GA less than 25 weeks and group "GA≥25" were infants with GA equal to or greater than 25 weeks. Two tailed student's T-test and chi square test were used for statistical analysis.

Results: Table 1 and Table 2 provide demographic and eye examination results respectively for a total of 415 infants of which 7.3% (n=30) had GA<25. As expected, GA<25 infants had significantly lower birth weight compared to GA≥25 (656g vs 1150g, p<0.001) and significantly higher mortality (37% vs 8.11%, p<0.00001). There were no differences in sex or single/multiple births between the two groups. GA<25 infants had a significantly higher number of total examinations than GA≥25 (9.8 vs 4.2, p<0.001) and higher numbers of inpatients exams (7.8 vs 2.5, p<0.001). Outpatient exams were similar (2.1 vs 1.5). GA<25 had worst average stage of ROP at 1.33 compared to 0.224 for GA≥25 (p<0.001). Rates of Type I ROP were significantly higher for GA<25 compared to GA≥25 (20% vs 1.04%, p<0.001).

Conclusions: Infants with GA<25 required significantly more ophthalmologic exams, developed more severe ROP and had a higher treatment rate. It is important for ROP services, including neonatologists and ophthalmologists, to be aware of this increased clinical burden, especially as the number of such infants starts increasing in their NICUs.

CONTROL ID: 3543676

SUBMITTER (NAME ONLY): Michael Simpson

TITLE: Preclinical Estimation of Constants for Intraocular Lens Power Calculations

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Simpson, Simpson Optics LLC, Arlington, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Michael Simpson: Commercial Relationship(s);Simpson Optics LLC:Code E (Employment)

ABSTRACT BODY:

Purpose: Intraocular lenses (IOLs) are labeled with a lens power, but a corresponding “lens constant” is also needed for IOL power calculations. This is typically determined by back-calculation from earlier postoperative results, and initial patients may have less accurate refractive outcomes. To address this, a method for estimating the SRK/T A-Constant before any IOLs have been implanted is described. Parameters that have a strong effect on the A-Constant are also discussed, such as the shape factor, the asphericity, and the methods used for IOL testing.

Methods: The final axial location of the IOL is the greatest unknown, but this is primarily determined by the lens capsule, which contracts around the lens and haptics, while also being stretched flat by the zonules. A new IOL can be physically compared to an existing single-piece IOL to estimate the location, and image distances can be calculated or measured using the ISO2 model eye to estimate the optical effects (Fig. 1a). An average eye is assumed, and a central range of IOL powers (eg 19D–23D)). Zemax calculations demonstrate the method here for several conceptual high index (1.55) IOL styles that have different shape factors and spherical aberration values (Fig. 1b). The haptic location was used to position the lenses.

Results: The “best focus” image distances for a 3 mm pupil diameter are plotted against the labeled power values in Fig 2, along with estimated power changes relative to the equiconvex spherical lens. The calculations illustrate how changes to the shape factor and the asphericity can each change the effective power of the IOL by 0.5 D, with more than 2 D difference across this extreme range of potential styles. Differences can be used to adjust the A-Constant.

Conclusions: The focusing effect of IOLs in an average laboratory eye can be used to estimate the SRK/T “A constant” through comparison to an existing lens. The IOL axial location is envisaged to be constrained primarily by the capsule, and this is estimated by comparing design features (in this case, simply the haptic location). This estimation is the weakest part of the analysis. Calculations are useful, but the best results would come from actual lens measurements at 35 C in saline, to be close to actual eye conditions. The theoretical designs would then not be needed, and any unexpected effects would also be addressed, with the use of several powers averaging out any fabrication variations.

CONTROL ID: 3543681

SUBMITTER (NAME ONLY): Ana Rita Santos

TITLE: Degree and Location of Retinal Capillary Closure Indicate ETDRS grading of Non Proliferative Diabetic Retinopathy

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To explore the use of widefield OCTA (Swept-source OCTA PlexElite) to identify capillary closure in different regions of the retina (perifovea vs mid-periphery) in diabetes type 2, and its correlation with ETDRS severity stages.

Methods: 105 eyes from diabetic type 2 patients (66.6 ± 7.9 yrs) were imaged with the PlexElite 9000 (Zeiss, Dublin, CA) using Angio 15x9mm and Angio 3x3mm protocols. Data was processed by the Density Quantification of Averaged Data v0.3.5 algorithm available on the Advanced Research Imaging portal which uses multi-layer segmentation and calculates vascular density metrics for Superficial Capillary Plexus (SCP) and Deep Capillary Plexus (DCP). For retinal mid-periphery, 3 extra concentric rings were added to the standard 9 ETDRS areas. Images were checked for quality: signal strength ≥ 6 , minimal motion artefacts and no evidence of defocus. Diabetic eyes were classified using the ETDRS severity scale, Grade 10-15 ($n=16$), 20 ($n=17$), 35 ($n=37$), 43 ($n=15$) and 47 to 65 ($n=14$). Skeletonized Vessel Density (VD) measurements from diabetic patients were compared to an age matched healthy control population ($n=28$; 58.7 ± 17.9 yrs).

Results: Retinal capillary closure (CC) diabetes type 2 patients with mild ETDRS levels (10-35), predominates in the parafoveal region, with SCP VD values of 13.2 ± 1.6 in ETDRS 10-20 ($p < 0.001$) and 12.4 ± 2 in ETDRS 35 ($p < 0.001$), when compared with the healthy control population (14.6 ± 1.1).

The CC extends to the retinal mid-periphery in the more severe ETDRS stages, with DCP VD values of 10.8 ± 6.4 in ETDRS 43-47 ($p = 0.002$) and 10.1 ± 4.6 in ETDRS 53-61 ($p = 0.013$) comparing with healthy control population. Involvement of one or more retinal quadrants correlate with increase in ETDRS grade severity and allow discrimination between different ETDRS levels (see table 1). The 3x3mm acquisition protocol identifies well the initial DR stages (10-35), whereas 15x9 mm widefield SS-OCTA acquisitions of the midperiphery differentiates the more severe ETDRS levels.

Conclusions: Retinal CC, quantified by SS-OCTA, allows the identification and separation of different ETDRS levels, by combining 3x3mm and 15x9mm acquisitions and considering the number of retinal quadrants affected. SS-OCTA metrics of retinal CC, allowing measurements to be performed in the macula and in more retinal peripheral regions, may offer an objective and easier alternative to ETDRS severity grading.

CONTROL ID: 3543683

SUBMITTER (NAME ONLY): Jost Jonas

TITLE: Axial Length and Its Associations in a Very Old Population. The Ural Very Old Study

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the distribution of axial length and its determinants in a very old population.

Methods: The population-based Ural Very Old Study included 1526 (81.1%) participants out of 1882 eligible individuals aged 85+ years. The participants underwent a detailed ophthalmological and medical examination including sonographic axial length measurement.

Results: Biometric data were available for 717 (47.0%) individuals with a mean age of 88.0 ± 2.6 years (range:85-98 years; 25%). Mean axial length was 23.1 ± 1.1 mm (range:19.37-28.89mm) and 23.1 ± 1.1 mm (range:19.507-28.84mm) in the right eyes and left eyes, respectively. Prevalences of moderate myopia (axial length:24.5-<26.5mm) and high myopia (axial length ≥ 26.5 mm) were 47/717 (6.6%;95%CI:4.7,8.4) and 10/717 (1.4%;95%CI:0.5,2.3), respectively. Longer axial length was associated (correlation coefficient $r:0.37$) with taller body height ($P<0.001$;standardized regression coefficient $\beta:0.26$; non-standardized regression coefficient $B:0.03$; 95% confidence interval (CI): 0.02, 0.04), higher level of education ($P<0.001$; $\beta:0.12$; $B:0.06$;95%CI:0.02,0.11), and thinner peripapillary retinal nerve fiber layer thickness ($P=0.001$; $\beta:-0.15$; $B:-0.004$;95%CI:-0.006,-0.002), in addition to more myopic spherical refractive error ($P=0.001$; $\beta:-0.15$; $B:-0.08$;95%CI:-0.13,-0.03). In that model, axial length was not significantly associated with age ($P=0.52$), gender ($P=0.17$) and intraocular pressure ($P=0.21$).

Conclusions: Mean axial length (23.1 ± 1.1 mm versus 23.30 ± 1.10 mm) and prevalence of moderate axial myopia (6.6% (95%CI:4.7,8.4) versus 8.7% (95%CI:9.0,10.5)) and high axial myopia (1.4% (95%CI:0.5,2.3) versus 1.4% (95%CI:1.1,1.7)) in this old study population were comparable with values from the younger population of the Ufa Eye and Medical Study conducted in the same study regions. As in previous studies, higher axial length was correlated with higher level of education

CONTROL ID: 3543684

SUBMITTER (NAME ONLY): Kristin Josic

TITLE: Conversion of Central Subfield Thickness Measurements of Diabetic Macular Edema across Cirrus and Spectralis Spectral Domain Optical Coherence Tomography Instruments

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Josic, Jaeb Centre for Health Research, Tampa, Florida, UNITED STATES|K. Josic, DRCR Retina Network, Tampa, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kristin Josic: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To develop equations to convert automated central subfield thickness (CST) values among eyes with diabetic macular edema (DME) between Cirrus (Carl Zeiss Meditec) and Spectralis (Heidelberg Engineering) instruments.

Methods: A random sample of 70% of the data from participants in a cross-sectional observational study (DRCR Retina Network Protocol O) who underwent two replicate scans on both Cirrus and Spectralis instruments were used to develop the conversion equations. The remaining 30% of the data and data from an independent study (CADME) were used to validate the equations. Concordance correlation coefficients and Bland-Altman 95% limits of agreement (LOA) were used to evaluate conversion equation performance.

Results: A total of 262 CST scan pairs from 131 eyes of 75 participants in Protocol O were used to develop the equations. The validation samples included 112 scan pairs from 56 eyes of 32 participants in Protocol O and 150 scan pairs from 37 eyes of 37 participants in CADME. The proposed conversion equations with units of μm are (1) Spectralis = $40.78 + 0.95 \times \text{Cirrus}$ and (2) Cirrus = $1.82 + 0.94 \times \text{Spectralis}$. The concordance correlation coefficients between observed and converted measurements ranged from 0.96 to 0.99. Converting CST between Spectralis and Cirrus, 95% of the converted measurements are expected to be within $\pm 10\%$ or $\pm 32 \mu\text{m}$ of the observed measurements on the other instrument.

Conclusions: The conversion equations developed in this study are suitable for the transformation of values from individual scans taken with Cirrus or Spectralis machines as well as averaged values from cohorts of eyes with DME. Variability of observed versus converted measurements is similar to that of test retest. Although previous work enabled the conversion of Spectralis and Cirrus measurements to time domain OCT equivalents, time domain OCT is now obsolete. Thus, the ability to convert CST values from one SDOCT instrument to another will benefit both clinical research and standard care efforts.

CONTROL ID: 3543686

SUBMITTER (NAME ONLY): Ajay Ashok

TITLE: ARPE19 cells exposed to sodium iodate accumulate ferritin in lysosomes and release ferritin-rich vesicles in the extracellular milieu: Implications for in vitro model of AMD

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ashok, S. Chaudhary, A. S. Wise, A. E. Kritikos, N. Rana, N. Singh, pathology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|E. Lindner, Medical University of Graz, AUSTRIA|

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ABSTRACT BODY:

Purpose: Exposure of the retinal pigment epithelial cell line (ARPE19) to the oxidant sodium iodate (NaIO_3) is a well-established in vitro model of retinal degeneration, including age related macular degeneration (AMD). Higher levels of iron in AMD retinas and a protective effect of an iron chelator has been reported before by Hadziahmetovic et al. The underlying mechanism of NaIO_3 -induced iron accumulation and retinal degeneration, however, remains unclear. Here, we explored the mechanism of iron accumulation in NaIO_3 -treated ARPE19 cells.

Methods: ARPE19 cells were obtained from ATCC and used until passage 20. Cells were treated with 10 mM of NaIO_3 for 24 h, and the lysates were evaluated for various proteins with specific antibodies by Western blotting (WB). Additionally, NaIO_3 -treated cells were co-immunostained with organelle-specific antibodies to confirm the localization of ferritin.

Results: Immunoblotting of lysates from NaIO_3 treated ARPE19 cells revealed increased expression of LC3II, a marker of impaired autophagosomal activity, and ferritin relative to untreated controls. Cathepsin-D, a lysosomal enzyme, was significantly reduced in NaIO_3 -treated cells. Immunocytochemistry revealed co-localization of ferritin with LAMP-1 in NaIO_3 -treated cells, indicating accumulation in lysosomes. Surprisingly, exosomal structures co-immunostaining for ferritin and LAMP-1 were released in the extracellular milieu.

Conclusions: These data indicate that NaIO_3 inhibits lysosomal degradation of ferritin by inhibiting cathepsin-D. Accumulated ferritin is subsequently released to the extracellular milieu in vesicular structures that react for the lysosomal marker LAMP-1. Thus, accumulation of iron and iron-mediated retinal toxicity by NaIO_3 is mediated by accumulation of iron-rich ferritin and its release to neighboring cells. Since NaIO_3 is used to induce retinal degeneration in mice, the role of ferritin and other substrates of cathepsin-D requires consideration.

CONTROL ID: 3543687

SUBMITTER (NAME ONLY): JAISHREE GANDHI

TITLE: Prospective Evaluation of Galactomannan Enzyme Immunoassay and (1, 3) β -D-Glucan testing in the diagnosis of Fungal Endophthalmitis in Southern India

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. GANDHI, S. Gagan, J. Joseph Ruben, Jhaveri Microbiology, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|J. GANDHI, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|V. Dave, T. Das, Smt Kannuri Santhamma Centre for vitreo-retinal diseases, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|M. Ali, Centre for Clinical Epidemiology and Biostatistics, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Fungal endophthalmitis is a devastating intraocular inflammatory disease that represents ~17-25% of infectious endophthalmitis in India, but microbiological investigations have often failed to detect the causative agent, resulting in a clinical dilemma. Galactomannan (GM) and 1,3 β -D-Glucan (BG), have been previously evaluated in the diagnosis of invasive fungal infections, however, its utility in intraocular infections is not known. The aim of the study was to assess the clinical utility of vitreous GM and BG levels in the diagnosis of fungal endophthalmitis.<gdiv></gdiv>

Methods: Vitreous of 31 patients diagnosed clinically as fungal endophthalmitis between October 2018 and September 2020 and 11 patients diagnosed with non-infectious retinal disorders, as controls, were included in this study. Human GM and BG levels were determined by colorimetric assay kits (MyBioSource) and the receiver operating characteristic curves (ROC) were determined.<gdiv></gdiv>

Results: Of the 42 patients included in the infectious group, 16 were culture-positive and included *Aspergillus* spp. (44%), *Candida* spp. (31%), and other fungi (4/16; 25%). While, no significant association were found between GM and BG levels and visual outcome, significantly higher levels of vitreous GM (67.51 ± 22.08 pg/ml; $p=0.009$) and BG (1.53 ± 0.30 pg/ml; $p=0.0002$) were found in the culture-positive group compared to the control group. Additionally, both GM and BG levels were significantly higher in *Aspergillus* spp. compared to *Candida* spp. (p -value <0.05). The Area under the ROC curve (AUC) value for GM was 81% with a sensitivity of 88% and a specificity of 73% for a cutoff value of 51.36 pg/ml. Further, the AUC value for BG was 93% with sensitivity and specificity of 94% and 82% with the cutoff value being 1.19 pg/ml. Using that criteria, diagnosis of fungal infection was achieved in 12/15 (80%) culture-negative infectious samples by GM assay and in 15/15 (100%) by 1, 3 β -D-Glucan assays.<gdiv></gdiv>

Conclusions: Our study demonstrates the clinical utility of GM and BG as useful adjunctive biomarkers for the early diagnosis of fungal infections in patients with culture-negative endophthalmitis. A combination of both BG and GM assays would be the best approach, facilitating better predictive accuracy in vitreous fluids and may have a role in monitoring response to therapy.<gdiv></gdiv>

CONTROL ID: 3543689

SUBMITTER (NAME ONLY): Colleen McDowell

TITLE: Fibronectin extra domain A (FN-EDA) causes glaucomatous trabecular meshwork and optic nerve head damage in mice

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.M. McDowell, T. Mavlyutov, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Colleen McDowell: Commercial Relationship: Code N (No Commercial Relationship) | Timur Mavlyutov: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is a major risk factor for the development and progression of primary open angle glaucoma and is due to trabecular meshwork (TM) damage. We investigated the role of an endogenous Toll-like receptor 4 (TLR4) ligand, FN-EDA, in the development of glaucoma utilizing a transgenic mouse strain (B6.EDA^{+/+}) that constitutively expresses only FN containing the EDA isoform.

Methods: Eyes (n=3/strain) were processed for electron microscopy, polymerized in EPON, ultrathin sections (80 nm) were cut and placed on formvar coated slot grids, and poststained with uranyl acetate and lead citrate. Consecutive images of the entire TM area spanning from anterior to posterior parts of Schlemm's canal (SC) were collected at 2500x and montaged into a single image. ECM accumulation and basement membrane thickness were quantified by ImageJ analysis. TLR4 expression in ONH cells was conducted using RNAscope in situ hybridization and immunohistochemistry protocols (n=3 eyes/strain). IOP was measured using a rebound tonometer and ON damage assessed by PPD stain (n=20-22 eyes/strain).

Results: Ultrastructure analyses show the TM of B6.EDA^{+/+} mice have significantly increased accumulation of ECM between the TM beams with few empty spaces compared to C57BL/6J control mice (P<0.05). SC basement membrane is thicker and more continuous in B6.EDA^{+/+} mice compared to C57BL/6J control. No significant structural differences were detected in the TM of EDA null mice. The mRNA expression of TLR4, a known ligand of FN-EDA, was increased in the TM of B6.EDA^{+/+} mice compared to C57BL/6J control eyes (p<0.05). IOP was significantly higher in B6.EDA^{+/+} mice compared to C57BL/6J control eyes (p<0.01) and significant ON damage was detected at one year of age (p<0.001). TLR4 mRNA is expressed in the ONH, and is present in mouse ganglion cell axons, microglia, and astrocytes. There was no significant difference in astrocyte density in B6.EDA^{+/+} mice compared to C57BL/6J control eyes; however, there was a significant increase in the area occupied by Iba-1 positive microglia cells in the ONH of B6.EDA^{+/+} mice compared to C57BL/6J control eyes (p<0.01).

Conclusions: B6.EDA^{+/+} mice have increased accumulation of ECM in the TM, elevated IOP, enhanced proinflammatory changes in the ONH, and damage to retina ganglion cell axons. These data implicate B6.EDA^{+/+} mice as a novel mouse model of glaucoma.

CONTROL ID: 3543691

SUBMITTER (NAME ONLY): Suman Chaudhary

TITLE: β -cleavage of the prion protein is specific to the human eye and has implications for the spread of infectious prions and ocular disorders

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chaudhary, A. Ashok, A. S. Wise, N. Rana, A. E. Kritikos, N. Singh, Pathology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|E. Lindner, Ophthalmology, Medizinische Universität Graz, Graz, AUSTRIA|

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ABSTRACT BODY:

Purpose: Recently, we reported β -cleaved prion protein (PrP^{C}) in human ocular tissues. Here, we explored whether this is unique to the human eye, and its implications in ocular disorders.

Methods: The ratio of β - and α -cleaved PrP^{C} in ocular tissues and fluids was determined by Western blotting (WB). Processing of green-fluorescent-protein (GFP)-tagged PrP^{C} was evaluated in human retinal (ARPE-19) and neuronal (BE(2)-M17) cell-lines respectively.

Results: PrP^{C} was β -cleaved in human ocular tissues, and soluble N-terminal fragment (N2) was released in the aqueous and vitreous humor (AH & VH). In contrast, PrP^{C} was α -cleaved in human brain and retinal tissue of diurnal and nocturnal animals. Insertion of the GFP tag between N-terminal residues 37 and 38 of PrP^{C} interfered with β -cleavage in ARPE-19 cells, and was cytotoxic. In BE(2)-M17 cells, PrP^{C} -GFP was α -cleaved, and was nontoxic. Surprisingly, neither exposure to light, oxidizing agents, inflammatory stimuli, or anti-oxidants altered β -cleavage of PrP^{C} in ARPE-19 cells.

Conclusions: β -cleavage of PrP^{C} is obligatory in human ocular tissues, and N2 likely protects the cells from oxidative stress, an established function of this fragment. Paradoxically, β -cleaved C-terminus (C2) of PrP^{C} is susceptible to conversion by the pathogenic PrP-scrapie (PrP^{Sc}) form while α -cleaved fragment (C1) is resistant, increasing the susceptibility of the human eye to prion infection. Moreover, C2 includes the binding site for $\beta 1$ -integrin and amyloid- β ($\text{A}\beta$), molecules implicated in ocular disorders. These observations suggest re-evaluation of animal studies on prion infection of the eye, and underscore the significance of PrP^{C} in ocular disorders.

CONTROL ID: 3543693

SUBMITTER (NAME ONLY): Viridiana Kocaba

TITLE: Comparison of the protein composition between fresh and frozen acellular Descemet's membranes

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Kocaba, V. Venkatraman, D. Neo, G.S. Peh, J.S. Mehta, Tissue Engineering and Cell Therapy Group, Singapore Eye Research Institute, Singapore, SINGAPORE|V. Kocaba, NIIOS, Netherlands Institute for Innovative Ocular Surgery, Rotterdam, NETHERLANDS|J.S. Mehta, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: We compared the protein composition of completely decellularized Descemet's membrane (DM), using 2 different sample preparation methods. The DMs derived from paired donor cornea were either subjected to freeze-thaw cycle or not, before mass spectrometry (MS) analysis.

Methods: Two corneas were subjected to a freeze-thaw cycle to remove corneal endothelial cells (CECs) by freezing the cornea at -20° C for 48 hours and thawing it gently at RT while the other two corneas from the fellow eye were incubated with culture media at 37°C for 48 hours. The corneas were washed with cell culture media to remove all the CECs. The DMs were peeled and the proteins were extracted with 2% SDS in 100 mM Tris buffer using a bullet blender homogenizer (Next Advance, NY). The supernatant was collected from homogenized sample. Extracted proteins were quantified by BCA method and subjected to SDS-PAGE fractionation. Protein bands were excised and subjected to in-gel trypsin digestion. The digested peptides were used for LC-MS/MS analysis performed using a Q Exactive mass spectrometer coupled with an online Dionex Ultimate 3000 RSLC nanoLC system (Thermo Scientific; MA). Tryptic peptides were separated with a Dionex EASY-spray column (PepMap® C18, 3µm, 100Å) using a typical 120min gradient of mobile phase A (0.1% FA) and mobile phase B (0.1% FA in ACN) with a flow rate of 300nl/min.

Results: The LC-MS/MS-based analysis identified more proteins in the DMs that were subjected to the freeze-thaw cycle than the ones without the freeze-thaw cycle. A total number of 951 proteins were identified in the freshly processed group and a total of 1423 proteins were identified in the tissue subjected to freezing. The freeze-thaw cycle identified 33% more proteins compared to the samples that were processed fresh with mild enzymatic digestion. A total of 53 proteins were common among all samples in the freshly processed group while 117 proteins were common in the sample group subjected to free-thaw. The common proteins identified in all the samples were also analyzed manually using the Uniprot database for the sub-cellular localization and 98% of the protein were classified as extracellular or secreted proteins confirming that the identified proteins truly belong to the acellular DM.

Conclusions: The DMs that underwent a freeze-thaw cycle resulted in more proteins than DMs that were prepared fresh and subjected to mild enzyme digestion.

CONTROL ID: 3543695

SUBMITTER (NAME ONLY): Kristin Perkumas

TITLE: Differential effects of bimatoprost vs. bimatoprost free acid on outflow cell MMPs

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Perkumas, D.W. Stamer, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|D.J. Rhee, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kristin Perkumas: Commercial Relationship: Code N (No Commercial Relationship) | Douglas Rhee: Commercial Relationship(s);Allergan:Code F (Financial

Support);Allergan:Code C (Consultant) | Daniel Stamer: Commercial Relationship(s);Allergan:Code F (Financial Support);Allergan:Code C (Consultant)

ABSTRACT BODY:

Purpose: In clinical trials, the intracameral bimatoprost SR implant lowers intraocular pressure (IOP) well beyond cessation of drug release by the implant. Since matrix metalloprotease (MMP) activity underlies topical bimatoprost effects on IOP, we hypothesized that long-term effects of bimatoprost SR was due to effects of dramatically elevated outflow tissue levels of unmetabolized bimatoprost (amide, not bimatoprost free acid (BFA)) on MMP activity in outflow pathway cells.

Methods: Human outflow pathway cells (trabecular meshwork, TM, n=7; ciliary muscle, CM, n=6; scleral fibroblasts, SF as controls, n=4) in culture were treated with either implant tissue levels of bimatoprost (10–1000 μ M) or topical tissue levels of BFA (0.1–10 μ M). Cells were exposed to drug for 24 hours, and MMP gene expression was measured by PCR array and MMP1 protein by ELISA.

Results: Compared to all other treatments, implant levels of bimatoprost (1000 μ M) significantly altered expression of the greatest number of genes in all cell types (e.g.: n=11 partially overlapping genes in TM and CM cells, $p<0.05$). Despite these significant effects, there was noticeable strain to strain differences in responses to implant levels of bimatoprost. By comparison, only two genes were significantly altered in TM and CM cells with topical outflow tissue levels of BFA (10 μ M). In the one glaucomatous TM cell strain tested, implant levels of bimatoprost had similar effects on most genes compared to normal cells. However, 1000 μ M bimatoprost dramatically increased MMP1 and MMP10 expression in glaucomatous TM cells well above average responses of normal TM cells (183.8 vs. 62.9 ± 66.4 fold, and 52.1 vs. 2.89 ± 2.4 fold, respectively), both genes of which were dose-dependently upregulated in normal TM cells, but not CM cells. Similarly, MMP1 protein levels were dose-dependently upregulated in TM, but not CM cells.

Conclusions: Bimatoprost and BFA had differential effects on MMP gene expression, with a dramatic upregulation in MMP1 in TM cells seen only at “implant levels” of bimatoprost. These preferential effects of high dose bimatoprost on MMP expression on TM cells suggests that increased conventional outflow is due to durable tissue remodeling, underlying long term IOP benefit of implant in some patients.

CONTROL ID: 3543698

SUBMITTER (NAME ONLY): Noel Brennan

TITLE: High myopia prevalence as a function of myopia prevalence and age

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.A. Brennan, X. Cheng, Johnson and Johnson Vision, Jacksonville, Florida, UNITED STATES|M.A. Bullimore, Optometry, University of Houston System, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Noel Brennan: Commercial Relationship(s);Johnson and Johnson Vision:Code E (Employment) | Xu Cheng: Commercial Relationship(s);Johnson and Johnson Vision:Code E (Employment) | Mark Bullimore: Commercial Relationship(s);Johnson and Johnson Vision:Code C (Consultant)

ABSTRACT BODY:

Purpose: There are limited longitudinal data on refractive progression between teenage and senior adult years. A recent analysis suggests that the ratio of the prevalence of high myopia to that of myopia increases over this time.¹

Methods: The literature was reviewed to identify papers where both myopia and high myopia prevalence were reported. Adult studies largely comprised population-based cohorts whereas studies of children and teenagers were principally from school-based populations. To reduce confounding caused by lenticular changes, subjects over 70 years of age were excluded. Prevalence rates were adjusted to bring the thresholds for myopia and high myopia to -0.50 D and -5.00 D according to previously developed equations.¹

Results: Figure 1 plots the prevalence of high myopia versus that of myopia by age group for 292 cohorts from 76 studies (a total of 1,034,220 individuals). The ratio of the prevalence of high myopia to that of myopia increases with myopia prevalence, as has been previously reported. But, it also increased across the lifespan. Figure 2 presents modelled data for the prevalence of high myopia against that for myopia at different ages. This model predicts, for example, that high myopia prevalence will increase by about two-thirds between ages 20 and 70 years for a constant myopia prevalence of 80%. Race and gender had minimal influence on the ratio of high myopia to myopia.

Conclusions: While there are numerous possible explanations for this observation, the most likely is continued myopic progression during adulthood among moderate myopes such that they become high myopes later in life. The apparent substantial progression in this group across age has not been previously quantified and may mean that the already substantial projections of future morbidity from myopia underestimate the true likely toll.

1. Brennan et al. Optom Vis Sci 2020; 97:E-abstract 2053.

CONTROL ID: 3543700

SUBMITTER (NAME ONLY): yu yoneda

TITLE: Factors in low prevalence of Fuchs' heterochromic iridocyclitis in Japan

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. yoneda, K. Yoneda, K. Takayama, S. Sugaoka, H. Shimazaki, M. Takeuchi, Boei Ika Daigakko, Tokorozawa, Saitama, JAPAN|

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ABSTRACT BODY:

Purpose: Prevalence of Fuchs' heterochromic iridocyclitis (FHI) among total uveitis patients in Japan is approximately 0.5%, which is significantly lower than those of most western countries. In this study, we investigated whether lower frequencies of ocular findings characteristic of FHI in Japanese patients may be responsible for the less prevalence.

Methods: Clinical records of 10 uveitis patients diagnosed as FHI (5 male, 5 female) at our institute between April 2012 and March 2019 were retrospectively reviewed. Investigations contained patients' age at diagnosis, gender, clinical findings, follow-up duration, BCVA at initial and final visits, complications, and medical and surgical treatments. The reasons for referral to our hospital were also interrogated.

Results: Unilateral involvement was noted in 90%, and cell infiltration in the anterior chamber was observed in 70%. At the initial presentation, stellate-shaped keratic precipitates (KP) and iris atrophy with or without heterochromia were observed in all cases, followed by cataract in 80%, anterior segment inflammation in 70%, vitreous opacity in 40%, and iris nodule in 20%. Ciliary injection or high intraocular pressure was not noted in any cases. All were patients referred to our institute, and had been followed up for several months or years at the primary clinics. The most in the referral reasons was cataract (60%), followed by uveitis (30%), and there was no case referred as FHI.

Conclusions: Ocular findings characteristic of FHI except for high intraocular pressure were observed in Japanese FHI patients as well. It was suggested that the low prevalence of FHI in Japan was due to the fact that FHI was under diagnosed at the primary clinics, and had been followed up as idiopathic mild anterior uveitis and/or cataract.

CONTROL ID: 3543705

SUBMITTER (NAME ONLY): Oscar Otero-Marquez

TITLE: Imaging of Parafoveal Surface Macrophages in Thyroid Eye Disease

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Otero-Marquez, M.V. Castanos Toral, D.B. Zhou, A. Pinhas, Y. Seol, J. Andrade Romo, J.V. Migacz, H. Reddy, R.B. Rosen, T.Y. Chui, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|D.B. Zhou, R.B. Rosen, T.Y. Chui, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal macrophages play key roles in the regulation of immune reactions and tissue repair. Using clinical OCT, we examined the association of parafoveal surface macrophage density and capillary density in thyroid eye disease (TED) patients with low and high clinical activity scores (CAS).

Methods: 33 TED patients (33 eyes) and 13 healthy control subjects (13 eyes) were imaged using a clinical SD-OCT system (Avanti RTVue-XR; Optovue). 23 of the 33 TED patients had a CAS ≤ 3 and 10 had CAS > 3 . Ten 3x3mm scans centered at the fovea were acquired and averaged (PMID: 28068370). Axial length was obtained for ocular magnification correction of images. Automated macrophage identification was performed on a 3 μ m OCT-Reflectance (OCT-R) slab located above the ILM surface using MATLAB (Fig 1, Left Column) (PMID: 32574351). The OCT-A full vascular slab, located between ILM and 9 μ m below the OPL was used for capillary density measurements and foveal avascular zone (FAZ) delineation. (Fig 1, Middle Column) (PMID: 31106029). Macrophage density maps were generated for each subject to provide quantitative visualization of cell distribution across the 3x3mm scan area (Fig 1, Right Column).

Results: Surface macrophages within the FAZ were identified in 31% of controls, 87% of low CAS and 100% of high CAS groups. A statistically significant difference in macrophage density within the FAZ was observed between the control and TED groups (Kruskal-Wallis tests, $P = 0.0005$), with mean \pm SDs of 1 ± 1 , 6 ± 7 and 14 ± 6 cells/mm² in the controls, low CAS and high CAS, respectively. Linear regression showed no significant correlation between macrophage density within the FAZ and capillary density ($r = -0.1$; $P = 0.495$).

Conclusions: Clinical OCT is capable of imaging parafoveal surface macrophages in TED patients and healthy controls. Our findings suggest that the concentration of macrophages within the FAZ reflects the inflammatory burden in TED.

CONTROL ID: 3543708

SUBMITTER (NAME ONLY): Jeffrey Bair

TITLE: Identification of Human Epithelial Cell Type by Analysis of Cell Function in Cultured Conjunctival Epithelium

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Bair, R. Hodges, D.A. Dartt, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jeffrey Bair: Commercial Relationship: Code N (No Commercial Relationship) | Robin Hodges: Commercial Relationship: Code N (No Commercial Relationship) | Darlene Dartt: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We previously developed a method to culture human goblet cells using RPMI medium. Our purpose is to culture and characterize three types of cells found in the conjunctival epithelium: goblet, stratified squamous, and undifferentiated.

Methods: A co-culture of goblet cells, stratified squamous cells, and undifferentiated cells was established from pieces of human conjunctiva in IOBA medium. Immunofluorescence was used to determine the amount and phenotype of cells grown. To determine cell function intracellular Ca^{2+} concentration ($[\text{Ca}^{2+}]_i$) was measured using fura2/AM in cultured cells stimulated by exogenous stimuli. Additionally immunofluorescence microscopy on fura2/AM labeled cells was used to assign cell phenotype to individual intracellular Ca^{2+} measurements post hoc.

Results: Explants of human conjunctiva were grown in IOBA media for 14 days and stained by immunohistochemistry using two cell markers for each type: cytokeratin (CK) 7 and the lectin Ulex Europeaus Agglutinin 1 (UEA1) for goblet cells, CK4 and Bandeiraea Simplicifolia Lectin 1 for stratified squamous cells, and p63 and PAX6 for undifferentiated cells. All three cell types were present in cultures from twelve different individuals. $[\text{Ca}^{2+}]_i$ was significantly increased in both goblet and stratified squamous cells (identified post hoc) when stimulated by the β adrenergic agonist isoproterenol (10^{-5}M), the $\alpha 1$ adrenergic agonist phenylephrine (10^{-4}M), and the nonspecific adrenergic agonist epinephrine (10^{-6}M). Increases in $[\text{Ca}^{2+}]_i$ elucidated by the purinergic agonist ATP (10^{-5}M) and the cholinergic agonist carbachol (10^{-4}M) were significantly greater in goblet cells than stratified squamous cells.

Conclusions: In mixed cultures containing the three phenotypically distinct human cell types that comprise the conjunctival epithelium, stratified squamous and goblet epithelial cells can be differentially identified by their $[\text{Ca}^{2+}]_i$ response to purinergic and cholinergic agonists. Furthermore, the activity of goblet cells is regulated by systems that utilize adrenergic, purinergic, and cholinergic agonists.

Grant Support: NIH NEI R01EY029789

CONTROL ID: 3543716

SUBMITTER (NAME ONLY): William Miller

TITLE: REDD1 ablation in Müller glia inhibits diabetes-induced retinal pathology in mice

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.P. Miller, A.L. Toro, S. Sunilkumar, D.L. Williamson, M.D. Dennis, Cellular and Molecular Physiology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|D.L. Williamson, Kinesiology, School of Behavioral Sciences and Education, Penn State Harrisburg, Middletown, Pennsylvania, UNITED STATES|M.D. Dennis, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): William Miller: Commercial Relationship: Code N (No Commercial Relationship) | Allyson Toro: Commercial Relationship: Code N (No Commercial Relationship) | Siddharth Sunilkumar: Commercial Relationship: Code N (No Commercial Relationship) | David Williamson: Commercial Relationship: Code N (No Commercial Relationship) | Michael Dennis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Müller glia provide critical homeostatic, trophic, and structural support for both the retinal vasculature and neuronal layers. In diabetes, Müller cell dysfunction contributes to retinal inflammation, microvascular defects, and neuronal damage. Our laboratory has recently demonstrated a critical role for the stress response protein Regulated in Development and DNA damage response 1 (REDD1) in the development of diabetes-induced oxidative stress and retinal defects. Herein, we investigated the hypothesis that diabetes-induced REDD1 protein expression specifically in Müller cells contributes to the development of retinal pathology.

Methods: Conditional Müller-specific REDD1 knockout (REDD1 cKO) mice were generated using a PDGFRa-cre/lox recombination system. REDD1 cKO and floxed REDD1 control mice were administered streptozotocin to induce diabetes or received a vehicle control. The impact of diabetes was evaluated by optical coherence tomography and fluorescence microscopy. Retinal homogenates and nuclear isolates were also analyzed by Western blotting and ELISA.

Results: Müller glia from REDD1 cKO mice lacked REDD1, but expressed Müller cell markers similar to that of floxed REDD1 controls. In the retina of diabetic control mice, REDD1 protein expression was enhanced concomitant with an increase in oxidative stress and reduced activity of the antioxidant defense transcription factor nuclear factor erythroid-2-related factor 2 (Nrf2). These effects of diabetes were attenuated by conditional deletion of REDD1 in Müller glia. REDD1 cKO mice also exhibited a reduction in diabetes-induced retinal thinning and retinal ganglion cell death as compared to control mice

Conclusions: The findings support a key role for REDD1 in diabetes-induced retinal defects and provide new insight into the specific molecular events in retinal Müller glia that contribute to the pathology of diabetic retinopathy.

CONTROL ID: 3543718

SUBMITTER (NAME ONLY): Rivkah Lender

TITLE: Comparison of ocular parameters in cataract surgery candidates using different biometric devices

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lender, D. Kurland, R. Greenberger, Z. Boim, L. Ben-Yaakov, I. Chowers, H. Ben-Eli, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|H. Ben-Eli, Optometry and Vision Science, Hadassah Academic College, Jerusalem, Jerusalem, ISRAEL|

Commercial Relationships Disclosure (Abstract): Rivkah Lender: Commercial Relationship: Code N (No Commercial Relationship) | Devora Kurland: Commercial Relationship: Code N (No Commercial Relationship) | Riki Greenberger: Commercial Relationship: Code N (No Commercial Relationship) | Zipora Boim: Commercial Relationship: Code N (No Commercial Relationship) | Lee Ben-Yaakov: Commercial Relationship: Code N (No Commercial Relationship) | Itay Chowers: Commercial Relationship: Code N (No Commercial Relationship) | Hadas Ben-Eli: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Precise biometric measurements before cataract surgery are crucial for successful intraocular lens (IOL) calculation. We compared pre-cataract surgery measurements obtained using Heidelberg's new Anterior, the IOLMaster 700 (Zeiss), and the Pentacam (Oculus).

Methods: Biometric measurements were taken with the IOLMaster700 and the Anterior, as well as corneal topography with the Pentacam. Values were compared for measurements of axial length (AL), anterior chamber depth (ACD), steep and flat K, cylinder and axis. Statistical analysis was performed using paired sample t-test, Friedman test, Pearson's coefficient, and Cohen's d effect size. Clinical implications were derived from the IOL calculations for each device using the Barrett calculator.

Results: We compared measurements of 42 eyes (21 subjects; 38% female, mean age 65.2 ± 14.9 years). Of these, 24 eyes also had corneal parameters measured with the Pentacam. Mean AL was 23.62 ± 1.26 mm with the IOLMaster and 23.58 ± 1.31 mm with the Anterior ($P=0.004$; Cohen's d 0.02). Mean ACD was 3.29 ± 0.72 mm with the IOLMaster and 3.44 ± 0.79 mm with the Anterior ($P=0.04$, Cohen's d 0.12). There were no statistically significant differences in the steep or flat K values between the three devices. The strongest correlations were observed between the Anterior and the Pentacam in the steep and flat K values ($r=0.96$ and 0.97 , respectively; $p<0.001$). The weakest correlations were observed in the axis of the flat K between the IOLMaster and Anterior ($r=0.45$; $p=0.003$) and between the Anterior and Pentacam ($r=0.42$; $p=0.02$). When calculating the IOL using the Barrett calculator and mean values of the biometric devices, the Anterior values yielded a lower cylinder power by 0.75D.

Conclusions: Our results indicate excellent inter-device measurement agreement between the IOLMaster700 and the Anterior, rendering the two devices nearly interchangeable, with strong correlations also to the Pentacam corneal topography measurements. A clinically significant difference was observed only in the cylinder power of the calculated IOL.

CONTROL ID: 3543723

SUBMITTER (NAME ONLY): Karina Luiza Dias Teixeira

TITLE: Lacritin Proteoform Rescue of Epithelial Corneal Homeostasis Requires GPR87 Coupled to Syndecan-1

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Dias Teixeira, J. Romano, G.W. Laurie, Cell Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|G.W. Laurie, Biomedical Engineering, University of Virginia, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Karina Luiza Dias Teixeira: Commercial Relationship: Code N (No Commercial Relationship) | Jeff Romano: Commercial Relationship: Code N (No Commercial Relationship) | Gordon Laurie: Commercial Relationship(s);TearSolutions Inc. :Code F (Financial Support);UVa Licensing and Ventures Group:Code P (Patent)

ABSTRACT BODY:

Purpose: Dry eye disease affects 7 - 10% of people worldwide. Dry eye is characterized by chronic inflammation and damage of the ocular surface. Lacritin (and several of its C-terminal proteoforms) is a prosecretory growth factor in tears that, based on preclinical and cell culture studies, restores basal tearing and ocular surface health. We previously reported on identification of cornea expressed G protein-coupled receptor 87 (GPR87) as a lacritin signaling receptor out of a genome-wide CRISPR/Cas9 screen. Here we sought to validate this observation, and ask whether GPR87 couples with lacritin co-receptor syndecan-1 (SDC1).

Methods: Validation studies of GPR87 were performed by generation of GPR87 knockout cell lines by CRISPR/Cas9 editing and by shRNA depletion of transduced human corneal epithelial (HCE-T) cells with lentiviral GPR87 sgRNA or shRNA and non-target controls. Depletion of GPR87 protein level was confirmed by western blotting. Complementation assays were performed by transducing depleted HCE-T's with lentiviral GPR87 cDNA obtained from DNASU Plasmid Repository. To explore whether GPR87 can couple with SDC1, we blotted for GPR87 out of SDC-1 pulldowns from HEK2936E cells co-transfected with wild type or mutated GPR87 and SDC1 cDNA's. GPR87- lacritin binding was studied out of recombinant lacritin- or C-25-intein pulldowns. 'C-25', lacks lacritin's 'N-94' bioactive domain. N-94 is a synthetic peptide analogous to several lacritin C-terminal proteoforms naturally in tears.

Results: Depletion of GPR87 abrogated N-94 rescue of IFNG/TNF stressed HCE-T's, but was rescued by complementation with GPR87 cDNA. GPR87 complexes with SDC1 in the absence of N-94, but not with SDC1 lacking the PDZ binding domain nor lacking N-terminal domain heparan sulfate at S15 nor membrane proximal chondroitin sulfate at S184 and S185. SDC1 failed to bind GPR87 lacking the G-protein binding site "DRY" motif. Lacritin, but not C-25, binds GPR87.

Conclusions: N-94 targets a preformed SDC1-GPR87 complex, the latter linked in part by glycosaminoglycans, and apparently by cytoplasmic SDC1 and GPR87 domains to regulate ocular surface health.

CONTROL ID: 3543725

SUBMITTER (NAME ONLY): Ali Alghamdi

TITLE: Repeatability and reliability of density and morphology measurements of corneal and conjunctival epithelial dendritic cells using in vivo confocal microscopy.

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Alghamdi, Z. Tajbakhsh, I. Jalbert, F. Stapleton, B. Golebiowski, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Corneal and conjunctival epithelial dendritiform cells (CEDC, CjEDC) are an essential part of the ocular immune response, including the allergic response. Confocal microscopy allows observation of these cells in patients in real-time. This study examined inter-observer reliability of CEDC and CjEDC density and morphology measurements in normal and allergic patients.

Methods: In vivo confocal microscopy images (HRTIII-Rostock) from the corneal sub-basal and conjunctival epithelium of the right eye of 66 participants (mean age 36.6 ± 12.0 years, 56% female; 33 patients with normal corneas and 33 patients with active ocular allergy) were independently assessed by two experienced observers. Five best-focused, non-overlapping images were selected for each participant from the central cornea, temporal far peripheral cornea, temporal corneal limbus, temporal bulbar conjunctiva, and one image from the corneal whorl. CEDC and CjEDC density were counted manually, and the highest-grade morphology of corneal cells was recorded using grading scales for CEDC cell body size, dendrite length and dendrite shape. The level of agreement between observers was analysed for density by calculating the coefficient of repeatability (CoR, Bland and Altman method) and Intraclass Correlation Coefficient (ICC), and for morphology using Weighted Cohen's Kappa.

Results: There was a strong level of agreement between the two observers for CEDC density at the central (CoR ± 11.9 , ICC=0.99), far peripheral (CoR ± 14.3 , ICC=0.99) and limbal cornea (CoR ± 28.0 , ICC=0.96), with no significant bias between observers. There was a significant difference between observers for density measurements at the corneal whorl ($p < 0.001$; CoR ± 29.10 , ICC=0.98). Repeatability of density measurements at the conjunctiva was comparatively poorer (CoR ± 19.1 , ICC=0.97), with no significant inter-observer bias. For all three CEDC morphology parameters, there was good to strong inter-observer agreement at all corneal locations ($k = 0.69$ to 1.0).

Conclusions: The strong inter-rater agreement in CEDC density and good agreement in CEDC morphology and CjEDC density measurements supports the validity and reliability of in vivo dendritic cell assessment using confocal microscopy using manual counting, a novel morphology grading scale by trained observers.

CONTROL ID: 3543726

SUBMITTER (NAME ONLY): Toco Chui

TITLE: Assessing peripapillary surface macrophage density in eyes with glaucomatous damage using enface OCT

SESSION TITLE: Advanced imaging technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.Y. Chui, M.V. Castanos Toral, D.B. Zhou, O. Otero-Marquez, J.V. Migacz, R. Ritch, R.B. Rosen, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|T.Y. Chui, D.B. Zhou, R.B. Rosen, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|R.E. Linderman, J. Carroll, Cell Biology, Neurobiology & Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D.C. Hood, Department of Psychology, Columbia University, New York, New York, UNITED STATES|D.C. Hood, Department of Ophthalmology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To detect and quantify peripapillary surface macrophage density changes in patients with open angle glaucoma (OAG) using enface OCT-reflectance (OCT-R) images.

Methods: 27 controls and 12 moderate to severe OAG patients were imaged using a clinical SDOCT system (Avanti RTVue-XR; Optovue). Ten 4.5x4.5mm scans centered at the optic nerve head (ONH) were obtained and averaged (PMID: 32574351). Seven eyes of 6 OAG patients were imaged at two visits 11-29 months apart. Semi-automated macrophage cell identification was performed on a 3 µm OCT-R slab located between 3 and 6 µm above the ILM using MATLAB (PMID: 32574351). An annular ROI with 0.75mm in width centered at the ONH was created on the OCT-R image (PMID: 29795576) (Fig). This annular ROI was then divided into four quadrants (temporal, nasal, superior and inferior) for macrophage density measurements. Cell density maps were also generated for each subject to allow rapid visualization of cell distribution across the ONH area. Axial length was obtained for ocular magnification correction of each image.

Results: In control eyes, the highest cell density was found in the temporal quadrant with mean±SD of 35.7±12.6 cells/mm² followed by the nasal (23.4±7.3 cells/mm²), inferior (23.1±7.6 cells/mm²), and superior (22.9±9.4 cells/mm²). In the OAG eyes, the highest cell density was found in the temporal quadrant with mean±SD of 16.6±13.2 cells/mm² followed by the nasal (15.6±8.3 cells/mm²), superior (12.6±4.8 cells/mm²), and inferior (9.9±6.3 cells/mm²). Cell densities measured at 4 quadrants were significantly reduced in eyes with OAG (Mann-Whitney rank tests, P values <0.05). Focal loss of surface macrophages was observed at regions with retinal nerve fiber bundle (RNFB) defect progression in OAG eyes (Fig). Density mapping of peripapillary surface macrophages enabled us to quantitatively and visually identify this novel feature of progressive RNFB defects.

Conclusions: Clinical OCT is capable of imaging surface macrophages on the ILM in control and glaucoma eyes. Density of these cells appeared reduced in regions with glaucomatous damage. Characterizing the relationship

between surface macrophage density and the underlying retinal nerve fiber integrity may be a useful biomarker for active disease progression, and possibly response to treatment.

CONTROL ID: 3543729

SUBMITTER (NAME ONLY): Anita Ghosh

TITLE: Effects of chronic alcohol administration on the cornea in preclinical models

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Ghosh, J.M. Eby, Graduate Program in Biochemistry and Molecular Biology, Loyola University Chicago Health Sciences Campus, Maywood, Illinois, UNITED STATES|R. Cesna, A. Ziniauskaite, D. Neverauskas, S. Ragauskas, S. Kaja, Research and Development Division, Experimentica Ltd., Vilnius, LITHUANIA|S. Kaja, Ophthalmology and Molecular Pharmacology and Neuroscience, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a clinical association between acute and chronic alcohol consumption and the incidence of ocular surface disease, including dry eye disease. The goal of this study was to investigate if chronic moderate alcohol consumption leads to signs of DED in vivo, and to investigate oxidative stress pathways involved in alcohol-induced damage to human corneal epithelial cells in vitro.

Methods: Twelve week-old male C57BL/6JRj mice were acclimated to the ad libitum Lieber-DeCarli liquid diet for 5 days. After acclimatization, 5% (vol/vol) ethanol was added to the diet in the alcohol group while control animals were maintained on an isocaloric Lieber-DeCarli liquid diet for 10 days. Corneal fluorescein staining was performed on day 10. Corneal tissue was sectioned and processed for histopathological analysis. For in vitro studies, human corneal epithelial cells (HCE-T; Riken, Japan) were exposed to 0.5% ethanol (vol/vol in media). RNA was collected from cells at 2, 4, 6, and 12 h after ethanol treatment and mRNA levels of oxidative stress markers NFE2L2, HMOX1, and HMOX2 were quantified by qPCR.

Results: Mice who received alcohol exhibited significantly higher corneal fluorescein scores compared to control (median scores: control = 2; alcohol = 3; $P < 0.001$). The average total corneal thickness in the alcohol group was significantly lower than in the control group (74.4 μm and 122.8 μm , respectively; $n = 6-7$, $P < 0.05$). This reduction was predominantly attributed to a reduction in stromal thickness.

In vitro studies revealed a statistically significant 3-fold increase in NFE2L2 gene expression in response to alcohol treatment in HCE-T cells at 2, 4, and 6 h ($P < 0.002$). There was a trend towards increased HMOX1 expression but no change in expression of the non-inducible HMOX2 isoform.

Conclusions: Our data provide the first preclinical evidence that chronic moderate alcohol consumption can lead to pathological signs of ocular surface disease in vivo. In vitro, alcohol exposure causes activation of Nrf2-mediated oxidative stress pathways. Future studies will investigate the effects of alcohol on corneal barrier function and the implications of chronic moderate vs. binge alcohol use.

CONTROL ID: 3543734

SUBMITTER (NAME ONLY): Alexandre Lachance

TITLE: Automated Machine Learning Prediction of Visual Acuity from Preoperative OCT Images After Macular Hole Surgery

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lachance, M. Hébert, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Faculté de médecine, Université Laval, Québec, Québec, CANADA|A. Lachance, M. Hébert, S. Bourgault, M. Caissie, E. Tourville, A. Dirani, Département d'ophtalmologie et d'oto-rhino-laryngologie – chirurgie cervico-faciale, Centre Universitaire d'Ophtalmologie, Hôpital du Saint-Sacrement, CHU de Québec-Université Laval, Québec, Québec, CANADA|F. Antaki, Département d'ophtalmologie, Centre Hospitalier de l'Université de Montréal, Montréal, Québec, CANADA|

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ABSTRACT BODY:

Purpose: Analysis of baseline optical coherence tomography (OCT) in patients with macular hole (MH) can provide insight into surgical success and postoperative visual acuity (VA). Automated machine learning (AutoML) is a new area in artificial intelligence research. We designed a machine learning model using AutoML to predict the visual outcome from preoperative OCT images in eyes with successful MH closure following vitrectomy.

Methods: We developed a single-label classifier using AutoML (Google Cloud AutoML Vision) to predict the visual outcome (“<70 letters” vs. “≥70 letters”; Snellen equivalent: 20/40) at 6 months in eyes with successful primary surgery for idiopathic MH. We used retrospective data obtained from consecutive eyes with successful primary surgery for idiopathic MH between 2014 and 2018 at the Centre Hospitalier Universitaire de Québec – Université Laval (Canada). We included a single eye per patient and excluded eyes with ocular comorbidities with a potential detrimental effect on VA. Baseline horizontal fovea-centered high-definition 30-degree OCT scans were obtained in all patients using the Cirrus HD-OCT 5000 machine (Carl Zeiss Meditec, Germany). VA at 6 months was measured in Snellen and converted to ETDRS letters for analysis. Eyes were divided into two groups based on VA at 6 months: <70 letters and ≥70 letters. During model development, 80% of images were used for training, 10% for the validation process, and 10% were used for evaluating the model. Precision, recall and area under the precision-recall curve (AuPRC) were used to evaluate the performance of the model.

Results: The dataset included 383 patients (383 eyes), 69% (263/383) of which were women. The mean age was 68 ± 8 years and 24% (91/383) of eyes were pseudophakic. Baseline VA was 51 ± 14 letters and 49% (187/383) of eyes had VA of 70 letters or more at 6 months. The model correctly classified postoperative VA 68% of the time for the “<70 letters” category and 79% of the time for the “≥70 letters” category. The model had a precision (positive predictive value) of 73.68%, a recall (sensitivity) of 73.68%, and an AuPRC of 0.799.

Conclusions: The development of a deep learning model using AutoML for the prediction of postoperative VA from baseline OCT images in eyes with MH is feasible. The AutoML model displayed good discriminative performance, but more research is needed to determine external validity.

CONTROL ID: 3543735

SUBMITTER (NAME ONLY): Pujan Patel

TITLE: Visualizing Three-Layered Perifoveal Retinal Vasculature in Preterm Infants Using Handheld Optical Coherence Tomography Angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.R. Patel, R. Imperio, D. Tran-Viet, S. Chiu, V. Tai, C.A. Toth, X. Chen, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|P.R. Patel, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|C. Viehland, J. Izatt, Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Current understanding of retinal vascular development is largely based on histopathological studies of rare postmortem fetal eyes and by inference from non-human primates. Recent technological advances in handheld optical coherence tomography angiography (OCT-A) offer opportunity for direct imaging of the in vivo human retinal vascular development in preterm infants. Our goal is to establish offset parameters for macular microvasculature segmentation and visualize the three-layered perifoveal retinal vasculature in preterm infants using handheld OCT-A.

Methods: In this exploratory study, preterm infants were imaged using an investigational noncontact, handheld swept-source OCT-A device (UC3) under an IRB-approved protocol. Imaging occurred either at the bedside non-sedated or during examination under anesthesia with pharmacological pupillary dilation. Customized MATLAB scripts were used to segment retinal layers, test offset parameters, and generate depth-resolved OCT-A slabs. The superficial (SCP), intermediate (ICP), and deep (DCP) capillary plexuses were visualized and qualitatively assessed by three image graders.

Results: We selected six high-quality OCT-A volumes in two infant age groups for analysis and optimized offset parameters for vascular plexus visualization. A three-layered perifoveal retinal vasculature was successfully visualized in all three preterm infants in the 40 weeks postmenstrual age (PMA) group. No obvious ICP or DCP was found in the preterm infants in the 35 weeks PMA group, all of whom had retinopathy of prematurity (ROP).

Conclusions: Custom OCT-A segmentation parameters can be used to visualize the three-layered perifoveal retinal vasculature in preterm infants at term equivalent age. Prior to formation of the ICP and DCP, the perifoveal vasculature may be better visualized in two layers. Depth-resolved OCT-A of perifoveal retinal vasculature in preterm infants will inform human retinal vascular development and vascular pathologies of ROP.

CONTROL ID: 3543736

SUBMITTER (NAME ONLY): Gabor Somfai

TITLE: Choroidal response due to heavy physical exercise and its correlation with changes of the neuroretina

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is some evidence pointing towards outer retinal changes due to physical exercise. We could previously show the thinning of the outer retina and outer segments both in professional sportsmen and young amateurs shortly after excessive physical strain. In the current analysis we aim to provide evidence about choroidal changes in the same cohort and their effect on the observed outer retinal thinning.

Methods: Altogether 30 eyes of 15 professional sportsmen (Group S) and 16 eyes of 11 control adults (group C) were enrolled in our study, with a mean age of 22 ± 5 and 25 ± 5 years, respectively. We performed macular scanning with a Spectralis SD-OCT device before and following a vita maxima-type physical straining exercise until complete fatigue. OCT follow-up examinations were made 1, 5, 15, 30 and 60 minutes post exercise (p.e.). The OCT images were exported and analyzed using OCTRIMA 3D software and the thickness of 7 retinal layers was calculated, along with semi-automated measurement of the choroidal thickness. One-way ANOVA analysis was performed, the level of significance was 5%. The study was approved by the Science and Research Ethics Committee of Semmelweis University (272/2013).

Results: There was no significant change in choroidal thickness over time in both groups; however, there was a tendency towards thinning in the central subfield 1 minute and even more pronounced at 30 minutes p.e. in both groups S and C. The absolute changes in choroidal thickness in the central subfield did not show any correlation with the thickness changes of the intraretinal layers.

Conclusions: It seems that the changes of the outer retina induced by physical exercise are not directly linked with structural/thickness changes of the choroid as we previously hypothesized. However, in this study we did not measure changes in choroidal blood flow that could still be the underlying reason for the outer retinal changes described earlier by our group.

CONTROL ID: 3543739

SUBMITTER (NAME ONLY): Christopher Sutura

TITLE: Normalization of Oxygen-Induced Retinopathy by Myo/Nog Cell Supplementation

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.K. Sutura, R. Brahmbhatt, G. Wilgucki, C. Martineau, S. Adams, P. Lecker, J. Bernstein, K. Johal, J. Spikes, J. Tsai, G. Gorski, J.V. Gerhart, M. George-Weinstein, A. Bravo Nuevo, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania, UNITED STATES|N.J. Philp, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is the leading cause of blindness in children, particularly those born before 32 weeks of gestation. During the supplemental hyperoxic environment that premature infants are placed in postpartum, there is inadequate development of blood vessels supplying the retina, including the choriocapillaris and the superficial and deep plexuses from the central retinal artery. When the infants are returned to ambient air, the retina becomes hypoxic and there is compensatory and rapid angiogenesis and the development of neovascular tufts. This results in a compromised blood supply to the retina, leading to photoreceptor cell damage and death. Myo/Nog cells are a subpopulation of cells that express MyoD, Noggin and the angiogenesis inhibitor BAI1. They exist throughout the body and have been shown to have neuroprotective properties in the eye and brain. Myo/Nog cells have a potential role in reducing pathology and loss of vision that develops in a retinopathic eye by ameliorating the vascular and neuronal damage from hyperoxia and subsequent hypoxia that result from ROP.

Methods: An oxygen-induced retinopathy (OIR) protocol was utilized to mimic the pathology seen in ROP of premature infants. Neonatal mice spent postnatal days 7-12 (P7-P12) in 75% hyperoxia before returning to room air (21% oxygen). Intravitreal injections of pre-labeled Myo/Nog cells isolated from a brain by magnetic sorting and unsorted brain cells were performed at P15, followed by electroretinography (ERG) at P21 to test retinal function. Retinas were removed and vasculature was stained for analysis of vascular growth and quantification of neovascular tuft development.

Results: In animals who were subjected to the OIR protocol, addition of exogenous Myo/Nog cells reduced neovascular tuft formation and normalized overall vasculature of the retina. Retinal function assessed by ERG also showed significant improvement in these animals.

Conclusions: Intravitreal injection of exogenous Myo/Nog cells normalizes the effects of OIR at a vascular and functional level. Subsequently, Myo/Nog cells have therapeutic potential in the treatment of ROP.

CONTROL ID: 3543740

SUBMITTER (NAME ONLY): Leon von der Emde

TITLE: Organelle distribution of the human retinal pigment epithelium (RPE) in age-related macular degeneration (AMD)

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Human RPE cells contain numerous lipofuscin (LF), melanolipofuscin (ML), and melanosome (M) organelles that vary in number with retinal location (fovea, perifovea, and near periphery) and age (PMID: 32433758) as well as impact on clinical autofluorescence (AF) imaging. Here, we examined the effect of AMD on granule count and AF of RPE cell bodies.

Methods: Seven AMD-affected human RPE flatmounts (early: 3, late dry: 1; neovascular: 3) were imaged at three locations (fovea, perifovea, near periphery) using structured illumination microscopy (SIM) and confocal AF (both: excitation 488 nm). Z-stacks (step size: SIM 100 nm, confocal 390nm) were acquired from apical to basal through RPE cell bodies of 10 adjacent cells in each region. Subsequently, LF, ML, and M were marked, counted, and classified based on their AF properties using a customized ImageJ plug-in. AF/cell was calculated from confocal images. Furthermore, we analysed the impact of AMD on the total number of granules and AF/cell implementing a mixed effect ANCOVA, correlated granule count with cell size, and compared the results with data from normal RPE cells (PMID: 32433758).

Results: Of 152 RPE cells analyzed, average granule count/cell was 449 ± 276 LF, 532 ± 377 ML, and 4 ± 2 M, with early AMD demonstrating higher average granule count (987 ± 616) and lower LF (406 ± 287) compared with late-stage AMD manifestations. While there was a high variation in granule load among cells, the foveal RPE cells had lowest LF (194 ± 290) and total granule count (851 ± 917). AMD-affected RPE cells were larger than RPE cells in normal eyes, had a higher granule density (granules/ μm^2), but showed significantly lower AF at all three locations (fovea: < 0.01 ; perifovea: 0.02; near periphery: < 0.01).

Conclusions: The reduced histological AF signal in AMD eyes compared to healthy cells mirrors and helps to explain clinical AMD AF imaging. Enlarged AMD affected RPE cells might reflect cell fusion or failed cytokinesis (PMID 26875723), which increases net granule count and diminishes total AF. Interestingly, LF was lowest at the fovea

typically affected by accumulation of drusen in AMD as well as preservation of cone-mediated visual acuity. Here, we examined RPE cell bodies, but future studies should also focus on M within RPE's apical processes and their impact on RPE AF imaging (PMID 32648890).

CONTROL ID: 3543742

SUBMITTER (NAME ONLY): Christine Ha

TITLE: Adjunctive use of latanoprostene bunod in refractory glaucoma: 1-year retrospective analysis

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Latanoprostene bunod is a new medication whose main additional mechanism is nitric oxide donation. Its downstream effect improves trabecular meshwork outflow. Published studies have proven its efficacy alone as primary therapy in treatment-naïve eyes. This study retrospectively investigated the long-term efficacy of adjunctive use of latanoprostene bunod in refractory cases of glaucoma at a tertiary care glaucoma clinic. Refractory cases were judged as requiring ≥ 3 topical medications.

Methods: Retrospective chart review for patients on ≥ 3 topical medications who received add-on latanoprostene bunod was conducted from 01/01/2018 to 08/31/2020. Patients' baseline characteristics prior to add-on therapy were recorded and included type of glaucoma and prior topical, laser, and surgical treatments. A baseline IOP was calculated by taking the average of the two most recent IOP measurements prior to latanoprostene bunod add-on treatment. IOP was measured at 3-, 6-, and 12-month intervals ± 4 weeks. A Bonferroni corrected student's T-test was used to test differences between groups with statistical significance set at $p = 0.01$.

Results: 53 eyes in 36 patients were included in this analysis. Mean age (\pm SD) was 72.1 ± 11.0 . 18 (50%) patients were Caucasian, 13 (36%) African American, 2 (5%) Hispanic, 2 (5%) Indian American, and 1 (2%) Asian. Glaucoma diagnoses were as follows: 45 (85%) primary open angle, 6 (11%) neovascular, and 2 (4%) uveitic. Prior surgeries included: 11 (21%) trabeculoplasty, 9 (17%) seton, 2 (4%) trabeculectomy, and 2 (4%) iStent (Table 1). Mean IOP mmHg (\pm SD) at baseline was 19.9 ± 6.0 . Follow-up mean IOP mmHg (\pm SD) are as follows: 3-month 17.3 ± 5.5 ($p < 0.01$) in 49 eyes, 6-month 17.2 ± 6.6 ($p < 0.01$) in 35 eyes, and 12-month 16.1 ± 4.5 ($p < 0.01$) in 28 eyes (Table 2).

Conclusions: Adjunctive use of latanoprostene bunod in refractory glaucoma showed clinically and statistically significant IOP reductions. This study suggests that adding latanoprostene bunod to eyes with previous medical or surgical treatment can provide longer term IOP reduction. Further analysis is required to fully understand the effect of latanoprostene bunod in refractory glaucoma.

CONTROL ID: 3543747

SUBMITTER (NAME ONLY): Yi Zhai

TITLE: Five-year results after AAV2-REP1 gene therapy for choroideremia

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To assess the long-term safety and efficacy of a recombinant adeno-associated viral vector expressing REP1 (AAV2-REP1) in choroideremia patients.

Methods: For the six patients who received single subfoveal injection of AAV2-REP1, five of them were followed up for up to five years. The long-term safety was evaluated by the ophthalmic examination, spectral-domain optical coherence tomography (SD-OCT), and short-wavelength fundus autofluorescence (FAF). Functional and structural changes were determined by best-corrected visual acuity (BCVA) change from baseline in treated eyes compared to untreated eyes, sensitivity change in microperimetry, preserved retinal pigment epithelium (RPE) area measured from FAF, central macular thickness measured from SD-OCT and central V4e kinetic visual field measured with Octopus.

Results: One subject experienced a localized intraretinal immune response that resulted in significant loss of preserved RPE in FAF. Another subject experienced exacerbation of peripheral retinoschisis observed by OCT. One subject had a constant ≥ 15 -letter BCVA gain in the treated eye through one to four and half years after treatment, while one subject had a one time ≥ 15 -letter BCVA improvement in the untreated eye. Microperimetry sensitivity showed constant decline in both treated eyes and untreated eyes without significant difference between groups. Central (≤ 30 dg) V4e kinetic visual field was noted to decline at a similar rate between the treated and untreated eyes. For preserved RPE area, four out of five subjects had similar slopes of decline in both treated and untreated eyes while for one subject preserved RPE in treated eye was found to decline slower than the untreated eye ($p=0.02$). For central macular thickness measured from OCT, four subjects had similar declines in the rate between the treated eye and untreated eyes; one subjects had significantly more rapid central macular thickness decline ($p<0.01$) in the treated eyes possibly due to observed adverse event.

Conclusions: The intraretinal inflammation and regional RPE loss triggered by AAV2-REP1 gene therapy stabilized after two years. The potential long-term benefits for AAV2-REP1 gene therapy include improvement in visual acuity, preservation in RPE in small portion of the study subjects (1/6, respectively) though more data is needed to support this statement.

CONTROL ID: 3543748

SUBMITTER (NAME ONLY): mohamed Elmasry

TITLE: Agreement rates for predominantly peripheral lesion(PPL) grading assessed using qualitative and quantitative methods on ultrawide field color images(UWF-CI) and fluorescein angiography(UWF-FA) in diabetic retinopathy(DR).

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare agreement rates of DR PPL grading using UWF-CI and UWF-FA via qualitative and quantitative methods.

Methods: UWF-CI and UWF-FA images were acquired at the same visit from eyes without panretinal photocoagulation and graded for DR severity level at a centralized reading center. UWF-CI were graded qualitatively by 2 trained graders for presence or absence of PPL (qualitative PPL). UWF-FA images were graded for qualitative PPL by 2 separate masked graders. Hemorrhages and microaneurysm (H/Ma) manual counts inside and outside the ETDRS fields were obtained from UWF-FA images. Quantitative PPL-H/MA were defined as greater H/MA counts outside than inside each ETDRS field.

Results: Images from 280 eyes of 188 patients were evaluated. Distribution of DR severity based on UWF grading was 85 eyes (30.4%) mild nonproliferative DR (NPDR), 94 (33.6%) moderate, 66 (23.6%) severe and 35 (12.5%) proliferative DR (PDR). Agreement for qualitative PPL for the entire cohort was moderate for UWF-CI (exact agreement, 77.9%, $\kappa = 0.421$) but was substantially greater for UWF-FA (87.9%, 0.702). Within DR severity levels, agreement was similar in mild NPDR ($\kappa = 0.486$ UWF-FA vs $\kappa = 0.439$ UWF-CI) but substantially better using UWF-FA in all other DR severity levels; moderate NPDR ($\kappa = 0.743$ vs $\kappa = 0.538$), severe NPDR ($\kappa = 0.553$ vs $\kappa = 0.339$) and PDR ($\kappa = 0.639$ vs $\kappa = 0.212$).

Average agreement between qualitative PPL grading for UWF-CI and UWF-FA was poor (70.2%, $\kappa = 0.228$). Using a difference of 1 H/MA or more in the UWF fields, quantitative PPL-H/Ma had a moderate agreement with both qualitative PPL graders (72.8%, 0.447 and 73.8%, 0.468). Increasing the threshold difference to determine PPL-H/Ma from 2-8 did not improve the agreement rates with qualitative grading (70.3% - 72.8%, 0.330 – 0.447; 73.6% - 78.2%, 0.468 – 0.516).

Conclusions: Agreement between qualitative PPL grading on UWF-FA and UWF-CI is poor, suggesting that they are not readily interchangeable. Determining PPL qualitatively on UWF-FA is more reproducible than UWF-CI in eyes with moderate NPDR or worse. Given these differences, future studies will need to evaluate whether PPL graded on FA or CI is more associated with DR progression. If FA is deemed more prognostic, then the role of FA in assessing DR management may become more important.

CONTROL ID: 3543752

SUBMITTER (NAME ONLY): Dmitrii Lachinov

TITLE: Monitoring GA lesion size on OCT using automated deep learning-based image segmentation in the FILLY phase II clinical trial

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Lachinov, J. Mai, G.S. Reiter, S. Riedl, W. Vogl, U. Schmidt-Erfurth, H. Bogunovic, Dept. of Ophthalmology and Optometry, Medical University of Vienna, AUSTRIA|

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ABSTRACT BODY:

Purpose: In patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD), the rate of progression is variable. To evaluate the potential of artificial intelligence (AI) for active monitoring of GA progression, we trained and evaluated an automated deep learning-based image segmentation algorithm to detect and measure the size of retinal pigment epithelium (RPE)-loss on OCT scans.

Methods: OCT scans (512x49x496 voxels, Heidelberg Engineering) of study eyes of patients with complete RPE and outer retinal atrophy (cRORA) were evaluated. Patients were enrolled in the FILLY phase II clinical trial to study the effect of pegcetacoplan (APL-2), an investigational therapy targeting complement C3. The scans were first manually annotated for the presence of cRORA at an A-scan level, delineating the GA area. With the manual annotations as the reference, a deep learning image segmentation method using a 3D-to-2D convolutional neural network (CNN) was then trained to automatically segment a topographic 2D cRORA area on a 3D-OCT scan and its performance was evaluated using a five-fold cross-validation.

Results: 115 study eyes were included in the analysis that completed a one year follow-up and had a sufficient image quality to allow manual annotation of RPE-loss at baseline and year 1. The segmentation performance was evaluated as a precision, recall and Dice score (DSC), corresponding to the overlap between the reference and the automated segmentation. For the set of baseline scans, a mean DSC was 0.91, precision was 0.90, and recall was 0.94. For the year 1 scans, the mean DSC was 0.93, precision was 0.91, and recall was 0.95. Evaluation limited to the differential one-year growth area, resulted in the mean DSC of 0.57, precision of 0.49, and recall of 0.72.

Conclusions: Fully automated image segmentation of RPE loss on OCT is able to localize and delineate the GA area with high accuracy. Automated AI-based analysis was able to reproduce the findings of the phase II clinical trial complementing the results of centralized reading. The results of this pilot study represent a promising step toward AI-based clinical decision support tools that can monitor GA progression and therapeutic response, once the treatments for GA secondary to AMD become available.

CONTROL ID: 3543755

SUBMITTER (NAME ONLY): Raksha Urs

TITLE: Three Dimensional Ultrasound Functional Imaging of Blood-Flow in the Rat Eye

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Plane-wave (PW) ultrasound with a linear array probe is capable of visualizing and measuring retrobulbar blood flow. Because the retrobulbar vessels have a complex arrangement and are not situated in one plane, 2D images cannot capture their anatomic arrangement. The goal of this study was to determine if PW ultrasound could be used to visualize and measure flow dynamics in 3D in the retrobulbar vessels in a rat model.

Methods: Ultrafast PW imaging on the eyes of Sprague Dawley rats was performed with a Verasonics Vantage 128 ultrasound system using an 18 MHz linear array probe. Compound images were acquired by emitting unfocused wavefronts at multiple angles and combining echo data from all angles to form individual B-scans. 3D data were acquired by moving the probe on a linear translation stage over 2.5 mm at 1.5 mm/s, imaging at the rate of 3000 images/s. Plane thickness was approximately 0.5 mm, allowing sufficient dwell time in overlapping planes to both capture anatomy and measure flow dynamics in 3D data sets. A Singular Value Decomposition (SVD) filter was used to detect blood flow and produce power Doppler images. Velocity was measured using spectrogram analysis.

Results: 3D images were produced in ImageJ from the stack of image planes. By applying the SVD filter to overlapping sets of scan planes (i.e., within a beamwidth), we were able to visualize pulsatile flow of vessels. Figure 1 shows a projection image of grey-scale structural backscatter and blood-flow from a 3D scan set. Figure 2 (a) and (b) show spectrograms of the two arteries marked in Figure 1. Cosine-corrected peak-velocities (47.7 and 32.2 mm/s) can be seen at depths of 1.2 and 0.9 mm, corresponding to the locations of the arteries in the 2.5 mm translation axis, velocities which are comparable to observed values in Doppler B-scans (39.9 ± 14.4 , $n=20$).

Conclusions: While 3D ultrasound imaging is not new, 3D capture combining structural and functional information is novel. Although the axial and lateral resolution of the array are on the order of 0.1 mm, out-of-plane resolution is ~0.5 mm, which is disadvantageous in terms of interplane spatial resolution. This weakness is turned to advantage by SVD processing sets of overlapping data from regions approximating slice thickness to obtain both structural and functional data.

CONTROL ID: 3543756

SUBMITTER (NAME ONLY): Hannah Weindler

TITLE: Comparison of peripapillary and perimacular flow density of POAG eyes with normal IOP under Tafluprost therapy compared with post-surgery eyes

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Weindler, M.S. Spitzer, M. Schultheiß, R. Kromer, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) is a progressive neurodegenerative disease which leads to irreversible blindness. An elevated intraocular pressure (IOP) is considered to be the main risk factor for the disease progression. It is known that retinal blood flow is altered in POAG eyes. Tafluprost, a prostaglandin analogue which lowers the IOP, has shown to also improve the retinal blood flow in animals.

Methods: The current study therefore evaluated the retinal vessel density in the peripapillary and macular region of POAG patients with normal IOP treated with topical Tafluprost (n=20) compared to surgically treated patients (including deep sclerectomy, trabeculotomy and trabeculectomy) with normal IOP (n=22) using optical coherence tomography angiography (OCT-A Topcon DRI OCT Triton Tokyo, Japan). The OCT-A was performed in the superficial peripapillary Plexus as well as the superficial and deep perimacular Plexus. The retinal flow density was obtained after binarisation using Matlab® and evaluated in five sectors (superior, inferior, nasal, temporal, central). The statistic analysis was performed using the parametric t-test with Sidak correction.

Results: There was a significantly higher peripapillary flow density in all sectors in Tafluprost treated eyes when compared to post-surgery eyes (central $39.3 \pm 11.8\%$ versus $32.8 \pm 5.9\%$, $p=0.04$; superior $41.1 \pm 9.4\%$ versus $32.1 \pm 7.4\%$, $p = 0.001$; temporal $32.1 \pm 14.9\%$ vs $20.9 \pm 5.9\%$, $p < 0.0001$; inferior $42.6 \pm 12.4\%$ versus $30.4 \pm 8.9\%$, $p < 0.0001$; nasal $23.8 \pm 10.1\%$ versus $15.7 \pm 4.9\%$, $p = 0.03$). The flow density in the inferior sector of the superficial plexus in the macular region was also significantly higher in the Tafluprost group $26.6 \pm 10.5\%$ versus $19.7 \pm 3.2\%$, $p = 0.03$).

Conclusions: These results suggest that there is a significantly higher flow density with patients with POAG under Tafluprost therapy when compared to surgically treated POAG patients. This may indicate that IOP lowering surgeries should be performed rather late.

CONTROL ID: 3543761

SUBMITTER (NAME ONLY): Zelia Corradi

TITLE: Identification and functional analysis of novel deep intronic and structural ABCA4 variants in 876 Stargardt disease cases

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The ABCA4 gene, implicated in Stargardt disease (STGD1), is the most frequently mutated maculopathy gene. Despite ABCA4 being identified 24 years ago, for thousands of cases the mutations causing STGD1 remain unknown. Previously, 1054 unsolved STGD and STGD-like probands were analyzed using single molecule molecular inversion probes (smMIPs), revealing bi-allelic ABCA4 variants in 448 probands, including 13 novel causal deep-intronic variants (DIVs) in 18 alleles, and 11 novel structural variants (SVs) in 16 alleles (Khan et al. GenetMed, 22:1235-1246, 2020). Here, we aim to shed further light on the missing heritability of STGD1 by analyzing another large cohort of genetically unsolved STGD probands.

Methods: 876 STGD and STGD-like patients were collected from 27 collaborators worldwide, 725 probands carried no or one ABCA4 variant and 151 probands carried two alleles, one of which was p.Asn1868Ile or p.Gly1961Glu, which are sometimes found in cis with DIVs. The complete 128-kb ABCA4 gene was sequenced using previously designed smMIPs. The effect of putative splice defects was assessed through in vitro midigene splice assays in HEK293T cells. The breakpoints of SVs were determined by junction PCR and Sanger sequencing.

Results: ABCA4 sequence analysis revealed two causal alleles in 436 of 876 probands (49.8%), and 13 known (in 63 alleles) and 15 novel (in 20 alleles) causal DIVs. In vitro splice assays revealed, among others, a DIV (c.4539+1964G>T) leading to the in-frame insertion of a pseudoexon, a near exon variant (c.859-25A>G) leading to complex splicing defects and a splice variant (c.4667+5G>T) that is part of a novel complex allele. In addition, 4 novel and 1 known SV were identified and characterized in 5 alleles.

Conclusions: Similar to a previous ABCA4 sequencing study of STGD and STGD-like cases, in which we genetically solved 448/1054 (42.5%) probands, we were able to genetically solve 49.8% of the probands. The total number of novel DIVs and SVs, i.e. 24 in 872 alleles (2.8%) is similar to the previous study in which we discovered 34 in 896 alleles (3.8%), indicating that there still are many rare DIVs and SVs to be discovered in Caucasian STGD1 cases. The identification of 83 DIVs in 81 probands suggests these persons may be eligible for splice modulation therapies when available.

CONTROL ID: 3543763

SUBMITTER (NAME ONLY): Alec Bernard

TITLE: The Impact of the COVID-19 Pandemic and Mitigation Measures on Persons with Vision and Hearing Impairment

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: COVID-19 and associated mitigation measures have caused unprecedented global disruption. It is not known whether there are disproportionate challenges for persons with a sensory disability. Our cross-sectional study assesses this impact of the pandemic on persons with and without visual or hearing loss.

Methods: Experts from diverse disciplines developed a 34-item survey instrument, the Coronavirus Disability Survey, which includes items on general and psychological health, instrumental activities of daily living, isolation, financial and transportation challenges, and information access. The study population included 112 adults with moderate or worse visual impairment (<20/60 in better-seeing eye), 108 with hearing loss (defined using ICD-10 codes), and 155 age/sex-matched controls recruited from the University of Michigan (UM) Health System. Survey administration was via email or telephone. The UM IRB approved this study and all participants provided informed consent.

Results: Participants reported similarly high levels of disruption of their daily lives with 80% reporting “a fair amount” or “a lot” of disruption. Groups reported similar levels of COVID exposure (21%) and infection (45% of exposed). In the visual loss (VL) group, 18% reported “a lot” of difficulty or being “unable” to access routine medical care compared with 12% of hearing loss (HL) and 10% of control (C) groups ($p=.02$). The reasons for increased difficulty with instrumental activities of daily living varied: among those with VL 62% had difficulty due to fear of exposure (54% HL, 45% C); 38% said the person assisting them was worried about exposure (6% HL, 7% C); and 12% cited decreased availability of public transportation (2% HL, 3% C). A greater proportion with VL began relying more on family for assistance (31% VL, 7% HL, 13% C) ($p<.001$ for all comparisons). Among all participants, 30% reported difficulty accessing trusted information about the pandemic; 11% of those with VL found the information difficult to see or hear (1% HL, 2% C; $p<.001$).

Conclusions: Individuals with VL may face increased disruption of their daily activities stemming from the pandemic and related mitigation measures, including in accessing healthcare, transportation, and information. Data-driven public health and policy decisions may benefit from a deeper understanding of the differential impact of the pandemic on these vulnerable groups.

CONTROL ID: 3543766

SUBMITTER (NAME ONLY): Marianne Berdugo-Polak

TITLE: Long-term oral treatment with low dose glibenclamide reduces diabetic retinopathy damage in the Goto-Kakizaki rat model

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Berdugo-Polak, L. Radet, S. Perreau, T. Guyon, A. Daruich, J. Beltrand, E. Kermorvant-Duchemin, M. Polak, F.F. Behar-Cohen, Université de Paris, Faculté de santé, Centre de Recherche des Cordeliers, Université de Paris, Paris, Île-de-France, FRANCE|K. delaunay, M. Naud, E. Gelizé, L. Jonet, T. Guyon, E. Picard, P. Crisanti, F.F. Behar-Cohen, Inserm UMRs 1138, Centre de Recherche des Cordeliers, Sorbonne Université, Université de Paris, INSERM, Paris, Île-de-France, FRANCE|D. Rosa, Wesleyan University, Middletown, Connecticut, UNITED STATES|A. Daruich, Hopital Necker-Enfants Malades, Department of Ophthalmology, Hopital universitaire Necker-Enfants malades, Paris, Île-de-France, FRANCE|E. Kermorvant-Duchemin, Hopital Necker-Enfants Malades, Department of neonatology, Hopital universitaire Necker-Enfants malades, Paris, Île-de-France, FRANCE|J. Beltrand, M. Polak, Hôpital Necker-Enfants Malades, Department of paediatric endocrinology, gynecology and diabetology, Hopital universitaire Necker-Enfants malades, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Glibenclamide (Glyburide), a Sulfonylurea drug used to lower blood glucose in diabetic patients, was shown to be neuroprotective when administered either systemically or locally in rat models of hyperglycemia or excitotoxicity-induced retinal degeneration. Its administration, at non-hypoglycemic doses, protected retinal function and structure. It acts through its binding to the Sulfonylurea receptor SUR1, extensively expressed in rodent, monkey and human neuroretinas (Berdugo et al. 2020). In this study, we investigated the protective effects of life-long oral treatment with glibenclamide, at low dose, in the Goto-Kakizaki (GK) rat model of diabetic retinopathy (DR).

Methods: GK rats were force-fed with a glibenclamide oral suspension (Amglidia(ND), Ammtek/Nordic Pharma) or vehicle twice a day, 5d/wk, from 2-months (hyperglycemia onset) to 12-months of age (previously described stage of DR; Omri S, 2013; Rothschild PR, 2017). At 12 months, we measured neuroretinal thickness on Optical Coherence Tomography (OCT) pictures, we quantified retinal vascularisation and vascular diameters on fluorescent lectin-labeled neuroretinal flatmounts, photographed with a confocal microscope and using a self-made ImageJ macro. We evaluated retinal function evolution through electroretinography testing (ERG) in glibenclamide vs. vehicle treated diabetic animals and vs. non-diabetic Wistar rats (WS).

Results: Diabetes induced retinal thickening on OCT pictures (mean 337 ± 3.7 sem vs. 303 ± 3.8 microns) and treatment reduced this thickening (315 ± 4.5 microns $P < 0.05$). The proportion of retinal capillaries is increased by 7.8% in the treated group compared to vehicle-treated group ($P = 0.04$). ERG parameters reflecting the inner retina activity were damaged at 12 months in GK rats compared to WS rats (first scotopic oscillatory potential implicit time = 33.5 ± 0.3 vs. 30.4 ± 0.26 ms, $P = 0.0001$, $n = 15$ and 8) and partially protected in treated animals (32.4 ± 0.29 ms, $P = 0.03$, $n = 7$).

Conclusions: Long-term low-dose oral glibenclamide treatment partially prevents RD vascular, edematous and functional damage in diabetic GK rats. As the oral drug is already available for patients, we are now exploring incidence and severity of DR in patients treated by glibenclamide vs. other medications, and developing a local

formulation for ocular diseases.

CONTROL ID: 3543770

SUBMITTER (NAME ONLY): Tea Soon Park

TITLE: Modeling the outer blood-retina barrier using microfluidic chips and iPSC-derived RPE and endothelial cells

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Park, E. Nguyen, H. Pakhchanian, D. Ortolan, N. Vettikatu, R. Dejene, D. Bose, G. Liang, R. Sharma, A. Maminishkis, K. Bharti, Ophthalmic Genetics & Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal pigmented epithelium (RPE) and choroid vasculature form a highly specialized tissue that provides critical support for retinal function and homeostasis. Here, we combined human iPSC-derived RPE and endothelial cells (EC) with organ-on-a-chip technology, to model the outer blood-retinal barrier (oBRB). Using this platform, we aim to study patient-specific mechanisms of retinal degenerative disorders such as macular edema.

Methods: The commercially available Emulate organ-chip microfluidic system was used as the basis of the model. The apical channel of the chip was seeded with iPSC-derived RPE cells that had been differentiated for 42 days. ECs were deposited as a monolayer surrounding the chip basal channel to mimic the choroid capillaries. In order to characterize the functionality of the RPE-EC co-culture system in the chip, we assayed: (1) Dextran permeability, (2) fluid transport across apical to basal channels, and (3) RPE and EC morphology.

Results: Various genetically independent healthy and diseased iPSCs were differentiated into functional RPE and EC and cryopreserved. RPE cells formed a monolayer on the membrane of the apical channel and displayed highly pigmented polygonal morphology with expression of ZO-1 and tublin-1b. RPE tight junction integrity was confirmed using a fluorochrome conjugated dextran permeability assay, demonstrating that RPE barrier function was sufficient to block Dextran molecules. In addition, a fluid transport assay was performed to examine RPE transcytosis and homeostasis function. When compared to control chips seeded with only RPE cells, the fluid transport activity in RPE-EC chips was 2-fold higher and in range of physiological levels. These results support that both EC and RPE cells are critical components of fluid transport activity.

Conclusions: The combination of a microfluidic organ-chip system with patient-specific iPSC derivatives has provided us with a non-invasive ex vivo model to study outer retinal physiology. This micro-engineered RPE-EC chip system is a platform for the patient-specific study of diseased RPE-EC phenotypes as well as drug discovery and toxicity screening for the treatment of ocular degenerative diseases such as macular edema.

CONTROL ID: 3543771

SUBMITTER (NAME ONLY): Patrícia Barreto

TITLE: Genetic characterization of a Portuguese age-related macular degeneration population

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Barreto, C. Farinha, R. Coimbra, M. Cachulo, M.H. Madeira, J.G. Cunha-Vaz, R. Silva, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|C. Farinha, M. Cachulo, R. Silva, Ophthalmology, Centro Hospitalar e Universitario de Coimbra EPE, Coimbra, Coimbra, PORTUGAL|J.B. Melo, I.M. Carreira, Cytogenetics and Genomics Laboratory, Clinical Academic Center of Coimbra (CACC), Faculty of Medicine; University of Coimbra, Portugal, Coimbra, Please select, PORTUGAL|J.B. Melo, I.M. Carreira, Coimbra Institute for Clinical and Biomedical Research (iCBR), CIMAGO, CIBB – Centre for Innovative Biomedicine and Biotechnology., Coimbra, PORTUGAL|C. Hoyng, A.I. Den Hollander, Ophthalmology, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|P. Barreto, Coimbra Institute for Clinical and Biomedical Research (iCBR), CIBB – Centre for Innovative Biomedicine and Biotechnology., Coimbra, Please select, PORTUGAL|

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ABSTRACT BODY:

Purpose: The purpose of this study was to genetically characterize an AMD population from Portugal.

Methods: We performed the epidemiological Coimbra Eye Study (NCT02748824), and genotyped AMD patients and controls. Participants were classified based on the Rotterdam Classification. Patients were considered stages 2,3 and 4, whereas controls were considered stages 0 and 1b. For this analysis, we considered 243 patients and 598 controls. Genotyping was performed using a single-molecule molecular inversion probes and next generation sequencing to target single nucleotide polymorphisms (SNPs) and coding and splice-site regions of 13 genes: ARMS2, C3, C9, CD46, CFB, CFH, CFI, HTRA1, TIMP3, SLC16A8, ABCA4, CTNNA1, and PRPH2. The genetic assay was performed under the EyeRisk Project, of the E3 Consortium. A total of 841 samples and 69 SNPs were tested for association under an additive model, using the presence of AMD as a binary outcome. A logistic regression analysis was performed to assess allelic odds ratio (ORs) at 95% CI for each variant, adjusted for age and sex.

Results: We have identified 7 variants that may have a protective effect on the outcome of the disease:

C2_CFB_SKIV2L rs429608 (OR 0.518;CI 95% 0.342-0.765, p= 0.0013); CFH rs10922109 (OR 0.683;CI 95% 0.5657-0.891, p= 0.0032) and rs1410996 (OR 0.708;CI 95% 0.5629-0.886, p=0.0028); CETP rs5817082 (OR 0.738;CI 95% 0.5637-0.961, p= 0.0255); CNN2 rs10422209 (OR 0.683;CI 95% 0.4757-0.966, p= 0.0343; CB rs641153 (OR 0.659;CI 95% 0.4408-0.966, p= 0.0366) and RDBP_CFB rs760070 (OR 0.682;CI 95% 0.4565-0.997, p=0.0541).

Additionally, we have identified 4 SNPs associated with the presence of AMD: ARMS2 rs10490924 (OR 1.51; CI 95% 1,1369 - 2, p= 0,0042); ARMS2_HTRA1 rs3750846 (OR 1.5; CI 95% 1.1226- 1.99, p= 0.0057); SLC16A8 rs8135665 (OR 1.51; CI 95% 1.0893- 2.08, p= 0.0128) and CFH rs35292876 (OR 2.93; CI 95% 1.204- 7.15, p= 0.0166).

Conclusions: Our results are in line with other studies that have been published, namely the two major genetic studies of the IAMDGC and the EyeRisk Project, highlighting the importance of genetics in the disease. The genes associated with AMD act in different pathophysiology pathways, sustaining the multifactorial etiology of AMD. To our knowledge, this is the first genetic study of a Portuguese AMD population, and our results are compliant with literature.

CONTROL ID: 3543776

SUBMITTER (NAME ONLY): Vamsi Parimi

TITLE: Foveal cone mosaic disruptions in diabetic subjects

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Parimi, A.E. Elsner, B. Walker, R. Gilbert, T. Gast, S.A. Burns, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic subjects have alterations in the anatomical integrity of the foveal cone mosaic, e.g. disruptions in the foveal cone mosaic that could act as noise in the visual system and lead to a decline in visual performance. We estimated the magnitude of these disruptions in Adaptive Optics Scanning Laser Ophthalmoscope cone maps.

Methods: We quantified the disruptions to the cone mosaic in 11 diabetic subjects (35-71 yr, 51.0 +/-14.4 yr) who were previously found to have localized dark cone regions. Subjects were consented and tested in a manner approved by the Indiana University Institutional Review Board, which adhered to the Declaration of Helsinki. Confocal images with a 100-micron aperture were collected as a series of 100 frame video sequences. The image sequences were aligned and summed to provide a range of gray scale images that allowed cones to vary from bright to dark. A 3 deg region of interest was analyzed, centered on the region of highest cone density. Two independent graders quantified the extent of the disruptions in the cone mosaic using the following criteria: 1) Continuity of the dark regions, 2) length of at least 3 cones and 3) regions darker than nearby structures. The disruptions could be either gaps between cones or adjacent cones that lacked strong central reflections. We computed the Euclidian distance of each disruption of the cone mosaics.

Results: Both types of disruptions, gaps between cones and three or more cones in a row lacking reflective centers, were found. Disruptions of the cone mosaic of a size sufficient to create visual noise were typical, with 10 of 11 subjects, having more than 75% of all the disruptions identified by the graders being > 1 min of arc (5 microns/ ≤30 cpd). In 10 of 11 subjects, the presence of at least 5 disruptions of the cone mosaic > than 3 min of arc (15 microns/ ≤10 cpd) and one disruption > than 5 min of arc (25 microns/ ≤6 cpd) were found. These disruptions varied widely in shape and orientation, which negatively impacted the agreement between the graders.

Conclusions: In the foveal region of diabetic retinas, disruptions of the cone mosaic were typical. Previously, sensitivity to acuity targets was shown to be decreased in a region of an area of dark cones (Tu, 2017). Thus, we anticipate that visual noise produced by these disruptions is of sufficient size to interfere with detection of acuity targets and reading.

CONTROL ID: 3543777

SUBMITTER (NAME ONLY): Sasan Moghimi

TITLE: Predicting central 10 degrees visual field from peripapillary optical coherence tomography using deep learning approach

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Moghimi, A. Kamalipour, H. Hou, J.A. Proudfoot, L.M. Zangwill, R.N. Weinreb, Hamilton Glaucoma Center, Shiley Eye Institute, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|P. Khosravi, Department of Computer Science, University of California, Irvine, Irvine, California, UNITED STATES|M. Jazayeri, San Diego State University, San Diego, California, UNITED STATES|J.M. Liebmann, Department of Ophthalmology, Edward S. Harkness Eye Institute, Columbia University Medical Center, New York, New York, UNITED STATES|C.A. Girkin, Department of Ophthalmology and visual science, Callahan Eye Hospital, University of Alabama-Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a deep learning (DL) simulation of standard automated perimetry (SAP) in the central 10° based on spectral domain optical coherence tomography (SD-OCT) retinal nerve fiber layer thickness (RNFLT).

Methods: This study included 5352 pairs of SD-OCT and 10-2 SAP from 1365 eyes of 724 healthy, glaucoma suspect and glaucoma patients from the Diagnostic Innovations in Glaucoma Study (DIGS) and the African Descent and Glaucoma Evaluation Study (ADAGES). Each pair of SD-OCT and 10-2 SAP was obtained within a 6-month duration. The dataset was randomly divided into training (65%), validation (15%), and test (20%) sets at the patient level. A unidimensional DL convolutional neural network was used to map all 768 peripapillary RNFLT values of SD-OCT to 68 sensitivity thresholds of 10-2 SAP. Visual field indices were generated using CNN-predicted sensitivity thresholds at 68 10-2 SAP test locations and included Total deviation (TD) values, Pattern deviation (PD) values at each test location, Mean deviation (MD) and pattern standard deviation (PSD). The accuracy of the model at each test location was evaluated by calculating the average mean absolute error (MAE) and the Pearson correlation coefficients (r) of predicted and actual TD values. Global accuracy of the model was evaluated by calculating the MAE and r for MD and PSD predictions.

Results: The DL TD predictions had an average MAE of 4.04 dB and r of 0.59 ($P < 0.001$) over the 68 10-2 SAP test points. This model was capable of predicting 10-2 SAP MD and PSD with MAE (r) of 2.88 dB (0.74) and 2.30 dB (0.59), respectively (Fig. 1).

Conclusions: An artificial intelligence approach was capable of reconstructing SAP central 10° using peripapillary SD-OCT RNFLT measurements. Peripapillary RNFLT provides information about central visual field in glaucoma.

CONTROL ID: 3543778

SUBMITTER (NAME ONLY): Charlie Börjeson

TITLE: Design of a compact open-field wavefront sensor

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Börjeson, D. Romashchenko, L. Lundstrom, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN|

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ABSTRACT BODY:

Purpose: Many ocular wavefront sensors employ one or two telescopes to image the wavefront from an eye onto a Hartmann-Shack wavefront sensor (HSWS). Conventionally, the components are placed in a 4f setup, resulting in a rather long system, especially for an open field of view configuration. It would be useful to have a small and portable system that could be moved between different experimental setups. Therefore, this study tested the hypothesis that ocular wavefront sensors can be reduced in size by using a non-4f setup, while still maintaining the large eye-to-first-lens distance necessary for open-field sensing.

Methods: The paraxial imaging properties of conventional 4f setups and non-4f setups were compared theoretically. The analyzed non-4f setups had the same eye-to-first-lens distance as the 4f setups, but with shorter focal lengths and with the eye and HSWS conjugate planes shifted away from the focal planes of the telescope lenses. Optical aberrations of the setups with different off-the-shelf lenses were also simulated in Zemax.

A wavefront sensor was built using one of the shortest developed non-4f designs. The HSWS was placed as close to the second lens of the telescope as possible. The correct position for the eye was found by utilizing a double eye model with refractive errors of +5 D and -5 D, which at the conjugate plane of the HSWS would yield equal detected pupil sizes on the HSWS. For verification of the system, trial lenses were then placed in front of the eye models and the wavefront was recorded as Zernike coefficients by the HSWS.

Results: The paraxial calculations showed that the 4f and non-4f setups had identical imaging properties. Compared to a 4f setup, the maximum reduction in eye-to-HSWS distance was 50%, at which point the second-lens-to-HSWS distance was 0. At this limit, the first-lens-to-HSWS distance was reduced to $1/(M+2)$ of that of a 4f setup, where M is the angular magnification of the telescope. The Zemax simulations showed that the non-4f design could be made diffraction limited on-axis.

The measured defocus root-mean-square error for the eye models with trial lenses was 0.11 D, where the total defocus ranged from -5 D to +5 D in increments of 1 D.

Conclusions: It is possible to construct a functional and compact ocular open-field wavefront sensor by using a non-4f setup. However, the initial alignment is more difficult, as the eye and the HSWS are not placed in the focal planes of the telescope lenses.

CONTROL ID: 3543784

SUBMITTER (NAME ONLY): Lucian Del Priore

TITLE: Border Location Affects Local Progression Kinetics of Geographic Atrophy

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.V. Del Priore, M. Sun, A. Ahluwalia, B. Young, M. Park, L. Shen, Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the impact of geographic atrophy (GA) location on GA local progression rate and the distribution of GA lesions.

Methods: We manually delineated GA on color fundus photographs of eyes with non-exudative age-related macular degeneration in the Age-Related Eye Disease Study. We included 2 visits that were 1 year apart for each eye with GA and then registered the images using vessel bifurcations. We calculated GA border expansion rate (BER) as the linear distance that GA border traveled over 1 year using a Euclidean distance map. Eye-specific BER was defined as the mean BER of all pixels (pixel size=10 μ m) on GA border in each eye. We also determined GA prevalence and BER in 4 macular quadrants and at different distances from the foveal center.

Results: We included 237 eyes of 160 patients in the analysis. GA enlarged $1.51 \pm 1.96 \text{ mm}^2$ in area and $0.13 \pm 0.11 \text{ mm}$ in distance over 1 year. GA area growth rate (mm^2/year) was significantly associated with baseline GA area ($P < 0.001$), number of lesions ($P < 0.001$), and circularity index ($P < 0.001$); in contrast, eye-specific BER (mm/year) was not significantly associated with any of these 3 morphological factors. The percentage of the retina affected by GA decreased from 49% to 1% as the retinal eccentricity increased from 0 to 4 mm (Figure A). By comparison, GA BER increased linearly as a function of retinal eccentricity ($P < 0.001$), increasing from 0.07 mm/year at 0-0.5 mm from the foveal center to 0.18 mm/year at 3.5-4 mm from the foveal center (Figure B). The GA BER did not vary significantly across 4 macular quadrants ($P = 0.16$), but the percentage of retina affected by GA was higher in the temporal than nasal quadrant ($P = 0.02$), and was higher in the superior than inferior quadrant ($P = 0.01$).

Conclusions: Measurements of eye-specific GA BER allows evaluation of GA progression without significant confounding effects from baseline GA area, shape, and lesion number. The local progression rate of GA increased as a function of distance from the foveal center within the macula, and was different from GA distribution. These findings suggest that the underlying mechanism responsible for GA initiation may be different from the mechanism of GA enlargement.

CONTROL ID: 3543786

SUBMITTER (NAME ONLY): Rosario Fernandez-Godino

TITLE: RPE cells grown on AMD-like extracellular matrix activate the complement system via tick-over, which can be prevented with shRNAs anti-C3.

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Fernandez-Godino, B. Chinchilla Rodriguez, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cell-based models are valuable tools to study the mechanisms of pathology at early stages of age-related macular degeneration (AMD), including the formation of sub-retinal pigment epithelial (RPE) deposits mediated by the activation of the complement system. We propose that alterations in the extracellular matrix (ECM) of Bruch's membrane (BrM) caused by aging or mutations accelerate the rate of hydrolysis of complement C3 to C3(H₂O) (tick-over), which forms a stable C3(H₂O)-convertase on the ECM that activates C3 chronically and ultimately leads to deposit formation.

Methods: To test our hypothesis, we have used CRISPR-based gene editing tools to generate induced Pluripotent Stem Cells (iPSCs) carrying the mutation p.923delDG in C3, which allows complement activation via tick-over only. iPSC C3^{-/-} and C3^{WT/WT} were used as controls. The edited iPSCs were differentiated into RPE cells using direct differentiation methods and cultured on transwells coated with RPE-derived ECM that mimics BrM with AMD. To investigate the potential of C3 as a therapeutic target, C3 was inhibited with short hairpin (sh) RNAs in the iPSC-RPE cells grown on AMD-like ECM. Complement activation by tick-over or alternative pathway was quantified by the presence of C3(H₂O) and C3a respectively in conditioned media measured via ELISA. Formation of basal deposits was characterized by immunofluorescence and electron microscopy.

Results: iPSC-RPE cells C3^{WT/WT} and C3^{WT/923DG} grown on AMD-like ECM secreted elevated levels of C3(H₂O) and C3a compared to the same cells grown on normal ECM (ANOVA, **p<0.01). Abnormal deposition of collagen fibers underneath the RPE cultured on AMD-like ECM was also observed by immunostaining and electron microscopy after 3 months. Treatment with shRNA anti-C3 decreased the mRNA levels of C3 (ANOVA, ****p<0.0001) as well as the amount of C3(H₂O) secreted to the media of wild type cells grown on AMD-like ECM (ANOVA, **p<0.01). The deposition of collagens underneath the RPE was also diminished after the treatment with shRNAs anti-C3.

Conclusions: The results are consistent with our hypothesis that abnormalities in the ECM result in increased activation of C3 via tick-over, which can be inhibited with shRNAs. Thereby, the tick-over could be used as a therapeutic target to prevent increased complement activation in patients with early AMD.

CONTROL ID: 3543787

SUBMITTER (NAME ONLY): Tim Schilling

TITLE: Selective stimulation of the optic nerve head with blue light increases vitreal dopamine levels in rabbits

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is growing evidence that intrinsically photosensitive retinal ganglion cells (ipRGCs) modulate retinal activity. It has been demonstrated that selective stimulation of the optic nerve head with blue light (BL) can activate the melanopsin-containing ipRGCs axons located there. Stimulation of ipRGC axons also improves contrast sensitivity and alters retinal electrical activity, which may indirectly reflect an increase in retinal dopamine release. Retrograde signalling from ipRGCs to dopaminergic amacrine cells can influence the retinal dopaminergic system. This study aimed to directly investigate any change in dopamine release as a result of ipRGC activation. It was hypothesized that dopamine levels would be elevated after stimulation of the optic nerve head with BL.

Methods: Adult male New Zealand rabbits were stimulated for one and ten minutes with and without BL, being included five rabbits in each group. With a self-constructed stereotactic system, it was able to specifically stimulate the optic nerve head with BL (peak 470 nm) in rabbits' eyes. The BL stimulus was delivered by an optical fiber of 200 µm diameter inserted into the globe and positioned over the optic nerve head in the experimental eye only. In the control condition with no light, the optical fiber was inserted without light stimulation. The concentration of dopamine in the tears, aqueous humor, vitreous humor, and retina was measured using high-performance liquid chromatography. After normal distribution analysis, statistical comparisons were conducted between the contralateral eye and the experimental eye after stimulation using paired Student's t-tests, being considered $p < 0.05$ as statistical significance.

Results: No significant difference in absolute dopamine levels between eyes was found in the tears, aqueous humor, or retina ($p > 0.05$). In the vitreous humor, dopamine concentration was significantly higher in the experimental eye compared to the contralateral eye after BL stimulation ($p < 0.05$).

Conclusions: These results are consistent with research that suggests vitreal content is a better measure of the rate of retinal dopamine release than retinal dopamine levels. This is the first direct evidence that activation of melanopsin in the axons of ipRGCs at the head of the optic nerve results in measurable changes in dopamine concentration in the eye.

CONTROL ID: 3543788

SUBMITTER (NAME ONLY): Diana Beatriz Bayani

TITLE: Cost-effectiveness analysis of retinal imaging devices for diabetic retinopathy screening

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To estimate and compare the cost-effectiveness of mydriatic and nonmydriatic imaging devices for consideration in a community-based program for diabetic retinopathy (DR) screening in the Philippines

Methods: A decision-analytic model was developed to simulate the costs and outcomes of each device [Aurora (AU), Smartscope (SS), RV700 (RV), InView (NV) with dilation and without dilation of the pupil. The key measures of effectiveness were determined by the devices' operating characteristics including positive and negative predictive values and rate of ungradable images. These parameters, as well as the distribution of patients with varying severity levels of DR, were obtained from a validation study performed in Manila involving images from 177 eyes of 92 patients with diabetes. Associated costs of screening, referrals, panretinal laser photocoagulation for severe nonproliferative or proliferative DR, and corresponding cost of severe vision loss were estimated from the perspective of the patient. Health outcomes were reported as quality-adjusted life years (QALYs) based on utility values assigned to vision threatening DR and vision loss. The primary outcome measure is reported as cost in Philippine Peso (PhP) per QALY gained.

Results: Analyses from the patient perspective show that all devices were dominated when the clinic-based screening test was used as comparator. When using the dominance approach, the NV and AU NM were strongly dominated, whereas the RV7 MD/NM, and SS MD were weakly dominated. The AU MD was most cost-effective with an incremental cost-effectiveness ratio (ICER) value of 71,207 PhP per QALY-gained versus the Smartscope MD. Results were most sensitive to changes in the cost of the comparator, rate of ungradable image and incidence of DR.

Conclusions: The use of Aurora and Smartscope with pupil dilation yield good value for money based on their validity, and the reported ICER value falls below the country-specific threshold of 150,000 PhP, which shows great potential for being cost-effective in a community-based DR screening program. A broader and more comprehensive analysis is warranted to account for societal costs when the devices are used in a larger-scale, relative to their individual and population-level benefits while considering other factors such as burden and treatment of disease, and health system capacity.

CONTROL ID: 3543796

SUBMITTER (NAME ONLY): Meghal Gagrani

TITLE: The epidemiology of episcleral venous pressure (EVP)

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Gagrani, S. Fan, V. Gulati, S. Kedar, C.B. Toris, D.A. Gbate, Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|S. Kedar, Neurology, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|D. Reed, S.E. Moroi, Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|A.J. Sit, Ophthalmology and Visual Sciences, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: EVP is a significant determinant of intraocular pressure (IOP) in the Goldmann equation and is a potential rapid and non-invasive biomarker for intracranial pressure (ICP). The variability of EVP with demographic variables, systemic and ocular characteristics is yet to be elucidated. This study aims to evaluate the epidemiology of EVP.

Methods: A post hoc analysis was conducted of collated data from aqueous humor dynamics studies of healthy adults at UNMC (Nebraska), Mayo Clinic (Minnesota) and U Michigan (Michigan). Systemic parameters measured were weight, height, BMI, neck circumference (NC), pulse rate, systolic (SBP) and diastolic blood pressures (DBP). Mean arterial pressure (MAP) was calculated. Seated IOP was measured using a pneumatonometer (Reichert, USA). Seated EVP was measured using a slit lamp mounted venomanometer (Eyetechn USA). Two sites subjectively chose endpoints and the third site added video capture of endpoints. Two to three readings were collected and averaged. Central corneal thickness (CCT), anterior chamber depth (ACD) and axial length (AL) were collected with ultrasound instruments. Biweight midcorrelations were used to study the effect of different variables on EVP. Right eye (OD) and left eye (OS) of each subject were independently correlated with each variable.

Results: Data from 201 subjects (n = 201 eyes) (mean age of 46 ± 16 years and range of 15 to 81 years) were analyzed. 76% were females (Table 1) and 85% were White. All variables were normally distributed except age, which was bimodally distributed. Data is presented as mean \pm SD unless stated otherwise. Mean values were weight 78 ± 18 kg, height 166 ± 9 cm, BMI 28 ± 5 and NC 37 ± 4 cm. Pulse rate was 72 ± 13 beats per minute and SBP, DBP, and MAP were 123 ± 15 , 77 ± 10 , and 92 ± 12 mmHg, respectively. All ocular measurements were correlated between OD and OS. Ocular parameters were EVP 7.9 ± 1.6 mmHg (range 3 to 14 mmHg), IOP 15.7 ± 2.7 mmHg (range 7 to 22 mmHg), CCT 557 ± 40 mm, ACD 3.4 ± 0.3 mm and AL 24 ± 1 mm. None of the systemic or ocular measurements had any significant correlation with EVP or IOP (Figure 1). All variables showed similar relationships for OD and OS eyes and in males and females.

Conclusions: EVP was not found to be correlated with any systemic or ocular parameters. A small range of distribution and the ability to measure EVP non-invasively would make it an excellent biomarker for raised ICP.

CONTROL ID: 3543800

SUBMITTER (NAME ONLY): Rayanne Luke

TITLE: Fitting Simplified Models to Machine Learning-Identified Tear Film Breakup

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Luke, R.J. Braun, T. Driscoll, D. Sinopoli, V. Yawatkar, L. You, A. Phatak, Mathematical Sciences, University of Delaware, Newark, Delaware, UNITED STATES|C. Begley, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Six ordinary differential equation (ODE) tear film breakup (TBU) models are created to capture evaporation, osmosis, and different types of flow. A convolutional neural network designed after Su et al. (IEEE, 2018) and trained on over 40,000 image patches successfully identifies TBU and non-TBU in fluorescent (FL) images gathered in vivo with an accuracy of 92%. The ODE models are fit to the automatically identified TBU FL intensity data by optimizing TBU quantities such as evaporation and tangential flow rates. Best-fit determination of TBU parameters suggests which mechanisms cause the thinning.

Methods: The FL intensity data was originally recorded from 25 normal subjects with 20 trials taken over two visits (Awisi-Gyau, Indiana University thesis, 2020). We extract the experimental FL image data from the centers of TBU regions identified by a convolutional neural network. These are fit with the models designed to mimic evaporation-driven, tangential flow-driven, and combination thinning. We estimate parameters using a least squares minimization of the difference between experimental and computed intensities using the trust region-reflective method. Theoretical intensity dependent on tear film (TF) thickness and FL concentration was based on Nichols et al (2012, IOVS, 53:5426). Separate procedures were used to estimate initial FL concentration and localized TF thickness (Wu et al, IOVS 2015, 56:4211). The fits use up to four parameters: evaporation rate v , a (steady) and b_1 (decaying) extensional flow rates, and decay rate b_2 . All computations are via custom Python programs.

Results: Optimal evaporation rates fall near or within experimental ranges (Nichols et al, IOVS, 2005). An example fit is shown in the Figure. The best-fit model determines that the evaporation rate is $-3.25 \mu\text{m}/\text{min}$ and that the instance exhibits strong, outward tangential flow that decays, allowing evaporation to take over in importance.

Conclusions: Intensity decay in automatically identified TBU areas can readily be fit with simplified models that capture essential thinning dynamics and yield physically relevant quantities. This procedure can be applied to a wide range of instances to obtain statistical information that cannot be directly measured during breakup.

CONTROL ID: 3543801

SUBMITTER (NAME ONLY): Ines Lains

TITLE: Plasma Metabolomic Profiles Associated with Three-Year Progression of Age-related Macular Degeneration

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I. Lains, A. Nigalye, K. Mendez, R. Katz, V.P. Douglas, I.K. Kim, J. Miller, D.G. Vavvas, J.W. Miller, D. Husain, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|K. Mendez, R.S. Kelly, J.A. Lasky Su, Systems Genetics and Genomics Unit, Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Metabolomics can provide unique insights into the understanding of the pathophysiology of multifactorial diseases. We and others have shown that plasma metabolomic profiles vary between patients with age related macular degeneration (AMD) and controls and across stages of AMD. However, to our knowledge, no longitudinal studies have assessed how metabolomic profiles relate to AMD progression. This work aimed to analyze the association between plasma metabolomic profiles and progression of AMD over a three-year period.

Methods: Prospective longitudinal study including patients with AMD and a control group (>50 years old). At baseline and three years later (\pm 3 months), all included participants (both eyes) were imaged with color fundus photographs (CFP) for AMD grading and fasting plasma samples were collected. Eyes were considered to have AMD progression if at three-years their AMD stage was more advanced than the baseline stage grading with the AREDS classification scheme using CFP. Metabolomic profiling was performed using Ultrahigh Performance Liquid chromatography – Mass Spectrometry. Multilevel mixed models (i.e. considering inclusion of two eyes of the same patient), accounting for age, body mass index, smoking and gender were used for analysis, using as outcome progression of AMD (yes/no).

Results: We included data on 196 eyes ($n=98$ patients), 13% ($n=26$) of them with progression at the three-years follow-up. After quality control, a total of 645 plasma endogenous metabolites were considered for analysis. Among the baseline plasma metabolites, 3 (N-palmitoyl-sphingosine, methylsuccinate and N,N-dimethylalanine) were significantly associated with three-year AMD progression ($p \leq 0.009$). When evaluating the association between changes in plasma metabolites (between baseline and 3 years) with progression of AMD, 10 significant associations were seen ($p \leq 0.009$).

Conclusions: Baseline metabolites and changes in metabolomic profiles were associated with clinical progression of AMD at 3 years. In particular, lipid and amino acid metabolites appear to be among the relevant metabolites linked to AMD progression. This work contributes to our understanding of AMD progression and to the development of future biomarkers to monitor and potential therapeutics for this blinding disease.

CONTROL ID: 3543803

SUBMITTER (NAME ONLY): Carmen María Lago

TITLE: Simulated Assessment of Presbyopia Correction IOLs in post-LASIK Patients

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Lago, A. de Castro, S. Marcos, Instituto de Óptica, Consejo Superior de Investigaciones Científicas, Madrid, SPAIN|C. Lago, L. Sawides, 2Eyes Vision S.L., Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To computationally assess the expected performance of a presbyopia correcting Intraocular Lens (PCIOL) in patients after LASIK surgery, in comparison with non-LASIK patients, and monofocal IOLs.

Methods: Presbyopia correcting IOL (PCIOL, Alcon Acrysof IQ Vivity) and Monofocal IOLs (MonoIOL, Alcon Acrysof IQ) of 22-D power were virtually implanted in an eye model (corneal power 43 D, corneal spherical aberration (SA) of 0.28 mm for 6-mm pupil diameter, anterior chamber depth 3.2 mm). LASIK corneas for myopic (-7.5 to -2.5 D) and hyperopic (+2.5 to +4.5 D) pre-operative spherical error were modeled by inducing SA ranging from 1.15 to -0.78 μ m, correlated with the corrected pre-operative spherical error (Marcos et al. 2002).

Image quality was evaluated in terms of Visual Strehl (VS) at best focus and through-focus. In addition, a metric to quantify retinal image halos was estimated by convolving the Point Spread Function with a 2-arcmin pinhole and calculating the ratio of light beyond 2 arcmin, for 5-mm pupils, ranging from 0 to 1 (maximum halo). Calculations were performed using a commercial optical design software (OpticsStudio, Zemax) and Matlab.

Results: For 5/3 mm pupil diameters VS @BestFocus was 0.93/0.99 and 0.78/0.52 for MonoIOL and for PCIOL (NoLASIK), and was 0.61 ± 0.38 and 0.5 ± 0.27 for MonoIOL and PCIOL (LASIK), on average (across LASIK conditions and pupils). VS at intermediate distances was 0.06/0.11 and 0.08/0.24 for MonoIOL and PCIOL (NoLASIK), and was 0.10 ± 0.06 and 0.17 ± 0.09 for MonoIOL and PCIOL (LASIK). The halo metric was 0.26 for MonoIOL and 0.64 for PCIOL (NoLASIK) and 0.59 ± 0.32 for MonoIOL (LASIK) and 0.71 ± 0.20 for PCIOL (LASIK). The impact of LASIK in combination with IOL on halos was largely asymmetric for hyperopic and myopic LASIK. For similar magnitude of pre-op LASIK refraction correction (+4.5 to -4.5 D), the average halo metric was 0.57 ± 0.26 / 0.85 ± 0.04 for MonoIOL/PCIOL for hyperopic LASIK and 0.73 ± 0.10 / 0.59 ± 0.08 for Monofocal/Presbyopia for myopic LASIK.

Conclusions: In (non LASIK) patients visual quality (VS) at best focus with a PCIOL lies within 16-18% of that with MonoIOL. However, the PCIOL outperforms the MonoIOL at intermediate distances (by 45-66%). The PCIOL performance is relatively immune to the presence of SA induced by LASIK. Furthermore, the PCIOL appears to interact favorably with positive SA (in myopic LASIK) to reduce halos.

CONTROL ID: 3543807

SUBMITTER (NAME ONLY): Vidisha Goyal

TITLE: AxoNet 2.0: A deep learning (DL)-based tool for morphometric analysis of retinal ganglion cell (RGC) axons

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A key outcome measure in animal models of glaucoma is the number and appearance of RGC axons, typically obtained from light micrographs of optic nerve (ON) cross-sections. However, this analysis is time-consuming and subjective. Here we expand on our RGC axon counting software (AxoNet 1.0, [1]) to also identify axoplasm ("Ax") and myelin sheath ("MySh") of normal-appearing RGC axons and extract their morphometric features.

Methods: Micrographs from 12 control and 14 hypertensive rat ONs were acquired as before [1], representing a wide range of glaucomatous damage. 1421 12x12 μm^2 sub-images were randomly selected from these micrographs, and Ax and MySh of normal-appearing axons were annotated by 16 trained individuals with cross-validation. Sub-images were randomly divided into training (90%), validation (5%), and test (5%) sets. A trained U-Net architecture generated segmentation of Ax and MySh of the normal-appearing axons, assigning a probability of each pixel being Ax or MySh. These maps were processed through an image processing pipeline to compute, for each axon: area, convex area, perimeter, eccentricity, average MySh probability (average probability over all MySh pixels of each pixel being MySh), and average Ax probability. Outcome measures included: (i) the soft-dice coefficient between predicted and ground-truth segmentation maps; (ii) R^2 regressing number of the normal-appearing axons counted automatically vs. ground truth. [1] Ritch+, Sci Rep, 2020

Results: The model performed well (Fig 1) with high soft-dice coefficients (Fig 2). AxoNet 2.0 outperformed AxoNet 1.0 as judged by agreement with ground truth (Fig 2).

Conclusions: A DL model can segment Ax and MySh of normal-appearing axons from ON sub-images with varying ON health. This approach will speed RGC axon counting and morphometric analysis in animal models of glaucomatous optic neuropathy.

CONTROL ID: 3543808

SUBMITTER (NAME ONLY): Ester Reina Torres

TITLE: Elevated IOP stimulates NO-mediated IOP homeostasis in mice

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Reina Torres, J.Y. Chang, J. van Batenburg-Sherwood, D.R. Overby, Bioengineering, Imperial College London, London, London, UNITED KINGDOM|D.W. Stamer, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Increased IOP results in narrowing of Schlemm's canal (SC), which increases the shear stress acting on SC cells. SC cells respond to shear stress by producing nitric oxide (NO), which increases outflow facility and lowers IOP. We hypothesize that increased IOP stimulates NO production by SC cells, comprising part of a homeostatic mechanism to regulate IOP. To measure in situ NO production within the outflow pathway of mice exposed to elevated IOP, we utilised a peptide-based biosensor that is sensitive to changes in NO. We also examined whether inhibition of NO synthase (NOS), which should block IOP-dependent NO production, exhibits a pressure-dependent effect on outflow facility (C).

Methods: NO levels were measured using peptide-functionalized fluorescent particles that convert to 3-nitrotyrosine in the presence of nitroxidative stress. These NO biosensors were perfused into the TM of enucleated mouse eyes at 8 or 16 mmHg (C57BL/6J, n=8 mice). Anterior segments were labelled using anti-nitrotyrosine antibodies and imaged by confocal microscopy. Fluorescent signal from the particles was used to normalise the nitrotyrosine signal in order to account for local differences in particle concentration. To examine NOS activity at different pressures, 50µM L-NAME was perfused into enucleated mouse eyes while contralateral eyes were perfused with vehicle (C57BL/6J, n=7 mice). Eyes were perfused at 9 pressure steps ranging from 4 to 16 mmHg using iPerfusion. Power law fittings to flow-pressure data were used to estimate C at each pressure.

Results: Eyes perfused at 16 mmHg exhibited higher nitrotyrosine levels than eyes perfused at 8 mmHg, relative pixel intensity was 1.15 times higher at 16 mmHg ($p < 0.001$). L-NAME decreased C, and its effect was pressure-dependent ($p = 0.02$). At 20mmHg, L-NAME decreased C by roughly one-third (-32 [-50, -7]%; $p = 0.02$), while at 8 mmHg L-NAME had a borderline significant effect (-17 [-34, 5]%; $p = 0.07$).

Conclusions: Elevated IOP stimulates NO production within the conventional outflow pathway of mice. L-NAME causes an IOP-dependent decrease in outflow facility, presumably by inhibiting NO production that would otherwise increase with IOP. Taken together, these data provide evidence for a rapid homeostatic mechanism involving IOP-dependent NO production that acts to increase outflow facility and oppose IOP elevation. Disruption of this homeostatic mechanism may contribute to ocular hypertension in glaucoma.

CONTROL ID: 3543812

SUBMITTER (NAME ONLY): Xavier Sánchez-Sáez

TITLE: CRISPR generated mouse model of central areolar choroidal dystrophy with a Prph2 mutation reproduces human dystrophy features.

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Sánchez-Sáez, H. Albertos-Arranz, M. Ruiz-Pastor, O. Kutsyr, N. Martínez-Gil, P. Lax, N. Cuenca, Physiology, Genetics and Microbiology, University of Alicante, Alicante, SPAIN|V. Maneu, Optics, Pharmacology and Anatomy, University of Alicante, Alicante, SPAIN|C. Aguilera, L. Méndez, P. Hernández-Carabias, Transgenic Facility, NUCLEUS. University of Salamanca., Salamanca, SPAIN|

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ABSTRACT BODY:

Purpose: Central choroidal dystrophies are retinal diseases that involve progressive retinal degeneration and the atrophy of the choriocapillaris. These dystrophies usually present an autosomal dominant inheritance pattern in which patients carry a single mutation in the PRPH2 gene. The aim of this work was to generate a mouse model with the same p.Arg195Leu mutation that was described in diagnosed human patients.

Methods: The heterozygous mouse model Prph2^{KI/WT} has been designed and generated using the CRISPR system to introduce the Arg195Leu mutation in the same allele as the patients. The functional state of the retina was studied using electroretinography under photopic and scotopic conditions and the optomotor test was used to determine visual acuity. In vivo structural state of retinal layers was assessed by optical coherence tomography imaging. The number of photoreceptor rows was quantified in cryosections using immunohistochemistry.

Results: Genetic sequencing of the Prph2^{KI/WT} mouse revealed the same codon mutation found in humans suffering from this dystrophy. Importantly, mice presented a degeneration pattern comparable to patients. From 3 months of age, the mouse optomotor response was significantly reduced indicating a visual acuity decrease. At 6 months, the mice presented reduced scotopic and photopic ERG responses, with smaller a-wave and b-wave amplitudes, and the number of photoreceptor rows was decreased as well as the retinal thickness.

Conclusions: The new Prph2KI/WT mouse model presents a similar degeneration pattern than that observed in patients and may facilitate the analysis of the pathophysiological process, being a suitable model for evaluating different therapeutic strategies.

Support. Ministerio de Ciencia e Innovación (FEDER- PID2019-106230RB-I00). Ministerio de Universidades (FPU16/04114, FPU18/02964). Instituto Carlos III (RETICS-FEDER RD16/0008/0016). Retina Asturias/Cantabria. FARPE-FUNDALUCE. Generalitat Valenciana (IDIFEDER/2017/064, ACIF/2020/203). Es Retina Asturias (2019/00286/001).

CONTROL ID: 3543813

SUBMITTER (NAME ONLY): Oksana Kutsyr

TITLE: High-fat consumption accelerates retinal degeneration and alters the gut microbiome in retinitis pigmentosa mice

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Kutsyr, A. Noailles, N. Martínez-Gil, L. Maestre-Carballa, M. Martínez-García, N. Cuenca, P. Lax, Physiology, Genetics and Microbiology, University of Alicante, Alicante, SPAIN|L. Fernández-Sánchez, V. Maneu, Optics, Pharmacology and Anatomy, University of Alicante, Alicante, SPAIN|

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ABSTRACT BODY:

Purpose: The consumption of high-fat diets (HFD) can lead to significant changes in the gut microbiome. Likewise, intestinal dysbiosis has been associated with the pathogenesis of several degenerative diseases. Thus, the purpose of this work was to analyze the gut microbiome changes associated with the consumption of HFD in mice with retinitis pigmentosa (RP).

Methods: Healthy C57BL/6J mice and dystrophic rd10 mice (RP) were fed either with normal chow (5.5% fat kcal) or with a HFD (61.6% fat kcal) for two weeks after weaning (P19). At the endpoint, retinal function was evaluated by optomotor test and electroretinography. The structure and integrity of the retina were studied by immunohistochemistry. Additionally, the gut microbiome was analyzed by 16S rRNA gene sequencing.

Results: Increased retinal degeneration was found in rd10 mice compared to C57BL/6J mice, both fed with normal chow. rd10 mice showed significantly diminished retinal responsiveness, with lower a- and b-waves, as well as reduced visual acuity. The loss of retinal function was accompanied by a fall in the number of photoreceptor rows, and the remaining photoreceptors exhibited morphologic anomalies. Additionally, the photoreceptor degeneration was associated to an inflammatory response of the retina, with the proliferation of microglial cells and reactive gliosis of Müller cells. Moreover, the gut microbiome analysis revealed differences in alpha and beta diversity at the genera, species and amplicon sequence variants (ASV) levels. Notably, four common ASV (*Rikenella* spp., *Muribaculaceae* spp., *Prevotellaceae* UCG-001 spp., and *Bacilli* spp.) in the gut of healthy animals were not found in the rd10 mice gut. HFD intake by rd10 mice resulted in a significant acceleration of the retinal function and morphology degeneration compared to rd10 mice fed normal chow. The consumption of HFD produced significant dysbiosis in the gut microbiome increasing potentially pro-inflammatory bacteria as *Bilophila* sp., *Alistipes* sp. and *Mucispirillum schaedleri* that probably contribute to the worsening of the degeneration process.

Conclusions: Retinal dysfunction and degeneration in retinitis pigmentosa is linked to significant changes in the gut microbiome, which can be further altered by diet, leading to a deterioration of the disease.

MINECOFEDER-BFU2015-67139-R, FEDER-PID2019-106230RB-I00, RETICS-FEDER RD16/0008/0016, IDIFEDER/2017/064.

CONTROL ID: 3543814

SUBMITTER (NAME ONLY): Kelly Mulfaul

TITLE: Local CFH synthesis protects choroidal endothelial cells from membrane attack complex formation.

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Mulfaul, N.K. Mullin, J.C. Giacalone, A. Shrestha, H.T. Daggett, E.M. Stone, B.A. Tucker, R.F. Mullins, Department of Ophthalmology and Visual Sciences, University of Iowa, Institute for Vision Research, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early in age-related macular degeneration (AMD), choroidal endothelial cells (CECs) in the choriocapillaris degenerate concurrently with the choroidal accumulation of the membrane attack complex (MAC), a multiprotein pore which causes cell lysis. MAC formation is controlled by negative regulators such as complement factor H (CFH). A polymorphism in CFH (Y402H) increases risk of AMD by 4-7-fold and results in reduced affinity for binding of this inhibitor to the choroidal extracellular matrix. We hypothesize that changes in local CFH protein levels lead to increased MAC formation on CECs early in AMD.

Methods: To assess the role of CEC-derived CFH, an immortalized CEC line generated from a healthy donor eye was transfected with a pool of 3 CFH siRNAs or a scrambled control for 48 h prior to treatment with 25% normal human serum (NHS) or 25% heat-inactivated NHS. Levels of CFH mRNA and protein were determined and MAC formation was quantified by immunofluorescence. In addition, we generated iPSC-derived CECs from a patient homozygous for the Y402H polymorphism and harboring a stop mutation in CFH. We divided differentiated cells into two populations one un-transduced and one transduced with a lentiviral vector to drive overexpression of wildtype CFH. iPSC derived CECs were treated with 25% NHS or 25% C5 depleted NHS. MAC formation was visualized by immunofluorescence and quantified by FACS analysis.

Results: siRNA delivery resulted in 60% knockdown of CFH mRNA ($p < 0.001$) and 50% knockdown of secreted CFH protein. In the absence of CEC-synthesized CFH, we observed an increase in the abundance of MAC immunofluorescence on CECs (2-fold change, $p < 0.001$). AMD iPSC-derived CECs produced negligible levels of secreted CFH protein by ELISA. Lentiviral overexpression resulted in an 18-fold increase of CFH protein, which was accompanied by decreased MAC immunofluorescence (Figure 1).

Conclusions: We have demonstrated that a reduction in local synthesis of CFH protein by CECs leads to increased MAC deposition in cells exposed to complement-intact serum and that overexpression of CFH locally can protect CECs from MAC. Thus, increased expression of local wildtype CFH protein to CECs may protect against choriocapillaris degeneration and AMD progression.

CONTROL ID: 3543816

SUBMITTER (NAME ONLY): Robert Kissling

TITLE: Comparative In Vitro Activity of Antibiotics Frequently Used in the Management of Staphylococcal Blepharitis

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.F. Kissling, Medical Affairs, Bausch + Lomb, Bridgewater, New Jersey, UNITED STATES|C.M. Sanfilippo, H.H. DeCory, Medical Affairs, Bausch + Lomb, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Both *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS; including *Staphylococcus epidermidis*) are implicated in staphylococcal blepharitis. Treatment options for this condition, often used in combination, include lid hygiene, topical anti-inflammatory agents, and topical and/or oral antibiotics. We examined the in vitro potency of antibacterial agents commonly prescribed in the management of blepharitis against staphylococcal isolates from ocular sources.

Methods: Minimum inhibitory concentrations (MICs; µg/mL) were determined for 8 antibiotics (6 drug classes) against methicillin-susceptible and -resistant isolates of *S. aureus* (MSSA and MRSA, respectively) and *S. epidermidis* (MSSE and MRSE, respectively), as well as other species of CoNS with undetermined methicillin resistance status (excluding *S. epidermidis*) previously cultured from ocular infections. In vitro susceptibility testing was conducted at a central laboratory per Clinical and Laboratory Standards Institute broth microdilution methodology.

Results: A total of 150 staphylococci (n=30 per grouping) were tested, and the MICs for 50% and 90% of isolates (MIC₅₀ and MIC₉₀) are presented in the table. MICs among all species were highest for macrolides and bacitracin. Besifloxacin exhibited lower MICs than ciprofloxacin. Against MRSA/MRSE specifically, the lowest MICs observed were for doxycycline and besifloxacin.

Conclusions: Antibacterial agents commonly used in the treatment of blepharitis had variable in vitro activity against ocular staphylococci. Doxycycline and besifloxacin generally demonstrated greater in vitro potency (lower MICs) against all tested isolates, including methicillin-resistant strains, compared to other agents. These data should be considered when treating staphylococcal blepharitis.

CONTROL ID: 3543818

SUBMITTER (NAME ONLY): María José Ruiz-Pastor

TITLE: Lipidomics analysis shows a prominent decrease of DHA in rd10 mouse retina.

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ruiz-Pastor, O. Kutsyr, N. Martínez-Gil, H. Albertos-Arranz, P. Lax, N. Cuenca, Universitat d'Alacant, Alacant, Comunitat Valenciana, SPAIN|V. Maneu, Optics, Pharmacology and Anatomy, Universitat d'Alacant, Alacant, Comunitat Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa is a hereditary retinopathy that courses with photoreceptor cell death. The rd10 mouse model is suitable for the study of the cellular and molecular alterations that occur during neurodegeneration. Fatty acids and, especially, the n-3 polyunsaturated docosahexaenoic acid (DHA), are abundant in photoreceptor cells and they impact in the phototransduction cascade. Thus, lipidomics analysis can contribute to the knowledge of the molecular pathways that are altered in retinitis pigmentosa.

Methods: C57BL/6J and rd10 mice were kept at a photoperiod of 12:12 (L:D) with a light intensity of 50 lux. At P25, animals were perfused to avoid contamination by blood fatty acids. Retinal fatty acids were assessed by lipid extraction with Folch method and resolution with GC/MS. Cryostat sections of the retina were obtained for morphological studies using immunohistochemistry.

Results: Photoreceptor cell rows were decreased in the retina of rd10 compared to C57BL/6J mice. Recoverin and cone arrestin immunolabeling revealed alterations in the morphology of rods and cones. Moreover, outer segments were shortened, and rhodopsin was mislocated to the cell body. The total amount of fatty acids decreased by 29.4 % in the retina of rd10 mice. Some specific short-chain as well as long-chain saturated fatty acids dropped significantly in the rd10 retina. We also found a dropped in the monounsaturated vaccenic acid and hypogeic acid. Polyunsaturated fatty acids dropped in the retina of the dystrophic mouse too. Concretely, we observed a significant decrease in the n-6 linoleic and arachidonic acid and in the n-3 DHA. But the fall of DHA was more pronounced than the decrease of n-6, and the balance between n-6 and n-3 was altered in the rd10 retina. Furthermore, we found a positive correlation between specific long-chain saturated fatty acids, hypogeic acid and DHA and the number of photoreceptor rows.

Conclusions: DHA fatty acid experiences the most pronounced decrease among fatty acids in the retina of retinitis pigmentosa mice model. The positive correlation between the number of photoreceptor cells and the content of fatty acid could be indicating the relevance of these fatty acids in cell survival. These results can apport new molecular targets and further therapeutic strategies. FEDER-PID2019-106230RB-I00. FPU16/04114, FPU18/02964. RETICS-FEDER RD16/0008/0016. IDIFEDER/2017/064, ACIF/2020/203.

CONTROL ID: 3543822

SUBMITTER (NAME ONLY): Victor Lozano Iturbe

TITLE: Molecular alterations in exosomes derived from corneal stromal cells of patients with keratoconus

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Lozano Iturbe, L. Quirós, C. Martin, I. Alcalde, H. Ordiales-Trabanco, J. Merayo-Llves, Fernandez-Vega University Institute, Oviedo, SPAIN|V. Lozano Iturbe, L. Quirós, H. Ordiales-Trabanco, Biología Funcional, Universidad de Oviedo, Oviedo, Asturias, SPAIN|L. Fernandez-Vega-Cueto, Fernandez-Vega Ophthalmological Institute, SPAIN|J. Merayo-Llves, Surgery, Universidad de Oviedo, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Keratoconus is one of the most abundant corneal degenerative disease in the developed world, affecting 1 in 2000 people and a major cause of corneal transplantation. It is characterized by a narrowing and bulging of the cornea, taking a conical shape, which makes it difficult for the patient to see. The cause of the disease is still unknown and it does not have molecular markers to make an early diagnosis. That is why, in our study, we analyzed the content of exosomes, small vesicles of around 100 nm, produced by corneal cells obtained from healthy patients and stromal cells isolated from the corneas of patients with keratoconus.

Methods: Corneal stromal cells were obtained from cadaver donors and from penetrating keratoplasty surgeries of patients suffering keratoconus. Exosomes were isolated from cell culture medium of the two different tissues. miRNAs were analysed by NGS (Next Generation Sequencing), and proteins by LC-MS (Liquid chromatography-mass spectrometry).

Results: A total of 466 proteins and 800 miRNAs were detected, showing 18 and 23 significant differences respectively. Among the proteins, two appeared exclusively in the exosomes produced by keratoconus stromal cells, VNN2 and VTN, while 6 proteins increased and another 10 decreased their levels significantly. Analysis of the miRNAs resulted in 2 of them not being expressed, 5 were under-expressed and 16 were overexpressed in keratoconus versus healthy tissue. These MiRNAs are related to the regulation of the synthesis of around 2,500 proteins involved in many processes such as apoptosis, cell migration, inflammation and others.

Conclusions: This study shows the existence of differences in the composition of the exosomes produced by corneal stromal cells of patients with keratoconus compared to healthy individuals. Furthermore, these differences may be related to disease progression due to the role played by differential molecules, mainly affecting inflammatory pathways or cell migration processes, such as VNN2, VTN, SERPINE1, hsa-miR-34a-3p or hsa-miR-101-3p. These differences may be important for the development of an early diagnosis of the disease and even a possible therapeutic use of the molecules that have been described in this study.

CONTROL ID: 3543823

SUBMITTER (NAME ONLY): Ellina Rakhimova

TITLE: Prevalence of Dry Eye and Meibomian Gland Dysfunction and their Associations in a Very Old Population. The Ural Very Old Study

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Rakhimova, M. Bikbov, G. Kazakbaeva, I. Ponomarev, Ufa Eye Research Institute, RUSSIAN FEDERATION | S. Panda-Jonas, J. Jonas, Department of Ophthalmology, Medical Faculty Mannheim, GERMANY |

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ABSTRACT BODY:

Purpose: Although dry eye disease (DED) and Meibomian gland dysfunction (MGD) are worldwide one of the most common ophthalmological complaints by patients, their prevalence in a very old population has remained unknown so far. We assessed DED and MGD prevalences in a very old population.

Methods: The population-based Ural Very Old Study was conducted in a rural and urban area in Bashkortostan/Russia from 2018 to 2020 and included 1526 (81.1%) participants out of 1882 eligible individuals aged 85+ years. A detailed systemic and ophthalmological examination with Schirmer test and slit-lamp based assessment of the Meibomian glands, and an interview with a questionnaire of >300 questions.

Results: The investigation included 1493 (97.8%) individuals with available information about dry eye. Mean age was 88.3±2.9 years (range: 85-103 years). Schirmer test was ≤5 mm in 160 (34.3%; 95% confidence interval (CI): 31.5, 37.1) eyes. The mean score of dry eye symptoms was 7.52±2.14 (95%CI:7.41,7.63). A MGD grade 1,2,3 and 4 in the worse eye was diagnosed in 367 (31.4%), 309 (26.4%), 89 (7.6%), and 39 (3.3%) eyes, respectively. The prevalence of DED diagnosis 1 (dry eye symptoms score ≥7, Schirmer test <5 mm), 2 (score ≥8, Schirmer test <5 mm), 3 (score ≥9, Schirmer test <5 mm), 4 (score ≥7, Schirmer test ≤5 mm, MGD grade 1 (telangiectasia at the lid margin)), and 5 (score ≥7, Schirmer test ≤5 mm, MGD grade 2 (plugged Meibomian gland orifices) or higher) were 18.2% (95%CI:16.0,20.5), 14.5% (95%CI:12.4,16.5), 8.1% (95%CI:6.5,9.7), 14.8% (95%CI:12.7,16.8), and 7.4% (95%CI:5.9,9.0), respectively. In multivariate analysis, a higher DED prevalence (dry eye symptoms score ≥8; Schirmer test <5mm) was associated with female sex (odds ratio (OR):2.36;95%CI:1.18,4.71;P=0.02), rural region of habitation (OR:2.72;95%CI:1.10,6.70;P=0.03), longer axial length (OR:1.30;95%CI:1.04,1.62;P=0.02), and higher hearing loss score (OR:1.03;95%CI:1.01,1.05;P=0.001) and lower self-reported salt consumption (OR:0.64;95%CI:0.54,0.75;P<0.001).

Conclusions: : In this population-based recruited study sample aged 85+years, DED prevalence (7.4% to 18.2% depending on the definition) and MGD prevalence (31.4%) was associated with female sex, rural region of habitation, longer axial length, higher hearing loss score and lower salt consumption.

CONTROL ID: 3543824

SUBMITTER (NAME ONLY): Sari Yordi

TITLE: Bacillary detachment (BD) in nAMD: Incidence, clinical features, and response to anti-VEGF therapy

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yordi, K. Sarici, L. Lunasco, T.K. Le, D. Sevgi, J. Reese, S. Srivastava, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R. Zahid, X. Meng, Novartis AG, Basel, Basel-Stadt, SWITZERLAND|

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ABSTRACT BODY:

Purpose: BD is a unique OCT signature identified in the outer retina. To our knowledge, it has not been described in nAMD. This preliminary analysis evaluates the incidence of BD in nAMD and response to anti-VEGF therapy.

Methods: A post hoc OCT image analysis was performed on the OSPREY phase II, prospective randomized clinical trial of anti-VEGF therapy in nAMD. BD was defined on OCT as a hyporeflective space above a hyperreflective linear structure continuous with the ellipsoid zone (EZ) band. Machine-learning-augmented feature extraction enabled characterization of parameters including retinal and sub-retinal pigment epithelium (RPE) compartment metrics, and retinal fluid volumes. This hypothesis-generating analysis was conducted without adjustment for multiple comparisons and was treatment agnostic.

Results: BD was identified in 6/81 eyes (7.4%) at Baseline. Baseline BCVA was similar between eyes with and without BD. At Baseline, BD eyes showed significantly higher mean central subfield thickness (CST, 610 μ m vs 479 μ m; $p < 0.05$), total retinal fluid volume (0.95mm³ vs 0.37mm³; $p < 0.01$), macular total retinal fluid index (TRFI, 7.8% vs 3.3%; $p < 0.05$), total EZ attenuation (51% vs 30%; $p < 0.05$), and sub-RPE compartment volume (1.80mm³ vs 0.78mm³; $p < 0.0001$) compared to eyes without BD.

Compared to Baseline, macular TRFI was 0.03% ($p = 0.034$) and CST was 331 μ m ($p = 0.006$) in the BD group at Week 4. At the end of the loading phase, 83% of eyes with BD had minimal to no fluid (i.e., volume < 0.001 mm³) vs 68% of eyes without BD. By Week 56, total macular EZ attenuation remained higher in eyes with BD compared to eyes without BD (40% vs 16%). At Week 56, eyes with BD did not demonstrate VA improvement (-1.7 letters; $p = 0.838$), while eyes without BD showed significant VA improvement (+6.9 letters; $p < 0.001$).

Conclusions: BD is identifiable in a proportion of nAMD eyes which have higher baseline fluid volumes and CST. Preliminary findings suggest that eyes with BD are responsive to anti-VEGF therapy (fluid resolution and CST reduction), yet persistent significant EZ attenuation may limit VA recovery. More data are needed to further validate the findings; however, this is important for understanding visual prognosis and enriching clinical trials.

CONTROL ID: 3543825

SUBMITTER (NAME ONLY): Stijn Van de Sompele

TITLE: Whole genome sequencing and UMI-4C provide novel insights into the genetic architecture and mechanisms underlying North Carolina macular dystrophy, a cis-regulatory disease

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: North Carolina macular dystrophy (NCMD) is a rare autosomal dominant disease, characterized by loss of central vision. With the identification of noncoding single nucleotide variants (SNVs) and duplications overlapping with a DNase I hypersensitive site (DHS) near PRDM13 or IRX1 as underlying genetic cause, NCMD is hypothesized to be a cis-regulatory disease. Here we investigate the genetic architecture of and mechanisms underlying NCMD, to further solve its missing heritability, and to provide mechanistic insight into its molecular pathogenesis.

Methods: Twenty-five unrelated NCMD families underwent targeted testing of PRDM13 and IRX1 regions followed by whole genome sequencing (WGS) in a selection of unsolved cases (n=11). Chromosome conformation capture, in particular UMI-4C sequencing, was applied on retinas from human donor eyes to fine-map interactions of cis-regulatory elements with the PRDM13 and IRX1 promoter. This data, together with other human retinal (epigen)omics data, were integrated in a UCSC browser session to advance the interpretation of the WGS data. Luciferase assays in ARPE-19 cells were performed to evaluate the functional effect of 6 previously reported (V1-V3, V10-V12) and 2 novel candidate NCMD-associated SNVs.

Results: A known noncoding SNV upstream of PRDM13 (V1) was found in a first family, while a novel SNV at the same position was identified in a second family. WGS revealed a novel tandem duplication, encompassing the known DHS upstream of PRDM13, in a third family. An additional novel noncoding SNV upstream of PRDM13 was found in a fourth family. Interestingly, UMI-4C showed an interaction of this region with the PRDM13 promoter. This region is active at a specific developmental stage (D103) that is compatible with the timepoint when retinal progenitor cells of the central retina exit mitosis. Using luciferase assays we demonstrated that the noncoding SNVs, located in two mutational hotspots, displayed up- and downregulation of expression, respectively.

Conclusions: Overall, the genetic architecture of NCMD was expanded with novel noncoding variants with a likely effect on PRDM13 regulation. The retinal interaction profiles of PRDM13 and IRX1 advance the interpretation of novel noncoding variants identified using WGS and provide insight into the cis-regulatory mechanisms underlying NCMD.

CONTROL ID: 3543827

SUBMITTER (NAME ONLY): Sampson Abu

TITLE: Assessing glaucoma progression with post-processed visual field data

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Abu, L. Racette, Department of Ophthalmology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S. Poleon, School of Optometry, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously showed that assessing glaucoma progression with visual field (VF) data post-processed with the dynamic structure-function (DSF) model resulted in a higher positive rate compared to the original (observed) data (Abu and Racette, IOVS 2020;61: ARVO E-Abstract 1991). The aims of this study were to validate this finding in an independent dataset and to assess the false positive rate of this approach.

Methods: We used VF data from 139 patients with open-angle glaucoma (203 eyes) with at least 15 visits selected from the Rotterdam Eye Study. The DSF and ordinary least square linear regression (OLSLR) models were applied to the observed mean deviation (MD) values to derive two post-processed datasets: DSF-predicted and OLSLR-predicted. Specifically, MD values from visits 1–3 were used to predict MD at visit 4, then MD values from visits 1–4 were used to predict MD at visit 5. This procedure was repeated until MD for visit 9 was predicted. Linear regression was then used to assess progression within the observed, DSF-predicted and OLSLR-predicted datasets. Positive rate was determined for each dataset at a specificity of 95%. To examine the impact of VF post-processing on false positive rate, we performed 1000 permutations of the MD series in each dataset and reassessed progression. The permutations disrupted the temporal order of the MD series; therefore, significant negative slopes were deemed to be false positives. Mean false positive rates were computed for the observed, DSF- and OLSLR-predicted datasets.

Results: The positive rate obtained with DSF-predicted data was 2.9% higher than OLSLR-predicted data and 12.8% higher than observed data at the 9th visit (Fig 1). DSF-predicted data flagged 72.9% and 59.7% of the eyes identified as progressing with observed data at the 12th visit and 15th visit, respectively. The false positive rates obtained for each of the datasets were similar to the proportion of eyes expected to be identified as progressing by chance (Fig 2).

Conclusions: Our results confirm that post-processing visual field data using the DSF model yields a higher positive rate without compromising specificity. The higher sensitivity of this approach may lead to earlier detection of progression.

CONTROL ID: 3543834

SUBMITTER (NAME ONLY): Miriam Stolwijk

TITLE: Characteristics and healthcare utilization among patients of low vision services: a retrospective population-based descriptive study with healthcare claims

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.L. Stolwijk, R.M. Van Nispen, G. van Rens, Department of Ophthalmology and Amsterdam Public Health research institute, Amsterdam UMC Locatie VUmc, Amsterdam, North-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Despite the individual and societal benefits of Low Vision Services (LVS), a discrepancy in the need and uptake of LVS has been reported internationally. Little is known about the characteristics and healthcare utilization of adult visually impaired people who receive LVS. This study aims to identify these parameters to explore LVS user profiles.

Methods: A retrospective cohort study based on a Dutch national health insurance claims database. Claims data from 2015 till 2018 of all visually impaired adults (aged 18 years or older) who received LVS at Dutch multidisciplinary organizations were examined. Descriptive statistics were used to assess socio-demographic characteristics (age, sex, socio-economic status, region), clinical characteristics (ophthalmic diagnosis, comorbidity) and healthcare utilization (ophthalmic and other medical care utilized in hospitals, general practitioner care, mental healthcare, low vision aids). Separate descriptive analyses were performed for different diagnosis groups within LVS patients.

Results: Between 2015-2018, 49,726 unique patients received LVS. The amount of unique patients that utilized LVS decreased with 16% between 2015 and 2018. The majority was aged 60y or older (62%, mean 65y), were female (54%), had a middle (38%) or low (38%) socio-economic status and lived in urban areas (51%). Most common ophthalmic conditions were macular degeneration (AMD, 22%), cataract (21%), subretinal neovascularization (15%) and primary glaucoma (11%). Half of the patients were treated for only one ophthalmic condition. Of all patients, 86% utilized general practitioner care, 69% ophthalmic care, 54% low vision aids, 41% cardiovascular care, 22% audiological care and 12% mental healthcare at least once. Of LVS patients who utilized specialized mental healthcare, most people were treated for depression 19% and/or anxiety 12%.

Conclusions: Our study shows that patients of LVS are mostly female elderly with retinal disease and (comorbid) cataract. The decrease in LVS uptake might be explained by increased deductible health insurance and new innovative treatments for ophthalmic conditions that can cause low vision. Future research needs to further examine differences in patterns between LVS users and non-users.

CONTROL ID: 3543835

SUBMITTER (NAME ONLY): Mirataollah Salabati

TITLE: Outcomes of Eyes with Retinal Vein Occlusion that are Lost to Follow-up after Anti-Vascular Endothelial Growth Factor Therapy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Salabati, R. Mahmoudzadeh, S.N. Patel, R.R. Soares, J.W. HINKLE, A. Obeid, J. Hsu, Mid Atlantic Retina, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J. Wong, Rowan University School of Osteopathic Medicine, Stratford, New Jersey, UNITED STATES|D. Patel, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect of loss to follow up (LTFU) on outcomes in eyes with retinal vein occlusion (RVO) treated with anti-vascular endothelial growth factor (VEGF) injections

Methods: In this retrospective single center case series, patients with RVO receiving intravitreal injections who were LTFU >6 months were eligible for inclusion. Visual acuity (VA) and optical coherence tomography features were collected from the visit before LTFU, the return visit, 3 months after return, 6 months after return, 12 months after return and the final follow-up visit.

Results: Ninety-one eyes of 84 patients with a mean age (\pm standard deviation) of 74.2 (\pm 11.2) years were included. Forty-nine (58.4%) of the patients were female. Fifty (54.9%) patients had branch RVO and 41 (45.1%) had central RVO. Mean LTFU duration was 278.2 (\pm 108.8) days and patients were followed for mean 739.8 (\pm 366.7) days after return. Patients had received a mean of 8.5 (\pm 5.7) injections before being LTFU and received a mean of 8.3 (\pm 7.6) injections after return. Mean logMAR VA at the visit before LTFU was 0.72 (\pm 0.67) [Snellen 20/104] which significantly worsened at the return visit [1.05 (\pm 0.79), Snellen 20/224, $p < 0.001$], 3 months after return [0.92 (\pm 0.70), Snellen 20/166, $p < 0.001$], 6 months after return [0.97 (\pm 0.80), Snellen 20/186, $p < 0.001$], 12 months after return [0.94 (\pm 0.78), Snellen 20/174, $p < 0.001$] and the final follow-up visit [1.02 (\pm 0.85), Snellen 20/209, $p < 0.001$] (Figure1). The mean central foveal thickness (CFT) increased when comparing the visit before LTFU [251 (\pm 129) μ m] to the return visit [404 (\pm 241) μ m, $p < 0.001$]. No significant difference in CFT was noted by 3 months [256 (\pm 139) μ m, $p = 0.68$], 6 months [241 (\pm 122) μ m, $p = 0.59$], or 12 months after return [250 (\pm 134) μ m, $p = 0.98$]. The CFT was significantly thinner at the final visit [214 (\pm 114) μ m, $p = 0.017$] (Figure2). Three (4.2%) eyes (2 CVRO, 1 BRVO) presented with neovascular glaucoma (NVG) and 4 (4.5%) eyes (3 CRVO, 1 BRVO) with new onset vitreous hemorrhage (VH) at the return visit.

Conclusions: RVO patients receiving anti-VEGF treatment who were LTFU for a prolonged duration experienced a significant decline in VA that did not return to the levels seen before LTFU despite restarting therapy and subsequent improvement in CFT. LTFU might also increase the risk of unfavorable outcomes like NVG and VH in RVO patients.

CONTROL ID: 3543837

SUBMITTER (NAME ONLY): Thasarat Vajaranant

TITLE: Lifestyles and Visual Disability among Hispanic/Latino Individuals of Diverse Backgrounds and Ages in the United States: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL).

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.S. Vajaranant, H. Pauls, L. Ulanski, C.E. Joslin, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|D. Wu, M. Daviglus, Institute for Minority Health Research, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|B.L. Lam, C. Mendoza, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|D. Lee, L. McClure, D.D. Zheng, Department of Public Health Sciences, University of Miami School of Medicine, Miami, Florida, UNITED STATES|N. Schneiderman, Department of Psychology, Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual disability relative to lifestyle has not been assessed across Hispanic/Latinos of diverse backgrounds. We examined the relationship between physical activity (PA) and diet score (DS) across Hispanic/Latinos, and their relationship to visual disability.

Methods: Design: Multicenter, prospective, population-based Hispanic Community Health Study/Study of Latinos (HCHS/SOL) include 9663 participants age ≥ 40 years(y) completing Visit #2 (2014-2017). Age-adjusted, sex-specific prevalence of visual disability was calculated weighting for study design. Analyses included those with Cuban (n=1455), Dominican (n=804), Mexican (n=3746), Puerto Rican (n=1485), Central American (n=965), South American (n=669) and Other (n=199) backgrounds. High PA, ascertained by a modified Global Physical Activity Questionnaire, was defined as the top 40%. Dietary intake was ascertained by two 24-hour dietary recalls administered 6 weeks apart. High DS, calculated by sex-specific quintile of daily intake of saturated fatty acids, potassium, calcium, and fiber, was defined as the top 40%. Main outcome measures: Visual disability, defined as "being blind or having serious difficulty seeing even when wearing glasses," based on the US Census Bureau's American Community Survey.

Results: Results: Analysis included 9324 participants with complete data (35.9% men), with a mean age of 55.4y men and 56.5y women. Overall age-adjusted visual disability prevalence was 10.6% (95%CI; (9.2, 12.1) men, and 13.5% (12.0, 14.9) women. Subjects with high PA had a lower prevalence of visual disability: men 9.7% (7.4, 12.0) and women 12.9% (10.7, 15.1). Cubans reported the lowest percent of high PA (Fig 1, $p < 0.001$). Participants with high DS reported a lower prevalence of visual disability both in men 8.2% (6.5, 9.9) and women 8.7% (7.2, 10.1). Puerto Ricans had the lowest percent of high DS (Fig 1, $p < 0.001$).

Conclusions: Conclusions: Results identify significant visual disability in US Hispanic/Latinos, with a higher prevalence in those with lower PA and poorer diet. The significant variability across diverse groups supports objectives of SOL Ojos, an ancillary HCHS/SOL study aiming to assess associations of lifestyle and objectively measured chronic eye disease in a diverse group of Hispanics/Latinos.

CONTROL ID: 3543839

SUBMITTER (NAME ONLY): Hugo Barba

TITLE: Effects of High-Fat Diet and Gut-Dysbiosis on Gut-Retina Axis Pathways

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Emerging data show that the gut-microbiome plays a role in retinal physiology and several retinal diseases such as: age-related macular degeneration (AMD), retinopathy of prematurity (ROP) and diabetic retinopathy (DR). Our team has described the retinal pathways of the gut-retina axis in retinal homeostasis under regular diet conditions. The gut microbiome is significantly affected by diet and, in particular, a diet rich in fats or high-fat diet (HFD). The HFD modifies the composition and diversity of the gut microbiota; a condition referred to as gut-dysbiosis. The retinal pathways of the gut-retina axis in HFD-induced gut dysbiosis conditions remain unknown. The purpose of this study is to delineate how HFD-induced gut dysbiosis modulates the gut-retina axis pathways by comparing the transcriptome of mice with HFD-induced gut dysbiosis with germ-free (GF) mice that have no microbiome fed on regular diet (ND).

Methods: We compared the retinal gene expression and biologic pathways of C57Bl/6J mice fed on 23% HFD for 8 weeks and GF mice age and gender matched fed on ND (4 per group). RNA-sequencing (RNA-seq) was performed on whole retinas using a base paired-end method on the NovaSEQ600 platform. We then identified Differentially Expressed Genes (DEGs) (P -value <0.01) and performed a functional enrichment network analysis using Toppgene to elucidate the biologic pathways affected.

Results: We identified 538 DEGs with a p -value <0.01 . Some of the DEGs identified were the regulatory associated Protein of MTOR Complex 1 (Rptor), peroxisome Proliferator-Activated Receptor Gamma Coactivator 1 Alpha (PPARGC1A) and activating Transcription Factor 2 (ATF2); all of which have been implicated in retinal diseases like AMD and DR. The enrichment network analysis showed numerous signaling and metabolic pathways affected including the phototransduction cascade, the Related Orphan Receptor A (RORA) and the mitochondrial biogenesis activation pathways.

Conclusions: Our data shows that several pathways of the gut-retina axis are affected in HFD-induced gut dysbiosis conditions. Further studies delineating the effects and interactions of diet and gut microbiome on retinal physiology are needed to reveal the relationship to retinal disease pathogenesis.

CONTROL ID: 3543840

SUBMITTER (NAME ONLY): Sirisha Tadepalli

TITLE: Inter and intra-observer variabilities in the measurement of aqueous flare with a custom-made ocular spot fluorometer

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In our previous study, the intensity of light scatter (ILS) from the anterior chamber was measured in cataract subjects as a measure of aqueous flare using a custom-made ocular fluorometer (TVST; 2018). While the data was sensitive, we observed a poor correlation between ILS and SUN grades for patients with mild to moderate inflammation (i.e., SUN grades 0 and 1+). To further explore the variability, we are continuing to establish the repeatability and reproducibility of ILS in uveitis patients.

Methods: Uveitis (n = 111; with SUN scores of 0 to 2+) and healthy subjects (n = 93) were included in the study. One clinician performed SUN grading. For repeatability, ILS was measured twice by the same observer. For reproducibility, ILS was recorded by two observers. We calculated the intra-observer variability (expressed as the repeatability coefficient (Rc)) and intra-class correlation coefficient (ICC) to assess intra- and inter-observer variability. The latter was further analyzed by Bland-Altman (BA) plots.

Results: The intra-observer measurements in healthy subjects revealed no statistical difference in the mean ILS (0.1480 ± 0.0700 mV; n = 93; p > 0.98). The corresponding within-subject standard deviation (Sw) is 0.0272 mV, which corresponds to a repeatability coefficient (Rc) of 0.0754 mV ($= 2.77 * Sw$). Uveitis patients with SUN scores of 2+ showed much higher ILS (0.3740 ± 0.1090 mV; n = 5) with Sw = 0.0418 mV, and Rc of 0.1159 mV. The inter-observer analysis with uveitis patients (n = 72 for SUN 0 and n = 8 for SUN 1) revealed an ICC of 0.63 and 0.95 for measurements with SUN grades 0 and 1, respectively. In healthy subjects (SUN grade 0), ICC was 0.73 (n = 76). Corresponding Bland-Altman plot analysis in uveitis subjects indicated 0.0044 mV and 0.0046 mV as the difference between the mean ILS between observers for SUN grades 0 and 1, respectively.

Conclusions: ILS in control and uveitis are ~ 6 and ~ 9 times larger than the maximum of Sw, respectively. The lowest inter-observer variability in ILS measurement is ICC > 0.6 in both healthy and uveitis patients. Thus, ILS measurements using the fluorometer are highly reliable and can be employed to provide a higher granularity in recording aqueous flare. Thus, we attribute the apparent variability in ILS of uveitis patients with 0 and 1+ to SUN scores' subjective grading.

CONTROL ID: 3543841

SUBMITTER (NAME ONLY): Gyulli Kazakbaeva

TITLE: Central Corneal Thickness and its Associations in a Russian Population. The Ural Eye and Medical Study

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Kazakbaeva, M. Bikbov, T. Gilmanshin, R.M. Zainullin, E. Rakhimova, I. Rusakova, Ufa Eye Research Institute, Ufa, RUSSIAN FEDERATION | S. Panda-Jonas, J. Jonas, Department of ophthalmology, Ruprecht-Karls-University of Heidelberg, Mannheim, GERMANY |

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ABSTRACT BODY:

Purpose: To assess central corneal thickness (CCT) and its associations in a Russian population.

Methods: The Ural Eye and Medical Study included 5899 (80.5%) out of 7328 eligible individuals (mean age:59.0±10.7 years;range:40-94 years). As part of an ophthalmological and general examination, CCT was measured by Pentacam HR (Oculus, Germany).

Results: The study included 5792 (98.2%) participants (mean age:58.8±10.6 years;range:40-94 years) with available bilateral CCT measurements. Mean CCT was 541.7±33.7µm (median:541µm;range:200-779µm). In multivariable analysis, thicker CCT was associated (regression coefficient r:0.43) with younger age (standardized regression coefficient beta:-0.09;non-standardized regression coefficient B:-0.29;95% confidence interval (CI):-0.39,-0.20;P<0.001), male sex (beta:0.05;B:3.10;95%CI:1.18,5.03;P=0.002), urban region of habitation (beta:0.10;B:6.83;95%CI:4.61,9.05;P<0.001), Russian ethnicity (beta:0.04;B:3.48;95%CI:1.04,5.91;P=0.005), higher level of education (beta:0.04;B:0.97;95%CI:0.29,1.66;P=0.006), higher serum bilirubin concentration (beta:0.05;B:0.15;95%CI:0.07,0.23;P<0.001), lower corneal refractive power (beta:-0.09;B:11.92;95%CI:-2.50,-1.35;P<0.001), smaller anterior chamber angle (beta:-0.07;B:-0.38;95%CI:-0.52,-0.24;P<0.001), higher IOP readings (beta:0.38;B:3.47;95%CI:3.21,3.73;P<0.001), and higher rise in IOP readings by medical mydriasis (beta:0.07;B:0.88;95%CI:0.54,1.22;P<0.001). In that model, CCT was not associated with body height (P=0.14), previous cataract surgery (P=0.10), axial length (P=0.18) or prevalence of glaucoma (P=0.11). The mean inter-eye difference in CCT was 8.52±13.9 µm (median:6.0;95CI:8.16,8.88). A higher inter-eye CCT difference was associated with older age (beta:0.08;B:0.11;95%CI:0.07,0.15;P=0.01), lower level of education (beta:-0.04;B:-0.34;95%CI:-0.60,-0.08;P<0.001) and status after cataract surgery (beta:0.04;B:2.92;95%CI:1.02,4.83;P=0.003).

Conclusions: In this typical, ethnically mixed,population from Russia with an age of 40+ years, mean CCT (541.7±33.7µm) was associated with parameters such as younger age, male sex, Russian ethnicity, and higher educational level. These associations may be taken into account when the dependence of IOP readings on CCT are considered. Glaucoma prevalence was unrelated to CCT.

CONTROL ID: 3543843

SUBMITTER (NAME ONLY): Clair Enthoven

TITLE: Gender predisposition to myopia shifts to girls in the young generation.

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Enthoven, A. Haarman, J. Swierkowska, W. Tideman, J. Polling, V.J. Verhoeven, C.C. Klaver, Ophthalmology & Epidemiology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Swierkowska, Instytut Genetyki Czlowieka Polskiej Akademii Nauk, Poznan, POLAND|J. Polling, Orthoptics & Optometry, Hogeschool Utrecht, Utrecht, Utrecht, NETHERLANDS|V.J. Verhoeven, Clinical Genetics, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|C.C. Klaver, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Previous studies have suggested that female gender is a risk factor for myopia. The underlying mechanism is not well understood, and gender-specific factors such as age of growth spurt have been proposed. The aim of this study was to explore gender differences in myopia development in two prospective population-based cohorts from different generations, and to find possible explanations.

Methods: Analyses were performed in the birth cohort study Generation R (n=7229) and in the elderly Rotterdam Study I-III (45+ yrs; n=8674). Cycloplegic refraction was measured in the children at 6, 9, and 13 years, automated refraction was measured in the adults, and axial length and height was measured in both. Myopia was defined as spherical equivalent $\leq -0.5D$ in at least one eye. Lifestyle factors including near work and outdoor exposure were assessed in the children and level of education in the adults, both by questionnaire. The association between gender and myopia was tested using Cox proportional hazards and logistic regression models adjusted for age; change in height, lifestyle factors and education were investigated as possible mediators.

Results: Myopia prevalence increased from 2.5%, to 11.5% and 22.5% at age 6, 9, and 13 years in the children, respectively; the prevalence was 30.6% in the adults. Female gender was associated with myopia in the children (HR=1.14 95% CI=1.02-1.27), but was inversely associated in the adults (OR=0.88 95%CI=0.80-0.96). Mediators of the association in children were outdoor exposure, growth in height, sport participation, reading time, and number of books read per month; these mediators together attenuated the effect of gender with 34.9% and reduced risk to HR=1.09 (95%CI=0.97-1.23). Education was the most important mediator of the association in adults, attenuating the effect with 89.7% to OR=0.98 (95%CI=0.90-1.09).

Conclusions: In our study, myopia was more common in girls in the young generation, but more common in men in the older generation. This paradigm shift and our mediation analysis provide compelling evidence that lifestyle factors and education are strong drivers of myopia. In the generations to come, particularly girls should be guided to adhere to protective behaviour.

CONTROL ID: 3543847

SUBMITTER (NAME ONLY): Jonathan Soucy

TITLE: SDF1 directs donor retinal ganglion cell migration into the retina following allotransplantation in mice

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Soucy, J. Oswald, P.Y. Baranov, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Soucy, J. Oswald, P.Y. Baranov, Harvard Medical School Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma and other optic neuropathies lead to permanent damage of the optic nerve and loss of retinal ganglion cells (RGCs). Cell transplantation has been proposed to restore the retinal neurocircuitry; however, current state-of-the-art studies show that most donor RGCs have limited capacity to integrate into the ganglion cell layer (GCL) following intravitreal delivery. Since a fully developed mammalian retina does not have the natural capacity to regenerate RGCs, we do not know the exact mechanisms and cues employed by stem cell-derived donor RGCs to migrate across the retina (XY plane) and into the GCL (Z-axis). Here, we investigate the migration of donor RGCs into and across the retina in the presence of a stromal cell-derived factor-1 (SDF1) gradient.

Methods: RGCs were differentiated from Thy1-GFP mouse iPSC (C57Bl/6 background) in 3D retinal organoid cultures. On day 21, RGCs were isolated from organoids by magnetic microbeads against CD90.2. The ability of stem cell-derived RGCs to migrate in vitro was tested using a microfluidic device. For transplantation RGCs were formulated at 5×10^6 cells/mL with slow-release GDNF & BDNF particles. 2 μ L of Thy1-GFP+ RGC suspension was injected intravitreally (IVT), and 1 μ L 10ng/ μ L SDF1 was injected subretinally (SR) to establish a chemokine gradient across the retina to direct RGC migration. Two weeks after transplantation, whole mounted retinas were stained for GFP and RBPMS to assess donor RGC integration and distribution with respect to host RBPMS+ cells (GCL). RGC distribution across the retina was calculated as the percentage of 344 x 344 μ m tiles within the whole mount that contained more than one integrated RGC.

Results: The expression of CXCR4, the receptor for SDF1, on donor cells was confirmed by qPCR and flow cytometry. Thy1-GFP+ donor RGCs integrate into GCL of host retinas with and without SR SDF1 and have the same morphology in both groups. The artificial SDF1 gradient increased the retinal coverage by donor cells from $54 \pm 8\%$ to $76 \pm 4\%$ (Figure 1), proposing a benefit of CXCR4-SDF1 interactions for enhanced donor RGC migration.

Conclusions: Establishing an SDF1 gradient across the host retina is an effective strategy to improve the distribution and structural integration of donor RGCs.

CONTROL ID: 3543848

SUBMITTER (NAME ONLY): Jesus Merayo-Lloves

TITLE: Role in adhesion and changes in cell surface proteoglycan expression in Candida keratitis

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Merayo-Lloves, L. Quirós, C. Martin, I. Alcalde, V. Lozano Iturbe, H. Ordiales-Trabanco, Instituto Universitario Fernández-Vega, Oviedo, Asturias, SPAIN|J. Merayo-Lloves, Surgery Department, Universidad de Oviedo, Oviedo, Asturias, SPAIN|L. Quirós, V. Lozano Iturbe, H. Ordiales-Trabanco, Biología Funcional, Universidad de Oviedo, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Corneal infections are caused by a variety of microorganisms, including bacteria, viruses, amoebae and fungi. Infectious keratitis is the 4th leading cause of blindness in the world, being represented by up to 60% by fungal keratitis in tropical countries and rural areas. In an infective process, a series of steps are taken, the first of which is the adhesion of the microorganism to the epithelium. Numerous studies have shown an intimate relationship of cell surface proteoglycans (PGs) and their glycosaminoglycans chains (GAGs) with the adhesion process in bacterial infections. The objective of this work is to determine the implication of these molecules in the adhesion of fungi to the corneal epithelium and to study the possible influence of this adhesion process in the gene expression of cell surface PGs.

Methods: The involvement of GAGs in the adherence of *Candida albicans* to the corneal epithelium was studied by determining the influence of its elimination with biosynthetic inhibitors or through the use of specific bacterial lyases on the adherence of the fungus. The alterations in the transcription levels of the cell surface PGs were analyzed by RT-PCR.

Results: The adherence of *C. albicans* in the form of yeast to corneal epithelial cells was limited by the elimination of cellular GAGs, showing their involvement in the process. On the contrary, when the yeast produces hyphae there was an increase in adherence. The adherence of the fungus induced significant alterations in the expression levels of the cell surface PGs, which affected both syndecans and glypicans. Within syndecans, SDC3 under-expressed with both yeast and *C. albicans* hyphae, while SDC4 only did so when interacting with yeast. In the case of glypicans, GPC6 showed an overexpression induced by both forms of *C. albicans*, while GPC1 only under-expressed induced by yeast. Furthermore, GPC3 was not expressed in corneal cells, but it did after contact with both forms of *C. albicans*.

Conclusions: Corneal surface GAGs are involved in the adherence of *C. albicans* in the yeast form, but not in the filamented cellular forms. The interaction of the microorganism with the epithelial cells induces alterations in the transcription levels of the cell surface PGs that are dependent on the cell form presented by the fungus.

CONTROL ID: 3543849

SUBMITTER (NAME ONLY): Claire Malley

TITLE: Progression of Age-Related Macular Degeneration measured by Ultrawidefield Imaging in the Age-Related Eye Disease Study 2 10 Year Follow-On

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.E. Malley, E. Agron, T.D. Keenan, W.T. Wong, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|T.E. Clemons, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|A. Domalpally, Department of Ophthalmology, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|T. Peto, W.T. Wong, Queen's University Belfast, Belfast, IRELAND|

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ABSTRACT BODY:

Purpose: To describe the age-related macular degeneration (AMD) features on ultrawidefield (UWF) retinal imaging in the participants of the Age-Related Eye Disease Study 2 (AREDS2) 10 Year Follow-on Study.

Methods: OPTOS (Dunfermline, Scotland) color and fundus autofluorescence retinal (UWF) images were obtained at year 10 study visit in AREDS2 participants with intermediate or late AMD in one eye (N=230). Reading centers (U. of Wisconsin and Queen's University, Belfast) graded the images for presence and extent of: macula change, neovascular AMD, geographic atrophy (GA), drusen, reticular pseudodrusen (RPD), RPE pigmentary changes (hyper and hypo), peripheral pathology including cobblestone and senile reticular pigmentary changes. The images were divided into 3 zones: posterior pole (zone 1), midperiphery (zone 2), and far periphery (zone 3) and further divided into four image quadrants. RPD was diagnosed based upon the fundus autofluorescence imaging. AMD features were summarized by each of the zones and the 4 quadrants.

Results: Of the 230 AREDS2 participants, mean age was 69 ± 1 year, 59% female, 90% have late AMD (Figure). Only 13% presented neovascular AMD while most had GA and a minority presented inactive neovascular AMD. Almost half of the GA lesions were unifocal, and about 89% of the macula had GA. More than 80% had super large drusen ($\geq 250 \mu\text{m}$) and 25% had RPD. 71% had peripheral retinal abnormalities. Zone 2 had marked drusen, pigmentary changes, floaters, and GA. All three zones had demonstrated extensive AMD lesions throughout the macula and in the periphery.

Conclusions: The results of the 10-year follow-on of AREDS2 participants demonstrate the extensive and relentless progression of the AMD lesions. The disease is not confined to the macula but extensive throughout the retinal and its periphery. Future evaluation of AMD progression will need to take into account lesions that occur in the retinal periphery as well as the macula. It will also be important to correlate structural changes with functional deficits. This study also demonstrates that AMD is a pan-retinal disease.

CONTROL ID: 3543850

SUBMITTER (NAME ONLY): C Ethier

TITLE: Deep learning (DL)-based morphometric analysis of retinal ganglion cell (RGC) axons in a rat model of glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.R. Ethier, G. Sánchez-Rodríguez, D. Brown, A.M. Toporek, M.D. Ritch, A. Feola, A.T. Read, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|V. Goyal, Electrical and Computer Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|B. Hannon, Mechanical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|A. Feola, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|C.R. Ethier, Biomedical Engineering, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We developed a DL algorithm to identify axoplasm ('Ax') and myelin sheaths of normal-appearing RGC axons from light micrographs of optic nerve (ON) cross-sections [Goyal+, submitted ARVO 2021]. Here we: (i) compare RGC Ax area ('Area') and eccentricity ('Ecc') between manually- and DL-segmented images; and (ii) compare axon density (axons/ μm^2) and axon size distributions between hypertensive and control eyes.

Methods: Ocular hypertension was induced unilaterally in 14 Brown-Norway rats (3-13 months; 12 male:2 female) by episcleral hypertonic saline or microbead injection. Contralateral eyes were controls. (i) To compare manual and DL segmentations, we extracted the mean and median Ax Area and Ecc from all images, and computed the mean absolute percentage error (MAPE) between them for all ON. (ii) To compare control vs. hypertensive eyes, we restricted analysis to pairs where the hypertensive eye had an IOP burden > 100 mmHg day (n=7 pairs). Axons were counted in ON sub-images, divided by sub-image area to obtain axon density, and compared hypertensive vs. control. Axons were grouped by Area into 9 bins, and for each ON and each bin the ratio (hypertensive axon density)/(control axon density) was computed and normalized following Quigley+ [PMID: 3583630].

Results: (i) Mean and median Area agreed well between manual and DL segmentations (MAPE < 4.6%, Fig 1), as did Ecc (MAPE < 1.41%). (ii) Hypertensive eyes showed lower axon density (0.19 ± 0.11 vs. 0.36 ± 0.08 axons/ μm^2), an approximate 40% decrease ($p = 0.038$, 2-sided paired t-test). We did not observe a preferential loss of large axons with hypertension (Fig 2).

Conclusions: Morphometric parameters of RGC axons extracted by a DL algorithm agreed well with manual segmentations. The algorithm detected decreased axon density in hypertensive eyes, but no preferential loss of large axons (perhaps due to the rat model used). This algorithm provides a fast and non-subjective method to quantify axonal loss in animal models of glaucoma; future consideration of axonal shape changes may add sensitivity to detection of glaucomatous damage.

CONTROL ID: 3543852

SUBMITTER (NAME ONLY): Dhiksha Balaji

TITLE: Fixation and Saccadic Abnormalities in Amblyopic Patients With and Without Nystagmus

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Balaji, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|J.

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ABSTRACT BODY:

Purpose: Fixation eye movements are physiologic eye movements elicited during attempted fixation to prevent visual fading by thwarting neural adaptation. Saccades are rapid eye movements between fixation that bring the object of interest onto the high-resolution fovea to achieve the best possible vision. Amblyopic patients have increased fixation instability due to nystagmus, along with reduced saccadic precision and prolonged latencies. The purpose of this study is to quantify and correlate fixation and saccadic abnormalities in amblyopia patients with and without nystagmus.

Methods: We recruited 22 controls and 23 amblyopic subjects. We recorded fixational eye movements (FEMs) using infra-red video-oculography and classified 12 subjects without nystagmus, 5 subjects with fusion maldevelopment nystagmus (FMN), and 6 subjects with nystagmus that do not meet the criteria of FMN. We measured visually-guided horizontal, vertical, and oblique saccades in all participants. Latency, precision, and disconjugacy (amplitude difference between viewing and non-viewing eye) were measured and correlated with FEM abnormalities.

Results: Saccadic latencies were prolonged in amblyopic patients during both amblyopic eye viewing [Controls: 159 ± 50 , None: 301 ± 186 , Nystagmus without FMN: 203 ± 184 , FMN: 194 ± 57 , $p < 0.0001$] and fellow eye viewing [Controls: 159 ± 50 , None: 262 ± 161 , Nystagmus without FMN: 173 ± 62 , FMN: 164 ± 72 , $p < 0.0001$] conditions. Amblyopic patients without nystagmus were better at initiating corrective saccades to minimize the saccadic inaccuracies. On the other hand, patients with nystagmus had greater frequency of staircase saccades, which were defined as abnormal multiple rapid saccades within 500 milliseconds, compared to other groups.

Conclusions: Fixation and saccadic eye movement abnormalities are seen in both the amblyopic and the fellow eye, suggesting that amblyopia is a binocular vision disorder. The fixation and saccadic abnormalities are closely interlinked. These abnormalities likely contribute to reading and daily visuo-motor task difficulties and should be assessed to identify and provide proper academic accommodations to young children with amblyopia.

CONTROL ID: 3543855

SUBMITTER (NAME ONLY): Diana Tavares

TITLE: Association between visual acuity loss and disease pathways in the initial stages of nonproliferative retinopathy in type 2 diabetes

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Tavares, I. Marques, M.H. Madeira, A. Santos, T. Santos, J. Figueira, C.F. Lobo, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|I. Marques, M.H. Madeira, J. Figueira, C.F. Lobo, J.G. Cunha-Vaz, Coimbra Institute for Clinical and Biomedical Research, Universidade de Coimbra Faculdade de Medicina, Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To examine the association of changes in best corrected visual acuity (BCVA) occurring in a 5-year prospective longitudinal study of eyes with mild diabetic nonproliferative retinopathy (NPDR), with the three main disease pathways: microvascular changes, neurodegeneration and edema.

Methods: 212 patients with type 2 diabetes (T2D) and mild NPDR (ETDRS grades 20 or 35) were followed in a 5-year longitudinal study. Ophthalmological examinations were performed at baseline and annually.

BCVA was measured using Snellen chart for the patients and then converted to logarithm of the minimum angle of resolution (logMAR) VA. ETDRS and severity progression was assessed in T2D individuals by grading of 7-fields CFP performed at the initial and last visits. Microaneurysm turnover (MAT) was evaluated using the RetMarkerDR. Optical coherence tomography (OCT) was performed to evaluate average thickness of the ganglion cell layer (GCL).

Results: Of the 212 individuals with type 2 diabetes (T2D) and mild NPDR, one eye per person, followed for 5 years with annual visits, 171 completed the study or developed an outcome. BCVA worsening occurred in 118 eyes (69%) during the 5-year follow-up. BCVA worsening is associated with GCL thinning in the central macular area, representing neurodegeneration (difference V6-V1, $p=0.038$), but did not show association with MAT (considering $MAT \geq 6$ vs $MAT < 6$), representing microvascular changes ($p=0.633$) or central retina thickness, representing edema ($p=0.634$).

For the ones that completed the study, BCVA was also associated with age ($p=0.002$) and sex ($p=0.055$). No association was found with ETDRS level worsening.

Conclusions: BCVA worsening in eyes with mild NPDR, during a 5-year follow-up, is associated with neurodegenerative changes identified by GCL thinning in the macula, but not with the presence and progression of edema and/or ischemia.

CONTROL ID: 3543856

SUBMITTER (NAME ONLY): Aditya Josyula

TITLE: In vitro markers predict in vivo efficacy of a nano-structured glaucoma shunt

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Josyula, Y. Ha, L. Ensign, Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|A. Josyula, A. Mozzer, S. Chung, J. Szeto, L. Ensign, K. Parikh, I.F. Pitha, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|K. Parikh, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|B. Smith, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cell-biomaterial interactions and aqueous soluble factors regulate the initiation and progression of fibrosis, which is a primary cause of glaucoma drainage implant (GDI) failure. We created smooth and nano-structured electrospun scaffolds to evaluate and compare the expression of fibrosis-related genes in fibroblasts in vitro. We then designed two nano-structured, partially degradable GDIs and evaluated their performance in rabbit eyes.

Methods: Fibroblasts were seeded on scaffolds made from electrospun polyethylene terephthalate (PET) nanofibers or smooth PET films. Transcription of fibrosis-related genes in unstimulated and activated fibroblasts was quantified by qPCR. Predictive fluid flow modeling was applied to develop nano-structured GDIs of different lengths, both with an inner diameter of 75 μm and a 25 μm degradable polyglycolide core (Pressure Control Shunt, PCS1 and PCS2). Intraocular pressure (IOP), GDI patency, bleb morphology, and capsule thickness were evaluated for 91 days in normotensive New Zealand White rabbits.

Results: Fibroblasts cultured on nanofibers showed reduced levels of gene expression related to activation (MYOCD and SMA), collagen synthesis (COL6A6), focal adhesion-associated genes (rho-kinase signaling, ITGA6, ITGB1) and increased expression of MMP-1 and ITGA2 compared to cells cultured on smooth surfaces. In vivo, a mean reduction in IOP from baseline of 4 (PCS1) and 2.8 mmHg (PCS2) at 28 days and 1.8 (PCS2) and 0.9 mmHg (PCS1) at 91 days was observed post-operatively. Histological analysis revealed a fibrotic capsule thickness of $350 \pm 149 \mu\text{m}$ in PCS1 and $55 \pm 23 \mu\text{m}$ in PCS2 ($p=0.041$), likely due to decreased aqueous flow rate through the longer PCS2.

Conclusions: Nanofibers significantly attenuate expression of markers associated with fibroblast activation and collagen production in vitro. Nano-structured shunts can be designed to safely and effectively reduce IOP for a period of at least 91 days in vivo while minimizing fibrotic encapsulation.

CONTROL ID: 3543862

SUBMITTER (NAME ONLY): Tunde Peto

TITLE: Diabetic retinopathy contributes to global vision loss

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Peto, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|S. Resnikoff, Brien Holden Vision Institute, Sydney, Australia, Melbourne, Victoria, AUSTRALIA|J.H. Kempen, D.S. Friedman, Massachusetts Eye and Ear Infirmary and Harvard University, Boston, Massachusetts, UNITED STATES|J.D. Steinmetz, Institute for Health Metrics and Evaluation, Seattle, Washington, UNITED STATES|P.S. Briant, T. Vos, Institute for Health Metrics and Evaluation, Seattle, Washington, UNITED STATES|T.Y. Wong, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|A.M. Bron, Ophthalmology, Service d'Ophtalmologie CHU, Dijon, FRANCE|J. Jonas, Ophthalmology, Department of Ophthalmology, Medical Faculty Mannheim, Heidelberg University, Mannheim, GERMANY|T. Braithwaite, Medical Eye Unit, St Thomas' Hospital, London, London, UNITED KINGDOM|H.R. Taylor, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|R.R. Bourne, Anglia Ruskin University, Chelmsford, Essex, UNITED KINGDOM|A. Fernandes, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: The WHO initiative, VISION 2020: The Right to Sight showed that understanding global burden of eye diseases aids planning for appropriate care delivery. Here we report extensively updated estimates of the burden of vision loss due to diabetic retinopathy (DR) from 2000 to 2020, and distribution by sex and region.

Methods: A systematic review and meta-analysis of population-based surveys of eye diseases from January 1980 to October 2018 were carried out by the Vision Loss Expert Group of the Global Burden of Disease Study (GBD) and collated into the Global Vision Database. We fitted hierarchical models to estimate prevalence (with 95% uncertainty intervals [UIs]) of moderate and severe vision impairment (MSVI; presenting visual acuity from <6/18 to 3/60) and blindness (<3/60 and/or less than 10° visual field around central fixation) caused by DR by age, region, and year for those aged 50 years and older.

Results: Worldwide in 2020, due to DR an estimated 861,000 (592,000-1235,000) people aged 50+ years were blind and 2.95 million (2.14-3.95M) had MSVI. Since 2000, age-standardised prevalence (ASP) of DR-blindness and MSVI increased by 7.0% and 1.6% respectively. Reflecting growth in number of people aged 50+ and diabetes prevalence, overall DR-blindness increased by 89.9% with an 80.5% increase in DR-MSVI. Between 2000-2020, for DR-blindness the ratio of females/males increased to 1.20:1.00 from 1.06:1.00; DR-MSVI to 1.13:1.00 from 1.08:1.00. ASP for DR-blindness in males was unchanged (-0.1%) with a 12.9% increase in females.

In 2020, among GBD super-regions, the ASP of DR-blindness was highest in Latin America/Caribbean (LAC) (0.15%, 0.10-0.21) followed by North Africa/Middle East (NA/MI) (0.06%, 0.04-0.09). For MSVI, NA/MI had the highest prevalence (0.41%, 0.30-0.55), followed by LAC (0.30%, 0.22-0.40). The largest increase in ASP of DR blindness was in South Asia (+25.7%) followed by Southeast Asia, East Asia and Oceania (SA/EA/O) (+15.4%) and Sub-Saharan Africa (+2.5%), the 4 other super-regions showing a decrease. Only SA/EA/O showed an increase in ASP of DR-related MSVI of 2.3%.

Conclusions: There are regional differences in DR-related blindness and MSVI and females are increasingly disproportionately affected by DR-visual loss. Further targeted region-specific actions on reducing burden of diabetes

and its complications and improving female care access are essential to reduce DR-related blindness/MSVI.

CONTROL ID: 3543868

SUBMITTER (NAME ONLY): Aysegul Tura

TITLE: Differential expression of the genes involved in the response to insulin in the retinal pigment epithelium and choroid of patients with age-related macular degeneration

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Tura, S. Grisanti, Department of Ophthalmology, University of Lübeck, Lübeck, Schleswig-Holstein, GERMANY]

Commercial Relationships Disclosure (Abstract): Aysegul Tura: Commercial Relationship: Code N (No Commercial Relationship) | Salvatore Grisanti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Insulin resistance is a low-grade inflammatory and proangiogenic condition which is commonly detected in overweight people. Despite the positive association of a higher body-mass-index with the risk of developing age-related macular degeneration (AMD), it is not known whether the AMD patients exhibit insulin resistance in the primarily affected ocular tissues. Here, we analyzed the expression of n= 287 genes involved in the cellular response to insulin in the retinal pigment epithelium (RPE) and choroid of the AMD-patients versus age-matched controls using the transcriptome data of two independent cohorts from the Gene Expression Omnibus (GEO) database.

Methods: The list of genes involved in the cellular response to insulin was constructed using the Gene Ontology (<http://geneontology.org/>) and PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) databases. Analysis of mRNA expression was performed using the normalized microarray data of two independent studies available at the GEO database. The first study involved the RPE/choroid of early AMD patients (n=9, mean age: 81 years) and age-matched controls (n=7, mean age: 83 years, Accession number: GSE50195). The second cohort consisted of the RPE cells that were isolated from two patients with advanced CNV (mean age: 83.5 years, n=4 replicates for each culture) compared to the normal human RPE-cells (ScienCell, Carlsbad, CA, n=4 replicates, Accession number: GSE103060).

Results: A total of seven genes were significantly altered in both cohorts in the absence of multiple hypothesis testing. Despite the similar levels of insulin, the expression of the insulin-like growth factor 2 (IGF2) gene, which is positively correlated with insulin resistance, and the insulin-induced gene-1 (INSIG1) was significantly upregulated in the RPE/choroid of early AMD patients and the CNV-derived RPEs.

Conclusions: Our results provide the first clues for the altered potential to respond to insulin in the RPE/choroid of the AMD patients, suggestive of an insulin-resistant or hyperinsulinemic state in the course of this disease. Further research on this neglected aspect may enable the identification of novel modifiable mechanisms that are involved in the different stages of AMD.

CONTROL ID: 3543871

SUBMITTER (NAME ONLY): Jiaxing Wang

TITLE: Robust optic nerve regeneration in a mouse mutant

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Wang, R. King, Y. Li, E. Geisert, Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|D. Ashbrook, R. Williams, Genetics, Genomics and Informatics, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously we examined the effects of genetic background on optic nerve regeneration (ONR) using the BXD inbred strain set. One strain, BXD29-Tlr4^{lps-2J}/J, displayed robust axonal regeneration. This strain is known to have acquired a mutation in TLR4 since its initial production in 1976. The present study is designed to determine if the mutation in TLR4 is responsible for the profound regeneration.

Methods: The present study examined optic nerve regeneration in BXD29-Tlr4^{lps-2J}/J mice and BXD29/Ty (the cryopreserved original strain) mice, the F1 crosses and the F2 crosses. ONR protocols include knockdown of Pten and intravitreal injection of zymosan and cAMP. To identify the role of the known mutant gene Tlr4, we examined the effects of this treatment following optic nerve crush. Two days before sacrifice, Alexa Fluor® 647 Conjugated Cholera Toxin B was injected into the vitreous and at 14 days after crush, the optic nerves were fixed and cleared in FocusClear. The amount of regeneration was quantified by the number of axons at 0.5 mm and 1 mm from the crush, and the distance that the longest 5 axons and single axon had reached down the nerve. To explore other candidate genes, we explored the full genomic sequences of both BXD29-Tlr4^{lps-2J}/J and BXD29/Ty. All SNPs and INDELs were called and compared between the two strains to identify possible mutations that may have impact on the regeneration.

Results: There was a considerable amount of axonal growth on BXD29-Tlr4^{lps-2J}/J but not the BXD29/Ty. All the F1s and F2s have shown similarly robust regeneration as the BXD29-Tlr4^{lps-2J}/J, indicating that the genetic element that is regulating the regeneration could be autosomal dominant. There is no significant difference in the amount of regeneration between the homozygote F2s (+/+ for wild type Tlr4) and the heterozygote F2s (+/- for mutant Tlr4), indicating that the mutation of Tlr4 is not responsible for this robust regeneration response. Since the two sub-strains have been separated for over 40 years, other mutations may have occurred. After whole genome analysis, we have identified more than 5,000 variants between the two sub-strains with 293 variants in the protein coding region. We are currently evaluating the segregation of these SNPs to identify the genomic elements responsible for the increased regeneration.

Conclusions: The strong optic nerve regeneration found in the BXD29-Tlr4^{lps-2J}/J mice was not caused by the mutation in Tlr4.

CONTROL ID: 3543876

SUBMITTER (NAME ONLY): MHAMED OUZZANI

TITLE: Stability of Corneal Topographic Changes After Long-Term Orthokeratology

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study aims to assess the stability of topography parameters performed after wearing orthokeratology lenses for year

Methods: This is a retrospective study made on myopic patients seen at Université de Montréal Clinic, adapted for orthokeratology between January 2017 and December 2018, followed for at least 1 year, and having worn the same lens design during this period. Topographical data (Medmont) were extracted from tangential maps taken at baseline and after 1, 3, 6 and 12 months of wear. Following the map analysis method suggested by Marcotte-Collard et al, treatment zone diameter (TZD), mid-peripheral power (MPP), mid-peripheral power width (MPPW) were measured horizontally (180 deg) and vertically (90 deg) at each visit. These values were compared over time. Statistically, the repeated within-subject measures resulted in clusters of possibly correlated data. Models were fit that accounted for within-subject correlation. The predictors of main interest were Month and Quadrant. Also included were gender, ethnicity, age, flat keratometry (KF), Steep keratometry (KS), initial refraction (RX) and axial length.

Results: Clinical population is composed of 99 participants (58% Female; 54% Asian), aged 11.75 +/- 2.15 showing an average refraction of -3.27 +/- 1.28D. Analysis of the results highlights all parameters remain stable during the first 6 months. However, at 12 months, TZD becomes smaller (-0.067+/-0.43mm) ($p=0.004$), MPP decreased by 0.89+/- 2.82D ($p<0.001$), whilst its width (MPPW) remain stable at 0.99+/-0.25mm over time. The measures along the vertical meridian show higher convex power and larger width compared to the horizontal ones ($p<0.001$).

Conclusions: This study demonstrates that topographic data can be compared over time. However, the convex power generated by the OK lens is significantly less at 12 months. Future work is needed to identify the causes of this loss of power. This could implicate that lenses must be changed more frequently in order to maintain their effectiveness.

CONTROL ID: 3543883

SUBMITTER (NAME ONLY): Yan Liu

TITLE: Ultrafast adaptive optics for imaging the living human eye

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, J.A. Crowell, K. Kurokawa, H. Jung, A. Lassoued, M. Bernucci, D.T. Miller, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics (AO) measures and corrects ocular wavefront aberrations, enabling cellular-resolution retinal imaging and stimulation. Most current ophthalmic AO systems correct dynamic aberrations up to 2 Hz, the commonly-known cutoff frequency for ocular aberrations. However, this cutoff is based on measurements acquired in healthy subjects under ideal conditions and thus do not capture many real-life clinical scenarios that induce high temporal frequency aberrations. To investigate, we developed ultrafast AO and evaluated its use with optical coherence tomography (OCT).

Methods: Our ultrafast AO system used (1) a fast Shack-Hartmann wavefront sensor (SHWS) with high spatial sampling and dynamic range, (2) efficient software that minimized data processing time, and (3) discontinuous exposure permitting a higher AO loop gain. The SHWS comprised a 20×20 microlens array that sampled a 6.7 mm eye pupil and a high-speed streaming camera (ORCA-Lightning, up to 342 Hz). A direct slope reconstruction method and an integral controller scheme with a gain of 1 determined the voltages for a deformable mirror (DM, ALPAO DM97-15). Our software processed frames in 0.5 ms. We analyzed AO performance in correcting rapid dynamic aberrations caused by tear film disruptions, eye blinks, displacement of a high-power contact lens, nystagmus, and absence of cycloplegia. Performance was compared to conditions mimicking conventional AO on the same eyes.

Results: The cutoff frequency of our AO system as determined from a power rejection curve measurement was 32.5 Hz, enabling correction of dynamic aberrations more than 16× faster than conventional AO. After AO activation, the RMS wavefront aberration from un-cyclopleged subjects dropped below the diffraction limit within 5 ms, 40× faster than the fastest previously-reported ophthalmic AO system. Unlike conventional AO, ultrafast AO achieved high image quality of cone photoreceptors immediately after an eye blink, even in a late-stage retinitis pigmentosa subject wearing a -8.5 D contact lens. This immediate recovery from blinks enables continuous data acquisition for simple and high-throughput imaging in the clinic. In an eye with nystagmus, ultrafast AO improved the Strehl ratio from 0.37 to 0.81 and produced sharper images of the cone mosaic compared with conventional AO.

Conclusions: Ultrafast AO corrects ocular wavefront aberrations that conventional AO cannot and improves the clinical utility of AO.

CONTROL ID: 3543885

SUBMITTER (NAME ONLY): Emmanuel Kobia-Acquah

TITLE: Relationship between choroidal thickness, axial length, and degree of myopia in European children

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kobia-Acquah, I. Flitcroft, G.M. Hernandez, E. Loskutova, J. Loughman, Centre for Eye Research Ireland, Technological University Dublin, Dublin, Dublin, IRELAND|I. Flitcroft, Department of Ophthalmology, Temple Street Children's University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Myopia has been associated with structural changes such as axial elongation and thinning of the retina and choroid. The relationship between choroidal thickness (CT), axial length (AL) and myopia has been studied in adult populations, however, there is little evidence available in children. Baseline data of 248 myopic children aged 6-16 years and enrolled in the Myopia Outcome Study of Atropine in Children (MOSAIC) clinical trial (ISRCTN36732601) were analysed to investigate the relationship between CT, AL and myopia in European children.

Methods: Myopia was categorized into three subgroups: low myopia (≤ -0.50 D to -3.00 D); moderate myopia (< -3.00 D to > -6.00 D); high myopia (≤ -6.00 D). Macular CT images were obtained using Triton Swept Source OCT; AL was measured with the Topcon Aladdin; cycloplegic spherical equivalent refraction (SER) was measured with the Grand Seiko Open Field autorefractor. Multiple linear regression analysis was used to explore associations between CT and age, gender, AL, and SER. A P-value of .05 was considered statistically significant.

Results: The mean \pm SD age of participants was 11.3 \pm 2.4 years (63% females). There was a statistically significant difference in mean CT across the three myopic groups ($P=.0002$). A negative correlation between CT and AL was observed, with each additional millimeter in AL equating to a 21.2mm lower CT ($P<.0001$). There was a statistically significant positive correlation between CT and SER, with each additional diopter of myopia equating to a 11.5mm greater CT ($P<.0001$). Only AL was significantly associated with CT after adjusting for age, sex, and SER in the studied population. CT was thicker in females than in males (240.0mm vs 230.8mm; $P=.29$); thicker in younger (age 6-11) than older (age 12-16) children (242.9mm vs 229.5mm; $P=.11$).

Conclusions: The current study showed that CT was thinnest in high myopes and was associated with AL in European children. The MOSAIC trial will evaluate longitudinal changes in CT in children with progressive myopia to understand the relationship between CT, AL and other ocular parameters both with (0.01% atropine treatment group) and without (placebo control group) myopia control treatment with low dose atropine.

CONTROL ID: 3543888

SUBMITTER (NAME ONLY): Gopal Jayakar

TITLE: Modelling structure-function relationship in patients undergoing screening for hydroxychloroquine toxicity

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Jayakar, T. De Silva, C.A. Cukras, Unit on Clinical Investigation of Retinal Disease, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: The American Academy of Ophthalmology issued recommendations on annual screening of patients using hydroxychloroquine (HCQ) including functional testing with a Humphrey 10-2 visual field and structural evaluation using spectral domain optical coherence tomography (SD-OCT). This study investigates the association between retina microstructure and visual function in a cohort with long-term HCQ use.

Methods: Methods: The case-control study included 87 participants (173 eyes, mean age 60, 93% female, 55 without toxicity, 32 with toxicity) and SD-OCT imaging (Heidelberg Spectralis) and Humphrey 10-2 visual field (VF) testing were obtained during each visit. Quantitative metrics computed using OCT included total and outer retina thickness, minimum intensity (along A-scans within total and outer retina), and ellipsoid zone (EZ) loss. Enface 2D maps of OCT metrics were sampled in 68 circular regions (288 μ m diameter) corresponding to VF loci. First, correlations were analyzed between each OCT metric and corresponding VF sensitivity by locus using a linear model. Second, ability to predict VF sensitivity from the combination of OCT metrics were analyzed using a multi-variate, non-linear random forest regression using leave-one-out cross-validation.

Results: Results: In linear regression, the strongest relationship with VF sensitivity in the parafoveal ring was found with EZ loss, with $R^2=0.60$. Linear analyses using total and outer retinal thickness revealed $R^2=0.57$ and 0.40 , respectively, while total and outer retinal minimum intensity yielded $R^2=0.10$ and 0.22 , respectively. Using the multivariate model that included all five OCT metrics, the VF prediction markedly improved with $R^2 = 0.79$ and measured root mean squared error of 3.5 dB. Feature importance analysis identified EZ loss as the most relevant predictor.

Conclusions: Conclusions: Multiple OCT-derived quantitative metrics exhibited high correlation with VF sensitivity with the multivariate model achieving a high-degree of predictability of visual function from combined structural metrics. The results indicate a confluence of features available in SD-OCT and VF demonstrating the potential predictability of function from structure. With further analysis, this data could provide evidence to streamline the early detection of toxicity.

CONTROL ID: 3543890

SUBMITTER (NAME ONLY): Moying Wang

TITLE: Qualitative and Quantitative Comparison of Spectral Domain and Swept Source OCT Angiography Devices in Retinal Diseases

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare retinal vascular and foveal avascular zone morphology on OCT-angiography (OCTA) images and macular OCT images in subjects with retinal or choroidal abnormalities using two different OCT-angiography devices.

Methods: The retina of 31 study eyes of 21 participants with retinal or choroidal abnormalities including age-related macular degeneration, diabetic retinopathy, branch retinal vein occlusion and central retinal occlusion underwent fovea-centered 3×3mm and 6×6mm volume scans using the Topcon DRI-OCT Triton Swept-source OCT and Optovue RTVue-XR. The device-software generated en-face OCT-A images of the superficial (SCP) and deep capillary plexuses (DCP) and OCT images. By using the automatic segmentation, vessel length density (VLD), foveal avascular zone (FAZ) area, foveal avascular zone perimeter of OCTA images in the SCP and DCP and foveal center point thickness of 6 patterns of OCT images using image J software were compared between devices.

Results: After skeletonization of vessels to remove variation related to vessel width, mean (95% CI) difference of VLD between Topcon and Optovue was 8.40% (5.7%-1.1%, $P<.001$) and 3.33% (0.9%-5.7%, $P=.008$) in the SCP and DCP of 3×3mm volume scans, respectively. The mean difference of VLD was 7.72% (5.35%-10.09%, $P<.001$) and 8.93% (5.97%-11.88%, $P<.001$) in the SCP and DCP of 6×6mm volume scans, respectively. The mean difference of FAZ area was -0.17mm^2 (-0.25 – -0.10 , $P<.001$) and 0.31mm^2 (0.20 – 0.42 , $P<.001$) in the SCP and DCP of 3×3mm volume scans, respectively. The mean difference of FAZ area was -0.04mm^2 (-0.24 – 0.15 , $P=.647$) and 0.62mm^2 (0.39 – 0.85 , $P<.001$) in the SCP and DCP of 6×6mm volume scans, respectively. The mean difference of FAZ perimeter was -0.76mm (-1.22 – -0.31 , $P=.002$) and 0.94mm (0.47 – 1.42 , $P<.001$) in the SCP and DCP of 3×3mm volume scans, respectively. The mean difference of FAZ perimeter was -0.14mm (-0.62 – 0.34 , $P=.540$) and 1.40mm (0.95 – 1.84 , $P<.001$) in the SCP and DCP of 6×6mm volume scans, respectively.

Conclusions: These findings suggest VLD on Optovue was smaller than that on Topcon in either SCP or DCP on both volume of scans. FAZ area and perimeter in SCP on Optovue appeared larger than that on Topcon, but smaller in DCP. Further studies would be needed to determine if these differences are clinically relevant and how they vary across diseases, patients, and eye characteristics.

CONTROL ID: 3543891

SUBMITTER (NAME ONLY): Kristina Ertel

TITLE: Tolerability and efficacy of a rAAV-mediated glaucoma gene therapy in brown norway rats

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.J. Ertel, N.W. Li, E.R. Nettesheim, C.A. Reid, D.M. Lipinski, Ophthalmology and Visual Science, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|K.J. Ertel, Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|D.M. Lipinski, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of blindness affecting 2.9 million people in the US and is characterized by progressive optic nerve degeneration owing to imbalances between aqueous inflow and drainage. Prostaglandin analogs are effective at reducing IOP but are critically undermined by poor patient compliance. Herein, we set out to evaluate the effectiveness of a single use recombinant adeno-associated (rAAV)-mediated gene therapy treatment aimed at permanently lowering IOP through over-expression of prostaglandin F2a synthase (PTGS2) and receptor (PTGFR).

Methods: Brown norway rats (N=30) underwent baseline electroretinography (ERG), confocal scanning laser ophthalmoscopy (cSLO), optical coherence tomography (OCT), and tonometry. Rats were randomized following baseline characterization; each received a unilateral intracameral injection of rAAV packaging PTGS2 and PTGFR and a tetracycline inducible OFF-switch at either low (3.9×10^9 vector genomes(vg)/ml), medium (3.9×10^{10} vg/ml), or high (3.9×10^{11} vg/ml) dose. Tonometry was repeated at 1, 3, 6, 9, 12, and 13 months post injection and imaging/ERG repeated at 12 months to assess tolerability and efficacy. Gene expression was switched OFF at 12-months by administration of 5% tetracycline diet ad libitum. Eyes were harvested for histology at 12 and 18 months.

Results: Tonometry showed a dose-dependent reduction in IOP of -12.6% (low, NS), -21.87% (medium, $P=0.0036$) and -43.2% (high, $P<0.0001$) maintained until 12-months. Decreased IOP correlated to increased anterior chamber depth in low (+5.2%, $P=0.0125$), medium (+8.1%, $P=0.0447$) and high (+24.3%, $P<0.0001$) dose treatment (Unpaired T-test) at 12-months. No difference in reflectivity/autofluorescence (cSLO), corneal/retinal thickness (OCT), or ERG were observed in any treatment group. Slit lamp examination showed increased cell (12%), flare (36%), iris exfoliation (88%) and hyphema (20%) in the high dose treatment group. Placement on 5% tetracycline diet increased IOP in high (+22.5%) and medium (+21.5%) dose eyes, representing a partial or complete reversion to normal tension, respectively.

Conclusions: This study demonstrated dose-dependent reduction in IOP following a single injection of vector and excellent tolerability in low and medium dose treatment groups. Critically, IOP reduction could be reversed through oral administration of tetracycline; a critical safety feature for future clinical translation.

CONTROL ID: 3543894

SUBMITTER (NAME ONLY): Christine Curcio

TITLE: Transdifferentiated retinal pigment epithelium (RPE) visible in vivo, of relevance to cell-based therapies in age-related macular degeneration (AMD)

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Curcio, D. Cao, J. Messinger, L. Chen, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|D. Ferrara, Genentech Inc, South San Francisco, California, UNITED STATES|K. Freund, Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|L. Chen, The First Affiliated Hospital of Chongqing Medical University, Chongqing, Sichuan, CHINA|

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ABSTRACT BODY:

Purpose: Clinical trials for RPE transplantation for AMD have shown black pigment in the post-operative fundus. Black pigment in neovascular AMD is ascribed to melanotic cells, i.e., RPE-originated and packed with large spherical melanosomes (PMID 26024109). To inform interpretation of trial imaging outcomes, we provided histology of a clinically imaged eye with neovascular AMD and black pigment; in donor eyes, we performed immunohistochemistry to test whether melanotic cells are transdifferentiated RPE.

Methods: A white woman with inactive subretinal fibrosis OD was followed for 9 years using fundus color and autofluorescence imaging, and optical coherence tomography (OCT). After patient death at age 90 years, OD was preserved 6.25 hours later and prepared for epoxy resin sections aligned to OCT and light and electron microscopy. Regions of distinct gray-black pigmentation in the fibrotic scar were identified in histology. To assess cellular functional repertoire, we used enzyme-linked colorimetric immunohistochemistry to detect retinoid (RPE65) and immune (CD68) proteins, in bleached sections of donor eyes with nvAMD and lacking clinical history.

Results: Black and gray non-autofluorescent pigment appeared within the fibrotic scar and expanded during follow-up. The black pigment corresponded to cells with densely packed spherical black melanosomes. These contrasted both with spindle-shaped melanosomes of normal RPE, which were found infrequently, and tightly packed small spherical melanosomes in choroidal melanocytes. Some moderately pigmented melanotic cells expressed RPE65 and CD68. Only CD68 immunoreactivity, a marker for abnormal RPE (Cao ARVO2020), was seen in heavily pigmented cells.

Conclusions: Black fundus pigment corresponds to melanotic cells, shown previously to arise from RPE entombed in fibrotic scars or enveloping neovascular membranes (PMID 26024109, 32855855). Large spherical melanosomes likely arise from organelles such as lipofuscin or newly described spherical melanosomes (PMID 32433758) rather than from native melanosomes, which are sparse in advanced disease. Cell based therapies should anticipate possible dynamism of lysosome-related organelles including melanosomes. Trial outcome measures should include multimodal imaging with autofluorescence to assess health of implanted cells.

CONTROL ID: 3543901

SUBMITTER (NAME ONLY): Yuntian Xue

TITLE: Analysis of Retinal Organoids Long-term Development by Functional Imaging and Realtime Polymerase Chain Reaction

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Xue, W.C. Tang, A.W. Browne, Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|B. McLelland, G. Nistor, H. Keirstead, AIVITA Biomedical, California, UNITED STATES|M. Rouhizadeh, V. Giang, Biological Sciences, University of California Irvine, Irvine, California, UNITED STATES|J. Garcia, Chemical Engineering, Massachusetts Institute of Technology, Cambridge, Massachusetts, UNITED STATES|A.W. Browne, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|M.J. Seiler, Physical Medicine & Rehabilitation, University of California Irvine, Irvine, California, UNITED STATES|M.J. Seiler, Stem Cell Research Center, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stem cell-derived retinal organoids (RtOgs) can be used for transplantation in retinal degeneration (RD) models. The purpose of this study was to understand RtOgs' long-term metabolic and genetic changes in vitro to improve quality control for biomanufactured transplantable tissues.

Methods: Ten GMP-compatible lots of RtOgs manufactured by AIVITA Biomedical Inc (Irvine, CA, USA) and were used for long-term functional imaging and qPCR analysis. We used two-photon microscopy (Zeiss LSM 780, 740 nm pulsed laser) coupled with fluorescence lifetime imaging (FLIM) and hyperspectral imaging (HSPEC) to characterize the RtOgs' metabolic activity and structure. RtOg samples ranged from days 51 to 159 of differentiation during longitudinal imaging. In qPCR analysis, we used 12 retinal progenitor and photoreceptor genes and 1 housekeeping gene to identify and quantify the gene expression profile. Human fetal (n=1) and adult retinal tissue (n=3) were used as positive controls. Stem cell line CSC14 was used as a negative control.

Results: The free/bound NADH (f/b NADH) ratio demonstrated that a metabolic shift from glycolysis to oxidative phosphorylation occurred between day 54 and 87. The total metabolic activity shifted slightly back toward glycolysis between day 90 and 100. Consistency in organoid development among production lots was shown. Organoids demonstrated similar metabolic signatures over 5-6 months. Retinal progenitor genes were expressed in all groups between days 51 and 159. Photoreceptor genes expression emerged around the 2nd month of differentiation, which corresponded to the shift in f/b NADH ratio. RtOgs between 3-6 months of differentiation had photoreceptor gene expression levels between the human fetal retina and human adult retina gene expression levels. The occurrence of OPN1 SW and OPN1 LW indicated the maturation of photoreceptors in 4 months of differentiation, which was concurrent to the stabilized level of f/b NADH ratio starting from 4 months.

Conclusions: Long-term imaging data showed that RtOgs in different lots exhibited a reproducible metabolic development from more proliferative to more differentiated at an early stage. After 4 months, the metabolic signature stabilized consistent with gene expression profile stabilization.

CONTROL ID: 3543902

SUBMITTER (NAME ONLY): Dragos Rezeanu

TITLE: Explaining the Absence of Functional Tetrachromacy in Females with Four Cone Types

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D.L. Rezeanu, J. Kuchenbecker, R. Barborek, M. Mazzaferri, M. Neitz, J. Neitz, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Due to random X-inactivation and polymorphism in the spectral sensitivity of the L and M cones, some females have four distinct cone classes in their retinæ. However, psychophysical studies of females with the gene for four cones have found the vast majority of subjects do not exhibit four-dimensional color vision (Jordan et al., JoV, 10, p1, 2010), even when the three middle-to-long wavelength photopigments are well-separated in spectral peak. We propose that the absence of functional tetrachromacy in this population is a result of the circuitry in the outer retina and a dearth of visual experience that would train the visual system to distinguish an additional color axis.

Methods: To test this hypothesis, we created a receptive field response and detection algorithm based on the theory of color appearance put forward by Schmidt et al. (JOSA A, 31, pA195, 2014). According to this theory, all conscious vision is mediated by the midget ganglion cell system: achromatic vision is mediated by L vs M receptive fields, while hue perception is mediated by double opponent receptive fields formed when S-cone signals are combined with L vs M signals in the outer retina. The resulting model was presented with millions of colored edges and correlations between the response of each receptive field were calculated in order to ascertain how many distinct outputs the brain could distinguish. Our model differs from previous attempts, which relied on individual cone responses rather than the outputs of midget ganglion cells.

Results: We found that any 4th cone added to the model, no matter how well spaced between the M and L cone photopigments, produced a response that was highly correlated to the existing receptive fields of trichromats. Receptive fields with the 4th cone as a center were consistently classified as achromatic L vs M in the absence of S-cone input, or Blue vs Yellow when S-cone signals were included.

Conclusions: These results show that it is unlikely the brain would be able to differentiate the signal produced by receptive fields with a fourth cone without consistent exposure to scenes in which their activity is decorrelated from those that mediate the red-green, blue-yellow, and black-white percepts of normal trichromatic vision. As a result, functional tetrachromacy is exceedingly rare in the general population despite the significant number of females born with four well-separated cone photopigments.

CONTROL ID: 3543903

SUBMITTER (NAME ONLY): Lingge Suo

TITLE: Proteomics Analysis of Excitotoxicity Neurodegeneration in Retinal and Optic Nerves: N-Methyl-D-Aspartate-induced Ferroptosis, Autophagy, and Apoptosis

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Suo, D. Zhang, C. Zhang, Peking University Third Hospital Ophthalmology Department, Beijing, CHINA|

Commercial Relationships Disclosure (Abstract): Lingge Suo: Commercial Relationship: Code N (No Commercial Relationship) | Di Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Chun Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Various retinal disorders, such as glaucomatous, retinal ischemia reperfusion, and traumatic optic neuropathy, are involved in the pathogenesis of neurodegeneration via glutamate excitotoxicity. However, the proteomic characteristics and modulation of the neural microenvironment with NMDA-induced neurodegeneration in the retina and optic nerve remain incompletely understood.

Methods: We established a model of NMDA-induced injury by comparing the proteomes of phosphate-buffered saline (PBS)-operated, NMDA-operated and control groups. We performed mass spectrometry-based label-free quantitative mechanisms and identify key proteins that spatially regulate neural cell death related signaling pathways in the retina and optic nerve.

Results: Using LC-MS/MS proteomics analysis, we identified 3532 proteins in retinal tissues and 2593 proteins in optic nerve tissues. Using Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses, protein changes and energy metabolism in the retina and optic nerve tissue were comprehensively evaluated. Pearson's correlation coefficients revealed the excellent biological reproducibility of the proteomic results. We identified the key cellular signaling events triggered by glutamate overstimulation based on protein-protein interaction analysis. We found that the ACSL3 (Q63151) and Prnp (P13852) proteins are key factors in ferroptosis regulation in the retina; the Gabarapl2 (P60522) protein is the key factor in autophagy in the optic nerve. In PRM validation, we confirmed 16 up- and downregulated key proteins among the different groups.

Conclusions: This study provides the basis for further studies linking NMDA-induced neural cell death in the retina and optic nerve and may shed light on the advanced molecular mechanism of disease biology and accelerated targeted therapy.

CONTROL ID: 3543905

SUBMITTER (NAME ONLY): Melis Kabaalioğlu Güner

TITLE: Effects of IGFBP-3 on Mitochondrial Fitness in Corneal Endothelial Cells

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kabaalioğlu Güner, W. Stuard, D.M. Robertson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Melis Kabaalioğlu Güner: Commercial Relationship: Code N (No Commercial Relationship) | Whitney Stuard: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Robertson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Previous studies have shown that storage of donor corneal endothelial cells (dCEncs) at 4°C and subsequent rewarming prior to transplantation can damage mitochondria and decrease cell viability. The Insulin-like growth factor binding protein-3 (IGFBP-3) is a pleiotropic protein with known roles in cell growth and survival. This study investigated the effect of IGFBP-3 on mitochondrial fitness in dCEncs subjected to hypothermic storage.

Methods: Human donor corneas were obtained from Tissue Transplant Services at UT Southwestern Medical Center. dCEncs were harvested by removal of Descemet's followed by trypsinization. Cells were plated on collagen IV coated plates and cultured in medium containing 4% fetal bovine serum. Cells were serum starved for 24 hours prior to cold exposure (4°C) for 15 minutes, 2 or 6 hours with and without recombinant human (rh)IGFBP-3. Mitochondrial respiration and glycolysis were measured in real time using a Seahorse assay. Mitochondrial fragmentation and polarization were further assessed by double-labeling with MitoTracker and TMRE, respectively. Amplex red was used to quantify levels of reactive oxygen species (ROS). Western blotting was used to determine the expression of mitochondrial proteins.

Results: Short term cold exposure induced cell migration that was visible at 2 hours. By 6 hours, dCEncs formed distinct morphological clusters that were not evident in cells cultured at 37°C or rhIGFBP-3 treated cells. At the 6-hour time point, dCEncs also demonstrated a reduction in cell-substrate adhesion that was recovered by co-treatment with rhIGFBP-3, while cell-cell adhesion appeared unchanged. Despite a measurable increase in mitochondrial oxygen consumption, cold exposure induced mitochondrial hyperpolarization and fragmentation. Co-treatment with rhIGFBP-3 significantly increased oxygen consumption. This was associated with an improvement in mitochondrial morphology. Expression levels of Superoxide dismutase (SOD) 1 and SOD2 were decreased following 6 hours of cold exposure but returned to near normal levels when treated with rhIGFBP-3. There were no detectable differences in ROS levels between groups.

Conclusions: IGFBP-3 promotes mitochondrial fitness and cell-substrate adhesion in dCEncs in cell culture in vitro. Further studies are needed to determine the effects of IGFBP-3 on dCEncs during transplantation in vivo.

CONTROL ID: 3543906

SUBMITTER (NAME ONLY): Carrie Garufis

TITLE: System Settings for Intraocular Pressure (IOP) Performance with 25-Gauge Dual-Cutting 20,000cpm Beveled Vitrectomy Probes

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Garufis, Y. Zhu, Alcon Laboratories Inc, Lake Forest, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Carrie Garufis: Commercial Relationship(s);Alcon:Code E (Employment) | Ying Zhu: Commercial Relationship(s);Alcon:Code E (Employment)

ABSTRACT BODY:

Purpose: As IOP maintenance during vitrectomy surgery is a critical parameter, the study aims to 1) understand the IOP performance of 25+Gauge (Ga) dual-cutting, 20K cuts per minute (cpm) beveled vitrectomy probes under different system settings, and 2) help surgeons to optimize their system settings during surgery.

Methods: 25+® HYPERVIT® beveled 20K cpm vitrectomy probes were driven by a CONSTELLATION® Vision System (Alcon Vision, LLC.) to aspirate sterile irrigating solution (BSS®) in a hollow acrylic eye model. A digital transducer (OMEGA, PX409-001GUSBH) was connected to the bottom of eye model to detect IOP change during aspiration. Six samples were tested under core duty cycle and vacuums of 250mmHg, 450mmHg and 650mmHg. Cut rate ranged from 2500cpm to 20,000cpm. Both system IOP compensation enabled and disabled were used. Average IOP during aspiration was calculated for each test setting and statistical analyses were performed using Kruskal-Wallis test with statistical significance level of $p < 0.05$.

Results: At 450mmHg, without IOP compensation, the IOP ranged from 13.93 ± 0.96 to 14.32 ± 1.11 mmHg when the cut rate changed from 2500cpm to maximum cut rate of 20,000cpm. When IOP compensation was enabled, IOP ranged from 33.21 ± 1.06 to 33.25 ± 1.55 mmHg for cut rates from 2500cpm to 20,000cpm. Statistical analysis indicated that there was no significant difference between results using various cut rates for both IOP compensation enabled and disabled ($p > 0.05$).

At the maximum cut rate and without IOP compensation, IOP was 21.96 ± 0.60 mmHg under 250mmHg, 14.32 ± 1.11 mmHg under 450mmHg and 7.47 ± 0.98 mmHg under 650mmHg. Corresponding average flow rate was 6.54 ± 0.13 cc/min under 250mmHg, 10.64 ± 0.1 cc/min under 450mmHg and 14.08 ± 0.09 cc/min under 650mmHg. When IOP compensation was enabled, IOP at maximum cut rate significantly increased to 32.32 ± 1.07 mmHg (47% improvement) for 250mmHg, 33.25 ± 1.55 mmHg (132% improvement) for 450mmHg, 37.12 ± 4.04 mmHg (397% improvement) for 650mmHg compared with result without system's intervention ($p < 0.05$).

Conclusions: 25+® Ga Dual-Cutting 20K cpm vitrectomy probes have constant IOP performance under different cut rates. IOP compensation keeps the eye at improved IOP ranges during aspiration. 25+® Ga 20K cpm vitrectomy probe using IOP compensation offer surgeon flexible operation settings as well as a controllable and efficient process.

CONTROL ID: 3543907

SUBMITTER (NAME ONLY): Tianxiao Huan

TITLE: Identifying Genetic Variants in Immune Pathways for Age-related Macular Degeneration

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Huan, R. Widjajahakim, Z. Yang, J.M. Seddon, Department of Ophthalmology and Visual Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|J. Atkinson, Department of Medicine, Washington University School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly. Genome-wide association studies (GWAS) have identified common and rare variants in genes in the complement pathway associated with AMD. To identify additional AMD risk variants and better understand the underlying disease mechanisms, we sequenced the genomic regions of genes in the alternative complement system, coagulation, and inflammatory pathways in 481 advanced AMD (AAMD) and 277 unaffected subjects.

Methods: This study included 758 subjects, of which 340 subjects were from 76 families densely affected by AAMD. Targeted sequencing was performed on the genomic regions of 150 genes in 111 samples. Whole exome sequencing was performed on the other 647 samples. Single-variant tests were performed on 3062 variants shared among ≥ 5 AAMD subjects using logistic regression. Gene-based tests were used to evaluate aggregate effects from rare and low frequency variants (at minor allele frequency [MAF] $< 5\%$) in a gene using burden tests and SKAT. Analyses were adjusted for age, sex, smoking, four principal components, and family structure.

Results: At false discovery rate (FDR) < 0.05 , we identified a protein-altering variant, rs2274700 in CFH (Odds ratio = 0.61, $P = 1.78 \times 10^{-5}$) in association with AMD by single-variant analysis. rs2274700 is a perfect proxy of a well-known AMD intronic SNP rs1410996 (linkage disequilibrium, $r^2 = 1$). Gene-based tests identified a burden of 24 variants in OPRM1 ($P_{\text{SKAT}} = 0.002$) and 18 in LCT ($P_{\text{SKAT}} = 0.003$) at FDR < 0.2 . For densely AAMD affected families whose members had low genetic risk score (< 0.8) and no known rare variants of AMD, we hypothesized that some of those families may be explained by variants that are highly penetrant. Among the 82 extremely rare variants with MAF < 0.001 in the 1000 genomes reference panel and being predicted in silico to have functional impact on proteins, we identified one highly penetrant protein-altering variant, whose risk allele was found in $\geq 80\%$ affected AMD members in a family, but not in any of the other samples.

Conclusions: Our study suggested novel pathogenetic rare variants and genes in immune pathways for AMD. Further functional studies will be necessary to validate our findings that will guide the design for novel therapeutic strategies for the disease.

CONTROL ID: 3543908

SUBMITTER (NAME ONLY): Ji Won Bang

TITLE: Sleep-regulating systems are impaired in glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Bang, C. Parra, G. Wollstein, J.S. Schuman, K. Chan, Department of Ophthalmology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|G. Wollstein, J.S. Schuman, Department of Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|K. Chan, Department of Radiology, New York University Grossman School of Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma patients present a high prevalence of sleep disorders, yet its underlying mechanisms remain unclear. Intrinsically photosensitive retinal ganglion cells (ipRGCs), which are involved in circadian rhythms are also known to be injured in glaucoma. The ipRGCs provide input to the ventrolateral preoptic nucleus (VLPO), a major sleep-inducing subcortical structure. VLPO induces sleep by delivering inhibitory signals to the subcortical arousal systems and the cortex. In the current study, we investigated whether the sleep-regulating subcortical systems involving VLPO and their inhibitory projections to the cortex are impaired in glaucoma.

Methods: 37 glaucoma patients and 22 healthy subjects underwent 3T anatomical MRI and resting-state functional MRI (fMRI) with eyes closed. Additionally, 15 glaucoma patients and 4 healthy subjects were scanned for 3T anatomical MRI and proton magnetic resonance spectroscopy (MRS). For MRS, we recorded gamma-aminobutyric acid (GABA), glutamate and N-acetyl-aspartate (NAA) signals from the same single voxel ($2.2 \times 2.2 \times 2.2 \text{ cm}^3$) placed in the occipital cortex (Figure 2A).

We analyzed the fMRI data using CONN. Brain regions-of-interest included VLPO, a main sleep-promoting area, and the arousal systems including posterior hypothalamus (PH), dorsal raphe (DR), median raphe (MR), locus coeruleus (LC), and habenula and cortical networks. We fitted glutamate and GABA separately using LCModel. The amount of GABA and glutamate were normalized by NAA values. The excitatory and inhibitory balance (E/I balance) was calculated by dividing the amount of glutamate by that of GABA.

Results: At the subcortical level, enhanced functional connectivity (FC) was observed between VLPO and PH, a main arousal structure ($P=0.048$; Figure 1A,B,D), and between habenula and MR ($P=0.006$; Figure 1A,C,E) in glaucoma patients. At the cortical level, reduced FC was observed between VLPO and the medial occipital cortex ($P=0.014$; Figure 1F,G,H) and the posterior occipital cortex ($P=0.006$; Figure 1F,G,I). The occipital cortex of glaucoma patients also presented reduced amount of GABA ($P=0.001$; Figure 2C) but not glutamate ($P=0.486$; Figure 2D), resulting in increased E/I balance ($P=0.048$; Figure 2B).

Conclusions: Our study shows that the sleep-regulating subcortical systems involving VLPO and their projections to the occipital cortex are impaired under glaucoma. Such alterations may underlie the high occurrence of sleep disorders in glaucoma.

CONTROL ID: 3543909

SUBMITTER (NAME ONLY): Aftab Taiyab

TITLE: Role of Transcription Factor AP-2 β in the Development of the Trabecular Meshwork and Schlemm's Canal

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Taiyab, M. Akula, M. Rzepka, J.A. West-Mays, McMaster University Faculty of Health Sciences, Hamilton, Ontario, CANADA|J. Dham, Medical Sciences, McMaster University, Hamilton, Ontario, CANADA|T. Williams, University of Colorado - Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|T. Borrás, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anterior segment dysgenesis stems from anomalies in anterior ocular structures, including the trabecular meshwork (TM), leading to abnormalities in aqueous humor production and outflow. In order to determine the specific contribution of transcription factor activating protein-2 β (AP-2 β) in the development of TM, we have recently developed a novel mouse model by deleting AP-2 β specifically from the developing TM region (TMR) using a novel MgpCre mouse line, known to be expressed in periocular mesenchyme (POM), giving rise to the future TM.

Methods: MgpCre^{+/-}; Tfap2b^{+/-} mice were bred with Tfap2b^{lox/lox}; tdTomato^{lox/lox} mice to generate MgpCre^{+/-}; Tfap2b^{-/lox}; tdTomato^{lox/+} mice (AP-2 β TMR KO) with Tfap2b, encoding AP-2 β , deleted from the TMR. When crossed with tdTomato mice, control (MgpCre^{+/-}; tdTomato^{lox/+}) and knockout (KO) mice (MgpCre^{+/-}; Tfap2b^{-/lox}; tdTomato^{lox/+}) expressed an RFP variant that was used to trace MgpCre-expressing cells in frozen sections. H&E and immunohistochemistry (IHC) of paraffin sections was carried out using antibodies for the TM markers, α SMA and myocilin, the Schlemm's canal marker, Prox1, and retinal ganglion cell (RGC) marker, Brn3a, while intraocular pressure (IOP) was acquired using a tonometer.

Results: In control, MgpCre was expressed at embryonic day (E) 15.5 in the POM that was observed to be similar in AP-2 β TMR KO as well. By P7 and P14, fewer tdTomato-positive cells were observed in the TMR of KO mice when compared with control mice. Fewer TM cells were observed in the KOs, as seen using H&E staining, and by the reduction in α SMA and myocilin staining. Further, absence of Prox1 staining was observed in the anterior angle of KO when compared to the control mice. A significant increase in IOP at P30 (n=6 eyes, p<0.001) followed by a significant reduction in retinal thickness (n=3 eyes, p<0.01) and Brn3a positive cells (n=3 eyes, p<0.01) at P40 was observed in the KO mice when compared with control.

Conclusions: The reduction in tdTomato-positive cells and the reduced expression of TM and Schlemm's canal markers in the AP-2 β TMR KO mice suggests that AP-2 β is critical for the development and differentiation of TMR. The increased IOP at P30 in the KO mice likely resulted from abnormal differentiation of the POM cells into TM cells. The decreased retinal thickness and Brn3a positive cells at P40 shows loss of RGCs that can be attributed to increased IOP.

CONTROL ID: 3543911

SUBMITTER (NAME ONLY): Sangeetha Kandoi

TITLE: Development of a novel iPSC-derived 3D-retinal organoid model system from cone-dominant Tree Shrews

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Kandoi, C. Martinez, D.A. Lamba, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|M.H. Phay, P.Y. Baranov, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, MA, US, academic/medres, Boston, Massachusetts, UNITED STATES|M.H. Phay, P.Y. Baranov, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual dysfunctions affecting the central retina including highly prevalent age-related macular degeneration occurs due to degeneration of the cone-dominant central macula region leading to high-acuity vision loss.

Unfortunately, there is a lack of an easily accessible animal model that resembles the human retinal macula. *Tupaia belangeri* (Tree Shrews, Ts) exhibit an extremely high cone: rod ratio (~95%), have large eyes with a more human-like lens: globe ratio, and exhibit highly visual behaviors. Hence the goal of this study was to develop a novel stem cell-based 3D retina from the diurnal, cone-dominant, non-rodent primate-like, Ts.

Methods: Neural progenitor cells (NPC) obtained from a neonatal male, Ts (Gift by Brian Samuels, UAB) was used to generate a stable induced pluripotent stem cell (iPSC) line using CytoTuneTM-iPS 2.0 Sendai Reprogramming Kit. Individual iPSC clones were expanded and assessed for pluripotency markers via immunofluorescence (IF). 3D-retinal differentiation was carried out using a three-step transitioning protocol (3D-2D-3D) with neural induction media. Retinal organoids (RO) collected at various time-points of differentiation (Day 25, 40, 60) were evaluated for retinal cell types by IF and qRT-PCR, and phenotypically compared with neonatal Ts eyes.

Results: iPSC lines (n=3 clones) generated from Ts-NPCs exhibited typical morphological characteristics: compact colonies with clear borders and high nucleus: cytoplasm ratio by bright field microscopy. IF confirmed the expression of pluripotent markers - Oct3/4, Sox2, and Nanog. Undifferentiated Ts-iPSCs directed towards retinal fate generated self-assembled laminated 3D-RO. Protein and gene expression analysis confirmed markers of multipotent retinal progenitor cells (Lhx2, Pax6, Sox2), ganglion/amacrine cells (Brn3a, Islet, HuC/D), and photoreceptors (Otx2, Blimp1, Crx, Rcvrn).

Conclusions: This is the first study to demonstrate the establishment of iPSCs from a novel primate-like tree shrew with cone-dependent visual ecology. Additionally, we have successfully developed a method to generate photoreceptors containing 3D-RO. This approach has a great potential to both understand the feasibility of cone photoreceptor replacement and facilitate the development of novel cone-degeneration models in vitro for understanding and ameliorating catastrophic vision loss using this clinically relevant primate-like animal model.

CONTROL ID: 3543915

SUBMITTER (NAME ONLY): Teele Palumaa

TITLE: Absence of melanopsin leads to altered circadian rhythms of the retinal transcriptome

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Palumaa, L. Taylor, R. Foster, A. Jagannath, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Melanopsin, the photopigment of pRGCs, modulates retinal function as its genetic deletion leads to disruptions in cone ERG and the baseline and circadian rhythmicity of contrast sensitivity. By analysing retinal gene expression over a circadian time course with RNA-seq, this study aimed to uncover the molecular mechanisms of how melanopsin affects retinal circadian rhythms.

Methods: Retinas of wild-type (WT) and melanopsin-deficient ($Opn4^{-/-}$) mice were collected on the first day in constant darkness every 6 hours at circadian times (CT) 4-28 (n=4) and subjected to RNA-seq and qPCR analyses. Circadian rhythmicity and global differences in gene expression were analysed with MetaCycle and DESeq2, respectively. The KEGG database was used to analyse pathway enrichment and the dataset by Siebert et al. (Nat Neurosci 2012) for gene enrichment in retinal cell types.

Results: WT retinas displayed circadian rhythmicity in 647 genes, and $Opn4^{-/-}$ retinas in 691, while only 178 genes were circadian in both genotypes. Despite these differences, the peak phases of gene expression were remarkably similar between genotypes, with the largest number of genes peaking around CT18. The genes rhythmic in both genotypes showed significant enrichment for dopamine signalling (e.g. *Drd1* and *Drd4*), gap junction and circadian pathways, and cone-associated genes. The genes exclusively circadian in WT retinas were enriched for phototransduction and sphingolipid signalling pathways, and those exclusively rhythmic in $Opn4^{-/-}$ retinas for carbon metabolism. On a global level, 450 genes were differentially expressed between the genotypes and those with higher levels in $Opn4^{-/-}$ were enriched for sphingolipid signalling. The core clock genes *Bmal1*, *Per2* and *Cry1* showed circadian rhythmicity in WT, but, interestingly, not in $Opn4^{-/-}$ retinas.

Conclusions: We demonstrate that retinal circadian genes are associated with dopamine signalling and gap junctions, and are cone-enriched in both WT and $Opn4^{-/-}$ retinas. As demonstrated by Dkhissi-Benyahya et al. (Cell Mol Life Sci 2013), we also find that $Opn4^{-/-}$ retinas lose rhythmicity in core clock gene expression. These findings highlight a critical role for melanopsin in regulating the circadian rhythmicity of the retinal transcriptome and suggest that the circadian disruptions of retinal function in $Opn4^{-/-}$ mice might be a result of disrupted visual transduction and sphingolipid signalling pathways.

CONTROL ID: 3543916

SUBMITTER (NAME ONLY): Gabriella Rogers

TITLE: In situ forming collagen-PEG hydrogel as a matrix therapy for corneal defects: 2 month in vivo response

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.F. Rogers, F. Chen, P. Le, D.C. Mundy, C.M. Logan, D. Myung, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal injuries and subsequent scarring collectively represent a major global human health challenge, affecting millions of people worldwide. We have previously shown that in situ-forming PEG-collagen hydrogels supported epithelial wound closure by 1 week after treatment. Here we aim to evaluate the longer-term benefits of the hydrogel on corneal epithelial layer maturation and stromal scarring, 2 months after treatment.

Methods: Lamellar keratectomies were performed in rabbit corneas followed application of the in situ forming collagen-PEG hydrogel followed by bandage contact lens and partial tarsorrhaphy placement which were both removed on day 7. The healing and curvature of the treated cornea was monitored by OCT and photography, along with corneal thickness and intraocular pressure (IOP). Two months after the injury, the corneas were fixed for immunohistochemical analysis.

Results: Multi-layered epithelialization with normal morphology and cytokeratin 3 expression was observed at 2 months. Alpha smooth muscle actin expressed was reduced compared to injured, untreated corneas. The hydrogels were partially observed in the central corneal suggesting degradation and near-complete stromal remodeling. Corneal nerves were observed through beta-tubulin expression in the area of the stroma where the gel was placed. Corneal thickness and IOP were measured to be within normal limits by post-op month 1 and after.

Conclusions: The in situ-forming collagen-PEG hydrogel supports normal epithelial wound healing and stromal remodeling return to baseline corneal thickness by two months.

CONTROL ID: 3543918

SUBMITTER (NAME ONLY): Raghu Krishnamoorthy

TITLE: Endothelin-1 Mediated Decrease in Mitophagy is Involved in Neurodegeneration of Retinal Ganglion Cells in a Rodent Model of Glaucoma

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.R. Krishnamoorthy, B. Kodati, S. He, D.L. Stankowska, Department of Pharmacology and Neuroscience, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|R.M. Chaphalkar, Department of Ophthalmology, School of Medicine, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endothelin-1 (ET-1) is a vasoactive peptide whose levels are elevated both in the aqueous humor and circulation of primary open angle glaucoma patients as well as in animal models of glaucoma. Intravitreal ET-1 treatment in rodents has been shown to produce retinal ganglion cells (RGCs) loss, axonal injury, and disruption of nerve fiber layer. However, the precise mechanisms underlying these effects are still not completely understood. The purpose of the study was to assess mitochondrial mechanisms underlying ET-1 mediated neurodegeneration of RGCs in culture as well as in the Morrison model of ocular hypertension in rats.

Methods: Primary RGCs isolated from rat pups were treated with ET-1 (100 nM) for 24 h and reactive oxygen species were detected with the CellRox Green reagent and mitochondrial membrane potential was measured with the JC-1 dye. Mitophagy was assessed in the RGCs by treating with MitoTracker (labels mitochondria in live cells) and LysoTracker (tracks lysosomes in live cells). To confirm these findings in vivo, intraocular pressure (IOP) elevation was carried out in one eye of retired breeder Brown Norway rats. Two weeks post-IOP elevation, retina sections from IOP-elevated eyes and contralateral eyes were analysed for expression of LC3B (a marker of autophagosomes), LAMP-1 (lysosomal marker) and TOM20 (mitochondrial marker).

Results: ET-1 treatment of primary RGCs for 24 h produced a significant decrease ($n=3$, $p < 0.05$) in reactive oxygen species and a decrease in mitochondrial membrane potential. A decreased co-localization of MitoTracker and LysoTracker was found in primary RGCs treated with ET-1, indicative of decreased mitophagy. IOP elevation for 2 weeks in rats, produced a significant decrease in co-localization of LC-3B and TOM-20 ($n=4$, $p<0.05$) as well as LAMP-1 and TOM-20 in ganglion cell layer and nerve fiber layer.

Conclusions: Treatment of primary RGCs with ET-1 produced an elevation in reactive oxygen species which could result in mitochondrial damage. Following IOP elevation in rats, a decreased colocalization of TOM-20 with LC-3B as well as with LAMP-1 could be indicative of ET-1 mediated decrease in mitophagy in RGCs. Mitochondrial damage in conjunction with reduced mitophagy will exacerbate oxidative damage and neuronal injury, which could be one of the mechanisms underlying ET-1 mediated neurodegeneration of RGCs in glaucoma.

CONTROL ID: 3543923

SUBMITTER (NAME ONLY): Cecile Lebon

TITLE: Evaluation of a new ROCK inhibitor in a rat model of diabetic retinopathy

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lebon, M. Berdugo, K. delaunay, M. Naud, P. Lassiaz, F.F. Behar-Cohen, Physiopathology of ocular diseases, Centre de Recherche des Cordeliers, Paris, Île-de-France, FRANCE|C. Lebon, M. Naud, P. Lassiaz, INSERM, Paris, Île-de-France, FRANCE|F.F. Behar-Cohen, Ophtalmopole, Hopital Cochin, Paris, Île-de-France, FRANCE|M. Berdugo, K. delaunay, Universite de Paris, Paris, Île-de-France, FRANCE|J. Prestle, H. Fuchs, H. Neubauer, R. Bakker, Cardio-metabolic Diseases Research, Boehringer Ingelheim Pharma GmbH & Co. KG, GERMANY|

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ABSTRACT BODY:

Purpose: Rho-associated kinase (ROCK) activation contributes to micro-vascular closure, retinal hypoxia and disrupted retinal pigment epithelium (RPE) barrier in Diabetic Retinopathy (DR) rat model. ROCK inhibition seems to be a promising therapeutic target as previous results with Fasudil, a clinically approved ROCK inhibitor, showed a better retinal perfusion and reduced edema. However, its short life-time in the vitreous is not compatible with a long-term treatment. In this study, we evaluate the potential of a new treatment, BIRKI, a slow-release ROCK Inhibitor from Boehringer Ingelheim.

Methods: 10 to 16 month-old male Goto-Kakizaki (GK) type 2 diabetic rats were injected intravitreally with 3µl of either BIRKI or Vehicle. The diabetic status was defined by measurement of the plasma concentration of glycosylated hemoglobin (HbA1c). Eyes were enucleated and dissected 8 or 28 days after the injection. Immunohistochemistry was performed on flat mounts and cryosections to evaluate retinal hypoxia and vasodilatation, RPE morphology and barrier disruption 28 days after the treatment. Western Blots were performed to assess ROCK activity and expression 8 days after the treatment (significance of results was evaluated using non parametric tests).

Results: ROCK activity, quantified through the specific phosphorylation of one of its substrates, MYPT1, was significantly reduced in RPE/choroid complex of BIRKI injected rats compared to Vehicle rats ($p=0,028$). Moreover, a pimonidazole staining showed a significant reduction of retinal hypoxia in BIRKI rats compared to Vehicle ($p=0.004$). This result is consistent with the dilation of retinal vessel observed in BIRKI rats ($p=0.017$). The RPE morphology seems to be partially restored as well as its function as barrier, through quantification of cell size, cell shape and leakage. No signs of toxicity of BIRKI have been observed so far.

Conclusions: Our results are consistent with ROCK inhibition as an interesting new therapeutic concept for diabetic retinopathy. A single injection of BIRKI showed similar effects at 28 days than 3 consecutive injections of Fasudil at 48h. Further studies are needed to confirm that BIRKI would be a good candidate in the treatment of diabetic retinopathy, especially in regard of improvement of retinal vascular infusion and protection of the outer retinal barrier.

CONTROL ID: 3543925

SUBMITTER (NAME ONLY): Modesto Rojas

TITLE: Novel role of acyl-coenzyme A: cholesterol transferase (ACAT1) in ischemic retinopathy

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In cardiovascular disease CVD, ischemia increases the lipid load in macrophages, driving an inflammatory phenotype and promoting vascular damage. This process is poorly understood in ischemic retinopathy. Our studies in a model of oxygen-induced retinopathy have shown that macrophage activation during retinal neovascularization (RNV) is characterized by increased expression of the inflammation amplifiers TREM-1 (triggering receptor expressed on myeloid cells 1) and M-CSF (macrophage colony stimulator factor). Inhibition of TREM-1 reduces vascular injury and limits RNV. Here we examined upstream activators of the TREM1/MCSF pathway. In macrophages, ACAT1 esterifies LDL cholesterol (LDLc) with fatty acids to form cholesterol esters (CEs).

Methods: Wild-type and LDL receptor knockout mice were maintained in 75% oxygen from postnatal day 7 (P7) to P12 followed by normoxia until P17. Wild-type pups were treated with an ACAT inhibitor (N-[3-(4-hydroxyphenyl)-1-oxo-2-propenyl]-L-phenylalanine, methyl ester 10 mg/Kg, i.p) or vehicle (PBS) on alternate days from P7 to P16. The retinas were collected on P17 and prepared for immunofluorescence or western blot. Human macrophages were maintained in hypoxia (1% O₂) or normoxia (21% O₂) for 16 hrs, treated with the ACAT inhibitor (10µg/ml) or PBS, and prepared for western blot.

Results: Wild type mice showed significant increases in LDL receptor expression, lipid accumulation, and CE formation in areas of RNV along with increased expression of ACAT1, TREM-1, M-CSF, and VEGF (p<0.05). ACAT inhibitor treatment significantly abrogated those changes and reduced the areas of RNV and vaso-oblivation (p<0.05). LDL receptor knockout blocked RNV underscoring the role of LDLc metabolism in the pathology. In vitro, hypoxia-induced increases in expression of ACAT1, TREM-1, M-CSF and VEGF were prevented by ACAT inhibitor (p<0.05).

Conclusions: Hypoxia-induced increases in ACAT1 activity and CE formation are associated with upregulation of TREM-1, M-CSF, VEGF, LDLR and pathological RNV. Limiting the ACAT1 pathway offers a new therapeutic strategy for the treatment and prevention of vascular pathologies during ischemic retinopathy.

CONTROL ID: 3543926

SUBMITTER (NAME ONLY): archana jalligampala

TITLE: Rho 1-2 meganuclease, an allele-specific gene-editing therapy, rejuvenates rod photoreceptor structure and function in a pig model of autosomal dominant Retinitis Pigmentosa (adRP).

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. jalligampala, J. Noel, J.W. Fransen, W. Wang, M. Jabbar, N. Hasan, G. Pangeri, B. Sahu, M.A. McCall, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|N. Hasan, Biochemistry and Molecular Genetics, University of Louisville, Louisville, Kentucky, UNITED STATES|W. Lewis, J. Smith, V. Bartsevich, K. Viles, D. Jantz, Precision Biosciences Inc, Durham, North Carolina, UNITED STATES|M.A. McCall, Anatomical Sciences and Neurobiology, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: The P23H mutation in the rhodopsin (RHO) gene represents the most common form of adRP in North America. Elimination of the causative mutant allele, while leaving the wild-type (WT) allele intact should eliminate vision loss in adRP patients. To this end, we studied the efficacy of the engineered Meganuclease, Rho1-2, in the transgenic P23H human rhodopsin (TgP23H) pig model of adRP.

Methods: Rho1-2, packaged in a self-complementary AAV5 vector and driven by the GRK1 photoreceptor-specific promoter was delivered subretinally (40 ul) to one eye of TgP23H piglets postnatally (P3-7,n=23). The fellow eye served as a control and either was uninjected or injected with vehicle. The efficacy of 2×10^9 , 6×10^9 , 2×10^{10} , and 6×10^{10} vg were compared at regular post injection intervals. Fundus imaging and optical coherence tomography (OCT) assessed retinal structure. Full-field electroretinography (ffERG) assessed rod and cone function (ISCEV protocol). All pigs were assessed through P140 and a subset was assessed through P300. Immunohistochemistry/confocal assessed retinal morphology.

Results: From birth, untreated TgP23H pigs have no rod isolated ffERG response (Fernandez de Castro et al., IOVS, 2014). Regardless of dose, treatment with Rho1-2 was well tolerated, with no signs of an immune response. Treatment with two Rho1-2 doses (2 or 6×10^{10}) produced a significant rod isolated ffERG b-wave response as early as P60 (~ 14 uV; $p = 0.04$ and 0.0003) $n = 6$ and 12 pigs, respectively). Mean b-wave amplitudes increased at P120 (~ 25 - 30 uV; $p = 0.002$, <0.0001 respectively) and were maintained through P300. There is a strong correlation between rod isolated function and rod morphology. Rho1-2 treated Tg P23H rods are more numerous, have elongated outer segments, and correctly localized rhodopsin in contrast to untreated areas in the same retina or in untreated Tg retinas. The ONL measured in OCT and retinal sections was significantly thicker in the treated vs. untreated areas/retinas ($p < 0.001$).

Conclusions: Our results show that Rho1-2 meganuclease effectively rejuvenates rod structure and function in this TgP23H pig model of adRP and this gene therapy is well tolerated. This strongly indicates that Rho1-2 has the potential to effectively treat rod degeneration in P23H adRP patients

CONTROL ID: 3543928

SUBMITTER (NAME ONLY): Yash Shah

TITLE: A National Study of Open Globe Injuries in Pregnant Women and Non-Pregnant Women

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Shah, R. Malhotra, A. Uppuluri, P.D. Langer, N. Bhagat, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Open globe injury (OGI) is one of the leading causes of mono-ocular blindness in the world. The pregnant population is vulnerable to traumatic injuries especially to domestic violence and is far understudied in the literature in regard to the epidemiology of traumatic ocular injuries. In this study, we analyzed the differences in demographics and outcomes of OGIs in pregnant women and non-pregnant women.

Methods: The National Inpatient Sample was queried for diagnoses of OGIs from the years 2002 to 2014. The age was restricted inclusively between 15 to 45 and for the female gender. The status of pregnancy was recorded using built-in variables and ICD-9 codes. Descriptive statistical analysis using SPSS 25 was conducted with weighted data by the status of pregnancy. Demographics and outcomes were analyzed for both pregnant and non-pregnant groups.

Results: Pregnant women with OGI were younger in age compared to non-pregnant women (26.22 vs 29.93, $p<0.001$, Table 1), more likely to be Hispanic (29.0% vs 12.4%), more likely to be insured (87.4% vs 66.1%), and also more likely to use drugs (13.7% vs 6.3%, $p<0.001$). Pregnant women were less likely to have a “rupture” type of OGI (3.3% vs 14.6%, $p<0.001$, Table 2), but more likely to have a “penetrating without intraocular foreign body” type of OGI (78% vs 69.3%, $p=0.024$). Pregnant women were less likely to have a concurrent orbital floor fracture (0.0% vs 12.4%, $p<0.001$). Both groups underwent similar rates of surgical repair, but pregnant women were less likely to undergo an enucleation (0.0% vs 6.0%, $p=0.002$). Pregnant women had a higher mortality during the admission (3.3% vs 0.8%, $p=0.001$), but had shorter average duration of hospital stay (2.40 vs 4.31, $p<0.001$).

Conclusions: Pregnant women with OGIs have significantly different demographics compared to non-pregnant women with OGIs; they are more likely to be younger, be of Hispanic ethnicity and have a history of drug use. They were less likely to have a concurrent orbital floor fracture or undergo enucleation which may either suggest less severe injury or modified surgical management criteria to avoid general anesthesia related complications to the fetus. Further studies are needed to evaluate the circumstances of OGIs in pregnant women.

CONTROL ID: 3543929

SUBMITTER (NAME ONLY): Richard Foerster

TITLE: Autophagy inhibition-induced alterations of energy metabolism and fluorescence lifetime of the retinal pigment epithelium ex vivo

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Reduced autophagy function of retinal pigment epithelial (RPE) cells is suggested as one of the key factors in the pathogenesis of degenerative chorioretinal disorders, such as age-related macular degeneration. The purpose of this study is to investigate the energy metabolism of ex vivo RPE under the inhibitory condition of autophagy, and its correlation with its fluorescence lifetime (FLT) using fluorescence lifetime imaging ophthalmoscopy (FLIO).

Methods: Porcine ex-vivo RPE/choroid-explants were exposed to the autophagy inhibitor Bafilomycin A1 (1×10^{-8} M) for 24 h. The viability of the RPE cells was examined with a calcein test. The inhibitory effect of Bafilomycin A1 on autophagy was verified by measuring intracellular autophagosomes. To understand the influence of the autophagy inhibition on the energy metabolism of the RPE, the oxygen consumption rate (OCR) and extracellular acidification rate (ECAR) were measured by a Seahorse-XF-Analyzer after 24 h of Bafilomycin A1 incubation. The FLT of the RPE was examined by FLIO (excitation: 473 nm, detection in the short spectral channel (SSC): 498-560 nm and in the long spectral channel (LSC): 560-700 nm). In order to enable the FLIO on the tissues placed in a culture plate with culture medium, the horizontal stage and a 45-degree-angled mirror were built in front of the FLIO camera.

Results: Incubation of the explants with 1×10^{-8} M Bafilomycin A1 for 24 h did not cause increased cell death compared with the non-treated control group, whereas Bafilomycin A1 was proven to inhibit autophagy. The OCR of the treated tissue was significantly reduced (e.g., basal respiration from $220 \text{ pmol/min} \pm 43 \text{ pmol/min}$ to $147 \text{ pmol/min} \pm 62 \text{ pmol/min}$, $p < 0.05$). The ECAR, an indicator of the glycolytic activity was not significantly altered. In FLIO, Bafilomycin A1 significantly extended the FLT (mean FLT: τ_m) of the RPE by about 350 ps in both detection channels.

Conclusions: The results of the metabolic analysis clearly showed that the autophagy inhibition may induce mitochondrial dysfunction in RPE cells. In this study, it was experimentally demonstrated that FLIO may indicate alteration of mitochondrial function in RPE cells and could be utilized to assess it in clinical practice.

CONTROL ID: 3543930

SUBMITTER (NAME ONLY): David Le

TITLE: Quantitative optical coherence tomography reveals photoreceptor change in diabetic retinopathy

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Le, T. Son, X. Yao, Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|J.I. Lim, X. Yao, Department of Ophthalmology & Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Psychophysical and electrophysiological measurements have provided evidence for photoreceptor dysfunction in patients with diabetic retinopathy (DR). The purpose of this study is to conduct quantitative optical coherence tomography (OCT) analysis of outer retina, and thus to verify the feasibility of noninvasive OCT detection of photoreceptor abnormality in early DR.

Methods: OCT images were acquired from normal eyes, diabetic eyes with no diabetic retinopathy (no DR) and with mild DR. Nine quantitative features, including inner and outer retinal thicknesses, photoreceptor inner and outer segment bandwidths, reflectance intensities of the external limiting membrane (ELM), inner segment ellipsoid (ISe), and retinal pigment epithelium (RPE) were measured and intensity ratios of ELM/ISe and RPE/ISe were determined. Comparative parafoveal and perifoveal features (Figure 1a) were analyzed within retinal quadrants, i.e., superior, inferior, temporal, and nasal regions (Figure 1b). The quantitative features were determined using the averaged A-line reflectance intensities (Figure 1c).

Results: Outer retinal thickness was observed to have significant differences ($p < 0.05$) among the normal controls, no DR, and mild DR groups within the superior and inferior quadrants. Reflectance abnormalities of the ELM and ISe ($p < 0.05$) were observed within the temporal and nasal quadrants. Similarly, reflectance abnormality of the RPE was observed in the parafovea region of the nasal quadrant ($p < 0.05$). Comparative analysis consistently revealed decreased reflectance intensity of the ISe compared to that of the RPE, and the relative intensity ratio ISe/RPE discloses significant differences among the cohorts ($p < 0.001$) in the parafoveal region of all quadrants.

Conclusions: Quantitative OCT analysis consistently revealed outer retina changes in diabetic patients with no DR and with mild DR. The abnormalities of outer retinal thickness and OCT reflectance are retinal region/quadrant dependent. The normalized ISe/RPE measurement reveals retinal abnormalities in all quadrants, promising a sensitive biomarker for OCT detection of early DR.

CONTROL ID: 3543931

SUBMITTER (NAME ONLY): Gareth Hastings

TITLE: Modeling optical and visual image quality across the retina

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G.D. Hastings, A.J. Roorda, Center for Innovation in Vision and Optics, University of California Berkeley, Berkeley, California, UNITED STATES|G.D. Hastings, A.J. Roorda, School of Optometry and Vision Science Graduate Group, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We aimed to 1) create anatomically plausible individual eye models for cohorts of emmetropic and myopic eyes that define wavefront error (WFE) across the visual field and 2) apply neural anatomical weighting functions to those WFE to model visual performance.

Methods: Discretely measured WFE of 24 emmetropic (spherical equivalent (SE) +0.5 to -0.5D) and 18 myopic eyes (SE -1.5 to -3.5D) obtained from 4 laboratories (ranging ± 21 to $\pm 40^\circ$ horizontally and ± 16 to $\pm 25^\circ$ vertically around fixation) were used to optimize anatomical eye models in Zemax. Models comprised biconic anterior and posterior corneal surfaces, gradient refractive index lenses with aspheric surfaces, and aspheric retinas. All 27 anatomical parameters (including thicknesses, tilts, and translations) were constrained within typical norms from literature. Visual field angles were converted to mm of (aspheric) retina per eye.

Results: Of the 8 emmetropic and 3 myopic eyes completed to date (optimizing 27 parameters takes multiple days per eye), models accurately reproduced 2nd, 3rd, and 4th order input aberrations: mean \pm SD total RMS difference $0.237 \pm 0.166\mu\text{m}$ (4mm pupil). Foveal chromatic aberration of each model matched published population data to within 0.1D.

Mean field positions of best RMS WFE and Strehl ratio in emmetropic models were: RMS 1.4° and 0.3° ; Strehl 2.0° and 0.6° , in inferior and nasal fields respectively, which agreed closely with input data. Optical quality generally worsened monotonically with eccentricity in all directions from those peaks. Peripheral optical quality in myopic eyes depended on the form of modeled refractive corrections.

Degrees-to-mm factors were non-linear with eccentricity in each eye and varied with retinal curvature, asphericity, and nodal point position across eyes.

Relative cone- and mid-ganglion cell-weighted metrics mimicked experimental literature on detection and resolution as functions of eccentricity respectively.

Conclusions: Optical and visual (neurally-limited) image qualities across the retina are valuable in understanding onset and progression of ametropias as well as guiding development of wide-field head-mounted displays, ophthalmic corrections, and retinal imaging technologies. These models are more anatomically accurate than previous, they effectively return measured input WFE, allow continuous interpolation of WFE as a function of eccentricity, and represent mean samples and variability of typical eyes.

CONTROL ID: 3543934

SUBMITTER (NAME ONLY): Abinaya Priya Venkataraman

TITLE: Impact of peripheral optical errors in AMD and healthy eyes

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Venkataraman, L. Lundstrom, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN| A. Venkataraman, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|R. Rosen, A. Alarcon, C. Canovas, P. Piers, Johnson & Johnson Surgical Vision, NETHERLANDS|

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ABSTRACT BODY:

Purpose: People with advanced age-related macular degeneration (AMD) rely on their peripheral vision for many daily tasks where foveal vision is normally used. Sometimes magnification is used, but that comes at the cost of reduced visual field. Peripheral optical errors differ from central errors and can depend on factors such as the presence of an intraocular lens. In the current study, we evaluated the peripheral vision with naturally occurring average errors and a condition of larger errors on a group of AMD subjects as well as a control group.

Methods: High contrast grating resolution acuity and contrast sensitivity were evaluated in 11 control subjects with no ocular disorders and 9 AMD subjects. All measurements were performed monocularly at 20° nasal visual field. We tested 2 different optical conditions with an adaptive optics vision simulator designed for peripheral vision evaluations: 1) Simulated average phakic optical errors in 20° nasal visual field (-0.60 D spherical equivalent, -1.00 D cylinder with axis 90° and 0.09 µm horizontal coma for a 4 mm pupil); 2) larger errors in 20° nasal visual field (-1.20 D spherical equivalent, -2.90 D cylinder with axis 90° and 0.09 µm horizontal coma for a 4 mm pupil). The individual errors of the subjects were corrected. Contrast sensitivity (CS) was evaluated at 1 cycle/degree in the control subjects. For AMD subjects, only 6 subjects were able to perform the CS measurements and the CS was evaluated at a spatial frequency logarithmically midway between 1 cycle/degree and the resolution acuity cut-off.

Results: Reduced peripheral optical errors improved high contrast resolution significantly for both groups. The mean improvement was 0.08 and 0.16 logMAR in control and AMD, respectively. The CS was also significantly improved, with gains in control and AMD subjects of 0.29 and 0.39 logCS.

Conclusions: The average phakic peripheral optical error condition provides significantly better peripheral vision, with larger improvements in patients with AMD than in healthy eyes. Therefore, patients with AMD are likely to benefit more than healthy by controlling the peripheral optical errors, it may for example reduce the need of magnification.

CONTROL ID: 3543935

SUBMITTER (NAME ONLY): Tyler Miller

TITLE: Epidemiological Analysis of Causes of Ocular and Orbital Tissue Contusions Presenting to Emergency Departments Nationwide

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.T. Miller, J. Ong, S.J. Charles, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|K.K. Dansingani, Eye and Ear Institute, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular emergencies related to contusions of the eye & orbit often require immediate attention in the emergency department (ED). This study characterizes the circumstances and age distribution of patients with ocular contusions, highlighting common causes that may be prevented with proper eye protection.

Methods: A multi-year analysis of the CDC National Hospital Ambulatory Medical Care Survey (NHAMCS) database from 2011-2017 was conducted. We assessed the burden of contusions of the eye and orbit (ICD-9 921, ICD-10 S05) in the ED setting. Differences in variables across age groups were evaluated using logistic regression, controlling for potential confounders. All analyses were conducted using STATA 16 statistical software.

Results: We analyzed 166,395 emergency visits from 2011 to 2017. There were 297 contusions of the eye and orbit, representing 2,019,365 ocular contusions that had presented to EDs nationwide. Of these, roughly 17.8% were of unknown or not documented cause. The most common documented causes were striking against or accidentally struck by objects or persons (30.2% of injuries), assault (14.1%), falls on steps, level ground, or at sporting events (8.57%), firearm/labor/construction-related injuries (6.24%), and motor vehicle related injuries (5.13%). Injuries secondary to activities that warrant eye protection (firearm/labor/construction) made up a larger proportion of all injuries for adults aged 55-64 (27.7%) and children aged 5-11 (21.5%). Individuals aged 5-11 and 25-34 were 2.7 times ($p = 0.005$; 95% CI: 1.36 – 5.41) and 2.6 times ($p = 0.001$; 95% CI: 1.46-4.68), respectively, more likely to visit the ED with a contusion of eyeball and orbital tissues compared to adults who were 65 years and older (Figure 1). Comorbidities, including substance use, were not associated with injuries.

Conclusions: Contusions of the eye and orbit that present to the ED have a wide range of causes. Activities known to warrant eye protection were the 4th most common cause of ocular contusion. Older adults and children were most at risk for preventable injuries, possibly due to decreased visuospatial awareness, disregarding eye protection due to familiarity with occupational equipment, or being too young to acknowledge the importance of eye safety. Individuals of all ages could benefit from education on the importance of eye protection.

CONTROL ID: 3543938

SUBMITTER (NAME ONLY): Shyla McMurtry

TITLE: The accuracy of telemedicine screening compared to an ophthalmology follow-up appointment in an underserved community.

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. McMurtry, A. Hang, A. Husain, J. Jia, W. Kung, L. Cheng, J. Grachevskaya, J.D. Henderer, Y. Zhang, Ophthalmology, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, UNITED STATES|P. Kung, Ophthalmology, Stony Brook University Renaissance School of Medicine, Stony Brook, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fundus photography at primary care or internal medicine clinics can be utilized as a way to monitor patients for diabetic retinopathy (DR) without increasing the burden of care on the patient. Telemedicine screening should be accurate in diagnosing severity of DR to ensure only patients with appropriate disease severity get referred for treatment. We performed a retrospective chart review assessing the concordance between screening results and final diagnosis made at a follow-up ophthalmic appointment in patients who screened positive for DR.

Methods: 1902 adult patients were screened at general medicine clinics through Temple University Hospital (TUH) and Temple Physicians, Inc. (TPI) from March 2018 to March 2020. Technicians were trained to take 2-field non-dilated fundus photos at these clinics and screening photos were interpreted remotely by an optometrist using the ICDR classification system. Individuals with more than mild DR, other eye diseases, or ungradable images because of poor image quality were scheduled for a follow-up appointment with a TUH ophthalmologist for a dilated fundus exam. Screening results were compared to follow-up diagnosis using chi square analysis.

Results: 133 patients yielded a follow-up appointment and 85 patients had ungradable photos. For the 48 remaining patients, the correlation between screening results and final diagnosis showed mixed results (Table 1). Excluding unspecified DR, there was no correlation of the severity being the same or different upon follow-up ($\chi^2=8.95$, 0.34). 17 (35%) screening results had the same diagnosis upon follow-up, 17 (35%) had a decrease in severity, 3 (6%) had an increase in severity to PDR, and 11 (23%) were unspecified severity (Figure 1). The majority of differing severities decreased upon follow-up ($\chi^2=7.78$, 0.10).

Conclusions: Screening yielded identical or higher retinopathy severity scores compared to follow-up diagnosis. Overscoring screening photos can add referral visits and increase the anxiety of the patient, but does provide security that false-negatives are minimized. The level of disagreement and the presence of unspecified DR during screening indicates quality control issues that will need to be addressed.

CONTROL ID: 3543939

SUBMITTER (NAME ONLY): James Qiao

TITLE: Probiotic Bacterial Metabolite Inhibits Toll-Like Receptor 5 Agonist Induced Production of IL-6 by Human Corneal Epithelial Cells

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Qiao, M. Seu, Stritch School of Medicine, Loyola University Chicago, Maywood, Illinois, UNITED STATES|C.S. Bouchard, P. Bu, Department of Ophthalmology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) is a condition that currently affects over nine million people in the United States. This condition results in symptoms such as eye irritation, eye dryness, and pain in the eye. The pathogenesis of DED involves the production of proinflammatory cytokines (TNF α and IL-6) and one of the effective treatments is the use of anti-inflammatory agents. Probiotic bacteria are well known inhibitors of inflammation. The purpose of this study is to identify which Toll-like receptors (TLRs) contribute to the inflammatory response in human corneal epithelial cells (HCECs) and to determine whether the metabolites produced by *Lactobacillus fermentum* can suppress the activation of TLRs on HCECs to reduce inflammation.

Methods: SV40-immortalized HCECs were cultured in DMEM/F12 medium. HCECs were pretreated with a probiotic bacteria-derived metabolite (JE) produced by *Lactobacillus fermentum* and subsequently exposed to TLR4 agonist (LPS) or TLR5 agonists (flagellin from *Pseudomonas aeruginosa*). The inflammatory cytokine IL-6 within the culture supernatants was evaluated by ELISA.

Results: HCECs did not produce any IL-6 in response to LPS. In contrast, HCECs produced large amounts of IL-6 in response to TLR5 agonist flagellin from *Pseudomonas aeruginosa*. This data indicates that HCECs responded to TLRs differently. Probiotic bacteria-derived metabolite (JE) produced by *Lactobacillus fermentum* suppressed the TLR5 agonist-induced IL-6 production.

Conclusions: HCECs only responded to flagellin from *Pseudomonas aeruginosa* but not to LPS, indicating HCECs does not respond to all TLRs. The data suggests this is a possible innate mechanism to prevent ocular inflammation. The probiotic bacteria metabolite (JE) produced by *Lactobacillus fermentum* can suppress production of the inflammatory cytokine (IL-6) by HCECs. This data suggests that JE has a potential to be used as an anti-ocular inflammatory agent.

CONTROL ID: 3543940

SUBMITTER (NAME ONLY): Manuel Soliño

TITLE:

Expanding the view: large-scale assessment of synaptic disassembly in experimental glaucoma

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Soliño, A.K. Yu, L. Della Santina, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose:

As synapse loss is an early biomarker in experimental glaucoma, we studied the temporal dynamics of synapse disassembly in the entire inner plexiform layer (IPL) at varying time points after transient ocular hypertension.

Methods: Unilateral intraocular pressure elevation was induced in adult CD-1 mice by laser photocoagulation of the limbal and episcleral vessels, and then sacrificed at 7d, 14d, and 30d. Retinas were processed as wholemounts and stained by immunohistochemistry against Brn3a (ganglion cell marker), CtBP2 (ribbon marker), PSD95 (postsynaptic marker), and TO-PRO-3 (nuclear marker). Four confocal image stacks of the entire IPL depth of each retina were obtained. We quantified pre and postsynaptic puncta and their spatial relationships. Statistical analysis was performed using mixed effects analysis.

Results:

We found that ribbon density drops at 30d (Mixed-effects analysis, $p=0.001$). PSD95 density also drops, significantly at 14d and 30d (Mixed-effects analysis, $p=0.024$ and $p=0.018$, respectively). When assessing synaptic puncta density as a function of IPL depth, we found that ribbon density progressively drops at 14d and 30d at most IPL depths but density is preserved or recovers in the ON sublamina (Mixed-effects analysis, $p<0.0001$ for IPL depth and time as fixed effects). Conversely, when assessed as a function of IPL depth, postsynaptic proteins appear more resilient to transient ocular hypertension. The maximum decrease of PSD95 density occurs at 14d and partially recovers by 30d (Mixed-effects analysis, $p<0.0001$). Again, the ON sublamina shows less damage than the OFF sublamina (Mixed-effects analysis, $p<0.0001$).

Conclusions:

Although the initial site of injury in glaucomatous neurodegeneration is thought to be axonal compression at the optic nerve head, we show that bipolar cell ribbons are lost earlier and to a greater degree than their postsynaptic counterpart PSD95. This raises the possibility that bipolar cells are an active participant in the degeneration process. We also show that this process of synapse disassembly is non-uniform across IPL sublaminae, potentially resulting in differential impairment of distinct functional sub-circuits.

CONTROL ID: 3543941

SUBMITTER (NAME ONLY): Naomi Haque

TITLE: VEGFA165 Activation of PLVAP Expression Utilizes the p38-MAPK and AKT Signaling Pathways in Primary Human Retinal Endothelial Cells

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Haque, W.A. Dailey, K. Moyer, J. Felisky, A. Guzman, B. Patel, S. Elias, K.P. Mitton, Eye Research Institute, Oakland University, Rochester Hills, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elevation of total VEGFA165 and switching of VEGFA165b isoform expression to the VEGFA165a isoform have been reported in the aqueous and vitreous humors of eyes with diabetic retinopathy and ROP. VEGFA165a elevates the gene expression and protein concentration of Plasmalemma Vesicle-Associated Protein (PLVAP), a protein involved in transcytosis across the endothelial barrier. PLVAP regulation in primary Human Retinal Microvascular Endothelial Cells (HRMECs) is poorly understood. We hypothesize that both VEGFA165 isoforms increase permeability and PLVAP gene and protein expression in primary HRMECs, and AKT and p38-MAPK intracellular signaling pathways are involved in PLVAP gene expression in primary HRMECs.

Methods: Primary HRMECs (26 year old male) were cultured using EndoGRO-LS Complete Culture Media, in 6-well format for total RNA extraction. T-25 flasks were used for PLVAP immunoblotting. 24-well 0.4 μ M pore polyester transwell inserts with 70 kDa RITC dextran were used for transcellular permeability assays. Pharmacological inhibition of signaling pathways used MK2206 (AKT) and BIRB796 (p38-MAPK) inhibitors.

Results: VEGFA165a and VEGFA165b (5000 pM, saturating) increased PLVAP gene expression over 19-fold and 13-fold, respectively. VEGFA165a and VEGFA165b (5000 pM) increased PLVAP protein expression over 14-fold and 5-fold, respectively. AKT pathway inhibition (0.02 μ M MK2206) suppressed VEGFA165a or VEGFA165b -mediated increase of PLVAP gene expression by 51% and 54%, respectively. P38-MAPK pathway inhibition (0.01 μ M BIRB796) suppressed VEGFA165a or VEGFA165b -mediated increase of PLVAP gene expression by 63% and 58%, respectively. Double inhibition of the AKT and p38-MAPK pathways further suppressed VEGFA165a or VEGFA165b -mediated increase of PLVAP gene expression by 73% and 70%, respectively. VEGFA165a and VEGFA165b (5000 pM) increased transcellular permeability by 22% and 40%, respectively.

Conclusions: VEGFA165a was a stronger activator of PLVAP gene and protein expression relative to VEGFA165b. Differences between the effects of VEGFA165a and VEGFA165b on PLVAP gene and protein expression suggest that the reported isoform switching in retinal vascular diseases could contribute to disease mechanisms. Most of the VEGFA165-mediated increase to PLVAP gene expression involves the p38-MAPK and AKT pathways.

CONTROL ID: 3543943

SUBMITTER (NAME ONLY): Samuel Stratton

TITLE: Smartphone-based Fundus Photography for Remote Glaucoma Assessment in a Low-Resource Setting

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Stratton, University of New England College of Osteopathic Medicine, Biddeford, Maine, UNITED STATES|J. Luna, Asociación Salvadoreña Pro-Salud Rural, Santa Ana, EL SALVADOR|S. Roh, A. Alwreikat, Y. Jiang, P. Cotran, D.J. Ramsey, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|S. Roh, N. Shaikh, A. Alwreikat, Y. Jiang, P. Cotran, M. Bhardwaj, D.J. Ramsey, Ophthalmology, Lahey Hospital and Medical Center, Burlington, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: This investigation examines the effectiveness of smartphone-based, nonmydriatic fundus photography in detecting glaucoma in patients in a low-resource setting and explores the potential for this technology to serve as a means of primary screening for risk of glaucoma.

Methods: Subjects between the ages of 40 and 70 years old were recruited to undergo nonmydriatic fundus photography during a visual health campaign at the Salvadoran Association for the Promotion of Rural Health (ASAPROSAR) clinic in Santa Ana, El Salvador in January 2020. Color fundus photographs were obtained with a PanOptic iExaminer attached to an iPhone 6S operated by a trained non-specialist. Stereoscopic image pairs were assembled from two “best view” images for each eye. These were graded by a team of ophthalmologists and optometrists experienced in teleophthalmology who were blinded to the clinical diagnosis of each patient.

Results: A total of 273 participants were screened. Gradable images were obtained from 509 eyes (93.2%) in 268 participants (98.1%). A total of 5,744 images were collected, averaging 10.5 ± 5.2 images per eye. The cup-to-disc ratio (CDR) judged from the stereoscopic images showed moderate reliability and good agreement with the CDR reported by the treating ophthalmologists (ICC 0.59; $r = 0.792$, $p < 0.001$). Overall agreement was fair for glaucoma risk determined by remote grading of stereoscopic image pairs compared with the glaucoma-related diagnoses by ophthalmologists who examined the participants ($\kappa = 0.32 \pm 0.09$). Accuracy of screening for risk of glaucoma using only features of the optic disc observable in stereoscopic images was low (66.8%), with a positive predictive value of 45.1% and negative predictive value of 87.7%, compared with the results from clinical examination.

Conclusions: Remote evaluation by experts of CDR from optic disc photographs obtained by using a low-cost, handheld non-mydratic fundus camera operated by a non-specialist showed good agreement with CDR assessment from in-person clinical examinations. As expected from previous studies, the performance of CDR alone in detecting glaucoma was only fair. Nevertheless, the capacity to obtain high-quality fundus photographs and generate stereoscopic image pairs for remote evaluation by expert graders could permit development of an affordable, high-volume, glaucoma screening strategy in resource-constrained areas of the world.

CONTROL ID: 3543944

SUBMITTER (NAME ONLY): Prathibha Srikantan

TITLE: Head-mounted tablet device for reading and navigation in low vision

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Srikantan, R.A. Deffler, S. Cooley, G. Hopkins, B.E. Dougherty, The Ohio State University, Columbus, Ohio, UNITED STATES|H. McCullough, B. Henry, EduTechnologic, LLC, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Realwear HMT-1™ is a head mounted tablet device with a camera and a micro-display in use primarily for industry applications. The device may be useful for people with low vision with modification of some its features. The purpose of this study was to modify the HMT-1 to provide better low vision functionality, pilot test the modified device for reading with low vision, and test the usefulness of addition of real time kinematic (RTK) device data on improving indoor location accuracy for future navigation uses.

Methods: The HMT-1 consists of a video display mounted to an adjustable arm and a camera with magnification and image enhancing capability. A custom Android application (Industrial Badger App™) was used to increase magnification capability and allow for text-to-speech conversion of printed reading material. Visual acuity and contrast sensitivity were measured with habitual correction and with the HMT-1. A previously validated passage reading test (300 words per passage with 3 comprehension questions per passage) was used to assess speed and comprehension using: habitual aids, HMT-1 with magnification, and text-to-speech. Device location accuracy was tested at 8 indoor locations for the stock HMT-1 location provider and with the addition of RTK data, and GeoJSON centroids were calculated to compare location error between conditions.

Results: Three participants with low vision were recruited for pilot reading testing. Mean±SD age was 64±5 and 66% were male. Mean better-eye baseline ETDRS letter VA was 45±12 (approximately 20/120) and improved to 78±11 (approximately 20/25, (p<0.001). Mean passage reading time with habitual aid was 183 seconds vs. 457 seconds with HMT-1 camera (one subject was unable to use the camera due to poor VA). Comprehension performance was worse with HMT-1 camera compared to both habitual aid and HMT text to speech. All subjects reported the device to be useful and 2/3 of subjects reported they would use HMT-1 in real life. The addition of RTK data resulted in reduction of the average error of the cluster centroid from 60m to 38.4m and generally faster responses.

Conclusions: A modified version of the HMT-1 showed promise as an aid for near tasks in people with low vision, especially with reading and indoor navigation. Future work will seek to improve reading speed and location accuracy for navigation.

CONTROL ID: 3543947

SUBMITTER (NAME ONLY): Margaret O'Connell

TITLE: Longitudinal Changes in Microaneurysm Count and the Correlation with Leakage Index and Leakage Patterns in Diabetic Retinopathy on Ultra-widefield Fluorescein Angiography Following Intravitreal Aflibercept in the PRIME study

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To quantify longitudinal changes in microaneurysm (MA) count on ultra-widefield fluorescein angiography (UWFA) and their correlation with panretinal leakage index (PLI) in eyes with diabetic retinopathy (DR) being treated with as needed intravitreal aflibercept (IAI) guided by real-time DR severity score (DRSS) and PLI evaluations.

Methods: The PRIME study is a randomized prospective clinical trial comparing real-time DRSS-guided IAI treatment to real-time PLI-guided IAI treatment. 41 eyes with DRSS of 47 to 71 were randomized 1:1 to receive as needed IAI as determined by DRSS (DRSS cohort, n=21) or PLI (PLI cohort, n=20). UWFA and fundus photos were obtained monthly. UWFA images were analyzed in real-time with an automated analysis platform to quantify MA count and PLI with manual validation. Two trained readers evaluated the baseline UWFA images and classified them as having predominantly perivascular leakage or non-perivascular (including focal) leakage.

Results: Mean MA counts and PLI indices did not differ significantly at baseline between the DRSS cohort and the PLI cohort, with 839 ± 307 and 884 ± 331 MAs ($P=0.66$), respectively. At year 1, the MA count improved significantly to 662 ± 334 ($P=0.03$) in the DRSS cohort and 744 ± 526 ($P=0.05$) in the PLI cohort. Total mean MA and PLIs were positively correlated at both month six ($r=0.35$, $P=0.03$) and year one ($r=0.46$, $P=0.007$).

Eyes with predominant perivascular leakage (n=19) demonstrated a larger but non-significant reduction in mean MA

count (-210) compared to eyes with predominant non-perivascular leakage (n=14, -109, P=0.28).

Conclusions: Both DRSS and PLI cohorts demonstrated a significant decrease in MA count after one year of image-guided IAI treatment. Total mean MA count and total mean PLIs were correlated at month six and year one. Eyes with predominant perivascular leakage at baseline had a nonsignificant greater reduction in MA count. Further research in larger datasets is needed to further explore the potential association of MA reduction with underlying leakage patterns and whether this may be indicative of specific active pathways.

CONTROL ID: 3543949

SUBMITTER (NAME ONLY): Daniel Lee

TITLE: A Multi-Center Study Assessing Refractive Outcomes Following Uveitic Cataract Surgery

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Prior literature has reported that approximately 93% of eyes undergoing cataract surgery achieve a postoperative spherical equivalent (SE) within 1 Diopter (D) of that predicted by preoperative biometry (Lundstrom et al, 2018). While prior studies have assessed vision outcomes and postoperative complications following cataract surgery in patients with uveitis, less is known about refractive outcomes in this population. Our study assessed the refractive outcomes following uveitic cataract surgery and factors associated with deviations from the target refractive goal.

Methods: A multi-center retrospective chart review of patients with a history of uveitis undergoing cataract extraction was performed between June 2015 and June 2020. Subject demographics, ocular history, pre and postoperative examination findings, and biometry measurements were obtained. The difference between the refractive target and postoperative refractive SE was determined. We tested for association between a postoperative deviation from target greater than 1 D and several factors including age at the time of surgery, location of uveitis, presence of preoperative keratic precipitates or posterior synechiae, history of cystoid macular edema, preoperative logMAR acuity, and persistent inflammation one month postoperatively using t-tests or chi-square tests.

Results: We examined two hundred eighty-three eyes from 216 subjects. 40.6% of subjects had a refractive outcome which deviated more than 0.5 D from the refractive goal, and 13.4% of subjects deviated more than 1 D from the refractive target. The mean difference from refractive goal was 0.57 ± 0.68 D (range 0 – 4.54 D). The mean preoperative logMAR acuity for eyes >1 D from refractive goal was 0.21 greater than eyes < 1 D ($p=0.008$). Average age at time of cataract surgery was less for eyes >1 D from their refractive target (51.6 vs 59.0 years, $p=0.014$). The presence of preoperative keratic precipitates was also associated with a refractive outcome >1 D from the planned target ($p<0.001$).

Conclusions: A notable portion of eyes undergoing uveitic cataract surgery deviated from the planned refractive target by at least 1 D. Poorer preoperative acuity, younger age at the time of surgery and preoperative keratic precipitates were associated with this outcome.

CONTROL ID: 3543950

SUBMITTER (NAME ONLY): Hao Zhou

TITLE: Morphometric measurements of Bruch's membrane and choriocapillaris in eyes with Sorsby Macular Dystrophy using SS-OCTA

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zhou, Q. Zhang, K. chen, R.K. Wang, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|P. Iyer, Y. shi, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The extrapolated retinal pigment epithelium (eRPE)/Bruch's membrane (BM) complex undergoes alterations with aging and in disease. Despite the importance of the eRPE/BM complex, few quantitative studies have reported its in vivo morphology and how it changes with disease. We have developed an automated method to measure morphological features of the eRPE/BM complex using a commercially available swept source OCTA (SS-OCTA) system and studied the correlations between the BM and choriocapillaris (CC) flow deficits (FD) in eyes with Sorsby Macular Dystrophy (SMD).

Methods: 6×6 mm macular scans were acquired using SS-OCTA imaging (PLEX® Elite, Carl Zeiss Meditec Inc.) from a patient with SMD and age-matched normal subjects. Structural OCT cubes were converted into linear scales to obtain higher contrast at the RPE layer. The locations of the RPE and CC in each subfield were determined by OCT/OCTA A-scan intensity profiles, which were used for enface mapping of the eRPE-to-CC distances, that is equivalent to the BM thickness (Fig 1). RPE structure images were obtained by sum projection of selected OCT slab. CC enface images were generated from a 20-μm OCTA slab beneath BM and CC FDs were calculated using a previously validated thresholding method.

Results: A patient with Sorsby Macular Dystrophy and age-matched normal subjects were recruited. The locations of reticular pseudodrusen (RPD) were observed on a 20-μm thick enface structure slab positioned 20-μm above the RPE. The regional changes in the BM thickness were visualized on the enface eRPE-to-CC distance maps. We correlated an increase in the eRPE-to-CC distance and a decrease of CC flow in the regions with RPD in eyes with SMD (Fig 2).

Conclusions: Co-localization of RPD, thickened BM, and CC flow impairment were observed in eyes with Sorsby Macular Dystrophy. The proposed morphology metric should be useful to reveal more details of eRPE/BM complex, providing an opportunity to investigate potential functional relationships between the RPE, BM and CC, and their involvement in ocular diseases.

CONTROL ID: 3543951

SUBMITTER (NAME ONLY): Cassandra Hays

TITLE: Properties of multi-vesicular release from rod photoreceptors support transmission of single photon responses

SESSION TITLE: Inner retinal function

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Vision under starlight requires rod photoreceptors to transduce and transmit single photon responses to the visual system. This remarkable sensitivity depends on a small voltage change reliably reducing the rate of glutamate release such that it can be robustly detected by post-synaptic rod bipolar cells. Our goal was to identify how small voltage changes at the rod terminal alter the statistics of vesicle release and how these changes support the transmission of single-photon responses.

Methods: We characterized voltage-dependent properties of glutamate release in mouse rods by recording presynaptic glutamate transporter anion currents ($I_{A(glu)}$) in ex vivo retinas.

Results: Spontaneous vesicle release events at -70 mV were univesicular and occurred at random intervals (i.e., Poisson). However, when rods were voltage-clamped at their normal membrane potential in darkness of -40 mV, release occurred in coordinated multiquantal release events of ~17 vesicles. The rate of these multiquantal events was ~2 Hz and the interevent intervals were 2-to-3-fold more regular than predicted by Poisson statistics. These multiquantal events involved vesicles in the readily releasable pool and were triggered by opening of nearby, ribbon-associated Ca^{2+} channels. Applying a voltage waveform to mimic single photon voltage responses reduced the likelihood of multivesicular bursts nearly to zero with a rebound increase in release at stimulus offset. Simulations of release dynamics indicate that this regularly timed form of multivesicular release promotes the transmission of single photon responses to post-synaptic rod bipolar cells.

Conclusions: Regularly timed multivesicular release from rods provides an efficient means of encoding single photon responses, requiring fewer total vesicles to be released per-second than vesicle release governed by Poisson statistics.

CONTROL ID: 3543954

SUBMITTER (NAME ONLY): Deborah Villafranca-Baughman

TITLE: Glia-derived S100 β promotes pericyte-mediated capillary constriction and reduced blood flow in glaucomatous and ischemic retinas

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Villafranca-Baughman, A. Di Polo, Neuroscience, Universite de Montreal, Montreal, Quebec, CANADA|D. Villafranca-Baughman, L. Alarcon-Martinez, N. Belforte, F. Dotigny, A. Di Polo, Neuroscience, Centre Hospitalier de l'Universite de Montreal Centre de Recherche, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Pericytes are crucial for microvascular dynamics regulation and blood flow. Capillary constriction has been linked to calcium (Ca^{2+}) increase in pericytes; however, the mechanism of Ca^{2+} influx and its role on vascular deficits is currently unknown. The S100 calcium-binding protein B (S100 β), an important regulator of Ca^{2+} dynamics, is produced by astrocytes. Here, we asked: i) does retinal glia-derived S100 β contribute to Ca^{2+} increase in pericytes, and ii) does S100 β regulate pericyte-mediated capillary dysfunction after injury?

Methods: Two-photon laser scanning microscopy (TPLSM) was used to visualize pericytes in living mice expressing red fluorescence or the Ca^{2+} indicator GCaMP6 in pericytes (NG2-DsRed, NG2-GCaMP6). Capillary blood flow was quantified by TPLSM as red blood cells crossing a pre-fixed location per unit time. Ocular hypertension was induced by magnetic microbeads occlusion, and transient ischemia by ligation of the central retinal artery. S100 β expression was examined by immunostaining, western blots, and qPCR, and its function was modulated by intraocular injection of recombinant S100 β (gain-of-function) or a function-blocking antibody (FBA) (loss-of-function)

Results: S100 β levels increased in astrocytes and Müller glia in glaucomatous and ischemic retinas, which correlated with reduced capillary diameter and blood flow at pericyte locations, along with intrapericyte Ca^{2+} increase (12.6 ± 2 a.u.) relative to controls (5.3 ± 2 a.u.) (T-test, $p < 0.001$, $n = 6$ mice/group). Intraocular administration of recombinant S100 β further increased Ca^{2+} influx to pericytes and exacerbated blood flow impairment (T-test, $p < 0.001$, $n = 6$ mice/group). In contrast, selective inhibition of S100 β with a FBA decreased intrapericyte Ca^{2+} , reduced the number of capillary constrictions at pericyte locations, restored capillary diameter (FBA: $4.9 \pm 0.2 \mu\text{m}$, control: $5.17 \pm 0.2 \mu\text{m}$), and improved single-capillary blood flow (FBA: 0 red blood cell (RBC)/sec, control: 16 RBC/sec) (T-test, $p < 0.001$, $n = 6$ mice/group)

Conclusions: Our data support that: i) intrapericyte Ca^{2+} plays a critical role in the regulation of capillary diameter and blood flow in glaucomatous and ischemic optic neuropathies, and ii) retinal glia-derived S100 β is an important regulator of Ca^{2+} influx into pericytes, thus exerting a crucial regulation on microvascular dynamics in physiological and pathological conditions

CONTROL ID: 3543955

SUBMITTER (NAME ONLY): Georgia Kaidonis

TITLE: Cellular effects of a demethylating agent on normal human corneal endothelial cells

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There is increasing evidence that differential DNA methylation plays a significant role in ophthalmic diseases. We previously identified DNA methylation changes in the corneal endothelial tissue of patients with Fuchs endothelial corneal dystrophy (FECD), in particular the hypermethylation of genes related to FECD. 5-Aza-2-deoxycytidine (5-Aza-CdR) is a demethylating agent used to treat human cancers with aberrant DNA methylation. The purpose of this study is to better understand the cellular effects of 5-Aza-CdR on normal human corneal endothelial cells (CEnC).

Methods: Primary CEnC were cultured from a non-FECD cornea obtained from an eye bank and transformed CEnC (HCEnC-21T) were cultured as previously published. Cell cultures were treated with 0.3 mM 5-Aza-CdR or PBS control for 24 hours and assayed for cell viability using the Cell Counting Kit-8 (Dojindo). The Illumina Infinium HM450 BeadChip assay was used to perform global DNA methylation analysis of over 485,000 methylation sites. Statistical and array analyses were performed using R and p-values less than 0.05 were considered statistically significant.

Results: The global DNA methylation profiles of primary and immortalized (HCEnC-21T) normal human CEnC were compared using the Illumina Infinium HM450 BeadChip assay and similar global DNA methylation patterns were observed. HCEnC-21T cells were then treated with either 0.3 μ M 5-Aza-CdR or PBS (control) for 24 hours and cell viability, cell growth rate, and global DNA methylation status were measured. No significant difference in cell viability was found between 5-Aza-CdR and PBS-treated cells. At 10 days post-treatment, the cell doubling time peaked at 33 hours for 5-Aza-CdR-treated cells compared with 24 hours in PBS-treated cells. Global demethylation of methylated probes ($\beta > 0.6$) was not observed 5 days post-treatment (mean decrease in β value of 0.007), despite an effect on cell growth rate at this time-point. Baseline global DNA methylation levels displayed minimal change following 5-Aza-CdR treatment.

Conclusions: These findings show that 5-Aza-CdR does not induce significant cell toxicity or demethylation changes in normal human corneal endothelial cells. Further analyses of the demethylating effect of 5-Aza-CdR on CEnC from FECD patients with aberrant hypermethylation changes are needed to test its potential as an epigenetic therapy for FECD.

CONTROL ID: 3543958

SUBMITTER (NAME ONLY): Elfriede Friedmann

TITLE: Adult Neurogenesis in the retina originated in Müller Cells after loss of neurons

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Teleost fish have the special property of completely restoring their retina after an injury. More precisely, so-called Müller cells can reprogram their function and contribute to the reproduction of neurons similar to stem cells. It is not known how and how many neurons are produced. We develop a model that describes the development of the cell population following a loss of neurons in the retina. Our goal is to use current biological data to calibrate our model to be able to represent adult neurogenesis and a possible differentiation behavior.

Methods: Our model differs between Müller, progenitor and neuronal cells and we transfer the biological behavior of each cell type in a parameter dependent model resulting in a system of three ordinary differential equations. We take in account asymmetrical division, symmetrical differentiation and self-renewal. These processes are combined through parameters which are estimated with an in-house software. The fits were performed to a set of published measurements.

Results: We were able to show that the true parameter values are obtained by our fits with a 95% probability. This shows that our model depicts the regenerative process effectively. Analysis of the research data revealed that 5 cell divisions of progenitor cells are needed to make 279 neurons out of 9 Müller cells if we assume that 66% of the Müller cells re-entered the cell cycle after 36 hours.

Conclusions: With our model we were able to show a possible differentiation behavior of the progenitor cells which is still open and we gain a better understanding of the development of the cell populations involved in this process. This could lead to new regenerative treatments for the retina.

CONTROL ID: 3543965

SUBMITTER (NAME ONLY): Andrea García Llorca

TITLE: Age-related changes in retinal structure and function in mice with different Mitf mutations

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of this study was to examine age-related changes in the retina of mice carrying mutations in the microphthalmia-associated transcription factor (Mitf) and estimate the rate of retinal degeneration with age and how it affects function and structure in the retina.

Methods: Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} and Mitf^{mi-wh/Mitf^{mi}} mice were examined and compared to C57BL/6J mice as a control. Mice were examined at 1, 3, 6 and 12 months of age. Mice were anesthetized by an intraperitoneal injection of 40 mg/kg⁻¹ and 4 mg/kg⁻¹ Xylazine. Electroretinography (ERG) was used to determine retinal function, while fundus imaging and optical coherence tomography (OCT) were used for structural examination.

Results: ERG recordings revealed a slow degeneration in Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} mice compared to wild type. This applies to dark- and light adapted recordings at all ages. Results show no significant difference in ERG amplitude at one month of age between wild type and Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} mice but a difference in amplitude appeared at 6 months of age when Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} mice show higher amplitude in all cases. ERG responses could not be evoked in Mitf^{mi-wh/Mitf^{mi}} mice with no a- and b-waves in dark- and light-adapted recordings at all ages. Consistent with the ERG results, the retinal infrastructure of Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} mice showed all retinal layer's present in OCT images while Mitf^{mi-wh/Mitf^{mi}} images revealed severe degeneration.

Conclusions: These results suggest that Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} mice have normal retinal function while Mitf^{mi-wh/Mitf^{mi}} mice have severe degeneration and impaired retinal function when compared to the control. Changes in retinal structure appears with increasing age where some layers appear thicker in Mitf^{mi-enu22(398)/Mitf^{mi-enu22(398)}} but retinal degeneration increases in Mitf^{mi-wh/Mitf^{mi}} with age compared to the control, with some retinal layers absent.

CONTROL ID: 3543967

SUBMITTER (NAME ONLY): William McKee

TITLE: A test of a model for adding nerve fiber bundle trajectories to OCT retinal nerve fiber layer bundle (RNFL) probability/deviation maps from eyes with glaucomatous damage.

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.E. McKee, E. Tsamis, D. Weng, S. La Bruna, D.C. Hood, Psychology, Columbia University, New York, New York, UNITED STATES|C. De Moraes, D.C. Hood, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To test 3 methods of applying the mathematical model proposed by Jansonius et. al. [1] to optical coherence tomography (OCT) retinal nerve fiber layer bundle (RNFL) probability/deviation maps from eyes with glaucomatous damage.

Methods: Jansonius et al.'s mathematical model describes the trajectories of RNF bundles as a function of the origin (angular position) around the disc.[1] Individual variance in the degree of trajectory curvature for a given angular position around the disc is explained by the parameter beta in the model. A custom program was used to compute and superimpose the model's trajectories on RNFL probability and thickness maps for 18 eyes with well-defined arcuate damage as seen in the abnormal region of the RNFL probability map (Fig. 1).[2] For Method 1, trajectories were fitted to this region by manually varying beta and the associated region (AR) (red and blue vertical lines in Fig. 1) on the circle scan (Method 1, Fig.1A). For Method 2, a linear regression was performed to determine a relationship between beta and fovea-to-disc distance. Then, beta was automatically determined for each eye by the regression relationship, with AR manually adjusted for best fit. For Method 3, the average beta value [1] was used for all eyes, with AR manually adjusted for best fit. Trajectory fit was then examined across all eyes for average beta with AR set as the portion of the circle scan with thickness less than 5% of normal (Fig. 2).

Results: Using regression-based beta values (Method 2) did not out-perform using the average beta value (Method 3). While manually adjusting the beta (Method 1) gave the best agreement between the model and the data (as expected), the differences between its performance and Method 3 were relatively small (Fig. 1). Further, testing Method 3 by fixing the AR based upon the circumpapillary RNFL thickness (Fig. 2), produced reasonably good fits.

Conclusions: While manual determination of a separate beta for each eye performs best, implementing this method clinically is not practical. Fortunately, simply using the same beta value for all eyes did well enough for clinical use. Application of this model should improve both qualitative and quantitative evaluation of glaucomatous damage on OCT RNFL probability plots.[2] 1. Jansonius et al Exp Eye Res 2009, 2012; 2. Hood et al, JoG 2020.

CONTROL ID: 3543968

SUBMITTER (NAME ONLY): Pui-Chuen Hui

TITLE: Seeing through the Boston Keratoprosthesis: A detailed optical assessment with natural scene imaging and characterization of the resolving power.

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Hui, L.A. Pereira, E. Taniguchi, J. Chodosh, C.H. Dohlman, E.I. Paschalis, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|P. Hui, Materials Science and Engineering, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|L.A. Pereira, CAPES Foundation, Ministry of Education of Brazil, Brasilia, BRAZIL|S. Chen, R. Dore, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To visualize the image formation through the Boston Keratoprosthesis (B-KPro) and assess its optical properties.

Methods: We simulated the realistic natural-scene imaging condition by building an imaging cage system which subjected the B-KPro's posterior surface to an aqueous medium. Specifically, the B-KPro (back focal length: 17mm) was centrally clamped with a diaphragm and was mounted on a water-filled cuvette. Images formed by the B-KPro were then relayed to a camera with a pair of achromatic doublets (magnification: 1x). Targets including a standard eye chart and the natural scenes were imaged to assess the image quality and any presence of optical aberrations. Imaging of the 1951 USAF Resolution Test Target and a pinhole was also performed in air with a 10x telescope to evaluate the B-KPro's resolution efficiency and modulation transfer function (MTF).

Results: The 20/20 line of the eye chart could be adequately resolved. It remained in focus within a field angle of 3.8 degrees, which is well within the foveal area that confers 50-100% of the highest visual acuity. Images of the outdoor scene were similarly in focus in the central field but became defocused peripherally. However, the peripheral images could be refocused by adjusting the imaging distance of the B-KPro. This suggests the presence of spherical aberration that may be corrected by introducing an aspheric shape in B-KPro's optical surfaces. Finally, the spatial frequency resolution achieved by the B-KPro device was 146 line pairs per millimeter (lp/mm) in air at an MTF value of 0.2, which is higher than 25 lp/mm for a human eye with a 3mm aperture. Compared to the theoretical resolution of 290.7 lp/mm, the resolution efficiency was 66% which is sufficiently high according to the ISO11979-2 recommendation for intraocular lenses.

Conclusions: The B-KPro provides sufficient resolution power to achieve 20/20 vision over an angular field of view of 3.8 degrees, as elucidated by the natural-scene imaging and benchtop resolution characterization. Further improvement in the optical design may reduce the spherical aberration and expand the surgical margins for implantation decentration which may otherwise lead to vision degradation.

CONTROL ID: 3543971

SUBMITTER (NAME ONLY): Manmohan Singh

TITLE: Compression optical coherence micro-elastography of the cornea

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Singh, A. Nair, K. Larin, Biomedical Engineering, University of Houston, Houston, Texas, UNITED STATES|S. Aglyamov, Mechanical Engineering, University of Houston, Houston, Texas, UNITED STATES|K. Larin, Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Measuring the biomechanical properties of the cornea has become increasingly important to understand its health, detect disease, and evaluate therapies such as corneal collagen crosslinking (CXL). Here, we present a technique capable of mapping the stiffness of the cornea utilizing compression-based optical coherence micro-elastography of the cornea under various conditions, including before and after CXL in vivo.

Methods: A ring based piezoelectric transducer induced low amplitude ($< 5 \mu\text{m}$) displacements in the cornea, which were then converted to strain using a vector-based technique. Experiments were conducted in in situ rabbit corneas in the whole globe configuration ($N=3$) under various intraocular pressures (IOP) (10, 15, 20, 25, and 30 mmHg) and before and after CXL. The IOP was controlled with a closed-loop system, and CXL was performed using the traditional "Dresden" protocol. In these samples, stiffness was further quantified by dividing the difference in IOP between the loaded and unloaded states (ΔIOP) by the calculated strain. In vivo experiments were also conducted on an anesthetized rabbit before and after CXL to evaluate the feasibility of the technique for live imaging. Here, the only strain was quantified.

Results: In the in-situ samples, there was a significant difference in stiffness ($\Delta\text{IOP}/\text{Strain}$) as a function of IOP ($P = 0.037$), and the stiffness increased by ~86% after CXL ($P = 0.016$). The strain decreased by ~85% after CXL in the in vivo rabbit cornea, which was significant ($P < 0.001$).

Conclusions: Compression based optical coherence elastography of the cornea was able to detect the changes in corneal stiffness as a function of IOP and before and after CXL in an in situ as well in vivo rabbit cornea model. This technique may be useful for quantifying changes in corneal elasticity for disease detection or therapy monitoring.

CONTROL ID: 3543972

SUBMITTER (NAME ONLY): Patrick Staropoli

TITLE: Endophthalmitis Caused by Streptococcal Species: Clinical Outcomes and Antimicrobial Susceptibilities 2014-2019

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Staropoli, H.W. Flynn, D. Miller, P. Persad, E. Vanner, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Antibiotic resistance, prevalence, surgical management, and the role of virulence factors are topics frequently debated in the literature about streptococcal endophthalmitis. We performed a retrospective consecutive case series to report the clinical settings, antibiotic susceptibilities, and outcomes of this condition.

Methods: Chart review of culture-positive streptococcal endophthalmitis from January 1, 2014 to December 31, 2019. Thirty-eight eyes met study criteria. Mann-Whitney U, Fisher's exact test, and the exact chi-square test were used for statistical analysis.

Results: The most common clinical setting was post-glaucoma surgery (33.3%, 12/36). The most frequent isolate was *S. viridans* (63.2%, 24/38). Isolates were susceptible to vancomycin (100%, 36/36), ceftriaxone (100%, 28/28), and levofloxacin (100%, 36/36). Final BCVA was better than 20/200 in 24.1% (7/29) but 20/200 or worse in 75.9% (22/29). Enucleation was performed in 11.1% (4/36). A subset (n=11) of cases were evaluated for streptococcal-specific virulence factors: pneumolysin was present in 18.2% (2/11), autolysin in 45.5% (5/11), and hyaluronidase in 54.5% (6/11). Clinical settings, antibacterial susceptibilities, timing of PPV, and virulence factor presence were not associated with better visual outcome or enucleation rate ($p>0.05$).

Conclusions: Visual prognosis for streptococcal endophthalmitis is poor despite early and appropriate antibiotic treatment.

CONTROL ID: 3543978

SUBMITTER (NAME ONLY): Achuth Nair

TITLE: Heartbeat Optical Coherence Elastography: Using Heartbeat to Assess Corneal Biomechanical Properties

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nair, M. Singh, K. Larin, Department of Biomedical Engineering, University of Houston, Houston, Texas, UNITED STATES|S. Aglyamov, Department of Mechanical Engineering, University of Houston, Houston, Texas, UNITED STATES|S. Aglyamov, Department of Biomedical Engineering, The University of Texas at Austin, Austin, Texas, UNITED STATES|K. Larin, Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Assessment of corneal biomechanical properties is essential for detecting disease and monitoring corneal treatments. Optical coherence elastography (OCE) is a tool for measuring these mechanical properties, but assessment is typically performed by measuring the corneal response to some sort of external excitation. Here, we demonstrate how Heartbeat Optical Coherence Elastography (Hb-OCE) can be used to measure the cornea's mechanical response to the natural heartbeat-induced ocular pulse in the in vivo model.

Methods: An SD-OCT system in the common path configuration was used to measure the biomechanical properties of the cornea in two anesthetized rabbits. The first rabbit was kept as an untreated (UT) control, and the second had its cornea collagen crosslinked (CXL) using the standard Dresden protocol. OCT images were acquired at the apex of the applanated rabbit cornea while cardiac activity was measured concurrently. Corneal displacement over time was measured and translated to strain.

Results: Strain fluctuations in the UT cornea shown mirror the cardiac activity (~4Hz heart rate) of the rabbit. The untreated cornea had a mean strain amplitude over 12 cycles of 3.07 ± 0.48 mε, and the CXL cornea had a mean strain of 0.87 ± 0.19 mε. There was a statistically significant difference between the corneas in each group. ($p < 0.05$).

Conclusions: We demonstrate how Hb-OCE may be useful to measure the biomechanical properties of the cornea using heartbeat as a passive source of displacement. Furthermore, we show how this technique can distinguish the stiffness difference between UT and CXL corneas. Future work will be geared toward developing noncontact Hb-OCE with a quantitative model of stiffness.

CONTROL ID: 3543980

SUBMITTER (NAME ONLY): Donato Colantuono

TITLE: Multimodal imaging and clinical characteristics of peripapillary choroidal neovascularization in age-related macular degeneration.

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Colantuono, E.H. Souied, F. Amoroso, V. Capuano, A. Miere, Centre Hospitalier Intercommunal de Creteil, Creteil, Île-de-France, FRANCE|G. Querques, IRCCS Ospedale San Raffaele, Milano, Lombardia, ITALY|

Commercial Relationships Disclosure (Abstract): Donato Colantuono: Commercial Relationship: Code N (No Commercial Relationship) | Eric Souied: Commercial Relationship: Code N (No Commercial Relationship) | Francesca Amoroso: Commercial Relationship: Code N (No Commercial Relationship) | Vittorio Capuano: Commercial Relationship: Code N (No Commercial Relationship) | Giuseppe Querques: Commercial Relationship: Code N (No Commercial Relationship) | Alexandra Miere: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To analyze and describe the clinical and imaging characteristics of a series of patients with peripapillary choroidal neovascularization (PCN) in the context of age-related macular degeneration (AMD) and to investigate a possible relationship between PCN and the pachychoroid disease spectrum (PDS).

Methods: Case series of patients diagnosed with PCN in the Department of Ophthalmology of the Centre Hospitalier Intercommunal de Créteil between January 2000 and January 2018 were retrospectively included. Multimodal imaging, including OCTA (Plex Elite, Carl Zeiss Meditec, Inc., Dublin, CA) was obtained for all patients. Choroidal thickness (CT) was measured horizontally across the fovea and circumferentially around the temporal side of the disk to study its relationship to neovascularization. PCN morphology, area and vascular density were investigated in all cases.

Results: Thirty-five eyes of 26 patients with PCN were included in this study, of which 32 eyes (91.4%) had a focal or diffuse increase in CT, 35/35 eyes had pachyvessels (100%), 10 eyes of 35 (28.6%) had choroidal vascular hyperpermeability and 34 eyes of 35 (97.1%) showed vessel attenuation of the inner choroid. Twelve out of 35 (34.2%) developed peripapillary aneurismal type 1 neovascularization colocalizing with the PCN during follow up. OCTA revealed a densely packed high flow network in the ORCC slab in all cases. The mean PCN area averaged 3.56 mm² and the VD averaged 67.2%.

Conclusions: Analysis of choroidal structure, previously described in PDS, performed consistently when applied to our PCN series, thus supporting the hypothesis that PCN may be a distinct PDS variant.

CONTROL ID: 3543982

SUBMITTER (NAME ONLY): Jennifer Noel

TITLE: SPVN06, a Novel Mutation-Independent AAV-based Gene Therapy, Protects Cone Degeneration in a Pig Model of Retinitis Pigmentosa

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Noel, A. jalligampala, M.A. McCall, Ophthalmology and Visual Sciences, University of Louisville, Louisville, Kentucky, UNITED STATES|M. Marussig, P. VINOT, M. MARIE, M. Butler, F. LORGET, S. Boissel, Sparing Vision, Paris, FRANCE|T.D. Leveillard, J.A. Sahel, Institut de la vision, Paris, Île-de-France, FRANCE|J.A. Sahel, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|M.A. McCall, Anatomical Sciences and Neurobiology, University of Louisville, Louisville, Kentucky, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jennifer Noel: Commercial Relationship(s);Sparing Vision:Code F (Financial Support) | archana jalligampala: Commercial Relationship(s);Sparing Vision:Code F (Financial Support) | Myriam Marussig: Commercial Relationship(s);Sparing Vision:Code E (Employment);Sparing Vision:Code I (Personal Financial Interest);Sparing Vision:Code P (Patent) | Pierre-Axel VINOT: Commercial Relationship(s);Sparing Vision:Code I (Personal Financial Interest);Sparing Vision:Code E (Employment) | Melanie MARIE: Commercial Relationship(s);Sparing Vision:Code E (Employment) | Melanie Butler: Commercial Relationship(s);Sparing Vision:Code C (Consultant) | Florence LORGET: Commercial Relationship(s);Sparing Vision:Code E (Employment);Sparing Vision:Code I (Personal Financial Interest) | Stephane Boissel: Commercial Relationship(s);Sparing Vision:Code E (Employment);Sparing Vision:Code I (Personal Financial Interest) | Thierry Leveillard: Commercial Relationship(s);Sparing Vision:Code F (Financial Support);Sparing Vision:Code I (Personal Financial Interest);Sparing Vision:Code C (Consultant);Sparing Vision:Code P (Patent) | Jose Sahel: Commercial Relationship(s);Sparing Vision:Code I (Personal Financial Interest);Sparing Vision:Code P (Patent) | Maureen McCall: Commercial Relationship(s);Sparing Vision:Code F (Financial Support);Sparing Vision:Code C (Consultant)

ABSTRACT BODY:

Purpose: Rod-Cone dystrophies (RCD) are inherited neurodegenerative diseases characterized by an initial loss of rod photoreceptors (rods) followed by loss of cone photoreceptors (cones) eventually causing blindness. Over 1.5 million people worldwide are affected by RCD with ~65 genes identified. The NXNL1 gene encodes two proteins produced by rods, rod-derived cone viability factor (RdCVF) and its full-length isoform, thioredoxin RdCVFL, also expressed by cones, that support cone survival by promoting glycolysis and preventing oxidative damage, respectively. Delivery of RdCVF/L via adeno associated viral (AAV) vectors to the retina promote cone survival in RCD mouse models (Byrne et al., 2015, J. Clin. Invest.). We delivered SPVN06, a novel mutation-independent AAV-based drug candidate encoding both human RdCVF and RdCVFL sequences, in a large animal model of autosomal dominant retinitis pigmentosa (adRP), the transgenic P23H human rhodopsin (TgP23H hRho) pig, and evaluated cone survival.

Methods: Eight neonatal TgP23H hRho pigs received a unilateral subretinal injection of SPVN06 at 6.1E10 vg/eye (50 µL). We conducted regular ocular exams and fundus imaging to assess tolerability and retinal structure. Animals were euthanized 3 (n=4) or 6 months (n=4) post injection. Retinas were collected and processed for immunohistochemistry. Morphological differences in SPVN06-treated retinas vs control fellow eyes were assessed in the four animals euthanized 3 months post injection. Morphological analysis of 6 months post injection retinas are currently underway.

Results: Subretinal administration of SPVN06 is well tolerated. In three of the four animals, cone morphology is better preserved compared to the same area in the fellow, control eye within the area of treatment. Among those three animals, treated cones have significantly longer inner and outer segments (39%; p<0.05), and significantly more cones express medium-wavelength opsin (m-opsin; 90%).

Conclusions: In the TgP23H hRho model of human adRP, SPVN06 subretinal administration is well tolerated and preserves cone morphology and m-opsin expression. SPVN06 is expected to protect against cone degeneration in RCD patients independent of the causative mutation.

CONTROL ID: 3543984

SUBMITTER (NAME ONLY): Susmita Das

TITLE: Assessment of innate immune responses in Staphylococcus epidermidis endophthalmitis

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Das, S. Singh, A. Kumar, Ophthalmology, Visual and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coagulase-negative staphylococci (CONS), including Staphylococcus (S) epidermidis are responsible for 70% of all exogenous bacterial endophthalmitis. However, the pathogenesis of CONS endophthalmitis is limited epidemiologically and in clinical case reports; in part, this could be due to lack of suitable experimental models. Here, we developed a mouse model of S. epidermidis endophthalmitis and evaluated retinal innate immune responses. In vitro studies were also performed using cultured retinal and myeloid cells.

Methods: Endophthalmitis was induced by intravitreal injections of S. epidermidis and both dose-dependent and time-course studies were performed. Disease progression was monitored by an eye exam using slit-lamp microscopy and ERG analyses. Eyes were enucleated for enumeration of bacterial burden and assessment of inflammatory mediators using RT-PCR and ELISA assays. For in vitro studies, muller glial cells, retinal pigment epithelium and mouse bone marrow-derived macrophages (BMDM) were challenged with S. epidermidis and the expression levels of pro-inflammatory cytokines and chemokines were deduced at various time points post infection. The induction of inflammatory signaling was assessed by western blot.

Results: Our data showed that S. epidermidis was rapidly cleared from mice eyes and a relatively higher dose was needed to cause endophthalmitis. A time-course study revealed that bacterial load peaked at 24h post-infection followed by a gradual decline up to 72h. The production of inflammatory mediators followed a similar trend with reduced levels as bacterial burden decreased. In vitro studies showed differential expression of inflammatory mediators, with BMDM cells showing increased levels as compared to RPE and Muller glia. Western blot analyses revealed the induction of NF-kB and other MAPK (ERK and p38) signaling in S. epidermidis infected mice eyes and cultured cells.

Conclusions: S. epidermidis evoked innate immune responses in both mouse eyes and cultured cells. However, it did not cause severe endophthalmitis even when injected at a higher dose, indicating robust retinal innate immunity to efficiently clear CONS.

CONTROL ID: 3543985

SUBMITTER (NAME ONLY): Haven Roberts

TITLE: Differential Responses of Human Juxtacanalicular and Trabecular Meshwork Beam Cells to Mechanical Stretch

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Roberts, M.L. De Ieso, D.W. Stamer, Duke University, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Haven Roberts: Commercial Relationship: Code N (No Commercial Relationship) | Michael De Ieso: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Stamer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The contractility status of the trabecular meshwork (TM) plays a major role in the regulation of aqueous humor outflow resistance. However, the TM contains two morphologically different cell types, the endothelial-like cells that cover the beams and plates of the inner TM and the myofibroblast-like cells that reside in the Juxtacanalicular region. The purpose of this study was to determine the contractile responses of TM cell cultures having endothelial versus myofibroblast appearance.

Methods: TM cells from healthy and glaucomatous donors were isolated and categorized as predominately “beam” or “JCT” cultures based on morphology at confluence. Each strain was plated at confluence into wells of Collagen Type IV flex plates and cultured in 10% FBS for 3 days. Media was changed to 1% FBS 1 hour before stretch began. Plates were then stretched using the FlexCell FX5K Tension Stretch machine at 20% stretch (1 hertz) for 24 hours. Cell lysates were collected and subjected to SDS-PAGE, followed by western blotting for total and phosphorylated myosin light chain (MLC), a surrogate measure for cell contractility. Quantitative analysis of MLC expression was achieved using Image Lab software.

Results: JCT strains (n=3) responded to stretch with a $40\% \pm 24\%$ decrease in pMLC levels. Conversely, the mixed morphology (n=1) and beam (n=1) TM cell strains showed a 39% and 30% increase in pMLC, respectively under the same conditions. Notably, the glaucomatous TM strain, characterized as a primarily beam morphology, showed a 10% decrease in pMLC. Furthermore, we noted a pattern of morphological change from beam to JCT as cell culture passages increased.

Conclusions: Contractile responses to mechanical stress are opposite between beam TM and JCT cell strains, likely reflecting their different roles in conventional outflow homeostasis. Interestingly, a beam cell strain isolated from a glaucomatous donor eye behaved more like a JCT cell strain.

CONTROL ID: 3543990

SUBMITTER (NAME ONLY): Aaron Kho

TITLE: Age-related Bruch's membrane changes in the mouse retina imaged with visible light Optical Coherence Tomography

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Kho, T. Zhang, Biomedical Engineering, University of California Davis, Davis, California, UNITED STATES|V.J. Srinivasan, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|V.J. Srinivasan, Ophthalmology and Vision Science, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Aaron Kho: Commercial Relationship: Code N (No Commercial Relationship) | Tingwei Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Vivek Srinivasan: Commercial Relationship(s);Optovue Inc.:Code P (Patent)

ABSTRACT BODY:

Purpose: One of the earliest signs of age-related macular degeneration (AMD) is deposits in Bruch's membrane (BM). Thus far, BM thickening has only been studied in enucleated eyes ex vivo. Here, we show that visible light Optical Coherence Tomography (OCT) imaging can resolve BM and potentially observe age-related BM thickening in pigmented mice in vivo.

Methods: A custom spectral-domain visible light OCT ophthalmoscope was built for ultrahigh resolution in vivo mouse retinal imaging. The system had a theoretical axial resolution of 1 μm in tissue. We optimized spectrometer spectral resolution and applied spatially-dependent dispersion compensation to ensure that this resolution was achieved experimentally. Experiments were performed on 1.5 month old (n=2), 12 month old (n=2), and 18 month old (n=2) C57BL/6J mice. An incident power of 300 microwatts on the cornea and a line rate of 10 kHz were used. The imaged field-of-view was 1.44 mm (fast axis) by 0.12 mm (slow axis). Images were acquired within 2 mm of the optic disc. RPE multiply scattering tails were extrapolated and subtracted from axial intensity profiles to accurately estimate BM thickness.

Results: Exemplary images and preliminary analysis are shown in Fig. 1 and Fig. 2. The BM band was well-separated from the RPE band in all images (Fig. 1B-D). After subtraction of RPE multiply scattering tails to yield BM axial profiles, we noticed a slight BM thickening with age (Fig. 2D-F). Interestingly, due to RPE multiple scattering, lower visibility of BM does not translate to a thicker BM.

Conclusions: BM was visualized and quantified in vivo in highly pigmented mice of various ages with visible light OCT. This capability will enable studying BM changes with aging and ocular diseases.

CONTROL ID: 3543993

SUBMITTER (NAME ONLY): Jan Alder

TITLE: Detection of early microvascular changes in diabetic patients with OCTA

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Controversy exists whether optical coherence tomography angiography (OCTA) is able to detect preclinical retinal microvascular alterations in diabetic patients. We performed a cross-sectional analysis of the German Diabetes Study and analyzed type 1 and type 2 diabetic patients with regard to early changes in retinal vasculature.

Methods: In a cross-sectional analysis of the German Diabetes Study, the flow density of 74 diabetic and 52 control subjects in the macular region was analyzed by OCTA (Spectralis®, Heidelberg Engineering®) (10x10°, 512 A-scans, EDI mode, centered on the fovea centralis). After segmentation control, en face OCTA images of superficial (SVP), intermediate (IVP), and deep vascular plexus (DVP) were binarized in ImageJ using Otsu's thresholding method and flow density (proportion of white pixels to total pixel count) was calculated. Ultra-widefield fundus images were captured (Optos®, Optmap, Marlborough, MA, USA) and the stage of diabetic retinopathy was classified according to the International Clinical Diabetic Retinopathy Disease Severity Scale. Statistical analysis was performed using PROC MIXED (SAS, V 9.4, Cary, North Carolina, USA), age- and sex-adjusted.

Results: 47 patients with type 2 diabetes (T2DM) (32 male, age 58.6±11.9 (SD) years (Y), diabetes duration 6.9±2.8 Y), 27 patients with type 1 diabetes (T1DM) (14 male, 42.6±10.6 Y, diabetes duration 7.7±2.6 Y), and 52 control subjects (26 male, 42±15.6 Y) were evaluated. 1 subject from T2DM (2.1%) and T1DM (3.7%) showed mild nonproliferative diabetic retinopathy. The flow density for T2DM in SVP was 0.25±0.04, which was lower than in controls (0.28±0.04; p=0.0433). The other values for IVP (0.32±0.06) and DVP (0.33±0.05) did not differ from controls (IVP: 0.36±0.05; p=0.2365, DVP: 0.37±0.06; p=0.0507). The same was true for T1DM (SVP: 0.27±0.05; p=0.1760, IVP: 0.35±0.05; p=0.6661 and DVP: 0.36±0.06; p=0.2812). The decrease in flow density with age (per year of life: SVP: -0.00086, IVP -0.00163, DVP -0.00147, p each <.0001) was taken into account.

Conclusions: With similar duration of diabetes, T2DM, in contrast to T1DM, have lower flow density in SVP compared with controls. Accordingly, capillary vascular changes in T2DM are clearly detectable with OCTA even without DR. Overall, there is an age-dependent decrease in flow density, so future studies should always use age-adjusted data.

CONTROL ID: 3543995

SUBMITTER (NAME ONLY): Avinash Soundararajan

TITLE: Mechanistic Role of Clusterin in Extracellular Matrix remodeling and Intraocular Pressure Homeostasis

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Soundararajan, P.P. Pattabiraman, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Avinash Soundararajan: Commercial Relationship: Code N (No Commercial Relationship) | Padmanabhan Pattabiraman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is a primary risk factor for glaucoma. IOP homeostasis relies on the regulation of aqueous outflow through trabecular meshwork (TM). ECM accumulation in TM elevates IOP. Clusterin, a secretory stress response chaperone protein, has been reported to regulate cell-matrix interactions. Studies have shown a putative linkage between clusterin and primary open angle glaucoma pathogenesis. We aim to study the- 1) effect of stressors known to increase IOP on clusterin expression in TM, 2) understand the role of clusterin in ECM remodeling, and 3) effect of loss of clusterin on IOP.

Methods: Using qPCR and immunoblotting, we studied the effects of - A) CTGF, Endothelin, Dexamethasone, TGF β 2, elevated pressure on clusterin expression, B) adenovirus-induced clusterin expression (AdCLU) on ECM, pro-fibrotic proteins, and ECM regulatory matrix metalloproteinases (MMPs) activity using zymography, C) recombinant clusterin (rhCLU) on TGF β 2-induced fibrosis and ECM accumulation, in vitro. TM cells were transfected with expression clones Clusterin-RFP-GFP (CLU-RG) or Signal peptide-RFP-GFP (SP-RG), followed by live cell imaging post TGF β 2 treatment. IOP was measured in clusterin knockout (Clu^{-/-}) mice by tonometry. Student's t-test was used for statistical analyses and results were significant if $p < 0.05$ with a sample size of $n = 3-7$ per experiment.

Results: AdCLU significantly decreased ECM mRNAs and proteins including, Collagen 1A ($n = 3$, $p = 0.04$) and fibronectin ($n = 3$, $p = 0.01$), Elastin ($n = 3$, $p = 0.05$), whereas MMP2 expression was increased. CTGF ($n = 3$, $p = 0.006$), Endothelin ($n = 3$, $p = 0.05$), TGF β 2 ($n = 3$, $p = 0.04$) and Pressure stress ($n = 4$, $p = 0.04$) significantly reduced clusterin protein expression. rhCLU attenuated significantly the effects of TGF β 2 on ECM proteins- COL1A ($n = 3$, $p = 0.01$), Fibronectin ($n = 3$, $p = 0.05$). TM cells transfected with CLU-RG showed decrease in clusterin availability under TGF β 2 treatment. Clu^{-/-} mice demonstrated an age-dependent elevation in IOP with significant increase at postnatal day 90 compared to wild type ($n = 7$, $p = 0.03$).

Conclusions: Our novel finding demonstrates the role of clusterin on ECM remodeling and loss of clusterin function elevates IOP signifying the importance of clusterin in IOP homeostasis. Further studies on the signaling events of clusterin-mediated ECM remodeling and IOP changes can help us identify novel IOP lowering therapies.

CONTROL ID: 3543996

SUBMITTER (NAME ONLY): Alessandro Iannaccone

TITLE: Auditory and olfactory findings from the Rate of Progression of USH2A-related Retinal Degeneration (RUSH2A) study

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Iannaccone, Duke University, Durham, North Carolina, UNITED STATES|C.C. Brewer, National Institute on Deafness and Other Communication Disorders, Bethesda, Maryland, UNITED STATES|J.L. Duncan, University of California San Francisco, San Francisco, California, UNITED STATES|P. Cheng, A. Ayala, Jaeb Centre for Health Research, Tampa, Florida, UNITED STATES|M.G. Maguire, R.L. Doty, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|I. Audo, Institut de la vision, Paris, Île-de-France, FRANCE|P.S. Bernstein, University of Utah Health, Salt Lake City, Utah, UNITED STATES|G.M. Bidelman, The University of Memphis, Memphis, Tennessee, UNITED STATES|J.K. Cheetham, T. Durham, Foundation Fighting Blindness Inc, Columbia, Maryland, UNITED STATES|R.B. Hufnagel, W.M. Zein, National Eye Institute, Bethesda, Maryland, UNITED STATES|M.H. Myers, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: While sensorineural hearing loss (SNHL) is a characteristic of Usher syndrome type 2 (USH2), less is known about SNHL in USH2A-associated non-syndromic autosomal recessive retinitis pigmentosa (ARRP) and olfaction in USH2A-associated retinal degeneration. We investigate SNHL and olfaction in patients with USH2A-related disease using cross-sectional baseline data collected in a multicenter natural history study.

Methods: The Rate of Progression of USH2A-related Retinal Degeneration (RUSH2A) study enrolled 127 participants, 80 USH2 and 47 ARRP (male/female = 59/68, 113 White). Hearing was measured by pure-tone thresholds and word recognition score, and olfaction by the University of Pennsylvania Smell Identification Test (UPSIT). Associations of participant characteristics with SNHL and UPSIT scores were assessed by linear regression models. Correlation of UPSIT scores with different visual measures were assessed by Spearman correlation coefficients. UPSIT scores were also compared to historical healthy control subjects of similar age and gender.

Results: SNHL was moderate in 72% of USH2 participants and severe or profound in 25%, while 9% of ARRP participants had moderate adult-onset sensorineural hearing loss. Pure-tone thresholds increased (worsened) with age in ARRP ($p < 0.001$) but not in USH2 participants ($p = 0.46$). The degree of SNHL was not significantly associated with gender, race/ethnicity or smoking status. Among 14 USH2 participants reporting newborn hearing screening results, 7 reported passing. Among RUSH2A participants, 7% had mild microsmia and 5% had moderate or severe microsmia; however, their mean (\pm SD) UPSIT score was 35 (± 3), similar to healthy controls [34 (± 3); $p = 0.39$]. Smell function differed by country ($p = 0.02$), but was not significantly associated with clinical diagnosis, age, gender, race/ethnicity, smoking status, visual measures, or hearing function.

Conclusions: Hearing loss in USH2A-related USH2 did not increase with age. ARRP patients do not appear to be at risk for significant hearing loss beyond that associated with aging. Newborn hearing screening did not identify all USH2-related hearing loss. Olfaction was not significantly worse than normal in participants with USH2A-related retinal degeneration. Pathogenic variants in USH2A variably affect auditory hair cells but have no significant impact on olfaction.

CONTROL ID: 3543997

SUBMITTER (NAME ONLY): Wang Jui-Kai

TITLE: Differentiation of Papilledema from Non-Arteritic Anterior Ischemic Optic Neuropathy (NAION) using 2D Image-Based Features and 3D Deep-Learning-Based Shape Features in Color Fundus Photographs

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Previous studies have shown that optical coherence tomography (OCT) can help differentiate papilledema from NAION based on peripapillary 2D/3D structural and morphological features (Miller et al., ARVO 2018, Wang et al., ARVO 2020). However, OCT is not always available (e.g., in the emergency room and primary care settings). To overcome this limitation, in this study, we focus on the automated differentiation in more available 2D color fundus images and include novel use of deep-learning-based 3D morphological features.

Methods: Using 102 OCT and fundus image pairs (51 papilledema and 51 NAION subjects; severity matched by the optic-nerve-head [ONH] volume measured in OCT) from the University of Iowa, a feature pyramid neural network was trained to estimate the OCT-like thickness maps from the color fundus photographs (Fig. 1A). Based on these 102 estimated thickness maps, seven statistical shape models were built using principal component analysis (PCA) covering 90% of the shape variance (Fig. 1B). Then, for each input fundus image, the corresponding seven 3D shape measures were computed. Meanwhile, 12 features based on the image intensity, 12 features based on a segmented vessel map, 24 features based on the image texture analysis, and six regional peripapillary volumetric measures were also computed (Fig. 2) for a total of 61 features. A random forest classifier was used to classify papilledema/NAION cases using leave-one-subject-out validation.

Results: When the random forest classifier considered the entire feature set (feature importance of 61 features are shown in Fig. 2), the classification accuracy was 84% (44/51: papilledema; 42/51: NAION). Without considering the 3D features (i.e., the 48 pure 2D image-based features), the accuracy dropped to 80% (42/51: papilledema; 40/51: NAION).

Conclusions: Deep-learning-based OCT-like thickness maps make retinal 3D structural and morphological analysis possible in 2D color fundus photographs, which is beneficial for differentiating papilledema from NAION when OCT is not available.

CONTROL ID: 3543998

SUBMITTER (NAME ONLY): Niranjan Pandey

TITLE: AXT107 an Inhibitor of Neovascularization, Vascular Leakage, and Inflammation, Is Well-Tolerated and Could Potentially Be Dosed Once a Year to Treat Retinal Vascular Diseases

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pandey, AsclepiX Therapeutics, Baltimore, Maryland, UNITED STATES|N. Pandey, Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Niranjan Pandey: Commercial Relationship(s);AsclepiX Therapeutics:Code E (Employment)

ABSTRACT BODY:

Purpose: To assess the safety and pharmacokinetics (PK) of AXT107, a synthetic 20-mer peptide that blocks VEGF receptor 2 and activates Tie2, in preclinical studies.

Methods: Safety, PK, and ocular tissue distribution of 100, 250, 500, and 1000 µg of AXT107 injected intravitreally were tested in rabbit and minipig. GLP safety was studied over 9 months and PK and ocular tissue distribution were tested in rabbit and minipig for 15 months and 9 months respectively. Mass spectrometry was used to quantify AXT107 in plasma, aqueous humor, vitreous humor, retina, and choroid-RPE

Results: AXT107 was well tolerated in rabbit and minipig for 9 months after a single intravitreal administration of all doses of AXT107 in GLP studies. No increase in intraocular pressure, no inflammation, and no changes in ERG were observed throughout the 9-month period in both species. Within a few minutes of administration of a liquid formulation of AXT107, it formed a gel, whose size and appearance were dose-dependent, in the vitreous. The gel was compact and remained below the visual axis over the observation period. AXT107 was quantifiable in the gel by mass spectrometry and found to decrease over the duration of the study in both species. AXT107 was found at efficacious levels on the retina and choroid-RPE and at low levels in the bulk vitreous, and below levels of quantitation (BLQ) in the aqueous humor and other ocular tissues. AXT107 levels were also BLQ in plasma over the duration of the studies in both species. The levels of AXT107 in the retina and choroid were comparable at all doses of AXT107 tested. The half-life of the gel in the vitreous was found to be about 180 days.

Conclusions: Multiple doses of a single injection of AXT107 injected intravitreally were found to be safe and well-tolerated in GLP safety studies over 9-months in two species. PK and ocular distribution studies in rabbit and minipig showed that AXT107 formed a gel upon intravitreal injection that stayed below the visual axis releasing AXT107 slowly over the course of the study with a half-life of 180 days. The released AXT107 was found to be present at efficacious levels in the retina and choroidal tissues. These studies suggest that AXT107 is safe for intravitreal injection and support potentially once a year dosing in the clinic.

CONTROL ID: 3544000

SUBMITTER (NAME ONLY): Eric Tang

TITLE: Point-scanning optimization for video-rate volumetric intraoperative OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Tang, Y. Tao, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Eric Tang: Commercial Relationship: Code N (No Commercial Relationship) | Yuankai Tao: Commercial Relationship(s);Leica Microsystems:Code R (Recipient);Vanderbilt University:Code P (Patent)

ABSTRACT BODY:

Purpose: Galvanometer scanner response fundamentally limits optical coherence tomography (OCT) imaging performance. Scanning nonlinearities distort anatomic features and reduce image quality/resolution; and underdamped impulse response increases mirror settling duration and total acquisition time. Here, we present hardware and software scanner response optimizations and demonstrate benefits for video-rate volumetric intraoperative OCT.

Methods: Scanners (Saturn 5B, ScannerMax) were optimized iteratively using servo tuning parameters. A Gaussian process regression (GPR) model of step responses was developed and used to identify optimal tunings (Fig. 1). Improved imaging performance was validated using a custom 400 kHz swept-source OCT system and custom volumetric scan waveforms (Fig. 2).

Results: Mirror settling time was reduced by 39-58% and 17-58% for the slow- and fast-axis mirrors, respectively, over default tunings (Fig. 1(d),(e)). OCT volumes were acquired of 25G forceps at 16 Hz volume rate with 2560x250x50 pix. and 250 return lines (Fig. 2(a),(c)-(f)) and at 20 Hz volume rate with 2560x400x50 pix. and 0 return lines (Fig. 2(b),(g)-(j)). Scanner tuning optimization increased the number of linearly sampled lines by 12-101% (Fig. 2(f) vs. Fig. 2(c)-(e)) and by 18-72% (Fig. 2(j) vs. Fig. 2(g)-(i)) over default tunings for each scan waveform. Removing return lines increased the number of linearly sampled lines by 33-64% for all tunings (Fig. 2(g)-(j) vs. Fig. 2(c)-(f)).

Conclusions: The combination of hardware and software optimizations significantly increased both volume acquisition speed and linear field-of-view of volumetric OCT. These optimizations can benefit intraoperative OCT by improving the response of the scanners and minimizing image distortions during video-rate volumetric imaging of surgical dynamics.

CONTROL ID: 3544002

SUBMITTER (NAME ONLY): Ting Wang

TITLE: Inactivation of the Transcription Factor Sterol Regulatory Element Binding Protein (SREBP) Lowers Intraocular Pressure

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Wang, P.P. Pattabiraman, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|J. Rabinowitz, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ting Wang: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Rabinowitz: Commercial Relationship: Code N (No Commercial Relationship) | Padmanabhan Pattabiraman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Trabecular meshwork (TM) biomechanics is important in regulating aqueous humor (AH) drainage and intraocular pressure (IOP). This study aims at understanding the role of activation and inhibition of the transcription factor SREBP which is the master regulator of lipid biogenesis on the regulation of TM extracellular matrix (ECM) content via the modulation of lipid synthesis.

Methods: Quantitative-polymerase chain reaction (qPCR), immunofluorescence, immunoblot were performed on human TM (HTM) cells and porcine TM (PTM) cells in culture to assess - 1) expression of transcript variants of sterol regulatory-element binding protein (SREBP) and SREBP cleavage- activating protein (SCAP), and 2) effects of SREBP activation via clozapine, inhibition of SREBP-SCAP complex via fatostatin on - SREBP activation, regulation of ECM like fibronectin (FN), collagen (Col1A) in TM, SREBP target genes expression related to lipid biogenesis. Porcine anterior segment perfusion cultures were used to assess the effects of SREBP activation and inhibition on IOP changes. Student's t-test and two-way ANOVA were used for statistical analyses and results were significant if $p < 0.05$ with a sample size of $n = 3-5$.

Results: Transcript variants of SREBP-F1V1, V2, V3, and -F2V1 and SCAP were expressed in HTM and PTM cells. Activation of SREBP by clozapine significantly increased IOP ($p = 0.0440$, $n = 5$) after 17h clozapine perfusion. Clozapine treatment on HTM cells increased FN and Col1A fibril formation. Perfusion with fatostatin lowered IOP. HTM cells treated with fatostatin decreased ECM distribution and reduced gene expression of SREBP1, SREBP2, and their target genes involved in fatty acids, triglycerides, and cholesterol biosynthesis. Interestingly, we found a significant decrease in acetyl-CoA carboxylase (ACC) and low density lipoprotein receptor (LDLR) genes ($p = 0.0001$, $n = 3$).

Conclusions: Our study identifies that modulating SREBP alters TM lipids and IOP. Of significance is the decrease in ACC which catalyzes the carboxylation of acetyl-CoA into malonyl-CoA, a rate-limiting step in fatty acid biosynthesis. Acetyl-CoA metabolism is implicated in primary open-angle glaucoma and ACC1 regulates ECM turnover and tissue fibrosis. Future studies on SREBP in TM will identify the potential regulation of membrane properties, AH outflow resistance, and novel therapeutics.

CONTROL ID: 3544007

SUBMITTER (NAME ONLY): David Miller

TITLE: Enhancing visible-light optical coherence tomography image quality for mouse retinal nerve fiber analysis

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Miller, H. Zhang, Biomedical Engineering, Northwestern University Robert R McCormick School of Engineering and Applied Science, Evanston, Illinois, UNITED STATES|M. Grannonico, M. Liu, X. Liu, Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|X. Liu, Psychology, University of Virginia, Charlottesville, Virginia, UNITED STATES|H. Zhang, Ophthalmology, Northwestern University, Evanston, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): David Miller: Commercial Relationship: Code N (No Commercial Relationship) | Marta Grannonico: Commercial Relationship: Code N (No Commercial Relationship) | Mingna Liu: Commercial Relationship: Code N (No Commercial Relationship) | Xiaorong Liu: Commercial Relationship: Code N (No Commercial Relationship) | Hao Zhang: Commercial Relationship(s);Opticent Health:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Our recent studies on visible-light optical coherence tomography (vis-OCT) make it possible to assess optic neuropathy progression in vivo based on retinal ganglion cell (RGC) axon bundle size. However, accurate quantification of these structures by vis-OCT is complicated by speckle noise. We thus implemented two techniques, temporal speckle averaging (TSA) and a novel resampling technique, to improve the visualization of RGC axon bundles in fibergrams and B-scans.

Methods: TSA images were acquired from an anesthetized C57BL/6 mouse using vis-OCT. We positioned the optic nerve head (ONH) in one corner of the field of view (FOV) and acquired 5 OCTA volumes consisting of 512 A-lines×512 B-scans with each B-scan repeated 5 times. We repeated this acquisition process with the ONH in each corner of the FOV. A single OCTA volume produced a fibergram, averaged five times, and an unaveraged angiogram. All fibergrams and angiograms at each location were registered and averaged using non-rigid demon registration. Speckle reduced circular scans were reconstructed from 4 rectangular OCT volumes acquired with the ONH positioned in each corner of the FOV. For each volume, an 11 pixel-thick (~15 µm) ring with a 400 µm radius centered on the ONH was plotted. A-lines located along the ring were sorted as a function of angle and averaged within 0.1° sectors to produce a speckle reduced B-scan (SRB-scan).

Results: Fig. 1a shows a montaged fibergram after TSA. Compared to before (Figs. 1b-c), the fibergram and angiogram after TSA (Figs. 1d-e) show smoother structures with greater contrast. RGC axon bundle contrast to noise ratio (CNR) increased 1.5 dB after TSA. Compared to the traditional scan (Fig. 2(a)), individual RGC axon bundles are visible in the SRB-scan (Fig. 2(b)). RGC axon bundle CNR increased 2.4 dB using our novel resampling method.

Conclusions: The combined TSA and resampling greatly enhanced visualization of RGC axon bundles in fibergram and B-scan images, enabling more accurate bundle size analysis.

CONTROL ID: 3544008

SUBMITTER (NAME ONLY): Jingyi Gao

TITLE: Subtype-specific ipRGC survival and visual behavioral changes in an experimental mouse model of glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gao, E. Griner, M. Liu, I. Provencio, X. Liu, Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|I. Provencio, X. Liu, Ophthalmology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jingyi Gao: Commercial Relationship: Code N (No Commercial Relationship) | Erin Griner: Commercial Relationship: Code N (No Commercial Relationship) | Mingna Liu: Commercial Relationship: Code N (No Commercial Relationship) | Ignacio Provencio: Commercial Relationship: Code N (No Commercial Relationship) | Xiaorong Liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is the second major cause of blindness worldwide and is characterized by the loss of the retinal ganglion cells (RGC) which convey visual information from the retina to the brain. More than 40 subtypes of RGCs have been identified and studies suggest that their susceptibility to insults differ. In particular, one type of retinal ganglion cells, intrinsically photosensitive retinal ganglion cells (ipRGC), has been shown to be relatively resistant to damage in glaucoma and similar injuries. ipRGCs consist of 6 subtypes, M1-M6, each one projecting to different brain areas and involved in distinct functions such as circadian entrainment, the pupillary light reflex, image forming vision, etc. Accordingly, it is important to determine the correlation between the loss of particular ipRGCs subtypes and behavioral deficits such as circadian dysfunction and vision loss. Such information will provide important insights to address the pathologies of glaucoma patients.

Methods: In this study, we used laser photocoagulation of the trabecular meshwork of the eyes to induce chronic ocular hypertension (OHT). Visual acuity and contrast sensitivity of the animals were measured by the optomotor test. We also assessed circadian rhythmicity and photoentrainment in these mice through the progression of the disease. Finally, retinas were dissected, immunostained for RGC subtypes, and flatmounted for confocal imaging. We quantified the survival of RGCs and ipRGC subtypes in mice with chronic OHT.

Results: We found that ipRGCs are more resistant to the ocular hypertension insult than the general RGC population. Moreover, the survival of ipRGCs depends on subtypes. Specifically, M1 and M2 cells survived better than M4s. Though the contrast sensitivity and visual acuity of the OHT group dropped significantly, circadian rhythmicity and photoentrainment were barely disrupted.

Conclusions: Our results suggest the circadian behaviors were relatively well maintained with glaucoma progression, which is correlated with the survival of ipRGCs. Future studies are needed to dissect out the neural circuit and its underlying mechanisms.

CONTROL ID: 3544009

SUBMITTER (NAME ONLY): Shwetha Mangalesh

TITLE: Association between maternal and perinatal systemic factors and macular optical coherence tomography characteristics in preterm infants at 36 weeks postmenstrual age

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mangalesh, N. Sarin, V. Tai, X. Chen, N. Younge, C.M. Cotten, S. Michalak, L. Vajzovic, C.A. Toth, Duke University, Durham, North Carolina, UNITED STATES|B. McGeehan, G. Ying, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|L. Shen, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Shwetha Mangalesh: Commercial Relationship: Code N (No Commercial Relationship) | Neeru Sarin: Commercial Relationship: Code N (No Commercial Relationship) | Brendan McGeehan: Commercial Relationship: Code N (No Commercial Relationship) | Vincent Tai: Commercial Relationship: Code N (No Commercial Relationship) | Liangbo Shen: Commercial Relationship: Code N (No Commercial Relationship) | Xi Chen: Commercial Relationship: Code N (No Commercial Relationship) | Noelle Younge: Commercial Relationship: Code N (No Commercial Relationship) | C. Cotten: Commercial Relationship: Code N (No Commercial Relationship) | Suzanne Michalak: Commercial Relationship: Code N (No Commercial Relationship) | Lejla Vajzovic: Commercial Relationship: Code N (No Commercial Relationship) | Gui-Shuang Ying: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Toth: Commercial Relationship(s);Duke University:Code P (Patent);Alcon:Code R (Recipient);Hemosonics:Code R (Recipient);Theia Imaging, LLC:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: To investigate the associations between maternal and perinatal systemic health factors and macular optical coherence tomography (OCT) characteristics in preterm infants at 36 weeks postmenstrual age (PMA).

Methods: We included 85 infants enrolled under STudy of Eye imaging in Preterm infantS (BabySTEPS, NCT02887157) with parental consent for research and OCT imaging at 36±1 weeks PMA. We evaluated associations between maternal and perinatal systemic factors and, vitreous pathologies, macular edema, and the following layer thicknesses at the foveal center and 1000µm nasal to the fovea: total retina, combined retinal nerve fiber layer (RNFL), ganglion cell layer (GCL) and inner plexiform layer (IPL), inner nuclear layer (INL), and outer retina. We averaged the thicknesses of the right and left eyes for all infants and tested the associations using multivariable regression models.

Results: Infants with lower gestational ages had thicker foveal RNFL+GCL+IPL (estimate=-4.76µm, 95% confidence interval=-6.12, -3.37; p=<0.001) and those with intracranial hemorrhage/periventricular leukomalacia/ventriculomegaly (n=30) had thinner RNFL+GCL+IPL at 1000µm nasal from fovea (mean± standard deviation = 124±3 versus 134±2µm, 0.004). Infants with septicemia/necrotizing enterocolitis (NEC) (n=16) had a significantly thicker outer retina (110±7 vs. 79±3µm, p=<0.001) and total retina (316±27 vs. 222±13µm, p=0.002) at the fovea and thicker INL (98±7 vs. 76±3µm, p=0.006) at 1000µm nasal from fovea. These associations remained statistically significant after adjusting for confounding variables such as gestational age.

Conclusions: Lower gestational age and intracranial hemorrhage/periventricular leukomalacia/ventriculomegaly independently impact inner retinal layers other than the INL. Parafoveal INL devoid of distorting cystoid spaces, and outer and total retinal thicknesses at the foveal center are affected by septicemia/NEC. Our study highlights the variable effects of different systemic health on preterm retina, independent of prematurity related birth factors.

CONTROL ID: 3544010

SUBMITTER (NAME ONLY): Shirin Hassan

TITLE: Comparing the Street-Crossing Performance of Subjects with Simulated AMD against Patients with Real AMD

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Hassan, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Shirin Hassan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously developed a method of simulating a central scotoma, as found in age-related macular degeneration (AMD), using centrally-opaque contact lenses (CLs). The aim of this study was to determine how realistic our AMD simulation was of real AMD by comparing the street-crossing decision-making performance of subjects with real AMD to those with simulated AMD using our simulation tool.

Methods: Street-crossing decisions along a non-signalized, one-way street were collected in 17 AMD subjects with a scotoma, 34 AMD subjects without a scotoma and 20 normally-sighted subjects wearing centrally-opaque CLs that induced a central scotoma. Subjects observed approaching traffic for a two second period after which they reported whether or not they believed that the vehicular gap time was long enough to afford a safe crossing. When subjects indicated that they would cross when the measured vehicular gap time was shorter in duration than their actual crossing time, this was considered an unsafe decision. When subjects indicated that they would not cross when the measured vehicular gap time was longer in duration than their actual crossing time, this was considered a missed decision. For each subject, the percentage of unsafe (%unsafe) and missed (%missed) decisions were calculated. A generalized linear mixed model with binary logistic function, repeated measures for subject and a covariate to adjust for age differences was used to determine if the %unsafe and %missed decisions changed as a function of subject group (AMD with a scotoma versus AMD with no scotoma versus simulated AMD with a scotoma).

Results: The simulated AMD subjects made as many %unsafe and %missed decisions as those with real AMD with a scotoma ($p=0.98$ and $p=0.66$ for %unsafe and %missed, respectively) and without a scotoma ($p=0.19$ and $p=0.13$ for %unsafe and %missed, respectively). While those AMD subjects with no scotoma made as many %missed decisions as AMD subjects with a scotoma ($p=0.26$), they did have a tendency to make more %unsafe decisions ($p=0.09$).

Conclusions: Our method of AMD simulation appears to mimic the street-crossing decision-making performance of people with real AMD. This simulation tool may therefore be beneficial to future studies assessing the functional performance of people with AMD.

CONTROL ID: 3544011

SUBMITTER (NAME ONLY): MONSURAH SALAMI

TITLE: Evaluation of Masked Associated Dry Eyes using AS-OCT Tear Meniscus Parameters and OSDI Scores

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.O. SALAMI, S. Bains, S. Shankar, R. Thangarajah, E. Sogbesan, Ophthalmology, McMaster University, Hamilton, Ontario, CANADA|

Commercial Relationships Disclosure (Abstract): MONSURAH SALAMI: Commercial Relationship: Code N (No Commercial Relationship) | Sharnjit Bains: Commercial Relationship: Code N (No Commercial Relationship) | Sushmitha Shankar: Commercial Relationship: Code N (No Commercial Relationship) | Rishi Thangarajah: Commercial Relationship: Code N (No Commercial Relationship) | Enitan Sogbesan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study is to determine the effect of prolonged use of a surgical mask on tear meniscus parameters using anterior segment ocular coherence tomography (AS-OCT) and Ocular Surface Disease Index (OSDI) score amongst healthcare workers during the COVID-19 pandemic.

Methods: Fifty healthcare workers from St. Joseph's Healthcare Hamilton in the Hamilton Regional Eye Institute Department, Hamilton, Ontario participated in the study. All participants completed OSDI Questionnaire and provided demographics data. Participants had an average of three AS-OCT imaging of the tear meniscus (TM) at baseline and 8hrs later, after their regular shift. During this 8hr period, participants were required to wear medical masks continuously throughout their shift. Data was analyzed using SPSS V27.

Results: Participants' (n = 50) mean age was 38.9 ± 12.9 years; 22.0% were male and 78.0% were female. Of these participants, 62.0% wear spectacles and 28.0% wear contact lens. 54.4% of participants (n = 100 eyes) had normal OSDI scores of <12, 34.0% had mild OSDI scores, 4.0% had moderate OSDI scores, 8.0% had severe OSDI scores. Baseline mean AS-OCT TM height was $385.4 \pm 172.6 \mu\text{m}$ and mean TM area was $46,496.7 \pm 41,875.5 \mu\text{m}^2$; after 8 hours shift the parameters reduced to mean TM height of $296.6 \pm 99.9 \mu\text{m}$ and mean TM area of $28,187.8 \pm 18,761.3 \mu\text{m}^2$. With the resultant mean TM height and area difference of $88.8 \pm 142.8 \mu\text{m}$ ($p < 0.001$) and $18,308.9 \pm 35,901.9 \mu\text{m}^2$ ($p < 0.001$), respectively. Participants had a mean reduction in tear meniscus parameters in left eye (TM height: $90.1 \pm 149.3 \mu\text{m}$ and TM area: $18,290.9 \pm 39,538.78 \mu\text{m}^2$) and right eye (TM height: $87.5 \pm 137.5 \mu\text{m}$ and TM area: $18,326.9 \pm 32,262.7 \mu\text{m}^2$), regardless of OSDI scores and significance between the left and right eye (Area Difference $p = 0.996$; TMH Difference $p = 0.927$).

Conclusions: This study shows that prolonged use of medical mask especially during COVID-19 may reduce tear meniscus parameters. There was a 23.0% reduction in tear meniscus height and 39.4% reduction in tear meniscus area compared to the initial parameters, regardless of the presence of OSDI scores.

CONTROL ID: 3544014

SUBMITTER (NAME ONLY): Nathan Fisher

TITLE: Ophthalmic Procedure Training During COVID-19: Virtual and In-Person Training of the Suprachoroidal Injection Procedure

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Fisher, S. Hancock, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nathan Fisher: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment) | Shelley Hancock: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment) | Thomas Ciulla: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: The purpose of this analysis was to evaluate virtual and in-person training modalities to educate retinal specialists and other ophthalmology professionals on suprachoroidal injection with the SCS Microinjector®. Significant travel and site visitation restrictions associated with the COVID-19 pandemic required that alternative virtual methodologies be developed to continue training when traditionally utilized in-person, wet lab instruction was not permitted.

Methods: Trainees for the suprachoroidal injection procedure included retina physician-investigators participating in clinical trials and non-physicians, including medical science liaisons and other ophthalmology professionals. Both training modalities included a review of a short film on the procedure, a slide review of key procedural steps, and practice injections with a custom-designed synthetic eye, moderated by a certified trainer providing live feedback. Virtual training was conducted via teleconference; both trainee and trainer connected via webcam and audio connection, with all supplies mailed prior to training. Following completion of training, a follow-up survey was sent to every trainee. Trainees were asked about training component preferences and confidence to perform the procedure on a 5-point Likert scale.

Results: A total of 31 trainees completed the survey following suprachoroidal injection training, including 21 physicians and 10 non-physicians. A total of 12 training sessions were completed virtually and 19 were completed in person. Physicians reported an average confidence to perform the procedure of 4.8 (range 4-5), while non-physicians reported an average of 4.2 (range 3-5), although non-physician trainees will not be performing the procedures in patients. Across all groups, the most useful component of training was the hands-on wet lab with the synthetic eye (71%) followed by the live trainer feedback and Q&A (26%). Nearly two-thirds of trainees felt that the training was comprehensive and no additional training elements were required.

Conclusions: Among trainees who completed virtual or in person training on the suprachoroidal injections, physician trainees felt highly confident to perform the procedure with patients. Training experience with a synthetic eye model and live feedback should be incorporated into training curriculums, whether virtual or in person.

CONTROL ID: 3544015

SUBMITTER (NAME ONLY): Elsayed Elbasiony

TITLE: Mast cells directly activate corneal allograft-primed T cells

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Elbasiony, S. Mittal, W. Cho, S. Chauhan, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Elsayed Elbasiony: Commercial Relationship: Code N (No Commercial Relationship) | Sharad Mittal: Commercial Relationship: Code N (No Commercial Relationship) | WonKyung Cho: Commercial Relationship: Code N (No Commercial Relationship) | Sunil Chauhan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously reported that inhibition of mast cell activation prolongs corneal graft survival following transplantation. The purpose of the current study is to investigate whether mast cells directly activate T cells to secrete IFN γ , a critical inflammatory molecule for their effector function.

Methods: Single-cell suspensions of corneal tissue and peritoneal lavage were prepared to evaluate levels of major histocompatibility complex II (MHC II) expression (Mean Fluorescent Intensity; MFI) on Fc ϵ R1⁺cKit⁺ mast cells using flow cytometry. Bone marrow cells were harvested from femurs and tibias of balb/c mice and cultured for 3-4 weeks in the presence of IL-3 (10 ng/ml) and SCF (50 ng/ml) to generate bone marrow mast cells. Alloprimed CD4⁺ T cells were sorted from the draining lymphoid tissues of C57BL/6 transplant recipients (grafted with Balb/c corneas) using flow cytometry. To evaluate the effect of mast cells on T cell stimulation, purified C57BL/6 CD4⁺ T cells were cultured with balb/c mast cells. Co-cultures of alloprimed CD4⁺T cells and antigen-presenting cells (APCs; CD90.2- from balb/c splenocytes) served as a positive control. Intracellular expression of IFN γ by CD4⁺ T cells was assessed after 48 hours using flow cytometry.

Results: A high expression of MHC II was observed in mast cells harvested from ocular tissues (P<0.001) peritoneal fluid (P<0.001) and bone marrow (P<0.05), compared to isotype controls. Furthermore, mast cells upregulated MHC II expression by 2-fold following IFN γ stimulation (100 ng/ml), compared to unstimulated controls (P<0.05). Alloprimed CD4⁺T cells co-cultured with mast cells showed an approximate 3.5 fold increase in the expression of IFN γ , compared to T cells cultured alone (P<0.05). Similarly, allogenic APCs induced a 2-fold increase in the expression of IFN γ by CD4⁺ T cells (P<0.03), which was comparable to allogenic mast cells mediated T cell activation.

Conclusions: Our data demonstrate that mast cells express antigen-presenting molecule, MHC II, and directly activate alloprimed T cells to secrete their signature molecule, IFN γ .

CONTROL ID: 3544016

SUBMITTER (NAME ONLY): Gopa Kumar Gopinadhan Nair

TITLE: Exosome Mediated Reactive Retinal Gliosis in the Development of Proliferative Vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Gopinadhan Nair, J.S. Hocker, D. Pollalis, S. Lee, Ophthalmology, Dean McGee Eye Institute, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|S. Lee, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Gopa Kumar Gopinadhan Nair: Commercial Relationship: Code N (No Commercial Relationship) | James Randolph Hocker: Commercial Relationship: Code N (No Commercial Relationship) | Dimitrios Pollalis: Commercial Relationship: Code N (No Commercial Relationship) | Sun Young Lee: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We have previously reported that elevated levels of GFAP and vimentin in the vitreous humor (VH) from patients with proliferative vitreoretinopathy (PVR) were significantly correlated with PVR severity. To explore how intracellular structural proteins such as GFAP and vimentin, hallmarks of reactive gliosis, were released into the VH during the development of PVR, we performed proteome analysis of exosomes isolated from VH in PVR patients.

Methods: Exosomes were isolated from undiluted VH from patients with PVR (N=4), Macular hole (MH; N=5), or epiretinal membrane (ERM; N=5) using differential ultracentrifugation. We confirmed their size, morphology, and exosome markers using nanoparticle tracking analysis (NTA), transmission electron microscopy (TEM), and an exosome detection antibody array. Tryptic fragment sequencing of exosome contained proteins was performed using liquid chromatography tandem mass spectrometry (LC-MS/MS) and a Thermo Lumos Fusion tribrid Orbitrap mass spectrometer. The pathway analysis of MS data was performed using Ingenuity Pathway Analysis (IPA).

Results: We recovered a range of $1.5\text{--}4.0 \times 10^9$ exosomes per vitreous sample (500 μL), characterized by their size (peak ~ 131 nm), morphology, and positive exosome markers including FLOT1, ICAM, ALIX, EpCAM, ANXA5, TSG101, CD81 and CD63 (Figure 1). We observed a large pool of GFAP and vimentin in VH of PVR patients was contained in the vitreal exosomes. We also identified 627 proteins from vitreal exosomes (533, 431, and 318 in PVR, MH, and ERM, respectively). Of the 94 exosomal proteins related to “reactive gliosis” and “gliosis of retina,” 42 (45%) exosomal proteins were only present in PVR (Figure 2A). The gliosis-related exosomal proteins in PVR were also connected with key pathways related to PVR development, including inflammation, epithelial-mesenchymal transition, tissue healing, cellular proliferation, and growth of connective tissue (Figure 2B).

Conclusions: Our results suggest that vimentin and GFAP were released into the VH in a controlled fashion by exosomes in association with PVR development and the exosome mediated reactive gliosis may play a key role in PVR formation.

CONTROL ID: 3544018

SUBMITTER (NAME ONLY): lucas quagliato

TITLE: Psychological impairment in neurophthalmologic patients before/during the COVID-19 pandemic-Comparative study with retina patients

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.B. quagliato, Retina, Instituto Penido Burnier, Campinas, SP, BRAZIL|P. Dechichi, V.A. Filho, T.V. Batistel, M.D. Pacheco, G.A. Beckedorff, Instituto Penido Burnier, Campinas, SP, BRAZIL|E.B. Quagliato, Neurology, Particular Clinic, Campinas, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: Assess the presence of anxiety, depression and stress in a group of patients with neuro-ophthalmic disorders, before and during COVID-19 pandemia and compare to a group of patients with retinopathies. Evaluate the relation between visual loss and symptoms intensity in both groups.

Methods: Cross-sectional study with a questionnaire evaluating the relation between psychological characteristics of neuro-ophth. and retinal diseases patients (Depression, Anxiety and Stress Scales-DASS-21) in 16 patients of each group. The neuro-ophthalmic patients were assessed before and during COVID-19 pandemia. The clinical data were collected by chart review and analyzed through the same application.

Results: Within the 16 neuro-ophthalmic patients (12 women/4 men), 10 presented optical neuritis, 4 NAION, 1 Ischemic Stroke and 1 Devic disease. The evaluation before COVID-19 pandemia showed 12 (75%) with depression, 13 (81%) with anxiety and 8 (50%) with stress.

During COVID-19 pandemia the results were the same in 12 patients, one patient presented less anxiety levels and 2 increased stress levels. One patient did not answer.

Within the 16 retinal disease patients (6 women/10 men), 7 presented Diabetic Retinopathy, 6 AMD, and 3 Retinal Detachment. Evaluation showed 12 (75%) with depression, 14 (87,5%) with anxiety and 8 (50%) with stress.

VISUAL ACUITY IN THE AFFECTED EYE AND PSYCHIC SYMPTOMS – NEURO OPTH. PATIENTS

100% of patients (3) with visual acuity(VA) <20/40 in the affected eye presented very severe depression, anxiety and stress.

77% (13) of patients with VA >20/40 in the affected eye 10(80%) presented mild to very severe symptoms.

RETINOPATHY GROUP

13 patients with VA <20/40 in the affected eye, 12(92,3%) presented mild to very severe symptoms.

3 patients with VA >20/40 in the affected eye, 2(66,6%) not presented any symptom and the other presented mild anxiety and depression.

Conclusions: 81.2% of neuro-ophthalmic patients presented symptoms of depression, anxiety and/or stress. There was no differences between the scores before/during the COVID-19 pandemia in this group. Among the retinal disease patients 81,2% presented symptoms of depression, anxiety and/or stress, like neuro-ophthalmic patients. There is a correlation between low visual acuity and the presence of anxiety, stress and depression in both groups, more evident in neuro-phthalmological patients

CONTROL ID: 3544020

SUBMITTER (NAME ONLY): Alfredo Dueñas Rey

TITLE: Exploring the role of putative cis-regulatory variants within the 5'UTR of the ABCA4 gene in ~6,900 cases with inherited retinal disease

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Dueñas Rey, M. Bauwens, E. De Baere, F. Coppieters, Department of Biomolecular Medicine, Universiteit Gent Faculteit Geneeskunde en Gezondheidswetenschappen, Gent, BELGIUM|A. Dueñas Rey, M. Bauwens, T. Rosseel, E. De Baere, F. Coppieters, Universitair Ziekenhuis Gent Centrum Medische Genetica Gent, Gent, BELGIUM|M. Khan, Universitair Medisch Centrum Groningen Pathologie en Medische Biologie, Groningen, NETHERLANDS|D. Sharon, Hadassah Medical Center Department of Ophthalmology, Jerusalem, ISRAEL|R.K. Koenekoop, Paediatric Surgery, Montreal Children's Hospital, McGill University Health Center, Montreal, Quebec, CANADA|G. Arno, A. Webster, UCL Institute of Ophthalmology, London, UNITED KINGDOM|C. Toomes, Leeds Institute of Medical Research, School of Medicine, University of Leeds, St James's University Hospital, Leeds, UNITED KINGDOM|C. Dhaenens, Univ. Lille, Inserm, CHU Lille, U1172 - LiNCog - Lille Neuroscience & Cognition, Lille, FRANCE|M. Khan, F.P. Cremers, Radboudumc Department of Human Genetics, Nijmegen, NETHERLANDS|G. Arno, A. Webster, Moorfields Eye Hospital, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: ABCA4-retinopathy (including Stargardt, STGD1) is by far the most common single-gene inherited retinal disease (IRD). Although a plethora of pathogenic coding and an increasing number of noncoding splicing ABCA4 variants are known, a significant fraction of STGD1 cases remains genetically unexplained. It is becoming clear that noncoding variants in ABCA4 represent an emerging source of missing heritability in STGD1. Here we explored one of such regions, the 5' untranslated region (5'UTR) of ABCA4 in IRD cohorts, in search of rare potentially pathogenic cis-regulatory variants.

Methods: Data derived from ~6,900 IRD probands from three cohorts – (i) ERDC4000, a targeted IRD gene sequencing project of the European Retinal Disease Consortium (n=3,200), (ii) ABCA4 locus (re)sequencing of STGD1 cases (n=1,054), and (iii) WGS data from a Genomics England IRD cohort (n=2,615), were mined to search for 5'UTR variants of ABCA4. Candidate variants were evaluated for potential effects on gene regulation by means of computational tools and interrogation of retina-derived epigenomic datasets.

Results: We identified eight rare (MAF < 0.001) ABCA4 5'UTR variants, three of which are ultra-rare (absent from public databases). All variants were heterozygous and found in IRD cases for which an ABCA4-associated disease was suspected, 4 of which are monoallelic for ABCA4 variants. Most variants were predicted to significantly disrupt secondary structure formation and/or affect motifs representing retina-specific transcription factor binding. Furthermore, two variants were found to create an upstream open reading frame in a favorable Kozak sequence context. Validation and segregation analysis of these alleles, and luciferase assays to assess their functional activity are ongoing.

Conclusions: Although often under-recognized, 5'UTR variants are known to influence post-transcriptional and translational regulation. Thus far, no (likely) pathogenic cis-regulatory variants within the 5'UTR of ABCA4 have been reported. Here we present a comprehensive analysis of the ABCA4 5'UTR in ~6,900 IRD cases. Exploring the functional consequences of these eight rare and other putative regulatory noncoding ABCA4 variants will not only

expand our understanding of its cis-regulation but also provide mechanistic insight into STDG1.

CONTROL ID: 3544021

SUBMITTER (NAME ONLY): Deepayan Kar

TITLE: Morphological variants of mitochondria in neurons surrounding the deep capillary plexus in human retina

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kar, C.A. Curcio, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|Y. Kim, O. Packer, D.M. Dacey, Department of Biological Structure, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptors are metabolically demanding first-order neurons. The deep capillary plexus sustains synaptic interactions between photoreceptors and horizontal and bipolar cells. Mitochondria produce energy in the form of ATP to support the activities of retinal cells via uptake of oxygen from the retinal vasculature. Prior studies showed mitochondrial migration towards blood sources during retina development (PMID 18048005). The purpose of this study was to determine the distribution of mitochondria in cells participating in the neurovascular unit of the outer plexiform layer in human retina, of relevance to retinal vascular disease.

Methods: Parafoveal retina of a 21-year-old male organ donor was dissected and placed into oxygenated Ames medium and fixed in 4% glutaraldehyde. Vertical sections were acquired using serial block-face electron microscopy at a voxel size of $5 \times 5 \times 50 \text{ nm}^3$ and registered using TrakEM2 (NIH). In the outer plexiform layer surrounding the deep vascular plexus, cone and bipolar cells and within them, individual mitochondria was reconstructed in 3-dimensions using supervised deep-learning enabled segmentation (ORS Dragonfly, Canada).

Results: Complete reconstructions of processes in and near the deep capillary plexus revealed numerous cone bipolar dendrites encircling a vessel. The capillary was also ensheathed by Müller cells without identifiable mitochondria. Mitochondria within bipolar neurons surrounding the capillary exhibited a long and slender morphology extending through the dendritic course encircling the capillary. Reconstructions of outer plexiform layer revealed multiple bipolar cells with mitochondria-filled blind processes lacking synaptic terminals and descending into the Henle fiber layer. Reconstructions of cone pedicles revealed clusters of ovoid mitochondria. Mitochondria counts in cone pedicles adjacent to the capillary were higher (mean 54.4 ± 9.7 , range 66-44, $n=6$) than in pedicles distant from the capillary (35.2 ± 7.75 , 43-27; $n=6$).

Conclusions: Initial findings of this ongoing study suggest cellular-level variations in mitochondrial morphology and distribution in cone pedicles and bipolar dendrites in relation to vascular oxygen sources. Findings are relevant to the cellular basis of underlying mechanisms involved in compromised oxygen supply to the outer plexiform layer in type 3 neovascularization and paracentral acute middle maculopathy.

CONTROL ID: 3544027

SUBMITTER (NAME ONLY): Princia Anney

TITLE: 3D environment and intraocular pressure increase corneal endothelial cell sodium-potassium pump activity.

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Anney, M. Thériault, S. Proulx, CHU de Quebec-Université Laval Research Center, section of regenerative medicine; and LOEX Research center of Université Laval, Quebec city, Quebec, CANADA|P. Anney, S. Proulx, Dept. of ophthalmology, Faculty of medicine, Université Laval, Quebec city, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The corneal endothelium acts as a barrier and controls the diffusion of fluid and nutrients between the aqueous humor and the stroma through intercellular junctions and the Na⁺/K⁺-ATPase pump. The purpose of this study is to assess the influence of intraocular pressure (IOP) and fluid flow on the functionality of the corneal endothelium.

Methods: Human corneal endothelial cells (CECs) were extracted from donor corneas. Cells were seeded at 2,500 cells/mm² either on plastic (2D cultures) or on devitalized human corneas (3D tissue model) (N=3 pairs). After 7 days of culture, the tissue-engineered corneal endothelia were placed in a corneal bioreactor in the presence of an IOP of 16 mmHg and fluid flow of 5ul/min for one of the 2 corneas. The mate cornea was cultured without IOP. Following 3 days of culture in the bioreactor, the activity of Na⁺/K⁺-ATPase was assessed (ATPase assay, Abcam). Results were relativized using total DNA (Genomic DNA purification Kit, New England Biolabs).

Results: Na⁺/K⁺-ATPase activity of CECs cultured on plastic (2D model) was low (-0,01 ±0.9x10⁻³ nmol/min/uL/ngDNA). However, the same cells cultured on a devitalized stroma (3D model) showed an increase in Na⁺/K⁺-ATPase activity (6.33x10⁻³ ± 3.9x10⁻³ nmol/min/uL/ngDNA), which was further increased by 2.38-fold in the presence of IOP (1.5x10⁻² ±3.1x10⁻³ nmol/min/uL/ngDNA). This increase of Na⁺/K⁺-ATPase activity in the presence of IOP was also observed using 2 other cell populations. Indeed, in 3D models, the activity of the Na⁺/K⁺-ATPase pump following IOP increased 2.0-fold (1.04 x10⁻³ ±1.24x10⁻⁵ nmol/min/uL/ngDNA without IOP and 2.08x10⁻³ ±7.4x10⁻⁵ with IOP); and 2.1-fold (4.40x10⁻⁴ ±6.3x10⁻⁵ nmol/min/uL/ngDNA without IOP to 9.15x10⁻⁴ ±1.4x10⁻⁴ with IOP).

Conclusions: These results indicate that culturing CECs in a 3D environment increases the activity of the sodium-potassium pump, which is further increased by adding IOP. A better understanding of how the in vivo environment influences CEC functionality may help to provide better tissue engineered corneas.

CONTROL ID: 3544028

SUBMITTER (NAME ONLY): Isis Vazquez

TITLE: Association of Vessel Density, Perfusion and Flux Index with Glaucoma Severity Assessed by OCT Angiography.

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.F. Vazquez, J.A. Paczka, A. Orozco Garcia, A. Tornero-Jimenez, A.M. Ponce Horta, Instituto de Oftalmologia y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|I.F. Vazquez, A. Orozco Garcia, A. Tornero-Jimenez, A.M. Ponce Horta, Research, Unidad de Diagnostico Temprano del Glaucoma, Guadalajara, Jalisco, MEXICO|J.A. Paczka, C.D. Ortiz-Moreno, Research and Development, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) is a noninvasive imaging technique that provides a quantitative assessment of the microcirculation of the retina and choroid. OCTA might allow us to expand our understanding on the pathophysiology of glaucoma and its clinical outcomes. The aim of this study is to investigate the association of vessel density, perfusion and flux index in the peripapillary/macular regions with different structural and functional variables at different stages of the disease

Methods: A cross-sectional retrospective study of consecutive cases which underwent a battery of ancillary tests to assess glaucoma patients was performed. A total of 135 eyes from 65 patients (glaucoma suspects and glaucoma patients) were included. Complete medical records and good quality results from a battery of tests were analyzed, including peripapillary and macular OCTA (Cirrus 6000, Carl Zeiss). Multiple functional and structural variables were assessed in different stages of glaucoma. A P-value of ≤ 0.05 was considered as statistically significant.

Results: Patients had a mean age of 63.35 ± 13.44 years. The sample had a greater proportion of female (66.1%), primary open-angle glaucoma (53.8%), and early stages of the disease (63.07%). The mean thickness values of retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) demonstrated a good correlation ($r \geq 0.5$). All of the mean values of peripapillary perfusion and flux index were statistically significance in each eye ($P = 0.0001$), with exception of flux index in the left eye, in which the correlation was modest ($r > 0.36$) but maintaining a level of statistical significance ($P \leq 0.002$). A statistically significant ($P < 0.005$) but modest correlation ($r \geq 0.34$) was found between CFNR and GCC as well as the variables, macular perfusion and macular vessel density. When the mean values of peripapillary perfusion and flux index were compared between two subgroups of severity (mild glaucoma vs. glaucoma suspect), statistically significant differences were found in both eyes (table 1).

Conclusions: In our study, peripapillary perfusion and flux index are variables derived from OCTA assessment that correlates well with important structural elements at different stages of glaucoma. Well-designed studies could determine the diagnosis and prognosis capacities of such technology in order to improve therapeutic decisions.

CONTROL ID: 3544029

SUBMITTER (NAME ONLY): Sai Supriya Vuda

TITLE: Cathepsin K Activity in Trabecular Meshwork Outflow Pathway Regulates Intraocular Pressure Homeostasis.

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vuda, S.A. Ghag, P.P. Pattabiraman, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: A sustained increase in intraocular pressure (IOP) is a major risk factor for primary-open angle glaucoma (POAG). Extracellular matrix (ECM) accumulation in the trabecular meshwork (TM) outflow pathway results in IOP elevation. Among the major ECM components in the TM outflow pathway, increased accumulation of collagen 1A is found in POAG. Cathepsin K (CTSK) is a lysosomal protease and a potent collagenase known to degrade helical and non-helical regions of collagen 1A. We studied the role of CTSK activity on ECM modulation in the TM outflow pathway and on IOP.

Methods: Porcine TM (PTM) cells were isolated, cultured and were treated with 10uM Balicatib, a potent cell-permeable CTSK activity inhibitor, for 1, 4, 8, 16, 24hrs to study time-dependent inhibition of CTSK activation and assessed for its effect on ECM modulation using immunoblotting. Porcine anterior segment organ culture perfusion was used to assess the effect of Balicatib on - a) IOP, b) changes in tissue distribution and expression of ECM like collagen, fibronectin, and elastin using immunofluorescence and immunoblotting. Student's t-test was used for statistical analyses and results were significant if $p < 0.05$ with a sample size of $n=3-9$ in each experiment.

Results: Balicatib treated PTM cells decreased CTSK activity by 80%. Time-dependent balicatib treatment in porcine TM cells showed no changes in active CTSK but a significant increase in pro-CTSK ($p=0.001$) as well as in ECM proteins like COL1A ($p=0.004$), FN ($p=0.009$). Perfusion of balicatib in the porcine anterior segment perfusion cultures increased IOP nearly two-fold ($n=5$, $p < 0.05$). TM isolated from perfused globes showed increased elastin protein expression by nearly seven-fold ($n=2$, $p=0.023$). Immunofluorescence data showed an increase in collagen 1A and fibronectin distribution in the TM outflow pathway

Conclusions: Firstly, this proof of concept study shows that directly perturbing the activity or function of an ECM degrading enzyme-like CTSK increases intraocular pressure by altering the ECM degradation. Secondly, we demonstrate that CTSK is a critical regulator of IOP homeostasis. This study also reinforces the fact that ECM in the outflow pathway is very important for maintaining IOP. Finally, activation of CTSK is an attractive therapeutic strategy to lower IOP

CONTROL ID: 3544031

SUBMITTER (NAME ONLY): Sook Hyun Chung

TITLE: Cellular origins of VEGF family members in laser-induced choroidal neovascularization using single-cell transcriptomic analysis.

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chung, B.Q. Dang, G. Yiu, Ophthalmology, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify the cellular origins of vascular endothelial growth factors (VEGF) and potential new therapeutic targets for ocular angiogenic disorders, we performed single-cell transcriptomic analysis on retinal, retinal pigment epithelium (RPE), and choroidal tissues from mouse eyes after laser-induced choroidal neovascularization (CNV).

Methods: Eight to ten laser CNV spots were created in wild-type adult C57/BL6 mouse eyes. One week after laser injury, retinal and RPE-choroidal tissues were dissected from the CNV lesions from 9 animals for single-cell preparation. Single-cell RNA sequencing libraries were prepared using Chromium technology, and barcoded libraries were pooled and sequenced at 300 million reads per library using the Illumina HiSeq 4000 platform.

Results: A total of 16,321 cells (14,966 from retina and 1,355 from RPE-choroid) were recovered and approximately 1200 gene were identified from each cell. Nine major transcriptionally distinct cell populations were identified from unsupervised clustering (Figure 1), including rod/cone photoreceptors, cholinergic/GABAergic/glycinergic amacrine cells, rod/cone bipolar cells, and RPE. One major cluster was further subdivided into Muller glia, horizontal, retinal ganglion cells, endothelial cells, stromal cells, and melanocytes. Among these cell types, we found that VEGFa and VEGFb were expressed in all major cell types except rod and cone photoreceptors, with the highest levels of expression found in Muller glia and RPEs. By contrast, VEGFc and VEGFd were minimally expressed in all cell types.

Conclusions: Single-cell transcriptomic analysis demonstrate differential expression of VEGF family members across different retinal and choroidal cell types after laser-induced CNV in mouse eyes, providing critical guidance for cell-specific targeting of anti-angiogenesis retinal gene therapies. Analyzing differentially expressed genes may help identify other novel therapeutic targets for ocular angiogenic disorders.

CONTROL ID: 3544033

SUBMITTER (NAME ONLY): Seher Yuksel

TITLE: Establishing the role of dietary lipids in meibogenesis

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yuksel, A. Wilkerson, I.A. Butovich, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|I.A. Butovich, Graduate School of Biomedical Sciences, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Seher Yuksel: Commercial Relationship: Code N (No Commercial Relationship) | Amber Wilkerson: Commercial Relationship: Code N (No Commercial Relationship) | Igor Butovich: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Meibomian glands (MG) play a vital role in ocular physiology producing meibum – a complex mixture of cholesterol (Chl), Chl esters (CE), triacylglycerols (TAG), and other classes of lipids, in a process termed meibogenesis. The purpose of this study was to establish the role of dietary Chl and TAG in meibogenesis, and determine if dietary lipids can be directly incorporated in meibum without undergoing deep anabolic/catabolic transformations first.

Methods: Wild type C57Bl/6J mice (n=16) were gavaged daily with Chl-2,2,3,4,4,6-d₆ (d₆-Chl) and triolein-1,2,3,7,8-¹³C₅ (¹³C₅-TO) dissolved in a vehicle. At Days 0, 7, 14, and 28 of gavaging, the mice were euthanized (4 mice at each time point) and their tarsal plates, small intestine, liver, plasma, and feces specimens were collected. Then, lipids were extracted from all tissue samples and analyzed using ultra-high-performance liquid chromatography/high-resolution mass spectrometry to determine the fate of the tracers in the tissues.

Results: We established that ¹³C₅-TO and its metabolites could be detected in the small intestine, plasma and liver in diminishing quantities, but not in the feces or meibum even after 4 weeks of gavaging. Our results demonstrate that ¹³C₅-TO underwent deep catabolic transformations and could not be directly incorporated into meibum neither as an intact TAG, nor as its metabolized products (diacylglycerols, monoacylglycerols, free fatty acids, or their esters with other compounds). On the other hand, d₆-Chl was detected in all tested tissues, including meibum. Moreover, in MG d₆-Chl underwent successful esterification into long- and ultra-long-chain CE typical of Meibomian lipids. Importantly, enrichment studies demonstrated that d₆-Chl could be accumulated in meibum in excessive quantities suggesting that increased levels of Chl in blood can increase levels of Chl in MG and meibum.

Conclusions: Our experiments demonstrated that dietary Chl may directly affect Chl and CE homeostasis in MG, while dietary TAG seem to be extensively catabolized in the small intestine, liver, and blood before reaching MG, and, thus, could not directly influence the outcome of meibogenesis.

CONTROL ID: 3544034

SUBMITTER (NAME ONLY): Laura Bohrer

TITLE: Pre-clinical toxicity analysis following subretinal transplantation of an iPSC-derived retinal cell graft in immune suppressed rats.

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.R. Bohrer, I. Han, J.A. Cooke, E.R. Burnight, K.R. Anfinson, E.K. Kaalberg, M.J. Ulferts, J.M. Hoffmann, K.L. Wieland, L.A. Wiley, K.S. Worthington, R.F. Mullins, E.M. Stone, B.A. Tucker, Ophthalmology & Visual Sciences, Institute for Vision Research, University of Iowa, Iowa City, Iowa, UNITED STATES|K.S. Worthington, Department of Biomedical Engineering, University of Iowa, Iowa City, Iowa, UNITED STATES|K.N. Gibson-Corley, Pathology, Microbiology and Immunology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Induced pluripotent stem cell (iPSC)-derived retinal progenitor cells are a promising cell type for restoring vision in patients with advanced retinal degeneration. Traditional bolus cell suspension injection often results in poor cell survival and limited synaptic integration following transplantation. To address this problem, we have focused our attention on tissue engineering to reduce post-transplant cell loss while promoting cellular alignment and proper packing density. The purpose of this study was to evaluate local and systemic toxicity following transplantation of human iPSC-derived retinal cell grafts in an immune suppressed rat model.

Methods: Polycaprolactone (PCL) scaffolds were generated by injecting a prepolymer solution into a photopolymerization chamber containing a photomask with 50um spots separated at 25um intervals. Scaffolds were seeded with iPSC-derived retinal progenitor cells generated from 1 of 5 patients. 1mm punches were transplanted into the subretinal space of immune suppressed RNU^{-/-} rats (N=150) followed by necropsy with complete histopathology, clinical chemistry and hematology performed at 1-, 3-, and 6-months post-transplantation.

Results: Two weeks following scaffold seeding, iPSC-derived retinal precursor cells expressing recoverin and OTX2 were densely packed into vertical columns throughout the scaffold, recapitulating the outer nuclear layer of the retina. Following subretinal transplantation in RNU^{-/-} rats, retinal reattachment was noted in all eyes. No evidence of treatment induced retinal or systemic toxicity/tumorigenicity was detected by gross or histopathologic evaluation. No significant difference in mean body and/or organ weight was detected between control vs treatment groups at any of the time points evaluated (P>0.05). Finally, no significant treatment induced adverse events were detected via hematology or clinical chemistry (P>0.05).

Conclusions: We successfully developed a high-throughput platform for evaluating local and systemic toxicity following subretinal transplantation of patient derived retinal cell grafts.

CONTROL ID: 3544035

SUBMITTER (NAME ONLY): Sayantan Biswas

TITLE: The drive for myopia control: interactions between bright light and optical refocus

SESSION TITLE: Effects of Light Intensity and Blur on Refractive Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Biswas, M. Arumugam Ramachandran, V.A. Barathi, W. Low, J. Fianza Busoy, D. Milea, R. Najjar, Singapore Eye Research Institute, Singapore, SINGAPORE|V.A. Barathi, D. Milea, R. Najjar, Duke-NUS Medical School, Singapore, SINGAPORE|N.A. Brennan, Johnson and Johnson Vision Care Inc, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the synergetic impact of bright light (BL) and optical refocus (RF) on myopia development in a chicken model of lens induced myopia (LIM).

Methods: One day old chicks (Golden Comet/White Leghorn) were assigned to 7 groups of 13 chicks each. Chicks were housed for 7 days in a temperature-controlled enclosure under a 12/12h light-dark cycle (150 lux). Myopia was induced randomly in one eye from the day of hatching (BSL) until day 7 post-hatching (D7) using -10D lenses. The fellow eye was used as uncovered control. Six groups were exposed every day to continuous 4 hours (h) or 6h of either BL (15,000 lux); RF (removal of -10D lens); or both (BL+RF). One group served as control without BL or RF interventions. On BSL and D7, ocular axial length (AL), refractive status and choroid thickness were measured using ultrasonography, infra-red refractometry and optical coherence tomography, respectively. Outcome measures were expressed as the difference between the experimental and control eyes in each animal, and compared between groups and across days using a 2-way repeated measures ANOVA.

Results: By D7, LIM led to significant increases in AL (0.36 ± 0.15 mm) and myopic refraction (-8.51 ± 1.35 D), as well as choroid thinning (-62.1 ± 61.1 μ m) in the control group (all, $P < 0.001$). Both 4h and 6h of BL or RF reduced axial elongation and myopic refraction induced by LIM (Fig. 1) while only 6h of BL or RF prevented choroid thinning (Fig. 1F; $P < 0.05$). RF was more effective than BL in preventing axial elongation and myopic refraction development (Fig 1). BL+RF (4h) was less effective in slowing LIM compared to RF ($P = 0.04$; Fig. 1B), while 6h of BL+RF stopped axial elongation, refractive error development and choroid thinning induced by LIM, compared to BL ($P < 0.001$) and RF ($P = 0.03$).

Conclusions: Daily exposure to 4 or 6 hours of BL or RF slows LIM in chickens. Combined with RF, only 6h of BL can stop LIM. The synergetic effect of BL and RF is dependent on the duration of the intervention.

CONTROL ID: 3544040

SUBMITTER (NAME ONLY): Meital Ben-Dov

TITLE: Regenerative effect of adipose derived mesenchymal stem cell on ganglion cells in the hypoxic organotypic retina culture

SESSION TITLE: Blood flow, ischemia, reperfusion

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Ben-Dov, I. Nakdimon, M. Benhamou, A. Klein, S. Schwartz, A. Loewenstein, A. Barak, A. Barzelay, Tel Aviv University Sackler Faculty of Medicine, Tel Aviv, ISRAEL|M. Ben-Dov, I. Nakdimon, M. Benhamou, A. Klein, S. Schwartz, A. Loewenstein, A. Barak, A. Barzelay, Ophthalmology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, ISRAEL|

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ABSTRACT BODY:

Purpose: To examine whether ischemic retinal ganglion cells (RGC) will be salvaged from apoptosis by co-culture with adipose-derived mesenchymal stem cells (ADSC) by direct contact or by paracrine activity.

Methods: Retinas of wild type C57Bl/6 mice were harvested. Deprived of arterial oxygen supply, retinas were cultured as ex vivo organotypic cultures on an insert membrane. First, number of surviving RGC was evaluated at different time points (T0, T48, T72 hours) by Brn3a staining and confocal microscopy. Then, the therapeutic potential of ADSC on ischemic retinas was evaluated either by co-culture of ADSC with organotypic retinas with direct contact of ADSC (ADSC seeded above the retina) or by a co culture of ADSC with organotypic retinas allowing a paracrine activity of ADSC (ADSC seeded on tissue culture plate below the retina) (n=7). Retinas were flat-mounted and the number of surviving RGC was assessed using Brn3a staining and confocal microscopy. We also examined the cytokine secretion profile of ADSC related to their paracrine effect on ischemic retina by analyzing the protein expression in ADSC-conditioned medium using protein array.

Results: We demonstrated a time-dependent decrease in number of viable RGC in non-treated ischemic retinas evident by Brn3a+ staining. When co cultured with ADSC, the number of surviving RGC was significantly higher in treatment groups compared to controls of retinas treated with standard medium (Brn3a+ cells treated with ADSCs seeded above the retina = 29 ± 10.9 , $p < 0.001$, Brn3a+ cells treated with ADSCs seeded below the retina = 29 ± 7.2 , $p = 0.001$, controls = 4.5 ± 2.5 SD). Evaluating ADSCs cytokines secretion profile, we showed secretion of anti apoptotic and pro- proliferative cytokines (threshold > 1.4).

Conclusions: Our results demonstrate that transplantation of ADSC in a co culture with organotypic ischemic retinas significantly improved recovery of the RGC. The effect was similar when ADSC were seeded above and below the retina suggesting the beneficial effect seen was related to paracrine activity of ADSC rather than to direct contact of ADSC. These data correlated with secretion profile of ADSCs anti-apoptotic and pro proliferative cytokines. In summary, ADSC could direct future development of autologous cell therapy modalities to repair ischemic retinal and/or optic nerve damage.

CONTROL ID: 3544043

SUBMITTER (NAME ONLY): Jose Rico-Jimenez

TITLE: Real-Time OCT Image Denoising Using Self-Fusion Neural Network

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rico-Jimenez, Y. Tao, Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|D. Hu, I. Oguz, Computer Science and Computer Engineering, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) imaging has benefitted ophthalmic diagnostics by enabling depth-resolved volumetric imaging of ocular structures. Inherent speckle noise degrades the OCT image quality complicating the identification of anatomical features and pathologic features. Frame-averaging is a ubiquitous method for increasing signal-to-noise ratio (SNR), however, the need to acquire multiple repeated frames increases the imaging time, introduces motion artifacts, and adds to potential patient discomfort. We recently introduced a method called self-fusion, which reduces speckle noise and enhances OCT SNR using adjacent frames, thus reducing the need to repeated image the same location and extending imaging time. Uniquely, self-fusion integrates image similarity metrics between adjacent frames to maintain lateral resolution. We have trained a convolutional neural network to offset the computational overhead of self-fusion and, here, present a framework for performing self-fusion in real-time.

Methods: The neural network was designed in PyTorch based on the U-net architecture. The training and validation sets were first processed with using self-fusion to yield ground truth images and then both the noisy and self-fused images were fed into the training algorithm to fit the model and optimize the hyperparameters (Fig. 1A). An independent test set was used for unbiased evaluation of a final model. Since the data acquisition software (DAQ) was written in C++, the pretrained model was exported to a file to interface with the DAQ (Figure 1B). A self-fusion network that was pretrained to fuse 3 frames was implemented to further increase display rates.

Results: Figure 1C shows a noisy OCT B-scan, a 7-frame averaged image, and a 3-frame self-fused image. There is a clear gain in peak SNR in the 3-frame self-fused image (20.2 dB) over both the raw and 7-frame averaged image (13.8 dB).

Conclusions: This approach delivers a fast and robust OCT denoising alternative to frame-averaging without the need for repeated image acquisition. Real-time self-fusion image enhancement will enable improved localization of OCT field-of-view relative to features-of-interest and improved sensitivity for anatomic features of disease.

CONTROL ID: 3544044

SUBMITTER (NAME ONLY): William White

TITLE: Generation of an in vitro retinal ganglion cell (RGC) model by expressing the POU domain, class 4, transcription factor 2 (Pou4f2) gene in R28 retinal precursor cells

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. White, T. Hollingsworth, M.M. Jablonski, Ophthalmology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is an unmet need for in vitro RGC models to better understand the underlying cellular pathogenesis of glaucoma. While there has been success with enriching for RGCs from intact retinas, the procedure is technically complex and the resulting RGCs are viable only for a short period of time (roughly 2 weeks). We hypothesized that Lentiviral transduction of R28 retinal precursor cells with Pou4f2, a transcription factor associated with RGCs, would drive R28 cells toward an RGC fate. The goal of this study was to generate an in vitro RGC model using R28 retinal precursor cells that constitutively express Pou4f2.

Methods: R28 cells were transduced using a Lentivirus carrying the Pou4f2 gene fused to green fluorescent protein or mCherry. After antibiotic selection using puromycin, the Pou4f2-transduced R28 cells were cultured for 14 days in Neurobasal Plus Medium containing B27 supplement. The cells were observed using confocal microscopy to verify Pou4f2 expression and neuronal morphology. Immunocytochemistry was performed to detect RGC markers. Non-transduced R28 cells cultured in supplemented Dulbecco's Modified Eagle Medium served as the control for all experiments.

Results: Confocal microscopy of Pou4f2-transduced R28 cells confirmed the presence of the fluorescent fusion protein, the presence of axonal projections, and the formation of synaptic junctions. The expression and localization of at least 10 RGC and neuronal markers were confirmed in the transduced R28 cells including: β -tubulin 3 (TUBB3); POU domain, class 4, transcription factor 1 (POU4F1); Islet 1 transcription factor (ISL1); very long chain enoyl-CoA reductase (TECR); microtubule-associated proteins 1 and 2 (MAP-1 and MAP-2); RNA binding protein with multiple splicing (RBPMS); synaptosomal-associated protein, 25kDa (SNAP25); synaptotagmin 11 (SYT11); and Thy 1.1 cell surface antigen.

Conclusions: Pou4f2-expressing R28 cells demonstrate neuronal morphology and protein expression patterns similar to that of in situ RGCs, indicating that these cells can differentiate into RGC-like neurons. Thus, the Pou4f2 R28 cells show strong potential as a new in vitro RGC model.

CONTROL ID: 3544047

SUBMITTER (NAME ONLY): Wei Chieh Huang

TITLE: OCT Biomarkers in Ocular CLN2 Disease

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Huang, C.M. Ohnsman, REGENXBIO Inc, Rockville, Maryland, UNITED STATES|Y. Atiskova, S. Dulz, Department of Ophthalmology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, GERMANY|

Commercial Relationships Disclosure (Abstract): Wei Chieh Huang: Commercial Relationship(s);Regenxbio Inc.:Code E (Employment) | Yevgeniya Atiskova: Commercial Relationship: Code N (No Commercial Relationship) | Christina Ohnsman: Commercial Relationship(s);Regenxbio Inc.:Code E (Employment) | Simon Dulz: Commercial Relationship(s);Regenxbio Inc.:Code C (Consultant);Biomarin Pharmaceuticals Inc.:Code C (Consultant);Neurogene Inc.:Code C (Consultant)

ABSTRACT BODY:

Purpose: Cone-rod degeneration is a prominent feature of neuronal ceroid lipofuscinosis Type 2 (CLN2) disease. While bilateral progressive, symmetrical loss of central retinal thickness (CRT) has been well-characterized, other OCT anatomical biomarkers have not been described in as much detail. This study was therefore undertaken to further explore progression of anatomical retinal changes in CLN2 disease.

Methods: SD-OCT macular cube scans were collected in 31 subjects, ages 5 to 157 months, with classic CLN2 disease. Horizontal B-scans through the fovea from one eye per subject were segmented manually to determine thickness of six retinal parameters: full retinal thickness (FRT), retinal nerve fiber layer, inner nuclear layer, outer nuclear layer (ONL), photoreceptor (PR) plus retinal pigment epithelium (RPE), and outer segment plus RPE (OS+RPE). Ellipsoid zone (EZ) integrity was also examined. FRT was measured in standard Early Treatment Diabetic Retinopathy Study (ETDRS) sectors. In addition to cross-sectional analysis, longitudinal data for individual patients were analyzed when available.

Results: CRT loss correlated to disease severity and Weill Cornell Late Infantile Neuronal Ceroid Lipofuscinosis Severity Scores. A linear relationship between loss of CRT and foveal ONL thickness confirmed the connection between PR loss and disease progression. Retinal degeneration in the macula showed a predictable pattern on horizontal scans, with relative foveal sparing and parafoveal involvement in early disease, followed by more profound foveal degeneration with additional ONL thinning beyond the central retina later in the disease. Focal EZ changes in the macula were an early signal of PR degeneration, progressing to more extensive EZ loss in later stages. PR degeneration in OS+RPE preceded ONL loss. Marked FRT reduction was also observed in ETDRS para- and peri-central sectors in late stages. Analyses of longitudinal data confirmed these observations.

Conclusions: CRT is a useful anatomical biomarker in CLN2 until maximal foveal thinning has occurred late in the disease, when para- and peri-central sector changes become more significant for understanding disease progression and treatment efficacy. Further studies using en face images will further clarify progression of retinal degeneration in CLN2 disease. Additional longitudinal data are needed to characterize the pattern and progression of EZ loss in CLN2 disease.

CONTROL ID: 3544048

SUBMITTER (NAME ONLY): Peter Kaiser

TITLE: Feasibility of ellipsoid zone quantification as identified on optical coherence tomography using a customized software algorithm in the clinical trial of Allogeneic Human Retinal Progenitor Cells (hRPC) for the Treatment of Retinitis Pigmentosa.

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.M. Kaiser, M.A. McDonald, C. Chen, D. Burton, K. Baynes, J.P. Ehlers, S. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|R. Kammer, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the feasibility of ellipsoid zone quantification on spectral domain optical coherence tomography in a clinical trial assessing the treatment of retinitis pigmentosa (RP).

Methods: A customized OCT platform using logic based identification of OCT layers was utilized. 97 line macular spectral domain OCT scans (Heidelberg) obtained at baseline visits on 25 patients were analyzed using this software. OCT layers were then identified and manually corrected by trained graders. Ellipsoid zone (EZ) metrics were then calculated including thickness and volume. EZ thickness maps were also created.

Results: 29 eyes from 29 subjects with advanced RP (mean BCVA 1.02logMAR or 34 letters; mean age 46) were included. All eyes were successfully mapped and graded. Logic based identification successfully identified more normal areas of EZ, but required manual correction often in areas of severe EZ loss. The mean central subfield thickness was 206.53 µm. The mean EZ-RPE central subfield thickness was 11.35 µm (range 0.76 – 37.04 µm) Mean EZ-RPE volumetric measures of the central subfield, mid subfield and macula were 0.0089 mm³, 0.025 mm³ and 0.087 mm³ respectively. En face zero micron and less than 20 micron EZ-RPE thickness coverage maps of the macula were created. The mean zero micron coverage within the macula was 84.36% (range 59-98%); the mean less than 20 micron thickness was 96% (range 84-100%).

Conclusions: This study provides important insight into the use of OCT EZ-RPE analysis for advanced RP. EZ-RPE thickness and volume was measurable, but required manual correction. In contrast to normal OCTs (0.87% mean attenuation with a mean of 0.12% total attenuation), significant EZ attenuation occurred in RP subjects with marked loss noted beyond the midsubfield (central 2 mm) area. OCT analysis of the EZ layer provides important information about the severity of photoreceptor loss in retinitis pigmentosa.

CONTROL ID: 3544050

SUBMITTER (NAME ONLY): Sudha Swamynathan

TITLE: Secreted Ly-6/uPAR Related Protein-1 (SLURP1) suppresses epithelial cell proliferation by upregulating cell cycle inhibitors and downregulating cyclins and cyclin dependent kinases

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Swamynathan, G. Campbell, A. Tiwari, S.K. Swamynathan, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sudha Swamynathan: Commercial Relationship(s);Patent number: US 9,731,014:Code P (Patent) | Gregory Campbell: Commercial Relationship: Code N (No Commercial Relationship) | Anil Tiwari: Commercial Relationship: Code N (No Commercial Relationship) | Shivalingappa Swamynathan: Commercial Relationship(s);Patent number: US 9,731,014:Code P (Patent)

ABSTRACT BODY:

Purpose: Previously we demonstrated that the Secreted Ly-6/uPAR Related Protein-1 (SLURP1), abundantly expressed in the cornea and secreted to the tear film, is an anti-proliferative and pro-differentiative protein. Here we have studied the mechanistic basis for its anti-proliferative effect on the Human Corneal Limbal Epithelial (HCLE) cells.

Methods: HCLE cells were stably transfected with pCMV-SLURP1 and two different clones overexpressing SLURP1 were selected for the present studies. The effect of SLURP1 overexpression on HCLE cell cycle progression was quantified by flow cytometry. The expression, quantity and subcellular localization of cyclins, cyclin-dependent kinases (CDKs) and cyclin inhibitors were determined by QPCR, immunoblots, and immunofluorescent staining, respectively.

Results: Flow cytometry revealed that the percent of cells in G0/G1 phase is significantly higher in SLURP1-expressing HCLE clones (73.8% and 81.6%) compared with the WT HCLE (63%). QPCR revealed an upregulation of p21 (1.1- and 2-fold), and downregulation of Cyclin-B1 (0.66- and 0.68-fold), and Cyclin D2 (0.48- and 0.64-fold) in HCLE-SLURP1 clones relative to the WT control. Immunoblots revealed elevated expression of cell cycle regulators p15 (1.5- and 1.6-fold), lower CDK-4 (0.9- and 0.57-fold) and cyclin-E (0.93- and 0.77-fold) in HCLE-SLURP1 relative to WT HCLE cells. HCLE-SLURP1 clone with a higher level of SLURP1 expression displayed decreased CDK6 (69% of the WT) and Cyclin-D1/D2 (60% of the WT) expression. Immunofluorescent staining revealed an increased cytoplasmic and decreased nuclear localization of CDK-2, -4 and -6 in HCLE-SLURP1 cells compared with the WT.

Conclusions: SLURP1 serves as an anti-proliferative protein by promoting the expression of cell cycle inhibitors p15 and p21 and suppressing the expression of cyclins-D1/D2 and -E, and CDK-4 and -6. Further cell cycle regulation is facilitated by altered sub-cellular localization of CDKs in the cytoplasm of SLURP1-overexpressing cells.

CONTROL ID: 3544053

SUBMITTER (NAME ONLY): Jody Summers

TITLE: Single Cell Transcriptomics Identifies Distinct Choroid Cell Populations Involved in Visually Guided Eye Growth

SESSION TITLE: Role of choroid and sclera in myopia development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.A. Summers, E. Martinez Cano, R. Sharp, K. Jones, Cell Biology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jody Summers: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Martinez Cano: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Sharp: Commercial Relationship: Code N (No Commercial Relationship) | Kenneth Jones: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Many studies suggest that the choroid participates in regulation of postnatal ocular growth and refractive development. This study was designed to characterize the cell populations in the chick choroid and compare gene expression changes in these cell populations during the recovery from induced myopia.

Methods: Choroids were isolated from normal chick eyes as well as from treated and control eyes of chicks reared for 10 days with occluders to induce form deprivation myopia, followed by a recovery period of 24 hrs. Single cells were isolated, labelled with ethidium homodimer III and calcein-AM to fluorescently label dead and living cells, respectively, and living cells were sorted using flow cytometry. 50,000 cells from three separate pools of control and treated eyes were used to generate transcriptome libraries using the 10x genomics Chromium Controller and Single Cell 3' library. Single Cell RNA-Seq data was processed using Cellranger and analyzed in R using the Seurat package.

Results: UMAP clustering analysis identified 24 distinct cell clusters in all chick choroids. 7 clusters were identified as fibroblasts based on Col1a gene expression; 6 clusters were identified as endothelial cells based on CDH5, PECAM1, and VWF expression; 4 clusters were CD45+ immune cells and 2 clusters were identified as melanocytes based on PMEL expression. Significant changes in gene expression between control and treated choroids were identified in 17 cell clusters. The majority of significant gene expression changes were relatively small (< 2 fold), however the gene NOV/CCN3 was significantly overexpressed in two fibroblast clusters (\uparrow 3.45 and \uparrow 2.52, fold over control cells). The highest gene expression changes were identified in a rare cell population (\approx 0.26% of total choroidal cells) (C4A, \uparrow 12 fold; CST3, \uparrow 8 fold; CTSV, \uparrow 9 fold; and TMSB4X, \downarrow 0.6 fold). This rare cell population expressed high levels of GAL, CHRNA3, VIP, ELAVL4, and SCN9A, suggestive of a neuronal cell population.

Conclusions: Several populations of choroidal cells, representing 95% of total choroidal cells exhibit significant changes in gene expression in response to visual stimuli. The large changes in gene expression identified in a rare neuronal cell population is suggestive of a role for intrinsic choroidal neurons in the choroidal recovery response.

CONTROL ID: 3544054

SUBMITTER (NAME ONLY): Andrea Orozco Garcia

TITLE: Decision-Making Usefulness to Treat Glaucoma with a Combination of Water-Drinking Test and 24-Hour IOP curve with Icare Home.

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Orozco Garcia, J.A. Paczka, I.F. Vazquez, A.M. Ponce Horta, A. Tornero-Jimenez, Instituto de Oftalmologia y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|A. Orozco Garcia, I.F. Vazquez, A.M. Ponce Horta, A. Tornero-Jimenez, C.D. Ortiz-Moreno, F.M. Guerrero-Cuevas, Research Department, Unidad de Diagnostico Temprano del Glaucoma, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Research & Development, Asistencia e Investigacion en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: The main risk factor for the development and progression of glaucoma is elevated intraocular pressure (IOP); thus, the mainstay of glaucoma treatment is to reduce IOP to a safe level. Measurement of IOP is crucial to the diagnosis and management of glaucoma. Alternative methods to measure IOP, as with the water-drinking test (WDT) and a 24-h profile of IOP (24HP), have been reported as useful ways to determine pressure control. The purpose of this study was to determine if a combination of a WDT and a 24HP of IOP with the device Icare Home, is a useful approach to make clinical decisions in regards of glaucoma management.

Methods: A retrospective study of 20 consecutive glaucoma patients who underwent an expanded profile of IOP (EPIOP) consisting of a combination of traditional WDT and a 24HP of IOP with Icare Home. IOP results for each test per eye were analyzed. Central corneal thickness, clinical examination data, including prior applanation IOP, were also assessed. The clinical impact for each test interpretation was determined.

Results: Patients had a mean age of 53.6 ± 14.3 years. A larger proportion of female patients (75%), with a primary open-angle glaucoma diagnosis (65%), and usage of antiglaucoma medication (55%) were observed. Mean previous highest IOP values were 14.4 ± 3.63 mm Hg (RE) and 14.1 ± 3.7 mm Hg (LE). Mean CCT values were 541.9 ± 35.9 microns (RE) and 540.7 ± 36.8 (LE). WDT abnormality was found in 60% of the RE and 65% of the LE. Mean IOP fluctuation was significantly different in both eyes (10.50 ± 4.55 mm Hg, RE; 11.05 ± 4.81 mm Hg; $P = 0.0001$). Clinically significant results with the 24HP with Icare Home was obtained in 80% of both eyes. Integrated information with results derived from both tests supported the decision of starting antiglaucoma medications in 12 eyes, adding medications in 6 eyes, indicating SLT in 4 eyes, performing peripheral iridotomy in 2 eyes, and re-treating 1 eye with SLT.

Conclusions: An EPIOP (combined approach of WDT and a 24HP of IOP with the Icare Home device) seems to be a useful, although time-consuming, way to support the clinicians decision-making process in the management of glaucoma.

CONTROL ID: 3544057

SUBMITTER (NAME ONLY): Sneha Singh

TITLE: SARS-CoV-2 infects human corneal epithelium and elicits an antiviral immune response.

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Singh, R.E. Wright, A. Kumar, Ophthalmology, Visual and Anatomical Sciences (OVAS), Wayne State University, Detroit, Michigan, UNITED STATES|G. Garcia, V. Arumugaswami, School of Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|A. Jha, Department of Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Kramergy, A.V. Ljubimov, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently reported the presence of SARS-CoV-2 RNA, Spike, and Envelope proteins in the corneas of COVID-19 donors. However, the presence of viral RNA and antigens does not necessarily equate to infection. In this study, using RNA-seq of COVID-19 corneal tissue, and SARS-CoV-2 infection of human corneal epithelial cultures, we now examined whether SARS-CoV-2 could replicate in the cornea and elicits an innate immune response.

Methods: Eyes from healthy and COVID-19 donors were from the Eversight eye bank. The corneal tissue was used for IHC detection of SARS-CoV-2 by RNA-FISH. In another experiment, total RNA was extracted from corneas for RNA-seq analysis to identify genes/ pathways altered by infection. In vitro studies were performed by infecting primary human corneal epithelial cells (HCECs) from normal and diabetic donor corneas with SARS-CoV-2. Bioinformatics analysis was performed to determine the differential gene expression. qPCR was used to assess the expression of innate inflammatory and antiviral genes and to confirm RNA-seq data in corneal tissue and cells.

Results: RNA-FISH analysis showed the presence of both positive and negative strands of SARS-CoV-2 viral RNA in the epithelium of COVID-19 donor corneas. This coincided with infiltration of CD45+ cells in the stroma and induced expression of inflammatory (IL-6, IL-1 β) and antiviral (ISG15, OAS2) genes. RNA-seq analysis revealed significant upregulation of genes involved in the viral response, inflammation, and injury along with induction of lncRNA XIST and TSIX involved in modulation of the immune response. The primary HCECs were found permissive to SARS-CoV-2 infection, as evidenced by increase viral replication which peaked at day 3 p.i. along with an induction of p-STAT1. Interestingly, HCECs from diabetic cornea had higher viral RNA on day 1 p.i. compared to non-diabetic cells. SARS-CoV-2 infected HCECs also exhibited induced expression of antiviral innate response genes, which was elevated in diabetic donor cornea cells.

Conclusions: Our study confirms the presence of replicating SARS-CoV-2 viral RNA and antigen in the cornea of COVID-19 affected donors resulting in the production of inflammatory mediators and recruitment of CD45+ immune cells to the cornea. Moreover, HCECs from diabetic corneas had increased SARS-CoV-2 replication and immune response, suggesting that diabetes is a potential risk for ocular transmission of COVID-19.

CONTROL ID: 3544058

SUBMITTER (NAME ONLY): Kirsty Clarke

TITLE: Vision-specific quality of life in a cohort of Alport Syndrome patients

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Patients with Alport syndrome (AS) can display a range of ocular abnormalities with variable effects on visual function and quality of life. We report results from the National Eye Institute 25 item Visual Functioning Questionnaire (NEI-VFQ25) in a cohort of AS patients.

Methods: As part of a wider phenotyping study patients with AS undertook the NEI-VFQ25. This questionnaire is a widely used and validated shortened version of the NEI 51-item visual function questionnaire. It is multidimensional and yields a total score and several subscales. Here, the total score was analysed. Where possible, patients were also contacted some years after their initial visit, and the questionnaire was repeated to explore stability. Particular note was made of those patients who underwent lens exchange surgery for anterior lenticonus.

Results: 32 patients with AS were evaluated: 19 were males with X-linked AS; 8 were females with X-linked Alport variants; 5 had autosomal recessive AS. Mean (SD) age was 36 (16) years. Mean (SD) VFQ25 for the cohort was 84.9 (13.9). The lowest score was 35.4 in a patient with severe recurrent corneal erosions. Five patients had significant anterior lenticonus, and were listed for surgery; these patients had a mean (SD) score of 68.9 (11.9), which was significantly lower than the overall mean ($p < 0.05$). Eighteen patients completed the VFQ25 questionnaire on a second occasion after a median (and mean) period of 6 years. For this cohort, there was no significant change in VFQ25 score. However, in a subgroup of 4 patients who underwent surgery for lenticonus and also completed the questionnaire on a second occasion, there was a significant increase in scores ($p < 0.05$), with initial and final mean (SD) scores of 68.5 (13.7) and 94.1 (4.9) respectively.

Conclusions: We present average VFQ25 scores from a cohort of over 30 patients with Alport syndrome. For 18 patients who completed the questionnaire on a second occasion following a median interval of 6 years, scores were largely stable. The questionnaire appeared to be sufficiently sensitive to show an adverse effect of lenticonus on vision-related quality of life, and a noticeable improvement following surgery.

CONTROL ID: 3544060

SUBMITTER (NAME ONLY): Min Gao

TITLE: Reconstruction of high-resolution OCT angiograms of retinal intermediate and deep capillary plexuses using deep learning

SESSION TITLE: Deep learning for classification and segmentation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Gao, T.T. Hormel, J. Wang, Y. Guo, S. Bailey, T.S. Hwang, Y. Jia, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: We propose to use deep learning to reconstruct flow signal from under-sampled 6×6-mm optical coherence tomographic angiography (OCTA) images of the intermediate capillary plexus (ICP) and deep capillary plexus (DCP).

Methods: 6×6-mm macular scans with a 400×400 A-line sampling density and 3×3-mm scans with a 304×304 A-line sampling density were acquired on one or both eyes of 180 participants (including 230 eyes with diabetic retinopathy (DR) and 44 healthy controls) using a 70-kHz commercial OCT system (RTVue-XR; Optovue, Inc.). Projection-resolved OCTA algorithm was applied to remove projection artifacts in voxel. ICP and DCP angiograms were generated by maximum projection of the OCTA signal within the relevant plexus. We proposed a deep-learning-based method, dubbed “deep capillary angiograms reconstruction network” (DCARnet), to reconstruct 6×6-mm high-resolution ICP and DCP en face OCTA images from sparsely-sampled, low-resolution scans of the same area. DCARnet takes registered 3×3-mm ICP and DCP angiograms with proper sampling density as the ground truth reference. Same network can also be applied on 3×3-mm angiograms. We evaluated the reconstructed 3×3- and 6×6-mm angiograms based on vessel connectivity, false flow signal (flow signal erroneously generated from background), and the noise intensity in the foveal avascular zone (FAZ).

Results: Compared to the originals, the angiograms reconstructed by DCARnet significantly reduced noise intensity (ICP, 7.38 ± 25.22 , $p < 0.001$; DCP, 11.20 ± 22.52 , $p < 0.001$), improved vascular connectivity (ICP, 0.95 ± 0.01 , $p < 0.001$; DCP, 0.96 ± 0.01 , $p < 0.001$), and did not generate false flow signal at the level of noise intensity in normal FAZ. DCARnet not only enhanced the image quality of 6×6-mm ICP and DCP angiograms, but also reduced noise and improved connectivity in 3×3-mm ICP and DCP angiograms. Furthermore, DCARnet preserves the appearance of the dilated vessels in the reconstructed angiograms.

Conclusions: DCARnet can reconstruct high-resolution ICP and DCP angiograms from low-definition 6×6-mm en face OCTA images. The enhanced angiograms may improve characterization of biomarkers such as non-perfusion area and vessel density.

CONTROL ID: 3544062

SUBMITTER (NAME ONLY): Andrea Tornero-Jimenez

TITLE: Effect of Acute Intraocular Pressure Reduction on Vascular Density and Perfusion of Optic Nerve and Macula as Measured by Optical Coherence Tomography Angiography.

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Tornero-Jimenez, J.A. Paczka, A. Orozco Garcia, I.F. Vazquez, A.M. Ponce Horta, Instituto de Oftalmologia y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|A. Tornero-Jimenez, A. Orozco Garcia, I.F. Vazquez, A.M. Ponce Horta, C.D. Ortiz-Moreno, Research Department, Unidad de Diagnostico Temprano del Glaucoma, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Research & Development, Asistencia e Investigacion en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Optical coherence tomography angiography (OCTA) qualitatively assesses the microcirculation within the optic nerve and macula. Vascular density quantification is also measured with this technique. Long-standing ocular hypertension can lead to a varied chronic structural change including the capillary bed. Although a decreased intraocular pressure (IOP) due to antiglaucoma therapy may improve perfusion of the optic nerve, it would be desirable to know if an abrupt reduction in IOP could have an effect on the microcirculation. The objective of this study is to investigate the effect of two clinical settings of abrupt IOP reduction on OCTA variables in the ON and the macula.

Methods: Eighteen eyes of 18 non-consecutive patients which underwent either a bleb needling (BN) procedure or post-trabeculectomy digital compression (DC) were evaluated by applanation tonometry, ON and macula OCT, and OCTA. Baseline measurements were followed by any one of the ocular hypotensive maneuvers. The studied variables were cup to disc (CD) ratio, thickness of retinal nerve fiber layer (RNFL), thickness of the ganglion cell complex (GCC), and perfusion (ONP) and flux index (ONFI) of the optic nerve, as well as perfusion (MP) and vessel density (MVD) of the macular area.

Results: Patients included in the study (10 males, 8 females) had a mean age of 61.9 ± 17.7 years. A post-procedure IOP (9.4 ± 4.7 mmHg) was significantly less ($p=0.0001$) than before the procedures were carried out (23.1 ± 8.9 mmHg). No significant changes in the RNFL, GCC, and CD ratio were found before and after the procedures, neither in the intervened eyes nor in the control ones. Pre-procedure ONFI (0.3 ± 0.65), MP (63.6 ± 7.2) and MVD (16.0 ± 3.6) were significantly different ($p=0.01$, $p=0.03$, and $p=0.0001$; respectively) as compared to post-procedure values (0.37 ± 0.04 , 62.7 ± 8.0 and 17.3 ± 2.6), but not with ONP (40.1 ± 3.8 vs. 40.1 ± 3.2 ; $p=0.89$). IOP reduction was inversely correlated with pre- ($r=-0.62$; $p=0.005$) and post-procedural ONFI ($r=-0.56$; $p=0.01$), as well as pre-MVD ($r=-0.6$; $p=0.007$).

Conclusions: Acute IOP decrease after either BN or DC, is associated with a modest but significant change in several OCTA variables (ONFI, MVD, MP). The clinical impact of such microvasculature changes is still a matter to be elucidated.

CONTROL ID: 3544064

SUBMITTER (NAME ONLY): Julien Blouin

TITLE: Protection of RPE cells against oxidative stress-induced cell death by choroidal melanocytes and their secreted factors

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The goal of this project is to study the involvement of the choroid and its most abundant cells, the melanocytes, in the protection of retinal pigment epithelial (RPE) cells against oxidative stress.

Methods: RPE were seeded on a choroidal substitute that was produced using the self-assembly approach of tissue engineering (3D models). Choroidal melanocytes were added (or not) to the choroidal stromal substitutes. These different cell combinations of 3D models were exposed to oxidative stress (tert-butyl hydroperoxide: TBHP, 250 μ M, 2h). Levels of reactive oxygen species (CellRox) and cellular death (Ethidium-homodimer) were then assessed. In 2D models, RPE cells were exposed to oxidative stress (500, 1000 μ M, 2h), then incubated with either fresh media or media conditioned by melanocytes that were previously exposed to oxidative stress (500 μ M, 2h) using different dilutions. Death of the RPE cells was measured using LDH release assay and by viability assays (Annexin/ Propidium iodide; Caspase 3/7). Proteins and cytokines secreted by melanocytes, fibroblasts and RPE cells in 2D cultures were identified and measured (Human XL Cytokine Array Kit; ELISA).

Results: The presence of melanocytes in the engineered tissues reduced CellRox intensity by 45% and decreased RPE cell death by 90%. Oxidative stress-induced cell death of RPE cells was reduced by 5% when the RPE cells were left to recover in the media conditioned by melanocytes (1:1 ratio with fresh culture media). Compared to choroidal fibroblasts and RPE cells, melanocytes secreted respectively 49 and 46-times more pigment epithelium-derived factor (PEDF) and 6 and 4-times more osteopontin (OPN).

Conclusions: Overall, our results demonstrate that choroidal melanocytes protect RPE cells against oxidative stress-induced cell death. PEDF and OPN were identified as proteins mainly secreted by melanocytes, and may be involved in this protection. The identification of factors that prevent RPE cell death could help to find a cure for diseases where RPE needs protection, such as dry AMD.

CONTROL ID: 3544065

SUBMITTER (NAME ONLY): Yogeshwari Sanjayrao Ambekar

TITLE: Assessing biomechanical properties of ex vivo murine retinas using Brillouin microscopy

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Ambekar, M. Singh, K. Larin, Biomedical Engineering, University of Houston, Houston, Texas, UNITED STATES|E.M. Rueda, B.M. Hall, R.A. Poché, K. Larin, Molecular Physiology and Biophysics, Baylor College of Medicine, Houston, Texas, UNITED STATES|J. Zhang, G. Scarcelli, Fischell Department of Bioengineering, University of Maryland at College Park, College Park, Maryland, UNITED STATES|
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ABSTRACT BODY:

Purpose: The retina is a crucial part of the eye and plays an important role in vision. Assessing the biomechanical properties of retina could provide critical information for disease detection and guiding precision therapeutic interventions. Previous work assessing retinal elasticity has been limited to global assessments and destructive methods, but in this work we demonstrate Brillouin microscopy to noninvasively assess the layer by layer distribution of retinal stiffness. Furthermore, we were able to measure the changes in retinal stiffness caused by fixation and the effects of n-methyl-d-aspartate (NMDA) induced damage.

Methods: Dissected fresh (n = 3) and paraformaldehyde-fixed (n = 2) adult C57/BL6J mice retinas were used in this experiment. The retinas were mounted flat on microscope slides with the vitreous layer on the top and the photoreceptor layer on the bottom. Optical coherence tomography (OCT) images were acquired to visualize the retina structure and ensure there was no damage. Next, Brillouin microscopy was used to obtain the layer by layer distribution of biomechanical properties of the retinas. As a proof-of-concept study, mice were intravitreally injected with 100 mM NMDA and imaged using OCT and Brillouin microscopy.

Results: We observed that the average Brillouin modulus of all fresh retinas over entire depth was 2.48 ± 0.06 GPa whereas the average Brillouin modulus of all fixed retinas was 2.73 ± 0.09 GPa. Figure 1 (a) shows layer by layer distribution of stiffness within the retina using Brillouin microscopy. Retinal ganglion cell (RGC) layer of NMDA-damaged retina had a greater Brillouin modulus compared to the control retina sample.

Conclusions: We showed that Brillouin microscopy can noninvasively assess the stiffness over the entire depth of ex vivo mouse retinas. We observed that the retina is a heterogeneous tissue and has different biomechanical properties for its different layers. Fixed retinas were stiffer compared to fresh retinas. Results showed the biomechanical properties are highly affected by the cellular density and PFA-fixing. Increased Brillouin modulus in the RGC layer of NMDA-induced retina may indicate cell death in that layer.

CONTROL ID: 3544066

SUBMITTER (NAME ONLY): Ana Ponce Horta

TITLE: Comparative Performance of Würzburg Classification System and a Novel Classification System by Anterior Segment Optical Coherence Tomography in Assessing Filtering Blebs

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Ponce Horta, J.A. Paczka, A. Tornero-Jimenez, A. Orozco Garcia, I.F. Vazquez, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|A.M. Ponce Horta, A. Tornero-Jimenez, A. Orozco Garcia, I.F. Vazquez, S. Garcia y Otero Sánchez, Research Department, Unidad de Diagnóstico Temprano del Glaucoma, Guadalajara, Jalisco, MEXICO|J.A. Paczka, D. Valencia Paredes, Research & Development, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Trabeculectomy is the most practiced glaucoma surgery; however, its success depends on the presence of a filtering bleb and its lowering pressure capacity, usually related to its morphology and permeability. Multiple clinical classification systems have been proposed to describe filtering bleb appearances and their functionality. Optical coherence tomography (OCT) technology has been used to describe the inner morphology of such blebs. The objective of this study is to determine the correlation between the IOP-lowering capacity of a series of post-trabeculectomy filtering blebs and the Würzburg classification (WC) system, as well as with a new anterior segment OCT (AS-OCT) classification system (NOCTCS).

Methods: A cross-sectional study of non-consecutive cases that underwent primary supplemented-MMC trabeculectomy was carried out. Fifty-eight eyes from 39 patients with glaucoma were included. Anterior segment and filtering bleb photographs of the included cases were examined by two independent and masked observers using the WC (score range, 0-12). A series of AS-OCT images were also evaluated by the same observers, using NOCTCS (score range, 0-6) that evaluates 3 tomographic traits of the filtering bleb (wall thickness, cystic spaces and wall inner reflectivity). A weighted score was assigned to each item for every examined case. The data were analyzed with SPSS 25 statistical software, considering significant a p value ≤ 0.05 .

Results: Patients had a mean age of 61.4 ± 17.8 years. The cases consisted in a greater proportion of female (71.8%), primary open-angle glaucoma (53.8%), and required digital compression (69.4%). The mean time after trabeculectomy was 52.2 ± 32.1 months. A WC of 9.4 ± 2.7 , inversely correlated with mean post-operative IOP values ($r = -4.30$, $p = 0.001$). The mean NOCTS also correlated but in a weaker manner with the mean IOP ($r = -2.41$, $p = 0.034$). However, it did not correlate with the mean percentage reduction of IOP ($r = 0.133$, $p = 0.159$). In addition, NOCTS and WC, correlated fairly well ($r = 0.412$, $p = 0.001$).

Conclusions: The Würzburg system outperformed the NOCTS. A combined assessment with clinical and tomographic traits might be more useful to establish key findings associated to better post-trabeculectomy outcomes. Prospective trials using clinical and AS-OCT images of filtering blebs are required.

CONTROL ID: 3544067

SUBMITTER (NAME ONLY): Javier Zarranz-Ventura

TITLE: COVID-19 pandemic lockdown international impact on nAMD, DME and RVO intravitreal therapy outcomes: Fight Retinal Blindness International registry

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the impact of COVID-19 pandemic lockdown on the clinical outcomes of an international cohort of neovascular AMD (nAMD), diabetic macular edema (DME) and retinal vein occlusion (RVO) treated eyes in eight countries: Australia, France, Ireland, Italy, Netherlands, New Zealand, Spain and Switzerland.

Methods: Multicenter international nAMD, DME and RVO database observational study. Data was internationally collected using a validated web-based tool (Fight Retinal Blindness! Project). Baseline visit was defined as the closest visit prior (up to 3 months) to the initial lockdown date, which differed by country. Pre- and post-lockdown periods were defined as 6 months prior and post-baseline visit. Data collected included: demographics, visual acuity (VA) in logarithm of the minimum angle of resolution (logMAR) ETDRS letters at baseline and pre- and post-baseline visits, number of injections and visits.

Results: 5271 eyes of 4288 patients were included. In nAMD eyes (n=4240), mean VA change post-lockdown ranged from -0.3 to -3.3 letters, and the median number of injections/visits decreased from a pre-lockdown range of 4-5/4-7 to a range of 2-4/2-4 post-lockdown, respectively. In DME eyes (n=605), mean VA change ranged from -4 to +2.3 letters, and the median number of injections/visits decreased from a pre-lockdown range of 2-5/4-6.5 to 1-3/2-3. In RVO eyes (n=426), mean VA change ranged from -2.4 to +3 letters, and the median number of injections/visits decreased from a range of 3-7/4-7.5 to 1-6/2.5-6 post-lockdown. The dropout rates for the 6 months post-lockdown period were 34% for nAMD (n=1458), 43% for DME (n=264) and 44% for RVO (n=188). Study drugs included ranibizumab (33.5%), aflibercept (50.9%) and bevacizumab (15.5%).

Conclusions: This study provides accurate estimates of the impact of COVID-19 pandemic lockdown on the visual outcomes of an international cohort of eyes treated with intravitreal therapy. The data reported in this study may serve clinicians to prepare strategies to mitigate vision loss in future scenarios of the COVID-19 pandemic evolution.

CONTROL ID: 3544069

SUBMITTER (NAME ONLY): Farzad Pakdel

TITLE: Efficacy of Anti-TNF-alpha agents in Active Thyroid Eye Disease

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The key role of tissue necrosis factor alpha (TNF alpha) has been shown in the pathophysiology of thyroid eye disease. In this study we aimed to report the effect of anti-TNF alpha agents in treatment of patients with active thyroid eye disease (TED) who could not take or failed to respond to corticosteroids.

Methods: Data of all patients with active TED from January 2014 to December 2018, that received anti-TNF alpha agents because they could not take steroids or showed resistance to them, were reviewed. Data included visual acuity, clinical activity score (CAS), extra-ocular motility, eyelid swelling and erythema, conjunctival injection and chemosis, caruncular congestion, keratopathy and dysthyroid optic neuropathy. Those with follow-up less than 9 months were excluded.

Results: Data of eight eligible patients were analyzed. Mean age was 54.6 (SD= 7.08, range=42-65) years. Five were male. The reason for abandonment from corticosteroid included: gastrointestinal bleeding (n=1), congestive heart failure (n=1), diabetic hyperosmolar state (n=1), non- or inadequate response to corticosteroid regimen (n=5). Patients received one anti-TNF alpha agent as single main treatment including infliximab (n=3), etanercept (n=3), Adalimumab (n=2). CAS score decreased from baseline 5.5 (SD= 1.69) to 0.5 (SD= 0.75) (p=0.0001). Proptosis value showed decreased from baseline 24.12 mm (SD= 2.23) to 22.12 (SD=1.88) after treatment (p=0.037). The patients that received adalimumab showed resolution of diplopia and decrease in proptosis in comparison to none of the other six patients. Mean follow up time was 27.75 (range: 15-46, SD= 10.30) months. Four (50%) patients were current smokers. Five patients had DON before anti-TNF alpha. Four of them were smokers. Three of them improved by anti-TNF alpha medication only. We did not observe any complication associated with the use of anti-TNF alpha agents.

Conclusions: This study supports the efficacy of anti-TNF alpha agents in active TED. Further they may be considered in patients that cannot take corticosteroids or are resistant to steroid therapy. Results of this study justify future comparative studies to verify efficacy of this modality of treatment in patients with active TED.

CONTROL ID: 3544071

SUBMITTER (NAME ONLY): Taewoo Lee

TITLE: Developing Behavior-Based Diabetic Retinopathy Screening Guidelines

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Personalized screening guidelines can be an effective strategy to prevent diabetic retinopathy (DR)-related vision loss. However, these strategies typically do not capture behavior-based factors such as a patient's compliance or cost preferences. This study develops a mathematical model to identify screening policies that capture both DR progression and behavioral factors to provide personalized recommendations.

Methods: A partially observable Markov decision process model (POMDP) is developed to provide personalized screening recommendations. For each patient, the model estimates the patient's probability of having a sight-threatening diabetic eye disorder (STDED) yearly via Bayesian inference based on natural history, screening results, and compliance behavior. The model then determines a personalized, threshold-based recommendation for each patient annually—either no action (NA), teleretinal imaging (TRI), or clinical screening (CS)—based on the patient's current probability of having STDED as well as patient-specific preference between cost saving (\$) and QALY gain. The framework is applied to a hypothetical cohort of 40-year-old African American male patients.

Results: For the base population with TRI and CS compliance rates of 65% and 55% and equal preference for cost and QALY, NA is identified as an optimal recommendation when the patient's probability of having STDED is less than 0.72%, TRI when the probability is [0.72%, 2.09%], and CS when the probability is above 2.09%. Simulated against annual clinical screening, the model-based policy finds an average decrease of 7.07% in cost/QALY (95% CI; 6.93-7.23%) and 15.05% in blindness prevalence over a patient's lifetime (95% CI; 14.88-15.23%). For patients with equal preference for cost and QALY, the model identifies 6 different types of threshold-based policies (See Fig 1). For patients with strong preference for QALY gain, CS-only policies had an increase in prevalence by a factor of 19.2 (see Fig 2).

Conclusions: The POMDP model is highly flexible and responsive in incorporating behavioral factors when providing personalized screening recommendations. As a decision support tool, providers can use this modeling framework to provide unique, catered recommendations.

CONTROL ID: 3544072

SUBMITTER (NAME ONLY): Gavin Li

TITLE: Outcomes of Sjögren's versus non-Sjögren's Related Dry Eye in a Longitudinal, Tertiary Clinic-Based Sample

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Li, D. Cui, P. Mathews, S. Van Court, E. Akpek, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the long-term treatment outcomes of dry eye in patients with and without primary Sjögren's Syndrome (SS) in a retrospective cohort study.

Methods: SS and non-SS dry eye patients with clinic visits for a minimum of 5 consecutive calendar years at a tertiary, dedicated dry eye clinic were included. Electronic health records were reviewed to collect data regarding demographics, objective dry eye parameters (Schirmer's test without anesthesia, tear osmolarity, corneal and conjunctival staining) at baseline and final visit, treatments utilized, and corneal complications during follow-up.

Results: Two hundred and two patients (101 SS and 101 non-SS) were included, with mean follow-up of 7.1 years (range 3.8 to 15.4). At baseline, patients had significant mean conjunctival (2.9) and corneal (2.0) staining. Notable improvement in staining score for cornea (-1.1, $P < .001$) and conjunctiva (-1.8, $P < .001$) was seen equally in both SS and non-SS dry eye groups. A great majority of patients (89.1%) received escalation of treatment at final visit with equal rates in both groups ($P = .259$). Half (48.9%) of the patients had no conjunctival staining and a third (34.4%) had no corneal staining at last visit. Twenty (9.9%) patients experienced a vision-threatening corneal complication including ulcers and melt with no difference between the groups ($P = .638$).

Conclusions: The majority of patients in this longitudinal, tertiary clinic-based sample had improvement in ocular surface staining score by final visit owing to proper treatment escalation. Treatments used, improvement achieved, and corneal complication rates were similar in both SS and non-SS dry eye groups.

CONTROL ID: 3544073

SUBMITTER (NAME ONLY): Katherine Derouin

TITLE: Multimodal photoacoustic microscopy and OCT molecular imaging of choroidal neovascularization in rabbits using indocyanine green

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Derouin, V. Nguyen, Y. Li, J. Henry, W. Zhang, X. Wang, Y.M. Paulus, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection of neovascularization is essential for early diagnosis and treatment of diseases such as diabetes and macular degeneration, yet it remains challenging. We tested whether an FDA-approved exogenous contrast agent, indocyanine green (ICG), could enhance photoacoustic microscopy (PAM) significantly enough to differentiate neovascularization from normal vasculature in rabbits.

Methods: ICG was conjugated with RGD peptide to bind to integrin expressed in neovascularization. A custom-built multimodal PAM and Thorlabs Ganymede-II-HR OCT retinal imaging system was utilized. New Zealand white rabbits (N=6) were treated with subretinal injection of Matrigel and human vascular endothelial growth factor (VEGF-165) to induce choroidal neovascularization (CNV) and imaged before and at 2 h, 24 h, 48 h, 72 h, 4, 5, 7, 9, 11 and 14 days after intravenous administration of ICG 0.4 mL at 2.5 mg/mL after approval by the UM IACUC.

Results: In indocyanine green angiography (ICGA) and PAM imaging at 700 nm, no signal was observed pre-injection of ICG-RGD. 2 h post-injection the binding of ICG-RGD at CNV was identified with a strong PAM signal. 24 h post injection, the CNV was visualized with ICGA. PA image contrast at 700 nm was improved by 13-fold from $.03 \pm .001$ a.u. pre-injection to $.39 \pm .03$ a.u. at 2 h post-injection ($p < .001$). The peak PA amplitude within CNV was achieved at 24 hours post-injection and increased by 15.7-fold (PA signal = $.47 \pm .03$ a.u.). PAM imaging also showed ICG-RGD present in CNV for up to 5 days post-injection in living rabbits with a model of CNV, allowing for extended evaluation.

Conclusions: Injection of ICG-RGD led to increase in PAM imaging contrast. This signal peaked at 24 hours and continued for up to 5 days. This allowed for successful differentiation between neovascularization and normal vasculature. This work demonstrates the possibility that ICG-RGD paired with PAM imaging can assist in early detection of CNV.

CONTROL ID: 3544074

SUBMITTER (NAME ONLY): Nicole Ross

TITLE: Input following first time use of visual assistance mobile apps by seniors with low vision

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mobile phone applications(apps) have become important tools for everyday life and can offer additional accessibility for patients with low vision. It is unknown whether seniors with low vision will be able to use and embrace apps.

Methods: Fourteen participants were interviewed during one of 5 focus group sessions conducted via zoom videoconferencing; n=8 from Boston, n=6 from L.A. They had no prior experience with 3 visual assistance apps (Aira, SuperVision+, SeeingAI), received a study loaner iPhone with the three apps, a brief demonstration of the apps' features, then tried the apps for ~5 minutes during the focus group, after which their feedback was solicited. Median age was 66 years (IQR 58-77), and median visual acuity in the better eye was 0.6 logMAR (IQR 0.4-0.8 logMAR). Qualitative analyses were used to explore themes from the discussion and Wilcoxon Sign Rank tests evaluated for differences according to participants' characteristics.

Results: A greater number of participants reported they would use Aira or SuperVision+ outside the home (57% for Aira, 50% for SuperVision+; e.g., shopping in stores, navigating streets, airports) than inside the home (28% for Aira, 21% for SuperVision+; e.g., reading, identifying objects, computer), which was not significantly influenced by age or visual acuity.

The primary theme to encompass comments about Aira from 9 subjects (64%) was: "Always there for you with a human element" as they would appreciate relying on the personalized service when others were not available to assist; additionally, they felt public use was inconspicuous and less stigmatizing than other visual aids. The primary theme for SuperVision+ (from 71%; n=10) was "convenience at your fingertips: one less thing to weigh you down" as it eliminates the need to take a magnifier along with a smartphone. Preferences for the SeeingAI features and usability were more varied, with less consensus.

Five participants (36%) were unable to try all three apps due to difficulty using or understanding the technology; their median age was 76 years (range 66-81) and all had age-related, acquired vision loss. Eight (57%) cited the need for additional assistance with the apps.

Conclusions: Low vision seniors were more likely to report indications for visual assistive apps in public places than at home. Participants appreciated the concept and convenience of the apps, but some will require further training.

CONTROL ID: 3544085

SUBMITTER (NAME ONLY): Alexandra Boehm

TITLE: Variation in unique yellow for small foveal spots

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Boehm, J.E. Vanston, G.D. Hastings, A.J. Roorda, W.S. Tuten, School of Optometry and Vision Science Graduate Group, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Individuals are remarkably consistent in the color that they perceive to be uniquely yellow, despite several sources of anatomical variability. Studies using larger stimuli (≥ 1 deg) have shown that unique yellow (UY) is invariant to differences in L/M cone ratio, suggesting that color appearance is normalized to be consistent across observers. Whether this invariance is maintained at smaller spatial scales is not well understood. Otake and Cicerone (2000) showed that foveal estimates of UY shifted toward longer wavelengths when measured with small stimuli (3 arcmin), although the extent to which optical factors may have contributed to these findings, or whether this trend persists at even smaller spatial scales, is not clear.

Methods: We used an adaptive optics scanning laser ophthalmoscope (AOSLO) to correct ocular aberrations and examine how stimulus size and duration influence foveal estimates of UY. UY estimates were obtained at three stimulus sizes (1, 3, 11 arcmin diameter) and three durations (1, 4, 15 frames at 30 fps) using a multi-wavelength AOSLO, which provided simultaneous retinal imaging and aberration-corrected stimulus delivery. Stimuli were composed of varying mixtures of green (543 nm) and red (680 nm) monochromatic lights to produce metamers to intermediate wavelengths. Axial and transverse chromatic aberrations were corrected. Stimuli were viewed against a white background. Participants ($n = 4$) reported on each trial whether the stimulus appeared redder or greener. Primary mixtures were adjusted using an adaptive staircase procedure, and UY was defined as the mixture that was equally likely to be judged as red or green.

Results: In the 11 arcmin/15 frame condition, the mean wavelength of UY was 585 nm (range: 580-592 nm), roughly consistent with previous estimates obtained with larger stimuli. For all subjects, UY tended toward longer wavelengths as stimulus size decreased, with an average UY at 591 nm (range: 580-602 nm) for the 1 arcmin/15 frame condition. UY was mostly constant as a function of duration, except in the case of the smallest and briefest stimuli, where UY was 3-12 nm longer.

Conclusions: Our results demonstrate that restricting the spatio-temporal profile of the stimulus on the retina causes UY to (1) shift to longer wavelengths and (2) exhibit more variability between observers. These findings suggest that the normalization of UY for large-field stimuli does not persist at the smallest spatial scales.

CONTROL ID: 3544087

SUBMITTER (NAME ONLY): Harry Flynn

TITLE: Acute-Onset Postoperative Endophthalmitis After Cataract Surgery Performed by Resident and Attending Physicians at a University Teaching Hospital (2015-2020)

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.W. Flynn, A.L. Kunkler, K.E. Donaldson, D. Miller, N.A. Yannuzzi, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate nosocomial acute-onset postoperative endophthalmitis following cataract surgery at a university teaching hospital and to compare frequency among resident and attending physicians.

Methods: This study was a retrospective, consecutive case series of patients diagnosed with acute-onset postoperative endophthalmitis within 6 weeks of cataract surgery performed at at Bascom Palmer Eye Institute, Miami, Florida between January 1, 2015, and November 30, 2020. Resident physician case totals were obtained from self-reported case logs.

Results: In a six-year period, there were 22 cases of acute-onset postoperative endophthalmitis following cataract surgery at a single institution. The overall frequency of endophthalmitis was 0.068% (22/32,505). The most common bacterial isolate was Coagulase-negative Staphylococcus (7/22, 31.8%) followed by Streptococcus spp. (3/22, 13.6%). Cultures were negative in 11 eyes (11/22, 50%). Initial treatment with tap and injection was performed in 21 eyes (21/22, 95.4%) and vitrectomy in one eye (1/22, 4.5%). Injection of vancomycin 1.0mg and ceftazidime 2.25mg was performed in all eyes and dexamethasone 400ug was added initially in 18 eyes (18/22, 81.8%). Vitrectomy was performed as a second treatment in 9 patients (9/22, 40.9%). Visual acuity (VA) at last follow up was 20/40 or better in 13 eyes (13/22, 59%) and hand motions or worse in 3 eyes (3/22, 13.6%). The frequency of endophthalmitis for resident physicians was 0.09% (6/6,447), compared to 0.06% (16/26,058) for attending physicians, but this difference was not statistically significant (P=0.55). There was no difference (P=0.14) between average VA outcomes among resident (logMAR VA 1.19 ± 1.06) and attending physican (logMAR VA 0.53 ± 0.80) cases.

Conclusions: At a university teaching hospital, the frequency of acute-onset postoperative endophthalmitis following cataract surgery remains low. When stratified between resident and attending physicians, the frequency of endophthalmitis and visual outcomes were similar.

CONTROL ID: 3544088

SUBMITTER (NAME ONLY): Crystal Colón Ortiz

TITLE: Endothelial caspase-9 signaling alters glial response in a mouse model of retinal vein occlusion (RVO)

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.K. Colón Ortiz, M. Avrutsky, J. Lawson, J. Smart, C. Troy, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vascular diseases present increased glial activity, inflammation, and release of inflammatory cytokines. But the signaling mechanisms that connect vascular damage to a glial response have not been elucidated. Studies in the laboratory showed that non-apoptotic activation of endothelial caspase-9 (EC-Casp9) regulated activation of astroglial caspase-6 in a mouse model of retinal vein occlusion (RVO). We investigated the effect of EC-Casp9 signaling on astroglial and microglial response in RVO.

Methods: RVO was performed in inducible EC-Casp9 (iEC-Casp9 WT/KO) adult male mice by tail vein injection of Rose Bengal and photocoagulation of major retinal veins. After induction of RVO we collected the retinas one and two days post RVO (P-RVO). Immunohistochemistry for Iba-1, CD68, cl-Caspase-6, GFAP, and AQP-4 was done and analyzed by blinded quantification using thresholding analysis in FIJI. Data was evaluated in injured iEC-Casp9 WT (n=6-8) and iEC-Casp9 KO (n=4-9), and uninjured groups (iEC-Casp9 WT, n=3, iEC-Casp9 KO, n=3). Kruskal-Wallis followed by Dunn's and Brown-Forsythe and Welch ANOVA tests were used for statistical analysis.

Results: EC-Casp9 did not modify the total number of Iba-1 or CD68 microglial cells, but the latter increased in injured animals two days P-RVO ($p=0.02$) compared to uninjured iEC-Casp9 WT. The area of microglial CD68 particles of injured retinas was bigger P-RVO ($p=0.01$, $p=0.001$), and rescued to normal levels in injured iEC-Casp9-KO 1 day P-RVO ($p=0.03$). EC-Casp9 led to higher astroglial cl-caspase-6 in injured iEC-Casp9 WT at assessed time points ($p=0.02$, $p=0.004$) compared to injured iEC-Casp9 KO. However, injured retinas did not show differences in GFAP expression P-RVO, but had a downward trend in AQP-4 2 days P-RVO compared to uninjured iEC-Casp9 WT, independent of EC Casp9.

Conclusions: EC-Casp9 expression caused increased microglial activation in a timely manner and led to higher astroglial cl-caspase-6 expression, but not GFAP or AQP-4. These data demonstrate that EC-Casp9 signaling affects glial activity in our model. Further studies will help determine whether these glial responses are detrimental to the neuroretina.

CONTROL ID: 3544090

SUBMITTER (NAME ONLY): Hamzah Aweidah

TITLE: A Deep Intronic Substitution in CNGB3 is One of the Major Causes of Achromatopsia among Jewish Patients

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Aweidah, M. Salameh, C. Yahalom, A. Blumenfeld, M. Macarov, E. Banin, D. Sharon, Department of Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|N. Weisschuh, S. Kohl, Centre for Ophthalmology, Universitätsklinikum Tübingen Forschungsinstitut für Augenheilkunde, Tübingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: Although most (and perhaps all) genes that can cause achromatopsia (ACHM) when mutated are known, some patients with an ACHM phenotype are still negative for mutations in the coding region of known genes. Our aim was to characterize genetic and clinical aspects of a deep intronic (c.1663-1205G>A, IVS14-1205G>A) CNGB3 variant.

Methods: Clinical evaluation included visual acuity testing, refractive error, color vision testing, full-field electroretinography, and multi-modal retinal imaging. Genetic analysis was performed by Sanger sequencing of PCR products.

Results: Screening for the CNGB3 c.1663-1205G>A variant revealed 17 patients belonging to 12 unrelated families who were either homozygous (7 cases, 5 families) or compound heterozygous (10 cases, 7 families) with another known CNGB3 mutation on the counter allele. All patients were diagnosed with a cone-dominated disease, mainly complete ACHM. In all cases, the disease had an early congenital onset. Visual acuity was markedly impaired, ranging between 0.07 and 0.32 ETDRS (LogMAR +1.18 to +0.50), with a mean visual acuity of 0.15 ETDRS (LogMAR +0.80). Additional typical signs of ACHM including impaired color vision, light aversion, and nystagmus were also noted in all patients. As is common in ACHM, fundus exam was largely unremarkable in the majority of patients, with mild foveal retinal pigment epithelium changes seen in some cases at older ages. Electroretinography was available for 14 out of 17 patients and in all of them cone responses were non-detectable, including infants from the age of 6 months. In a few cases, rod involvement was also evident, with mild reduction of amplitudes. Optical coherence tomography imaging showed irregularity of the ellipsoid zone in the foveal area in some of the patients.

Conclusions: CNGB3 is the most common cause of ACHM in patients of European descent, mainly due to a panethnic founder mutation, c.1148del. Here we report of an intronic CNGB3 variant which is more frequent than the c.1148del mutation in the Jewish population. Among our ACHM cohort, 64% have biallelic CNGA3 mutations and 32% have biallelic CNGB3 mutations. The phenotype of patients harboring the intronic mutation falls largely within the spectrum commonly seen in ACHM. As gene therapy for CNGB3 is currently under investigation, these patients might benefit from this promising therapy.

CONTROL ID: 3544091

SUBMITTER (NAME ONLY): Aaron Lindeke-Myers

TITLE: Pentosan Polysulfate Maculopathy: Prospective Longitudinal Study of Disease Course after Drug Cessation

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lindeke-Myers, R. Lyons, J. Brower, N. Jain, Ophthalmology, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies have demonstrated an association between long-term pentosan polysulfate (PPS) use and a novel maculopathy. No study has prospectively evaluated long-term disease course after drug cessation. Here, we report year 1 outcomes of a long-term prospective study of retinal structure and function in PPS maculopathy.

Methods: Thirteen PPS maculopathy patients were followed prospectively with multimodal assessments of retinal structure and function; 11 (22 eyes) completed year 1 visits. Functional testing endpoints at year 1 included: microperimetry (MP) mean and percent reduced thresholds, and ETDRS best corrected visual acuity (BCVA). Structural endpoints included: central subfield retinal thickness (CST), subfoveal choroidal thickness (SFCT), and geographic atrophy area (defined as complete retinal and outer retinal atrophy). Baseline and year 1 outcomes were compared using a Wilcoxon signed rank test. To account for inter-eye correlation, mean results were computed for the two eyes for each patient.

Results: Patients had a median age of 63 (range 38-77) and median 2.04 kg (IQR 1.15 – 2.58) PPS exposure. Patients stopped PPS use a median of 9.9 (IQR 5.6 – 20.5) months prior to baseline. Median change in ETDRS BCVA during the study period was -3 letters (IQR -4.75 – 1.5) [baseline: 81.5 letters (IQR 79 – 86.3), year 1: 78.5 letters (IQR 74.5 – 86.8) ($p = 0.07$)]. Seven of 11 (64%) patients had BCVA decline. Four (18%) eyes, each with progressive atrophy, lost ≥ 10 letters. Median MP average thresholds declined from 25.7 (IQR 17.8 – 26.7) to 25.2 (IQR 16.5 – 27.6) ($p = 0.18$). Median MP percent reduced thresholds increased from median 23.0% (IQR 9.5% – 54.1%) to 25.2% (IQR 14.2% – 28.6%) ($p = 0.88$). Fifteen eyes (68%) had atrophy at baseline; with an increase from a median of 5.64 mm² (IQR 0.36 – 17.9) to a median of 7.23 mm² (IQR 0.45 – 20.8) ($p < 0.01$) and median linearized increase of 0.21 mm (IQR 0.08 – 0.39) per eye. Median CST decreased from 278 μ m (IQR 243 – 287) to 267 μ m (IQR 238 – 290) ($p = 0.08$). Median SFCT decreased from 268 μ m (IQR 159 – 324) to 261 μ m (IQR 161 – 334) ($p = 0.47$).

Conclusions: This prospective study demonstrates continued evolution of structural and functional deficits in patients with PPS maculopathy even after drug cessation. Geographic atrophy enlarged in all eyes with atrophy present at baseline, and thus may pose a long-term threat to central vision.

CONTROL ID: 3544093

SUBMITTER (NAME ONLY): Shehnaz Bazeer

TITLE: Have SARS-CoV-2 virus (COVID-19) lockdown restrictions impacted the prevalence and severity of retinopathy of prematurity in a London population?

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bazeer, A. Mahtani, A. Das, A. Khaier, M. Posner, Barking Havering and Redbridge University Hospitals NHS Trust, Romford, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is the leading cause of blindness associated with pre-term births. Globally, numerous centres have reported a reduction in pre-term hospital births during the SARS-CoV-2 virus (COVID-19) lockdown restrictions. Lockdown measures may have influenced the health and wellbeing of pregnant women.

A survey of ROP screening ophthalmologists in London indicated a perceived reduction in the number of babies screened during lockdown measures in 2020 compared to previous years.

The aim of this study was to determine whether there has been a change in the severity or prevalence of ROP due to COVID-19 lockdown restrictions in the UK.

Methods: A pilot study of 113 participants screened for ROP in an East London Hospital were included. Babies whose last 4 weeks of gestation fell within the UK's first lockdown window of 23rd of March and 28th of August 2020 were compared to data from corresponding dates in 2019.

A student t -test was used to compare the gestational ages, birth-weight, ethnicity, and severity of ROP stage, COVID-19 status and multiple pregnancies.

A chi-squared test was used to compare the prevalence of various stages of ROP between the two groups and a t-test was used to compare the demographics.

Results: This study showed no statistical significance ($p=0.09$) in the prevalence of babies with various stages of ROP between 2019 ($n=68$) and 2020 ($n=45$).

Overall, this pilot study showed no statistical significance ($p>0.05$) in birth-weight, gestational age or ethnicities between the two groups.

Conclusions: In conclusion, our pilot study showed no statistical significance in the prevalence of babies with ROP between 2019 and 2020. Although subjectively we have noted there to be a trend in fewer babies born below 32 weeks or 1500g birthweight during lockdown corresponding to fewer ROP screenings at our London hospital, we were unable to demonstrate a statistically significant difference due to our small sample size.

We aim to increase the power of the study by including data from other screening units in London and collecting further control data from 2018.

We believe that our study has the potential to indicate how the UK's lockdown measures may impact the prevalence and severity of babies with ROP associated with preterm births.

CONTROL ID: 3544094

SUBMITTER (NAME ONLY): Bhavana Chhunchha

TITLE: Prdx6-Loaded PLGA Nanoparticles Protect Lens Epithelial Cells From Oxidative Stress And Prevent Lens Opacity

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Chhunchha, P. Singh, D.P. Singh, Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|E. Kubo, Ophthalmology, Kanazawa Medical University, Kanazawa, Ishikawa, JAPAN|U.B. Kompella, Ophthalmology, University of Colorado Anschutz Medical campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress-evoked aberrant Sumoylation of proteins is linked to aging etiopathologies. We previously reported that TAT transduction domain fused Prdx6 mutated at Sumoylation sites, Prdx6^{K(lysine)122/142R(Arginine)}, enhanced protection of human lens epithelial cells (hLECs) by escaping Sumoylation. Herein, we formulated TAT-His-Prdx6 and TAT-His-Prdx6^{K122/142R}-loaded poly (lactic-co-glycolic acid) (PLGA) nanoparticles (NPs) to further enhance protective efficiency in vitro and in vivo.

Methods: PLGA-based TAT-Prdx6(TAT-His-Prdx6-PLGA) and TAT-Prdx6^{K122/142R}(TAT-His-Prdx6^{K122/142R}-PLGA) NPs were prepared by nano-precipitation method. The properties of TAT-His-Prdx6 and TAT-His-Prdx6^{K122/142R} NPs were characterized by dynamic light scattering(DLS) and atomic force microscopy (AFM). Release assay was done using Prdx6-ELISA. The Prdx6-NPs were delivered to rat lenses cultured under H₂O₂ stress or delivered subconjunctivally to Shumiya Cataract Rat (SCR), to assess the formulation's protective ability. MTS and Dye assays examined cell viability and reactive oxygen species (ROS) levels. Western blot and ELISA analyzed Prdx6 levels using His/Prdx6 antibodies. Two-tailed Student's t-test and one-way ANOVA were used for statistical analysis.

Results: Prdx6 analog loaded PLGA NPs (~56-62% efficiency) were cytocompatible. DLS and AFM analyses showed that the NPs were spherical and of submicron size (220-250nm), with a negative zeta potential of ~23 mV. Release studies revealed that encapsulated Prdx6 analogs were biologically active with ~6-7.5% cumulative release within 24h, followed by slower release thereafter and retained the Prdx6 integrity (~35kDa). NPs with TAT-Prdx6^{K122/142R} (4µg/ml) provided 35% more protection (p<0.05), with ROS reduction in hLECs exposed to H₂O₂ (50µM/72h) compared to TAT-Prdx6-NPs. Lenses cultured with TAT-Prdx6^{K122/142R}-NPs were clear compared to control lenses facing H₂O₂ stress (100µM/72h). Subconjunctival delivery of Prdx6 formulations revealed that TAT-Prdx6^{K122/142R}-NPs released the Prdx6 in vivo and could reduce lens opacity by 58% and delayed cataractogenesis in SCR.

Conclusions: A single application of TAT-Prdx6^{K122/142R}-NPs provided increased cytoprotection and prevented the cataractogenesis compared to TAT-Prdx6-NPs in vitro and in vivo, providing a proof of concept for potential delivery of TAT-Prdx6^{K122/142R} via NPs to delay cataract formation.

CONTROL ID: 3544095

SUBMITTER (NAME ONLY): Gonzalo Carracedo

TITLE: A comparison between aberrometry-based automated subjective refraction and traditional subjective refraction in keratoconus patients

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Carracedo, C. Carpena Torres, C. Pastrana, A. Privado, M. Serramito, T. Espinosa Vidal, M. Rodriguez Lafora, Optometry and Vision, Universidad Complutense de Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the agreement between the Eye Refract, a new instrument to perform aberrometry-based automated subjective refraction, and the traditional subjective refraction in keratoconus patients.

Methods: A total of 50 eyes of 50 keratoconus patients were randomly evaluated, dividing the sample into two groups: 27 eyes without intracorneal ring segments (ICRS) (37.78 ± 9.35 years) and 23 eyes with ICRS (39.26 ± 13.62 years). An optometrist conducted the refraction with the Eye Refract and another different optometrist conducted the traditional subjective refraction on the same day, also randomly. Spherical equivalent (M), cylindrical vectors (J0 and J45), corrected distance visual acuity (CDVA), and time spent performing refraction were compared between both methods of refraction. Additionally, Bland-Altman analysis was performed to assess the agreement between both methods of refraction.

Results: There were no statistically significant differences ($P \geq 0.05$) in terms of M, J0, J45, and CDVA between the Eye Refract and the traditional subjective refraction in either group. However, the Eye Refract was faster for performing refraction than the traditional method ($5:37 \pm 1:35$ min:s vs. $8:36 \pm 2:37$ min:s, $P < 0.001$). Without ICRS, the mean difference and 95% limits of agreement were -0.20 [$+1.50, -1.89$] D for M, -0.14 [$+1.40, -1.68$] D for J0, and $+0.05$ [$+1.23, -1.14$] D for J45. These values worsened with ICRS to -0.62 [$+3.89, -5.12$] D for M, $+0.06$ [$+2.46, -2.34$] D for J0, and -0.02 [$+2.23, -2.28$] D for J45.

Conclusions: The Eye Refract would offer faster refraction compared to the traditional method, and also similar refractive results in keratoconus patients not implanted with ICRS. However, some patients could show abnormal measurements, especially those with ICRS, who should be treated with caution in clinical practice.

CONTROL ID: 3544096

SUBMITTER (NAME ONLY): Karina Patasova

TITLE: UK Biobank study of 340, 419 participants identifies four novel loci associated with the age of first spectacle wear

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Patasova, P.G. Hysi, C.J. Hammond, O.A. Mahroo, Twins Research and Genetic Epidemiology, King's College London Faculty of Life Sciences and Medicine, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Refractive errors and the age of first wearing glasses or contact lenses are correlated both observationally and at a genotypic level. Individuals who require vision correction at an earlier age often progress to high-grade myopia, and thus are at a greater risk of complications. The purpose is to identify genetic risk factors associated with the age of first spectacle wear in a large genome-wide association study.

Methods: For the purposes of this work, we conducted a survival analysis in the age of first spectacle or contact lens correction. This phenotype was available for 340,419 UK Biobank participants of European descent, self-reported through an electronic questionnaire. In addition, direct phenotypic information about spherical equivalent and other ocular measurements were available for a subset of participants (N=90,550). The genetic associations with the age of first spectacle wear were tested using Cox proportional hazards-ratios model, adjusted for age and sex.

Results: We found genetic associations with 44 independent genetic regions, most of which previously associated with refractive error. The strongest association was observed for TSPAN10 ($p=1.71 \times 10^{-35}$). Although an early onset of refractive correction correlated well with spherical equivalent in adulthood, several genes such as PRSS56, LAMA2, RDH5 had stronger effects and led to earlier manifest refractive errors, while other genes, such as AGPS, contributed to stronger than expected later life refractive error.

We were able to identify six loci at genome-wide significance, not previously reported as associated with refractive error, for example, LOC100287944 ($p=1.96 \times 10^{-08}$), and successfully validated four of them in an independent cohort.

Conclusions: This study confirmed the correlation between age of first spectacle wear and magnitude of refractive errors. In addition, this study identified genes associated specifically with early and late-onset refractive errors which may improve understanding of the mechanisms affecting spherical equivalent measurements in the general population.

Our study also illustrates the additional power gained by the use of longitudinal and survival methodologies and contributed several novel associations with refractive error traits, adding to our knowledge of the genetic risk architecture of these conditions.

CONTROL ID: 3544098

SUBMITTER (NAME ONLY): Henry Wiley

TITLE: Oral HIF-2 α inhibitor belzutifan for ocular von Hippel-Lindau (VHL) disease

SESSION TITLE: Advances in Diagnosis and Management of Retinoblastoma and Congenital Eye Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Wiley, E.Y. Chew, National Eye Institute, Bethesda, Maryland, UNITED STATES|H.R. Coleman, Digital Angiography Reading Center (DARC), New York, UNITED STATES|E. Jonasch, The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES|R. Srinivasan, National Cancer Institute, Bethesda, Maryland, UNITED STATES|F. Donskov, Aarhus Universitetshospital, Aarhus, DENMARK|J.K. Maranchie, J. Chhablani, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|T. Else, H. Demirci, University of Michigan, Ann Arbor, Michigan, UNITED STATES|B.L. Maughan, M. Hartnett, University of Utah, Salt Lake City, Utah, UNITED STATES|R.F. Perini, E.K. Park, Merck & Co Inc, Kenilworth, New Jersey, UNITED STATES|A. Kruse, Aalborg Universitetshospital, Aalborg, North Denmark Region, DENMARK|

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ABSTRACT BODY:

Purpose: VHL disease is a rare hereditary disorder caused by VHL gene mutation, resulting in overexpression of hypoxia-inducible factors (HIFs) and tumorigenesis. We report results for retinal hemangioblastomas (RH) in patients with VHL disease-associated clear cell renal cell carcinoma (VHL-RCC) receiving small molecule HIF-2 α inhibitor belzutifan (MK-6482).

Methods: In this open-label, single-arm, phase 2 study (NCT03401788), patients with VHL-RCC received belzutifan, 120 mg orally daily. Evaluations included visual acuity assessment, ophthalmic exam, and imaging every 3 months for patients with baseline active ophthalmic disease. The primary endpoint was objective response rate (ORR) of VHL-RCC by Response Evaluation Criteria In Solid Tumours (v1.1). Efficacy for RH was a secondary endpoint, measured as an eye-level best overall response by an independent reading center (DARC, Great Neck, NY) based on assessment of color fundus imaging. Each eye was evaluated for RH number/size/location; degree of feeding/draining vessel dilation; and presence of intraretinal/preretinal/vitreous hemorrhage, exudation, and/or fibrosis. Eyes were assigned a summary grade of improved, stable, or progressed at last follow up.

Results: 61 patients were enrolled between 2018 and 2019. As of June 2020, median follow-up was 69 weeks (range, 18–105). Confirmed ORR for VHL-RCC was 36% (95% CI, 24–49), with a disease control rate of 98% (95% CI, 91–100). The most common adverse events were anemia (90%) and fatigue (61%) for the entire study population.

Color fundus images were obtained for 29 eyes (16 patients) having ≥ 1 RH. 16/29 eyes (55%) were graded as improved, 12/29 eyes (41%) were stable, and 1/29 eyes (3%) was not evaluable (poor image quality). No eye was graded as progressed and no new RH occurred. 1/29 eyes (3%) had a decrease in visual acuity >15 letters equivalent, secondary to retinal detachment in the setting of RH, epiretinal membranes, and myopia.

Conclusions: Belzutifan demonstrated promising activity, including reduction in size, vascularity, and/or exudation in a subset of RH, in addition to beneficial effects on RCC in patients with VHL disease.

CONTROL ID: 3544101

SUBMITTER (NAME ONLY): Pratheepa Rasiah

TITLE: Neurotrauma induced retinal basement membrane Col4a1 defects are restored by Adipose tissue derived mesenchymal stem cell concentrated conditioned medium

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The goal of our study was to determine if Col4a1 deficiency exacerbates the visual deficits after mild traumatic brain injury (mTBI), and demonstrate the efficacy of COL4A1 enriched ASC concentrated conditioned medium (ASC-CCM) in restoring retinal vascular health after mTBI and mitigating visual deficits

Methods: Two-month-old C57Bl/6 mice were subjected to retina-specific knockdown of Col4a1 with intravitreally delivered AAV2-Col4shRNA and later to a 50-psi air pulse to the left side of the head, resulting in an mTBI, and compared to Control-shRNA treated mice with mTBI. Post blast, ASC-CCM (~100ng/eye/1mL) was delivered intravitreally, followed by visual assessment, immunohistology, and gene expression analysis after 4 weeks. Immune depletion of COL4A1 from ASC condition media was evaluated for the role of COL4A1 in the anti-inflammatory effects of ASC-CCM on microglial activation and endothelial permeability in vitro. Human retinal endothelial cells (HREC) with knockdown of Col4a1 via siRNA transfection were assessed for endothelial migration and leukocyte transmigration with COL4A1-enriched ASC-CCM

Results: mTBI resulted in a significant reduction in visual acuity and contrast sensitivity in mice, worsen with Col4a1 knockdown ($p<0.001$). An intravitreal injection of ASC-CCM rescued visual function in mTBI mice with Col4a1 knockdown ($p<0.05$). Immunohistological and gene expression analysis of retinas of mTBI mice with Col4a1 knockdown demonstrated increased gene transcripts indicative of glial and endothelial activation ($p<0.05$) and retinal vascular and synaptic junction defects, which were significantly improved in blast mice with Col4a1 knockdown receiving ASC-CCM. COL4A1-enriched but not COL4A1-immunodepleted ASC-CCM prevented cytokine stimulated microglial nitrite release as well as TNF- α induced endothelial permeability in vitro. HRECs with knockdown of Col4a1 (~90%) mimicked known pathogenic vascular defects, exhibiting impaired HREC migration and increased transmigration of leukocytes, which was remedied by COL4A1 enriched ASC-CCM ($p<0.05$)

Conclusions: Our studies demonstrate that pre-existing Col4a1 deficiency can exacerbate the TBI outcome and thus be a TBI risk factor in humans. Additionally, our studies confirm the efficacy of ASC-CCM administration in treating Col4a1 deficiency in neurotrauma

CONTROL ID: 3544102

SUBMITTER (NAME ONLY): Chris Mesnard

TITLE: Synaptotagmins 1 and 7 in vesicle release from rods and cones of mouse retina

SESSION TITLE: Inner retinal function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Mesnard, C. Hays, J. Grassmeyer, C.L. Barta, K.K. Hinz, W. Thoreson, Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|

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ABSTRACT BODY:

Purpose: Synaptotagmins are the primary Ca^{2+} sensors for synaptic exocytosis. Previous evidence suggested synaptotagmin-1 (Syt1) mediates evoked vesicle release from cones, but release from rods involves Syt1 and another sensor.

Methods: We performed immunohistochemistry, electroretinograms (ERG) and single-cell recordings using mice in which Syt1 and Syt7 were conditionally removed from rods (Rho-Cre) and/or cones (HRGP-Cre). Glutamate release was measured in rods from anion currents activated during glutamate re-uptake.

Results: Deletion of Syt1 from rods abolished fast glutamate release evoked by short depolarizations but not slower release evoked by long steps. Immunohistochemical labeling showed syntaptotagmin-7 (Syt7) in rod terminals and deletion of Syt7 reduced slow but not fast glutamate release. Deleting both sensors from rods fully abolished depolarization-evoked glutamate release. Using Ca^{2+} buffers, we found that fast release involves vesicles close to ribbon-associated Ca^{2+} channels whereas slow release involves more distant sites. Confirming that Syt1 is the sole sensor in cones, eliminating Syt1 from cones abolished photopic ERG b-waves, matching responses of GNAT2KO mice that lack functional cones. Eliminating Syt1 from rods reduced scotopic ERG b-waves. However, selective elimination of Syt7 from rods, as well as global knockout of Syt7, did not significantly reduce scotopic or photopic b-waves. Furthermore, mice lacking both Syt1 and Syt7 in rods showed the same responses as mice only lacking Syt1 in rods. Eliminating Syt1 from both rods and cones abolished photopic b-waves and left almost no scotopic b-waves. These b-waves did not differ significantly from those of mice lacking both Syt1 and Syt7 in rods and cones.

Conclusions: Syt1 is the principal sensor shaping rod and cone inputs to bipolar cells during light flashes. Syt7 contributes to slow non-ribbon release from rods, but has little impact on ERG b-waves suggesting it plays a modulatory role (e.g., shaping synaptic cleft glutamate levels).

CONTROL ID: 3544103

SUBMITTER (NAME ONLY): Leroy Muya

TITLE: Long-acting potential of suprachoroidally delivered BCX4161, a selective plasma kallikrein inhibitor, for diabetic macular edema

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Muya, V. Kansara, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|Y. El-Kattan, Y. Babu, Biocryst Pharmaceuticals Inc, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: BCX4161 is a potent and selective inhibitor of human plasma kallikrein activity. Elevated plasma kallikrein (PKal) levels have been reported in the vitreous humor of patients with diabetic macular edema (DME). Inhibition of PKal activity can be an effective therapeutic strategy for the treatment of DME. Suprachoroidal delivery of BCX4161 suspension may result in sustained and safe therapeutic drug levels in the retina-choroid. Hence, the purpose of this study was to assess ocular pharmacokinetics (PK), durability and tolerability of suprachoroidally delivered BCX4161 in rabbits.

Methods: A single bilateral suprachoroidal injection (100 µL) of BCX4161 suspension was administered to male Dutch-Belted (DB) pigmented rabbits (N=2-3 rabbits/ timepoint) at a dosage of 0.5 mg/eye. Ocular tissues (RPE-choroid-sclera (RCS), retina, vitreous humor, aqueous humor), and blood were collected, at pre-determined timepoints for up to 12 weeks, and analyzed for drug content. An 8-mm biopsy punch was used to collect the central retina and the central RCS around the optic nerve. Ocular tolerability was assessed via in-life clinical observations including slit-lamp and indirect ophthalmoscopy.

Results: Suprachoroidally delivered BCX4161 was generally well tolerated in rabbits. No overt signs of toxicity were observed in rabbits during this 12-week study. Sustained and high exposure of BCX4161 was observed in the RCS and the retina throughout the study duration. Mean retina concentrations reached a maximum value (C_{max}) of 75 µg/gm (peripheral retina) and 13 µg/gm (central retina) at 24 hours postdose (T_{max}). On day 84 (the last timepoint), mean BCX4161 levels in the central retina (30 µg/gm) and the peripheral retina (21 µg/gm) were 1-2 orders of magnitude higher than the in-vitro IC99 (100 nM) levels. The dose depot (RCS) had 1 to 2 orders of magnitude higher mean concentration than the retina, and the retina had 1 to 2 orders of magnitude higher mean concentration than the vitreous humor. Low levels of BCX4161 were observed in some samples of aqueous humor and plasma.

Conclusions: Suprachoroidally delivered BCX4161 suspension provided sustained and targeted delivery of BCX4161 to the chorioretina, has the potential to be a safe, effective and long-acting therapy for the treatment of DME, and warrants further studies.

CONTROL ID: 3544106

SUBMITTER (NAME ONLY): Reem Almagati

TITLE: Visual Perceptual Abilities in Young Children Diagnosed With CVI Versus Those With Ocular Disorders

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Almagati, B.S. Kran, D. Mayer, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Currently, there is no available standard approach to diagnose Cerebral Visual Impairment (CVI). Vancleef et al (2020) showed that the Children's Visual Impairment Test for 3- to 6-year-olds (CVIT 3-6) differentiated children with CVI from three groups: typically developing children, children with intellectual disorders, and typically developing children with simulated reduced visual acuity. We performed a prospective clinical study to assess the ability of this visual perceptual test to differentiate children with CVI from children with ocular and/or ocular motor disorders.

Methods: The CVIT 3-6 is an objective test that uses a simple matching technique to assess the child's visual perceptual abilities. In-person testing was not feasible due to the COVID-19 pandemic. We developed and tested a virtual model first in a small sample of typically developing young children. Study participants were later recruited from a pediatric low vision clinic. Our clinical cohort consisted of two groups, children with a previous diagnosis of CVI and children with ocular and/or ocular motor disorders only. The examiner was unaware of the participant's diagnosis prior to data collection. A validated parent questionnaire regarding CVI, the Flemish cerebral visual impairment questionnaire, was also administered.

Results: Preliminary data show a small, non-significant difference in overall CVIT 3-6 scores between participants with CVI and those with ocular disorders. (means 56 vs. 64.7, respectively. $p = 0.151$). For the Flemish CVI questionnaire, participants in the CVI group had a significantly higher % abnormal scores on average than those with ocular disorders ($p = 0.003$). Our virtual testing protocol was successful in all participants tested to date.

Conclusions: In this preliminary study, collected data suggest that the CVIT 3-6 did not differentiate between children with CVI compared to those without CVI. This study is ongoing. Results from a larger sample will be needed to verify this finding. The Flemish (Ortibus) questionnaire differentiated between children with CVI from children without CVI.

CONTROL ID: 3544107

SUBMITTER (NAME ONLY): Heather Broyles

TITLE: Outcomes of Minimally Invasive Glaucoma Surgery in a Veteran Population

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Broyles, Ophthalmology, University of Arkansas for Medical Sciences, Little Rock, Arkansas, UNITED STATES|V. Ly, University of Arkansas for Medical Sciences College of Medicine, Little Rock, Arkansas, UNITED STATES|R. Braswell, Central Arkansas Veterans Healthcare System John L McClellan Memorial Veterans Hospital, Little Rock, Arkansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the outcomes of combined phacoemulsion and minimally invasive glaucoma surgeries (MIGS) performed by residents and attendings in a veteran population. Eye care is the third busiest clinical service in the VA system, with an increasing prevalence of glaucoma as a result of extended life-span in this population. There is currently no data that exists on the use of MIGS in the veteran population.

Methods: Retrospective chart review based on CPT codes of patients who underwent combined phacoemulsification and MIGS procedure from 2015 to 2020. Inclusion criteria involved veterans of all races, aged 18 or older, male or female, currently taking at least one anti-hypertensive eye drop medication, with the diagnosis of either ocular hypertension, glaucoma suspect, open angle glaucoma, pseudoexfoliative glaucoma, pigmentary glaucoma, or mixed mechanism glaucoma. Excluded were all patients with previous glaucoma surgery, except for cataract extraction or laser surgery, and any patients with the diagnosis of severe glaucoma.

Results: The study comprised 55 eyes of 40 veterans with a mean age of $72 \pm$ SD years. In conjunction with phacoemulsion, 10 (18%) eyes received endoscopic cyclophotocoagulation, 21 (38%) eyes underwent Kahook Dual Blade goniotomy, 7 (13%) eyes underwent gonioscopy-assisted transluminal trabeculotomy, 9 (16%) eyes received iStent, and 8 (15%) eyes had a combination. IOP was reduced by 22% on average at 1-year follow-up. The number of required IOP-lowering eye drop medications decreased for 24 eyes (44%). 9 (16%) eyes required no drops after MIGS. The overall rates of complications and failure were 12% and 16%, respectively. There was no statistically significant difference in the rates of operative complications ($p = 0.302$) and treatment failure ($p = 0.149$) between residents and attendings.

Conclusions: MIGS are safe with low rates of adverse events, and have the potential to decrease IOP and medication burden in veterans. This is in alignment with the current literature regarding MIGS in the civilian population. MIGS outcomes do not differ between resident surgeons and attending surgeons. To our knowledge, this is the first study that has compared MIGS performed by residents to those performed by attendings.

CONTROL ID: 3544109

SUBMITTER (NAME ONLY): Geeta Lalwani

TITLE: DR progression analyses and its association with race and diabetes type in real-world patients with diabetes in the US

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the impact of DR severity on the risk of DR progression to clinically significant macular edema (CSME) or proliferative DR (PDR) in patients with diabetes mellitus (DM) screened at primary care centers in the US; and the association of ≥ 2 -step DR worsening with race or DM type.

Methods: Eyes of 22,109 patients with DM were analyzed based on DR severity data collected by masked professional reading center graders from 1999–2016 (Inoveon Corporation, OK). DR severity was graded using the Early Treatment Diabetic Retinopathy Study (ETDRS) DR Severity Scale (DRSS). Eyes with valid baseline (BL) and ≥ 1 post-BL DRSS value (42,011 eyes) were analyzed. Rate of ≥ 2 -step DR worsening was assessed in the overall population; the development of CSME (using ETDRS criteria) or PDR was analyzed among eyes with no CSME and no PDR at BL, respectively. Association analyses were performed in a subset where patients reported race and DM type.

Results: For all eyes evaluated, time to first ≥ 2 -step DR worsening was 2.7% at year 2 and 7.1% at year 4 (Kaplan-Meier analysis). Rate of ≥ 2 -step DR worsening was greatest among eyes with BL DRSS 43–53. Analysis of time to first development of PDR or CSME in all eyes showed the presence of 3 distinct clinical subtypes: increased risk of CSME, increased risk of PDR, and increased risk of CSME and PDR (smallest subset). This trend was not dependent on BL DRSS. Only 4058 (18%) and 11,334 (51%) patients reported race and DM type, respectively. Of these, >95% patients had BL DRSS 10–35; in this subset, a higher rate of ≥ 2 -step DR worsening was associated with Black and White races (Fig) and type 1 DM (T1D).

Conclusions: Eyes with BL DRSS 43–53 were at greatest risk of progression to CSME or PDR. Existence of 3 distinct clinical DR subtypes, which were not driven by BL DR severity, was also observed. The association analyses, conducted in subsets where race and/or DM type was reported (>95% with BL DRSS 10–35), showed a trend of faster DR progression in Black and White patients and those with T1D; more research is needed as our data may not accurately reflect DR dynamics in underrepresented minorities. Study limitations were: small sample size of the Black and T1D patient subsets; majority of patients reporting race and/or DM type were from OK or FL; and more thorough targeted screening conducted for patients with DM in the Native American population.

CONTROL ID: 3544120

SUBMITTER (NAME ONLY): Jie Gong

TITLE: Increased Reactive Oxygen Species (ROS) production in Patient-specific iPSC-derived RPE from AMD patients

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gong, H. Cai, L.V. Del Priore, M.A. Fields, Department of Ophthalmology and Visual Sciences, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress plays an important role in RPE cell injury and is also a risk factor of AMD. Tert-butyl hydrogen peroxide (TBHP) is an agent used to induce oxidative stress in RPE and serves as a reproducible model that mimics key aspects of AMD pathology. We have previously demonstrated our ability to derive iPSC-derived RPE from AMD patients and age-matched controls. These cells perform critical functions such as phagocytosis of photoreceptor outer segments, the ability to form tight junctions, and retinol metabolism. A decrease in metabolic capacity was also observed in iPSC derived RPE from AMD patients. Here we seek to detect the cellular ROS production of iPSC-derived RPE from AMD patients and age-matched controls.

Methods: iPSCs were generated from AMD (n=3) and age-matched patients with no history of AMD (n = 2) using mRNA. iPSCs were differentiated into RPE using an established protocol. RPE lines were verified by morphology, immunohistochemistry and confocal microscopy. Cells were labeled with 20 μ M 2', 7' -dichlorofluorescein diacetate (DCFDA), and then cultured for another 2 hours with or without 150 μ M TBHP, and then quantified using a BioTek FLx800 plate reader.

Results: Human iPSC-derived RPE expressed specific RPE cell markers RPE65, CRALBP, and ZO-1. In the presence of TBHP, both groups of iPSC-derived RPE cells expressed higher level of ROS. In normal control group, ROS were 42.10% (p<0.001) higher in TBHP than untreated group. In AMD group, ROS were 23.70% (p<0.001) higher in TBHP than untreated group. A comparison of iPSC- derived RPE cells with PBS treatment from normal controls (n = 2) vs. AMD patients (n = 3) revealed no significant difference in ROS production in all 5 lines. However, iPSC-derived RPE from normal controls with TBHP treatment revealed higher ROS production 18.47% (p<0.05) vs AMD patients with TBHP treatment.

Conclusions: In this study, we generated RPE from AMD patients and individuals with no history of AMD. Higher levels of ROS production was observed in iPSC-derived RPE from both AMD patients and normal controls. However, no differences were observed when comparing TBHP-treated AMD and control lines. Further, exploration of various inflammation related growth factors and metabolic pathways among normal and AMD-derived RPE should reveal mechanisms of disease-related phenotypes and pave the way for novel therapeutic strategies.

CONTROL ID: 3544122

SUBMITTER (NAME ONLY): Belinda Hernandez

TITLE: Chronic Oxidative Stress in Primary Retinal Pigmented Epithelium Monolayers Increases Basolateral Exosome Release and Changes Both Exosome and Extracellular Matrix Proteomes

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Hernandez, M. Klingeborn, N. Skiba, D. Grigsby, U. Kelly, M. Caday, T. Watkins, W. Stamer, C. Bowes Rickman, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|A. Maminishkis, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|S.S. Miller, NEI Office of the Director, National Eye Institute, Bethesda, Maryland, UNITED STATES|W. Stamer, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|C. Bowes Rickman, Department of Cell Biology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress is implicated in the pathobiology of age-related macular degeneration (AMD). Exosomes are small extracellular nanovesicles (EVs) of endocytic origin that mediate different signals between cells and can be modified by oxidative stress. We hypothesize that oxidative stress affects retinal pigmented epithelium (RPE) exosome release and content and contributes to basal deposit extracellular matrix (ECM) changes. Here, we characterize ECM changes and RPE exosome release and content in response to oxidative stress.

Methods: We have previously shown that exosomes can be isolated apically and basally from fully differentiated and polarized primary porcine RPE cells grown on Transwell cell culture inserts. To induce chronic oxidative stress, these cultures were treated daily with 0.2mM H₂O₂ for 4 weeks. Basolateral exosome yield was assessed by Nanoparticle Tracking Analysis (NTA) and immunoblotting for exosomal markers along with total protein quantitation. Purity and protein content of exosome preparations were analyzed by immunoblotting for exosomal markers, and markers for known contaminants. In-depth proteomic mass spectrometry analyses were done on both exosomes and ECM preparations.

Results: Unbiased proteomic analyses of the content of highly purified basolateral exosomes isolated from RPE cultures under chronic oxidative stress revealed changes to a number of ECM proteins. One such protein, Keratin 10 (KRT10), was increased 3-fold in basolateral exosomes and this was mirrored by a 6.5-fold increase of KRT10 in proteomic analyses of the basal extracellular matrix (ECM) and correlated with a 4-fold increase in basolateral exosome secretion as measured by NTA. Treatment of RPE cultures with an inhibitor of exosome release effectively reduced basolateral EV secretion. Proteomic analyses of exosomes and ECM from these cultures will also be presented.

Conclusions: We show for the first time that chronic oxidative stress in primary RPE monolayers induced proteomic changes in exosomes and increased basolateral EV secretion which could be prevented by inhibition of exosome release. We also show examples of protein changes in exosomes that correlate with protein changes in the underlying ECM. These findings have the potential to open up a completely novel avenue for therapeutic intervention in AMD.

CONTROL ID: 3544124

SUBMITTER (NAME ONLY): Pamela Tsuruda

TITLE: UBX1325, a small molecule inhibitor of Bcl-xL, attenuates vascular dysfunction in two animal models of retinopathy

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tsuruda, S. Chaney, S. Dasgupta, S. Rao, S. Armstrong, D. Marquess, P. Beltran, UNITY Biotechnology, South San Francisco, California, UNITED STATES|A. Dejda, S. Crespo-Garcia, P. Sapieha, Hopital Maisonneuve-Rosemont Centre de Recherche, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Retinal vasculopathies account for the primary causes of loss of sight in the industrialized world and current standards present significant side effects. To develop novel treatment paradigms, we developed UBX1325, a novel small molecule inhibitor of specific subtypes within the B-cell lymphoma 2 (Bcl-2) family of apoptosis regulatory proteins and assessed its efficacy in senescence-associated models of retinopathy.

Methods: Target engagement (TE), decreased Bcl-xL:Bim or Bcl-2:Bim complexes, was measured by an electrochemiluminescence-based assay in retinal lysates from C57BL/6 mice after intravitreal (IVT) injection of UBX1325. Initiation of apoptosis (mechanism engagement, ME) was measured by caspase-3/7 activation. Adult mice and neonatal mice from oxygen induced retinopathy (OIR; 75% O₂ from post-natal day (P)7-P12) or normoxic controls were used for TE and ME measurements. Vascular endpoints (neovascular and avascular area) were evaluated at P17 by isolectin B4 staining in OIR mice given a single IVT injection of UBX1325 at P12. UBX1325 was also studied in the streptozotocin (STZ)-induced retinopathy model. UBX1325 was injected IVT at weeks 8 and 9 post-STZ, and retinal endpoints were measured at week 10. Vascular leakage was evaluated by Evans blue dye extravasation into the retina after intravenous injection. The dark-adapted electroretinogram was used to assess retinal function with increasing flash intensity. Retinal gene expression was evaluated for a limited panel of targets by qRT-PCR.

Results: IVT administration of UBX1325 lead to a reduction of anti-apoptotic Bcl-xL:Bim complexes in the mouse retina. Bcl-xL TE (37-81%) in OIR animals resulted in caspase-3/7 activation (3-9-fold) and improvements in both retinal neovascularization (58-71%) and avascular area (32-52%). In the diabetic mouse, UBX1325 injection resulted in reduced retinal vascular permeability (78-90%) and an improved ERG (a- and b-wave amplitude).

Conclusions: Inhibition of retinal Bcl-xL by UBX1325 promotes apoptosis in the senescence-associated OIR model. UBX1325 improves retinal vasculature in both the OIR and STZ mice, and demonstrates differentiation over anti-VEGF agents in OIR. Collectively, our data support development of UBX1325 for retinal vasculopathies and initial clinical evaluation of UBX1325 in patients with diabetic macular edema (DME).

CONTROL ID: 3544129

SUBMITTER (NAME ONLY): Amogh Iyer

TITLE: Relationship between Intraretinal and Subretinal Fluid with Visual Acuity in Patients with Neovascular Age-Related macular Degeneration Treated with Anti-Vascular Endothelial Growth Factor

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Iyer, J. Muste, A. Kalur, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-vascular endothelial growth factor (VEGF) treatment is used to treat neovascular age-related macular degeneration (nAMD). Fluid resolution by OCT is used both as an indicator of disease control and to guide the frequency of treatment since anti-VEGF therapy reduces neovascularization-related exudation. The variability in treatment response is considered a poor prognosis for visual acuity (VA). This study seeks to characterize the specific fluid compartment drives this variability. The hypothesis is that there will be poorer VA outcomes for eyes in the highest quartile of IRF volumes and no significant correlation between SRF and VA.

Methods: A retrospective cohort study of 301 treatment-naïve nAMD eyes was performed at the Cleveland Clinic Cole Eye Institute. Spectral domain optical coherence tomography (OCT) scans were obtained for patients over a 12 month period at 3 month intervals from January 1st, 2012 to October, 31st, 2019. Patients were excluded if they had maculopathies unrelated to nAMD that would interfere with analysis. IRF and SRF quantification was performed by the Notal Optical Coherence Tomography Analyzer (NOA), which employs machine learning and image recognition computational techniques. Baseline demographics and VA were also recorded at each visit. A linear mixed-effects regression model (LMER) was used to analyze the effect of IRF and SRF on VA over 12 months by quartiles.

Results: Mean IRF was $122.23 \pm 270.14 \text{ mm}^3$ (mean \pm SD) at baseline and $24.39 \pm 106.56 \text{ mm}^3$ at 12 months ($p < 0.001$). Mean SRF at baseline was $215.52 \pm 394.86 \text{ mm}^3$ and $64.42 \pm 173.70 \text{ mm}^3$ at 12 months ($p < 0.001$). Mean number of injections was 8.25 ± 2.47 . Mean VA at baseline was 60.13 ± 18.79 ETDRS letters and 65.68 ± 17.19 ETDRS letters at 12 months ($p < 0.001$). The LMER showed that eyes in the highest quartile of IRF volume had a significant VA loss of -4.26 ± 2.54 ETDRS letters compared to those not in this quartile ($p = 0.001$) after adjusting for baseline factors and injections. There was no significant relationship between SRF and VA.

Conclusions: High levels and high variability of IRF volume are associated with poorer VA outcomes in patients with nAMD treated with anti-VEGF. Further studies can provide insight into treatment patterns in nAMD patients with IRF and SRF and how that relates to VA.

CONTROL ID: 3544130

SUBMITTER (NAME ONLY): Noam Sapiens

TITLE: Accommodation mitigation in reverse Shack-Hartmann refraction measurement

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Sapiens, EyeQue Corp., Newark, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accommodation is one of the most prevalent impediments of accurate refraction measurements. As accommodation is part of the eye refraction, measurements are often incapable of discerning between the eye accommodation state and the refraction error of an eye. A method to control accommodation during a refraction measurement is required. The desired method would not require cycloplegia and could be implemented anywhere.

Methods: A low-cost, handheld, self-administered refraction measurement prototype device based on the reverse Shack-Hartman technology with accommodation mitigation was developed. The device has two optical channels per eye that are optically overlaid on the retina. An accommodation mitigation channel with a 30° field of view and large depth of focus presents a 3D stereoscopic visual stimulus during the test. A measurement channel implements the reverse Shack-Hartman technology.

An exploratory, single-center, open-label study in healthy volunteers was conducted to compare this device with an autorefractor. 21 subjects between the ages of 18 and 30 are included in the analysis. Each subject underwent 3 autorefractor measurements and 3 measurements on the device. Average refraction numbers were calculated for each device. Double blind BCVA measurements using trial lenses were conducted by an optometrist using ETDRS charts.

Results: The correlation between the autorefractor and the device spherical equivalent are presented in figure 1. Results show good linear correlation with slight negative bias.

BCVA results were statistically analyzed and a graphical representation of is presented in figure 2. The results show that the average difference between the device and the autorefractor is less than half a letter with 95% confidence interval of achieving normal vision.

Conclusions: The performance of the new device is substantially equivalent to the autorefractor. The expected cost of the device is to be orders of magnitude less than that of the autorefractor. Furthermore, the device is handheld and simple to use. Therefore, it is an accurate alternative to traditional refraction measurements. It provides users with an ability to perform accurate, self-administered refraction measurements conveniently at home.

CONTROL ID: 3544131

SUBMITTER (NAME ONLY): Russell Chan

TITLE: Cerebrovascular reactivity decreases in the visual cortex and increases in the basal forebrain with glaucoma severity

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Dampened cerebrovascular reactivity (CVR) impairs blood delivery to brain regions. Multiple studies have suggested a role of the basal forebrain (BF) in glaucoma (PMID: 31242454; ARVO 2020: 4336). However, CVR changes in BF with glaucoma severity have yet to be explored. Recently, relative CVR (rCVR) mapping was introduced using resting-state functional MRI (rsfMRI) without gas challenges. Here, we investigate rCVR changes in the visual cortex and basal forebrain with glaucoma severity.

Methods: Normal (n=22), early-stage (n=18), and advanced-stage (n=19) glaucoma patients underwent anatomical MRI and rsfMRI. The optic nerve and optic chiasm volumes were measured using ImageJ. rCVR maps and regional rCVR values were generated and extracted with MriCloud online tool. Age, optical coherence tomography measurements, and Humphrey visual field perimetry were obtained from clinical records. Results are presented as mean±SEM. One-way ANOVA followed by post-hoc Bonferroni's multiple comparisons test, and trend analysis were applied.

Results: Demographics, clinical ophthalmic assessments, and volumetric MRI assessments illustrated the characteristics of the anterior visual pathways in the normal control, early-stage glaucoma and advance-stage glaucoma groups (Fig. 1). The averaged rCVR map from normal controls is consistent with previous studies (PMID: 27888058, 32278094) (Fig. 2). Advanced-stage glaucoma patients [1.03 ± 0.03 relative unit (r.u.); $p < 0.05$] have significantly lower rCVR in the visual cortex compared to normal controls (1.20 ± 0.06 r.u.; early-stage: 1.09 ± 0.05 r.u.), and exhibit a decreasing trend in more severe disease. These corroborate with a previous Doppler ultrasound study (PMID: 23816432). Interestingly, rCVR in BF has an increasing trend with severity. No significant rCVR change was observed in the somatosensory cortex.

Conclusions: Visual cortical rCVR decreases with glaucoma severity, while rCVR in the basal forebrain increases with severity. Our results verify visual cortical CVR reduction in glaucoma patients and further solidify that the basal forebrain plays a role in glaucoma.

CONTROL ID: 3544133

SUBMITTER (NAME ONLY): Antonio Iskandar

TITLE: Transscleral optical phase imaging in non-neovascular age-related macular degeneration

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Mantel, Medical Retina, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|L. Kowalczyk, C. Moser, Laboratory of Applied Photonic Devices, Ecole Polytechnique Federale de Lausanne, Lausanne, VD, SWITZERLAND|I. Mantel, Universite de Lausanne Faculte de biologie et medecine, Lausanne, VD, SWITZERLAND|A. Iskandar, L. Kowalczyk, A. Gryczka, A. Navarro, F. Jeunet, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|M. Kunzi, T. Laforest, Innovation Park, Early Sight SA, Ecole Polytechnique Federale de Lausanne, Lausanne, VD, SWITZERLAND|F.F. Behar-Cohen, Centre de Recherche des Cordeliers, Inserm, Sorbonne Universite, Paris, Île-de-France, FRANCE|F.F. Behar-Cohen, Cochin Hospital, Assistance Publique - Hopitaux de Paris, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To report the results of transscleral optical phase imaging (TOPI) in age-related macular degeneration (AMD). This image modality has been developed to visualize in vivo the cellular structure of the human retinal pigment epithelium (RPE).

Methods: Non-neovascular AMD cases with clear optic media and good fixation were recruited for TOPI, associated with conventional imaging: spectral domain optical coherence tomography, autofluorescence, color and infrared fundus imaging. Six squares of 5.04x5.04 degrees were acquired with TOPI: one foveal, four localized in the macular quadrants with 3.8° eccentricity, and one to the investigators discretion. The TOPI images were optimized for contrast and confronted with information from conventional multimodal imaging.

Results: Included were 10 eyes of 8 AMD patients (mean age 75.5 years, 50% females).

Prominent features on the TOPI images were the reticular pattern of the choriocapillaris, particularly well contrasted on areas of geographic atrophy and RPE hypopigmentation, and the presence of additional dark spots irregularly distributed. Drusen showed dark with a white halo around. Within atrophic zones there were irregularly formed, sharply demarcated dark spots of variable size, correlating with degenerative remnants of RPE cells on OCT. The dark spots were the dominating element for the image contrast, leading to very low contrast of the RPE cell visualization on the same image.

Conclusions: TOPI revealed in AMD the detailed structure of the choriocapillaris. Different types of dark spots were identified, corresponding to drusen and degenerated RPE cells.

CONTROL ID: 3544134

SUBMITTER (NAME ONLY): Justin Wang

TITLE: Short-Term Normobaric Hyperoxia Treatment for Dry Age-Related Macular Degeneration: An Exploratory Study

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wang, C. Lemire, B. Seto, K. Yamada, J.G. Arroyo, Ophthalmology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry age-related macular degeneration (AMD) is a complex ocular disorder that is thought to result in outer retinal hypoxia and can lead to the growth of choroidal neovascularization. Computational models of dry AMD demonstrate that the presence of drusen and distance between the choroid and retinal photoreceptors affect levels of retinal hypoxia; however, few studies have investigated normobaric hyperoxia treatment for dry AMD. We performed an exploratory study to evaluate the functional and anatomic effects of short-term normobaric hyperoxia in patients with dry AMD. We hypothesized that normobaric hyperoxia would be most effective in retinas with greater separation between the photoreceptors and choriocapillaris.

Methods: Patients with dry AMD (23 eyes in 18 patients) were categorized based on the presence of: hard drusen (n = 10), drusenoid pigment epithelium detachments (PED) (n = 8) or geographic atrophy (GA) (n = 5). Macular OCT scans and ETDRS visual acuity measurements were obtained before and after 3-hour administration in a blinded fashion of either normobaric hyperoxia (40% FiO₂) or normobaric normoxia (20% FiO₂).

Results: Three-hour normobaric hyperoxia treatment in dry AMD patients with drusenoid PED demonstrated significant decreases in foveal volume ($-0.003 \pm 0.005 \text{ mm}^3$, $p = 0.02$) and drusen height ($-6.8 \pm 7.6 \text{ } \mu\text{m}$, $p = 0.002$) as well as an increase in visual acuity (LogMAR: -0.06 ± 0.07 , $p = 0.02$) relative to pre-O₂ baseline using Two-tailed Student's dependent samples t-test. These differences were also significant when compared to normobaric normoxia controls using Two-tailed Student's independent samples t-test. There was a moderate positive correlation between change in drusen height and change in visual acuity in the 3-hour drusenoid PED condition ($r^2 = 0.42$). In contrast, no significant differences in functional and anatomic measures tested were found after three-hour normobaric hyperoxia treatment in patients with hard drusen or geographic atrophy.

Conclusions: These results support our hypothesis that retinas with larger drusen, resulting in greater separation between the choroid and photoreceptors, respond more to hyperoxia. These findings support the role of hypoxia in AMD and suggest that hyperoxia treatment should be investigated further in these patients.

CONTROL ID: 3544136

SUBMITTER (NAME ONLY): Omar Ibrahim

TITLE: Physiology-enhanced data analytics to evaluate the role of ocular hemodynamics in glaucoma progression

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Ibrahim, D. Zou, N.M. Marazzi, J. Keller, G. Guidoboni, Electrical Engineering and Computer Science, University of Missouri, Columbia, Missouri, UNITED STATES|A. Harris, B.A. Siesky, A. Verticchio Vercellin, R. Zukerman, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|A. Verticchio Vercellin, Università degli Studi di Pavia, Pavia, Lombardia, ITALY|

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ABSTRACT BODY:

Purpose: Many studies have identified ocular hemodynamics as relevant in glaucoma; however the specific link between vascular biomarkers, blood pressure (BP), intraocular pressure (IOP), and the progression of open angle glaucoma (OAG) remains uncertain. Herein we address this issue via a novel physiology-enhanced approach to analyze data from the Indianapolis Glaucoma Progression Study.

Methods: 115 OAG patients were evaluated twice yearly over 5 years. Functional and structural OAG progression was monitored by visual field testing, optical coherence tomography and Heidelberg retinal tomography. A validated model of the retinal circulation (Guidoboni et al 2014) was used to simulate 8 individualized hemodynamic outputs (Fig.1) based on 4 inputs (SBP, DBP, IOP, HR) measured on each patient. In the retinal model, changes in IOP and BP induce changes in transmural pressures and, therefore, vascular resistances. The model is capable of predicting hemodynamic variables of physiological interest that cannot be measured directly, thereby producing a physiology-enhanced dataset with 12 instead of 4 variables for each patient and visit. The 12 baseline variables for each patient were then fed into an unsupervised machine learning model, Fuzzy c-means (FCM) clustering algorithm to identify patient clusters with similar ocular hemodynamics. The relationship between clusters and OAG progression was analyzed statistically with p-values<0.05 considered statistically significant.

Results: The FCM clustering algorithm generated 4 clusters based on the 12 variables and were plotted based on IOP and mean arterial pressure ($MAP = 2/3 \cdot DBP + 1/3 \cdot SBP$), Fig. 2. A statistically significant difference was found between the occurrence of OAG progression in Cluster 4 (n=35; 20 progression, 15 no progression) when compared to the other clusters (n=80; 62 progression, 18 no progression), p=0.026. Further, HR and Rv in Cluster 4 were found to be markedly lower than the other clusters (Fig.2).

Conclusions: Our analysis suggests that physiology-enhanced data analytics based on mathematical modeling and unsupervised machine learning of ocular hemodynamics may be effective in glaucoma risk stratification. The integration of modeling, machine learning and the clinical outcomes of glaucoma patients has the potential to improve OAG screening and treatment paradigms.

CONTROL ID: 3544137

SUBMITTER (NAME ONLY): Minhaj Nur Alam

TITLE: Automated region of interest selection improves the deep learning based segmentation of hyper-reflective foci in optical coherence tomography images

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Alam, D.L. Rubin, Biomedical Data Science, Stanford University, Stanford, California, UNITED STATES|M. Pfau, Rheinische Friedrich-Wilhelms-Universitat Bonn, Bonn, Nordrhein-Westfalen, GERMANY|M. Pfau, Ophthalmic Genetics and Visual Function Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|D. Yi, J. Hallak, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|D.L. Rubin, Radiology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hyper-reflective foci(HRFs) are associated with age-related macular degeneration(AMD), and with visual outcomes in diabetic retinopathy. Automating the HRF segmentation in retinal tissues would be beneficial for feature extraction and overall disease management. This work presents a fully automated approach for HRF segmentation in spectral domain optical coherence tomography(SD-OCT) images.

Methods: This study includes SD-OCT data acquired at the University of Bonn (Heidelberg Spectralis; image resolution of 786x496 pixels,scan width 30°). The dataset contained 3669 B-scans from 56 patients (10 diabetic macular edema,46 AMD).

A modified U-Net architecture with a densenet-169 backbone was implemented for the semantic segmentation. A point of innovation is the use of a patch-based strategy that ensures the model encoder is trained on enough pixels of interest. To elaborate, as a pre-processing step, we define the retinal pigment epithelium(RPE) layer for each B-scan (using a previously trained model for OCT layer segmentation). An automated dataloader takes the B-scan, HRF ground truth annotation and the RPE denotation as inputs and generates random patches(8x64x64) for each image around the HRF and RPE denoted pixels(location chosen randomly). These patches are then fed into the U-Net encoder, trained with a compound loss function derived from Dice and focal loss. This strategy allows the encoder to train on pathologically important pixels around the inner/outer retina.

Results: Our trained model performed well,considering the high class-imbalance of the HRF and non-HRF pixels. The current reported HRF segmentation performance in the literature is an average precision(AP) of 0.71. Our baseline AP was similar(AP 0.70) following a similar strategy. Using our patch-based strategy with region of interest selection, the AP improved to 0.75. The AP was 0.69 when trained with a ResNet50 backbone. Overall, the combination of Dice-focal loss generated higher segmentation performance.

Conclusions: This study presents a pipeline for semantic segmentation of HRFs corresponding to hard exudative and hyperpigmentation. Implementation of a patch-based strategy to improve region of interest selection for the model encoder, and combination of Dice and focal loss improve the current state of the art performance for HRF segmentation.

CONTROL ID: 3544140

SUBMITTER (NAME ONLY): Rifah Gheyas

TITLE: Role of PI3K Signaling Inhibition in Inducing Autophagy-Dependent Organelle Elimination

SESSION TITLE: Lens Development and Differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Gheyas, A. Menko, Anatomy, Cell Biology, and Pathology, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Rifah Gheyas: Commercial Relationship: Code N (No Commercial Relationship) | A Sue Menko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Blocking of PI3K/Akt signaling is known as a canonical autophagy-inducing pathway. Previous studies performed in our lab have linked autophagy mechanisms to the removal of mitochondria and ER from the center of the developing lens to form the Organelle Free Zone (OFZ). Our new studies have investigated the role of PI3K pathways in autophagy-dependent elimination of mitochondria, ER, and nuclei during lens development.

Methods:

At E12, prior to formation of the OFZ, chick embryo lenses are exposed for 24 hrs in organ culture to the pan-PI3K inhibitors, LY294002 or CH5132799, or the PI3K/Akt-specific inhibitor, MK-2206, with DMSO as the vehicle control. Differentiation state-specific regions were microdissected for immunoblot analysis. Whole lenses either cryosectioned for immunostaining with antibodies to organelles, autophagy markers, or signaling molecules, or labeled live for mitochondrial potential with Rhodamine123 prior to confocal image analysis. Development-stage-specific studies were also performed.

Results: In studies of the lysosomal protein LAMP1 we provide evidence that lysosomes are induced as OFZ formation begins at E13. Exposure of E12 lenses to either LY294002 or MK-2206 induces LAMP1, along with other autophagy-specific proteins, and the premature elimination of mitochondria and ER in lens fiber cells. While mitochondrial depolarization is known to occur before mitochondrial removal, blocking PI3K signaling with LY294002 had no impact on mitochondrial polarity, demonstrating that the link between suppression of PI3K signaling and mitochondrial loss was a direct result of autophagy induction. The two distinct pan-PI3K inhibitors lead to premature elimination of organelles. Pan-PI3K inhibition induced removal of nuclei, with nuclear loss associated with DNA cleavage as demonstrated by TUNEL assay, without impacting cell survival. In contrast, specifically blocking just the PI3K/Akt signaling axis alone induced premature loss of mitochondria and ER within 24 hrs without inducing DNA cleavage or nuclear loss.

Conclusions: The loss of mitochondria and ER to form the OFZ is by an autophagic-dependent mechanism activated by suppression of the PI3K/Akt signaling axis. While the elimination of nuclei is also PI3K-regulated, its induction involves suppression of multiple downstream effectors of PI3K.

CONTROL ID: 3544144

SUBMITTER (NAME ONLY): Vasantha Rao

TITLE: Dexamethasone-induced robust upregulation of ArgBP2, an actin crosslinking, ZO-1 and focal adhesion interacting adaptor protein, in human trabecular meshwork cells.

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Rao, W. Bachman, N. Skiba, A. Chakraborty, C. Eldawy, R. Maddala, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|V. Rao, Pharmacology and Cancer Biology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To understand the cytosolic and nuclear role(s) of actin cytoskeletal and cell adhesive proteins in trabecular meshwork (TM) cells in the context of aqueous humor outflow

Methods: Nuclear and cytosolic fractions isolated from primary cultures of human TM cells treated with dexamethasone for various lengths of time were subjected to quantitative proteomics analysis. The distribution and colocalization of ArgBP2 and its related c-Cbl associated protein (CAP/Ponsin) with actin cytoskeletal and focal adhesions proteins, and the dexamethasone-induced reorganization of these proteins in human TM cells were evaluated by immunofluorescence and immunoblotting analyses.

Results: Dexamethasone treatment (0.5 μ M for 5-7 days) led to a significant increase in the levels of ArgBP2 (SORBS2) and CAP (SORBS1), which are the sorbin and SH3-domain containing, and flotillin interacting adaptor proteins, in both, the nuclear and cytosolic fractions of human TM cells. The increase in ArgBP2 levels was consistent in more than ten biological replicates of TM cells analyzed. While CAP exhibited a focal adhesion-specific distribution profile, ArgBP2 was found to colocalize with actin stress fibers and ZO-1, and distribute to the focal adhesions, lamellipodia, and nucleus. Upregulation of ArgBP2 and CAP in dexamethasone treated TM cells was associated with increased levels of chromatin remodelers including BRG1, MAT1 and MECP2. The Abl and Arg kinase inhibitor, dasatinib, was found to suppress dexamethasone-induced association of ArgBP2 and CAP with focal adhesions. Interestingly, the chromosomal localization of ArgBP2 at 4q35.1 is a recognized locus for an autosomal dominant POAG.

Conclusions: Taken together, ArgBP2 and its related cell adhesive proteins (CAP and Vinexin) appear to play a key role in dexamethasone-induced actin cytoskeletal crosslinking and cell adhesive interactions in TM cells, which are known to influence aqueous humor outflow and intraocular pressure.

CONTROL ID: 3544146

SUBMITTER (NAME ONLY): Nawaf Almutairi

TITLE: Chromatic Filters Restore the Accommodation Control Mechanism in mTBI Patients

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Almutairi, C. Liu, J. Hayes, Optometry, Pacific University, Forest Grove, Oregon, UNITED STATES|N. Almutairi, Optometry, Qassim University, Buraidah, Al Qassim, SAUDI ARABIA|

Commercial Relationships Disclosure (Abstract): Nawaf Almutairi: Commercial Relationship: Code N (No Commercial Relationship) | Chunming Liu: Commercial Relationship: Code N (No Commercial Relationship) | John Hayes: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Accommodation dysfunction following mild traumatic brain injury (mTBI) can lead to symptoms such as blur, asthenopia, and photosensitivity, impairing patients' near-work comfort and efficiency. Accommodative insufficiency is widely reported in mTBI patients who show significantly higher accommodative error (AE). Chromatic filters (CF) have been used as a clinical treatment to improve these symptoms. This study aimed to explore the potential mechanism underneath the CF treatment effect by assessing the effective threshold to blur (ET), a concept introduced by Jiang's modified control model for steady-state accommodation to account for the sensory component.

Methods: Data was obtained from 54 healthy (age 21-30 years) and 30 mTBI subjects (age 18-33 years) using Power Refractor 3. Monocular static accommodation was recorded continuously for 1 minute at 5 distances (6m-20 cm) under 3 conditions: baseline without filter (NF), subjects' selected CF using the Intuitive Colorimeter, and transmission-matched neutral density filters (ND). Further subgrouping was based on subjects' high vs. low color preference. ET was averaged for all distances. The longitudinal chromatic aberration (LCA) was calculated for each selected CF.

Results: Consistent with previous report, AE significantly correlated with ET for non-TBI subjects for all conditions. This correlation was disrupted in the mTBI group and restored by CF and ND Fig.1. The non-TBI group did not show any correlation between ET and LCA Fig.2. Similar result was found in mTBI subjects with low color preference. In contrast, the mTBI subjects with high preference selected a wavelength that induced ET change which was highly correlated with the LCA ($r=-0.90$, $p=0.001$), indicating a potential link between the color and accommodative sensory control.

Conclusions: Our data suggested that accommodation sensory control was impaired in mTBI patients. CF and NF rescued this impairment by altering wavelength and/or luminance. Subjects with high color preference selected color that might modify the ET via LCA, restoring the control through blur sensitivity. This finding provided the first evidence supporting the hypothesis that the CF treatment effect in mTBI might rely upon improving accommodation control.

CONTROL ID: 3544147

SUBMITTER (NAME ONLY): Grace Xiao

TITLE: Association Between Over Time Changes in Visual Field and Contrast Sensitivity in Glaucoma Patients

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Xiao, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|A. Mihailovic, J. E. S.K. West, P.Y. Ramulu, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Maryland, UNITED STATES|D.S. Friedman, Massachusetts Eye and Ear, Harvard Medical School, Massachusetts, UNITED STATES|L.N. Gitlin, Drexel University College of Nursing and Health Professions, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the association between changes in visual field [VF] and contrast sensitivity [CS] in glaucomatous eyes over a 3-year study period.

Methods: Glaucoma patients who underwent a minimum of three Humphrey 24-2 SITA-Standard VFs and three MARS CS tests were evaluated. Univariate linear regression was used to calculate within-eye slopes of changes in VF mean deviation (MD) and CS over time. Multivariable generalized estimating equation models accounting for within-individual clustering were used to assess the relationship between MD and CS at the baseline and changes over time.

Change in concordance/discordance between MD and CS in terms of defining the eye with better vision was evaluated over time using the test of proportions and survival analysis. Agreement of better eye MD / CS in defining longitudinal stability (± 0.5 dB/year for MD and ± 0.04 logCS units/year for CS) vs. change was also examined.

Results: 338 eyes from 180 glaucoma patients were included. Participants were on average 70 years old and about a third of participants were Black and half were female. There was a significant association between MD and CS at baseline ($\beta = 1.53$ dB decline for every 0.1 logCS unit decline, $p < 0.001$) and change in MD and CS over time ($\beta = 0.13$ dB decline for every 0.1 logCS unit decline, $p = 0.002$).

At baseline, MD and CS tests did not identify the same eye as the better eye for 33.8% of patients. 50% of eyes that were discordant at baseline remained discordant (95% confidence interval (CI) = 0.34-0.66) while 80% of eyes concordant at baseline remained concordant (95% CI = 0.71-0.89). At the end of 3 years, the probability of concordant eyes at baseline remaining concordant over time was 66%, significantly greater than the probability of discordant eyes at baseline remaining discordant ($p < 0.001$).

Over the 3-year period, 77% of subjects who had stable better eye MD also had stable CS while 45% of subjects who had worsening better eye MD also had worsening CS. Similarly, 83% of subjects who had stable CS over the years also had stable MD while 37% of subjects who had worsening CS also had worsening MD.

Conclusions: We found that change in CS over time predicts change in MD in those with glaucoma. However, more work is required to determine if CS could serve as an ancillary test to help judge disease progression.

CONTROL ID: 3544152

SUBMITTER (NAME ONLY): Stuart Tompson

TITLE: Intronic variant in sonic hedgehog associated with autosomal dominant pediatric cataract, myopic astigmatism, familial exudative vitreoretinopathy, and primary open-angle glaucoma

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.W. Tompson, K.N. Whisenhunt, T.L. Young, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|A.W. Hewitt, Department of Ophthalmology, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|D.A. Mackey, Lions Eye Institute, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|D.A. Mackey, Eye Department, Royal Hobart Hospital, University of Tasmania, Hobart, Tasmania, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To identify the genetic etiology of an autosomal dominant constellation of pediatric cortical cataract, asymmetric myopia with astigmatism, familial exudative vitreoretinopathy, and primary open-angle glaucoma phenotypes in a large Australian pedigree of European decent we performed linkage analysis, as well as exome and whole-genome sequencing (WGS).

Methods: Twelve affected and 4 unaffected individuals were genotyped at 713K SNPs using HumanOmniExpress-24 BeadChips, and 103K high quality and informative markers were selected via GenomeStudio software. Multipoint linkage analysis and haplotyping were performed by Superlink-Online software (dominant inheritance, 0.99 penetrance). Four affected individuals were exome sequenced using a Roche Nimblegen SeqCap EZ Exome V3 capture kit and an Illumina HiSeq2000 platform (2x100bp, 100x coverage). WGS was performed on an affected individual and his unaffected father using an Illumina HiSeq X Ten platform (2x150bp, 30x coverage). Reads were aligned to hg19 with BWA. SNPs/InDels, structural variants, and copy number variants (CNVs) were called with GATK, Delly, and control-FREEC, respectively. Variant analysis was performed using Golden Helix SVS. Combined Annotation Dependent Depletion (CADD) analysis prioritized variants by predicted deleteriousness.

Results: Linkage mapped the genetic locus to chromosome 7q36 (LOD 3.3). A co-segregating disease haplotype delimited the interval containing 27 protein coding and 17 non-protein coding genes. No candidate coding variants were identified. WGS discovered 136 rare (allele frequency <0.0001) non-coding variants, of which 77 were associated with 13 genes. CADD analysis determined only 1 variant within the top 1% of deleterious variants in the genome (scaled score 21.7) - a novel base substitution located in a highly conserved CpG island between exons 1 and 2 of sonic hedgehog (SHH; NM_001310462.2: c.300+290C>T). Extensive published animal studies link SHH to the phenotypes of this family. ENCODE data suggested that the region may act as a distal enhancer during early development of human eye and retinal tissues.

Conclusions: We identified an intronic variant in SHH as a potential cause of this rare constellation of ocular phenotypes. Disruption of the cis-regulatory enhancer element in SHH may lead to abnormal ocular development.

CONTROL ID: 3544154

SUBMITTER (NAME ONLY): Lisa Beckmann

TITLE: Visible-Light Optical Coherence Tomography Imaging of the Developing Inner Retinal Layer Structure in Mice

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Beckmann, Z. Cai, D.A. Miller, H. Zhang, Northwestern University, Evanston, Illinois, UNITED STATES|J. Cole, M. Liu, M. Grannonico, P. Netland, X. Liu, University of Virginia, Charlottesville, Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lisa Beckmann: Commercial Relationship: Code N (No Commercial Relationship) | Zhen Cai: Commercial Relationship: Code N (No Commercial Relationship) | James Cole: Commercial Relationship: Code N (No Commercial Relationship) | David Miller: Commercial Relationship: Code N (No Commercial Relationship) | Mingna Liu: Commercial Relationship: Code N (No Commercial Relationship) | Marta Grannonico: Commercial Relationship: Code N (No Commercial Relationship) | Peter Netland: Commercial Relationship: Code N (No Commercial Relationship) | Xiaorong Liu: Commercial Relationship: Code N (No Commercial Relationship) | Hao Zhang: Commercial Relationship(s);Opticent Health:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Visible-light optical coherence tomography (vis-OCT) provides high axial resolution and unique backscattering information compared with conventional OCT. However, vis-OCT signal quality is lower in young mice, chiefly due to attenuating hyaloid vessels that persist for several weeks after birth, potentially preventing the use of vis-OCT in mouse models of pediatric eye diseases. We explore the feasibility of using vis-OCT to track developmental changes in the murine inner retinal structure in vivo, starting at eye-opening.

Methods: Wildtype C57BL/6 mice from P12 to P60 were separated into four age groups: 1) P13-P16, right after eye-opening, 2) P18-21, 3) P24-31, and 4) P40-P60 (mature). We acquired vis-OCT images centered on the optic nerve head with a field-of-view of 1.1 mm × 1.1 mm. We utilized a resampled circular B-scan averaging technique in post-processing to improve inter-layer retinal contrast (example resampled circular B-scan shown in Figure a). Histology images were acquired via confocal microscopy. For both vis-OCT and histology data, we measured the thickness of the retinal nerve fiber layer + ganglion cell layer (RNFL/GCL), inner plexiform layer (IPL), inner nuclear layer (INL), and total retina using ImageJ. Figure b is a magnified view of the orange box from Figure a with relevant layers used for measurements labelled. All measurements were taken 300-550 µm from the optic nerve head.

Results: We averaged nine acquisitions and developed a resampled circular B-scan method, which enabled repeatable retinal layer thickness measurements from vis-OCT datasets in all age groups. The correlation constant between OCT and histology, defined as the ratio of the OCT thickness measurement to the histology thickness measurement, ranged from 0.68 to 1.18 across the different retinal layers and age groups. These results are consistent with previously published values of correlation constant in healthy adult mice. The correlation coefficient between OCT and histology, defined as Pearson's correlation coefficient (R^2) for the line of best fit under a preassumed linear relationship between OCT and histology layer thickness measurements, is 0.996.

Conclusions: Vis-OCT retinal layer thickness measurements agreed well with histology for all layers and age groups examined. Vis-OCT can visualize and track developmental changes in the murine retinal layer structure in vivo from eye-opening.

CONTROL ID: 3544156

SUBMITTER (NAME ONLY): Inés López Cuenca

TITLE: Assessment of macular thickness changes by OCT in asymptomatic relatives of Alzheimer's disease patients

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. López Cuenca, R. de Hoz, E. Salobar-García, J. Fernández-Albarral, P. Rojas, L. Elvira-Hurtado, A. Ramirez, J. Salazar, J. Ramirez, Inst.Inv.Oft.Ramón Castroviejo, UCM and RETICs OFTARED-ISCIII, Madrid, Madrid, SPAIN|R. de Hoz, E. Salobar-García, A. Ramirez, J. Salazar, Departamento de Inmunología, Oftalmología y ORL., Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|P. Rojas, , Instituto Oftálmico de Madrid, Hospital General Universitario Gregorio Marañon Unidad de Glaucoma y Neuro-oftalmología, Madrid, Comunidad de Madrid, SPAIN|A. Barabash, Endocrinology and Nutrition Department, Hospital Clinico Universitario San Carlos, Madrid, Madrid, SPAIN|A. Barabash, Centro de Investigacion Biomedica en Red de Diabetes y Enfermedades Metabolicas Asociadas, Madrid, Madrid, SPAIN|J. Ramirez, Departamento de Inmunología, Oftalmología y ORL., Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|

Commercial Relationships Disclosure (Abstract): Inés López Cuenca: Commercial Relationship: Code N (No Commercial Relationship) | Rosa de Hoz: Commercial Relationship: Code N (No Commercial Relationship) | Elena Salobar-García: Commercial Relationship: Code N (No Commercial Relationship) | Jose A. Fernández-Albarral: Commercial Relationship: Code N (No Commercial Relationship) | Pilar Rojas: Commercial Relationship: Code N (No Commercial Relationship) | Lorena Elvira-Hurtado: Commercial Relationship: Code N (No Commercial Relationship) | Ana Ramirez: Commercial Relationship: Code N (No Commercial Relationship) | Ana Barabash: Commercial Relationship: Code N (No Commercial Relationship) | Juan J. Salazar: Commercial Relationship: Code N (No Commercial Relationship) | Jose Ramirez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Alzheimer's diseases is a neurodegenerative disease, whose pathophysiological features show decades before the main cognitive symptoms appear. In addition to age, genetic factors are one of the most important risk factors.

The aim of the present study was to analyze the retinal thickness changes by optical coherence tomography (OCT) in first-degree relatives of Alzheimer's disease patients who are carriers of $\epsilon 4$ allele for the ApoE, which are two of the main risk factors for developing the disease.

Methods: Sixty- four participants, who were free of ocular pathology were analyzed. A complete eye examination and OCT were performed. The two study groups were formed by 35 subjects with a family history of AD (FH+) and ApoE $\epsilon 4$ carriers and 29 age-matched control subjects without a family history of AD (FH-) and ApoE $\epsilon 4$ non-carriers.

Results: In FH+ ApoE $\epsilon 4$ carriers compared to FH- ApoE $\epsilon 4$ non-carriers we found a statistical significant thinning ($p < 0.05$) in the next sectors and layers: the foveal area of the macular retinal nerve fiber layer (11.89 ± 1.95 , FH+ vs 12.86 ± 1.62 , FH-); the inferior and nasal sectors, both in the outer (26.77 ± 2.74 , FH+ vs 28.17 ± 2.82 , FH- for inferior) (29.49 ± 2.89 , FH+ vs 30.93 ± 3.85 , FH- for nasal) and inner (40.49 ± 2.51 , FH+ vs 42.10 ± 3.48 , FH- for inferior) (41.94 ± 2.74 , FH+ vs 43.52 ± 3.57 , FH- for nasal) macular ring in the inner plexiform layer; the foveal area (18.82 ± 3.61 , FH+ vs 21.21 ± 3.88 , FH-) and the inferior sector in the outer macular ring (30.91 ± 2.72 , FH+ vs 32.10 ± 2.81 , FH-) in inner nuclear layer, and the inferior sector of the outer macular ring (27.60 ± 2.75 , FH+ vs 29.97 ± 3.82 , FH-) in outer plexiform layer. No statistically significant differences were found in the peripapillary thickness of RNFL between both study groups.

Conclusions: In asymptomatic relatives of Alzheimer's disease patients with high genetic risk for the development of AD, initial changes appeared in the macular area. These slight retinal thickness changes measured by OCT could be used as an early biomarker of the disease.

CONTROL ID: 3544159

SUBMITTER (NAME ONLY): Alex Bowers

TITLE: Pilot study of a tactile hazard warning device for drivers with central vision loss

SESSION TITLE: Visual Impairment - Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.R. Bowers, S.W. Savage, J. Xu, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A.R. Bowers, S.W. Savage, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|G.N. Dyszak, F.M. Kölsch, C. Lehsing, Chair of Ergonomics, Department of Mechanical Engineering, Technische Universität München, München, Bayern, GERMANY|J. Xu, Envision Research Institute, Kansas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Alex Bowers: Commercial Relationship: Code N (No Commercial Relationship) | Georg Dyszak: Commercial Relationship: Code N (No Commercial Relationship) | Felix Kölsch: Commercial Relationship: Code N (No Commercial Relationship) | Steven Savage: Commercial Relationship: Code N (No Commercial Relationship) | Christian Lehsing: Commercial Relationship: Code N (No Commercial Relationship) | Jing Xu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: People with central vision loss (CVL) are permitted to drive in most states in the USA; however, CVL may cause delayed responses to hazards. Advanced driver assistance systems that provide hazard warnings are available, but little is known about the extent to which such systems might mitigate crash risk of drivers with CVL. We therefore developed a prototype hazard warning device and evaluated its impact on the responses of drivers with CVL to pedestrian hazards in a simulator.

Methods: Seven subjects with CVL (36 – 74 y; median VA 20/80) and 7 subjects with normal vision (NV) (34 – 78 y; median VA 20/15) participated. They completed 2 drives with and 2 drives without a custom-designed vibrotactile warning device embedded in the seat cushion. There were 10 realistic pedestrian hazards per drive which appeared mid-block from either the left or right and crossed the road in front of the driver's vehicle, requiring a natural braking response by the driver to avoid a collision. If collision risk (computed continuously) exceeded a pre-defined threshold, the device gave a directional vibration to warn of the approaching hazard. Gaze position and driving metrics were monitored at 50 Hz for analysis. The virtual city environment was populated with other distractor pedestrians, crowds, and traffic.

Results: Overall, CVL subjects took longer to fixate hazards (1.2s vs 0.6s, $p = .01$), received more warnings (77% vs 66%) and were involved in more collisions (2.9% vs 0.4%, $p = .01$) than NV subjects. When collision risk exceeded the threshold, warnings had no effect on the time to fixate the hazard, but significantly reduced the time taken by CVL subjects to press the brake (from 2.4s to 2.0s, $p = .004$). Thus, the warnings significantly improved response safety of CVL subjects ($p < .001$), reducing their collision rate from 8.5% to 0% for events exceeding the collision threshold. In contrast, the warnings had no effect on safety of NV drivers (interaction $p < .001$). CVL subjects liked the design of the warnings (intensity, duration, timing and frequency), rated the device as more helpful than NV subjects, and would be more likely to use it if available on their car.

Conclusions: Our results provide preliminary evidence that tactile directional warnings of potential hazards may reduce collision risk of CVL drivers by decreasing the time required to perceive the risk level and initiate a braking response.

CONTROL ID: 3544161

SUBMITTER (NAME ONLY): Qitao Zhang

TITLE: Differential Susceptibility of Primary Human Adult vs. Fetal RPE Cultures to AMD-Relevant Insults

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is characterized by progressive retinal pigment epithelial (RPE) dysfunction and eventual atrophy. Numerous pathogenic mechanisms have been proposed, including accumulation of lipofuscin, shifts in RPE metabolism, and alterations in the RPE's underlying extracellular matrix. Our goal is to identify pathways in RPE that contribute to resiliency and can be pharmacologically manipulated to protect RPE in AMD.

Methods: Primary human adult RPE (ahRPE) and fetal RPE (hfRPE) were cultured based on established protocols. Lipofuscin-like granules accumulate through repeated feedings of photo-oxidized outer segments to cultures. Glycolysis and mitochondrial function were assayed by a Seahorse Analyzer. Calcium deposition in the extracellular matrix was determined using a variety of standard stains. Gene expression differences between ahRPE and hfRPE were assessed by RNASeq using DESEQ2 for differential expression and iDEP90 with both GSEA and PGSEA for pathway analysis.

Results: Lipofuscin-like granule accumulation was significantly higher in ahRPE compared to hfRPE, despite more ingestion of OS in the hfRPE group. Further, lipofuscin-like granules are associated with a reduction in oxidation consumption rate, a marker of mitochondrial capacity, only in ahRPE. RNASeq comparing ahRPE with hfRPE demonstrates generally similar expression of RPE-specific genes, but differences in fatty acid degradation, ketogenesis, and lysosomal function that may account for hfRPE's resistance to lipofuscin accumulation and toxicity. RNASeq also revealed an ectopic extracellular calcification program robustly expressed in ahRPE only. Ongoing studies are determining whether the basolateral extracellular matrix is more calcified in ahRPE compared to hfRPE cultures.

Conclusions: Compared to hfRPE, ahRPE demonstrates increased susceptibility to several AMD-relevant stresses. Initial RNASeq analysis also suggests ahRPE may uniquely express a basolateral extracellular membrane calcification program that could account for calcified drusen, a significant risk factor for AMD progression. Ongoing studies are cataloging other AMD-relevant insults that preferentially affect ahRPE over hfRPE. Comparative gene expression and secreted metabolomic analysis are being used to identify pathways contributing to hfRPE's resiliency.

CONTROL ID: 3544162

SUBMITTER (NAME ONLY): Daisy Shu

TITLE: Differential effects of TNF α on Mitochondrial Function and Metabolic Activity in the Retinal Pigment Epithelium

SESSION TITLE: Mitochondria in ocular diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The retinal pigment epithelium (RPE) acts as a metabolic gatekeeper between photoreceptors and the choroidal vasculature to maintain healthy retinal function. RPE dysfunction is a key feature of age-related macular degeneration (AMD), the leading cause of blindness in developed countries. Tumor necrosis factor- α (TNF α), a potent pro-inflammatory cytokine, has been implicated in the pathogenesis of AMD. Growing evidence supports metabolic dysfunction as another key mechanism driving AMD. To date, there is no literature on the metabolic effects of TNF α on RPE and thus, this study sheds light on the impact of TNF α on mitochondrial morphology and metabolic function in RPE.

Methods: Matured ARPE-19 were treated with TNF α (10 ng/ml) for up to 72h. Glycolysis and oxidative phosphorylation (OXPHOS) were examined by high-resolution respirometry on the Seahorse XF24. Gene expression of EMT and metabolic markers were assessed by qPCR. Mitochondrial morphology was assessed by confocal imaging and ImageJ processing of MitoTracker Orange-stained ARPE-19.

Results: TNF α induced ARPE-19 to elongate into spindle-shaped cells, reminiscent of epithelial-mesenchymal transition (EMT). However, qPCR showed that TNF α reduced EMT genes expression (Col1A1: 1.2 vs 0.39, $p=0.015$; α -SMA: 1.01 vs 0.66 $p=0.001$) indicating that the elongated cells were not mesenchymal. TNF α increased basal OXPHOS levels (OCR = 2.2 vs 3.7 pmol/min/ μ g, $p=0.042$) and increased glycolytic capacity (ECAR = 0.68 vs 0.92 mpH/mol/ μ g, $p=0.03$). Paradoxically, TNF α induced a reduced expression of OXPHOS genes (COX4I1: 1.02 vs 0.16, $p < 0.0001$; COX5B: 1.02 vs 0.24, $p<0.0001$). TNF α significantly upregulated expression levels of the mitochondrial antioxidant SOD2 (1.14 vs 14.8, $p<0.0001$) and disrupted mitochondrial network morphology exhibiting increased sphericity and fragmentation.

Conclusions: Taken together, we find that TNF α robustly disrupts mitochondrial function and morphology in RPE, although shifting the bioenergetic profile in a paradoxical manner, i.e. TNF α raised the levels of basal respiration and glycolysis despite the suppression of genes regulating OXPHOS. These findings highlight the potential of targeting metabolic pathways in RPE as a promising therapeutic avenue for AMD. Further research is required to elucidate the mechanisms underlying the intriguing TNF α -driven metabolic changes.

CONTROL ID: 3544163

SUBMITTER (NAME ONLY): Abraham Olvera-Barrios

TITLE: Foveal curvature and its associations in UK Biobank participants

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To analyse the foveal curvature in macular optical coherence tomography (OCT) scans, and evidence its associations in a large cohort.

Methods: We analysed a sample of 73,032 participants from the UK Biobank study, who as part of their enhanced ophthalmic examination had macular spectral-domain OCT. Mean age $56.5 \pm$ standard deviation (SD) 8.02 years, 46% were male. A deep learning model was used to segment the retinal pigment epithelium, and foveal curvature was calculated by polynomial fit. Age, gender, refractive status (spherical equivalent [SE]), visual acuity, intraocular pressure (IOP), birth weight, maternal smoking, average income, and deprivation (Townsend index) were included as part of the analysis in a linear regression model. This research used data from the UK Biobank Resource, under data access request number 60554.

Results: The mean fovea curvature was 0.0722, interquartile range (IQR) 0.0464-0.0981. Males had a more pronounced foveal curvature (0.0771 ± 0.0201) than females (0.0681 ± 0.0185 ; $p < 0.001$). The flatter fovea curvature tertile (mean 0.0519, IQR 0.0404-0.0634) was more frequently observed in hyperopes; i.e. 60.3% of high hyperopes ($SE \geq +6.00$ diopters [D]) and 38.5% of hyperopes ($SE > +0.50 < +6.00$ D). Conversely, the steeper fovea curvature tertile (mean 0.0942, IQR 0.0781-0.1103) was more frequently observed in myopes; i.e. 37.8% of high myopes (< -6.00 D) and 36.8% of myopes ($SE < -0.50 > -6.00$ D). The multivariable linear regression analysis showed negative associations between fovea curvature and SE, worsening visual acuity and increasing material deprivation (flatter curvature measurements for each extra unit increase of these variables). Male gender, birth weight, maternal smoking, higher intraocular pressure and income greater than £100,000 showed a positive association with foveal curvature (more pronounced curvature).

Conclusions: Visual acuity, SE and poorer socioeconomic profile showed negative associations with foveal curvature. High income showed a positive association with foveal curvature. Additional research is warranted to further characterise the foveal curvature and its associations with retinal development and disease.

CONTROL ID: 3544166

SUBMITTER (NAME ONLY): Sylvia Gasparini

TITLE: HiPSC-derived cones incorporate, mature and survive long-term in a mouse model of cone-degeneration

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Humans rely on high acuity and daylight vision – both of which are mediated by cone photoreceptors. Once photoreceptors die, they do not regenerate. Thus cell transplantation has emerged as a treatment strategy. While retinal organoids hold promise as an unlimited cell source, human cone transplantations have so far been hampered by a lack of efficient cone cell enrichment by surface markers. In this study a cone specific GFP-reporter hiPSC line was generated, facilitating this cone transplantation study.

Methods: A mArr3-GFP hiPSC line was utilized in an optimized protocol to produce robust numbers of cones (up to 45%) in retinal organoids. FAC-sorted cones of day 200 organoids were transplanted into cone photoreceptor function loss 1 mice (Cpfl1) which exhibit rapid cone loss. Using local immune suppression, the transplants survived well, allowing long term follow up at 3, 10 and 26 weeks (wk). Transplants were examined via immunohistochemistry, electron microscopy and RNA sequencing.

Results: At 3wks the human cones remained largely in the subretinal space, but, by 10wks a bulk migration of the graft into the host outer nuclear layer was observed, a behavior which has not been described previously. Transplanted cones appeared to be well tolerated by the mouse retina – rather than forming a glial barrier, Müller Glia cells enveloped the graft. In addition, bipolar and horizontal cells extend processes to the human cones, a requisite for synaptic connectivity. Transplanted cones continued to mature in vivo, where by 10wks, some cones developed characteristic photoreceptor features of ribbon synapses and inner segments. By 26wks the human cones further matured, developing outer segment structures. Of note, only cones interacting with the host retina developed these features, while cones within the subretinal space lacked signs of maturation. Remarkably, the xenogeneic environment did not negatively alter maturation of the human cones, as evidenced by the high degree of similarity between the RNA expression profiles of in vivo vs in vitro matured cones, as well as to primary fetal human cones.

Conclusions: Overall these results indicate that human cones are well tolerated, mature normally and interact readily with the dystrophic mouse retina. This is an important achievement in photoreceptor transplantation research and opens up possibilities for further research towards clinical application.

CONTROL ID: 3544172

SUBMITTER (NAME ONLY): James Im

TITLE: Trends in prevalence of self-reported visual impairment in Canadians with and without diabetes: findings from population-based surveys from 1994 to 2014

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Few studies have evaluated the prevalence of visual impairment (VI) and associated trends in diabetes and non-diabetes. This study assessed the prevalence of and changes in VI among Canadians with and without diabetes from 1994 to 2014.

Methods: Data from respondents aged 40+ participating in seven nationwide surveys were analyzed: the National Population Health Survey in 1994/1995 (n=17,626), 1996/1997 (n=81,804) and 1998/1999 (n=17,244) and the Canadian Community Health Survey in 2000/2001 (n=130,880), 2008/2009 (Healthy Aging, n=30,865), 2009/2010 (n=124,188) and 2013/2014 (n=127,462). VI was self-reported as unable to see close or distance when wearing glasses/contact lenses. Diabetes was self-reported. Using the 2016 Canadian population as the standard, the age- and sex-standardized prevalence of VI was calculated. For analyses stratified by levels of education and income, sex-standardized prevalence was calculated.

Results: In any survey year, the age- and sex-standardized prevalence of VI was about 2 times higher in people with diabetes versus those without (e.g. 2.96% vs 1.57% in 2013/2014). Among people with diabetes, the standardized VI prevalence was 7.11% (95% confidence interval (CI): 6.99%-7.24%) in 1994/1997 and gradually decreased to 2.96% (95% CI: 2.91%-3.01%) in 2013/2014, a 58% reduction over 20 years (standardized prevalence ratio: 0.42 (95% CI: 0.23-0.75) for prevalence in 2013/2014 versus 1994/1997).

Among people without diabetes, the standardized VI prevalence decreased from 3.38% (95% CI: 3.35%-3.40%) in 1994/1997 to 1.57% (95% CI: 1.56%-1.58%) in 2013/2014, a 54% reduction (standardized VI prevalence ratio: 0.46 (95% CI: 0.42-0.52) for prevalence in 2013/2014 versus 1994/1997).

Decreases in sex-standardized VI prevalence were observed among people with and without diabetes from 1994/1997 to 2013/2014 after stratification by education and income levels.

Conclusions: From 1994 to 2014, VI was roughly 2 times higher in people with diabetes versus those without. For both people with and without diabetes, the standardized VI prevalence decreased in those with high and low levels of education and income. These results likely reflect the effectiveness of the collective efforts by eye care providers, researchers, the public and government.

CONTROL ID: 3544175

SUBMITTER (NAME ONLY): Manjing Cao

TITLE: Microglia phagocytosis contributes to clearance of photoreceptor outer segment following retinal detachment

SESSION TITLE: Glial Cells

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Cao, D. Kong, S. Shanmugam, H. Hager, B.X. Ross, D.N. Zacks, S.F. Abcouwer, Department of Ophthalmology and Visual Science, University of Michigan, Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal detachment (RD) occurs when photoreceptors (PR) are separated from the retinal pigment epithelium (RPE), compromising PR cell survival. PR outer segments (OS) are continuously renewed by a process including daily shedding and phagocytosis by RPE cells, which is interrupted by RD. RD also triggers an innate immune response, with the activation and attraction of retinal microglia to the subretinal space. We hypothesized that subretinal microglia replace the function of RPE by actively phagocytose OS.

Methods: To lineage trace microglia, tamoxifen (Tam)-inducible Cre-driver mice (CX3CR1-CreERT2) were crossed with mice with Cre-dependent expression of tdTomato red-fluorescent protein (RFP). A 4-week period after Tam treatment was used to eliminate RFP-expressing monocytes. The mice then received subretinal injections of 1% hylaluronic acid to cause partial RD. Retinal sections were obtained at 3, 7 and 14 days post-retinal detachment (dprd). Untreated fellow eyes were used as controls. Retinal and subretinal cells were examined by immunofluorescence for expression of RFP and phagocytosis markers. Lysosomal receptor CD68 and phagocytic receptor MerTK were used as phagocytosis markers. Rhodopsin and PNA lectin, were used to identify OS of rods and cones, respectively. Imaris software was used to construct 3D images.

Results: RFP-labeled retinal microglia were observed to migrate to the subretinal space at 3, 7 and 14 dprd. Lineage tracing confirmed that the vast majority of subretinal cells were microglia, averaging $87 \pm 2\%$ at 14 dprd. Dramatically increased CD68 and MerTK immunoreactivity were observed in microglia, indicating phagocytic activity. Anti-rhodopsin and PNA-reactive OS were observed anchoring to microglial membranes and drawn within the cell bodies of microglia, indicating phagocytosis of POS. The co-localization of CD68 and rhodopsin implied OS internalization and transfer into phagolysosomes.

Conclusions: The initial innate immune response to RD involves microglia infiltration in the subretinal space. The results reveal microglia OS phagocytosis provides OS clearance in the absence of PR-RPE interaction.

CONTROL ID: 3544176

SUBMITTER (NAME ONLY): Aneela Raja

TITLE: Outcomes of glaucoma referrals for narrow anterior chamber angles: real world data

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The UK Joint College Guidance advises referral of all patients with “a narrow anterior drainage angle on Van Herick testing consistent with a significant risk of acute angle closure within the foreseeable future”.¹ However, recently published data do not support widespread prophylactic laser peripheral iridotomy (LPI) for primary angle closure suspects (PACS).² This study aims to investigate the outcomes of glaucoma referrals from community optometrists specifically for narrow anterior chamber angle on Van Herick.³⁻⁵

Methods: This retrospective study, conducted at Moorfields Eye Hospital at Bedford (UK) included all glaucoma referrals received between April 2018 – March 2019 for “narrow Van Herick” (or synonym terms) in the absence of other glaucoma-related factors, such as raised intraocular pressure and ‘suspicious’ optic discs or visual fields. Data were collected manually via electronic medical records (Medisoft). Patients were retrospectively classified as PACS, Primary Angle Closure (PAC), and Primary Angle Closure Glaucoma (PACG).^{6,7}

Results: We received 438 glaucoma referrals for ‘narrow angles’ alone, of which 400 (91.3%) had a full glaucoma assessment (37 did not attend; 1 could not be found). Of these 400 patients, only 45 (11.3%; 95% Confidence intervals (CI) 8.5-14.7) had an occludable angle on gonioscopy. With regard to management decisions, 194/400 patients (48.5%; 95% CI 43.6-53.4) were discharged at first visit, 116/400 (29%; 95% CI 24.8-33.6) were monitored and 90/400 (22.5%; 95% CI 18.7-26.9) received treatment: 55/400 (13.8%; 95% CI 10.7-17.5) had LPI and 35/400 (8.8%; 95% CI 6.3-12) had phacoemulsification. The 45 patients with a confirmed occludable angle were retrospectively classified: 44/400 (11%; 95% CI 8.3-14.5) PACS, 1/400 (0.3%; 95% CI <0.01-1.6) PAC, and 0 PACG. Among the 44 PACS, 34 (77.3%; 95% CI 62.8-87.3) had LPI, 6 (13.6%; 95% CI 6-27.1) had phacoemulsification and 4 (9.1%; 95% CI 3-21.7) were monitored without treatment.

Conclusions: The diagnostic accuracy of ‘narrow Van Herick’ for occludable iridocorneal angles was found to be low. The majority of those with a confirmed occludable angle were at low risk for glaucoma (PACS). Nonetheless, most of them underwent prophylactic LPI. The guidance for glaucoma referrals needs to be reconsidered; the clinical management of angle closure also needs to move away from the widespread use of prophylactic LPI in low risk patients.

CONTROL ID: 3544179

SUBMITTER (NAME ONLY): Calvin Robbins

TITLE: An initiative to improve follow-up of patients with glaucoma

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Adherence to follow-up for glaucoma is known to be poor, especially among asymptomatic patients or those with mild disease. This study reports on an initiative aimed at reducing the number of patients with glaucoma-related diagnoses lost to follow-up (LTF) and reviews its short-term outcomes.

Methods: An electronic medical record (EMR)-based tool was designed to identify patients with glaucoma-related diagnoses who were seen at a hospital-based outpatient eye clinic within a six-month period in the prior year and who had not scheduled or returned for follow-up care. Providers were given lists of patients designated as potentially LTF and asked to review the EMR and re-engage patients, as appropriate. One month later, the initiative was evaluated by retrospective chart review.

Results: 3,666 unique patients were seen during the study period. 3,167 patients were not LTF (86.4%) and 115 patients were deceased (3.1%), leaving 384 patients as LTF (10.5%). The number of prior ophthalmology appointments attended was inversely related to the risk of being LTF (Pearson correlation $r=-0.067$, $P<0.0001$). Not surprisingly, history of missing a scheduled appointment increased the risk of being LTF (OR 1.51, 95% CI 1.22 to 1.86 $p=0.0002$). Patients with low-risk findings such as glaucoma suspects or ocular hypertensives were more likely to be LTF than those with other forms of glaucoma (OR 1.26, 95% CI 1.01-1.58, $p=0.038$). Patients with primary open angle glaucoma were less likely to be LTF than those with other glaucoma-related diagnoses (OR 0.77, 95% CI 0.62-0.95, $p=0.016$). One month following the re-engagement initiative, 124 (32.3%) of the LTF patients had been re-engaged: 49 had completed a telemedicine visit (39.5%), 70 had a new in-person appointment ordered or scheduled (56.5%), and 5 had documentation that they declined re-engagement when contacted (4.0%). Of the remaining 260 patients (67.7%) without documented re-engagement, an order to schedule a follow-up appointment had been submitted for 238 individuals (91.5%). At the end of the initiative, only 22 patients (5.7%) had no documented plan for follow-up.

Conclusions: An EMR-based reporting system can be an effective tool to alert providers and allow for the re-engagement of patients with glaucoma-related diagnoses at risk of being LTF. This should promote better management of glaucoma and related diagnoses, enhance clinical productivity, and reduce potential medicolegal liability.

CONTROL ID: 3544180

SUBMITTER (NAME ONLY): Emily Wiecek

TITLE: Longitudinal Change of Refractive Error in Retinopathy of Prematurity Treated with Bevacizumab or Laser Photocoagulation

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Myopia is the most common clinical sequela of preterm birth and is especially common following retinopathy of prematurity (ROP). However, reported rates of myopia are lower in children whose ROP was treated with anti-vascular endothelial growth factor (anti-VEGF) agents as compared to conventional laser photocoagulation. We examined the progression of refractive error, over a period of up to nine years, in preterm-born children with ROP treated with either injection of the anti-VEGF agent Bevacizumab or laser.

Methods: We performed a retrospective review of records of premature infants treated for ROP at Boston Children's Hospital from 2011-2020 with Bevacizumab (n = 24) or laser (n = 54). Bevacizumab dosage ranged from 0.02mg-0.75mg. We analyzed cycloplegic refractions from 349 cumulative visits (mean 4±3 visits per individual; mean 2.3±2.7 years under observation), using a linear mixed effects model, to evaluate how refraction changed with corrected age following treatment.

Results: In aggregate, the model estimated a significant ($P < 0.001$) trend in refraction, from slight hyperopia to relatively more myopic states, as is common in emmetropization. However, the progression in laser-treated eyes was significantly ($P = 0.002$) more rapid: The estimated progression in individuals treated with laser was -0.79 diopters per year compared to only -0.02 diopters per year in eyes treated with Bevacizumab. Random effects, including individual subject variation with nested variance for left and right eye, accounted for 70% of the remaining variance not explained by corrected age and treatment.

Conclusions: Our analysis suggests that children with ROP who are treated with laser photocoagulation will tend to progress to myopia at a higher rate compared to those individuals treated with Bevacizumab.

CONTROL ID: 3544181

SUBMITTER (NAME ONLY): Emmanouil (Manos) Tsamis

TITLE: Evaluation of standard and novel structural and functional methods for detecting progression in glaucoma

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To assess standard and novel optical coherence tomography (OCT) and visual field (VF) methods for detecting glaucomatous progression

Methods: Disc circle and macular cube OCT scans and 24-2 and 10-2 VF data were obtained from 100 eyes [71 patients/suspects and 29 healthy controls (HC)], as part of a prospective, longitudinal study (P-group)(ClinicalTrials.gov Identifier: NCT02547740). All eyes had a minimum of 4 OCT and VF tests (mean 9.2 tests), with the last visit at least 1 year after the baseline visit. We evaluated standard OCT and VF metrics, combinations of OCT-OCT and OCT-VF, and a metric based on a region-of-interest (ROI) approach (Table 1, left-most column). For event-based, test-retest variability was estimated based on 176 eyes (146 patients/suspects, 30 HC). Repeated OCT and VF data collected within 4 months were analyzed with quantile regression to define cut-offs (the 95th percentile defined 'statistical progression'). Those cut-offs were then applied to the first vs. last test of the P-group. For trend-based, based on least squares regression eyes were categorized as "progression" if the slope was significantly negative (one-tail $p < 0.05$). Finally, 2 OCT experts (E-OCT) reviewed all OCT information and judged whether each eye had progressed on a scale of 0 (definitely did not progress) to 100% (definitely did progress). Eyes with scores $\geq 95\%$ were labelled "progrsors" (P), and those with scores $\leq 5\%$ "not progrsors" (NP). The E-OCT identified 13 P eyes, none of which was a HC

Results: We used the 60 NP and 13 P eyes as proxies for specificity and sensitivity (see Tables -bold columns). For the Event Analysis (Table 1) only one metric, TI (green in Tables), had a percent agreement greater than 90% for both proxies, while for the Trend Analysis (Table 2) none of the metrics had percentages greater than 90% for both. In general, an event-based approach performed better than trend analyses (Tables 1&2)

Conclusions: All objective methods so far explored miss clear progression revealed in some eyes by a careful examination of circumpapillary b-scans, with or without the aid of OCT probability maps, as well as identify "progrsors" that are clearly not progressing. We recommend that a qualitative evaluation of OCT images and thickness/probability maps be included at least as part of a post-hoc analysis.[1,2] 1. Hood et al. JoG 2020; 2. Eguia et al. TVST 2020

CONTROL ID: 3544182

SUBMITTER (NAME ONLY): Miltiadis Tsilimbaris

TITLE: Evolution of macular atrophy in eyes with neovascular age-related macular degeneration treated with anti-VEGF agents compared to fellow dry AMD eyes

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Macular atrophy (MA) is a basic characteristic of age-related macular degeneration (AMD), in both its neovascular and dry form. The purpose of this study is to evaluate the evolution of MA in patients with neovascular AMD (nAMD) treated with anti-vascular endothelial growth factor (anti-VEGF) agents, compared with the fellow eyes exhibiting dry AMD.

Methods: Participants in this retrospective study were 124 patients, treated for nAMD with anti-VEGF injections in one eye and followed-up for dry AMD in the fellow eye, in three different retinal departments. We analyzed data of 60 patients with a total of 4 years of follow-up. MA was evaluated in an annual basis using near-infrared and spectral-domain optical coherence tomography images, according to criteria proposed by the Classification of Atrophy Meetings group. Incidence and progression of MA were evaluated.

Results: Presence of MA until the 4th year of follow up in treated eye (TE) was recorded in 56% (34/60) patients and 30% (18/60) in fellow eye (FE). Repeated measures ANOVA with 2 within factors [time with 5 levels (0 to 4 years) and eye with 2 levels (TE, FE)] revealed significant time ($p < 0.001$), eye ($p = 0.012$) and time-eye interaction ($p < 0.001$) effects. Treated eye MA exhibits a steady significant increase up to year 4, whereas in the FE the significant increase is halted at year 2. The annual increase in the TE is 0.107mm/y for year 1, jumps to 0.304mm/y for year 2 and to 0.343mm/y for year 3, to drop to 0.281mm/y for year 4. The respective annual increase for the FE is 0.143mm/y, 0.143mm/y, 0.092mm/y and 0.086mm/y. Focusing on the subset of the 22/60 patients, who started with no baseline MA in TE, we observed the previously described pattern in a more pronounced manner. Following a slower growth in the TE at year 1 (0.066mm/y vs 0.147mm/y), MA growth in the TE is much faster than the FE (0.388mm/y vs 0.155mm/y for year 2, 0.39mm/y vs 0.083mm/y for year 3 and 0.353mm/y vs 0.075mm/y for year 4).

Conclusions: In this study we documented a significant difference in MA incidence and progression in eyes treated for nAMD compared to their fellow eyes exhibiting dry AMD. Treated nAMD eyes tend to develop more often MA; moreover MA progresses in a faster rate in these eyes compared to fellow dry AMD eyes.

CONTROL ID: 3544184

SUBMITTER (NAME ONLY): Xingjun Fan

TITLE: Cellular FLICE-like inhibitory protein (cFLIP) critically maintains apoptotic resistance in human lens epithelial cells

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The present study aims to understand the mechanism of lens epithelial cells' strong anti-apoptosis capacity and survival rate in the mature human lens that, on the one hand, maintains lens transparency over several decades, while on the other hand increases the risk of posterior capsule opacification (PCO).

Methods: Cell viability and apoptosis were analyzed in FHL124 cells under TNF α stimulation and were compared with HeLa cells. The TNF α mediated inflammatory signaling, cell survival genes were screened by real-time PCR, and key genes were confirmed by shRNA knocking down and immunoblot analysis.

Results: FHL124 cells demonstrate strong resistance to TNF α mediated cell death compared to HeLa cells. Harsh stimulation with TNF α and cycloheximide (CHX) triggers almost entire HeLa cell death within 7hr but not FHL124 cells even after 24hr stimulation. Further studies suggest that FHL124 cells are able to block caspase 8 activation and subsequently preventing caspase 3 activation, PARP-1 cleavage, and cell death. Interestingly, despite spontaneous activation of transcription factors, NF κ B and AP-1, and upregulation of multiple cell survival and anti-apoptotic genes in both cell types, only FHL124 cells managed to survive under TNF α challenge. By screening and comparing the cell survival genes, the cellular FLICE-like inhibitory protein (cFLIP) is found highly expressed in FHL124 cells and substantially upregulated by TNF α stimulation. FHL124 cells with a mild cFLIP 37 knockdown manifest a profound apoptotic response to TNF α and CHX treatment similar to HeLa cells.

Conclusions: Lens cells demonstrate a high level of resistance to stress-induced apoptosis relative to HeLa cells. cFLIP is abundant in lens epithelial cells and is further upregulated in the presence of stressors. A reduction in cFLIP renders lens epithelial cells more susceptible to apoptosis and therefore suggest that cFLIP plays a critical role in lens cell survival.

CONTROL ID: 3544185

SUBMITTER (NAME ONLY): Samuel Kyei

TITLE: Objectively-measured adherence to hypotensive ocular medication in patients with glaucoma in Ghana

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is the leading cause of irreversible blindness in Ghana, where it affects nearly 7.7% of the population aged over 30 years and 8.5% of those aged over 40 years. Reduction of intra-ocular pressure via ocular hypotensive eye drops is the first line of treatment for glaucoma. Current estimates of adherence to this treatment in Africa were obtained through self-report, which is known to overestimate adherence. In this study, we used electronic monitors to objectively assess adherence among glaucoma patients in Ghana.

Methods: Glaucoma patients on Timolol eye drops (N=139) were recruited from the Christian Eye Centre, Cape Coast, Ghana. These 4 questionnaires were administered at baseline: Self-Reported Adherence, Glaucoma Medication Self-Efficacy (GMSE), Eye Drop Technique Self-Efficacy (EDTSE) and Brief Illness Perception (BIP). Medication adherence was measured objectively using Medication Event Monitoring System devices (MEMS) (Aardex, Switzerland) and by self-report during a 3-month period. Adherence was computed as the percentage of days medication was used as prescribed within the 3-month monitoring period. Participants with < 75% adherence score were classified as non-adherent. The association between adherence and demographic information and medical history were assessed using chi-square tests and logistic regression. The relationship between adherence and GMSE, EDTSE and BIP scores were also determined using Pearson correlation coefficient.

Results: Of the 139 participants, 47 (33.8%) and 107 (77.0%) were classified as non-adherent based on self-report score and objective score. Mean (\pm SD) adherence was 49% \pm 30. Objectively-measured adherence was not significantly associated with GMSE ($r = -0.065$, $p = 0.45$), EDTSE ($r = 0.119$, $p = 0.16$) and BIP scores ($r = 0.068$, $p = 0.43$). Significant associations were observed between adherence and educational level ($\chi^2 = 9.179$, $p = 0.01$) and the number of systemic comorbidities ($\chi^2 = 6.029$, $p = 0.049$), with those without systemic comorbidities being 70.4% less likely to be adherent ($p = 0.045$).

Conclusions: Non-adherence to ocular hypotensive medication is common in Ghanaian patients with glaucoma. Future work should focus on identifying the factors associated with non-adherence with a goal of assisting patients efforts to adhere with their treatment.

CONTROL ID: 3544187

SUBMITTER (NAME ONLY): Lisa Vinikoor-Imler

TITLE: Profiles of women with choroideremia diagnosis codes

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Vinikoor-Imler, D. Yoon, S. Eaton, Biogen Inc, Cambridge, Massachusetts, UNITED STATES|D.C. Hayflinger, Hayflinger Analytic Services, LLC, Wilmington, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Choroideremia (CHM) is an X-linked recessive inherited retinal dystrophy (IRD) resulting in progressive vision loss, ultimately leading to blindness. Women are typically carriers, although a few studies have shown some women to be symptomatic. Our objective was to perform an epidemiologic study using electronic medical records to better understand women with diagnosis codes for CHM.

Methods: Optum[®] de-identified Electronic Health Record dataset (2007-2019) was used. Women with at least one recorded ICD-9 or -10 diagnosis code for CHM (ICD-9: 363.55; ICD-10: H31.21) were included. The women's records were examined for age at first diagnosis within the database, other IRDs, provider type, and notes/measures of vision.

Results: Fifty-seven women had CHM ICD codes recorded while enrolled in the database. The median time in the database was 8 years, and during that time 35% of the women had more than one physician visit with a CHM code. The age at first CHM code in the database ranged in age from 6-87 years, with a median of 54 years. At the first diagnosis in the database, 63% of women were seen by an ophthalmologist and 12% were seen by an optometrist. Other provider specialties included Family Medicine (12%) and Obstetrics/Gynecology (9%). Sixteen percent of women also had an ICD code or physician note for retinitis pigmentosa. Thirty-nine percent of women had an ICD code or physician note mentioning a family history of eye genetic disease and/or blindness. Using physician notes, ICD codes, and/or reported visual acuity measurements, 13 (23%) women were categorized as having poor/low vision, severe visual impairment, and/or blindness. Among women aged 60 and older, 40% had poor/low vision, severe impairment, or blindness. Many of these women had other eye conditions (e.g., glaucoma, cataracts); therefore, it is not possible to know whether the vision loss is attributable to the other issues or CHM. Often visual acuity measurements were lacking and physician notes were not descriptive enough to understand specific vision levels among the women.

Conclusions: A proportion of women with CHM have visual impairments. Further research on women with CHM is warranted to determine the level of visual impairment experienced by these women and if it is attributable to CHM or other eye conditions.

CONTROL ID: 3544189

SUBMITTER (NAME ONLY): Sabiha Hacibekiroglu

TITLE: Safe and immune-tolerant 'designer' RPE cells towards the treatment of age-related macular degeneration

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Frequent anti-VEGF injections and use of immunosuppressive drugs during RPE cell therapy can cause severe side effects. Also, the fear of tumorigenicity of grafted cells remains an issue. We test the hypothesis that cells, grafted into a diseased eye, expressing our local acting anti-VEGF biologics, 'VEGF Sticky-trap', with FailSafeTM and immune cloaking technologies, is safe and controllable as a long-term treatment option for AMD. This approach combines the cells' positive therapeutic effect with that of local acting biologics, avoiding potentially harmful side effects.

Methods: In a mouse model of AMD, we have grafted engineered human RPE to replace the lost cells in the recipient's eye that a) produce a drug-inducible, local acting anti-VEGF biologic (VEGF Sticky-trap, PMID: 24705878) and b) control cell growth by introducing a suicide switch to the cell's genome (FailSafeTM, PMID: 30429614). The RPE cells generated in vitro from hES cells were further modified to make them "invisible" (iACT StealthTM, PMID: 31417198) to the immune system (cloaked cells), or not (uncloaked cells). To assess the efficacy, safety and toxicology of all genetic modifications, cells (cloaked and uncloaked) were injected in the subretinal space (40,000 cells per eye) and subcutaneously (either 1 million cells per flank or 100,000 cells intradermal in ear pinnae) in albino BL6 mice. Immune-compromised NSG mice served as a control and cell survival and efficacy was followed through life eye imaging or BLI imaging.

Results: We have demonstrated the function of all three genome altering systems (FailSafeTM, iACT StealthTM and VEGF Sticky-trap) separately, in pilot studies and are moving forward to a pre-clinical phase with small (mouse) and large animal models (rabbit, pig) to test in cell therapy settings. Thus far we have demonstrated, in vitro and in vivo (in mice), that cells survive up to 10 months in subretinal spaces and that each genetic modification continues to function in tandem.

Conclusions: Immuno-cloaking is essential to avoid graft rejection and/or immunosuppressive drugs, while tight regulation of cell proliferation (FailSafeTM system) and drug-induced VEGF Sticky-trap expression was demonstrated. No adverse events were reported in mice receiving genetically modified cells. We expect our genome edited therapeutic cells to advance the development of novel and improved therapies for AMD and beyond.

CONTROL ID: 3544192

SUBMITTER (NAME ONLY): Philipp Mueller

TITLE: Prevalence and Associations of Dome-Shape Macular Configuration – A Macular Curvature Study on UK Biobank data

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the prevalence and potential associations of dome-shape macular configuration in general population.

Methods: A total of 65440 subjects with a mean age (\pm standard deviation, SD) of 57.3 ± 8.11 years with spectral-domain optical coherence tomography (OCT) data from a unique contemporary resource for the study of health and disease that recruited more than half a million people in the UK (UK Biobank) was analyzed in this study. A deep learning model was used to segment the RPE, and the macular curvature of the OCT scan was calculated by polynomial fit. The curvature was evaluated and associations with refractive error (spherical equivalent), corneal curvature, visual acuity, intraocular pressure, age, sex, ethnicity, fluid intelligence, birth weight, maternal smoking were examined.

Results: The overall macular curvature values followed a gaussian distribution with a mean (\pm SD) of 0.0021 ± 0.0014 . There was a high inter-eye agreement. While all factors but 'sex' were significantly associated with the curvature in a multilinear analysis (adjusted R^2 , 0.122), the highest correlation could be found for the factors refractive error and ethnicity. The prevalence of a macular dome-shape configuration was overall 4.78%, most common in Chinese subjects as well as hypermetropic eyes. An increasing frequency was found towards extreme refractive error (hypermetropia and myopia). Extreme dome-shape configuration (defined by the fourth quartile of concave curvature values), however, was more frequently found in myopic eyes; in particular in eyes with high (spherical equivalent, <-6 diopters) and extreme (spherical equivalent, <-9 diopters) myopia with a frequency of 3.76% and 6.49%, respectively. The odds ratio for this particular macular configuration in individuals of Chinese ethnicity for high and extreme myopia was 4.83 and 7.91, respectively.

Conclusions: Dome-shape macular configuration can be found in general population, more commonly in eyes with high refractive error. Further investigation of determinants of this macular configuration might provide new insights into normal eye development and maldevelopment like staphyloma.

CONTROL ID: 3544193

SUBMITTER (NAME ONLY): Heather Pauls

TITLE: Prevalence of Visual Disability Among Hispanic/Latinos without Access to Healthcare and Those with Health Insurance: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Context: The Affordable Care Act excludes undocumented immigrants from coverage, which may decrease healthcare access among Hispanic/Latinos. Objective: To characterize the prevalence of visual disability among Hispanic/Latinos without access to healthcare and those with health insurance.

Methods: Methods: Design, Setting, and Participants: Multicenter, prospective, population-based Hispanic Community Health Study/Study of Latinos (HCHS/SOL) including 9,663 participants aged ≥ 40 y completing Visit #2 (2014-2017). Participants include those with Cuban, Dominican, Mexican, Puerto Rican, Central American, South American and Other backgrounds from 4 US cities. The age-adjusted, sex-specific prevalence of visual disability was calculated weighting for study design and non-response. For healthcare access, participants were asked "In the past 12 months, was there a time when you needed healthcare but could not get it?" Health insurance represented a presence or absence of coverage. Data was collected at Visit #2. Main Outcome Measure: Prevalence and 95% confidence interval (95%CI) of self-reported visual disability defined using the US Census Bureau definition, "being blind or having serious difficulty seeing even when wearing glasses."

Results: 9324 participants were analyzed; mean age was 55.4y in men and 56.5y in women. The overall prevalence of visual disability was [estimate and 95%CI; 10.6(9.2-12.1)] in men and 13.5(12.0-14.9) in women. Among participants with health insurance, the age-adjusted prevalence was similar at 10.8(9.1-12.5) in men and 14.5(12.8-16.2) in women. Among participants without access to healthcare, the age-adjusted prevalence was elevated at 15.9(7.1-24.8) in men and 17.6(11.8-23.5) in women.

Conclusions: Sex-specific results demonstrate an elevated prevalence of visual disability among diverse Hispanic/Latinos without access to healthcare. Results are important, as they suggest prevalence rates of chronic eye disease estimated from clinical registries may underestimate disease as they fail to include those without access. Results also support SOL Ojos objectives, an ancillary HCHS/SOL study designed to estimate the prevalence of chronic eye disease across Hispanic/Latino backgrounds, and to assess the impact of lifestyle factors, including healthcare access, with disease outcome.

CONTROL ID: 3544196

SUBMITTER (NAME ONLY): Yang Zhang

TITLE: Multi-scale imaging of mouse corneas using optical coherence tomography and single-molecule localization microscopy

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhang, Z. Cai, L. Beckmann, H. Zhang, Biomedical Engineering, Northwestern University Robert R McCormick School of Engineering and Applied Science, Evanston, Illinois, UNITED STATES|C. Sun, Mechanical Engineering, Northwestern University Robert R McCormick School of Engineering and Applied Science, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Abnormality of the cornea can lead to blindness and vision loss. The corneal endothelial cells (CECs) play a significant role in maintaining corneal function. We developed a multi-scale imaging workflow to visualize the mouse cornea at the microscale and the underlining subcellular variations of CECs in corneal flatmount at the nanoscale. We used a visible-light optical coherence tomography (vis-OCT) to image a mouse model of intraocular hypertension in vivo and revealed the nanoscopic cytoskeleton changes in the CECs using single-molecule localization microscopy (SMLM).

Methods: The left eyes of wild-type mice were maintained at 40 mmHg intraocular pressure (IOP) for 1 hour using anterior chamber puncture. The right eyes were used as controls without any procedures. The vis-OCT images of cornea were acquired using a home-built vis-OCT system. The mice were sacrificed and the cornea was isolated, fixed, and immunostained to visualize the ZO-1 tight junction structure variations using indirect immunofluorescence labeling. The cornea sample was flat-mounted for SMLM imaging in a commercially available STORM imaging buffer in a home-built SMLM system.

Results: The vis-OCT images of corneal tissues revealed the typical edema after maintaining 40 mmHg IOP in the epithelium and stroma layers of the cornea. The SMLM images showed characteristic hexagonal CECs and revealed significant changes in tight junction proteins' filament density and thickness after exposure to high IOP. Such disruptions of cell tight junctions are likely related to the blurred vision in diseases associated with elevated IOP. Further, it reveals the native cell responses in tissue that would be challenging for imaging cell cultures.

Conclusions: We developed a multi-scale imaging workflow to correlate microscopic variations in corneal tissue and nanoscopic variations in CECs of corneal flatmount in response to high IOP in mouse models. These results demonstrate the utility of multi-scale imaging for studying tissue- and molecular level variations for corneal diseases and glaucoma.

CONTROL ID: 3544198

SUBMITTER (NAME ONLY): Ayeswarya Ravikumar

TITLE: Image segmentation to grade Lid Wiper Epitheliopathy

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ravikumar, H.M. Queener, E.R. Ritchey, Optometry, University of Houston, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ayeswarya Ravikumar: Commercial Relationship: Code N (No Commercial Relationship) | Hope Queener: Commercial Relationship: Code N (No Commercial Relationship) | Eric Ritchey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The lid wiper region is responsible for tear distribution along the ocular surface during the blink. Disruption to the tear film increases the coefficient of friction under boundary lubrication conditions at blink initiation. This irritates the epithelium, resulting in staining termed lid wiper epitheliopathy (LWE). LWE is a critical clinical marker to identify and track abnormal lid/cornea interaction. We propose a semi-automated LWE grading algorithm using hue and value channels of staining images

Methods: 37 images representative of LWE staining, observed after instillation of 2% sodium fluorescein and 1% lissamine green, were analyzed. Using a custom MATLAB program, a region of interest around the lid-wiper region was manually defined. Using the hue and value channels of the image, the algorithm identified stained pixels within this region and fit a curve to these pixels. The number of stained pixels along bisector lines perpendicular to the curve were sampled at regular intervals, defining the height of staining at each bisector. LWE height (mm) was calculated as the average extent of LWE staining along all perpendicular bisectors after subtracting average Marx line height calculated from 11 images without LWE staining. LWE width in mm was determined from the length of the curve scaled by the fraction of the curve that included staining beyond the Marx line.

Results: 31 images (15 upper and 16 lower eyelids: 84%) were successfully analyzed by the algorithm, with 6 images where LWE staining was not successfully detected. Average Marx line height for eyelids without LWE was 0.06 ± 0.02 mm. The mean LWE staining height was 0.12 ± 0.11 mm and 0.12 ± 0.07 mm for the upper and lower eye lid respectively. The mean LWE staining width was 10.70 ± 3.84 mm and 10.40 ± 3.84 mm for the upper and lower eye lid respectively. No significant difference between upper and lower lids were observed LWE height or width (t-test, $p > 0.05$).

Conclusions: This novel automated hue and value algorithm eliminates the potential human error in subjective grading. Automated LWE grading may allow practitioners to observe subtle changes in LWE staining between different CL materials or clinical conditions over time.

CONTROL ID: 3544200

SUBMITTER (NAME ONLY): Sophia El Hamichi

TITLE: Large Optic Disc Colobomas: Interest of OCT and OCT-Angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. El Hamichi, T. Murray, Murray Ocular Oncology and Retina, Miami, Florida, UNITED STATES|S. El Hamichi, Pediatric Retina, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|D. Acon, Pediatric Retina, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A.M. Berrocal, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optic disc coloboma is a rare congenital anomaly of the optic nerve. Only a few studies describing the OCT and the OCT-Angiography aspects of congenital optic disc anomalies have been published. The OCT-Angiography studies only described the small optic disc colobomas. This study mainly focuses on assessing the utility of OCT and OCT-Angiography in the particular setting of large optic disc coloboma.

Methods: A retrospective study of patients who were referred to the department of pediatric retina at Bascom Palmer Eye Institute, Miami, Florida between January 2019 and January 2020.

Six eyes of 3 patients were identified. All patients were seen in the clinic and brought to the operating room for exam under anesthesia to perform a full ophthalmological exam, fundus photographs, fluorescein angiography, OCT and OCT-A using the Heidelberg Spectralis Flex Module. Then, necessary treatment was implemented as needed. The OCT and OCT-A were performed by trained experienced photographers.

Results: We provide multimodal imaging results of large optic disc coloboma in 3 children. The first case was associated with cat eye syndrome, the second case was associated with CHARGE syndrome (coloboma, heart defects, atresia choanae, growth retardation, genital abnormalities, and ear abnormalities), and the third case was associated with branchio-oculo-facial syndrome. In all these cases, we were able to capture fundus photographs, fluorescein angiography and OCT images. This allowed a proper evaluation of the coloboma, its associated complications and therefore, it helped establish appropriate management. However, the OCT-Angiography could not capture clear images of large nerve coloboma due to its depth.

Conclusions: Large optic disc colobomas are more challenging than small optic disc colobomas. They are often associated with complications and require long term treatment management and follow up. While OCT has proven its utility in monitoring choroidal neovascularisation and retinoschisis that could be associated with optic disc coloboma, OCT-Angiography in its current form is unable to capture large optic disc coloboma and therefore is of limited interest.

CONTROL ID: 3544201

SUBMITTER (NAME ONLY): Ashley Kramer

TITLE: A comparative analysis of gene and protein expression during retinal regeneration in adult zebrafish using 3'mRNA sequencing and quantitative immunohistochemistry

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kramer, R. Thummel, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|K. Gurdziel, Genome Sciences Core, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Following ablation of photoreceptors by intense light lesion, the zebrafish is capable of complete regeneration due to the ability of their Müller glia (MG) to re-enter the cell cycle, creating progenitors which differentiate into new photoreceptors. The purpose of this study was to determine if 3'mRNA sequencing, paired with a detailed morphological and immunohistochemical (IHC) analysis, is an effective and unbiased method to investigate the regenerating zebrafish retina.

Methods: Adult albino zebrafish were subjected to three days of intense phototoxic lesion to destroy photoreceptors. Tissue was collected at 8 timepoints during the regeneration process. Right eyes were designated for IHC with subsequent mean fluorescence intensity analysis using ImageJ. Left eyes were designated for RNA isolation, cDNA library preparation, 3'mRNA sequencing, and bioinformatics. Differential gene expression analysis was performed at each time point and PCA and a time series analysis was performed across the entire dataset.

Results: Early in the damage response, photoreceptors were destroyed as evidenced by morphological and gene expression losses of the opsins. A dynamic response by immune cells cleared the photoreceptor debris as GFAP-positive and reactive MG re-entered the cell cycle to produce pools of progenitors. Finally, our data highlight a distinct window of time between 5 and 10 days post lesion as a transition from progenitor proliferation/migration to differentiation into new photoreceptors. PCA analysis of the top 200 significantly differentially regulated genes demonstrated distinct clustering of each of the time points over two experimental replicates, confirming the method's precision. And transcript analysis largely mimicked morphological and protein changes at each time point, suggesting that this database can be utilized to search for novel genetic players in the regenerative process.

Conclusions: 3'mRNA sequencing presents an economical alternative to traditional RNA sequencing for investigations of regenerative biology in the zebrafish retina, with minor limitations. These transcriptomic data, paired with detailed IHC quantitative and morphological analysis, present a powerful method to observe the stem cell processes in a model capable of a robust regeneration response.

CONTROL ID: 3544209

SUBMITTER (NAME ONLY): Mitchell Wolin

TITLE:

A Novel Approach to Handling Eyelid Biopsies of Low Malignancy Suspicion

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Wolin, Surgery, Prisma Health, Greenville, South Carolina, UNITED STATES|E. Zhou, G.B. Caudill, University of South Carolina School of Medicine Greenville Campus, Greenville, South Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose:

It is the standard of care to submit for pathological evaluation any eyelid lesions that are considered suspicious or likely to show malignancy. There is less clarity on how to handle lesions felt to be of low malignancy risk. Many ophthalmologists feel comfortable discarding certain lesions without pathologic evaluation based on a convincingly non-malignant appearance. However, there are always some lesions that are not clearly malignant or benign, and therefore are typically submitted.

In general, the estimated malignancy rate of eyelid lesions is 10-20 percent.^{1,2} However, in biopsied eyelid lesions thought to be benign by the clinician, the rate of malignancy drops to between 2-4.6 percent.¹ As a result, a large number of pathologic evaluations are performed with the result being a benign diagnosis in up to 80-90 percent of all lesions and up to 97 percent of lesions thought to be benign clinically.^{1,2}

A significant downside of pathologic evaluation is cost, with uninsured patients at our institution paying 75 dollars out of pocket. Therefore, a way to substantially reduce or eliminate this expense without compromising risk to the patient would be desirable.

Methods:

We propose therefore a new paradigm of the management of eyelid biopsy specimens (Figure 1).

Results:

This protocol allows subsequent submission of pathology specimens if regrowth appears to be occurring, while substantially reducing unnecessary pathology submissions and cost to patients.

One possible downside to our approach is that malignancies such as sebaceous carcinoma (SC) traditionally require a fixation method other than formalin for histological analysis.⁴ However, IHC staining has emerged as a helpful tool in differentiating SC from other common eyelid malignancies like BC and remains an option for even formalin fixed samples.⁵ In addition, basal cell carcinoma (BC)—by far the most common eyelid malignancy—has low propensity to spread metastatically, reducing the risk of any delayed diagnosis that may result from the use of this paradigm.³

Conclusions:

In order to assess the safety and efficacy of this new treatment paradigm, we hope to perform a controlled study comparing it to the current standard of practice. Given the common nature of eyelid lesions, the cost savings could potentially be in the millions of dollars for the medical system.

CONTROL ID: 3544210

SUBMITTER (NAME ONLY): Kimberly Wong

TITLE: Retinal ganglion cell survival and axon regeneration after optic nerve injury: crosstalk among early injury signals

SESSION TITLE: Glial Cells

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.A. Wong, T. Marthaswaran, J. Msaddi, V. Patel, S. Peterson, L. Benowitz, Neurosurgery, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|K.A. Wong, S. Peterson, L. Benowitz, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|Y. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Our limited understanding of the signals that regulate retinal ganglion cell (RGC) death and axon regeneration after optic nerve injury has prevented development of curative therapies. Recently, three phenomena have been identified that contribute strongly to RGC death after injury: elevation of mobile zinc (Zn^{2+}) in the inner retina, activation of microglia and neurotoxic astrocytes, and activation of transcriptional networks via MAP3K kinase cascades (DLK/LZK). Inhibition of individual events is partially neuroprotective, but effects are incomplete, transient, or counteract axonal regenerative capacity, respectively. The objective of our studies was to investigate possible crosstalk among these signals and determine whether synergistic inhibition may enhance neuroprotection and axon regeneration.

Methods: In the mouse optic nerve injury (ONI) injury model, Zn^{2+} -selenite autometallography was used to visualize Zn^{2+} in retinal sections. Microglial activation was assayed morphologically and transcriptionally after ONI. DLK/LZK signaling was assessed via downstream transcription factors (TFs), c-JUN, ATF2, MEF2A, and SOX11. Loss-of-function for each signal was utilized to assess crosstalk: reduction of retinal Zn^{2+} by intraocular chelator (ZX1) injections or genetic deletion of Zinc Transporter 3 (ZnT3: Slc30a3); systemic microglia ablation (CSF-1R inhibitor, PLX5662); and conditional deletion of DLK/LZK in RGCs ($\text{DLK}^{\text{fl/fl}}$; $\text{LZK}^{\text{fl/fl}}$).

Results: Within 1 dpi, we observed simultaneous elevation of mobile zinc (Zn^{2+}), activation of DLK/LZK-dependent TFs, and increased microglial proliferation and activation in the retina. DLK/LZK activation and microglia activation persisted, peaking at 5 dpi concomitant with the onset of RGC death. ZX1 treatment or ZnT3 knockout partially repressed the activation of both DLK and microglia. PLX5622 treatment reduced microglial density in the retina by 96% and reduced expression of inflammatory markers, but did not repress Zn^{2+} elevation or DLK signaling. DLK/LZK deletion blocked injury-induced transcriptional activity to prevent RGC death and partially inhibited microglia activation.

Conclusions: Our data suggest that Zn^{2+} elevation contributes to the activation of microglia and DLK/LZK signaling after ONI. Thus, crosstalk exists between the early injury signaling pathways to regulate RGC cell death after axon injury.

CONTROL ID: 3544211

SUBMITTER (NAME ONLY): Christopher Starr

TITLE: Dry Eye Disease Flares: A Ten-Year Literature Review

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Starr, Weill Cornell Medicine, New York, New York, UNITED STATES|D.V. Owen, K. Brazzell, S. Zhang, Kala Pharmaceuticals, Massachusetts, UNITED STATES|S.C. Pflugfelder, Baylor College of Medicine, Houston, Texas, UNITED STATES|R. Dana, Harvard Medical School, Boston, Massachusetts, UNITED STATES|E. Holland, Cincinnati Eye Institute, Cincinnati, Ohio, UNITED STATES|S. Lucas, Envision Pharma Group Limited, Horsham, West Sussex, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To evaluate the existing literature on dry eye disease (DED) and to report the features of DED flares including triggers, characteristics (signs and symptoms), and biomarkers.

Methods: A 10-year literature review was conducted of 2093 publications identified from MEDLINE, Embase, and PubMed databases using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol (PRISMA-P) guidelines. The literature review was performed on English language publications only of clinical trials or observational studies in adults with DED from 2009-2019 using an array of keywords associated with dry eye flares. The searches were designed to identify any observational studies or clinical trials published in the 10-year period that reported dry eye flares or short-term exacerbations of the signs and symptoms of DED.

Results: Screening using PICOS criteria identified 22 studies that met the inclusion criteria. To meet the study objectives, evidence was drawn from studies reporting exacerbations of signs and symptoms following exposure to environmental triggers encountered during daily life, following cataract and refractive surgery, and following exposure to controlled adverse environments. These studies suggest that exacerbations, or flares, of the signs and/or symptoms of DED occur in response to environmental triggers and/or ocular surgeries. Studies evaluating tear biomarkers following controlled adverse environment exposure found significant increase in inflammatory biomarkers matrix metalloproteinase 9 (MMP-9) and interleukin 6 (IL-6), and significant decrease in homeostatic biomarker epidermal growth factor (EGF). Other chronic inflammatory conditions such as chronic asthma, Sjogren syndrome, and rheumatoid arthritis have similar immune-mediated pathways as DED and feature subgroups of patients who experience episodes of flare and remission similar to those in DED.

Conclusions: DED flares are exacerbations of a patient's signs and/or symptoms and can be caused by a variety of triggers. Episodic exacerbation is a common feature of chronic inflammatory diseases.

CONTROL ID: 3544212

SUBMITTER (NAME ONLY): Jessica Bills

TITLE: Characterization of retinal cell types in the African spiny mouse (*Acomys cahirinus*)

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Bills, A.C. Morris, Biology, University of Kentucky, Lexington, Kentucky, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jessica Bills: Commercial Relationship: Code N (No Commercial Relationship) | Ann Morris: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal structure and cell type composition are generally well conserved across all vertebrate species. Differences in the precise complement of retinal cell types among closely related species can reflect functional adaptations to daily activity and/or life history. Among the order Rodentia, retinal anatomy and physiology are predominantly studied in mice and rats, but there is renewed interest in incorporating additional rodent models that exhibit interesting behaviors and visual adaptations. The African spiny mouse has been studied for its unique behavioral qualities, precocial development, and recently, for its regenerative abilities. However, the spiny mouse retinal anatomy has not been rigorously studied. Here, we present a comparative analysis of retinal cell type morphology and number in *Acomys cahirinus* and *Mus musculus* adult retinas.

Methods: All animal procedures were performed in accordance with guidelines established by IACUC and the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Retinal tissue sections were obtained from adult eyes and subjected to histological staining or immunohistochemistry with antibodies for various retinal cell types. Sections were imaged by light, fluorescence, and confocal microscopy. Cell number and morphology were assessed. Comparison of cell number between species was assessed using a Student's t test. Data are presented as mean \pm SD.

Results: Overall, the general features of retinal anatomy between *Acomys* and *Mus* are similar. With roughly triple the eye size, the retinal layers of the *Acomys* are of similar thickness and, for the majority of retinal cell types, the morphology appears comparable in the two species. However, *Acomys* bipolar cells show an increased number and altered laminar positioning compared to *Mus*. Intriguingly, we also observe a differential patterning and distribution of *Acomys* photoreceptors, particularly the cones.

Conclusions: Taken together, the differences in photoreceptors and bipolar cells could suggest differences in visual acuity between the two species, possibly due to visual adaptations for foraging food in their unique desert environment. These results set the stage to investigate retinal cell type diversity and visual function in this interesting mammalian model.

CONTROL ID: 3544213

SUBMITTER (NAME ONLY): Anne Kunkler

TITLE: Trends in Moxifloxacin Nonsusceptibility Among Coagulase-Negative Staphylococcus Isolates Causing Endophthalmitis, 2005-2020

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Kunkler, J. Sengillo, N.A. Yannuzzi, D. Miller, H.W. Flynn, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coagulase-negative Staphylococcus (CoNS) is the most common cause of acute-onset post-cataract surgery endophthalmitis. Moxifloxacin, a fourth-generation fluoroquinolone, is frequently used prophylactically to prevent infection after cataract surgery, either topically or intracamerally. The purpose of this study is to report the trends in moxifloxacin resistance of CoNS isolates causing endophthalmitis over a 16-year period.

Methods: This study was a retrospective, consecutive case series of vitreous CoNS isolates causing endophthalmitis between January 1, 2005, and December 31, 2020, at Bascom Palmer Eye Institute, Miami, Florida. The study was deemed exempt from IRB approval as no identifying patient information was collected. Microbiology testing was used to determine the sensitivities for moxifloxacin derived by the E-test and VITEK testing of isolates. Statistical analysis was performed using two-tailed Fisher's exact test.

Results: The moxifloxacin sensitivities of 236 CoNS endophthalmitis isolates were reviewed. The nonsusceptibility rates of 68 CoNS isolates to moxifloxacin from 2005-2009 were 78.8% for methicillin-resistant Staphylococcus epidermidis (MRSE, 23/33), 41.4% for methicillin-sensitive Staphylococcus epidermidis (MSSE, 18/49), and 0% for other CoNS (0/6). The nonsusceptibility rates of 100 CoNS isolates to moxifloxacin from 2010-2015 were 84.6% for MRSE (44/52), 41.9% for MSSE (13/31), and 11.8% for other CoNS (2/17). The nonsusceptibility rates of 68 CoNS isolates to moxifloxacin from 2016-2020 were 50.0% for MRSE (10/20), 25.9% for MSSE (7/27), and 9.5% for other CoNS (2/21). The average nonsusceptibility of all CoNS isolates to moxifloxacin decreased from 59.0% (n=59/100) between 2010 and 2015 to 27.9% (n=19/68) between 2016 and 2020 (P <0.0001).

Conclusions: In the current study, the nonsusceptibility of CoNS to moxifloxacin has decreased over the last 5 years. Moxifloxacin resistance remains higher among MRSE isolates. Further investigation is needed to determine the clinical implications of these findings.

CONTROL ID: 3544215

SUBMITTER (NAME ONLY): Catarina Castro

TITLE: The impact of covid-19 on delivering intravitreal therapy to patients with diabetic macular edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Castro, J. Coelho, N. Correia, P. Menéres, B. Pessoa, Ophthalmology, Centro Hospitalar Universitário do Porto EPE, Porto, Porto, PORTUGAL|P. Menéres, B. Pessoa, Universidade do Porto Instituto de Ciencias Biomedicas Abel Salazar, Porto, Porto, PORTUGAL|

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ABSTRACT BODY:

Purpose: To evaluate the effectiveness of our treatment guideline for intravitreal injections (IV), which was implemented in diabetic macular edema (DME) patients.

Methods: Retrospective analysis of medical case reports in patients who had an IV appointment at Centro Hospitalar e Universitário do Porto. The first aspect of this analysis was the impact of COVID-19 on treatment appointments by comparing the lockdown period (22 March 2020 – 2 May2020) with the same period in 2019. The second aspect quantified the number of DME patients with delayed treatments based on a COVID-19 treatment guideline (see Figure 1). The impact of delayed appointments was assessed based on best-corrected visual acuity (BCVA) and central foveal thickness (CFT) prior to COVID-19 and then immediately after a missed appointment at the outset of COVID-19 and 6 months after the pandemic began.

Results: In 2019, 693 medical retina patients received an IV. During the same period in 2020, 272 maintained their IV appointment, 391 patients experienced a delay and 80 patients missed their IV. 132 DME patients (mean age 70.6 ± 9.7 years; 59.1% females) had a delayed IV and were subsequently evaluated following a missed appointment and then 6 months after lockdown began. Prior to COVID-19, mean BCVA was 61.9 ± 19.0 ETDRS letters and CFT was 361 ± 140 μm . Then, immediately after the COVID-19 lockdown and the missed appointment, BCVA and CFT were 59.4 ± 21.1 ETDRS letters and 355 ± 132 μm , respectively. These then improved to 67.7 ± 15.6 ETDRS letters and 314 ± 84 μm , respectively, 6 months after the onset of COVID-19. In the appointment after the delayed IV, a clinical decision was taken to increase the time between IV in 50.8% of patients; to shorten it in 4.5%; in 39.0% it could be kept the same; and, in 5.7%, therapy was switched.

Conclusions: These data show that during the enforced COVID-19 lockdown, about half of all our IV appointments were delayed. This had an immediate impact on DME patient's vision as demonstrated by the small reduction in BCVA, which was reversed after re-implementation of DME treatment according to the standard of care, with BCVA and CFT improvement. This highlights the importance of treatment guidelines but also the value of longer duration treatments that can be used to minimize the potential negative impact of interruptions to DME therapy.

CONTROL ID: 3544216

SUBMITTER (NAME ONLY): Shanawar Waris

TITLE: Readability Analysis of the American Society of Ophthalmic Plastic & Reconstructive Surgery Patient Brochures

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Pakhchanian, C. Geist, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|S. Waris, R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The American Medical Association and the National Institutes of Health recommend that health materials should not exceed the 6th grade reading level. However, a general review of patient educational material (PEM) in ophthalmology has found that PEM is consistently written at a level that exceeds this recommendation. Our goal was to evaluate the readability of patient educational brochures from the American Society of Ophthalmic Plastic & Reconstructive Surgery (ASOPRS).

Methods: Patient educational brochures from the ASOPRS website were transcribed onto a Microsoft Word document. During the reformatting process, all titles, figures, disclaimers, acknowledgments, citations, references, and hyperlinks were removed. The reformatted patient education resources were then analyzed for readability with Readability Studio Professional Edition 2019.3 (Oleander Software Ltd). The body of text from all 18 ASOPRS patient brochures were analyzed by ten validated tests for readability assessment: Flesch Reading Ease Test (FRE), Flesch-Kincaid Grade Level (FKGL), Simple Measure of Gobbledygook (SMOG), Coleman-Liau Index (CLI), Gunning Fog Index (GFI), New Dale-Chall Readability (NDC), FORCAST, Fry Graph Readability (FG), Raygor Readability Estimate (RRE), and New Fog Count (NFC).

Results: The mean (\pm SD) readability scores from the 18 ASOPRS patient brochures were 48 (4.3), 11.2 (0.8), 13 (0.7), 11.7 (0.8), 13.6 (0.9), 11.6 (1.3), 11.1 (0.5), 12 (1.4), 12 (1.0), and 10.6 (1.3) for FRE, FKGL, SMOG, CLI, GFI, NDC, FORCAST, FG, RRE, and NFC, respectively. All ten of the mean readability scores were well above the sixth-grade reading level as recommended by the National Institute of Health and the American Medical Association for patient educational materials (Figure 1).

Conclusions: These findings show that the average patient would have difficulty understanding the medical information provided by ASOPRS patient brochures, thereby hindering their ability to make informed decisions on their healthcare. More attention is needed in creating patient educational brochures that is more comprehensible by the general public.

CONTROL ID: 3544220

SUBMITTER (NAME ONLY): Peyton Grisso

TITLE: Correlations Between AMD Severity and OCT Thickness

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate how optical coherence tomography (OCT) measured macular thickness of the retina and retinal pigment epithelial drusen complex (RPEDC) varies with intermediate age-related macular degeneration (iAMD) severity and the presence of subretinal drusenoid deposits (SDD).

Methods: In this longitudinal prospective study (NCT01352975), we followed 158 eyes from 89 participants (mean age = 71.5 yr, stdev 8.77 yr), with a range of AMD severities, excluding advanced disease, for 5 years with multimodal imaging and grading performed by the Wisconsin reading center. We investigated correlations between the thickness of the RPEDC (RPE to Bruch's membrane) and neurosensory retina (NSR = total retina – RPEDC) and AREDS severity grade and SDD presence in cross-section. We also investigated the correlation of longitudinal changes in macular thickness with AMD severity progression and SDD presence.

Results: At baseline, 14 eyes with AREDS severity scale grades 5-8 were evaluated to have SDD, 34 eyes were in step 0 (control), and 112 eyes were in steps 1-8.

In the cross-sectional data, NSR measures in the 1mm and 3mm rings revealed that eyes with SDD were significantly thinner than eyes in step 0. Comparisons of RPEDC in the 1mm and 3mm rings revealed that eyes in later AMD steps (5-6 and 7-8) were significantly thicker than eyes in step 0. SDD eyes had thicker RPEDC measures in the 3mm ring. Over 5 years, a subset of eyes in each AMD severity step progressed at least one step scale score. Longitudinal analysis in the 1mm and 3mm rings demonstrated that eyes in later AMD steps 7-8 that progressed and eyes with SDD underwent NSR thinning.

Eyes in steps 1-2 and 3-4 that progressed showed significant RPEDC thickening in the central 1mm ring, whereas eyes in steps 7-8 that progressed showed significant RPEDC thinning. In the 3mm ring, eyes in steps 3-4 showed significant RPEDC thickening, whereas eyes in steps 7-8 that progressed showed significant thinning.

Conclusions: Macular thickness in iAMD varies with disease severity, disease severity progression, and the presence of SDD. NSR measures were thinner in eyes with SDD. Eyes in steps 7-8 that progressed in AMD severity demonstrated NSR thinning. Eyes in earlier steps (3-4) that progressed in AMD severity showed RPEDC thickening, while progression in steps 7-8 was associated with RPEDC thinning. Future work will include multivariate analyses to associate AMD progression with OCT measured changes.

CONTROL ID: 3544221

SUBMITTER (NAME ONLY): Jennifer Grossman

TITLE: Identifying patterns of glaucomatous progression in the circumpapillary retinal nerve fiber layer using OCT circle scans

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.L. Grossman, E. Tsamis, S. La Bruna, D.C. Hood, Psychology, Columbia University, New York, New York, UNITED STATES|J.M. Liebmann, C. De Moraes, D.C. Hood, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify and understand patterns of progressive, glaucomatous damage around the circumpapillary retinal nerve fiber layer (cpRNFL) using optical coherence tomography (OCT) circle scans and custom cpRNFL thickness difference plots.

Methods: 116 eyes [86 early glaucoma, 30 healthy controls (HC)] from 116 patients were identified from a prospective, longitudinal study and comprised the study group (SG). Eyes had baseline OCT disc circular and macular cube scans and a follow-up scan at least 1 year from the baseline date. RNFL thickness difference plots (Fig. 1C) were generated using a custom program to show the change in cpRNFL thickness between the first baseline (Fig. 1A) and most recent (Fig. 1B) circle scans. Fig. 1C shows an example with 95% confidence interval (dotted curves) based upon short-term variability in 176 eyes using all tests within 4 months of baseline. For the 116 eyes in the SG, an OCT expert identified 15 definite progressing eyes (P) and 68 definite non-progressors (NP), after evaluation of the OCT information. Patterns of progressive RNFL changes in the P eyes were defined based upon the difference plots. A mixed-effect linear model was used to assess sector differences among the HC, P and NP groups.

Results: Progression was present in the inferior disc in 14 of the 15 P eyes, and always included the TI region. However, 11 of the 15 P eyes showed significant progression in both the inferior and superior disc on the difference plots, while progression was restricted to one hemidisc in the other 4. 3 of these 4 showed static glaucomatous damage in the non-progressing hemidisc. Only 1 eye had both damage and progression confined to a single hemidisc. None of the eyes had significant diffuse damage, defined as significant progression in all regions of the disc on the difference plots. However, for all regions of the disc, except the nasal region, the P group, but not the NP group, showed statistically significant progression as compared to the HC group (Fig. 2).

Conclusions: In early glaucoma, most of the RNFL loss due to progression tended to be relatively local. While in general inferior and superior regions of the disc were involved, in 14 of the 15 P eyes progression included the TI region of the disc, a region susceptible to early glaucomatous damage [1,2]. 1. Hood et al., PRER, 2013. 2. Hood PRER 2017.

CONTROL ID: 3544225

SUBMITTER (NAME ONLY): Julia Arciero

TITLE: Metabolic status of the retina predicted using a hybrid mathematical model

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study introduces a hybrid mathematical model of the human retina that combines a heterogeneous vascular network description of the arterioles with a compartmental representation of the capillaries and venules to predict retinal blood flow and tissue oxygenation.

Methods: A previous heterogeneous model of the retinal arterioles is adapted here into a hybrid model of the retinal vasculature in which every terminal arteriole is connected in series to compartments representing capillaries, small venules, and large venules (Figure 1A). An overall pressure drop of 16 mmHg is assumed across the arterioles, yielding a total flow of 36,670 nL/min to the retinal microcirculation. A Green's function method is used to model oxygen transport in the arterioles, and a Krogh cylinder model is used in the capillaries and venules (oxygen demand is $1 \text{ cm}^3 \text{ O}_2 / 100 \text{ cm}^3 / \text{min}$). A metabolic wall signal is calculated from blood and tissue PO_2 and is conducted upstream to communicate the metabolic status of the retina to the arterioles.

Results: The wall signal conducted upstream from the capillaries and venules is shown in Figure 1B. The signal generated by the hybrid model is compared with the signal generated by an entirely compartmental model to demonstrate the role of spatial heterogeneity in the system. A more than two-fold range of wall signal values is communicated upstream and depends on vascular path lengths (Figure 1B) and PO_2 (Figure 1C). A 25% reduction in blood PO_2 leads to a doubling of the signal in many pathways.

Conclusions: A hybrid vascular model is introduced that accounts for spatial heterogeneity and oxygen transport in the retina. The model predicts that a higher metabolic wall signal is generated in pathways with a lower PO_2 at the terminal arteriole. This model provides the geometric and hemodynamic framework necessary to predict blood flow regulation in the human retina and will ultimately be used for early detection and treatment of ischemic and metabolic disorders of the eye.

CONTROL ID: 3544229

SUBMITTER (NAME ONLY): Andrea Waksmunski

TITLE: All Eyes on Us: Community-based perspectives on eye health and vision care in Cleveland, Ohio

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.R. Waksmunski, S. Kennedy, S. Koopman-Gonzalez, B. Croniger, R. Laux, L. Cummings, L. Castaneda, L. Richards, G. Blackshire, B. McIntosh, E. Trapl, J. Cooke Bailey, Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|A.R. Waksmunski, J. Cooke Bailey, Cleveland Institute for Computational Biology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|S. Koopman-Gonzalez, B. McIntosh, E. Trapl, Prevention Research Center for Healthy Neighborhoods, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|E. Pike, University Settlement, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection of primary open-angle glaucoma (POAG), a leading cause of blindness, is essential for mitigating severe visual impairment. The World Health Organization has highlighted the importance of engaging with communities about vision care and early disease intervention. We established the All Eyes on Us (AEOU) study in collaboration with University Settlement in the Broadway-Slavic Village neighborhood of Cleveland, Ohio to assess community-based perceptions of vision care and barriers to seeking vision care.

Methods: In collaboration with University Settlement, a community resource center for over 90 years in the Broadway-Slavic Village community of Cleveland, Ohio, we established a Community Advisory Board (CAB) comprised of community members interested in learning more about vision care and health. The CAB helped design our interview guide, which we administered to Broadway-Slavic Village community members over age 40 as semi-structured interviews designed to illuminate perceptions of and obstacles to vision care. Interviews with 60 individuals (30 self-reported African American and 30 self-reported White) were 30-45 minutes in length and audio-recorded. Of these, we transcribed and coded 59 interviews for thematic elements using the NVivo 12 Plus qualitative software package. One interview was coded manually.

Results: While study interviews demonstrated a wide array of perspectives of vision care, there were several common themes. Some reasons people reported for not going to the eye doctor included cost, insurance issues, lack of transportation, and not knowing where to seek eye care. Several individuals mentioned that they did not have general knowledge about eye health and were unaware of the importance of seeking vision care. Interestingly, when asked about their frequency of eye doctor visits compared to what they would suggest for others, study participants commonly said that people should seek vision care annually but said that they personally go less frequently.

Conclusions: We obtained perspectives of 60 Cleveland, Ohio community members; interview topics ranged from how they value vision care for themselves and other members of their community to the reasons that they are unable to access vision care. This information will help illuminate the needs of the community and inspire research into interventions by which improved access to adequate eye care can be achieved.

CONTROL ID: 3544230

SUBMITTER (NAME ONLY): Edward Ryan Collantes

TITLE: A prospective study of the natural history of MYOC-associated juvenile open-angle glaucoma

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Juvenile open angle glaucoma (JOAG) can lead to irreversible blindness if not detected and treated at early stages of disease. Myocilin (MYOC) mutations are known to cause JOAG in individuals and families worldwide. We have identified a large Filipino family with JOAG due to a novel MYOC stop-loss mutation, c.1515A>G (p.*505Wext*42). Examining this family over 4 years has allowed for determining the natural history of disease related to this mutation, including information about the onset of intraocular pressure (IOP) elevation, timing of treatment and therapeutic outcomes.

Methods: Fifty-seven members of a 4-generation family were screened for the novel MYOC stop loss mutation. 26 family members carried the mutation and were recruited for the clinical study. Clinically unaffected mutation carriers were monitored over the course of 51 months including visual acuity (VA) assessment, slit-lamp exam, applanation tonometry, gonioscopy and fundus exam.

Results: Twenty six of the 57 family members were carriers of the novel stop loss mutation. 13 mutation carriers were affected by JOAG (mean age of diagnosis 28.6 years; SD=7.9; range 16-43). Despite treatment, 11 mutation carriers had no light perception in at least one eye. Five mutation carriers were newly diagnosed with JOAG as part of the family ascertainment.

Of the 26 mutation carriers, 8 subjects (mean age 7 years; SD=4.9; range 1-15) did not have clinical evidence of glaucoma. These 8 subjects were examined regularly over the course of 51 months. One subject developed IOP elevation at age 14. The average intraocular pressure was within the normal range for the remaining 7 subjects (range: 12-20 mmHg). There was no significant change in the VA and cup to disc ratio and no indication of an upward IOP trend in this subgroup.

Conclusions: This is the first stop-loss MYOC mutation that has been described. In this family, this mutation appears to exhibit variable age of onset with 100% penetrance by age 49. It does not seem to cause elevated IOP in the first decade of life. Similar to a common MYOC mutation (GLN368X), the variable age of onset could suggest that other factors, including POAG polygenic risk score can modify disease development. Evaluation of unaffected mutation carriers provides insight into the natural history of MYOC-associated JOAG. This information will be of critical importance as gene-based therapies become available in the future.

CONTROL ID: 3544231

SUBMITTER (NAME ONLY): Annapurna Hanumanthu

TITLE: Utilizing Higher-Order Quantitative SD-OCT Biomarkers in a Machine Learning Prediction Model for the Development of Subfoveal Geographic Atrophy in Age-Related Macular Degeneration

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hanumanthu, K. Sarici, J. Whitney, L. Lunasco, D. Sevgi, H. Cetin, S. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|J.R. Abraham, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study sought to evaluate higher-order SD-OCT features, including ellipsoid zone integrity and drusen burden, as predictive imaging biomarkers for a machine learning (ML) prognostic model for the development of subfoveal geographic atrophy (sfGA) in non-neovascular age-related macular degeneration (NNVAMD) over 5 years.

Methods: This was a retrospective cohort study of eyes with NNVAMD without sfGA with a 5-year follow-up interval. Based on sfGA status at year five, eyes were categorized into two subgroups: non-converter and sfGA converter. The macular scans at baseline were evaluated using an automated machine learning-enhanced multi-layer segmentation platform with expert reader verification for assessment of retinal anatomy, including outer retinal integrity [e.g., ellipsoid zone (EZ)] and the sub-RPE compartment (e.g., drusen burden). The feature complexities were compared using multiple decision trees and random forest ML modeling for a prediction assessment. Model performance was evaluated with a 5-fold cross-validation.

Results: One hundred and thirty-seven were included in this assessment, including 116 non-converters and 21 sfGA converters. Multiple higher-order OCT features, including EZ integrity metrics and sub-RPE compartment metrics, that were associated with sfGA conversion were analyzed. Feature selection for model inclusion was based on univariate analysis significance. Utilizing 7 significant baseline imaging features, the predictive performance of the ML sfGA prediction model was evaluated and achieved an area under the receiver operating characteristic (ROC) curve (AUC) of 0.85. SD-OCT features were ranked on their predictive ability to identify the development of sfGA and demonstrated that the most important feature was associated with EZ integrity and drusen burden.

Conclusions: Utilizing a ML classifier, higher-order SD-OCT quantitative biomarkers (i.e., EZ integrity, sub-RPE compartment) appeared to provide a high-performance model for predicting the development of sfGA in NNVAMD within 5 years of baseline assessment.

CONTROL ID: 3544232

SUBMITTER (NAME ONLY): Steven Pittler

TITLE: Retinal gene expression analysis of mouse models of RP59

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.J. Pittler, M.N. Nguyen, E. Monson, A.A. Frith, D. Chakraborty, Optometry and Vision Science, Vision Science Research Center, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S. Ramachandra Rao, L.A. Skelton, S.J. Fliesler, Ophthalmology and Biochemistry, SUNY-The State University of New York at Buffalo, Buffalo, New York, UNITED STATES|S. Ramachandra Rao, L.A. Skelton, S.J. Fliesler, Research Service, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: RP59 is due to mutations in the essential gene, dehydrodolichyl diphosphate synthase (DHDDS), which is ultimately required for protein N-glycosylation. A subset of DHDDS mutations cause non-syndromic RP. To identify genes and pathways that are affected by disruption of the Dhdds locus, we analyzed the retina RNA profiles of two RP59 mouse models, in comparison to controls.

Methods: Total RNA was isolated from the retinas (2/sample) of N=3 mice/genotype: Dhdds^{K42E/K42E} knock-in (KI, 4 wks.; an RP59 mutation); Dhdds^{flx/flx} Rho iCre (KO; rod-specific Dhdds knockout, 4 wks.); Dhdds^{flx/flx} without iCre littermates; and WT (C57Bl/6J) controls. RNA was analyzed using the NanoString platform by the UAB Nanostring Core Laboratory. Data from three panels were analyzed: Neuropathology (770 genes), Glial (770 genes), and a Custom Panel (479 genes) with retina- and glycosylation pathway-related genes. Data were combined and analyzed using NanoString software nSolver 4.0 and advanced analysis 2.0, setting a fold-change cutoff of 2.0. In Situ Hybridization (ISH) and cytokine array analysis were performed to validate transcript/protein level increases of selected target genes. Statistical analysis: Student's t-test; significance threshold, P<0.001.

Results: Excluding overlap among panels, 1466 unique genes were analyzed, resulting in 11 up- (range: 2- to 6-fold) and 31 down-regulated (range: -2 to -131-fold) transcripts identified in KI retinas and 89 up- (2- to 15-fold) and 28-down-regulated (range: -2 to -8-fold) transcripts found in KO retinas. Pathway analysis showed significant changes in the adaptive immune system, intracellular signaling by second messengers and cytokines, toll receptor cascades, extracellular matrix reorganization, and neutrophil degranulation genes. In KI retinas, significant changes were seen in neuronal systems, signaling by nuclear receptors and rho GTPases, and vesicle-mediated transport pathways genes. ISH analysis suggested upregulation of C1qb, an inflammatory marker, in activated microglia.

Conclusions: The results are consistent with the previously observed early degenerative changes, neuroinflammation and cytokine upregulation observed in rod-specific Dhdds KO retinas and the physiologic changes previously observed in DhddsK42E/K42E KI mice. Since several of the identified genes yield proteins that become glycosylated, they may be candidates for primary and secondary effects relevant to altered Dhdds function.

CONTROL ID: 3544236

SUBMITTER (NAME ONLY): Omar Ali

TITLE: Identifying Barriers to Follow-Up After Teleretinal Screening for Diabetic Retinopathy

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetes mellitus and its primary ophthalmic complication, diabetic retinopathy (DR), continue to increase in prevalence worldwide. A large-scale teleretinal screening program has been utilized in the Harris County, the largest county in Texas, since 2013. While screening has improved DR screening compliance overall, a significant proportion of patients with sight-threatening diabetic eye disease (STDED) are lost to follow-up (FU). This study aims to identify barriers that may hinder patients from FU after a positive initial screening.

Methods: Retrospective cohort analysis of patients in the Harris Health System (HHS) who were screened via nonmydriatic fundus photography at 13 primary care clinics in 2018. Of the 11,622 screened patients, 891 patients were detected to have STDED on teleretinal screening, and 333 patients failed to FU for an in-clinic evaluation by a retina specialist within 1 year of initial screening. Of this final cohort, 103 patients responded to a telephone survey questionnaire designed to explore their perceived barriers to FU.

Results: The majority of survey respondents were English speakers (52.43%), and self-identified as Hispanic/Latino (61.17%). The most common reported barriers by nearly 47% of survey respondents were cost of the healthcare and lack of clarity in processes post-screening (Figure 1). Patients reported a mean commute time of 35.19 minutes (SD 25.52) to see a retina specialist and the average number of barriers reported by each patient was 2.46 (SD 1.58). No statistically significant relationship was found between language preference, screening location, commute time, or age/race/sex and the mean number of barriers reported.

Conclusions: The HHS teleretinal screening program has significantly increased access to DR screening, but compliance following positive screening for STDED remains a challenge. Among patients found to have STDED on teleretinal screening in 2018, approximately 37.4% were lost to FU. Our study identified several factors that may preclude patients from FU, including cost, employment demands, transportation issues, and lack of understanding in post-screening instructions. Future quality improvement interventions, such as a refined process in providing patient instructions, are being planned based on these findings.

CONTROL ID: 3544238

SUBMITTER (NAME ONLY): YINGZI XIONG

TITLE: Estimates of Direction and Distance by People with Vision and Hearing Impairment

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Accurate judgements of direction and distance are important for safe mobility. For people with vision or hearing impairment, it is important to optimally utilize their residual vision and hearing in such activities. Here we asked how people with various combinations of vision and hearing impairment integrate their residual vision and hearing in judging direction and distance.

Methods: There were three groups—vision impairment (VL, N = 9); dual sensory impairment with combined vision and hearing impairment (DSL, N = 6); and healthy controls (N = 6). Their mean acuities were 0.73, 0.42 and 0.0 logMAR; mean contrast sensitivities were 0.98, 1.35 and 2.0 logCS; and mean hearing thresholds were 9.1, 36.0 and 7.5 dB, respectively. Subjects were asked to walk to a briefly presented (5 s) target on the floor in a room under dark or normal lighting conditions. There were three types of targets—1) broadband auditory sound pulses, 2) visual LED flashes (8.4 cd/m²), and 3) both auditory pulses and visual flashes (audiovisual targets). In a direction trial, the target was presented from one of six directions on the horizontal plane ($\pm 6^\circ$, $\pm 13^\circ$ and $\pm 20^\circ$). In a distance trial, the target was presented at one of six distances from straight ahead (0.9m to 5.4m). Precision was calculated as the standard deviation of 6 trials for each subject response for each target modality.

Results: The lighting conditions did not significantly affect the subjects' distance or direction precision. For both distance and direction estimation, the three groups had similar precision in the visual condition, but the DSL group showed significantly lower precision in the auditory condition than the other groups. Within each group, the auditory condition always showed lower precision than the visual and audiovisual conditions, regardless of the lighting conditions. The audiovisual condition always had similar precision to the visual condition in all three groups, possibly indicating that subjects primarily relied on their vision while the auditory signal provided little additional benefit.

Conclusions: Our preliminary results showed that visual localization remains intact with vision impairment, but sound localization is susceptible to hearing impairment. In both direction and distance judgments, when localizing multimodal targets subjects primarily rely on their vision regardless of their vision and hearing status.

CONTROL ID: 3544240

SUBMITTER (NAME ONLY): M Francesca Cordeiro

TITLE: DARC as a biomarker of endothelial cell stress in retinal angiogenesis

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Cordeiro, L. Guo, V. Luong, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|M. Cordeiro, P. Corazza, S. Younis, ICORG, Western Eye Hospital, London, London, UNITED KINGDOM|J. Maddison, Novai Ltd, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): M Francesca Cordeiro: Commercial Relationship(s);Novai Ltd:Code I (Personal Financial Interest);Novartis:Code F (Financial Support);Bayer:Code F (Financial Support) | Li Guo: Commercial Relationship: Code N (No Commercial Relationship) | Vy Luong: Commercial Relationship: Code N (No Commercial Relationship) | John Maddison: Commercial Relationship(s);Novai Ltd:Code I (Personal Financial Interest) | Paolo Corazza: Commercial Relationship: Code N (No Commercial Relationship) | Saad Younis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: DARC (Detection of Apoptosis Retinal Cells) consists of a fluorescently-labelled annexin A5 molecule (ANX776) which binds to externalised phosphatidylserine (PS) on retinal cells undergoing apoptosis and stress. However, recently, endothelial cell PS externalisation has been demonstrated as one of the earliest stages in neovascularization. Here we assess if DARC can be used as a biomarker of vascular leakage and angiogenesis in vivo.

Methods: Pilot experiments were performed on 3 New Zealand White (NZW) rabbits to evaluate the natural history of vessel leakage and neovascularisation using FFA. Following this, 6 NZW rabbits had intravitreal injections humanVEGF165 (1 ug, Sigma, UK) into the left eye only of each animal, with 3 being given ranibizumab treatment. Animals were assessed 2 and 4 days later, using intravenous ANX776 (0.2mg) and 1% sodium fluorescein after baseline autofluorescence.

Results: Although not present at 2 days, all control rabbit eyes treated with hVEGF had fluorescein leakage at 4 days compared to ranibizumab eyes. All left hVEGF eyes were found to have significantly ($p<0.05$) more DARC positive-staining compared to the untreated contralateral right eye 2 days after treatment; however, ranibizumab eyes had significantly less ($p<0.05$) than untreated hVEGF eyes.. Staining appeared as single spots localised to the vascular branches of the main stems of the retinal vessels.

Conclusions: This is the first time in vivo that DARC has been shown to identify phosphatidylserine in angiogenic processes, and illustrates its use as a biomarker for anti-angiogenic treatments. DARC can be therefore used in vivo to identify the earliest stages of leakage and angiogenesis in choroidal neovascularisation, diabetic eye disease and potentially any retinal disease in which pathological angiogenesis occurs.

CONTROL ID: 3544241

SUBMITTER (NAME ONLY): Andrea Cabrera

TITLE: Novel Genetic Variants Identified in “Poor” Responders to Anti-VEGF Therapy in Patients with Diabetic Macular Edema—A Whole Exome Sequencing Approach

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Cabrera, L. Marek, F. Monickaraj, A. Das, Ophthalmology and Visual Sciences, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|S. Rangasamy, C. Legendre, Translational Genomics Research Institute, Phoenix, Arizona, UNITED STATES|A. Das, New Mexico VA Health Care System, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: All major clinical trials have shown that only 27-40% of diabetic macular edema (DME) patients show vision improvement of >15 letters with intravitreal anti-VEGF injections. Thus, a substantial proportion of patients are “poor” responders to anti-VEGF therapy. Our goal was to identify genetic variants, if any, that may help determine “good” vs “poor” response to anti-VEGF therapy.

Methods: We conducted whole-exome sequencing (WES) on two cohorts, “Good” Responders (reduction of baseline central retinal thickness, CRT >25% after three monthly anti-VEGF injections; n=10) and “Poor” Responders (reduction of CRT <10% or increase in CRT after three monthly injections; n=10). DNA was isolated from white blood cells followed by quality evaluation and quantification. DNA libraries were constructed using HiFi Library Amplification Kit followed by exome region capturing by Agilent SureSelect XTLI and Human All Exon V7 capture. Exome sequencing was performed on the Illumina NovaSeq 6000 for 100X coverage. The sequenced data were processed and aligned to the reference genome (Hg19/GRCh38) using TGen pipeline and Constitutional variant calling with high functional impact performed with DeepVariant caller.

Results: After comprehensive exome variant analysis to identify coding variants with functional impact, we identified that “Poor” responders had increased burden of missense mutation. Further, gene enrichment analysis revealed enrichment of ultra-rare variants in Sphingomyelin Phosphodiesterase 4 (SMPD4), Golgi Associated, Gamma Adaptin Ear Containing, ARF Binding Protein 2 (GGA2), and Mucin 12 (MUC12) in the “poor” responder cohort. These genes have been shown to play an important role in signaling of cell proliferation, apoptosis, and cell adhesion.

Conclusions: Our data provides evidence for protein-coding genetic variants that may influence patient response to anti-VEGF therapy. A thorough understanding and functional validation of the mechanistic consequences of these variants using cell and animal model of diabetes will help in the identification of risk genes that play a role in the anti-VEGF response in DME patients and may help identify personalized treatment strategies.

CONTROL ID: 3544242

SUBMITTER (NAME ONLY): Diamond Brunt

TITLE: Impacts of Vision and Hearing Impairment on Egocentric Straight-ahead

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Brunt, Y. XIONG, Envision Research Institute, Wichita, Kansas, UNITED STATES|G.E. Legge, Psychology, University of Minnesota, Minneapolis, Minnesota, UNITED STATES|Y. XIONG, G.E. Legge, Center for Applied and Translational Sensory Science, University of Minnesota, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Diamond Brunt: Commercial Relationship: Code N (No Commercial Relationship) | YINGZI XIONG: Commercial Relationship: Code N (No Commercial Relationship) | Gordon Legge: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Egocentric perception of straight-ahead is an important internal reference for spatial orientation. For people with sensory impairment who receive reduced external sensory input, such internal reference may affect mobility and judgments of spatial layout. This study investigates the impacts of vision and hearing impairment on the perception of egocentric straight-ahead and the relationship to real-life tasks such as walking without veering.

Methods: Subjects with vision impairment (VL, N = 9), dual sensory impairment (DSL, combined vision and hearing impairment, N = 6), and healthy controls (N = 6) participated in this study. Across all subjects, the acuity ranged from -0.14 to 1.66 logMAR, the contrast sensitivity ranged from 0 to 2.25 logCS, and the hearing threshold ranged from -1.3 to 55 dB. The egocentric straight-ahead was measured in three modalities: proprioception, vision and audition. In measuring proprioception, subjects closed their eyes and pointed to their perceived straight-ahead. To measure vision and audition, subjects adjusted a LED light or clicking sound in the horizontal plane to their perceived straight-ahead. Each condition was tested with eight trials. The center point between the two eyes was measured as the reference for body center. Bias was calculated as the mean error in the angle between the reported straight-ahead and a straight-ahead line defined by body center. Precision was calculated as the standard deviation across the eight trials

Results: There was no significant group difference in bias in any of the three modalities. The biases were also not significantly related to hearing asymmetry, hearing threshold, binocular acuity or contrast sensitivity. When comparing the precision, only the auditory condition showed a significant group difference. Post-hoc analysis showed that the control group had significantly higher precision than both VL and DSL groups. Hearing threshold and binocular acuity were both significant predictors for the auditory precision, with higher hearing threshold and worse acuity related to reduced precision.

Conclusions: Our preliminary results showed that vision and hearing impairment did not significantly affect the perception of proprioceptive and visual straight-ahead, but both reduced the precision of auditory straight-ahead. The impacts of vision and hearing impairment on other real-life tasks such as walking without veering is currently under investigation.

CONTROL ID: 3544243

SUBMITTER (NAME ONLY): Zsolt Ablonczy

TITLE: A tetravalent bispecific anti-angiopoietin-2/anti-VEGF antibody suppresses neovascular lesion and leakage in a laser-induced rat choroidal neovascularization model

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Ablonczy, C. Schillo, C. O'Connor, A. Whitlock, Preclinical R&D, Ora, Inc, Andover, Massachusetts, UNITED STATES|J. Lulo, S. Wan, M. Muda, AbPro, Woburn, Massachusetts, UNITED STATES|R. Patil, R&D, Ora, Inc, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zsolt Ablonczy: Commercial Relationship(s);Ora, Inc:Code E (Employment) | James Lulo: Commercial Relationship(s);AbPro:Code E (Employment) | Shengqin Wan: Commercial Relationship(s);AbPro:Code E (Employment) | Christopher Schillo: Commercial Relationship(s);Ora, Inc:Code E (Employment) | Ciara O'Connor: Commercial Relationship(s);Ora, Inc:Code E (Employment) | Raj Patil: Commercial Relationship(s);Ora, Inc:Code E (Employment) | Andy Whitlock: Commercial Relationship(s);Ora, Inc:Code E (Employment) | Marco Muda: Commercial Relationship(s);AbPro:Code E (Employment)

ABSTRACT BODY:

Purpose: Abnormal angiogenesis underpins vision loss associated with several diseases including wet age-related macular degeneration (AMD), diabetic retinopathy, diabetic macular edema (DME), and macular edema following retinal vein occlusion. Anti-vascular endothelial growth factor (VEGF) therapies have shown consistent success in these pathologies. However, in addition to VEGF, the angiopoietin-Tie2 pathway has also been shown to play a role in angiogenesis. ABP-201, our tetravalent bispecific antibody, was engineered with the goal of inhibiting VEGF and angiopoietin-2 concomitantly. This is the first study assessing the activity of ABP-201 in the eye, using a rat laser-induced choroidal neovascularization (CNV) disease model.

Methods: Brown-Norway rats received a single 5 µL intravitreal injection of ABP-201 in three concentrations, vehicle, or aflibercept (EYLEA[®]) in the right eye. Four or five lesions were burned within two discs from the optic nerve using a laser. Fundus imaging and optical coherence tomography (OCT) verified the lesions immediately following challenge. On Days 7 and 15, fluorescein angiography and OCT assessed lesion leakage and volume. Data were expressed as means ± SEM and analyzed using one-way ANOVA.

Results: On Day 7, all three doses of ABP-201 induced a highly significant reduction in both lesion volume (27%, 27%, and 40%, respectively, for all $p < 0.01$) and in leakage (33%, 35%, and 37%, respectively, for all $p < 0.0002$) when compared to vehicle. On Day 15, the mid and high doses of ABP-201 induced a significant reduction in lesion volume (26% and 27%, respectively, for both $p < 0.05$) and all three doses induced a significant reduction in leakage (28%, 33%, and 36%, respectively, for all $p < 0.05$). For both lesion volume and leakage, the performance of ABP-201 was similar or better than aflibercept.

Conclusions: Our study demonstrated that ABP-201 was beneficial for reducing neovascular lesion formation and vascular leakage in rat model of laser-induced CNV. These results pave the way to begin to utilize this bispecific antibody, engineered to improve both efficacy and durability compared to current VEGF therapies, for the treatment of wet-AMD and DME, as well as other angiogenic eye diseases.

CONTROL ID: 3544244

SUBMITTER (NAME ONLY): Shivany Condor-Montes

TITLE: Repeatability, Reproducibility, and Bias of the Tracking Scanning Laser Ophthalmoscope

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Condor-Montes, C. Sheehy, A.J. Green, Department of Neurology, University of California San Francisco, San Francisco, California, UNITED STATES|E. Bensinger, A.J. Roorda, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|E. Bensinger, A.J. Roorda, Vision Science Graduate Group, University of California Berkeley, Berkeley, California, UNITED STATES|Y. Sherkat, College of Engineering, University of California Berkeley, Berkeley, California, UNITED STATES|Z. Helft, C. Light Technologies, Berkeley, California, UNITED STATES|A.J. Green, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the sources of variation and accuracy of the tracking scanning laser ophthalmoscope (TSLO) as an eye-tracking measurement system

Methods: Gauge Repeatability and Reproducibility (Gauge R&R) was assessed on TSLO outputs to examine variability from apparatus, operator, signal input, and interaction between operator/signals. Twelve total pre-determined amplitude and frequency values of sinusoidal motion, representing the span of human fixation, were input into a custom-built steerable model eye. Three operators (AA,AB,AC) recorded three 10-second videos for each input on three separate days. The second frequency input at 30 Hz was discarded due to overlap with the device framerate. We completed a variance component analysis, and linearity and bias analyses to assess TSLO's precision and accuracy. Bias was measured as the difference between the true value and observed value.

Results: Variance component analysis showed that part-to-part variation was the main contributor to variance for both frequency (99.99%) and amplitude (99.93%) inputs. The repeatability and reproducibility variance components contributed minimally to variability, at 0.007% for frequency and 0.14% for amplitude. There was a positive correlation between frequency signal input value and bias for all operators ($\max p=1.7e^{-13}$), indicating the presence of linearity (i.e., higher frequencies have lower accuracy). For amplitude measurements, there was a tendency to underestimate large amplitudes, with linearity being present for operator 2 ($p=0.03$) and 3 ($p=8.7e^{-6}$). However, the maximum significant bias was 3.75 Hz at a frequency of 100Hz and -12 arcsecs at an amplitude of 360 arcsecs.

Conclusions: The TSLO can reliably distinguish between signals of different values, with very minimal contribution from apparatus error or operator bias. A large proportion of the TSLO variation stemmed from differences between signal inputs, 99.99% for amplitude and 99.3% for frequency. Gage R&R contribution fell well below 10%, at 0.007% for frequency and 0.14% for amplitude. Overall, TSLO showed excellent operator repeatability and apparatus reproducibility. Biases noted would be likely to be clinically insignificant.

CONTROL ID: 3544246

SUBMITTER (NAME ONLY): Khelly Shah

TITLE: Optimization of Glaucoma Management During a Pandemic: Drive-Through IOP Checks

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Shah, A. Ooms, A.S. Khouri, M. Habel, Rutgers New Jersey Medical School
Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Khelly Shah: Commercial Relationship: Code N (No Commercial Relationship) | Ashley Ooms: Commercial Relationship: Code N (No Commercial Relationship) | Albert Khouri: Commercial Relationship: Code N (No Commercial Relationship) | Miriam Habel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In this pilot study, we compared the efficacy of drive-through intraocular pressure (IOP) checks in combination with E-health visits to E-health visits alone in the management of glaucoma patients during the COVID-19 pandemic.

Methods: We performed a retrospective chart review for visits from April 2020 – November 2020 to compare subjects that received E-health visits (Group 1) versus subjects that received E-health visits with a drive-through IOP check (Group 2). Drive-through visits consisted of temperature screening with a non-contact infrared thermometer, near visual acuity check, and IOP measurements using a Tono-Pen XL Tonometer (Reichert, Depew, NY) followed by a video E-health visit with a glaucoma specialist. Group 1 patients only attended a video visit. We compared the proportion of interventions done at the visit as well as changes in visual acuity (VA) and IOP after the tele-visits between the 2 groups. The 4 types of interventions were: change in drop type, change in drop frequency, change in number of drops, and recommending surgical or laser intervention.

Results: 28 subjects were included in our pilot study (mean age 74.9 +/- 3.8 years, 57.1% female). There was no significant difference in baseline characteristics between group 1 (n=15) and group 2 (n=13, Table 1). 6.7% of Group 1 patients had an intervention done compared to 38.5% of group 2 patients. Fisher exact probability testing showed a significant increase in the proportion of interventions done in group 2 subjects compared to group 1 subjects (p=.041), with the most common interventions being changing number of drops and drop frequency. There was no significant difference in changes in VA or IOP between the 2 groups (Table 1).

Conclusions: Drive-through IOP checks in combination with virtual visits resulted in more interventions than virtual visits alone in the care of glaucoma patients during the COVID-19 pandemic. This novel healthcare modality can address the mismatch between capacity and demand for glaucoma care both during a pandemic and can further expand access to sub-specialized care.

CONTROL ID: 3544247

SUBMITTER (NAME ONLY): Zhongfa Yang

TITLE: Characterizing trans Regulatory Networks of Human Plasma Proteomics in Relation to Age-related Macular Degeneration

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Yang, T. Huan, J.M. Seddon, Department of Ophthalmology and Visual Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zhongfa Yang: Commercial Relationship: Code N (No Commercial Relationship) | Tianxiao Huan: Commercial Relationship: Code N (No Commercial Relationship) | Johanna Seddon: Commercial Relationship(s); Gemini Therapeutics, Inc.: Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Genome-wide association studies (GWAS) have identified common and rare variants in association with age-related macular degeneration (AMD). Despite the success of GWAS, the molecular mechanism underlying AMD gene-disease associations, however, is largely unknown. The human proteome plays direct role in biological processes and is major resource for druggable therapeutic targets. In this study, we systematically evaluated the causal influence of plasma proteins on AMD by cross-linking GWAS of plasma proteins with AMD.

Methods: We curated published GWAS of human plasma proteome which identified cis- and trans- protein quantitative trait loci (pQTLs) for approximately 2600 proteins. cis-pQTLs were defined as the SNPs residing within +/- 1Mb of the protein-coding genes, and the other pQTLs were trans. AMD GWAS studies included the International AMD Genomics Consortium (16,144 cases and 17,832 controls), the Boston-French-FINRISK study (4332 cases and 25,268 controls), and the UK Biobank (5860 cases and 126,726 controls). GWAS of proteins and AMD were conducted in independent populations. Two-sample Mendelian randomization (MR) and colocalization analysis were used to infer causal associations between proteins and AMD using pQTLs as instrument variables.

Results: We identified trans-pQTL hotspots across different chromosomes which harbored causal variants for AMD and multiple proteins, such as genetic loci near CFH (chr.1), C7 (chr.5), CTRB2 (chr.16), and APOE (chr.19). We proposed a remotely regulatory mechanism of AMD showing AMD risk loci regulated distant proteins (trans-proteins) by altering local genes or proteins, which in turn may affect the disease. Gene ontology enrichment analysis suggested that the trans-proteins were enriched for genes involved in response to nutrient ($P=0.005$) and retina homeostasis ($P=0.01$). MR and colocalization analysis identified putatively causal pathways for AMD. For example, the APOE loci drive the causal effects of APOE on AMD in cis ($\text{Beta}=-0.52$, $P_{\text{MR}}=1.5 \times 10^{-23}$), and may also through vertical pleiotropic effects on multiple trans-proteins including MAN2B2, NAPB, and LRRN1.

Conclusions: Our study not only identified novel proteins associated with AMD, but also defined network structures that shed light on the regulatory mechanism of AMD pathogenesis.

CONTROL ID: 3544252

SUBMITTER (NAME ONLY): Geoffrey Broadhead

TITLE: Dietary Nitrate Consumption And Risk of Progression in Age-Related Macular Degeneration

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G.K. Broadhead, E. Agron, D. Peprah, T.D. Keenan, E.Y. Chew, National Eye Institute, Bethesda, Maryland, UNITED STATES|T.E. Clemons, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|T. Lawler, J.A. Mares, Ophthal and Visual Sci, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: To assess potential relationships between dietary nitrate intake and risk of progression in age-related macular degeneration (AMD).

Methods: Methods: Post hoc analysis of 2 large prospective clinical trial cohorts: Age-Related Eye Diseases Study (AREDS) and AREDS2. Dietary nitrate intake was calculated for each participant by analysis of food frequency questionnaire. AMD progression was evaluated by reading center grading of annual fundus photographs. Cox proportional hazard analyses were performed for AMD progression, according to quartiles of dietary nitrate intake (quartile 1 as reference), with adjustment for age, gender, smoking status, and caloric intake.

Results: Results: In the combined AREDS/AREDS2 cohort (n=7788 eligible participants without late AMD in either eye at baseline), higher dietary nitrate intake was associated with decreased risk of late AMD (HR 0.80 for quartile 4, 95% CI 0.72-0.90). Risk of each late AMD subtype was also reduced, with both risk of geographic atrophy (GA; HR 0.78, 0.67-0.91) and neovascular AMD (NV-AMD; HR 0.61, 0.53-0.71) reduced. Similar associations were observed in each cohort, considered separately: HR 0.70 (0.59-0.83), 0.74 (0.60-0.90), and 0.73 (0.59-0.91), in AREDS, and 0.85 (0.74-0.97), 0.86 (0.70-1.06), and 0.88 (0.72-1.07), in AREDS2, respectively. In additional analyses of the AREDS cohort (n = 4288 eligible participants), adjustment was made also for dietary lutein/zeaxanthin intake (since this is correlated with nitrate intake); higher nitrate intake was still associated with decreased risk of late AMD (HR 0.68, 0.56-0.82), GA (0.67, 0.53-0.85), and CNV (0.73, 0.57-0.92). Also in the AREDS cohort, higher nitrate intake was also associated with decreased risk of progression to large drusen: HR 0.82 (0.68-0.99).

Conclusions: Conclusions: Higher dietary nitrate intake has protective associations against progression to late AMD. This is true for both subtypes of late AMD. Higher intake also appears associated with decreased risk of large drusen, so nitrate intake may be protective across the spectrum of AMD severity. The associations are independent of lutein/zeaxanthin intake, with which nitrates share some food group sources. These findings may justify further studies of nitrate supplementation, including randomized controlled trials.

CONTROL ID: 3544255

SUBMITTER (NAME ONLY): Julie Kim

TITLE: Systemic immunosuppression and risk of endophthalmitis after intravitreal anti-vascular endothelial growth factor injections

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Kim, S.N. Patel, A. Obeid, J. Hsu, S.J. Garg, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|P.P. Storey, Austin Retina Associates, Austin, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The impact of systemic immunosuppressive therapy on the rates and outcomes of endophthalmitis following intravitreal anti-vascular endothelial growth factor (VEGF) injections remains largely unexplored. The aim of this study was to examine whether systemic immunosuppressive therapy alters a patient's risk for developing endophthalmitis after anti-VEGF injections.

Methods: This is a retrospective, single-center cohort study examining all eyes that underwent intravitreal anti-VEGF injections (bevacizumab, ranibizumab, or aflibercept) from January 2016 to September 2019. Two cohorts (no immunosuppression vs immunosuppression) were created based on immunosuppressive status at time of intravitreal injection. The primary outcome was the occurrence of endophthalmitis rates, while visual acuity (VA) and culture-positive cases were secondary outcomes. Within both cohorts, patients who developed presumed post-injection endophthalmitis that underwent ocular tap with intravitreal antibiotics were identified and compared using Chi-Square or Mann-Whitney U. $P < 0.05$ was considered significant.

Results: Of 270,347 anti-VEGF injections administered to 23,252 patients, 1300 (0.48%) injections were administered to 412 patients who were on systemic immunosuppressive therapy. In this cohort of eyes, five developed endophthalmitis for a rate of 0.38% (1 in 260 injections) compared to 100 eyes not on systemic immunosuppressants for a rate of 0.037% (1 in 2690 injections) with an odds ratio (OR) of 9.86 (95% CI: 4.0-24.3, $P < 0.001$). Among the five eyes with presumed endophthalmitis, 3 had positive cultures (0.023%, 1 in 433 injections) compared to the 2 (0.012%, 1 in 8,407 injections) in the immunocompetent group for an OR of 19.4 [95% CI: 5.9-63.4, $P < 0.001$]. Symptom onset occurred 2.51 (95% CI: 0.15-4.87, $P = 0.040$) days earlier in the immunosuppressed patients; however, visual outcomes at 6 months were similar between the two groups.

Conclusions: Eyes receiving intravitreal anti-VEGF injections who are concurrently on systemic immunosuppressive therapy may be at an increased risk for developing PIE. However, final visual outcomes following post-injection endophthalmitis treatment is similar regardless of systemic immunosuppression status. Additional studies are indicated to further elucidate the role, if any, of immunosuppressive therapy in the management of PIE.

CONTROL ID: 3544265

SUBMITTER (NAME ONLY): Hannah Youngblood

TITLE: Identification of ESR1 in aqueous humor outflow pathway tissues

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Youngblood, J. Cai, H. Yu, Y. Liu, Augusta University Department of Cellular Biology and Anatomy, Augusta, Georgia, UNITED STATES|K. Perkumas, W. Stamer, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|M.A. Hauser, Department of Medicine, Duke University, Durham, North Carolina, UNITED STATES|Y. Liu, Augusta University Center for Biotechnology and Genomic Medicine, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is the only treatable risk factor for primary open-angle glaucoma (POAG). Our previous pathway analysis of IOP-associated loci identified 2 networks focused on an unspecified estrogen receptor and estrogen receptor 1 (ESR1), respectively (Liu 2020). Here we seek to confirm the role of ESR1 signaling in the aqueous humor (AH) outflow pathway.

Methods: We examined which 17 IOP-associated genes in the estrogen receptor networks were specifically expressed in a single-cell RNA sequencing (scRNA-Seq) dataset of human outflow tissue (van Zyl 2020) as well as an RNA-Seq dataset of nonglaucomatous human TM (n=4) and Schlemms Canal (SC) (n=2) cells. To confirm ESR1 activity in the outflow pathway, we examined its protein expression in nonglaucomatous human (n=4) and mouse outflow tissues (n=2) by antibody-based immunofluorescence, using tissue from an *Esr1*^{-/-} mouse as a negative control (n=1). We also measured 17 β -estradiol (E2) concentration in glaucomatous (n=4) and nonglaucomatous (n=4) human AH using an ELISA kit (Enzo Life Sciences).

Results: Seven IOP genes from the estrogen receptor networks (i.e., CAV2, FBXO32, SIX3, FOXC1, SPTBN1, TCF7L2, and TNXB) were expressed in ≥ 1 cell clusters defined by scRNA-Seq, including cell clusters localized to the TM, SC, collector channels, ciliary muscle, Schwalbe's line, vascular endothelium, etc. As confirmation, in a separate RNA-Seq study of human TM and SC cells, 8 genes of interest (i.e., CAV2, ETS1, FBXO32, VEGFC, FOXC1, SPTBN1, TCF7L2, and TMEM119) were highly expressed (i.e., FPKM ≥ 10) in either TM or SC cells, with SPTBN1 having the highest expression (i.e., 85.85 FPKM and 85.83 FPKM). *Esr1* protein was expressed in the iridocorneal angle of female B6J wild-type, but not *Esr1*^{-/-} mice. Similarly, ESR1 protein was expressed in human TM/SC. E2 was present in both glaucomatous (34.46 ± 7.08 pg/mL) and nonglaucomatous human (37.90 ± 14.80 pg/mL) AH ($p > 0.05$).

Conclusions: Many IOP-associated genes within the estrogen receptor networks are highly expressed in the outflow pathway including in the TM, SC, ciliary muscle, and vascular endothelium. The confirmation of ESR1 protein expression in human and mouse outflow tissues and the presence of E2 in AH further supports a possible function of ESR1 signaling in IOP regulation through modulation of AH outflow.

CONTROL ID: 3544268

SUBMITTER (NAME ONLY): Dongfeng Cao

TITLE: Expression and distribution of Ionized calcium binding adaptor molecule 1 (Iba1) and transmembrane protein 119 (TMEM119) in age-related macular degeneration (AMD)

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Microglia and macrophages play roles in AMD-relevant processes of immune surveillance, neurodegeneration, and neovascularization. We analyzed the distribution of cells expressing Iba1 and TMEM119, specific markers for microglia/ macrophage and brain microglia, respectively, in human donor eyes at different AMD stages.

Methods: Twelve µm-thick sections of maculae from 20 eyes of white donors were immuno-stained with Iba1 (Wako 019-19741) and TMEM119 (Abcam ab185333), using red-substrate enzymatic detection and scanned with a 40X objective. Immunoreactivity presence was assessed by one observer as 0 (none), 1 (a few cells), 2 (some cells) and 3 (all over or all cells). Positive controls were resident microglia cells in the inner retina, choroidal macrophages, and Kupffer cells in surgically excised human liver. Negative control experiments omitted primary antibody. RPE cells were phenotyped by published methods (PMID 25813989, 26024109).

Results: In all eyes (4 normal,16 AMD; 7 early-or-intermediate (e-i)AMD, 6 geographic atrophy (GA) AMD, 3 neovascular (nv)AMD), elongated and dendritic cells in inner retina and in choroid were Iba1+, and only in these locations, in normal eyes. Iba1+ cells appeared in outer retina in e-iAMD eyes. In advanced AMD, Iba1+ cells were amoeboid and found in GA areas and in fibrotic scar (nvAMD), where photoreceptors (PR) and RPE layer are absent (both stages) or scarred (nvAMD). Fewer Iba1+ cells were found in inner retina and choroid compared normal and e-iAMD eyes. A few RPE cells were stained (sloughed, intraretinal and subducted phenotypes); most were not. Like Iba1, TMEM119+ cells were found in inner retina and choroid in normal eyes and additionally in outer retina of AMD eyes. Unlike Iba1, TMEM119 signal was found in PR inner segment ellipsoids, ganglion cells, and Müller cells, as seen in mouse (PMID 31853425).

Conclusions: Iba1+ and TMEM119+ cells in outer retina of advanced AMD eyes are most likely activated microglia; we cannot exclude choroidal cells. Some RPE phenotypes that express immune markers in AMD (Cao ARVO 2020) were Iba1+ and TMEM119+ but most RPE cells were unlabeled. TMEM119 signal in PR ellipsoids possibly localizes to mitochondria. Results will assist interpretation of planned single-cell RNA sequencing studies.

CONTROL ID: 3544270

SUBMITTER (NAME ONLY): Dhimas Hari Sakti

TITLE: Incidence of electronegative findings in tertiary ophthalmology referral centre

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Negative electroretinogram (ERG) reflecting inner retinal dysfunction can be used as diagnostic tool to determine the anatomical abnormality location in eye disease. The aim of this study is to determine the frequency and etiology of negative ERG in an electrophysiology referral centre.

Methods: Retrospective review of ERGs performed at the Save Sight Institute from January 2011 to December 2020 . ERGs were performed according to ISCEV standard. The b:a ratio was analyzed in Dark Adapted (DA) 3.0 or 12.0. Data were then divided into 2 groups: Group A true negative ERGs (b:a wave ratio of ≤ 1.0) and group B mild negative ERG (b:a wave ratio between 1 and 1.5).

Results: 4,530 patients had ERGs performed, of which 178 (3.9%) had an electronegative ERG consisting of 112 male and 66 female. 142 (3.1%) patients were in Group A and 36 (0.8%) patients were in Group B indicating that 20.2% of the electronegative ERG diagnoses were mild type. The median age at referral time was 36 (2-91) years. Photoreceptor dystrophy was the largest causative etiology with 53 (45A+8B) patients (28%) followed by Congenital Stationary Night Blindness (CSNB) with 42 (33A+9B) (16.5%), retinoschisis with 18 (15A+3B) (7.1%), retinal ischemia with 16 (15A+1B)(6.3%) and Paraneoplastic Autoimmune Retinopathy (PAIR) and nonPAIR with 14 patients (11A+3B)(5.5%). Batten disease, inflammatory retinopathy, Melanoma Associated Retinopathy and retinal detachment each had 5 (4A+1B)(2%), 3 (3A)(1.2%), 2 (2A)(0.8%), 2 (1A+1B) (0.8%) patients respectively. Birdshot chorioretinopathy, vigabatrin toxicity and foveal hypoplasia were diagnosed in 3 patients (0.4%) and 20 patients had an unclassified diagnosis.

Conclusions: The incidence of true negative ERG and mild negative ERG in our referral center was 3.1% and 0.8% with photoreceptor dystrophy as the main etiology followed by CSNB, retinoschisis, ischemia, and PAIR and nonPAIR. Classic negative ERG diagnoses such as CSNB and retinoschisis both had patients with mild negative ERG (Group B) suggesting the conceivable need to reconsider the traditional negative ERG definition of ≤ 1 .

CONTROL ID: 3544271

SUBMITTER (NAME ONLY): Naga pradeep Rayana

TITLE: Inhibition of TGF β 2-induced ocular hypertension using CRISPR interference

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Rayana, W. Mao, C.K. Sugali, J. Dai, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies have shown that elevated TGF β 2 induces pathological changes in the trabecular meshwork (TM) leading to ocular hypertension (OHT) which are similar to the phenotypes observed in primary open-angle glaucoma. Our published studies suggest that elevated TGF β 2 may be due to promoter region hyperacetylation in the TM. dCAS9 is a mutated form of CAS9, the key enzyme in the CRISPR system. When fused with KRAB, a repression domain, and guided by sgRNA, dCAS9-KRAB can repress gene expression without altering genomic DNA (CRISPR interference). In this study, we showed that CRISPR interference is a useful tool in decreasing intraocular pressure (IOP) by repressing TGF β 2 in mouse eyes.

Methods: Lentiviral dCAS9-KRAB and sgRNA expression vectors were co-transduced into TM cells at an MOI value of 1 to 50. On the fifth day post-transduction, cell lysate and condition medium were extracted and the expression of TGF β 2 and dCAS9 were determined using western immunoblotting. Lentiviral CRISPR interference vectors or control vectors were injected into mouse eyes followed by a second injection of adenoviral vectors expression active TGF β 2.

Results: Our initial screening showed two guide RNAs from a pool of sgRNAs were able to decrease the expression of TGF β 2 compared to control sgRNA in GTM3 cells. We also found similar efficiency of the sgRNAs in the inhibition of TGF β 2 in primary TM cell strains. ChIP-qPCR showed enrichment of dCAS9-KRAB at the TGF β 2 promoter region. In addition to TM cells, we tested our system in a mouse model. We injected male (n=6) and female (n=6) mouse eyes with lentiviral vectors expressing dCAS9-KRAB together with sgRNA targeting the CMV promoter or non-targeting sgRNA as control. We then injected both eyes with Ad5-CMV- Δ hTGF β 2. We found that specific sgRNA expressing eyes did not develop OHT while control sgRNA expressing eyes developed OHT (p<0.05).

Conclusions: CRISPR interference can be used as an important tool in decreasing TGF β 2 and TGF β 2-induced OHT. It can be used as an alternative for siRNA.

CONTROL ID: 3544274

SUBMITTER (NAME ONLY): Elena Schiff

TITLE: The clinical features and variability of retinopathy consequent upon homozygous mutation of LAMA1 in three affected siblings

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Biallelic mutations in LAMA1 (laminin subunit alpha 1) (OMIM #150320) cause Poretti-Boltshauser Syndrome (PBS), a rare non-progressive cerebellar dysplasia disorder with ophthalmic manifestations including oculomotor apraxia, high myopia and retinal dystrophy. Only 32 variants nearly all loss-of-function, have been previously reported in 29 patients from 23 families. Clinical presentation included consistent as well as unspecific and variable features such as intellectual disability. Here we report 3 affected siblings, homozygous for a novel frameshift mutation in LAMA1 and their detailed retinal manifestations.

Methods: Whole genome sequencing (Illumina 150bp paired-end reads, average x30 read-depth) was conducted on members of a consanguineous family with myopia and retinal dystrophy in three of five adult children. Filtering for rare variants in known retinal genes and genome-wide variants in shared homozygous regions in affected individuals was employed. Clinical evaluation included full ophthalmic examination, detailed colour, autofluorescence retinal imaging, retinal optical coherence tomography (OCT) and electroretinography.

Results: Genetic analysis revealed a novel homozygous LAMA1 frameshift variant, c.1492del p.(Arg498GlyfsTer25), in two male and one female affected siblings. Two had oculomotor apraxia in childhood; none had symptoms nor signs of neurological failure as adults. Corrected visual acuities ranged from 6/6 to 6/24. All three had myopia, and a qualitatively similar retinopathy of wide-ranging severity, involving pigmentary changes in the temporal retina in the two lesser affected siblings and in the posterior pole in the more severely affected sibling. Electrophysiology showed mild to severe cone rod dystrophy.

Conclusions: This report describes the detailed retinal structural and functional consequences of LAMA1 deficiency in three siblings and these exhibit much variability. Biallelic mutations should be considered in myopia and retinopathy, even in the absence of systemic signs.

CONTROL ID: 3544275

SUBMITTER (NAME ONLY): Andrea Naranjo

TITLE: Comparison of PRAME antigen detection by Immunohistochemistry (IHC) and polymerase chain reaction (PCR) in Uveal Melanoma.

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Uveal melanomas (UM) are the most common primary intraocular malignancy in the adult population. Based on gene expression profiles, UM can be categorized as Class 1 (low risk for metastasis) or Class 2 (high risk for metastasis). PRAME (PReferentially expressed Antigen in MELanoma) protein is a member of the cancer-testis antigen family and has been suggested as an independent UM prognostic biomarker. PRAME can be detected in UM tissue by either RT-PCR or IHC but concordance in techniques has not been determined.

Methods: We retrospectively identified UM patients who had PRAME detected on RT-PCR testing (Decision Dx UM PRAME, Castle Biosciences, TX) following globe enucleation. In house PRAME IHC was performed on these specimens with cutoff of 50% for positive detection after slide review. ICH results, based on clinical stage, were compared.

Results: 15 UM patients (11 males (73%), average age 60.7 years) were analyzed. AJCC 8th edition staging was varied (Stage 1 n=2), Stage 2 (n=6), Stage 3 (n=6), Stage 4 (n=1) and Class 1 in 9 eyes (60%) and Class 2 in 6 eyes (40%). 11/15 (73%) cases showed concordant PRAME detection results by both RT-PCR and IHC. In 4/15 (27%) discordant cases, ICH did not reach significance for PRAME positivity. Tumor grade for these cases included 1a, 2b, 3d and 4e and 3 cases were low risk Class 1. No patients with discordance developed metastatic disease with 13 months mean last follow up (range 0.1-17 months).

Conclusions: Our findings reveal that PRAME RT-PCR and IHC provide concordant results in 73% of enucleated UM eyes. The discordant results differed in tumor stage and may be due to a lack uniform standardization of IHC based nuclear PRAME detection or geospatial variations within each tumor. Further studies are required to determine the methodologic and prognostic implications.

CONTROL ID: 3544277

SUBMITTER (NAME ONLY): Arunkumar Ranganathan

TITLE: Lutein and zeaxanthin reduce A2E and iso-A2E levels and improve visual performance in $Abca4^{-/-}/Bco2^{-/-}$ double KO Mice

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Ranganathan, A. Gorusupudi, B. Li, D. Blount, F. Chang, P.S. Bernstein, Moran eye center, University of Utah Health, Salt Lake City, Utah, UNITED STATES|J.R. Sparrow, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In autosomal recessive Stargardt disease (STGD1) and dry age-related macular degeneration (AMD), excessive accumulation of lipofuscin is associated with retinal pigment epithelium (RPE) cell death, photoreceptor cell damage, and vision loss. A2E and iso-A2E are prominent fluorophores of ocular lipofuscin that mediate phototoxicity and degeneration. Previous work from our lab in vitro, in quail eyes, and in human donor eyes have indicated that macular carotenoids (MC) can attenuate bisretinoid formation and phototoxicity, but mouse studies have been hampered by poor carotenoid uptake due to their very active carotenoid cleavage enzyme, Bco2. In this study, we have crossed Bco2 KO "macular pigment mice" with a mouse model of STGD1.

Methods: $Abca4^{-/-}/Bco2^{-/-}$ and $Abca4^{-/-}$ mice on C57BL6/J background were fed with lutein, zeaxanthin, or a placebo chow (~2.6 mg of carotenoid/mouse/day; DSM, Kaiseraugst, Switzerland; n=12/group) for 3 months, and their optokinetic response (OKR), electroretinography (ERG) and optical coherence tomography (OCT) were measured after 1-3 months of carotenoid supplementation. Mice were sacrificed after 3 months of supplementation, and their blood and tissues (eye, liver, and brain) were collected. A2E and iso-A2E levels from RPE/choroid and carotenoid levels from the retina were quantified by HPLC

Results: Lutein and zeaxanthin supplemented $Abca4^{-/-}/Bco2^{-/-}$ mice had 33-71% lower levels of RPE/choroid A2E and iso-A2E compared to control mice fed with placebo chow ($p<0.05$) and had improved visual performance. Carotenoid supplementation in $Abca4^{-/-}$ mice minimally raised retinal carotenoid levels and did not show much difference in bisretinoid levels or visual acuity compared to the control diet-fed group. There was a statistically significant inverse correlation between MC levels in the retina and A2E and iso-A2E levels in the RPE/choroid. Scotopic and photopic a and b-wave response and photoreceptor cell viability did not show any significant differences relative to WT mice of same age in either mouse line, irrespective of their supplementation status.

Conclusions: Supplementation with MC effectively reduces bisretinoid formation and improves visual acuity in a mouse model of STGD1 genetically enhanced to accumulate carotenoids in the retina. These results provide further impetus to pursue oral carotenoids as therapeutic interventions for STGD1 and AMD.

CONTROL ID: 3544278

SUBMITTER (NAME ONLY): Jose Ramirez

TITLE: Visual acuity and contrast sensitivity are slightly modified in young asymptomatic relatives of Alzheimer's disease patients

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Ramirez, I. López Cuenca, E. Salobar-García, J. Fernández-Albarral, P. Rojas, L. Elvira-Hurtado, J. Salazar, A. Ramirez, R. de Hoz, Inst.Inv.Oft.Ramón Castroviejo, Universidad Complutense de Madrid (UCM); and RETICs OFTARED-ISCI, Madrid, SPAIN|J. Ramirez, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|E. Salobar-García, J. Salazar, A. Ramirez, R. de Hoz, Departamento de Inmunología, Oftalmología y ORL., Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|P. Rojas, Instituto oftálmico de Madrid, Hospital General Universitario Gregorio Marañón Unidad de Glaucoma y Neuro-oftalmología, Madrid, Comunidad de Madrid, SPAIN|A. Barabash, Endocrinology and Nutrition Department, Hospital Clínico Universitario San Carlos, Madrid, Madrid, SPAIN|A. Barabash, Centro de Investigación Biomedica en Red de Diabetes y Enfermedades Metabólicas Asociadas, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Alzheimer's disease is a neurodegenerative disease, whose signs can appear decades before clinically detectable symptoms. In addition to age, genetic factors are one of the most important risk factors. One population at increased risk are first-degree relatives of AD patients, at a 2- to 3-fold increased risk for developing dementia. This probability increases if relatives are carriers of the apolipoprotein E (APOE) $\epsilon 4$ allele.

The aim of the present study was to analyze the possible changes that may occur in visual acuity (VA) and contrast sensitive test (CST) in first-degree relatives of Alzheimer's disease patients who are carriers of $\epsilon 4$ allele for the ApoE.

Methods: A complete eye examination was performed in all participants, who were free of ocular pathology. This case-control study was conducted in 28 subjects with family history of AD (FH+) , ApoE $\epsilon 4$ carriers and with a mean age of 53.39 years and 16 age-matched control subjects without a family history of AD (FH-), ApoE $\epsilon 4$ non-carriers and with a mean age of 53.94 years.

Results: In comparison with FH- ApoE $\epsilon 4$ non-carriers, in FH+ ApoE $\epsilon 4$ carriers we found statistical significant increase ($p < 0.05$) both in VA (1.04 ± 0.10 , FH+ vs 0.98 ± 0.04 , FH-) and in CS in the spatial frequency (SF) of 12 cycles/degree (1.68 ± 0.18 , FH+ vs 1.54 ± 0.17 , FH-).

Conclusions: The VA and CST registered changes in FH+ ApoE $\epsilon 4$ carriers compared to FH- ApoE $\epsilon 4$ non-carriers. In first-degree relatives of AD patients, an increase of VA and CS in the 12 cycles/degree SF could be the first functional changes to appear.

CONTROL ID: 3544279

SUBMITTER (NAME ONLY): Robert MacLaren

TITLE: Visual function improvements with BIIB112 (NSR-RPGR) in X-linked retinitis pigmentosa: XIRIUS (dose-expansion) and XOLARIS (natural disease progression) studies

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: X-linked retinitis pigmentosa (XLRP) is a severe phenotype of retinitis pigmentosa clinically characterized by onset of night blindness in childhood, followed by progressive vision loss that results in blindness for most individuals. BIIB112 (NSR-RPGR) is an AAV8 vector-based gene therapy that uses codon optimization to express the full-length, correctly sequenced retinitis pigmentosa GTPase regulator (RPGR) protein in the photoreceptors of individuals with XLRP caused by mutations in RPGR. Here, we present results from 2 ongoing trials in participants with XLRP: XIRIUS, a dose-expansion study of BIIB112, and XOLARIS, a natural disease progression study.

Methods: Part 1 of XIRIUS is a Phase 1, 3+3, six-dose-escalation study (NCT03116113) of BIIB112 in participants with XLRP aged ≥18 years. A subgroup of participants was identified from XOLARIS who met XIRIUS part 1 inclusion and exclusion criteria and completed 12 months of follow-up (N=69). Retinal sensitivity responder criterion was

defined as an achievement of ≥ 7 dB improvement from baseline at ≥ 5 loci.

Results: Overall, 18 participants were treated with BIIB112. Treatment with the 4 highest doses (n=12) resulted in early (Month 1 responders, 6/12 [50%]) and durable (Month 12 responders, 4/12 [33%]) improvements in central retinal sensitivity. No untreated participants in XOLARIS who met the inclusion criteria for XIRIUS achieved central retinal sensitivity response (improvement of ≥ 7 dB at ≥ 5 loci) at Month 12 (33% difference in response rate between groups). Improvements in low-luminance visual acuity (LLVA), assessed by a gain of ≥ 15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters, were observed in treated eyes in XIRIUS as early as Month 1 and through 12 months of follow-up (Month 12 proportion of participants with gain of ≥ 15 ETDRS letters: treated eyes, 3/11 [27%]; untreated eyes, 0/11 [0%]; one participant was missing a baseline LLVA assessment score). Most adverse events were mild and resolved, and no dose-limiting toxicities occurred at any dose. Inflammation, mostly observed at the higher doses, was successfully treated with oral corticosteroids.

Conclusions: Treatment with BIIB112 was well tolerated and, in cohorts 3-6, led to early and durable improvements in 2 measures of visual function.

CONTROL ID: 3544281

SUBMITTER (NAME ONLY): Praveen Bandela

TITLE: Real-time manipulation of blur-driven accommodation using an electrically-tunable lens: a feasibility study

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.K. Bandela, A. Ho, E.B. Papas, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|P.K. Bandela, A. Ho, Brien Holden Vision Institute Limited, Sydney, New South Wales, AUSTRALIA|S.R. Bharadwaj, Brien Holden Vision Institute of Optometry and Vision Sciences, L V Prasad Eye Institute, Hyderabad, INDIA|

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ABSTRACT BODY:

Purpose: The ability to manipulate accommodative response real-time during an experiment will be useful to study the properties of feedback-driven accommodation and its interaction with vergence and pupils. Usage of pinholes or low spatial frequency targets may render the blur-feedback open-loop, but they do not allow real-time manipulation of blur input. This feasibility study describes a technique for real-time manipulation of blur-driven accommodation using an electrically- tunable lens coupled with a dynamic, infrared (IR) photorefractor.

Methods: Real-time manipulation of an accommodative response was achieved by measuring the response of one eye dynamically at 50 fps using the Plusoptix PowerRef 3 photorefractor (PR) and synchronously feeding a low-pass filtered version of its output to a calibrated electrically-tunable lens (ETL, Optotune, EL-16-40-TC-VIS) placed along the visual axis of the participant. In Experiment 1, the PR output of the target fixing eye was added to the ETL placed in front of the fellow eye occluded using an IR filter. In Experiment 2, the ETL dynamically subtracted the PR output of the consensual accommodative response from the IR filter occluded eye from the direct response of the eye viewing an accommodative target. These experiments were performed on two young adults (26 and 34 yrs) viewing a broadband spatial frequency target located at 100 and 40 cm from the fixating eye.

Results: Low-pass filtering of the PR output by 50Hz resulted in the ETL smoothly altering its dynamic power, with a fixed delay of only 20 ms. In Experiment 1, the mean refraction of target fixing and the fellow eye was -0.69 ± 0.04 D and 1.00 ± 0.10 D in both subjects before initiation of manipulation. The fellow eye PR output decreased to 0.36 ± 0.19 D after initiation of manipulation, as predicted from the addition of optical power by the ETL. In Experiment 2, the mean consensual accommodative response was 1.03 ± 0.14 D before initiation of manipulation. The direct PR output decreased to 0.41 ± 0.06 D after manipulation, as may be predicted from the subtraction of optical power by the ETL.

Conclusions: These results indicate that the dynamic coupling between the PR and ETL allows real-time manipulation of blur-driven accommodation with negligible temporal delays. This set-up has the potential to be used in studies of the near-triad seeking dynamic manipulation of blur input.

CONTROL ID: 3544285

SUBMITTER (NAME ONLY): Eleftherios Paschalis

TITLE: Anti-inflammatory medication after corneal trauma or surgery to prevent subsequent late glaucoma.

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.I. Paschalis, C. Zhou, F. Lei, S. Kim, D.G. Vavvas, J. Chodosh, G. Papaliodis, C.H. Dohlman, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|A. Urtti, Division of Pharmaceutical Biosciences, University of Helsinki, Kuopio, FINLAND|

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ABSTRACT BODY:

Purpose: Since late glaucoma is the most damaging complication after acute corneal events such as surgery or trauma, our aim has been to develop effective prophylaxis. We have administered antibody against TNF- α for the purpose of protecting the retinal ganglion cell against apoptosis (the hallmark of glaucoma)—and to compare with the effect of corticosteroids.

Methods: Rabbits with normal corneas or with alkali-burned corneas were injected subconjunctivally with the biologics. They were evaluated clinically and with dark- and light-adapted ERG, OCT, and IOP manometrically. The tissues were stained ex vivo in 3 days experiments with TUNEL, DAPI, and H&E. The optic nerves was evaluated after 50 days with paraphenylenediamine staining.

Results: Subconjunctival administration of 0.4 mg or 4.0 mg of adalimumab, and 1.0 mg, 10.0 or 100 mg infliximab were all well tolerated. 40 mg adalimumab showed toxicity. 4.0 mg of adalimumab suppressed apoptosis the most. Local subconjunctival injection, compared to systemic infusion, resulted in substantially higher retinal bioavailability which should reduce systemic side effects. Analysis of the optic nerve axons confirmed the safety of 100 mg infliximab and the 4.0 mg adalimumab.

Conclusions: A subconjunctival injection of 4.0 mg adalimumab has excellent protective effect against retinal ganglion cell apoptosis and no observed toxicity. Corticosteroids, especially triamcinolone 20 – 40 mg sub-Tenon or subconjunctivally, are also having a suppressive effect against apoptosis, but limited applicability because of their side effects. A clinical study for anti-glaucoma prophylaxis after corneal surgery or trauma is proposed.

CONTROL ID: 3544287

SUBMITTER (NAME ONLY): Avinash Aher

TITLE: Spatial properties of L- and M-cone driven incremental (on-) and decremental (off-) electroretinograms: normal subjects Vs. glaucoma patients

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.J. Aher, F. Horn, C.R. Huchzermeyer, R. Lämmer, J.J. Kremers, Department of Ophthalmology, University Hospital Erlangen, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: To compare the electroretinographical (ERG) responses elicited by L- and M-cone isolating incremental (On) and decremental (Off) sawtooth stimuli in normal subjects and glaucoma patients.

Methods: Twenty-one normal subjects and 44 primary open angle glaucoma patients participated in the present study. L- and M-cone isolating rapid On- and Off-sawtooth (4Hz) stimuli were generated using the triple silent substitution technique. The cone contrast was 18% with a mean luminance of 284 cd/m^2 . ERGs were recorded with Full-Field (FF) and 70 deg diameter stimuli. The On- and Off-ERG responses were summed (called Ladd and Madd) to study the response asymmetries to increments and decrements. The steady state pattern ERG (PERG) was also recorded in a subpopulation of each group with 0.8 and 16 deg black and white checkerboard stimuli at the rate of 15 reversals/s. The initial positive (P) and subsequent late negative (LN) ERG components of Ladd and Madd were compared between the subject groups and correlated with retinal nerve fiber layer thickness (RNFLT) and PERG.

Results: The responses to L-On stimuli resembled those to M-Off stimuli and vice versa particularly with 70° stimuli. The P_{Ladd} amplitudes were not significantly different between the two subject groups. However, the P_{Ladd} with 70 deg stimuli was significantly ($P < 0.01$) smaller compared to those of FF stimuli. The amplitudes of the LN_{Ladd} in FF were similar in the two subject groups, whereas, for the 70 deg stimuli, the LN_{Ladd} amplitude was significantly ($P < 0.01$) smaller in the glaucoma patients. Both P_{Madd} and LN_{Madd} were not significantly different between the subject groups. The PERG amplitude in response to 0.8 deg check sizes and the ratio of the amplitude of responses to 0.8 deg over that to 16 deg checks (PERG Ratio) were significantly ($P < 0.05$) different between the subject groups. The LN_{Ladd} amplitude with 70 deg diameter stimuli and the PERG amplitude with 0.8 deg checks were significantly correlated with the retinal nerve fiber layer thickness.

Conclusions: The responses to cone isolating sawtooth stimuli elicited ERGs that strongly reflect (parvocellularity based) cone opponency. Compared to (magnocellular) luminance based responses (PERG), the cone opponent ERG responses have little diagnostic value, indicating that the magnocellular system is functionally more affected by glaucoma.

CONTROL ID: 3544288

SUBMITTER (NAME ONLY): Roy Joseph

TITLE: In Vitro and In Vivo Role of FGFR2 in Corneal Stromal Keratocytes

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Joseph, O.P. Srivastava, Optometry and Vision Science, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|R.R. Pfister, Ophthalmology, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the role of FGFR2-mediated signaling in keratocytes during corneal development by phenotypic characterization of stromal specific FGFR2 knockout (KO) mouse

Methods: In vitro analysis of FGFR2 knockdown was performed in cultured normal corneal keratocytes using Silencer® Select FGFR2 siRNA and siCtr (control), based on manufacture's protocol. The cells were processed after 48 h post-transfection. The immunohistochemical analysis of FGFR2 knockdown in cells was determined by confocal microscopy. To determine the in vivo effect of FGFR2, a FGFR2 KO mouse model was generated. FGFR2 flox mice (Jackson Labs) were crossed with inducible keratocyte specific-Cre mice (Kera-rtTA/tet-O-Cre, Dr. Winston Kao, University of Cincinnati). The pregnant females were fed doxycycline chow (600 mg/kg) to induce tissue-specific FGFR2 KO pups. The flox-, Cre-, and wild-type (wt) mice were used as controls. Corneal thickness were determined using an ultrahigh resolution spectral domain optical coherence tomography instrument (SDOCT, Bioptigen).

Results: In vitro, FGFR2 gene silencing severely inhibited pluripotency of stromal keratocytes when cultured in the presence of FGF2 (FGFR2-ligand) compared to control siRNA. The FGFR2 gene silenced-cells also exhibited pluripotency in the presence of IGF, suggesting that FGFR2 was needed for the pluripotency maintenance of keratocytes. OCT-based analysis of the FGFR2 KO mice corneas showed relatively thinner cornea compared to control mice. Immunohistochemical analysis also showed thinner cornea in FGFR2 mice compared to the control mice. Collagen-1 immunostaining was significantly down-regulated in KO mice corneal stroma compared to control mice.

Conclusions: Our earlier results showed that FGFR2 was significantly downregulated in keratoconus corneal stroma. In vitro analysis showed FGFR2 knockdown affected the pluripotency of stromal keratocytes. The FGFR2 KO mice showed stromal thinning. Suggesting that the stromal-specific conditional FGFR2 KO mouse model will provide the functional understanding of FGFR2 in stromal keratocytes and also serve as a keratoconus animal model.

CONTROL ID: 3544293

SUBMITTER (NAME ONLY): Ankur Mehta

TITLE: Low temperature vacuum-dehydrated amnion membrane (Omnigen) - Case series for the treatment of ocular surface burn and related complications at a tertiary eye unit in the UK.

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mehta, S. Pradhan, F. Figueiredo, Ophthalmology, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|F. Figueiredo, Faculty of Medical Sciences, University of Newcastle upon Tyne, Biosciences Institute., Newcastle upon Tyne, Tyne and Wear, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Cryopreserved amniotic membrane (AM) is widely used in the management of ocular surface burns (OSB). A novel low-temperature vacuum-dehydrated AM product called Omnigen (NuVision, Nottingham, UK-Licensed 2015) is available, but its clinical use is not broadly reported. Omnigen (OG) is delivered to the eye as a pre-mounted device using a special contact lens (OmniLenz -OL). This case series aims to document and describe the use of OG for the treatment of ocular surface burns and its complications.

Methods: A retrospective analysis of consecutive patients with acute OSB and related complications undergoing treatment with pre-mounted OG was identified from a registry between September 2019 to December 2020. Electronic medical records were reviewed and the following data extracted at 2 time points (OG insertion and last follow up): demographics, best corrected visual acuity (BCVA) in LogMAR; symptoms; epithelial defect (ED) recorded in largest axis. Successful treatment was defined as no loss of BCVA (or improvement) or resolution of ED (less than 0.5mm).

Results: A cohort of 11 patients had unilateral OSB as their primary diagnosis, 5 (45.5%) patients had repeat OG treatments giving a total of 17 OG treatments, consisting of 2 acute alkali OSB and 15 chronic OSB (14 alkali and 1 thermal). All OSB were classified as Roper Hall grade 4 at presentation. Mean age of 35.6 (SD 12.7), 9.1% of which were female. Of the total treatments, 12 were left eyes (70.6%).

Pain was the most common presenting symptoms (n=12; 70.6%), then foreign body sensation in 5 cases (29.4%). Mean presenting BCVA was +2.4 (SD 1.2). Mean BCVA at last review was +2.3 (SD 1.1) mainly due to deeper corneal stromal damage. Mean ED was recorded as 3.4 (SD 2.9 mm). Mean follow-up was 3.3 (SD 3.8) months. Successful treatment was achieved in terms of BCVA in 16 (94.1%) of eyes treated and in terms of ED, in 13 (76.5%) eyes treated. There were no documented complications.

Conclusions: This study demonstrates Omnigen to be a successful and safe treatment for OSB in both acute and chronic setting. This study reports small numbers and a mixture of acute and chronic OSB. Therefore, further studies are needed to demonstrate the overall long-term efficacy and safety of OG in a clinical setting of acute and chronic OSB.

CONTROL ID: 3544296

SUBMITTER (NAME ONLY): Sonali Ghosh

TITLE: Transient Mitomycin C treatment of human corneal epithelial cells impacts expression of autophagy and cytokine genes and increases phagocytosis

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Ghosh, J. Thomasian, B. Karpinski, G. Tadvalkar, M. Stepp, Department of Anatomy and Cell Biology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|M. Morasso, Laboratory of Skin Biology, National Institutes of Health, Bethesda, Maryland, UNITED STATES|S. Brooks, Biodata Mining and Discovery Section, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland, UNITED STATES|M. Stepp, Department of Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: A single MMC treatment enhances reinnervation of the intraepithelial corneal nerves after debridement injury. RNAseq studies performed on mouse corneas revealed that MMC enhanced protease inhibitor expression in the epithelium. To confirm that the gene expression changes in mouse corneal epithelial cells was due to a direct impact of MMC on corneal epithelial cells, we performed RNAseq studies on transiently treated telomerase immortalized human corneal limbal epithelial (HCLEs) and primary human corneal epithelial (PHCLE) cells before and after MMC treatment.

Methods: HCLE and PHCLE cells were cultured in KSFM media to 70% confluence. Cells were treated with 0.0025% MMC for 3h followed by RNA extraction. For each variable, 4 replicate sets of RNA were isolated. mRNA expression profiling was performed in the NIAMS Genome Core Facility at the NIH. Single end, 50 base reads were mapped to the mouse genome mm10 using TopHat 2.1.0. For phagocytosis studies, fluorescent 1.0 mm latex beads were opsinized with BSA and added to cell cultures for 1 hr. Cells were washed, fixed and stained with phalloidin. The fluorescence intensity of the beads present per cell were corrected for difference in cell size.

Results: Comparing 5-fold up and down regulated genes, we determined genes that are altered in expression after MMC treatment in HCLE and PHCLE cells. There are 15 MMC signature genes with 11 upregulated and 4 down regulated. There are too few down regulated genes to determine shared gene ontology but the 11 up regulated genes show common gene ontology terms for cytokines with 4 of the genes falling into category [CXCL1, CXCL16, IL32, and ISG15]. In addition, MMC induced an increase in expression of autophagy and phagocytosis genes which was also shown by the phagocytosis studies.

Conclusions: MMC treatment impacts gene expression in the corneal epithelium both in vivo and in vitro in HCLE and PHCLE cells by inducing the up-regulation of numerous cytokines, autophagy and phagocytosis genes which lead to increased phagocytosis by corneal epithelial cells. The enhanced reinnervation seen in the mouse corneal epithelium after a single MMC treatment during debridement wounding may be due to its ability to alter immune cell recruitment via alterations in cytokine secretion and/or the improved ability to remove debris released by injured cells and severed axons.

CONTROL ID: 3544297

SUBMITTER (NAME ONLY): Raymond Warner

TITLE: Red Blood Cell Velocity Variability in Small Retinal Vessels

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Warner, T. Gast, K. Sapoznik, A. Carmichael-Martins, S.A. Burns, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: To understand the temporal and spatial variability of red blood cell velocity in small retinal vessels using a dual-beam Adaptive Optics Scanning Laser Ophthalmoscope

Methods: Experiment 1 measures temporal blood velocity variability in a local vascular region consisting of an arteriole, capillary, and venule by measuring blood velocities in 3 young healthy subjects repeatedly over two days. Data consisted of 10 imaging periods separated into two sessions: 1) Five 6-minute image acquisition periods with 30-minute rest intervals and 2) Five 6-minute image acquisition periods with 10-minute rest intervals. Experiment 2 measures spatial distribution of velocity variability by imaging three capillary segments in 5 young healthy subjects during three 2-minute imaging conditions: 1) A baseline imaging condition, 2) A full-field flicker and 3) no flicker condition again.

Images were collected in 3-second 100-frame videos at 29 Hz and processed via MATLABTM software. Red blood cells travelling through the selected capillaries were detected based on a z-score algorithm for the first channel. Then regions of interest centered on detected cells were averaged across all cell detections for each channel. Five videos were used for analysis during each condition. Regions of interests were averaged over three consecutive frames and the displacement of the average RBCs between both channels (3.32 ms) determines the velocity (mm/s).

Results: Red blood cell velocities were measurable in all subjects. The coefficient of variation (C.V.) was used to determine the physiological variability of the selected vessels among all subjects relative to the average velocity for each condition. Average C.V. for both days in arterioles was 7% (± 2), in capillaries was 19% (± 6), and in venules was 8% (± 2). ANOVA and post-hoc t-test showed significant differences in RBC variability in capillaries compared to arteriole and venules in Experiment 1 [$F(2, 118) = 199.70, p < 0.001$]. In Experiment 2, individual capillaries varied in their blood flow response despite changes in metabolic demand. Average C.V. was 16% during baseline, 15% during flicker stimulation, and 18% after flicker stimulation.

Conclusions: Small retinal vessels in humans exhibit unique spatial and temporal characteristics that are involved in meeting metabolic demand. This inherent variation places limits on studying vascular regulation at the single capillary level.

CONTROL ID: 3544299

SUBMITTER (NAME ONLY): Anderson Vu

TITLE: Quantitative evaluation of transplanted and host retinal tissues by optical coherence tomography

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Vu, V. Marwaha, J.K. To, A.W. Browne, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|V. Marwaha, University of California San Diego, La Jolla, California, UNITED STATES|B. Lin, M.J. Seiler, University of California Irvine Sue and Bill Gross Stem Cell Research Center, Irvine, California, UNITED STATES|B. McLelland, G. Nistor, H. Keirstead, I. Nasonkin, AIVITA Biomedical Inc., Irvine, California, UNITED STATES|A.W. Browne, Department of Biomedical Engineering, Institute for Clinical and Translational Science, University of California Irvine, Irvine, California, UNITED STATES|M.J. Seiler, Department of Physical Medicine & Rehabilitation, Anatomy & Neurobiology, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal organoids show great promise as a transplantable treatment for retinal degeneration. Quantifying organoid anatomical features and visual function recovery in vivo after organoid transplantation involves spectral domain optical coherence tomography (SD-OCT) and superior colliculus recordings (SCR). Volumetric analysis of organoid structures and its role in visual recovery has not been investigated. We sought to correlate transplant imaging characteristics on SD-OCT with SCR functional recordings in a model of retinitis pigmentosa with rhodopsin mutation (S334ter-3).

Methods: Human embryonic stem cells (hESC) were induced into retinal organoids and differentiated in vitro for 30-70 days. Retinal organoids suitable for transplantation were chosen based on outer tissue transparency and morphological criteria. Organoids were then transplanted into the subretinal space of S334ter-3 rats. SD-OCT were completed at 2 weeks and 1 month after transplantation, then every 1-2 months. After overnight dark adaptation, extracellular recording was utilized in the superior colliculus of the rats and the data was analyzed using MATLAB according to established procedures. SD-OCT were analyzed for native retina and transplant volume, morphology, and transplant distance to the optic disc using 3D Slicer and ImageJ, both open-source image analysis software.

Results: Preliminary data demonstrated rats with positive SCR had greater final organoid volumes than rats with no SCR. Further analysis is ongoing.

Conclusions: Our data showed that lower organoid transplant volumes were linked to lower visual function recovery. This pilot study suggests that quantitative and volumetric analysis of retinal organoid transplants using SD-OCT may predict the quality of retinal transplantation.

CONTROL ID: 3544301

SUBMITTER (NAME ONLY): Alyssa Coleman

TITLE: Frequency of known pathogenic gene mutations causing inherited retinal disease in a university and university-affiliated retina-only private practice

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Coleman, S.B. Patel, R.D. Sarran, M.W. MacCumber, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent promising results in the use of gene therapy for inherited retinal disease (IRD) have prompted the implementation of genetic testing to evaluate for the presence of mutations in relevant genes. This study reports the findings following a retrospective review of genetic testing results in patients diagnosed with IRD. Subsequent analysis of data will provide insight into the relative frequency of pathogenic retina-associated gene mutations within Chicago, IL.

Methods: A query was made of the Illinois Retina Associates (IRA) and Rush University Eye Center Physicians (RUECP) databases to identify patients with diagnoses representing IRD as identified by the following ICD-10-CM codes: pigmentary retinal disorder (H35.52), unspecified hereditary retinal dystrophy (H35.50), and other dystrophies primary involving the sensory retina (H35.53). Eligibility was confirmed via chart review. Patients were included if a prior diagnosis of IRD was present and associated with pending or returned genetic testing results. After confirming eligibility, the following de-identified data was entered into the study database: medical record number, age, gender, race, clinical diagnosis, genetic testing service, genetic panel used, and results.

Results: 487 patients at IRA and 49 at RUECP were identified as having appropriate codes between 1/1/2014 and 12/31/2020. 68 patients have been tested for retinal specific gene mutations through commercial genetic laboratories to date. 67 patients have testing resulted. 0/67 (0%) patients were positive for RPE 65. 49/67 (73%) patients had positive results of heterozygosity in at least one implicated gene. 54/67 (80%) patients had positive results of variants of unknown significance. Pathogenic variants were identified in 27 different genes, the most frequent being ABCA4, USH2A, and NR2E3 in decreasing order.

Conclusions: ABCA4 and USH2A were identified as the two most frequent implicated genes, consistent with previously published data. In contrast to prior publications, we found the third most frequent pathogenic variant to be NR2E3, which was previously reported as a rare cause of IRD. These contrasting findings suggest that additional analyses of IRD genetic testing results from large populations are required to provide those researching novel gene therapies with the target that will provide the greatest impact.

CONTROL ID: 3544307

SUBMITTER (NAME ONLY): Hamid Alemi

TITLE: Efficacy of Neuropeptide Alpha-Melanocyte Stimulating Hormone (α -MSH) in Suppressing Corneal Edema Following Acute Injury

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Alemi, S. Wang, N. Deshpande, T. Blanco, K. Pang, E. Yuksel, H. Nakagawa, R.B. Singh, T. Dohlman, J. Yin, U.V. Jurkunas, R. Dana, Department of Ophthalmology, Harvard Medical School, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal endothelial cells (CEnC) have minimal regenerative capacity, and insults to the endothelium may lead to significant corneal swelling. Studies have reported corneal nerve damage is associated with CEnC loss, suggesting nerves exert trophic effects on CEnC. Previously, we have demonstrated the cytoprotective function of the neuropeptide α -MSH against inflammatory and oxidative stress in CEnC ex vivo. Here, we investigate the efficacy of α -MSH in preventing corneal edema in a model of corneal endothelial injury.

Methods: Corneal injury was induced by transcorneal freezing in BALB/c mice (n=8/group) by placing a -196°C 2 mm-diameter steel rod on the center of the cornea for 10 seconds. Beginning immediately after injury, mice received subconjunctival injections of 10 μL of 10^{-4} M α -MSH or PBS (control) twice weekly for a total of 8 weeks. Corneal edema was evaluated by assessing corneal opacity on slit lamp biomicroscopy and central corneal thickness (CCT) via optical coherence tomography. CEnC density and variability in cell size (polymegathism) and shape (hexagonality) were evaluated by in vivo confocal microscopy.

Results: In the untreated control group, transcorneal freezing led to significant corneal edema on d1 post-injury (CCT:180 \pm 28 μm vs. baseline 101 \pm 2 μm , P=0.007) which remained elevated 8wk after injury (186 \pm 14 μm , P<0.001). There was a significant reduction in CEnC density (1821 \pm 42 cell/mm² vs. baseline 2954 \pm 67, P<0.001), an increase in polymegathism (CV: 41 \pm 3 vs. baseline 28 \pm 2, P=0.001) and a decline with a trend to significance in CEnC hexagonality (hexagonal cells%: 52 \pm 3 vs. baseline 59 \pm 4, P=0.079) at 8wk in the control group. In contrast, treatment with α -MSH restored normal (pre-injury) CCT (103 \pm 3 μm , P=0.60). Further, compared to untreated control, subconjunctival injections of α -MSH led to clearer corneas with a significant reduction in edema (117 \pm 12, P=0.004), improved CEnC density (2209 \pm 132, P<0.001) and reduced CEnC polymegathism (CV:34 \pm 2, P=0.001). Restoration of normal CEnC morphology occurred earlier in the α -MSH treatment group compared to the control group.

Conclusions: Our results demonstrate that following corneal injury, treatment with α -MSH reverses corneal endothelial function by reducing CEnC loss. Our findings suggest a therapeutic role for α -MSH in preventing/restoring endothelial function following corneal injuries.

CONTROL ID: 3544309

SUBMITTER (NAME ONLY): Yuna Park

TITLE: Investigating the Timing and Regulation of Developmental Retinal Ganglion Cell Death in Human Stem Cell-Derived Organoids

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y.K. Park, T. Brooks, A. Vielle, M. Vergara, CellSight Ocular Stem Cell and Regeneration Program, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|A. Vielle, M. Vergara, Linda Crnic Institute for Down Syndrome, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: During development, the proper histoarchitecture of the retina is achieved through a delicate balance between proliferation, differentiation, and cell death. Retinal ganglion cells (RGCs) in particular increase in numbers during development except for two periods of sharp decline that appear conserved in vertebrates. The mechanisms responsible for these phenomena are incompletely understood. Notably, we observed that the first wave of RGC death is replicated within human stem-cell derived retinal organoids. Thus, we took advantage of this model to investigate the mechanisms of RGC death in the developing human retina.

Methods: Retinal organoids were differentiated from human induced pluripotent stem cells (hiPSCs) and collected weekly between weeks 6 and 10 of differentiation. The timeline of the first wave of RGC death was characterized by immunofluorescent staining of RGCs and further confirmed in organoids generated from a fluorescent reporter line. Potential microglia involvement was evaluated at the transcriptional and translational levels. TUNEL and activated caspase 3 immunostaining were performed to assess for apoptotic cell death, and Western blot was used to identify the intracellular pathways involved.

Results: Retinal ganglion cell numbers consistently decreased at week 8 of differentiation, as observed by different quantitative methods. Immunofluorescent staining for IBA1 and RT-PCR for microglia markers verified the absence of microglia in this model, while a spike in cell death coinciding with the trough in RGC numbers was observed by TUNEL staining and cleaved caspase 3 immunofluorescence. Interestingly, we observed a decrease in the BAX/BCL2 ratio and a marked increase in cleaved caspase 8, suggestive of the involvement of the extrinsic apoptotic pathway.

Conclusions: Human retinal organoids recapitulate the first wave of developmental ganglion cell death in vitro. The absence of microglia in this model and the evidence of caspase-dependent apoptosis revealed an additional contributor to regulating RGC numbers in human retinal development. The activation of caspase 3 and caspase 8 suggest the recruitment of the extrinsic apoptotic pathway. This knowledge can lead to new insights regarding congenital retinal abnormalities.

CONTROL ID: 3544310

SUBMITTER (NAME ONLY): Sayali Pradhan

TITLE: Dupilumab induced ocular surface disease: a prospective study.

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We aimed to identify the incidence, risk factors, demographic and clinical profile for Dupilumab-induced ocular surface disease (DIOSD) in patients with atopic dermatitis (AD) and propose a standardised treatment protocol

Methods: Prospective case series including 40 eyes of 20 patients with AD developing ocular symptoms after commencing Dupilumab at the Royal Victoria Infirmary referred to the Corneal Service from dermatology department, between September 2018 to May 2019. Patients were evaluated using a standard history and examination protocol including subjective symptom severity grading and Ocular Surface Disease Index (OSDI) questionnaire on each visit. Patient demographics, onset and severity of ocular symptoms, BCVA and slit-lamp examination findings were evaluated. Standard treatment prescribed included topical dexamethasone 0.1% preservative free (PF) tapering dose, ketotifen 0.025% (PF), ciclosporin 0.1% PF, lubricants and hydrocortisone 0.5% ointment for lid margins.

Results: Thirty two (28.31%) Dupilumab treated AD patients out of 113 consecutive patients developed DIOSD, 20 (62.5 %) of which were evaluated in the Cornea Service. The median age was 38.0 years (SD 15.8; range 19 – 74). Equal male to female ratio. History of allergic conjunctivitis was reported in 50%. The average time to onset of ocular symptoms was 9.2 (SD 8.7) weeks. Symptoms included burning, itching, tearing, foreign body sensation, photosensitivity, and discharge. 90% of patients had bilateral conjunctival inflammation and blepharitis at presentation. Good response to treatment was noted with significant improvement in the subjective severity scale and the mean OSDI score (from 34.0 to 10.2). Median follow-up was 18 weeks (SD 9.4; range 10-44).

Conclusions: DIOSD is not uncommon. No difference in severity was noted in patients with a previous history of allergic conjunctivitis. Most cases responded well to topical anti-inflammatory treatment combined with anti-allergic eye drops. No patient discontinued Dupilumab. With timely referral and appropriate treatment better clinical outcomes and patient satisfaction can be achieved. Further prospective studies with longer follow-up with a focus on the efficacy of prophylactic topical treatment prior to starting Dupilumab and possible disease mechanisms are needed.

CONTROL ID: 3544311

SUBMITTER (NAME ONLY): J. Mark Petrash

TITLE: Structural and Functional Consequences of Aldose Reductase Overexpression in Retina

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Petrash, B. Shieh, M. Pedler, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

Commercial Relationships Disclosure (Abstract): J. Mark Petrash: Commercial Relationship: Code N (No Commercial Relationship) | Biehuoy Shieh: Commercial Relationship: Code N (No Commercial Relationship) | Michelle Pedler: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aldose reductase transgenic (AR-Tg) mice created to model diabetic eye disease showed an unexpected diabetes-independent phenotype involving cell swelling at the retinal nerve fiber layer and decreases in pattern ERG compared to controls. The purpose of our study was to identify the cell types and potential role of AR as a driver of this phenotype.

Methods: PCR genotyping ruled out the Rd8 mutation of the Crb1 gene in this model. Retinal morphology was routinely assessed by H&E staining. Immunofluorescence was used for detection and quantitation of Brn3a as a marker for RGCs, GFAP and CRALBP for Müller glia, and Iba-1 for microglia, and a species-specific antibody to human AR (AKR1B1) to map transgene expression. GraphPad Prism was used to measure differences in comparison groups according to either t-test or 1 way ANOVA followed by Tukey's Multiple Comparison Test.

Results: The human AR (hAR) transgene was designed using a hybrid lens crystallin gene promoter. As expected, strong immunostaining was observed in lens. Unexpectedly, we observed a significant ($p<0.01$) increase in the number of hAR-immunopositive cells in the RGC and inner nuclear layers compared to nontransgenic controls. By 18 weeks of age, and in the absence of experimentally-induced diabetes, AR-Tg mice developed a layer of swollen and vacuole-rich cells adjacent to the RGC layer ($p=0.003$). Treatment from birth with Sorbinil (0.25mg/ml in drinking water), a well characterized AR inhibitor, prevented these changes ($p=0.003$), suggesting that the change in cell morphology was associated with AR activity. Patterns of immunostaining with GFAP, CRALBP, and hAR species-specific antiserum suggest that the swollen cells are likely endfeet of Müller glia containing transgene-derived hAR. In addition, a proinflammatory phenotype characterized by increased numbers of activated retinal microglia was observed in AR-Tg retina compared to nontransgenic control ($p<0.001$) or after treatment with Sorbinil ($p<0.01$).

Conclusions: Elevated levels of AR gene expression typical of the diabetic retina induce a proinflammatory phenotype in mouse Müller glia and retinal microglia. Sorbinil substantially prevented these structural and functional changes, suggesting that suppression of retinal inflammation by AR inhibitors may represent a novel approach to prevention of diabetic retinopathy.

CONTROL ID: 3544312

SUBMITTER (NAME ONLY): Markus Schranz

TITLE: Does retinal fluid correlate with OCTA characteristics of choroidal neovascular membranes?

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schranz, R. Told, V. Hacker, P.K. Roberts, G.S. Reiter, A. Reumueller, W. Vogl, H. Bogunovic, S. Sacu, U. Schmidt-Erfurth, Medizinische Universität Wien Universitätsklinik für Augenheilkunde und Optometrie, Wien, Wien, AUSTRIA|G.S. Reiter, W. Vogl, H. Bogunovic, U. Schmidt-Erfurth, Laboratory for Ophthalmic Image Analysis, Medizinische Universität Wien, Wien, Wien, AUSTRIA|

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ABSTRACT BODY:

Purpose: To identify an association between the vascular properties of choroidal neovascularization obtained by optical coherence angiography (OCT-A) and the resulting amount of retinal fluid (RF) in neovascular age related macular degeneration (nAMD).

Methods: In this prospective observational study, 54 patients with type 1 and type 2 treatment naïve nAMD were included and treated according to a treat and extend regimen with intravitreal aflibercept.

At baseline and month 1 each patient underwent the following examinations:

A 97-line high resolution OCT volume scan using HR2 + OCT device (Spectralis, Heidelberg Engineering, Germany).

A deep learning algorithm was used to automatically detect, quantify and localize RF in OCT volume scans.

A 6x6mm volumetric flow scan was made using a swept-source OCTA device (PlexElite 9000, Zeiss). Angio Tool GUI was used to skeletonize MNV properties and quantify MNV area (VA), vessel density (VD), total number of endpoints (TNE), total number of junctions (TNJ), junction density (JD) and total vessel length (TVL). Subsequently linear regression models and mixed models were used to analyze.

Results: Fluid and MNV properties were not normally distributed, therefore logarithmization was performed to normalize data prior to linear regression.

The median amount of total RF was 173.7 nl (84.7; 614.5) at baseline, which consisted of 156.6 nl (60.3; 435.8) of subretinal fluid (SRF) and 2.3 nl (0.04; 22.3) of intraretinal fluid.

After the first anti-VEGF treatment the median amount of RF decreased to 5.0nl (0.96; 18).

RF at baseline was significantly associated with the numbers of TNE (coefficient= 0.50; $p=0.002$; $R^2=0.17$), SRF with TVL (coefficient= 0.33; $p=0.04$; $R^2=0.08$) and TNE (coefficient= 0.57; $p=0.000762$; $R^2=0.2$). IRF was significantly associated with VA (coefficient= 1.082; $p=0.04$; $R^2=0.08$).

None of the vessel parameters was significantly associated with the relative fluid decrease after the first anti-VEGF treatment.

Conclusions: In this study population the number of endpoints as well as the vessel length correlated with the volume of fluid at baseline, indicating that these vessel parameters were biomarkers for exudative activity. However, none of the vessel parameter had an influence on the treatment response.

CONTROL ID: 3544313

SUBMITTER (NAME ONLY): Todd McLaughlin

TITLE: The Neuroprotective Action of p58IPK is Independent of Macrophage Regulation in Retinal Disease Models

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. McLaughlin, J. Wang, J.J. Wang, S.X. Zhang, Ophthalmology and Ross Eye Institute, University at Buffalo, Buffalo, New York, UNITED STATES|T. McLaughlin, J.J. Wang, S.X. Zhang, SUNY Eye Institute, State University of New York, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: p58IPK is a multifunctional ER chaperone and a regulator of cell stress response in a variety of cell types and tissues including the retina, pancreas, and immune cells. The goal of the present study is to evaluate the neuroprotective effect of p58IPK overexpression in mouse retina and elucidate the mechanism by which p58IPK acts as a neuroprotectant involving regulation of macrophage activation.

Methods: Conditional knockout (cKO) of p58IPK in macrophages was achieved by crossing p58IPK floxed mice with a myeloid-specific Cre line (LysM-Cre). We determined knockout efficiency by qPCR in cultured bone marrow derived macrophages (BMDMs). Overexpression of p58IPK in wild type (WT) retina was accomplished by intravitreal injection of adeno-associated virus (AAV). Neurodegeneration was assessed at 14 days post-induction in two disease models, a microbead induced increase in intraocular pressure (IOP) and an ischemia-reperfusion (IR) model. The loss of RGCs was examined by immunohistochemistry (IHC) for Brn3a. The structure and function of the cKO eyes were assessed by IHC for multiple retinal markers, morphological measurements, and electroretinogram (ERG).

Results: We find that BMDMs from p58IPK fl/fl; LysM-Cre (p58IPK cKO) mice have a 97% knockdown of p58IPK mRNA compared to BMDMs from p58IPK fl/fl (WT) mice, validating the loss of p58IPK from macrophages. p58IPK cKO retina has no substantial differences from WT retina in retinal structure or cellular composition, including the number of Brn3a+ RGCs. p58IPK cKO mice have a trend for reduced b wave amplitudes in both light- and dark-adapted ERGs compared to WT mice. Injection of AAV-p58IPK in WT mice with increased IOP results in greater Brn3a+ RGC survival compared to AAV-GFP overexpression. However, in p58IPK cKO mice, in which p58IPK is lost only in macrophages, we find no difference in Brn3+ RGC survival compared to WT using the same IOP model. Similarly, p58IPK cKO mice suffer identical loss of Brn3a+ RGCs in the IR model, compared to WT.

Conclusions: Though broad p58IPK overexpression in retina reduces RGC loss in disease models, the loss of p58IPK specifically in macrophages does not substantially ameliorate RGC loss in the same model or in a second disease model. These results suggest that the neuroprotective effect of p58IPK does not likely involve a regulation of macrophage activation.

CONTROL ID: 3544316

SUBMITTER (NAME ONLY): Milan Patel

TITLE: In silico Characterization of Tyrp1 Molecular Docking and Associated OCA3 Mutants

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.H. Patel, M.B. Dolinska, Y.V. Sergeev, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Milan Patel: Commercial Relationship: Code N (No Commercial Relationship) | Monika Dolinska: Commercial Relationship: Code N (No Commercial Relationship) | Yuri Sergeev: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Oculocutaneous albinism type 3 (OCA3) is an autosomal recessive disorder caused by mutations in the TYRP1 gene. Tyrosinase-related protein 1 (Tyrp1) is involved in eumelanin synthesis, catalyzing the oxidation of dihydroxyindole carboxylic acid oxidase (DHICA) to indolequinone carboxylic acid (IQCA). Here, we used computational methods to assess molecular docking of DHICA and IQCA in Tyrp1 and associated OCA3 mutants.

Methods: The mutations for analysis, C30R, H215Y, D308N, and R326H, were selected from ClinVar and The Human Gene Mutation Database. The crystal structure of human Tyrp1 (5M8L) was minimized using molecular dynamics in water and subjected to global mutagenesis to ascertain the $\Delta\Delta G$ values of folding. In total, four known mutations of Tyrp1 and the wild type (chain A of 5M8L) were simulated for 100 ns in pH 5.5. Global mutagenesis was conducted to identify residues critical to protein folding, a Weighted Histogram Analysis Method (WHAM) was applied to compare free energy landscapes of the active site between the wild type and mutants, and Maestro software was used to dock DHICA and IQCA.

Results: C30R and H215Y exhibit greater instability according to experimental results, which is consistent with their unfolding parameters of 1, indicating protein misfolding. Global mutagenesis suggests that of the four mutants, D308N and R326H were the only ones that were not completely unfolded or misfolded, with unfolding parameters of 0.56 and 0.98, respectively. Free energy landscapes generated by WHAM indicate that the binding cleft (residues Y362, N378, and T391) of both of these mutants are larger and less well defined. The docking of DHICA in Tyrp1 highlights four interactions that remain constant between DHICA and the protein: three hydrogen bonds and one salt bridge. D212 and E216 are the most common recipients of these interactions.

Conclusions: Our observations are consistent with the results of biochemical analysis of recombinant Tyrp1 and four mutant variants from this study. The docking of DHICA, in the most stable protein conformations as determined by WHAM, indicate that the hydrogen bond and salt bridge interactions that stabilize DHICA remain similar among wild type Tyrp1, D308N, and R326H. However, the strength of these interactions and stability of the docked ligand may decrease proportionally to mutation severity due to the larger and less well-defined nature of the binding cleft in mutants.

CONTROL ID: 3544317

SUBMITTER (NAME ONLY): Nobuyoshi Unno

TITLE: Comparing Vessel Whitening Using Confocal Scanning Laser MultiColor and Color Fundus Imaging in Retinal Vein Occlusion

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Unno, University of California San Diego, La Jolla, California, UNITED STATES|V. Alex, M. Jhingan, W.R. Freeman, S. Borooah, Joan and Irwin Jacobs Retina Center, La Jolla, California, UNITED STATES|L. Lando, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Identification of sclerotic vessels resulting from ischemia can be challenging with conventional color fundus photography (CFP). We aim to use this pilot study to evaluate the detection of retinal vessel whitening from branch retinal vein occlusion (BRVO) using CFP and newer confocal scanning laser Multicolor (MC) imaging.

Methods: This retrospective study identified patients with BRVO using the imaging database at the University of California San Diego. Whitening on CFP and MC was graded by retinal specialists compared to reference images. Graders were asked to choose their preferred MC channel (infrared, blue, or green) to identify whitening. Vessel whitening by MC was further correlated to the area of ischemia on FFA and analyzed longitudinally.

Results: MC images from 32 BRVO patients (n=33 eyes, 21 females, mean age 69.7 years) and 29 healthy controls (n=29 eyes, 20 females, 70.1 years) were analyzed. To test the difference in MC versus CFP for vessel sclerosis detection, 24 patients (n=24 eyes) with available images in both modalities were graded and compared, showing a significantly higher grade of vessel whitening by MC compared with CFP ($p < 0.05$). The green channel was preferred in 70% of MC images to best identify whitening in cases with whitening visible on CFP (n=30 eyes, 3 eyes were excluded due to poor image quality), followed by blue (30%) and 0% infrared. Longitudinal analysis with MC images (n=32 cases/194 eyes) found significantly higher grading scores, indicating more vessel whitening, as time progressed ($p < 0.001$). Finally, MC images matched with same-date fluorescein angiography (n=28 cases/eyes) had a moderate correlation between vessel whitening and the area of ischemia ($r=0.438$, $p=0.022$).

Conclusions: MC imaging appears to better identify retinal vessel whitening compared with CFP in BRVO patients, preferably with the green MC channel. A limiting factor in this study was that in some cases MC and CFP images were not taken on the same day. However, the MC module may be a quick, non-invasive tool to highlight vessel whitening in ischemic BRVO.

CONTROL ID: 3544318

SUBMITTER (NAME ONLY): Kelly Coutant

TITLE: Impact of melanomic extracellular vesicles in the metastatic process of uveal melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Coutant, L. Piquet, S. Landreville, Ophthalmology, Université Laval, Québec City, Québec, CANADA|K. Coutant, L. Piquet, A. Mitchell, J. Bérubé, S. Landreville, Regenerative medicine, Centre de recherche du CHUQ, Québec City, Québec, CANADA|F. Bordeleau, Molecular biology, medical biochemistry and pathology, Université Laval, Québec City, Québec, CANADA|F. Bordeleau, Oncology, Centre de recherche du CHUQ, Québec City, Québec, CANADA|A. Brisson, UMR-CBMN, CNRS, Université de Bordeaux, Bordeaux, FRANCE|

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ABSTRACT BODY:

Purpose: Uveal melanoma is the most common primary intraocular tumor in adults and arises from the transformation of melanocytes. Despite the treatment of the eye tumor, the survival of patients is greatly reduced due to the development of metastases to the liver. Extracellular vesicles (EVs) are released by cancer cells, which allow oncoproteins or genetic material to be transferred to distant cells in order to modify their microenvironment and promote the spread of cancer. Our hypothesis is that EVs from the ocular tumor prepare the hepatic stroma for metastatic cell colonization via endothelial cells and by activating hepatic stellate cells. Our study aims to characterize the melanocytic and melanomic EVs and to study their impact on the hepatic microenvironment and their interactions with liver cells.

Methods: EVs were isolated from uveal melanoma cells and melanocytes by differential centrifugation. Their concentration/size were characterized by Western immunoblotting, high-sensitivity flow cytometry and cryogenic electron microscopy using exosomal or melanomic markers. The mechanisms of internalization of EVs in hepatic stellate cells and endothelial cells have been investigated by confocal microscopy using inhibitors of endocytosis pathways. The contractility of stellate cells on more or less rigid hydrogels and the tubular organization of endothelial cells on Matrigel post-exposure to melanomic EVs were determined by traction force microscopy or time-lapse. The selective biodistribution of EVs in organs was studied by fluorescence imaging in mice.

Results: The extravesicular fraction of uveal melanoma cells and melanocytes contained exosomes and microvesicles. The stellate cells that had internalized the melanomic EVs were more contractile, while the endothelial cells developed capillary-like tubular networks faster. Melanomic EVs were mainly accumulated in the liver and lungs of mice.

Conclusions: We have demonstrated that the extravesicular signaling from uveal melanoma cells activates hepatic stellate cells, which become more contractile. Melanomic EVs also have proangiogenic potential. The discovery of melanoma-specific proteins on the surface of the EVs of metastatic patients could lead to the development of new imaging modalities for micrometastases or drug vectors for targeted delivery to liver metastases.

CONTROL ID: 3544319

SUBMITTER (NAME ONLY): Gideon Obasanmi

TITLE: Granzyme B degrades extracellular matrix and promotes choroidal neovascularization in an ex-vivo microvascular angiogenesis model

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Obasanmi, Y. Tian, J.Z. Cui, J.A. Matsubara, Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|C.T. Turner, M.R. Zeglinski, D.J. Granville, Department of Pathology, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

Commercial Relationships Disclosure (Abstract): Gideon Obasanmi: Commercial Relationship: Code N (No Commercial Relationship) | Yuan Tian: Commercial Relationship: Code N (No Commercial Relationship) | Jing Cui: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Turner: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Zeglinski: Commercial Relationship: Code N (No Commercial Relationship) | David Granville: Commercial Relationship(s);viDa Therapeutics:Code E (Employment);viDa Therapeutics:Code P (Patent);viDa Therapeutics:Code S (Non-remunerative) | Joanne Matsubara: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Granzyme B (GzmB) is a cytotoxic serine protease that advances aging/age-related diseases and chronic inflammation via pathological extracellular matrix (ECM) degradation and increased vascular permeability. Extracellular GzmB is increased in the aging outer retina and in the choroid of donor eyes with neovascular AMD (nAMD) and with choroidal neovascularization (CNV), but its role in CNV is not known. This study determines the effect of exogenous GzmB using an ex vivo model of microvascular angiogenesis.

Methods: Ex vivo choroid sprouting assay (CSA) using peripheral retinal pigment epithelium (RPE)/Bruch's membrane (BrM)/choroid/sclera tissue explants from 3-month-old C57BL/6 mice was established and cultured for 10 days. Explants were stimulated with either exogenous GzmB (50nM) or PBS on Days 4, 6, 8 and 10 of culture. Western blot was performed to assess the expression and cleavage of ECM proteins, decorin and fibronectin in the CSA supernatant. Images of CSA explants were captured, vascular sprouting was analysed and quantified by a standardized SWIFT-Choroid macro based on ImageJ software. CSA relative vascular sprouting area (mm²) and western blot relative band intensity data were statistically evaluated.

Results: Relative vascular sprouting area was significantly ($p < 0.05$; $n \geq 11$ per group) increased in choroid explants stimulated with exogenous GzmB compared with controls. Western blot also reveals significantly increased cleavage of fibronectin ($p = 0.001$; $n = 3$ per group) and expression of decorin ($p < 0.05$; $n = 4$ per group) in GzmB-stimulated choroid explants compared with controls. ECM remodelling induced by GzmB cleavage of important ECM proteins could diminish outer retinal barrier function, promote vascular leakage and inflammation, and dysregulated angiogenesis in CNV.

Conclusions: GzmB cleavage of ECM proteins including decorin and fibronectin may contribute to CNV development in nAMD via an ECM remodelling/pro-angiogenesis pathway. Further studies are needed to investigate the possibility that pharmacological inhibition of extracellular GzmB could mitigate CNV in nAMD.

CONTROL ID: 3544322

SUBMITTER (NAME ONLY): Minjae Kim

TITLE: In-silico comparison of CB2 selectivity among endocannabinoid ω -6 and -3 epoxyethanolamides

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Kim, G.W. McCollum, J.S. Penn, Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Minjae Kim: Commercial Relationship: Code N (No Commercial Relationship) | Gary McCollum: Commercial Relationship: Code N (No Commercial Relationship) | John Penn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Cannabinoid (CB) receptors are G-coupled protein receptors, and two CB receptors have been identified so far, CB1 and CB2. There is abundant data suggesting that epoxyeicosatrienoic ethanolamides (EET-EAs) and epoxydocosahexaenoic ethanolamides (EDP-EAs), which are derived from ω -6 and -3 fatty acids, respectively, may inhibit retinal inflammation through CB2 activation. In this study, we aim to provide a comprehensive in-silico comparison of the regioisomers of EET-EA and EDP-EA on their affinities to CB1 and CB2.

Methods: CB1 (PDB:5TGZ) and CB2 (PDB:5ZTY) have been used for molecular docking of 5,6-, 8,9-, 11,12-, and 14,15-EET-EA as well as 4,5-, 7,8-, 10,11-, 13,14-, 16,17-, and 19,20-EDP-EA. Additionally, arachidonoyl ethanolamide (AEA), docosahexaenoyl ethanolamide (DHA-EA), CB1-selective AM-6538 (PubChem CID: 46912833), and CB2-selective AM-10257 (PubChem CID: 137321161) have also been investigated. Docking was carried out with AutoDock Vina (Scripps Research, USA) and scored by their binding free energy, ΔG in kcal/mol. Their protein-ligand interactions were visualized with PyMOL (Schrödinger, Inc., USA).

Results: AM-6538 and AM-10257 displayed CB1- and CB2-selectivity, respectively, and their predicted binding modes were consistent with their crystallographies in the literature. AEA and DHA-EA displayed preference for CB2 over CB1, and their metabolites, EET-EA and EDP-EA, shared a similar pattern but showed more CB2-selectivity. This is consistent with the literature in that the epoxygenation step of AEA and DHA-EA serves as a "bioactivation" event, since the products exhibit enhanced selectivity for CB2. Among EET-EAs, 11,12-EET-EA had the highest affinity to CB2 (ΔG of -8.3 kcal/mol). Among EDP-EAs, 19,20-EDP-EA had the highest affinity to CB2 (ΔG of -9.0 kcal/mol). The PyMOL visualization predicted that the intracellular region of CB receptors most likely contains the binding site, where phenylalanine at position 183 in CB2 associates with hydrophobic tails of EET-EA and EDP-EA.

Conclusions: The results predict that EET-EA and EDP-EA bind to the intracellular region of cannabinoid receptors and are more CB2-selective than their parent compounds, AEA and DHA-EA. Considering the rising interest in CB2 agonism to inhibit retinal inflammation, these epoxygenated fatty acids, specifically 11,12-EET-EA and 19,20-EDP-EA, can be potentially useful in inhibiting inflammation in DR.

CONTROL ID: 3544325

SUBMITTER (NAME ONLY): Jonathan Siktberg

TITLE: Visual acuity changes in eyes with poor presenting vision treated with bevacizumab for exudative age-related macular degeneration

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Siktberg, S. Berkowitz, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|S. Patel, Department of Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jonathan Siktberg: Commercial Relationship: Code N (No Commercial Relationship) | Sean Berkowitz: Commercial Relationship: Code N (No Commercial Relationship) | Shrijj Patel: Commercial Relationship(s);Alcon:Code F (Financial Support)

ABSTRACT BODY:

Purpose: The literature is limited on the visual acuity outcomes of patients with a poor presenting visual acuity (VA) who undergo bevacizumab treatment for neovascular age-related macular degeneration (nAMD), especially since the landmark bevacizumab trials excluded patients with VA < 20/320. We performed a retrospective, observational cohort study to investigate the annual visual acuity changes of patients who had a presenting VA worse than 20/320 and underwent bevacizumab therapy for nAMD.

Methods: Eyes with a presenting VA < 20/320 treated for nAMD with bevacizumab from January 1, 2012 to December 31, 2020 were included. Eyes with previous intravitreal anti-VEGF injections, previous non-cataract intraocular surgery, or < 12 months of treatment were excluded. Data on visual acuities, number of injections, and treatment regimen were collected annually. The primary outcome was the mean VA change from presentation at one year in Early Treatment Diabetic Retinopathy Study (ETDRS) letters. Secondary outcomes included the mean VA change at years 2-6 and the percentage of eyes that gained attained vision > 20/320 at one year.

Results: 120 eyes completed at least one year of treatment and qualified for the study. The mean VA change at 1 year was +20.5 letters (SD=26.0). 53 eyes (44.2%) achieved vision > 20/320 at one year. The mean VA change at 2 and 3 years was +16.0 letters (SD=23.8, N=89) and +17.8 letters (SD=27.5, N=59), respectively. The annual total number of injections and the VA change in subsequent years are summarized in Table 1.

Conclusions: Eyes with poor presenting vision treated for nAMD with bevacizumab can gain visual acuity in the first year of treatment and maintain some degree of improved vision in subsequent years.

CONTROL ID: 3544335

SUBMITTER (NAME ONLY): Jeffrey Hunter

TITLE: Intact hand kinematics in anisometropic children during visually-guided reaching

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Hunter, R. Jost, K.R. Kelly, Retina Foundation of the Southwest, Dallas, Texas, UNITED STATES|C. Beauchamp, L. Dao, ABC Eyes Pediatric Ophthalmology, PA, Dallas, Texas, UNITED STATES|B. Luu, Pediatric Ophthalmology and Adult Strabismus, Plano, Texas, UNITED STATES|E. Niechwiej-Szwedo, Kinesiology, University of Waterloo, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Coordination between eye and hand movements is essential for a child's interaction with the environment. We previously reported longer reach times in strabismic children, and in children with impaired binocularity, compared with controls (Kelly et al, ARVO, 2019, 2020). Anisometropia results in reduced binocularity, but to a lesser extent than strabismus. Thus, reaching in anisometropic children may not be disrupted. Here, we evaluate hand kinematics during visually-guided reaching in children with anisometropia.

Methods: Results from 21 children (age 7-12 years) diagnosed with anisometropia (visual acuity, 20/16–20/630; stereoacuity, 40"–nil) were compared to 20 age-similar controls. Hand movements were recorded using the LEAP motion device. Children reached and touched a small dot that appeared in 1 of 4 positions ($\pm 5^\circ$ or $\pm 10^\circ$ horizontally displaced from fixation). Kinematic measures were time-to-reach onset, reach duration, peak velocity, duration of acceleration, and duration of deceleration. Sensory factors were amblyopia (present n=15 vs not present n=5) and stereoacuity (nil n=6 vs measurable n=14).

Results: Anisometropic children did not differ on any hand kinematic measure compared with controls (time to reach onset, 333 ± 73 vs 334 ± 61 ms, $p=0.98$; reach duration, 516 ± 66 vs 526 ± 47 ms, $p=0.50$; peak velocity, 1.35 ± 0.24 vs 1.35 ± 0.16 m/sec, $p=0.91$; duration of acceleration 187 ± 26 vs 189 ± 24 ms, $p=0.85$; duration of deceleration 324 ± 48 vs 334 ± 37 ms, $p=0.43$). Hand kinematics did not differ with sensory factors (amblyopia, stereoacuity).

Conclusions: Despite decorrelated binocular experience during a critical period of visuomotor development, we found no significant impact of anisometropia on hand kinematics during visually-guided reaching in children. This finding may be due to better binocularity outcomes found in anisometropic children compared with strabismic children. Children, regardless of visual deficit, may increase their speed of reaching, but pay a price with precision. Children with normal vision may improve precision and accuracy with experience, but those with abnormal vision may compensate and adapt movements (increased duration of acceleration, reduced peak velocity) to reach normal levels of accuracy and precision, as seen in adults with anisometropic amblyopia (Niechwiej-Szwedo et al, 2011). However, spatial accuracy and precision cannot be measured reliably with the LEAP device.

CONTROL ID: 3544337

SUBMITTER (NAME ONLY): Bela Parekh

TITLE: Digital Media Effects on Glaucoma Eye Care During COVID-19

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Gauge the impact of digital medicine and associated tools on glaucoma management and medication adherence during the COVID-19 pandemic.

Methods: The study was conducted at EyeCare Consultants of New Jersey's two locations in Woodland Park and Edison, NJ. Eye care professionals (ECPs) (two ophthalmologists & two optometrists) surveyed 100 glaucoma patients during the first several months of the COVID-19 pandemic (March - August 2020). All those surveyed received previous digital instruction with CheckedUp, a patient education digital platform utilizing auditory, visual, and touch elements to engage patients with eyecare education during prior in-person visits. All patients were randomized into two groups: Group 1 received traditional phone calls while Group 2 received video calls (video with ECP and screen share of CheckedUp) during the pandemic to ensure adherence with ocular medications and address acute issues during this time period. All patients in Group 2 were shown the same glaucoma educational videos in English using the CheckedUp platform. Both groups received follow-up with an in-person visit in August. Surveys elicited responses to gauge consistency of ocular medication use.

Results: Adherence was defined as daily compliance with the glaucoma medication throughout the five-month period. The survey results demonstrated a significant difference between Group 1 and Group 2. Adherence during months without in-person office visits were compared to self-reported adherence for the same five-month time period in the year prior to the COVID-19 pandemic. Group 1's overall adherence was 64% (32/50 patients) at the August in-person visit and revealed that several patients used their drops inconsistently or differently from their prescribed regimen. Group 2's overall adherence was 90% (45/50 patients) at the August in-person visit and patients demonstrated continued comprehension of glaucoma risk and the importance of consistent medication use. A majority of Group 2 patients also commented that the ECP video call with CheckedUp helped reinforce the importance of eye pressure control in glaucoma.

Conclusions: This study illustrates the ability of digital medicine platforms to supplement in-person office visits to manage glaucoma, even during a pandemic such as COVID-19. Compliance remains an important issue in the medical management of glaucoma and digital solutions like CheckedUp assist with optimizing patient care.

CONTROL ID: 3544338

SUBMITTER (NAME ONLY): Theresa Akoto

TITLE: Identifying the target genes of PPIP5K2 in relation to keratoconus

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Akoto, J. Cai, Z. Chen, M.A. Watsky, Y. Liu, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|C. Gu, S.B. Shears, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, UNITED STATES|Y. Liu, Augusta University Center for Biotechnology and Genomic Medicine, Augusta, Georgia, UNITED STATES|M.A. Watsky, James and Jean Culver Vision Discovery Institute, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Keratoconus (KC) is the most common corneal ectasia and a major cause of corneal transplantation worldwide. Recent studies have suggested the contribution of two missense mutations (N843S and S419A) in the phosphatase domain of PPIP5K2 to the etiology of KC. PPIP5K2 is a cell-signaling kinase/phosphatase highly expressed in human and mouse cornea tissues. We aimed to identify the potential target genes of PPIP5K2 using human cancer cell line HCT116, primary human corneal epithelial cells (HCEC), and human corneal stromal fibroblast (HCSF).

Methods: First, differentially expressed (DE) genes were identified using Total RNA-Seq in HCT116 cells with stable PPIP5K2-knockdown (n=8). Data were analyzed by Ingenuity Pathway Analysis and WebGestalt's gene ontology analysis. Second, we knocked down PPIP5K2 expression in HCEC (n=3) and HCSF (n=3) for 24 hours using Dicer-Substrate Short Interfering RNAs (DsiRNA) via electroporation. Third, we validated changes in expression of six DE genes (MGMT, NR2F1, BMP4, HIST1H2AI, CDK6 and FUT8) in HCEC and HCSF using droplet digital PCR (ddPCR).

Results: We identified 81 genes with DE in HCT116 cells (|fold change| > 1.5, p<0.05). Pathway analyses implicated the enrichment of genes involved in protein degradation/synthesis, connective tissue disorders, cellular assembly and organization. The pathways affected include TGF β -signaling and LPS/IL-1 mediated inhibition of RXR function, which have been suggested to be involved in KC pathogenesis. We successfully decreased the expression of PPIP5K2 in human HCEC and HCSF cells for more than 80%. Following the successful knockdown of PPIP5K2 expression in HCEC and HCSF, our ddPCR data confirmed that CDK6 and HIST1H2AI were downregulated in HCEC whereas MGMT, NR2F1 and FUT8 were upregulated in HCSF, similar to those discovered in HCT116 cells.

Conclusions: We identified several target genes of PPIP5K2 in HCT116 cells and validated five target genes in primary HCEC and HCSF cells. In addition, we will perform Total RNA-Seq in PPIP5K2-knockdown corneal cells to identify DE genes and their pathways which may be more specific to corneal cells and contributing to KC.

CONTROL ID: 3544339

SUBMITTER (NAME ONLY): J Crawford Downs

TITLE: Microstructural Finite Element Modeling of the Entire Lamina Cribrosa in the Human Optic Nerve Head

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.C. Downs, C.A. Girkin, R.G. Grytz, A. Karimi, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|S.M. Rahmati, School of Biological Sciences, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The microstructure of the lamina cribrosa (LC), including the size, volume fraction, and orientation of the LC beams likely play a crucial role in protecting the retinal ganglion cell axons passing through the scleral canal. Prior computational models have been limited to multiscale approaches, in which a small chunk of the LC microstructure is subjected to displacement boundary conditions predicted from a parent mesoscale model. This regional approach cannot calculate the stresses and strains across the entire LC, and is unable to accurately represent the relatively compliant neural tissues (NT).

Methods: A finite element (FE) model of posterior pole of the eye was developed, including the LC microstructure that is constructed directly from the binary images of the LC microstructure (Figure). Models of three human donor eye were used to estimate the stresses and strains in the LC and NT under acute IOP elevation, and compared with identical models in which the LC was represented as a single material with either mapped connective tissue volume fraction (CTVF) and anisotropic properties based on local LC beam direction, or homogeneous isotropic neo-Hookean properties. The models were subjected to an IOP elevation to 45 mmHg after pre-stressing from 0 to 10 mmHg, and solved in CalculiX. ONH and LC displacements were matched across the three modeling approaches within each eye, and stresses and strains were compared for the LC and NT combined (continuum material and microstructural), and the LC and NT separately.

Results: The regional volumetric average von Mises stress, and 1st, 2nd, and 3rd principal stresses and strains showed that the microstructural model with neo-Hookean properties yielded similar results to our prior approach using an LC continuum representation with mapped CTVF/anisotropy, but the microstructural modeling approach allows analysis of the stresses and strains in the LC and NT separately. In the microstructural models, the LC beams carried most of the IOP load but exhibited less strain, while the encapsulated NT exhibited lower stresses and much higher strains. Strain levels matched prior experimental studies.

Conclusions: Microstructural modeling will provide greater insight into the biomechanical factors driving damage to the axons (NT) and connective tissue remodeling of the LC that occur in glaucoma.

CONTROL ID: 3544340

SUBMITTER (NAME ONLY): Verena Juncal

TITLE: Levels of systemic VEGF-A and ranibizumab in the infant of a nursing mother receiving intravitreal ranibizumab therapy followed by a 'pump and dump' strategy

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Juncal, R. Kohly, S.B. Marafon, N.A. Figueiredo, L. Hostovsky, Y. Diambomba, K. Koushan, R.H. Muni, University of Toronto, Toronto, Ontario, CANADA]

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ABSTRACT BODY:

Purpose: To analyze the levels of ranibizumab and vascular endothelial growth factor (VEGF)-A in the breast milk of a nursing mother and in the bloodstream of her infant after intravitreal ranibizumab injections followed by a 3-day 'pump and dump' strategy.

Methods: This is a prospective, interventional clinical study that included both a 34-year-old nursing patient who required bilateral ranibizumab injections post-partum and her newborn child. The mother received an injection of ranibizumab 0.5mg in each eye with 1-week interval between eyes. The infant was regularly breastfed, except for 3 days following each injection, when a 'pump and dump' strategy was adopted, where the mother regularly pumped and discarded the breast milk while the infant was fed exclusively with formula. Breast milk samples were obtained at baseline and then daily for 14 days after the first injection. The infant's blood samples were obtained daily for 11 days starting on the day before breastfeeding was resumed. Plasma and serum samples were obtained for VEGF-A and ranibizumab analysis, respectively. In addition, blood samples of 3 control infants of similar gestational age as the index infant were obtained and analyzed for plasma VEGF-A levels

Results: Ranibizumab levels remained below the lower limit of quantitation (LLOQ) of the assay at all time points in the mother's breast milk and in the infant's serum. VEGF-A levels in the breast milk gradually reduced from 5266pg/ml at baseline to 1537pg/ml at day 11, and then increased to 3438pg/ml at day 14. Plasma VEGF-A levels in the infant remained below the LLOQ at all time points, except for days 9 (20.45pg/ml) and 11 (13.19pg/ml). Plasma VEGF-A levels in the control patients were also below the LLOQ.

Conclusions: Ranibizumab was not detected in the infant of a nursing mother who received intravitreal ranibizumab injection followed by a 3-day 'pump and dump' strategy and systemic VEGF-A levels did not seem to be affected. This suggests that a 3-day 'pump and dump' strategy could possibly be a safe option for nursing mothers who require intravitreal ranibizumab therapy but want to continue breastfeeding.

CONTROL ID: 3544341

SUBMITTER (NAME ONLY): SUNDARARAJAN MAHALINGAM

TITLE: α B-crystallin super chaperone for treating protein aggregation diseases

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. MAHALINGAM, S. Srivastava, P. Santhoshkumar, K. Sharma, Department of Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|K. Sharma, Department of Biochemistry, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: α B-crystallin super chaperone (α B Δ 54-61) can be prepared by deleting 54-61 amino acid residues in α B-crystallin. The objective of this study was to evaluate the therapeutic potentials of α B Δ 54-61 super chaperone using cell culture systems and *C. elegans* model system. Additionally, whether heat- or urea-induced unfolding and refolding of α B Δ 54-61 and WT protein increases the proteins ability to protect cells from oxidative stress and apoptosis was also evaluated.

Methods: The therapeutic efficacy of the WT- and Δ 54-61- α B-crystallins was investigated a *C. elegans* model (CL4176) for Alzheimer's disease (AD). The α B-crystallin response to counter thermal and chemical-induced stress was studied using wild type (N2 strain) *C. elegans*. The chaperone-like activity of heat-/urea-activated wild-type and α B Δ 54-61 were measured using luciferase and lysozyme as client proteins. The structural and molecular changes in Δ 54-61- α B-crystallin after urea/heat activation were investigated using multi-angle light scattering analysis method. The cytoprotective effects of the native and heat/urea-activated α B-crystallins were evaluated in ARPE-19 cells using cell integrity assay and 2,7-dichlorofluorescein diacetate staining.

Results: The super chaperone protected *C. elegans* (N2 strain) from paraquat and juglone-induced oxidative stress to a greater extent than did by wild-type α B-crystallin. The mutant super chaperone also prevented A β -induced toxicity on ARPE-19 cells in a more effective manner when compared to the wild-type protein. The mutant α B-crystallin also delayed A β -induced paralysis in a *C. elegans* model for AD and showed 10% increase in lifespan of the worm. *C. elegans* pre-treated with mutant α B-crystallin and exposed to thermal stress (35°C) showed a 11% increase in survival. In contrast, the wild-type protein treated worms showed no significant increase in survival when compared to placebo. Heat- and urea-induced unfolding/refolding events showed two-fold increase in the chaperone-like function with a concomitant increase in surface hydrophobicity of the mutant protein, even though increased hydrophobicity didn't result in enhanced cytoprotective effects.

Conclusions: Our findings suggest that α B-crystallin super chaperone (α B Δ 54-61) has improved therapeutic potential in cell culture and *C. elegans* model system.

CONTROL ID: 3544342

SUBMITTER (NAME ONLY): Guilherme Motta

TITLE: How glaucoma patients balance between the advantages and disadvantages of adherence to the recommended treatment regimen in real-life: perspectives from a middle-income country

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.S. Motta, J. Andrade, N. Kasahara, Ophthalmology, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Patients primary open-angle glaucoma (POAG) are required to take long-term treatments with topical medications to halt disease progression. Measuring patients' acceptance of the use of the eyedrops prescribed should help to better understand and predict their behavior toward treatment. This issue has not been studied in glaucoma patients, especially in low-middle income nations. This cross-sectional survey aimed to describe the level of acceptance of Brazilian patients toward the long-term treatment with eyedrops and to find potential predictors of high acceptance.

Methods: POAG patient were recruited from the Glaucoma Service - Santa Casa of São Paulo, São Paulo, Brazil. Clinical and demographic data were retrieved from participants electronic records. All patients answered the ACCEPT® questionnaire. This is a generic patient-reported outcome questionnaire specifically developed to assess patients' acceptance of long-term medications. The questionnaire comprises seven independent dimensions: one on general acceptance (Acceptance/General) and six treatment-attribute specific, covering all specific attributes of drug: Acceptance/Medication Inconvenience, Acceptance/Long-term Treatment, Acceptance/Regimen Constraints, Acceptance/Numerous Medications, Acceptance/ Side effects, and Acceptance/Effectiveness. Scores based on categorical/ordinal data are linearly transformed to range from 0 to 100 with a higher score indicating greater acceptance.

Results: The sample comprised 96 patients with POAG. The mean age was 63.2 ± 8.9 years; 48 were male and 48 female; 55 (57.3%) were white, 36 (37.5%) African-Brazilian, and 5 (5.2 %) were of mixed color; most patients (97.9%) had less than high school degree and all had a family income $<USD8,000$. The mean ACCEPT score was 79.5 ± 6.0 .

Conclusions:

In this cohort of Brazilian patients with glaucoma, acceptance of treatment was high. The adequate interpretation of this data can provide valuable insights about patient priorities and current unmet needs.

CONTROL ID: 3544343

SUBMITTER (NAME ONLY): Juliet Moncaster

TITLE: α B-Crystallin Potentiates Alzheimer's Disease A β Neurotoxicity by Hetero-Oligomeric Stabilization

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: We previously reported A β accumulation in lenses from patients Alzheimer's Disease (AD) (Goldstein et al., 2003) and Down syndrome (Moncaster et al., 2010), a common chromosomal disorder in which age-related A β brain pathology is an invariant feature. A β co-localized with α B-crystallin in these lenses. Here we investigate the molecular mechanisms underpinning α B-crystallin interactions with A β and implications for AD pathogenesis.

Methods: Immunohistofluorescence, Confocal Microscopy, Immunogold electron microscopy, SDS-page and immunoblotting, electron paramagnetic resonance spectroscopy (EPR), quasi-elastic light scattering (QLS) spectroscopy, cell and organotypic slice culture, LDH and Propidium iodide assays.

Results: Electron paramagnetic resonance spectroscopy revealed that α B-crystallin dynamically interacts with and binds to A β in vitro in concordance with previous findings. Quasi-elastic light scattering spectroscopy showed that α B-crystallin suppresses formation of high molecular weight A β aggregates by stabilizing soluble hetero-oligomeric complexes. However, whilst co-incubation of α B-crystallin and A β suppressed A β fibrillogenesis, α B-crystallin potentiated A β neurotoxicity in mouse primary neurons and organotypic rat hippocampus slice culture as detected by LDH and Propidium Iodide assays.

Conclusions: These results indicate that α B-crystallin potentiates A β neurotoxicity by stabilizing soluble hetero-oligomers.

CONTROL ID: 3544345

SUBMITTER (NAME ONLY): Fiona Stapleton

TITLE: The effect of a novel selenium disulphide-containing treatment on ocular signs and symptoms in symptomatic contact lens wearers: An exploratory study

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Stapleton, J. Tan, T. Jia, School of Optometry and Vision Science, UNSW Sydney, Sydney, New South Wales, AUSTRALIA|V. DePuy, Bowden Analytics, Raleigh, North Carolina, UNITED STATES|M. Gleeson, C. Bosworth, Azura Ophthalmics, Melbourne, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To evaluate a novel topical ointment AZR-MD-001 1%, containing selenium disulphide, on ocular signs and symptoms in symptomatic contact lens wearers in a 4 month prospective placebo controlled double masked randomised trial.

Methods: Symptomatic contact lens wearers (Contact Lens Dry Eye Questionnaire-8 [CLDEQ-8] score >12) with signs of Meibomian Gland Dysfunction (Meibomian Gland secretion score [MGS] ≤12) were enrolled. Participants were randomly assigned to receive either the test AZR-MD-001 1% or vehicle ointment to the lower eyelid margin twice per week (NCT03972501). MGS and number of Meibomian glands yielding liquid secretion (MGYLS) were measured at baseline, after 2, 4, 6 weeks and 2, 3 and 4 months of treatment. CLDEQ-8 was completed at baseline, 1 and 4 months. Differences between active and vehicle were analysed relative to baseline using ANCOVA.

Results: Fourteen subjects (5 males, 9 females, aged 30.8 ± 13.8 years) completed the study. Compared to baseline, change in MGS significantly improved in the active treatment group after 2 weeks (Mean 3.4 ± 6.1 , $p < 0.05$) and continued to improve to four months (19.5 ± 7.6 , $p < 0.0001$). In the vehicle group, change in MGS from baseline improved at month 4 (Mean 16 ± 10.1 , $p < 0.005$). Compared to baseline, the change in MGLYS was not significant in the active group after 2 and 4 weeks (Mean 0.7 ± 1.8 ; 2.1 ± 3.4 , respectively), but improved after 6 weeks (3.5 ± 3.4 , $p < 0.001$) and remained significantly improved by month 4 (3.4 ± 4.1 , $p < 0.001$). In the vehicle group, change in MGLYS from baseline was improved at 4 months only. The active reached statistical superiority over the vehicle in both change in MGS and MGLYS at 6 weeks onwards. Both active and control showed a significant improvement in CLDEQ-8 score at 1 and 4 months. At 4 months a larger proportion of subjects using the active (5/7) showed a clinical improvement in CLDEQ-8 score compared with placebo (2/7, $p = 0.11$).

Conclusions: Use of a topical ointment containing selenium disulphide, designed to treat hyperkeratinisation at the gland orifices, appears to improve Meibomian gland patency and secretion by more than 30% in symptomatic contact lens wearers after six weeks of twice weekly use compared to placebo. Improvements were maintained to 4 months of use. These early findings including improved symptoms warrant further exploration.

CONTROL ID: 3544346

SUBMITTER (NAME ONLY): Abhishek Vats

TITLE: A non-retinoid chaperone of rhodopsin protects the Rho^{P23H/+} mouse retina in ex vivo culture.

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: RHODOPSIN (RHO) mutations accounts for ~25-30% of autosomal dominant retinitis pigmentosa (adRP). Structural instability of mutant rhodopsin (RHO) causes dominant negative effect leads to the death of rod photoreceptors and vision loss. We hypothesize to restore the RHO homeostasis and rescue rods from RHO-associated adRP using previously discovered non-retinoid chaperone of RHO. The goal of this study is to test this hypothesis in ex vivo culture of the Rho^{P23H/+} knock-in mouse retina.

Methods: We established retinal explant culture with RPE from the Rho^{P23H/+} and Rho^{+/+} mouse. Retinal morphology was analyzed by immunohistochemistry (IHC) of retinal explants at different days in vitro (DIV). To test the effect of small molecule chaperone on RHO homeostasis and retinal degeneration, Rho^{P23H/+} retinal explants were treated with the compound and DMSO for 10 DIV. Retinae were collected for IHC, immunoblots and RNA-seq. The safety of compound was examined by TUNEL assay using Rho^{+/+} retinal explants.

Results: IHC of RHO showed a gradual decrease of RHO level and outer segment (OS) length in both the Rho^{P23H/+} and Rho^{+/+} retinae along with time. The Rho^{P23H/+}, but not Rho^{+/+} retinal explants showed a time-dependent decrease of outer nuclear layer (ONL), confirming a progressive degeneration in dish as seen in vivo. Importantly, treated with the compound, the Rho^{P23H/+} retinae showed higher RHO level, improved RHO glycosylation, less ubiquitinated RHO, longer OS length, and thicker ONL, suggesting the compound indeed improved RHO homeostasis and supported photoreceptor survival. Interestingly, this small molecule increased the ratio of RHO in the OS/IS layer to that in the ONL of Rho^{P23H/P23H} retinal explants, consolidating its chaperone activity. The RNA-seq data suggests that the compound mitigated the primary immune response and reduced microglia activation. Additionally, protein homeostasis pathways were upregulated.

Conclusions: We showed that the non-retinoid chaperone improved RHO homeostasis and protected photoreceptors in the Rho^{P23H/+} knock-in mouse retinae in ex vivo culture. The efficacious dose of the compound showed no significant toxicity. Our results strongly support the notion that improving RHO homeostasis is sufficient to protect retina from RHO-associated adRP. Future development of a continuous ocular drug delivery system will allow us to test the efficacy of this compound in vivo.

CONTROL ID: 3544349

SUBMITTER (NAME ONLY): Rossen Hazarbassanov

TITLE: Evaluation of keratoconus detection from elevation, topography and pachymetry raw data using machine learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the performance of machine learning algorithms in detecting keratoconus (KCN) from corneal parameters in a tomography dataset, such as elevation, topography, and pachymetry.

Methods: We developed numerous machine learning models to detect keratoconus from corneal parameters. Elevation, topography and pachymetry dataset were obtained from 5881 eyes of 2800 patients in Brazil using a high-resolution rotating Scheimpflug camera system for anterior segment analysis (Pentacam® HR – Oculus, Optikgeräte GmbH). The accuracy of models was computed using each dataset of elevation, topography and pachymetry parameters separately. 10-fold cross validation of the area under the receiver operating characteristic curve (AUC) was used to evaluate the accuracy of different models. Thus, 3 independent datasets were created. Each of them was evaluated, and performance evaluation related to KCN detection was observed.

Results: A total of 1726 eyes were normal, and 4155 eyes were diagnosed as KCN. Figure 1 presents the distribution of the anterior cornea curvature radius (ACCR) of the cornea parameter versus the mean radius of cornea curvature (MRCC) in the 7 to 9 mm area parameter of normal versus KCN eyes. The cubic support vector machine (SVM) outperformed all other machine learning classifiers with an AUC of 1 for detecting KCN using elevation parameters only (Figure 2, ROC on left and confusion matrix on the right panel). The highest accuracy of classifiers for detecting KCN using pachymetry only and topography only parameters were 96.6% and 95.2%, respectively.

Conclusions: The results suggest that the cubic support vector machine (SVM) using elevation parameters provide the highest accuracy in detecting normal from KCN cases. This algorithm might be of help for detecting KCN patients in ophthalmological clinical sets.

CONTROL ID: 3544350

SUBMITTER (NAME ONLY): William Schultheis

TITLE: Effect of Taping Face Masks on Quantitative Particle Counts Near the Eye: Implications for Intravitreal Injections in the COVID-19 Era

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sharpe, Q. Zhang, S. Patel, A.E. Kuriyan, A. Chiang, S.J. Garg, J. Hsu, Wills Eye Health System, Philadelphia, Pennsylvania, UNITED STATES|W. Schultheis, S. Patel, A.E. Kuriyan, A. Chiang, S.J. Garg, J. Hsu, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: While one might expect that universal masking would decrease the risk of oral flora contamination during the injection procedure, anecdotal reports of oral flora-related endophthalmitis during COVID-19 have emerged. We performed a prospective observational cohort study to determine the effect of taping the top of face masks on air particle counts directed toward the eye during simulated intravitreal injections.

Methods: Thirteen healthy N95 qualitative fit tested human subjects were recruited, three women and ten men, with an age range of [24, 35]. Each wore a cloth, surgical, or N95 mask in randomized order. The number of air particles were quantified using a particle counter suspended over the right eye while each subject breathed normally, deeply, or spoke using a standardized script. Particle counts were obtained with the top of each mask taped and untaped. The main outcome measurements were particle counts in the size classes of 0.3 mm, 0.5 mm, 1 mm, 3 mm, 5 mm, 10 mm, and total particle count. The Wilcoxon signed rank test was used to test for paired differences between taped and untaped particle counts for each combination of mask type and respiratory mode, at each particle size.

Results: Taping cloth masks while subjects were speaking significantly reduced particle counts for the size classes of 0.3 mm ($p=0.03$), 0.5 mm ($p=0.01$), 1 mm ($p=0.03$), and total particle counts ($p=0.008$) compared to no taping. Taping the top of cloth masks during normal or deep breathing did not significantly affect particle counts compared to no taping. Taping the top of surgical or N95 masks did not significantly alter particle counts for any breathing condition tested.

Conclusions: Taping the top of cloth masks prior to simulated intravitreal injections significantly reduced air particle counts directed toward the eye when subjects were speaking compared to no taping. This may have implications for decreasing air particles reaching the eye during intravitreal injections, including aerosolized droplets from a patient's mouth that may carry oral pathogens.

CONTROL ID: 3544351

SUBMITTER (NAME ONLY): Adam Poe

TITLE: Parallel genomic and proteomic profiling of miR-10b targets in human limbal epithelial cells

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We previously showed that microRNA-10b (miR-10b) is one of the most abundant limbal miRNAs, which is upregulated in the limbus vs. central cornea and may regulate corneal epithelial homeostasis and stem cell functions. Additionally, we showed its upregulation in diabetic (DM) vs. normal limbus, which may contribute to diabetic corneal disease. Our purpose was to investigate miR-10b target genes and regulated proteins using combined genomic and proteomic analyses to elucidate its role in the limbus.

Methods: Human autopsy normal corneas were procured from the National Disease Research Interchange in Optisol medium. In vitro experiments were performed with stem cell-enriched human primary limbal epithelial cells (LECs). LECs were transfected with either miR-10b mimic, inhibitor, or their corresponding controls using Lipofectamine RNAiMAX (Thermo Fisher) following the manufacturer's instructions. At day 3 post-transfection cells were harvested for total RNA isolation using Trizol for next generation mRNA sequencing. A matching set of transfected cells was collected and analyzed by global proteomic analysis.

Results: Proteomics and mRNA-seq elucidated changes in pathways regulating limbal epithelial stem cells (LESC) maintenance and differentiation as a result of miR-10b overexpression in LECs. Our previous findings indicated major transcription factors controlling eye development and maintenance of the cornea as potential targets of miR-10b. Our current study found that miR-10b mimic downregulates KLF4, RAP2A, and EPHB2 that regulate epithelial-mesenchymal transition. Pathway analysis indicated a role in cell cycle regulation because of changes in related predicted miR-10b targets — E2F7 and CDK6. Previous findings showed that miR-10b increased LEC proliferation. Transfection with miR-10b resulted in downregulation of DKK1, GSK3B, CEMIP, and NEDD4/L that regulate canonical Wnt signaling pathway. There was a good concordance between the two methods.

Conclusions: Our data revealed potential direct targets of miR-10b and unveiled the underlying pathways affecting human limbal epithelial cell maintenance, proliferation and self-renewal. Combined approach of proteomics and genomics profiling provides insight into the regulation by microRNAs of their targets on a genome/proteome-wide scale.

CONTROL ID: 3544355

SUBMITTER (NAME ONLY): Manali Kamath

TITLE: Unfolded protein response is critical for the corneal pathogenesis of *Aspergillus fumigatus*

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kamath, J. Lightfoot, M. Montgomery, E. Adams, K.K. Fuller, Microbiology & Immunology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: The poor visual outcomes associated with fungal keratitis (FK) is attributable, in part, to the ineffectiveness of current antifungals. The development of novel therapy requires the identification of putative targets in the fungus, which we reasoned include pathways involved in the assimilation of corneal collagen (protein) as a nutrient source. The fungal unfolded protein response (UPR) is critical in this regard as it maintains the fidelity of the secretion pathway and, consequently, the release of collagenases into the cornea. Accordingly, we tested the hypothesis that the UPR is essential for corneal virulence in a predominant agent of FK, *Aspergillus fumigatus*.

Methods: The gene encoding HacA, a transcription factor essential for the UPR, was deleted in *A. fumigatus* using a CRISPR/Cas9 method, and the resulting mutant (hacA KO) was confirmed by PCR. Collagenase secretion was measured in culture supernatants using azocollagen hydrolysis (Millipore Sigma). Stress sensitivity assays were performed in rich (YPD) or minimal media as indicated. For the virulence studies, C57BL/6J mice were immunosuppressed with methylprednisolone (100mg/kg) on the days preceding and following infection. On the day of infection, corneas were abraded with an algerbrush and topically inoculated with germinated spores of the WT or hacA KO strains (n= 20/group). At 48 or 72 h post-inoculation, eyes were clinically scored and corneas were resected for histological analysis (PASH staining) or fungal burden assessment using colony-forming units (CFUs). WT and hacA KO data sets were compared by student's T-test.

Results: The *A. fumigatus* hacA KO mutant displayed hypersensitivity to stresses that induce protein misfolding, including increased temperature, DTT, and tunicamycin. The mutant was also deficient in secreted collagenase activity and could not grow on biological tissue ex vivo. Compared to mice infected with WT *A. fumigatus*, hacA KO-infected corneas displayed decreased clinical scores and fungal burden; this corresponded with the histopathology, which revealed reduced neutrophil infiltration and essentially no fungal invasion into the stroma.

Conclusions: Our results confirm our hypothesis that the UPR is essential for *A. fumigatus* nutrient acquisition on protein-rich substrates as well as virulence in a murine model of FK. These data suggest that the fungal UPR could serve as a target for antifungal intervention.

CONTROL ID: 3544356

SUBMITTER (NAME ONLY): Elmira Jalilian

TITLE: Interactions between mesenchymal stem cells (MSCs) and trigeminal ganglion (TGs) improve neurite growth and elongation

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Jalilian, I. Putra, E. Katz, G. Yazdanpanah, V.H. Guaiquil, X. Shen, K. Anwar, S. An, M. Rosenblatt, A.R. Djalilian, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|G. Yazdanpanah, Richard and Loan Hill Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sensory innervation of the cornea is essential for the perception of stimuli critical for blinking, maintenance of hydration, and injury avoidance. Disease, infection and ophthalmic surgical procedures can all damage corneal central nerves, resulting in scarring and vision problems. Corneal nerves regenerate over several years, however, sub-basal nerve density never returns to normal. Despite the clinical need to promote corneal nerve regeneration, few specific therapeutic interventions are available. Cell therapy, specifically MSCs presents an attractive treatment option for enhancing nerve regeneration in this critical ocular structure. In this project, we studied the role of MSCs in corneal nerve regeneration.

Methods: Mouse TGs neurons were isolated from Thy1-YFP mice which have fluorescent corneal nerves. Human corneal MSCs (CO-MSCs) and bone marrow MSCs (BM-MSCs) were used. 2D and 3D co-culture system was developed to grow TGs in presence of each type of MSCs. The morphology of the TGs was monitored over 7 days. Cells were then fixed and immune-stained on day 7. Immunocytochemistry was performed to observe $\beta 3$ tubulin and CD90 expression marker for TGs and MSCs respectively. Confocal microscopy and Neurolucida software used to analyze the density and length of the neurites in different conditions.

Results: Morphology observations illustrated enhanced axonal growth and survival over time in presence of MSCs compared to TG-only conditions. After 5 days, TGs started to shrink and finally die after 8 to 10 days whereas TGs in presence of MSCs showed enhanced survival after 2 weeks in culture. Immunostaining data ($\beta 3$ tubulin/CD90) and then analysis using Neurolucida illustrated a significant increase in density and the complexity of the TGs in the co-culture system versus TGs alone. Finally, a significant increase in neuron branching was observed in 3D versus 2D.

Conclusions: These results demonstrate the distinct effect of MSCs in maintenance, growth, and elongation of neurites nerve regeneration over time. Further functional experiments will be performed to study the effect of MSCs in vivo and the mechanisms by which MSCs can promote corneal nerve regeneration after injury. These studies will enable us to develop highly novel therapeutics for the restoration of damaged corneal nerves and potentially, other ocular diseases.

CONTROL ID: 3544359

SUBMITTER (NAME ONLY): Adam Tellier

TITLE: Anti-angiogenic activity of Complement Factor H in a laser-induced choroidal neovascularization mouse model

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Complement factor H (CFH) regulates alternative complement pathway activation. The non-canonical functions of CFH in the eye are also of interest, as recombinant human CFH (rhCFH; GEM103) is in development for the treatment of geographic atrophy in a genetically-defined age-related macular degeneration population. The hypothesis that rhCFH has anti-angiogenic activity in the eye was tested in a laser induced choroidal neovascularization (CNV) mouse model. To better understand the CNV phenotype reported in mice locally treated with polyethylene glycol (PEG;PMID:25088354), we tested the hypothesis that PEG treatment increases vascular endothelial growth factor (VEGF) production in retinal pigment epithelial (RPE) cells.

Methods: In mice, CNV was induced using a 532nm laser. Three days post laser, both eyes of each animal were intravitreally (IVT) treated with either rhCFH, aflibercept (anti-VEGF; positive control) or vehicle. CNV severity was determined by fluorescein angiography (FA), optical coherence tomography (OCT) in live animals on days 12 & 15, and isolectin B4 (ISB4) staining intensity on day 15 retinal flatmounts. In the cell-based model, induced pluripotent stem cell derived (iPS) RPE were treated for 28 days with either of PEG or vehicle. Conditioned media and cell lysates were collected on days 0, 2, 14 and 28 for VEGF protein and mRNA assessment, respectively.

Results: FA grades in rhCFH treated animals were decreased compared to vehicle at days 12 and 15 ($P<0.0001$) and were comparable to aflibercept treated mice ($P>0.99$). OCT-defined CNV area was also reduced in the rhCFH cohort at d12 ($P<0.001$) and 15 ($P<0.05$). A decrease in ISB4 staining intensity was observed in retinal flat mounts from rhCFH- vs PBS- treated mice ($P=0.008$). In cultured iPS RPE, an increase in VEGF mRNA and protein was observed following 2 or 4 weeks of treatment with PEG compared to vehicle ($P<0.0001$).

Conclusions: CNV severity was significantly reduced in rhCFH-treated mice compared to PBS group while being similar to aflibercept-treated controls, as measured by FA grading, OCT area, and ISB4 staining. These results demonstrate that IVT administration of rhCFH can provide anti-angiogenic effects in the eye and would not pose an increased risk of CNV development. In contrast, treatment with PEGylated molecules, has a potential to enhance VEGF secretion from RPE cells.

CONTROL ID: 3544361

SUBMITTER (NAME ONLY): Thomas Hwang

TITLE: Monitoring proliferative diabetic retinopathy with optical coherence tomography angiography

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.S. Hwang, Q. You, Y. Guo, C.J. Flaxel, S. Bailey, D. Huang, Y. Jia, Ophthalmology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the clinical value of optical coherence tomography angiography (OCTA) for monitoring proliferative diabetic retinopathy (PDR).

Methods: In this prospective cohort study, we enrolled PDR patients with neovascularization (NV) within the Early Treatment Diabetic Retinopathy Study fields 1 or 2. Clinicians treated the eyes per standard of care. Participants underwent high-definition (400x400) 6x6-mm OCTA scans centered on disc, fovea, and temporal retina consecutively with ~0.5mm overlap using a commercial spectral-domain OCTA system. A custom algorithm measured the NV vessel area and the central non-perfusion area (NPA) on en face OCTA. The OCTA images of baseline and 1-year follow-up visits were registered for comparison.

Results: We included 10 eyes of 9 PDR patients (6 male) with 13 NVs (2 NVs/eye in 3 eyes), including 1 NV at the disc and 12 NV elsewhere, detected on OCTA scans. The clinical characteristics of the study participants were summarized in table 1. From baseline to one-year follow-up visit, the macular NPA increased on average 8.6% ($P=0.25$); while the NV vessel area decreased on average 25.5% ($P=0.37$) (Figure 1). Four eyes did not receive any treatment during the follow-up, while 6 eyes were treated with multiple anti-VEGF injections. The NV vessel area in untreated eyes enlarged significantly more than that in treated eyes (increased 9.4% vs. decreased 48.7%, $P=0.017$). The NPA changes were similar in treated and untreated eyes (9.9% vs. 7.8%, $P=0.96$).

Conclusions: OCTA is useful for quantifying and monitoring NV in PDR. Anti-VEGF treatment reduces NV growth, but does not affect NPA enlargement.

CONTROL ID: 3544362

SUBMITTER (NAME ONLY): Tamara Voor

TITLE: Clinical characteristics and surgical outcomes of patients undergoing pars plana vitrectomy for complications of proliferative diabetic retinopathy

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.A. Voor, H. Patrick, J. Lee, A. Wang, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the outcomes of patients undergoing pars plana vitrectomy (PPV) surgery for complications of proliferative diabetic retinopathy (PDR).

Methods: Retrospective, observational chart review of 291 eyes of 217 patients that underwent PPV for complications of PDR at a large county hospital in Dallas, Texas from 2014 to 2019. Outcome measures included retinal re-attachment success rate, best-corrected visual acuity, and need for repeat PPV. Patients were excluded if they had less than 6 months of follow-up.

Results: Patients were 55.8% male and 44.2% female with an average age of 51 years (standard deviation (SD) of ± 9.5). Patients were followed for an average of 27.6 months, with a range of 6 to 71 months. The average Hgb A1c at time of surgery was 8.1 (SD ± 2.0). 72.3% of patients had their insurance covered by charity and 18.2% were covered by Medicaid/Medicare. 202 (93.1%) patients had other vascular risk factors or complications from diabetes, including hypertension (88.0%), hyperlipidemia (54.8%), chronic kidney disease (43.3%), need for dialysis (12.4%), coronary artery disease (8.8%), peripheral neuropathy (7.8%), need for amputation (7.4%), myocardial infarction (6.9%), and stroke (6.5%).

PPV surgery was performed for non-clearing vitreous hemorrhage in 110 eyes (37.8%), tractional retinal detachment (TRD) involving the macula in 98 eyes (33.7%), TRD not involving the macula in 50 eyes (17.2%), combined TRD and rhegmatogenous retinal detachment in 19 eyes (6.4%), and vitreomacular interface abnormalities in 14 eyes (4.7%). 81 eyes (27.8%) required gas tamponade and 29 eyes (10.0%) required silicone oil.

Average logMAR visual acuity was 1.75 (SD ± 0.74) pre-operatively and 0.92 (SD ± 0.87) at 1 year post-op. Retinal re-attachment success rate for patients with TRDs was 77.6% at 6 mo, 62.1% at 1 year, and 88.8% at most recent follow up. Common post-op complications included VH within 6 mos and cataracts. As of the most recent follow-up, 79 eyes (27%) needed repeat PPV and 91 (31.2%) needed cataract extraction (CE).

Conclusions: This study shows that vitrectomy is an overall safe and effective procedure that improves vision and stabilizes the retina in those with complications from PDR.

CONTROL ID: 3544367

SUBMITTER (NAME ONLY): Gwendolyn Schultz

TITLE: A glial point of view: investigating corneal Schwann cells in ex vivo murine organ and whole-eye cultures

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. Schultz, University of Connecticut School of Medicine, Farmington, Connecticut, UNITED STATES|P. Bargagna-Mohan, R. Mohan, Neuroscience, UConn Health, Farmington, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the setting of human corneal transplants and refractive surgery, incomplete stromal reinnervation and/or axonal degeneration pose clinical concerns. Corneal Schwann cells (cSCs) are glial cells that ensheath and provide trophic support to stromal axons. To investigate cSCs during corneal tissue preservation, as well as to study how stromal injury impacts cSCs, we analyzed the expression of cSC markers using ex vivo mouse corneal and eye-globe models.

Methods: We used adult wild-type (WT) C57LB6 mice, and PLP-eGFP transgenic mice (Bargagna-Mohan et al., J. Neurosci. Res., 2020). For the organ culture model, WT (n= 6) and PLP-eGFP (n=4) corneas including limbal tissue were excised, and cultured at 37°C in Opti-minimal essential medium containing 4% Dextran, 8% fetal bovine serum, and a cocktail of antibiotic/antimycotic for 6 days (6d). For the whole-eye model, after eye enucleation, using a 1.5-mm diameter trephine a circular incision was made on WT corneas to injure the stroma. Control (uninjured, n= 5) and injured eye-globes (n= 10) were cultured for 6d, and after fixation, corneas were isolated. All corneas were then processed for whole mount immunohistochemical analysis using the axonal marker b-III tubulin and cSC markers PLP-1 and DKK. Stained tissues were examined by epifluorescence microscopy.

Results: In the organ culture model, 6d post-culture caused a loss of axonal density mostly in the central zone in both WT and PLP corneas. At the limbus/peripheral zone, b-III tubulin+ axons co-stained with PLP-1+ and DKK+ cSCs, whereas in the mid-central cornea b-III tubulin staining was fragmented, and showed some axons lacking PLP-1 and DKK staining. In the whole-eye model, axonal integrity was more evident at the proximal sites where viability of cSCs was higher. At the distal sites trephine injury caused b-III tubulin fragmentation and downregulation of PLP-1 and DKK expression, suggesting these severed axons are highly sensitive to cSC loss.

Conclusions: Our results suggest that cSCs in the central cornea lose expression of PLP-1 and DKK after 6d in culture. This loss of expression appears to be associated with a certain degree of axonal degeneration, which is possibly due to a loss of trophic support from cSCs. Further studies will explore methods of how to best support the cSCs, and thus, the neural network that is crucial for corneal function.

CONTROL ID: 3544369

SUBMITTER (NAME ONLY): Omar Moussa

TITLE: Efficacy of Preoperative Risk Stratification of Resident Phacoemulsification Surgery

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: This study determines how a novel cataract surgery grading system at a single U.S. teaching institution may predict intra-operative complications and post-operative outcomes.

Methods: This is a retrospective observational study on non-consecutive cataract surgical cases performed by residents at Columbia University Irving Medical Center/Edward S. Harkness Eye Institute. Risk scores (Table), preoperative best-corrected visual acuity (BCVA), intra-operative complications, post-operative day 1 (POD1) and month 1 (POM1) BCVA, and POM1 exam findings were tabulated. Risk scores were used to stratify cases among residents at different levels of training. The relationship between preoperative risk scores and POD1/POM1 BCVA was modeled using linear regression. The relationship between preoperative risk scores and rates of each type of complication was modeled using logistic regression. Logistic regression was used to model the rates of complications across different levels of training, and odds ratios were calculated before and after adjusting for case mix using risk scores.

Results: Data was collected on 530 cases from January 2017 to May 2020 and risk scores ranged from 0 to 8 (mean = 1.31). Mean POM1 visual acuity was 0.37 LogMAR, and 80% of cases had visual acuity equal to or better than 20/30 at POM1. Average POM1 visual acuity for cases that had posterior capsular rupture was 0.56. Risk scores did not have a significant association with posterior capsule rupture. Risk scores were predictive of corneal edema (OR = 1.36, p = 0.0032), having any POM1 complication (OR = 1.20, p = 0.034), and having any complication overall (OR = 1.21, p = 0.014). Risk scores were also predictive of POD1 (β = 0.13, p < 0.0001) and POM1 (β = 0.057, p = 0.00048) visual acuity. There was not a significant association between level of training and rates of intra-operative or post-operative complications, both before and after adjusting for case mix (p > 0.05).

Conclusions: Our pre-operative cataract surgical risk score was highly correlated with post-operative visual acuity and the presence of POM1 corneal edema. Risk scores were also predictive for any POM1 complication and any complication overall. Rates of complications were not correlated to the year of training, both before and after adjusting for the risk score.

CONTROL ID: 3544372

SUBMITTER (NAME ONLY): Qi Cui

TITLE: Exposure to glucagon-like peptide 1 receptor (GLP1R) agonists is associated with reduced risk for glaucoma

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q.N. Cui, J. Sterling, P. Hua, J.L. Dunaief, B.L. VanderBeek, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glucagon-like peptide-1 receptor (GLP1R) agonists regulate blood glucose and are commonly used to treat type II diabetes. Recent work by our group showed that treatment with the novel GLP1R agonist NLY01 mitigated neuroinflammation and decreased glial activation to rescue retinal ganglion cells in an animal model of glaucoma (PMID 33147455). In this study, we used insurance claims data to examine whether GLP1R agonists impacted glaucoma risk.

Methods: A retrospective cohort of adult patients who initiated a new GLP1R agonist (i.e. exenatide, liraglutide, albiglutide, dulaglutide, semaglutide, or lixisenatide) was 1:3 age, gender, race, classes of active diabetes medication, and year of index date matched to a cohort of patients who initiated a different class of oral diabetic medication during their time in the database. Exclusion occurred for < 2 years in the database, < 18 years old, failure to visit an eyecare provider prior to the index date, a prior diagnosis of glaucoma, glaucoma suspect, or ocular hypertension, and prior glaucoma medication, procedure, or surgery. Primary outcome was a new diagnosis of primary open angle glaucoma, glaucoma suspect, or low tension glaucoma. Diabetes severity was assessed using hemoglobin A1c and the Diabetes Complications Severity Index (DCSI), a validated metric based on six categories of diabetic complications. Inverse probability of treatment weight (IPTW) was used within a multivariable Cox proportional hazard regression model to test the association between exposure to GLP1R agonists and the primary outcome. IPTW was derived from a propensity score model based on the DCSI, HbA1c, demographic factors, and other systemic health conditions.

Results: Cohorts were comprised of 1961 new users of GLP1R agonists matched to 4371 unexposed controls. After IPTW, age was the only imbalanced covariate between cohorts (SMD > 0.1). Ten new diagnoses of glaucoma (0.51%) were present in the GLP1R agonist cohort compared to 58 (1.33%) in the unexposed controls, conferring a reduced hazard of 0.54 (95%CI: 0.35-0.85, p=0.007) among GLP1R agonist initiators, suggesting that GLP1R agonists reduced the risk for glaucoma.

Conclusions: GLP1R agonists were associated with a statistically significant hazard reduction for a new glaucoma diagnosis. Our findings support further investigations into the use of GLP1R agonists in glaucoma prevention.

CONTROL ID: 3544379

SUBMITTER (NAME ONLY): Harpal Sandhu

TITLE: Bacterial or Fungal Co-Infection and Endogenous Endophthalmitis in Hospitalized Patients with Coronavirus Disease 2019

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.S. Sandhu, E. Dugan, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|W. Mattingly, J. Ramirez, Division of Infectious Diseases, Department of Internal Medicine, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coronavirus disease 2019 (COVID-19) is a pandemic viral illness which may predispose to co-infections and whose ophthalmic manifestations are still not well understood. This study was performed to determine the rate of bacterial or fungal co-infection and associated endogenous endophthalmitis in inpatients with COVID-19.

Methods: This was a retrospective cohort study of inpatients with COVID-19-associated pneumonia at seven general hospitals in Louisville, Kentucky from March to May 2020. All patients were positive by polymerase chain reaction for SARS-CoV-2 and had clinical evidence of pneumonia necessitating hospital admission. Records were reviewed for demographic data, clinical evidence of systemic bacterial or fungal co-infection, culture results, and evidence of endophthalmitis.

Results: There were 632 patients in this study. Median age was 63 (IQR 48-74), and 53% were female. 65 of them (10.3%) had a systemic, culture-positive bacterial or fungal co-infection (60 bacterial, 5 fungal). Of these 65 patients, 11 developed bacteremia (16.9% of co-infected patients; 1.7% of all COVID inpatients). One patient with Streptococcal bacteremia and septic arthritis developed endogenous endophthalmitis in one eye (1/65 co-infected patients, 1.5%; 1/632 total COVID inpatients, 0.16%), which was successfully treated with intravitreal antibiotics. No patients with negative blood cultures developed endophthalmitis, although the sole endophthalmitis patient presented with intraocular infection prior to blood cultures being positive.

Conclusions: Bacterial or fungal co-infection is relatively common in inpatients with COVID-19. Endogenous bacterial endophthalmitis, while rare, is still a possible and potentially devastating complication of the disease. Consequently, visual complaints in COVID-19 inpatients should be assessed promptly.

CONTROL ID: 3544380

SUBMITTER (NAME ONLY): Lachlan Knight

TITLE: Childhood and Early-Onset Glaucoma Classification and Genetic Profile in a Large Australasian Disease Registry

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Phenotypic and genotypic associations in childhood and early-onset glaucoma have not been well described in large datasets due to disease rarity, inconsistent use of disease definitions and limited availability of genetic testing. We performed a retrospective clinical and molecular study to report the relative frequencies of childhood and early-onset glaucoma subtypes and their genetic findings in a large single cohort.

Methods: We reviewed the referrals of individuals with childhood glaucoma (diagnosed 0 to <18 years) and early-onset glaucoma (diagnosed 18 to <40 years) recruited to the Australian and New Zealand Registry of Advanced Glaucoma (ANZRAG) over a 13-year period (2007-2020). Subtypes of glaucoma were determined using the Childhood Glaucoma Research Network (CGRN) classifications. DNA extracted from blood or saliva samples underwent sequencing of genes associated with glaucoma.

Results: 290 individuals with childhood glaucoma and 370 individuals with early-onset glaucoma were referred to the ANZRAG. Primary glaucoma was most prevalent in both cohorts. In the childhood cohort, 57.6% of individuals (167/290) had primary congenital glaucoma and 19.3% (56/290) had juvenile open-angle glaucoma (JOAG). JOAG constituted 73.2% of the early-onset glaucoma cohort (271/370). Genetic testing in probands resulted in a diagnostic yield of 24.7% (125/506) and a reclassification of glaucoma subtype in 10.4% of probands (13/125). The highest molecular diagnostic rate was achieved in probands with glaucoma associated with non-acquired ocular anomalies (56.5%). Pathogenic variants in 18 genes associated with childhood and early-onset glaucoma were found. Biallelic variants in CYP1B1 (n=29; 5.7%) and heterozygous variants in MYOC (n=24; 4.7%) and FOXC1 (n=21; 4.2%) were most commonly reported amongst probands. Biallelic CYP1B1 variants were reported in twice as many females as

males (66.7% vs. 33.3%; $p=0.01$).

Conclusions: We report on one of the largest international childhood and early-onset glaucoma cohorts using the CGRN classifications. Primary glaucomas were more prevalent than secondary glaucomas. Genetic diagnoses ascertained in 24.7% of probands supported clinical diagnoses and genetic counselling. International collaborative efforts to characterise genetic associations in rare phenotypes will improve genetic diagnostic rates and management of childhood and early-onset glaucoma.

CONTROL ID: 3544383

SUBMITTER (NAME ONLY): Chieh-Lin (Stanley) Wu

TITLE: Does bright light exposure affect in vitro choroid melanoma viability and secretion of pro-inflammatory chemokines?

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Cioanca, R.C. Natoli, John Curtin School of Medical Research, The Australian National University, Canberra, Australian Capital Territory, AUSTRALIA|C. Wu, M.C. Madigan, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|C. Wu, L. Zhu, Y. Chen, R. Conway, M.C. Madigan, Save Sight Institute, University of Sydney, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Cumulative UV exposure is significant in skin melanoma, and implicated in primary iris melanoma. UV, absorbed by the cornea, iris, lens, and vitreous, does not reach the posterior eye however visible (white) light radiates the retina, underlying retinal pigmented epithelium (RPE), and choroid. The effects of visible light exposure on the choroidal microenvironment and potential roles in choroidal melanoma progression are unknown. This preliminary study investigated if acute light exposure affected viability and secretion of pro-inflammatory CCL2 and IL8 (involved in macrophage and neutrophil migration) in human choroidal melanoma cells.

Methods: Choroidal melanoma cells were grown in RPMI with FBS, L-glutamine and sodium pyruvate (MP38 and MP46: RPMI+20% FBS; 92.1: RPMI+10% FBS). ARPE19 cells (DMEM+10% FBS, L-glutamine, and +/- pyruvate) were used as controls; RPE cells in vivo normally absorb abundant visible light. Cells were grown in 96 well black plates (8000 cells/well) (n=5 per cell line; in triplicate) for 18hrs, then fresh medium (with 1% FBS) for 16 hours. Cells were then exposed to 32,000 lux light (LED, λ : 400-700nm) for 4 hours (37°C); unexposed control cells were grown in parallel conditions. Viability of light-exposed and control cells was measured with alamarBlue. Conditioned medium (light-exposed and control) was assessed with ELISA for pro-inflammatory cytokines, CCL2 and IL8.

Results: Viability was reduced 10% to 15% immediately after light exposure for 92.1 and MP46 cells ($p<0.05$; t-test) but not MP38 cells ($p>0.05$). Surprisingly, ARPE19 cells showed dramatic cell death (~100%) after light exposure, that was mitigated by sodium pyruvate (110mg/ml). Secretion of CCL2 and IL8 was not induced following light exposure for any cell lines (light and control: ~20-100 pg/ml).

Conclusions: Acute light exposure reduced viability of MP46 and 92.1 melanoma cells but not MP38 cells, possibly due to melanin levels (MP38>MP46 and 92.1). No increase in CCL2 and IL8 secretion was noted following light exposure for melanoma cells, however, cumulative effects of light exposure, resembling real-life, remain to be clarified. Incidental light-induced ARPE19 cell death, ameliorated with sodium pyruvate, indicates effects on metabolism and reduced oxidative stress, and will be studied further.

CONTROL ID: 3544385

SUBMITTER (NAME ONLY): Peng Yan

TITLE: Prevalence of diabetic macular edema diagnosed with optical coherence tomography in patients with diabetes: a systematic review and meta-analysis

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Yan, Y. Jin, Department of Ophthalmology & Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|J. Im, University of Toronto Dalla Lana School of Public Health, Toronto, Ontario, CANADA|R. Chow, Department of Chronic Disease Epidemiology, Yale University School of Public Health, New Haven, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is a leading cause of vision loss among people of working age with diabetes. It is a major public health issue. Optical coherence tomography (OCT) technology allows for accurate assessment of DME but systematic reviews on the prevalence of DME diagnosed based on OCT are lacking. A systematic review and meta-analysis was performed to assess the global prevalence of DME diagnosed with OCT.

Methods: Three electronic databases (EMBASE, CINAHL and PubMed) were searched on May 25, 2020 using key words such as “diabetic macular edema”, “prevalence” and “optical coherence tomography”. The quality of retrieved studies was evaluated using the Joanna Briggs Institute Checklist for Prevalence Studies. Pooled prevalence estimates and 95% confidence intervals (CI) were calculated using a random-effects model following the assessment of heterogeneity (I^2).

Results: The search found 1524 studies. After removing duplicates, 1245 studies remained. After abstract screening and full-text assessment based on pre-established criteria, six studies were included in the meta-analysis. The sample size of included studies ranged from 75 to 978 patients, with a mean age of 50.6-68.2 years. Four studies had more females (51.1%-61.5%). The other two studies had predominantly males (64.5% and 74.4%). Three studies were conducted in developed countries and three studies in developing countries. The prevalence of DME ranged from 4.0% to 48.7% among individual studies. The associated I^2 value was 98.9%, suggesting that the random effects model was appropriate to combine individual studies. The pooled prevalence of DME was 17.9% (95% CI: 5.4%-35.5%) overall, 18.6% (95% CI 7.7%-32.8%) in developed countries and 17.7% (95% CI: 1.0%-47.7%) in developing countries. In comparison, using fundus photography exams, a meta-analysis published in 2012 reported a pooled prevalence of DME of 6.81%.

Conclusions: The prevalence of DME diagnosed based on OCT was 18%, which was 2-3 times higher than the prevalence of DME diagnosed with fundus photography. Modern OCT technology allows for early detection of DME before significant vision loss. Given the global pandemic of diabetes mellitus and obesity, there is an increasing need to inform physicians and educate people with diabetes regarding early detection and treatment of DME based on OCT.

CONTROL ID: 3544386

SUBMITTER (NAME ONLY): Emma Spowart

TITLE: The role of pH measurement at presentation in predicting outcomes from acute ocular surface chemical injury

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Spowart, S. Pradhan, C. Bruce, B. Salvador-Culla, G. Figueiredo, F.C. Figueiredo, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|F.C. Figueiredo, Biosciences Institute, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: In acute chemical ocular injuries, the role of pH measurement before irrigation is unclear. We performed a retrospective observational study to determine whether tear film pH measured at presentation in acute chemical eye injuries carries any prognostic value.

Methods: Data including demographics, pH values, nature of chemical, injury circumstances and severity, and clinical and visual outcomes were assessed from previously collated data from patients presenting to the emergency eye department in a UK tertiary hospital. All patients had pH measured before and after irrigation (irrespective of whether irrigation was started before attendance). Spearman rank correlation coefficient and univariate binary logistic regression analysis were used to assess associations between pH on arrival, injury severity, and clinical and visual outcomes.

Results: Pre-irrigation pH was recorded in 135 eyes (113 patients, 66.4% male, mean age 35.5 years [range 2 - 78; SD 15.4]; 15 acid, 108 alkali, 12 unknown). In patients presenting within 24 hours of injury (n = 108 eyes), pH positively correlated with injury severity at presentation ($r_s = 0.20$, $p = 0.02$). In patients with abnormal pH on presentation ($6.5 < \text{pH} < 7.5$; n = 26 eyes), pH correlated strongly with injury severity ($r_s = 0.72$, $p < 0.01$). There was no significant correlation with visual outcome ($r_s = 0.12$, $p = 0.11$). Presenting pH was a significant predictive factor for presence of limbal damage at follow up in patients presenting within 24 hours of injury and with follow up after the initial presentation (n = 70 eyes, 60 patients, follow up 1-3929 days, mean 579.4 days, SD 1206.0 days), ($p = 0.026$, Nagelkerke R^2 0.090)

Conclusions: In patients presenting within 24 hours of injury, pH at presentation positively correlated with injury severity and was a significant predictive factor for limbal damage at follow up. As well as guiding acute management, pH measurement is a useful test as a prognostic indicator to counsel patients.

CONTROL ID: 3544387

SUBMITTER (NAME ONLY): Jackson Townsend

TITLE:

Outcomes of bent ab interno needle goniotomy in primary open angle glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Townsend, A. Badar, S. Dixon, P. Parekh, E. Martin, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bent ab interno needle goniotomy (BANG) is a novel minimally invasive glaucoma procedure that has been developed to increase trabecular outflow. We performed this study to evaluate the reduction in intraocular pressure (IOP) and IOP lowering medication in primary open angle glaucoma (POAG) after bent ab interno needle goniotomy.

Methods: We performed a retrospective chart review of 43 eyes of 33 patients who underwent the procedure with cataract surgery from 7/18/19 to 9/29/2020 in our outpatient surgical center. Mild, moderate, and severe glaucoma were included. 24 eyes were classified as POAG. Mean age was 70, 76% of patients Caucasian, and 42% of patients were male. Cataract extraction was performed prior to repositioning patient for direct gonioscopy. 25-gauge needle was bent at the tip to form a nearly 90 degree bend and attached to a viscoelastic cannula. A nasal goniotomy was created, which was then stripped for at least 30 degrees of trabecular meshwork. Reflex heme was noted. Irrigation/aspiration was used to remove reflex heme and viscoelastic prior to hydrating main wound and filling anterior chamber with adequate depth of pressure.

Results: Average IOP reduction for all glaucoma patients at post op month 3 was 20.80% ($P<0.0001$). Average drop reduction was 0.88 ($P=0.0009$). The percentage of patients reaching IOP reductions of greater than 20% was 55.81%. When classified by type of glaucoma, POAG identified statistically significant decrease in IOP by 17.69% ($P=0.0301$) and drop reduction of 0.708 ($P=0.0389$). The percentage of patients reaching IOP reduction greater than 20% was 37.5%. When further stratified by severity of primary open angle glaucoma, the percent reduction was 25.893% ($P=0.0118$), 9.523% ($P=0.5235$), and 23.585% ($P=0.1114$) for mild, moderate, and severe POAG, respectively. The percentage of patients reaching IOP reductions of greater than 20% was 66.67%, 16.67%, and 50% in mild, moderate, and severe POAG, respectively.

Conclusions: There is significant reduction across all severity of glaucoma, when classified by POAG, and further stratified by mild POAG. BANG procedure is an economical option, and when combined with cataract extraction, demonstrates greater than expected improvement in IOP. For phakic patients, cataract extraction/BANG may represent a viable first step instead of more conventional and invasive surgical intervention for glaucoma.

CONTROL ID: 3544388

SUBMITTER (NAME ONLY): Daniel Maruri

TITLE: ECM stiffness regulates the myofibroblastic differentiation of cultured primary keratocytes via subcellular changes in contractility and focal adhesion assembly.

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Maruri, D. Schmidtke, V. Varner, The Department of Bioengineering, The University of Texas at Dallas, Richardson, Texas, UNITED STATES|M. Miron-Mendoza, M. Petroll, The Department of Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have suggested that focal adhesion size is correlated with the stiffness of ECM, but it remains unclear how signaling downstream of focal adhesion formation modulates changes in corneal keratocyte morphology and mechanical activation.

Methods: Polyacrylamide (PA) hydrogels of varying stiffness were fabricated on glass coverslips, functionalized with type I collagen, and used as substrata for two-dimensional (2D) cell culture. The gels were plated with primary corneal keratocytes (NRKs) in either serum-free media or media containing exogenous TGF- β 1. In some experiments focal adhesion kinase (FAK) inhibitor (PF-573228) was also added to the culture media. Afterward, NRKs were fixed and stained for F-actin, as well as markers for myofibroblastic activation (α -SMA), contractility (pMLC), or focal adhesions (vinculin). Focal adhesion size and traction stresses exerted by NRKs were also measured.

Results: Treatment with TGF- β 1 elicited distinct cellular phenotypes when NRKs were cultured on gels of varying stiffness. Cells cultured on either stiff (10 kPa) PA gels or collagen-coated glass coverslips formed abundant stress fibers, exhibited elevated levels of α -SMA immunofluorescence, and exerted large traction forces. These cells also formed abundant focal adhesions distributed across the entire cell body. NRKs cultured on soft (1 kPa) substrata, however, exhibited behaviors more indicative of a quiescent phenotype, even in the presence of TGF- β 1. They formed fewer stress fibers, retained a more elongated morphology, and exerted significantly lower traction forces, with small focal adhesions, localized primarily at the tips of cellular projections. pMLC immunofluorescence further revealed stiffness-dependent differences in subcellular contractility, with contractions localized in the tips of cellular projections in cells cultured on soft substrata. Traction force maps correlated strongly with these patterns of pMLC immunofluorescence. FAK inhibition blocked myofibroblast transformation and the associated phenotypic changes.

Conclusions: Taken together, these data suggest that mechanotransductive signaling downstream of FAK activation is required for TGF- β 1 induced myofibroblast transformation of corneal keratocytes.

CONTROL ID: 3544395

SUBMITTER (NAME ONLY): Jasleen Jolly

TITLE: Widespread Thinning of Human Primary Visual Cortex Following Focal Loss of Photoreceptors

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Visual field representation is preserved throughout the visual system. Inherited retinal dystrophies resulting in photoreceptor death cause characteristic patterns of visual field loss. Previous work has shown secondary remodelling in the inner retinal layers which raises the question of whether these changes are transmitted along the visual system to V1.

Methods: A cohort of patients with choroideremia (peripheral vision loss) and Stargardt disease (central vision loss), and age- and sex-matched control participants underwent visual field testing and T1 structural MRI scanning. Retinal thickness and visual field sensitivity were analysed in terms of degrees of visual space. Neuroimaging data was analysed using the free open cloud platform brainlife.io. An automated processing pipeline combining FreeSurfer and the approach developed by Benson and colleagues, was used to analyse V1-cortical thickness according to degrees of visual space represented. Repeated measures ANOVA with Huynh-Feldt adjustment were conducted for V1 thickness.

Results: In both patients groups, V1 thickness changed across eccentricities compared to controls ($P = 0.01$ in Stargardt patients and $P < 0.01$ in choroideremia). The key changes occurred across all eccentricities in choroideremia patients and between two and six degrees in the Stargardt patients. V1 thickness was not significantly correlated to microperimetry threshold ($p=0.08$, $P=0.56$) or octopus periphery score ($p=0.10$, $P=0.45$).

Conclusions: There is evidence of V1 thinning following retinal damage. A generalised effect of photoreceptor loss in the visual cortex due to retinal disease is not currently taken into account when planning retinal treatment. These effects along the visual pathway may require additional intervention to limit the impact of eye disease on brain tissue. We must consider the visual system as a whole rather than in terms of eye or brain.

CONTROL ID: 3544397

SUBMITTER (NAME ONLY): Jase Omizo

TITLE: Comparative Surgical Approaches Following Failed Pneumatic Retinopexy

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.N. Omizo, K.S. Lum, J.C. Lai, Retina Consultants of Hawaii, Aiea, Hawaii, UNITED STATES|J.N. Omizo, Hawaii Macula and Retina Institute, Aiea, Hawaii, UNITED STATES|J.C. Lai, Surgery, University of Hawaii John A. Burns School of Medicine, Honolulu, Hawaii, UNITED STATES|

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ABSTRACT BODY:

Purpose: Since its introduction in 1986, pneumatic retinopexy (PR) has been an effective procedure to repair select rhegmatogenous retinal detachments (RRD). However, in cases of re-detachment following PR, it is unclear which surgical option offers the best chance of reattachment. A retrospective observational clinical study was performed to examine the success rate of different surgical approaches to secondary RRD repair originally managed with PR.

Methods: A retrospective chart review was performed on patients presenting with RRD to four different doctors at the Retina Consultants of Hawaii from February 1, 2013 to December 31, 2019. Patients treated with PR for RRD repair who subsequently experienced a re-detachment were included in this study. Data collected included affected eye, date and type of procedures, and postoperative retina attachment status. A successful case was defined as an attached retina with no recurrence of retinal breaks or tears after one month following surgery. Cases where silicone oil remained in the post-operative eye or lacked a sufficient follow up time of three months after oil removal were excluded from the study. A Fisher's exact test was used to compare the success rate of different surgical approaches, a p value <0.05 was considered statistically significant.

Results: There were 15 eyes included in this study. Of these, 40% (6/15 eyes) were managed with pars plana vitrectomy (PPV) (3 with gas and 3 oil), 40% (6/15 eyes) were managed with a combination scleral buckle with PPV (5 with gas and 1 oil), and 20% (3/15 eyes) were managed with a repeat PR. The success rate was 50% for PPV, 83% for combination scleral buckle with PPV, and 0% for repeat PR. The success rate of reattachment with combination scleral buckle with PPV was significantly higher than with repeat PR ($p=0.048$). There was no significant difference in success rate between PPV vs. combination scleral buckle with PPV ($p=0.242$).

Conclusions: This study shows significantly better surgical outcomes when treating a failed PR RRD repair with combination scleral buckle with PPV rather than with a secondary PR. It raises the possibility that a scleral buckle is not necessary following a failed PR. Due to the small sample size and retrospective nature of the study, additional examination would be useful to further elucidate the best surgical approach following a failed PR.

CONTROL ID: 3544399

SUBMITTER (NAME ONLY): Annelies Bruinenberg

TITLE: Preparation of the Early Glasses Study: a randomized, controlled trial investigating the effect of early glasses for high refractive error on the development of amblyopia

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bruinenberg, M. Nordmann, W.L. Asjes - Tydeman, D. Sanders, H.J. Simonsz, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|R. van Ommen, Youth Healthcare, GGD Utrecht, Zeist, Utrecht, NETHERLANDS|J. Benjamins, Youth Healthcare, Icare, Meppel, Drenthe, NETHERLANDS|J. Hament, Youth Healthcare, Sante Partners, Tiel, Gelderland, NETHERLANDS|C.W. Wiersma-Hartman, Youth Healthcare, GGD Brabant-Zuidoost, Eindhoven, Noord-Brabant, NETHERLANDS|I. Tissen, Youth Healthcare, GGD Limburg-Noord, Venlo, Limburg, NETHERLANDS|N. Boonstra, Revalidation & Advice, Koninklijke Visio, Nijmegen, Noord-Brabant, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Photorefractive of young children is currently practiced nation-wide in Flanders, Belgium, at age one. Children with high refractive error are referred to an ophthalmologist and mostly prescribed glasses. Wearing of glasses has increased from 4.7% to 6.4% in four-year-olds in Flanders between 2012 and 2017 but it is unknown how many cases of amblyopia have been prevented from developing by the prescription of early glasses. In a randomized controlled trial (RCT), we will establish whether early glasses for high refractive error at age one reduce the development of amblyopia between age one and four. As a secondary outcome early literacy will be compared in groups with and without glasses.

Methods: In preparation of the RCT, Children's Healthcare Centers (CHCs), research-orthoptists and facilities for the examination of children were recruited. Youth healthcare physicians were contacted in most healthcare regions in the Netherlands, to engage clusters of CHCs in child-rich neighborhoods. Research-orthoptists were sought via orthoptic professional societies, meetings and announcements. Locations for examination of the children were sought among institutions for visually impaired, CHCs and hospitals.

Results: Five preventive healthcare organizations will participate with one cluster of CHCs in Utrecht: Neighborhood Leidsche Rijn, one cluster in Harderwijk, Ermelo and Putten, one cluster in Tiel, Geldermalsen and Culemborg, one cluster in Eindhoven-North, and one cluster in Venlo and Roermond. Study locations were ensured in two institutions for visually impaired, one in a CHC and one in a hospital. So far four study orthoptists have been engaged for retinoscopy in cycloplegia at age one, and randomization of children surpassing the AAPOS 2003 criteria and follow-up until age four.

Conclusions: Sufficient CHCs, youth healthcare physicians and nurses and research-orthoptists have committed themselves to this RCT. When the relation between the size and sort of refractive error at age one or two and the increased odds to develop amblyopia will have been established objectively, the use of practice-based referral criteria will no longer be necessary.

CONTROL ID: 3544404

SUBMITTER (NAME ONLY): Fabio Lavinsky

TITLE: The Degree of Intereye Asymmetry of Retinal Nerve Fiber Layer and Its Association with Other Structural and Functional Parameters Differences Between Eyes in Glaucoma.

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Lavinsky, F.F. Fujihara, R. Lindenmeyer, H. Pakter, J. Lavinsky, D. Lavinsky, Ophthalmology, Hospital de Clinicas de Porto Alegre, Porto Alegre, RS, BRAZIL|F. Lavinsky, A. Barros, H. Bohn, L.P. Bellini, MEDICAL SCHOOL, Universidade do Vale do Rio dos Sinos, Sao Leopoldo, RS, BRAZIL|F.F. Fujihara, Ophthalmology, Hospital Banco de Olhos, BRAZIL|H. Pakter, J. Lavinsky, D. Lavinsky, Ophthalmology, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, BRAZIL|E. Picceti, Ophthalmology, Hospital Conceicao, Porto Alegre, Rio Grande do Sul, BRAZIL|P. Mello, Ophthalmology, Universidade Federal de Sao Paulo Escola Paulista de Medicina, Sao Paulo, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: This study aims to evaluate the intereye asymmetry of selected structural and functional parameters in glaucoma and normal eyes between groups divided by the degree of circumpapillary retinal nerve fiber layer (cRNFL) thickness asymmetry between eyes.

Methods: Subjects with glaucoma and normal controls were included. Patients underwent 24-2 perimetry and Spectral Domain Optical Coherence Tomography (SD-OCT). Parameters analyzed were: cRNFL, average circumpapillary choroidal thickness (cChoroid), the hypotenuse of the vertical optic nerve head cup (HVOC) and VF mean deviation (MD). cChoroid was calculated as the mean between the measurements at 0°, 90°, 180° and 270° of the circular B-scan. For calculating HVOC the length and depth of the optic nerve cup were used as the sides of a right triangle. The length was measured as the distance between the innermost portion of the descending RNFL tissue at the Bruch's membrane opening level plan. The depth was measured as distance between the former line and the maximum depth of the anterior prelaminar tissue. Patients were divided into 3 groups based on the degree of asymmetry of cRNFL between eyes. Statistical analysis was performed using general estimate equations (GEE), One-way ANOVA and Tukey HSD test.

Results: 110 eyes (55 subjects) qualified for the study. The mean (SD) age was 65 (13.38) years. The number of subjects was 49 in the glaucoma and 6 in the control group. Three groups were divided by the terciles of the cRNFL difference between eyes: 1: $\leq 4 \mu\text{m}$ (n=21, 4 controls); 2: 5-13 μm (n=18, 2 controls) and 3: $\geq 14 \mu\text{m}$ (n=16, no controls). The mean (SD) cRNFL asymmetry within the groups was: 2.71 (1.35) μm , 9.28 (2.90) μm and 25.31 (12.56) μm (p<0.001), respectively. The average of the parameters in each group are depicted in table 1 showing that MD, cRNFL and HVOC were worse in the group with more intereye asymmetry. The MD, cRNFL and HVOC average differences between eyes comparing the 3 groups were significant (p<0.001)(Table 2).

Conclusions: The ONH parameter HVOC and the VF MD demonstrated significant intereye differences between the groups based on the degree of intereye asymmetry of the cRNFL. Evaluating additional SD-OCT parameters asymmetry may provide additional biomarkers and strategies for the diagnosis and monitoring of glaucoma.

CONTROL ID: 3544406

SUBMITTER (NAME ONLY): Arthur DeCarlo

TITLE: IOP regulation in the suprachiasmatic nucleus through glutamatergic and GABAergic neuronal pathways

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. DeCarlo, B.C. Samuels, Ophthalmology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Arthur DeCarlo: Commercial Relationship: Code N (No Commercial Relationship) | Brian Samuels: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of blindness in adults despite a variety of management strategies which help to slow its progression. In a quest to identify a new pharmacological approach for regulating intraocular pressure (IOP), a primary cause of glaucoma, this research focuses on the brain center that modulates most circadian rhythms, which potentially includes IOP variation. Our objective was to chemically stimulate the SCN directly by microinjection of either a glutamate receptor agonist, NMDA, or the GABA_A receptor antagonist, BMI, and determine the role of these two major signaling systems in the regulation of IOP within the SCN.

Methods: Male Sprague-Dawley rats (n=38) were placed under mild isoflurane anesthesia at midday. Using a stereotactic surgical approach, a 75 nL injectate of 0.4 mM BMI, or a dose range of NMDA 13-51 mM, or control 0.1M phosphate buffered saline, was delivered to the targeted area of the anterior hypothalamus after 10 minutes of stable baseline recordings of IOP, heart rate (HR), blood pressure (MAP), and intracranial pressure (ICP) were obtained. IOP, ICP and the cardiac responses were monitored for 60 minutes following injection.

Results: When injected directly into the SCN of anesthetized rats, both BMI (n=5) and saline (n=5) produced a rise in IOP (Fig. 1) that was 2.6 to 3.9-fold greater, respectively, than the NMDA response (n=5), which was near background level (saline-NMDA difference = 9.8 mm Hg, 3.9 fold +/- 1.5, n=10, AUC p=0.001; BMI-NMDA difference = 3.8 +/- 2.4 mm Hg, 2.7 fold +/- 1.5, n=10, AUC p=0.03). Alternatively, saline injected into either the ventricle (n=2) or the optic chiasma/supraoptic decussate region (och/sod) (n=5) did not stimulate a rise in IOP. BMI injected into the ventricle (n=3), however, led to a significant rise in IOP (3.6 +/- 1.0-fold relative to saline, p=0.03). Neither saline, BMI, nor NMDA injection into the SCN led to a significant rise in HR or MAP. ICP, however, was significantly increased by BMI microinjection into the SCN (3.1-fold rise relative to the saline response (p=0.03, n=9).

Conclusions: These data support the hypothesis that CNS regulation of IOP can be independent from HR, MAP, and ICP modulation, and suggest that IOP may be regulated through the SCN by both glutamatergic and GABAergic neuronal pathways.

CONTROL ID: 3544411

SUBMITTER (NAME ONLY): ELLEN ANTWI-ADJEI

TITLE: Assessment of night vision problems among drivers in Ghana

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.K. ANTWI-ADJEI, E.A. Addo, E.E. Dadzie, E. OwusuPoku, Optometry and Visual Science, Kwame Nkrumah University of Science and Technology, Kumasi, Ashanti, GHANA|E.K. ANTWI-ADJEI, Optometry, university of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess night vision problems among drivers to aid in traffic safety. Night visual problems are risk factor in most of the high way fatalities hence measuring only visual acuity in our Driver and Vehicle Licensing Authority (DVLA) is not enough. There is inadequate information on the various visual disturbances and complaints of drivers on the roads at night in Ghana. This research seeks to assess the visual problems encountered during night time driving in the Kumasi Metropolis in the Ashanti Region.

Methods: Night driving difficulties were assessed cross- sectionally using questionnaire comprising of demographics and night driving behaviors and characteristics, night visual problems and a preexisting Night Driving Questionnaire (VND-Q) among 311 drivers in Kumasi metropolis. The participants' aged, 20 to 72 years. Cross tabulations were used for age and gender of the participants with vision and night driving questionnaire (VND-Q) items used in assessing various difficulty levels. The statistical significance between age and gender with vision and night driving questionnaire (VND-Q) items were also analyzed using Pearson's Chi-square.

Results: Participants were mean \pm SD age of 36.58 ± 10.67 with more males (87.5%). Glare (40.8%) was the most prevalent night vision problem recorded in the metropolis. Most of the night driving difficulties correlated positively and significantly with age. The relationship between gender of participants and the difficulty levels in reading street signs ($p = 0.850$), seeing the road because of oncoming headlight ($p = 0.599$) and seeing because of glare when driving at dawn or dusk ($p = 0.193$) were not statistically significant. Driving during poor weather and rainy condition (20.4%), causing a lot of difficulty when driving on the road. Most drivers (<50years) have no difficulty in seeing dark colored cars, reading street signs, seeing pedestrians and animals, judging distance between drivers, and other cars at night.

Conclusions: Glare is the most occurring night visual problem with the highest prevalence for both male and female drivers among other night vision problems on the roads in the Kumasi metropolis. Due to night driving difficulties, among gender, men are 0.92 (CI 0.20-0.43) times more likely to drive at night than women. For traffic safety, simple tests for contrast and glare sensitivity should be reinforced as regular requirements for driving license issuance in Ghana.

CONTROL ID: 3544412

SUBMITTER (NAME ONLY): Edward Xie

TITLE: Drug-Gene Association Analysis to Identify Novel AMD Therapeutics

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Xie, Rosalind Franklin University of Medicine and Science Chicago Medical School, North Chicago, Illinois, UNITED STATES|U. Nadeem, Pathology, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|B. Xie, M.D. Souza, D. Sulakhe, Center for Research Informatics, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|H.A. Barba, D. Dao, D. Skondra, Ophthalmology and Visual Science, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|B. Xie, Medicine, University of Chicago Division of the Biological Sciences, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: By 2040, patients with age-related macular degeneration (AMD) are expected to reach 288 million; however, no cure or definite prevention exists to date. The purpose of this study is to use advanced bioinformatics tools to study drug-gene associations in order to identify drugs/compounds interacting with genes involved in AMD.

Methods: We queried PubMed Gene to compile a comprehensive list of genes described in AMD, wet AMD, dry AMD, intermediate AMD, and geographic atrophy (GA) to date. We also combined some of the sub-types to reflect the genes that play a role at distinct stages of the disease. Gene enrichment analysis was performed using ToppGene on AMD-related gene lists against the drug databases. This analysis estimates the statistical significance of overrepresented compounds from multiple drug-gene interaction databases to construct a Pharmacome. We selected compounds with adjusted p-value <0.05. Compounds with no clinical indications (e.g., paraquat and ethanol) were filtered out from the resulting drug lists.

Results: Among 77,146 candidate drugs/compounds in the database, our analysis revealed multiple drugs/compounds with significant interactions to genes involved in AMD. Amongst the top 20 most significant, drug classes such as anti-diabetics, antioxidants, statins, and flavonoids were identified. Metformin, the most common anti-diabetic medication, was identified as the drug with the strongest association to wet-AMD genes and was also in the top 20 for dry AMD subtypes. Curcumin, a flavonoid polyphenol, was identified as the drug with the strongest associations to all AMD-affiliated genes as well as to genes in the dry AMD subtype (both intermediate and GA). Other top compounds identified include statins and various antioxidants – glutathione, N-acetylcysteine, vitamins E & C – which were seen in the top 10 results of our AMD conditions.

Conclusions: This bioinformatics drug-gene interactions approach predicts drugs which can affect multiple genes involved in AMD. Multiple drugs with well-known pharmacodynamics and safety profiles like metformin and statin as well as antioxidants/nutrients like glutathione and curcumin are revealed by this analysis. Predicted bioinformatics studies require further validation from preclinical and clinical studies; however, this unbiased approach could identify potential candidates among existing drugs/compounds that could be repurposed for AMD.

CONTROL ID: 3544414

SUBMITTER (NAME ONLY): Swee Chai Teoh

TITLE: Axial length change with short-term exposure to visual stimuli with a limited range of spatial frequencies

SESSION TITLE: Effects of Light Intensity and Blur on Refractive Development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Teoh, M.J. Collins, S.A. Read, E. Pieterse, Queensland University of Technology School of Optometry and Vision Science, Kelvin Grove, Queensland, AUSTRALIA

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ABSTRACT BODY:

Purpose: Animals reared in environments with limited spatial frequency information can show changes in eye growth. The human eye shows short-term changes in axial length (AxL) in response to defocus, which limits the spatial information available to the eye. This study investigated the change in AxL with 60-minute exposure to videos filtered to present differing ranges of spatial frequencies, including full spectrum (FS), lowpass (≤ 1.5 cpd, LSF), bandpass (3 – 6 cpd, MSF) and highpass (≥ 10 cpd, HSF) (Figure 1), all viewed in the distance with no blur present.

Methods: Thirteen participants were tested on four separate days. Each session involved a 20-min washout (watching the FS video) and then 60-min exposure to a spatially filtered video (randomized order). Participants watched all videos binocularly, with optimum distance refractive correction. AxL of the RE was measured with Lenstar LS 900 at baseline (after washout), and then at 30 and 60 min. A still image was used as a fixation target when measuring the AxL and to measure the accommodation response with a binocular autorefractor WAM-5500. The ON- and OFF-retinal response stimulated by the videos was also analysed using the “Realtime ON OFF analysis of the visual world” software.

Results: A two-way repeated measures ANOVA showed that AxL did not change significantly by viewing the spatially filtered videos ($F_{3,33} = 0.71$, $p = 0.56$). The AxL change with 60-min exposure to LSF ($+3 \pm 6 \mu\text{m}$), MSF ($+2 \pm 7 \mu\text{m}$) and HSF ($+4 \pm 6 \mu\text{m}$) and FS videos ($-0.5 \pm 4 \mu\text{m}$) were similar (Figure 2). The change in accommodation response (range: 0.03 D to 0.13 D) stimulated by the videos was minimal and not statistically significant ($P > 0.05$). All four videos were found to result in a bias towards an ON-retinal pathway stimulation.

Conclusions: The spatial frequency detail of the visual stimulus did not cause significant short-term changes in axial length, when the eye was optimally corrected. This result does not support the hypothesis that the spatial frequency content of the retinal image is the primary factor in short-term defocus mediated changes in axial length.

CONTROL ID: 3544415

SUBMITTER (NAME ONLY): Manuel Garza Leon

TITLE: Comparison of meibomian gland morphology in patients with evaporative dry eye versus healthy subjects.

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Garza Leon, R.R. Crespo Treviño, A.K. Salinas Sánchez, F. Amparo, Clinical Science, Universidad de Monterrey Division de Ciencias de la Salud, San Pedro Garza Garcia, Nuevo León, MEXICO|

Commercial Relationships Disclosure (Abstract): Manuel Garza Leon: Commercial Relationship(s);Alcon :Code C (Consultant);S4Oprik:Code F (Financial Support);SIFI:Code F (Financial Support) | Ricaurte Crespo Treviño: Commercial Relationship: Code N (No Commercial Relationship) | Anna Salinas Sánchez: Commercial Relationship: Code N (No Commercial Relationship) | Francisco Amparo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: There is no conclusive information regarding the impact of meibomian gland (MG) morphology in tear film physiology and disease. We present a retrospective and observational clinical study that investigated the prevalence of anatomical and morphological MG alterations between patients with evaporative dry eye disease and healthy controls, and the correlation between these alterations and common clinical parameters used during meibomian gland disease evaluation.

Methods: Retrospective chart review of patients with evaporative dry eye and healthy individuals. The inclusion criteria for healthy subjects included an OSDI (Ocular Surface Disease Index) score of <12 points, non-invasive tear film break-up time (NIKBUT) > 10 sec, and absence of ocular surface staining (any type of dry eye was excluded). Patients with evaporative dry eye were selected based on the International Workshop on Meibomian Gland Dysfunction criteria. Demographic data, OSDI questionnaire, meibomian gland characteristics, ocular surface staining, non-invasive tear film break-up time, and infrared meibography were analyzed. Descriptive statistics and linear and logistical regression were used to evaluate the correlation between the clinical parameters and MG morphology.

Results: 75 eyes of 75 subjects were studied with a mean age of 40.68±18.43 (56% women), 42 (56%) subjects presented dry eyes and 33 (44%) were healthy controls. 90.7% of the subjects presented a morphological alteration in the upper lid and only 44% in the lower lid. We did not find significant differences in MG alterations in the upper lid between healthy and dry-eye subjects. Patients with evaporative dry eye presented MG alterations in the lower lid more frequently than healthy subjects (54.8 vs 30.3%; p=0.03). However, the presence of shortened glands was the only MG alteration that was more prevalent in the lower lid in dry-eye patients than in healthy subjects (p <0.05).

Conclusions: In the studied population, subjects with evaporative dry eye presented more alterations in the lower lid than healthy subjects, and meibomian-gland shortening was the most common morphological alteration in patients with dry eye.

CONTROL ID: 3544417

SUBMITTER (NAME ONLY): John Giannini

TITLE: Adaptive optics retinal imaging with deep learning cone segmentation enables area-based analysis in RHO-associated retinitis pigmentosa

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Giannini, J. Liu, T. Liu, N. Aguilera, L.A. Huryn, J. Tam, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): John Giannini: Commercial Relationship: Code N (No Commercial Relationship) | Jianfei Liu: Commercial Relationship: Code N (No Commercial Relationship) | Tao Liu: Commercial Relationship: Code N (No Commercial Relationship) | Nancy Aguilera: Commercial Relationship: Code N (No Commercial Relationship) | Laryssa Huryn: Commercial Relationship: Code N (No Commercial Relationship) | Johnny Tam: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Adaptive optics (AO) retinal imaging with single-cell resolution has enabled the extraction of quantitative information about the human photoreceptor mosaic, but characterizing small changes remains challenging. In diseases such as RHO-associated retinitis pigmentosa (RP), where rod loss precedes cone loss, the structural integrity of the cone mosaic could be altered due to rod-dependent cone survival. In this study, we investigate area-based metrics enabled by cone segmentation and their utility in characterizing subtle disruptions in the cone mosaic of patients with RP.

Methods: Non-confocal split detection retinal images were acquired using a custom-built AO scanning light ophthalmoscope. Images from two patients with molecularly-confirmed RHO-associated RP were compared to images from two healthy volunteers at matched eccentricities (2-3 mm temporal from fovea). Cone boundaries were localized using deep learning segmentation (PMID: 31701095), and cone centers were derived from the extracted cone boundaries. Cone boundaries were used to generate area-based metrics such as cone size (area within each cone) and percentage of retinal area occupied by cones, and cone centers were used to generate point-based metrics such as cone density.

Results: Subtle disruptions to the cone mosaic were observed in patients with RHO-associated RP, including variable cone size and local inter-cone area (area enclosed by nearest neighbors). There was a 24.5% decrease in cone density in patients with RP (healthy: average \pm SD, 10747 \pm 947 cells/mm²; RP: 8631 \pm 656 cells/mm²; n=4,216 cones; p < 0.01, two-tailed t-test). The percentage of retinal area occupied by cones was similar across healthy (45.6 \pm 3.8%) and RP (46.0 \pm 3.2%), which could be explained by a 24.1% increase in the average size of cones (healthy: 42.4 \pm 8.1 μ m²; RP: 52.7 \pm 10.4 μ m²; n=4,216 cones; p < 0.01, two-tailed t-test). These metrics show how area-based cone metrics enrich the interpretation of changes in cone density and help characterize subtle structural changes to the cone mosaic.

Conclusions: Diseases involving progressive photoreceptor loss, such as RP, may benefit from the introduction of area-based metrics alongside existing point-based metrics for characterizing early changes to the cone photoreceptors secondary to rod degeneration.

CONTROL ID: 3544419

SUBMITTER (NAME ONLY): Brittany Tsou

TITLE: Clinical characteristics and outcomes in Latinx patients presenting to the Emergency Department with ophthalmic injuries at an urban Level 1 trauma center

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tsou, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|S. Zafar, St Agnes Hospital, Baltimore, Maryland, UNITED STATES|M.J. Fliotsos, D. Srikumaran, F. Woreta, Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the demographics, clinical presentation, management, and visual outcomes in the Latinx population presenting with ophthalmic injuries at the Wilmer Eye Institute. A high proportion of workplace injuries, up to 20% in fiscal year 2020, in Latinx patients was noted at our institution, and no prior studies focused on the nature of injuries in this population.

Methods: Retrospective chart review of 73 patients who presented with ophthalmic injuries to the Wilmer Eye Institute, Johns Hopkins Hospital between January 1, 2006 and March 31, 2018. Injuries identified using ICD codes included orbital fracture, open globe, lid laceration, superficial injury of eye/adnexa, hyphema, traumatic cataract, retinal detachment, corneal foreign body, orbital foreign body, chemical splash, partial-thickness corneal laceration, and optic or oculomotor nerve injuries.

Results: Of 73 participants, 61 (83.6%) were male. Mean age (\pm SD) was 33.4 (\pm 14.3) years. Of 46 (63.0%) employed, 26 (56.5%) worked in construction. Forty-five (61.6%) had medical insurance and 24 (32.9%) did not. Of 79 eyes injured, 32 (40.5%) were work-related injuries, 26 (32.9%) assault injuries, and 21 (26.6%) by another cause. Thirty-three (41.8%) eyes were injured by blunt object, 19 (24.1%) by sharp object, 9 (11.4%) by a fall, 6 (7.6%) by a chemical, and 12 (15.2%) by unknown mechanism. In 23 instances where the use of eye protection was documented, 6 (26.1%) were protected using eye protection. Injuries included 29 (36.7%) orbital fractures, 17 (21.5%) open globes, 15 (19.0%) lid lacerations, and 14 (17.7%) superficial injuries. Forty-one (51.9%) eyes required surgery, including 17 (41.5%) open globe repairs, 10 (24.4%) vitrectomies, and 12 (15.2%) eyelid laceration repairs. Final visual acuity (VA) was 20/40 or better in 50 (63.3%) eyes, 20/50-20/200 in 11 (13.9%) eyes, 1/200-19/200 in 4 (5.1%) eyes, CF-NLP in 12 (15.2%) eyes, and unmeasured in 2 (2.5%) eyes.

Conclusions: In Latinx patients, ophthalmic trauma occurred most commonly in the workplace, highlighting the importance of improving education regarding eye protection in this setting. Injury occurred most often by blunt object. Most common injuries were orbital fractures and open globes, and most common surgeries performed were open globe repairs and vitrectomies. Final VA was worse than 20/200 in about 20% of eyes.

CONTROL ID: 3544420

SUBMITTER (NAME ONLY): James Wong

TITLE: Phase 1 Study of an Intravitreal Axitinib Hydrogel-based Implant for the Treatment of Neovascular Age-Related Macular Degeneration (nAMD)

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.G. Wong, Strathfield Retina Clinic, Strathfield, New South Wales, AUSTRALIA|A. Chang, Sydney Retina Clinic, Sydney, New South Wales, AUSTRALIA|R.H. Guymer, CERA, Melbourne, Victoria, AUSTRALIA|S. Wickremasinghe, CERA, Melbourne, Victoria, AUSTRALIA|E. Reilly, N. Bell, S. Vantipalli, M.H. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|A.A. Moshfeghi, Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: OTX-TKI, an intravitreal, bioresorbable, hydrogel-based implant, is designed to deliver the small molecule tyrosine kinase inhibitor, axitinib, in a sustained-release formulation to the vitreous & can potentially address the need for a novel treatment approach for nAMD that provides a longer duration of action. Here we report the preliminary safety, tolerability & biological activity of OTX-TKI in subjects with nAMD.

Methods: Prospective, multi-center, open-label, dose escalation Phase 1 study is ongoing. Subjects with nAMD (treatment-naïve or with a history of anti-VEGF therapy) were eligible to receive intravitreal placement of OTX-TKI. Three cohorts were evaluated: Cohort 1: 200 µg (n=6); Cohort 2: 400 µg (n=7); Cohort 3 (enrolling): 3a) 600 µg (n=5/6) & 3b) 400 µg + anti-VEGF induction therapy (n=2/6). Assessments included: Spectral-domain optical coherence tomography (SD-OCT) imaging to assess central subfield thickness (CSFT), best-corrected visual acuity (BCVA), & adverse event collection. Assessments were performed at baseline, day 0 (injection), days 3, 7, 14, & continued monthly until implants were no longer visible.

Results: No ocular serious adverse events have been reported to date (200 µg: 9-10.5 months; 400 µg: 12+ months; 600 µg: 4.5 months; 400 µg + Anti-VEGF: 3 months ongoing follow-up). No changes in intraocular pressure were observed in any subject & no subject required steroids. CSFT was noted to remain mostly stable in the 200 µg group. In the 400 & 600 µg groups, many subjects showed a decrease in CSFT & demonstrated a clinically meaningful reduction in intraretinal &/or subretinal fluid by 2 months. Reduction was maintained for up to 13 months in one subject in the 400 µg group, while in the 600 µg group, up to 4.5 months (only subject to reach this time point so far). Implants exhibited little movement in the vitreous & were generally no longer visible after 9 - 10.5 months (200 µg).

Conclusions: OTX-TKI appears to be generally well-tolerated to date with a favorable safety profile. Preliminary signs of biological activity, as evidenced by a decrease in CSFT in the 400 µg & 600 µg groups by two months, has been observed in many subjects with durability up to 13 months. Minimal movement & consistent resorption of implants has been observed. Study is still enrolling, and additional follow-up of current dose groups is ongoing.

CONTROL ID: 3544421

SUBMITTER (NAME ONLY): Eunice Sze Yin Ng

TITLE: Cathepsin D deficiency in RPE cells mediates Stargardt Disease pathogenesis

SESSION TITLE: Retinal diseases: molecular and biochemical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Ng, J.G. Hu, Z. Jiang, M.B. Gorin, A. Matynia, R.A. Radu, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|E. Ng, J.G. Hu, Z. Jiang, M.B. Gorin, A. Matynia, R.A. Radu, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the retinal pigment epithelium (RPE), Cathepsin D (CatD) is the principal lysosomal protease responsible for breaking down internalized proteins. CatD activity and its maturation through the endolysosomes requires a low pH. Key pathological hallmark of Stargardt disease (STGD1) and its mouse model (*Abca4*^{-/-}) is the accumulation of autofluorescent lipofuscin in the RPE. Both STGD1 donor eye and *Abca4*^{-/-} RPE showed significant deposition of complement proteins on the RPE cells. These RPE lipofuscin granules contain A2E-bisretinoids, lipid and protein aggregates, including complement fragments. Notably, increased lysosomal pH in the RPE was previously evidenced in the *Abca4*^{-/-} mice. In this study, we investigated the specific role of CatD in the endolysosomes of STGD1 experimental models.

Methods: Age-matched wild-type (WT) and *Abca4*^{-/-} mice (n=3) were used to prepare RPE homogenates for immunoblotting analysis of mature CatD level. Pooled RPE sheets of 6-mo-old WT and *Abca4*^{-/-} mice (n=4) were used for proteomics analysis by liquid chromatography-mass spectrometry (LC-MS). Functional activity of CatD in RPE cells of WT and *Abca4*^{-/-} mice (n=3) were measured by fluorometric assay. Statistical significance was determined by paired t-test. CatD and α -synuclein, its physiological substrate, were evaluated by immunohistochemistry (IHC) in fixed mouse eyes (WT and *Abca4*^{-/-}) and induced pluripotent stem cell (iPSC) derived RPE cells from STGD1 patient vs control unaffected individuals.

Results: By LC-MS proteomics analysis, we found a ~1.6-fold (p<0.001) increase in level of total CatD (immature, intermediate, mature) forms in RPE cells of *Abca4*^{-/-} mice vs WT. Surprisingly, quantitative immunoblotting analysis showed a ~1.7-fold (p=0.042) decrease of mature CatD in the RPE of *Abca4*^{-/-} mice vs WT. Importantly, CatD functional activity was reduced in the RPE of *Abca4*^{-/-} mice by ~42% (p=0.024) compared to WT. By IHC, STGD1 iPSC-RPE cells but not normal controls showed significant accumulation of α -synuclein consistent with impaired CatD activity.

Conclusions: Our studies suggest that CatD is an integral component of maintaining the homeostasis of the RPE cells. In STGD1 RPE cells, decreased CatD functional activity and reduced protein maturation further exacerbate the endolysosomal dysfunction. Our findings introduce a molecular mechanism involving CatD in the pathophysiology of STGD1 with important therapeutic implications.

CONTROL ID: 3544426

SUBMITTER (NAME ONLY): David Grasic

TITLE: The role of Optical Coherence Tomography Angiography in detecting and monitoring inflammatory choroidal neovascular membranes

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.J. Grasic, W. Kongwattananon, H. Lin, H. Sen, S. Kodati, ophthalmology, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical Coherence Tomography Angiography (OCT-A) has emerged as a valuable adjunctive imaging modality for the detection of choroidal neovascular membranes (CNVM). The goal of this study is to investigate the utility of OCT-A for the detection of inflammatory CNVM (i-CNVM) and monitoring their response to treatment.

Methods: A retrospective review of patients with a diagnosis of uveitis and associated i-CNVs based on clinical exam and OCT (CIRRUS, Carl Zeiss Meditec, Inc, Dublin, OH) was conducted. 6 × 6-mm SD-OCTA (CIRRUS AngioPlex, Carl Zeiss Meditec, Inc, Dublin, OH) or 6 × 6-mm swept-source OCTA (Plex Elite 9000; Carl Zeiss Meditec, Inc) images were acquired and the outer retina to choriocapillaris (ORCC) slab evaluated by two graders for the presence of i-CNVM. Follow up images were qualitatively assessed in order to determine if regression of i-CNVM occurred following treatment.

Results: Thirteen eyes (punctate inner choroidopathy (n=4), persistent placoid maculopathy (n=2), sarcoid uveitis (n=2), tuberculous choroiditis (n=1), birdshot chorioretinopathy (n=1), syphilitic uveitis (n=1), serpiginous choroiditis (n=1) and idiopathic panuveitis (n=1)) with i-CNVM and OCT-A images were identified. I-CNVM was detected on OCT-A in 11/13 eyes (84.6%). Treatment for i-CNVM included intravitreal bevacizumab (n=1), intravitreal ranibizumab (n=2), intravitreal aflibercept (n=8), subtenon triamcinolone acetonide (n=2) and intravitreal dexamethasone implant (n=2). Of these 11 eyes with detectable i-CNVM, 7 (63.6%) had a new diagnosis of i-CNVM. Mean best corrected visual acuity post-treatment improved from 0.68 (range 0.1-1.5) to 0.57 (-0.2-1.5) (p=0.08). Notably, 10 eyes (90.9%) demonstrated regression in i-CNVM area on OCT-A with treatment and of those 10 eyes, 4 (40.0%) showed complete regression in i-CNVM with treatment.

Conclusions: Our results show that OCT-A is an effective modality for detecting i-CNVM and that visible regression of the CNVM is apparent in the majority of cases following treatment.

CONTROL ID: 3544427

SUBMITTER (NAME ONLY): Kemal Donlic

TITLE: Visual dysfunction in a zebrafish FASD model is associated with retinal proteostasis impairment

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Donlic, T. Sherpa, O.G. Canterbury, K. Holguin, P.C. Meighan, M.D. Varnum, Integrative Physiology and Neuroscience, Washington State University College of Veterinary Medicine, Pullman, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fetal alcohol exposure is associated with a myriad of nervous system impacts. Retinal abnormalities and visual deficits also have been observed in fetal alcohol spectrum disorder (FASD). The purpose of this study was to characterize retinal manifestations of binge-like ethanol (EtOH) exposure in a zebrafish model of FASD and to investigate the role of EtOH-mediated proteostasis impairment for visual dysfunction.

Methods: We exposed zebrafish to 1% EtOH from 5-7 days post fertilization, within a developmental period following early establishment of working cone vision but before maturation of rods. Functional assays were carried out 2- and 3-days post-exposure. We employed a transgenic reporter for ubiquitin-system impairment in cone PRs (gnat2:Ub-G76V-YFP), determining the effect of EtOH on reporter accumulation via immunoblotting. The functional effects of EtOH were assessed by optomotor response (OMR) assays and electroretinogram (ERG) recordings in intact zebrafish larvae.

Results: Exposure to 1% EtOH produced a concentration in larvae of 16 ± 4 mM (SEM, $n=5$), which returned to baseline levels after one day following washout. OMR performance was significantly impaired at 2 and 3 days post-EtOH exposure, which was evident across different stimulus contrast levels and spatial frequencies. Cone-dependent ERG responses exhibited altered maximum amplitudes, sensitivity, and/or response thresholds for b-waves and isolated a-waves. After 2-days recovery, maximum b and a-wave amplitudes were reduced by 43 ± 10 and $34 \pm 23\%$ compared to controls, respectively ($p < 0.05$; $n=13-22$); response thresholds for b and a waves were increased by 1.0 ± 0.2 and 0.6 ± 0.1 log intensity units, respectively ($p < 0.05$, $n=7-12$). We also observed accumulation of unstable Ub-G76V-YFP following EtOH exposure in transgenic zebrafish, suggesting ubiquitin-system impairment within cones. Pre-treatment with $0.5 \mu\text{M}$ Torin1, an mTOR1/2 inhibitor previously shown to enhance both autophagy and proteasomal function (Zhao et al., 2015, PNAS), robustly protected against some damaging effects of EtOH on visual function, as revealed by OMR performance and rescue of multiple ERG parameters.

Conclusions: Together, these results show that binge-like EtOH exposure in immature zebrafish larvae produces visual dysfunction, including effects on cone PR neurons. Part of the damaging effects of EtOH on retinal neurons may involve disruption of proteostasis.

CONTROL ID: 3544429

SUBMITTER (NAME ONLY): Ines Marques

TITLE: Microaneurysm Turnover in eyes with mild nonproliferative diabetic retinopathy is associated with progression and development of sight-threatening complications: a 5-year longitudinal study

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.P. Marques, L. Mendes, A. Santos, D. Tavares, M.H. Madeira, C.F. Lobo, J. Figueira, J.G. Cunha-Vaz, Associacao para a Investigacao Biomedica e Inovacao em Luz e Imagem, Coimbra, Coimbra, PORTUGAL|I.P. Marques, M.H. Madeira, J.G. Cunha-Vaz, Coimbra Institute for Clinical and Biomedical Research (iCBR), Coimbra, PORTUGAL|A. Santos, Department of Orthoptics, School of Health, Polytechnic of Porto, Porto, PORTUGAL|C.F. Lobo, J. Figueira, Ophthalmology, Centro Hospitalar e Universitario de Coimbra EPE Campus dos Hospitais da Universidade de Coimbra, Coimbra, Coimbra, PORTUGAL|

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ABSTRACT BODY:

Purpose: To evaluate microaneurysm turnover (MAT) as a predictive biomarker for retinopathy progression and development of sight-threatening complications, diabetic macular edema (DME) or proliferative retinopathy (PDR), in patients with type 2 diabetes and mild nonproliferative retinopathy (NPDR) in a 5-year follow-up.

Methods: A 5-year prospective, longitudinal study was designed to follow 212 patients with type 2 diabetes (T2D) and mild NPDR (ETDRS grades 20 and 35). Ophthalmological examinations of the study eye including color fundus photography (CFP) and optical coherence tomography were performed at baseline, at the first 6-months visit and annually. Outcomes were DME and/or PDR development. MAT analysis included determination of MA formation and disappearance rates, automatically assessed using the RetMarkerDR at 12-month visits. Retinopathy severity progression was evaluated using step increase in ETDRS severity grades.

Results: Of the 212 individuals with T2D and mild NPDR, 162 completed the 5-year follow up period of the study or developed an endpoint (n=25). MAT calculated on the first year showed significant association with the development of any endpoint ($p = 0.0178$), in particularly MA disappearance rate ($p = 0.007$). MAT showed also significant association with ETDRS severity worsening in the 5-year period ($p = 0.0353$). There were variations between MAT values in the first year of follow-up (2.04 ± 3.18) and the 5-year (2.26 ± 3.06 ; $p = 0.060$), with a clear increase in the MA disappearance rate being observed in the last year of the study (1.50 ± 1.93) compared with the first-year of follow-up (1.05 ± 1.99 ; $p = 0.003$).

Conclusions: MAT in eyes with T2D and mild NPDR is associated with retinopathy severity progression and development of DME and/or PDR in a period of 5-years.

CONTROL ID: 3544435

SUBMITTER (NAME ONLY): DRIRH KHARE

TITLE: Differential regulatory role of normal and diabetic limbal epithelial cell-derived exosomes in limbal stromal cells

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. KHARE, A. Poe, R. Shah, A.V. Ljubimov, M. Saghizadeh, Regenerative Medicine Institute, Cedars Sinai Medical Center Eye Program, Los Angeles, California, UNITED STATES|A.V. Ljubimov, M. Saghizadeh, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previously we have shown the regulatory roles of limbal stromal cell (LSC)-derived exosomes (Exos) in normal (N) and diabetic (DM) limbal epithelial cells (LEC) in vitro and ex vivo organ-cultured corneas. Our purpose was to evaluate the effects of N and DM LEC-derived Exos in N and DM LSC maintenance, proliferation and wound healing.

Methods: Human autopsy age-matched N and DM eyes were from the National Disease Research Interchange. LEC and LSC were isolated from dissected corneas using Dispase/Trypsin and collagenase type IV, respectively. Exosomes were prepared from N and DM LEC-conditioned media by ultracentrifugation. LEC-derived Exos were characterized by NanoSight for morphology and particle size, and by flow cytometry and western blot for their markers (CD63, CD81). Exos were labeled with PKH-67 dye to determine their uptake by LSCs and LECs using confocal microscopy. MTS proliferation assay and scratch wound assay were performed on Exo-treated LSC. Markers of mesenchymal stem cells (MSC) and differentiated keratocytes were assessed by western blot.

Results: Isolated Exos sizes ranged between 50-200 nm with the typical cup shape morphology. N and DM Exos were positive for CD63 and CD81 by both western blot and flow cytometry. The uptaken Exos were observed by confocal microscopy and confirmed by FACS analysis in PKH-67-labeled Exo treated LSC and LECs. FACS analysis showed significant five-fold higher LEC-derived Exo uptake by LSCs than LECs. N Exo treatment significantly stimulated LSC wound healing and proliferation, with the stronger effect than with DM Exo treatment. N Exo treatment increased, whereas DM Exo decreased the protein level of MSC marker, CD90, in N LSCs compared to untreated control by western blot. On the contrary, treatment of N LSCs with N Exo decreased keratocyte markers, ALDH3A1, lumican and keratocan, with a less pronounced effect after DM Exo treatment.

Conclusions: The increased uptake of LEC-derived Exos by LSCs than by LECs suggests the cross-talk between limbal epithelial and stromal cells. The greater effects of N Exos than DM Exos on cell proliferation, wound healing and marker expressions may be due to the differences in their cargos.

CONTROL ID: 3544436

SUBMITTER (NAME ONLY): Zheng Jiang

TITLE: The role of melanopsin phototransduction pathways in the injury-resistant ability of intrinsically photosensitive retinal ganglion cells

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Jiang, Y. Zhu, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Zheng Jiang: Commercial Relationship: Code N (No Commercial Relationship) | Yan Zhu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glutamate toxicity mediated by NMDA receptors is involved in many retinal diseases, including retinal ischemia and optic nerve injury, which affect many types of retinal ganglion cells (RGCs). Interestingly, a subpopulation of retinal ganglion cells, named intrinsically photosensitive retinal ganglion cells (ipRGCs), are known to be more resistant than other RGCs to retinal injuries. However, the underlying mechanism of their injury-resistant ability is unknown. Distinct from other RGCs, ipRGCs are capable of detecting light without rod and cone photoreceptor cells, owing to their intrinsically expressed light-sensitive GPCR, melanopsin. The relationship between their intrinsic photosensitivity and injury-resistant ability also is not clear. In this work, we used NMDA-induced excitotoxicity model to study the role of melanopsin-mediated phototransduction pathways in the neuroprotective effect of melanopsin.

Methods: NMDA-mediated neurotoxicity was induced by intravitreally injecting 1 mM NMDA and measured by RGC density change based on immunolabelling with RPBMS, a RGC marker. AAV2-OPN4 virus was intravitreally injected to test the effects of ectopic melanopsin in conventional RGCs. ON- and OFF- α -RGCs were distinguished by immunolabelling with SMI32 antibody on Opn4-Cre;Rosa-tdTomato retina. Trpc6 and Trpc7 double knockout animals were used to examine the involvement of TRP-dependent phototransduction pathway.

Results: We found that virally expressing melanopsin in conventional RGCs increases their survival rate in NMDA-toxicity model, suggesting that melanopsin is sufficient to provide a neuroprotective effect in RGCs. In addition, M4-ipRGCs, also known as ON- α -RGC, have a higher survival rate than OFF- α -RGCs after NMDA treatment, suggesting that low expression of melanopsin is still capable of providing a neuroprotective effect. Interestingly, knocking out TRPC6 and TRPC7 does not reduce the survival rate of ipRGCs, suggesting that the TRP-dependent transduction pathway is not required for the NMDA-toxicity-resilient ability of ipRGCs.

Conclusions: Our data indicate that the NMDA-toxicity-resilient ability of ipRGCs does not require TRPC channels and that virally expressed melanopsin is sufficient to provide a neuroprotective effect in conventional RGCs.

CONTROL ID: 3544438

SUBMITTER (NAME ONLY): Alireza Karimi

TITLE: Ocular biomechanics during improvised explosive device blast

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Karimi, C.A. Girkin, J.C. Downs, The University of Alabama at Birmingham

Department of Ophthalmology and Visual Sciences, Birmingham, Alabama, UNITED STATES|R. Razaghi, Research Department, Heel of Scene Ltd., Tokyo, Japan, Tokyo, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Eye injuries are found in 10-13% of all combat casualties and, more recently, among civilians with improvised explosive device (IED) injury. Bomb blast injuries exerts a shearing force on the air-tissue interfaces through the blast wave, invoking a significant acute IOP elevation. A sudden elevation in the IOP could significantly amplify the mechanical deformation and/or strain within the laminar region that result in neuronal cell death. This study is aimed to estimate the stresses and deformations in the ONH due to IED explosion using a set of two eye-specific fluid-structure interaction (FSI) ONH models.

Methods: Eye-specific FE models of the ONH, including the pia, optic nerve, LC, sclera, and retina were constructed based on the 3D delineation of anatomic surfaces of the posterior eye obtained from two human donors and then the generic anterior segment was added. An IED with the weights of 1 and 2 kg was placed within 2, 3, and 4 m of the victim's temporal (side) and frontal (front) while the ground was covered with a deformable soil to reflect the blast wave. Prior studies ignored the overpressure due to the blast reinforcement by the ground.

Results: Reflection of the bomb blast pressure from the ground reached to the eye prior to the bomb blast pressure itself, which suggests a crucial role for the ground in reinforcement of the blast pressure and ocular injury simulations. Results revealed an IOP elevation of ~ 6,000-48,000 mmHg, with the highest IOP for the IED weight of 2 kg/victim distance of 2 m (front blast) and the lowest for the IED weight of 1 kg/victim distance of 4m (side blast); this suggests the important role of the victim's position with respect to the blast wave in ocular injury analyses (Figure). IOP was elevated by ~2900 and ~2700 mmHg within 1.6 ms after the blast for the front and side blasts, respectively, matching values reported in the literature, but IOPs were much higher due to ground blast reinforcement after 1.6 ms. Stresses and strains were highest in the temporal quadrant of the eye.

Conclusions: The findings of this study have implications for not only understanding of the stresses and deformations in the ONH due to IED explosion, but also for providing information for the military experts to design a better visor (eye armor) to help break the stress of the wave pressure and protect against blast-induced injuries in the ocular-orbital region.

CONTROL ID: 3544439

SUBMITTER (NAME ONLY): Shaohui Wang

TITLE: Therapeutic potential of a gK peptide for control of ocular HSV-1 infection

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Wang, J. Yu, K. Tormanen, U. Jaggi, H. Ghiasi, Surgery, Cedars Sinai Medical Center Eye Program, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported that binding of HSV-1 glycoprotein K (gK) to signal peptide peptidase (SPP) is required for virus infectivity. The goal of this study was to map the gK binding region to SPP and to determine if blocking gK binding to SPP using gK peptides reduces HSV-1 primary infection, latency-reactivation, and corneal scarring.

Methods: The gK domain binding to SPP was mapped using co-immunoprecipitation assays. Effect of this peptide, which we call gK4, on virus infectivity was determined by plaque assay, FACS and RT-PCR. The effect of ocular administration of gK4 on ocular HSV-1 replication was evaluated in BALB/c and C57BL/6 mice.

Results: Using a combination of gK fragments and gK peptides the binding domain of gK to SPP was mapped to 5 amino acids. HSV-1 replication in Vero cells was significantly inhibited by gK4 peptide treatment compared to control peptide. BALB/c mice treated with gK4 peptide as eye drops showed significantly less virus replication in the tear film and significantly fewer viral transcripts in the cornea and trigeminal ganglia during primary ocular infection with virulent HSV-1 strain McKrae. Survival in BALB/c mice was improved after treatment with gK4 peptide. Similar results were obtained following treatment of C57BL/6 mice with gK4 peptide.

Conclusions: Our results suggest that the gK4 peptide significantly reduced virus replication both in vitro and in vivo. Thus, gK4 peptide may have therapeutic potential to control ocular HSV-1 infections.

CONTROL ID: 3544440

SUBMITTER (NAME ONLY): Adam Miltner

TITLE: A novel retinal ganglion cell reporter stem cell line for timing neurogenesis in retinal organoids

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Miltner, S. Kwong, Y. Mercado-Ayon, S.K. Cheema, T. Glaser, A. La Torre, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stem cell-derived retinal organoids are widely used to study complex developmental and disease mechanisms. Pluripotent cells can self-organize to form laminated retinal tissue in vitro, but it is unclear whether organoids follow the same histogenetic clock or molecular mechanisms as retinal progenitors in vivo. As a first step to improve organoid disease modeling and use in future therapy we charted the timing of retinal ganglion cell (RGC) neurogenesis in organoid cultures and tested the role of three late-progenitor micro RNAs (LP-miRNAs)—let-7, miR-9, and miR-125b—in retinal organoid differentiation in vitro.

Methods: We isolated induced Pluripotent Stem Cells (iPSCs) from Isl2-GFP BAC transgenic RGC reporter mouse embryonic fibroblasts by transduction with Nanog, Lin28, Sox2, and Oct4. To determine RGC birthdates, we added 5-ethynyl-2'-deoxyuridine (EdU) to organoid cultures during four different two-day windows, and we measured LP-miRNA levels over time by quantitative PCR. To inhibit LP-miRNAs, we stably targeted Isl2-GFP iPSCs with an inducible polysponge vector via CRISPR/Cas9 recombination.

Results: iPSC-derived RGCs expressing Isl2-GFP were born from differentiation days 7 to 15 with peak birthdates at day 10. These EdU labeling results suggest that LP-miRNAs may act to limit RGC genesis over time, as they do in vivo during normal retinal development. To directly test how LP-miRNAs affect organoid RGC production, we isolated Isl2-GFP iPSC clones that express a polymerized miRNA sponge under the control of a Tet-On system. The multivalent sponge targets all three LP-miRNAs, is incorporated into the 3' UTR of an RFP fluorescent reporter, and is strongly induced after doxycycline addition.

Conclusions: Retinal organoids possess great potential as therapeutic and disease model tools. The timing of RGC birthdates match in vitro and in vivo—and appear to be controlled by the same miRNA mechanisms, providing a basis to model disease and manipulate organoids to produce specific cell types or molecules.

CONTROL ID: 3544444

SUBMITTER (NAME ONLY): Anita Grover

TITLE: Pharmacokinetics and target engagement of intravitreal administration of ANX007, an anti-C1q antibody fragment, in nonhuman primates

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Grover, K. Mease, L.K. Taylor, S. Keswani, Clinical Development, Annexon Biosciences, San Francisco, California, UNITED STATES|S. Sankaranarayanan, V. Mathur, P. Suri, Y. Andrews-Zwilling, E. Cahir-McFarland, T. Yednock, Research, Annexon Biosciences, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: C1q and the classical complement cascade, key regulators of synaptic pruning in neuronal development, are aberrantly activated in neurodegenerative ophthalmic diseases, including geographic atrophy and glaucoma. ANX007 is a novel fragment antibody that specifically recognizes the substrate-binding head groups of C1q and functionally inhibits the classical complement cascade. Nonclinical studies were completed to assess ANX007 biodistribution and C1q target engagement in the eye and serum following intravitreal (IVT) administration in cynomolgus monkeys.

Methods: Three studies were completed. In a single dose study, animals received 1 or 5 mg/eye IVT (n=2/group/timepoint), and serum, vitreous, and non-perfused tissue samples were collected through Day 30 post-dose. In combined analyses of two repeat-dose studies, animals received two monthly IVT doses of 0, 1, 2.5, or 5 mg/eye on Days 1 and 29 (n=2-6/group/timepoint), and terminal serum, aqueous, and vitreous were collected on Day 44 or 59 in each study. In 0 and 5 mg/eye groups, animals were perfused, and retina, choroid and optic nerve samples were collected on Day 44 or 59. Free ANX007 and free C1q were measured using specific and sensitive ELISA-based assays.

Results: All doses were well-tolerated. Vitreous ANX007 levels were measurable up to 30 days following a single or repeat doses of ANX007 at all dose levels studied. The ANX007 half-life in the vitreous was 3 days. Aqueous and vitreous levels were highly correlated, and aqueous levels were 4-fold lower than in the vitreous. In perfused tissue following two monthly 5 mg/eye doses, ANX007 levels were measurable 30 days post-last dose in the retina and choroid, and through 15 days in the optic nerve samples, confirming the diffusion of drug to the back of the eye. Presence of free drug was associated with a complete reduction of free C1q in fluids and perfused tissues.

Conclusions: Following IVT administration, ANX007 distributes to relevant sites of neurodegenerative ophthalmic disease within the retina, with clear evidence of C1q target engagement. Engagement of C1q in the aqueous humor reflects inhibition in the vitreous and retinal tissue, and is hypothesized to be sufficient to mitigate classical complement activation in neurodegenerative ophthalmic disease. This data supports further clinical evaluation of ANX007 for the treatment of such diseases.

CONTROL ID: 3544445

SUBMITTER (NAME ONLY): Chevy Singh

TITLE: Alterations in Gene Expression of Human Trabecular Meshwork Cells in Response to Hyperglycemic Conditions

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Singh, A. Soundararajan, D. Jusufbegovic, J. Lind, P.P. Pattabiraman, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes mellitus (DM) and elevated Intraocular pressure are risk factors for glaucoma, however the mechanisms of this association has not been investigated. The purpose of this study is to understand the alteration in gene expression response in human trabecular meshwork (HTM) cells to hyperglycemic conditions.

Methods: Cultured HTM cells from three donor eyes were maintained in 1% fetal bovine serum (FBS) glucose-free Dulbecco's Modified Eagle Medium (DMEM) with glucose concentrations of 5.5 mM (physiologic serum glucose) or 30 mM (DM patients) for 5 days followed by RNA collection, cDNA conversion and qPCR. Statistical analysis was done via student's t-test where results were statistically significant if $p < 0.05$ for the sample size $n=3$. We particularly examined the gene expression involved in tissue fibrosis including extracellular matrix (ECM), endothelial mesenchymal transition (EndMT) and genes involved in lipid biosynthesis.

Results: Hyperglycemic conditions showed a significant decrease in the cholesterol biosynthetic enzymes 3-hydroxy-3-methyl-glutaryl-coenzyme A synthase (HMGCS) and reductase (HMGCR) ($p=0.04$) and its regulatory transcription factor Sterol regulatory element-binding protein - SREBP 1 and 2. Interestingly there was an increasing trend in - a) profibrotic genes - Collagen 1A, alpha smooth muscle actin, transforming growth factor beta 2 (TGFB2), and Serpin Family E Member 1 (SERPINE), b) extracellular matrix (ECM) components - Fibronectin (FN), Tenascin C (TNC), Collagen 4 alpha (COL4A), Collagen 6 alpha (COL6A), and Elastin (ELN), and c) transcription factors involved in EndMT associated with fibrosis - Snail family transcriptional repressor 1 (SNAIL), Snail family transcriptional repressor 2 (SLUG), and Twist-related protein 1 (TWIST1).

Conclusions: Our preliminary data reveals a negative relationship between cholesterol biosynthesis machinery and positive correlation to fibrotic phenotype in TM as a response to elevated glucose levels. Interestingly, increased ECM deposition in the TM outflow pathway is known to increase resistance to aqueous humor outflow and elevate IOP. Therefore we predict that EndMT resulting in TM fibrosis could be a potential mechanism of IOP elevation in DM subjects.

CONTROL ID: 3544449

SUBMITTER (NAME ONLY): LeAnn Mendoza

TITLE: Deep Learning Predicts Demographic and Clinical Characteristics from Optic Nerve Head OCT Circle and Radial Scans

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mendoza, M. Christopher, N. Brye, J.A. Proudfoot, A. Belghith, C. Bowd, J. Rezapour, M.H. Goldbaum, R.N. Weinreb, L.M. Zangwill, Viterbi Family Department of Ophthalmology, Hamilton Glaucoma Center, Shiley Eye Institute, University of California, San Diego, La Jolla, California, UNITED STATES|M.A. Fazio, C.A. Girkin, Department of Ophthalmology, School of Medicine, University of Alabama-Birmingham, Birmingham, Alabama, UNITED STATES|J.M. Liebmann, C. De Moraes, Department of Ophthalmology, Bernard and Shirlee Brown Glaucoma Research Laboratory, Edward S. Harkness Eye Institute, Columbia University Medical Center, New York, New York, UNITED STATES|J. Rezapour, Department of Ophthalmology, University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Rhineland-Palatinate, GERMANY|

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ABSTRACT BODY:

Purpose: To develop deep learning (DL) models for predicting age, sex, race, diabetes diagnosis, hypertension, cardiovascular disease, and axial length from Spectralis optical coherence tomography (OCT) retinal nerve fiber layer (RNFL) circle and radial scans.

Methods: Spectralis OCT circle and radial scans of the optic nerve head (ONH) acquired from healthy subjects, glaucoma suspects and glaucoma patients from the Diagnostic Imaging in Glaucoma Study (DIGS) and African

Descent and Glaucoma Evaluation Study (ADAGES) were randomly assigned to training (85%), validation (5%) and testing (10%) datasets by patient. DL models were trained on unsegmented circle and radial scans to predict age, sex, race, diabetes diagnosis, hypertension, cardiovascular disease (CVD), and axial length. The circle scan dataset included 52,552 individual B-scans from 1,772 patients. The radial dataset included 111,456 individual B-scans from 730 patients.

Results: The DL models of the best circle and radial scans predicted age with a mean absolute error (MAE (95% CI)) within 5.4 (4.9, 5.9) years and 5.1 (4.5, 5.8) years, respectively and a R^2 (95% CI) of 0.73 (0.67, 0.78) and 0.64 (0.49, 0.76), respectively. For Axial length, the circle scan model had a MAE of 0.7 (0.6, 0.9) mm and an R^2 of 0.3 (0.2, 0.4), and the radial scan model had a MAE of 0.8 (0.7, 1.0) mm and an R^2 of 0.4 (0.2, 0.5). Accuracies (AUROC (95% CI)) for predicting sex in the best circle and radial scans was 0.72 (0.65, 0.79) and 0.68 (0.59, 0.77), respectively. The AUROC for predicting race in the best circle and radial scans was excellent, both 0.96, with 95% CIs of (0.92, 0.98) and (0.91, 0.99), respectively. The AUROC for predicting diabetes diagnosis in the best circle and radial scans was 0.65 (0.52, 0.77) and 0.76 (0.64, 0.85), respectively. The AUROC for predicting hypertension in circle scans was 0.71 (0.59, 0.81) and in radial scans was 0.64 (0.54, 0.73). The AUROC for predicting CVD diagnosis in circle scans was 0.56 (0.47, 0.65) and in radial scans was 0.54 (0.48, 0.62).

Conclusions: These results suggest that there are indicators of demographic and clinical characteristics embedded within OCT images showing that DL can infer these characteristics from images of the ONH. With the exception of predictions of diabetes, the DL models of circle scans predicted clinical and demographic features as well or better than radial scans.

CONTROL ID: 3544450

SUBMITTER (NAME ONLY): Brianna Barrett

TITLE: Dual AAV vector strategy for expression of large genes targeted for Stargardt disease gene therapy development

SESSION TITLE: Gene therapy in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Barrett, S. Kerns, B. Kevany, L. Padegimas, Abeona Therapeutics Inc, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Brianna Barrett: Commercial Relationship(s);Abeona Therapeutics Inc:Code E (Employment);Abeona Therapeutics Inc:Code I (Personal Financial Interest) | Scott Kerns: Commercial Relationship(s);Abeona Therapeutics Inc :Code E (Employment);Abeona Therapeutics Inc:Code I (Personal Financial Interest) | Brian Kevany: Commercial Relationship(s);Abeona Therapeutics Inc:Code E (Employment);Abeona Therapeutics Inc:Code I (Personal Financial Interest) | Linas Padegimas: Commercial Relationship(s);Abeona Therapeutics Inc:Code E (Employment);Abeona Therapeutics Inc :Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Stargardt disease is an inherited, chronic, and progressive retinal dystrophy caused by mutations in the ABCA4 gene resulting in the most common form of juvenile macular degeneration, for which there are currently no therapeutic options. The ABCA4 coding sequence is 6,822 nucleotides in length and therefore exceeds the packaging capacity of a typical AAV capsid. To enable delivery of large genes, several dual AAV vector strategies have been employed, including homologous recombination, trans-splicing, and intein-mediated protein splicing, but each method has advantages and limitations. To overcome these hurdles, we have created a dual AAV approach that allows efficient recombination of N-terminal and C-terminal ABCA4 fragments by exploiting Cre recombinase.

Methods: The first AAV vector encodes the N-terminal region of the ABCA4 gene and also expresses Cre recombinase via a self-cleaving T2A peptide. The second AAV vector encodes the C-terminal region of the ABCA4 gene. Cre recombinase recognizes LoxP sites inserted into each ABCA4 construct and combines the N- and C-terminal fragments resulting in a full-size ABCA4 expression cassette that will exist episomally within the cell. During the same recombination process, the Cre recombinase gene loses its promoter and inactivates itself.

Results: We have demonstrated that infection in tissue culture with a 1:1 ratio of AAV.ABCA_N and AAV.ABCA_C vectors results in efficient ABCA4 coding sequence reconstitution and full-length ABCA4 protein production within 48 hours. Tissue culture cells infected with ABCA_N and ABCA_C vectors lacking Cre recombinase show no detectable full-length ABCA4 protein after up to 120 hours.

Conclusions: Full-length ABCA4 protein can be efficiently reconstituted from two independent AAV vectors by utilizing Cre recombinase. Future studies exploring Cre-mediated ABCA4 reconstitution in vivo and the ability of dual AAV-delivered ABCA4 to clear lipofuscin build-up will be essential milestones to move this early-stage program towards the clinic.

CONTROL ID: 3544452

SUBMITTER (NAME ONLY): Ying Guo

TITLE: The Sensitivity to Light Decrement Controls Rod Response to Flickering Light

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Guo, Y. Umino, E.C. Solessio, Ophthalmology, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ying Guo: Commercial Relationship: Code N (No Commercial Relationship) | Yumiko Umino: Commercial Relationship: Code N (No Commercial Relationship) | Eduardo Solessio: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The recovery kinetics of rod photoreceptor response controls rod response to sinusoidal flicker and consequently sets mouse behavioral flicker sensitivity (temporal contrast sensitivity, TCS) at mesopic lights (Umino Y et al., 2019). The purpose of this work is to study the mechanism underlying the control of rod flicker response by rod recovery kinetics. We hypothesize that faster rod recovery kinetics would enhance rod sensitivity to light decrement, leading to increased rod flicker response.

Methods: Rod flicker response was recorded by trans-retinal ERG in WT and a transgenic line (R9OE) over-expressing R9AP that has faster rod recovery kinetics due to increased G_{α^*} -E* inactivation. Retinas were perfused with Ames medium supplemented with DL-AP4 (50 μ M), CNQX (20 μ M) and BaCl₂ (100 μ M) to isolate photoreceptor response. Because the sinusoidal stimuli does not permit separation of response to light increments and decrements, we utilized square wave flicker of 75% contrast of 0.5 Hz at backgrounds 10–3200 R*/rod/s. All comparisons were done at equivalent suppression of circulating current to match the effect of calcium feedback on rod response.

Results: We used brief flashes of various intensities to measure the dim flash sensitivity and the EC₅₀ at different backgrounds to represent rod sensitivity to light increment. WT and R9OE mice display similar flash sensitivity and EC₅₀. We also found that WT and R9OE mice have similar ON responses to square flicker at all backgrounds. By contrast, WT and R9OE mice have similar OFF responses to square flicker which increase with background until 80 R*/rod/s, above which they diverge. WT mice response remains constant while, R9OE mice response keeps increasing, peaking at 800 R*/rod/s and then decreasing. Thus, R9OE mice exhibit larger OFF responses at 80-3200 R*/rod/s, consistent with behavioral flicker sensitivity. We also used 1.5-second steps of various negative contrasts to acquire the contrast gain to light decrement. WT and R9OE mice have similar contrast gain at <80 R*/rod/s. While, R9OE mice display higher contrast gain than WT mice at 80-3200 R*/rod/s.

Conclusions: At mesopic light, the rate of G_{α^*} -E* inactivation in rod phototransduction cascade sets rod sensitivity to light decrement. Thus, the rod sensitivity to light decrement, not increment, controls rod response and behavioral sensitivity to flicker.

CONTROL ID: 3544453

SUBMITTER (NAME ONLY): Jade Moon

TITLE: Application of Widefield Swept-Source Optical Coherence Tomography Angiography in the Assessment of Retinal Microvasculature and Choroidal Thickness in Myopia Patients

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Moon, I. Garg, R. Katz, Y. Lu, E.S. Lu, C.A. Ludwig, D.M. Wu, J.W. Miller, L.A. Kim, D. Husain, D.G. Vavvas, J. Miller, Retina Service, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|J. Moon, I. Garg, Y. Cui, R. Katz, Y. Zhu, R. Le, Y. Lu, E.S. Lu, C.A. Ludwig, T. Elze, D.M. Wu, J.W. Miller, L.A. Kim, D. Husain, D.G. Vavvas, J. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|Y. Cui, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangzhou, Guangdong, CHINA|Y. Zhu, Department of Ophthalmology, Xiangya Hospital Central South University, Changsha, Hunan, CHINA|R. Le, Department of Ophthalmology, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|T. Elze, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: In recent years, optical coherence tomography angiography (OCTA) has improved our understanding of microvascular changes in myopic macular degeneration. We performed a prospective cross-sectional study using widefield swept-source OCTA (WF SS-OCTA) to assess retinal microvasculature and choroidal thickness in myopia.

Methods: Patients with high myopia (HM; Spherical Equivalent (SE) ≤ -6 D or axial length ≥ 26.5 mm), mild/moderate myopia (MM; $-6\text{D} < \text{SE} \leq -1\text{D}$), and age-matched healthy subjects were imaged with PLEX Elite 9000 (Zeiss) using 3x3mm, 6x6mm, and 12x12mm scans centered on the fovea. Foveal Avascular Zone (FAZ) perimeter, area, and circularity, as well as vessel skeleton density (VSD), vessel density (VD), and choroidal thickness (CT) of entire retina, superficial, and deep slabs were analyzed using the ARI Network (Zeiss Portal).

Results: 186 eyes were analyzed; these eyes were categorized as 75 with HM, 43 with MM, and 68 age-matched controls. HM was associated with increased FAZ perimeter in 6x6 and 12x12 scans ($P < .05$, Table) and decreased circularity in all scans ($P < .002$, Table). HM and MM were associated with decreased VSD and VD in all slabs ($P < .03$, Table). Furthermore, HM was associated with a decrease in every ETDRS subfield, with a larger decrease temporally in 12x12 scans ($\beta_{\text{VSD}} = -13.21$, $\beta_{\text{VD}} = -0.40$, $P < .001$). HM was associated with decreased CT in all scan sizes ($P < .03$, Table). Changes in CT were unevenly distributed, with thinning most evident in the region between central fovea and optic disc and superior nasal subfields ($P < .02$, Figure C).

Conclusions: We identified decreased vessel density associated with myopia using WF SS-OCTA in a large, comprehensive cohort at a single center. We also observed regional differences including a greater decrease in VSD and VD in the temporal quadrant and uneven reductions in CT. Further work may help identify risk factors for the progression of pathologic myopia and other vision threatening complications.

CONTROL ID: 3544455

SUBMITTER (NAME ONLY): Julia Fallon

TITLE: Impact of Ophthalmic Infection on New York State Hospital Admission Length, Charges and Hospital Costs from 2010-2017

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fallon, J. Lin, A. Barash, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if ophthalmic infection was associated with increase in cost or duration of stay in those admitted for ocular disease in New York (NY) state from 2010-2017

Methods: The NY Statewide Planning and Research Cooperative System (SPARCS) database was queried for discharges categorized by "Major Diseases and Disorders of the Eye" (Code 2, All Patient Refined Major Diagnostic Category). These were subcategorized into those admitted for infections and inflammation related to the eye versus those that were admitted for other reasons, using the Clinical Classifications Software (CCS) Diagnosis code, based on the ICD code associated with the hospital stay. We did a statistical analysis of length of stay, costs and charges between these groups utilizing an unpaired two-tailed t-test.

Results: 32,494 discharges were available for analysis. 4 discharges were excluded as they lacked CCS diagnosis information and 7 were excluded for lacking reliable length of stay or cost data. 32,483 unique discharges were analyzed. 48% were female. Ages were 18% 0 to 17 years old, 10% 18 to 29, 21% 30 to 49, 28% 50 to 69, and 23% 70 and older. The average length of stay was 3.6 days (standard deviation 4.84). The average total patient charges and hospital costs for each admission were \$27,900 and \$9,888, respectively. Medicare and Medicaid accounted for majority of the primary payment means, accounting for 31% and 32% of discharges each. There were 11,696 admissions associated with a CCS Diagnosis code related to infection or inflammation, accounting for over 1/3 of all discharges (36%). Infection was significantly associated with a longer duration of admission (4.2 days vs. 3.3 days, p-value <0.01). However, these stays were associated with lower charges to the patient and overall cost (\$26,211 vs. \$28,850, p-value <0.01; \$9,234 vs. \$10,256 p-value <0.01).

Conclusions: Across NY state hospital discharges for ophthalmic complaints from 2010-2017, eye infection and/or inflammation was associated with increased length of stay, but overall decreased charges to the patient and overall cost to the healthcare system. To our knowledge, this is the first analysis of ophthalmology patients utilizing the SPARCS database.

CONTROL ID: 3544458

SUBMITTER (NAME ONLY): William Mitchell

TITLE: Disparities in Eyecare Utilization in Glaucoma – A National Medicare Study

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Understanding disparities in healthcare utilization can identify barriers to access and motivate efforts to overcome them. We examine disparities in eyecare utilization by race and socioeconomic status (SES) among Medicare beneficiaries with glaucoma.

Methods: A nationally representative 5% sample of Medicare beneficiaries >65 years with glaucoma (≥ 1 ICD-9/10 code, and a Chronic Conditions Warehouse glaucoma diagnosis) was assembled. Low SES was defined as ≥ 2 low-income indicators (dual Medicare/Medicaid eligibility; Part D limited income subsidies; eligibility for Part A/B state buy-in). Eye care utilisation was measured using CPT codes for in/outpatient visits, visual field (VF) and retinal nerve fibre layer optic coherence tomography (RNFL OCT) testing, and laser/surgical intervention between 6/30/2014-12/31/2016. We estimated adjusted incidence rate ratios (IRR) for eyecare utilization comparing race and SES.

Results: 79,787 glaucoma beneficiaries were included. Compared to Whites, Black beneficiaries were less likely have outpatient visits (IRR [95% CI] 0.90 [0.89-0.91]), VF testing (0.92 [0.91-0.94]), and RNFL OCT testing (0.77 [0.75-0.79]); but more likely to undergo glaucoma surgery (1.17 [1.04-1.30]). Hispanic beneficiaries were less likely to undergo RNFL OCT testing (0.90 [0.86-0.93]). Asian beneficiaries were more likely to have outpatient visits (1.06 [1.04-1.09]) and VF testing (1.10 [1.07-1.14]).

Low SES beneficiaries were less likely vs high SES to have outpatient visits (0.92 [0.91-0.93]), VF testing (0.81 [0.80-0.83]), RNFL OCT testing (0.77 [0.76-0.79]) and glaucoma surgery (0.79 [0.70-0.90]). White beneficiaries of low SES were less likely vs high SES to undergo outpatient visits (0.86 [0.84-0.87]), VF testing (0.76 [0.74-0.78]), RNFL OCT testing (0.76 [0.74-0.79]), selective laser trabeculoplasty (SLT) (0.74 [0.64-0.85]), and trabeculoplasty (0.60 [0.44-0.82]), aqueous shunt (0.63 [0.42-0.96]) and minimally invasive glaucoma surgery (MIGS) (0.74 [0.59-0.92]). There was no difference in all eyecare utilization by SES among Black beneficiaries.

Conclusions: Black and Hispanic beneficiaries with glaucoma generally receive less eyecare than Whites. Even when adjusted, the association of low SES with eyecare utilization differed by race. Further research is needed to understand reasons for these disparities.

CONTROL ID: 3544460

SUBMITTER (NAME ONLY): Hernan Dieguez

TITLE: EXPOSURE TO ENRICHED ENVIRONMENT PROTECTS THE CENTRAL RETINAL PIGMENT EPITHELIUM AND RETINA ON A DRY-AMD EXPERIMENTAL MODEL IN MICE.

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Dry age-related macular degeneration (dAMD), the main blindness cause in the elderly, is characterized by retinal pigment epithelium (RPE) and photoreceptors (PR) atrophy circumscribed to the macular area. At the moment, there are no effective therapies to prevent or delay the vision loss affecting dAMD patients. We have developed a dAMD model induced by superior cervical ganglionectomy (SCGx) in C57BL/6J mice, which reproduces the disease hallmarks exclusively circumscribed to the RPE/outer retina temporal region. Environmental enrichment (EE) is a complex condition that boosts physical and social stimulation. Several reports show that EE provides a better recovery from different neuropathology and retinal alterations. In this context, our aim was analyzing the effect of EE on the alterations induced by experimental dAMD.

Methods: Adult male C57BL/6j mice were submitted to unilateral SCGx, where the contralateral side was submitted to a sham procedure. Animals were continuously exposed to SE or EE during different intervals. Visual function (electroretinography and visual behavior tests) was analyzed at 4, 6 and 10 weeks post-SCGx. Retinal histology and ultrastructure were analyzed at 10 weeks post-SCGx. RPE mitochondria and oxidative stress markers were assessed by Western blotting, specific probes, and immunofluorescence at 6 weeks post-SCGx.

Results: SCGx induced a reduction of the melanin content and RPE65 immunoreactivity at the temporal RPE, as well as a decrease in mitochondria mass, an increase in mitochondria superoxide and lipid peroxidation products. Moreover, SCGx induced ultrastructural alterations at the temporal RPE and PR. EE did not prevent SCGx-induced choroid alterations but significantly prevented the visual dysfunction, histology and ultrastructure alterations, mitochondria and oxidative stress. Moreover, EE reversed the functional and structural damage induced by SCGx when started at 4 weeks post-surgery.

Conclusions: Therefore, exposure to EE prevented, and reversed the damage induced by experimental dAMD, probably through RPE mitochondria protection and RPE oxidative damage prevention, thus becoming as a promising novel therapeutic strategy for dAMD.

CONTROL ID: 3544463

SUBMITTER (NAME ONLY): Luis De Sisternes

TITLE: ARI Network Hub: Establishing a cloud-based collaborative solution for advancing eye research

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. De Sisternes, G. Klose, B. Sandhoefner, D. Cosette, G. Michalec, G.C. Lee, S. Magazzeni, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We designed the ARI Network Hub: an online platform to share and process swept-source (SS) OCT angiography data. Our goal was to bring together leading clinicians with scientists and developers to accelerate retinal research through collaboration. In this work we analyze the success of this cloud-based solution in the 4 years since origination.

Methods: We set up a platform where different sites can upload deidentified data directly from a PLEX® Elite 9000 (ZEISS, Dublin, CA) instrument into the ARI Network Hub, and share it in collaboration with other sites as well as execute prototype algorithms. The initial 4-year goal was to add up to 220 sites on board. Prototype algorithm development for innovation was shaped by the clinicians part of this collaborative effort. We tracked number of sites, collaborations started between them, data uploaded, prototype algorithms shared and algorithms executed within the system. We analyzed scalability needs in terms of data storage, processing power and bandwidth to further understand the optimal design of such a cloud-based solution.

Results: 195 sites joined within the 4 years, leading to more than 289 independent publications derived from this collaborative effort. Data uploads were minimal during year 1 but increased during year 2 at a stable rate of ~100 and ~0.7TB per year quarter (/y.qtr) in terms of independent OCT volume datasets and size, respectively. Growth increased ~150%/y.qtr in both number and size in the remaining 2 years (Figure 1). Data uploaded after 4 years was a total of 22000 datasets holding 17TB. 23 processing algorithms were shared across participating sites, with macular density quantification algorithms being of highest usage. Algorithm usage saw an increase with the number of algorithms made available and data shared within the system. There was high non-uniformity across sites in terms of data shared, as well as in algorithm use both across sites and over time, highlighting the need of quick scalability of the design both in storage and calculations.

Conclusions: The proposed cloud-based solution was adopted and proved to accelerate research, especially considering the streamlined collaboration between institutions and device manufacturers. The vast amount of data acquired and collected represents high potential for future collaborative research and algorithm development.

CONTROL ID: 3544464

SUBMITTER (NAME ONLY): Francisco Figueiredo

TITLE: Rising incidence of ocular chemical injury secondary to assault in the Northeast of England

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.C. Figueiredo, C. Bruce, C. Cartes, S. Pradhan, Ophthalmology, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|F.C. Figueiredo, Biosciences Institute, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To report the rising incidence of ocular chemical assaults and analyse the epidemiologic and clinical profile of these injuries at a tertiary eye centre in the Northeast (NE) of England. These acts of violence affect the victims physically, psychologically and impact their quality of life negatively. Hence, constitute a significant social concern

Methods: Retrospective review of all consecutive cases with ocular injuries secondary to chemical assault presenting to the Eye Emergency Department, Royal Victoria Infirmary, Newcastle upon Tyne, UK between November 2015 and October 2020. The incidence, patient demographics, nature of chemicals, severity, management and clinical outcomes were recorded

Results: During the study period, 126 eyes of 90 patients endured these injuries secondary to an assault. Number of chemical assaults was 7 (9 eyes), 22 (31 eyes), 23 (30 eyes), 15 (21 eyes) and 23 (35 eyes) in the 1st, 2nd, 3rd, 4th and 5th year respectively. The mean age was 32.3 years (SD 11.7; Range 13-78). Male (92.2%) preponderance was noted. The ocular injury was unilateral in 54 patients (60.0%) and bilateral in 36 (40.0%). Ammonia was the commonest chemical used (67.8 %). Roper Hall severity grading at presentation was grade 1 in 61.9% (n= 78), Grade 2 in 12.7% (n=16), grade 3 in 12.7% (n=16), grade 4 in 7.9% (n= 10) and undocumented in 4.8% (n=6). Out of the 90 eyes, 82 (91.1%) were acutely managed medically. Eight eyes (8.9 %) needed amniotic membrane transplant, 7 of which were Roper Hall Grade IV and 1 was Grade III. Five of these patients progressed to total limbal stem cell failure despite maximal medical and surgical management

Conclusions: A rise in incidence of eye injuries caused by chemical assault, also known as “acid attack”, has been observed in young adult men over the past 5 years in NE of England. This can be vision threatening and is a rather serious medical and social concern requiring further investigation to be able to increase public awareness, implement stricter regulations, better surveillance and means of prevention and provide adequate support to the victims

CONTROL ID: 3544465

SUBMITTER (NAME ONLY): Jasmine Geathers

TITLE: The R345W-fibulin-3 mutation increases the sensitivity of the outer retina to damage caused by sodium iodate

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Geathers, J. Liao, S.L. Grillo, A.J. Barber, J. Sundstrom, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|W. Wang, The University of Texas at Austin, Austin, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Malattia Leventinese (ML), an autosomal dominant inherited degenerative eye disease, is caused by a point mutation (R345W) in the fibulin-3 (Fib3) gene (efemp1) that results in hyperreflective foci (detected by optical coherence tomography) in association with sub-retinal pigment epithelium (RPE) drusen and hyper-pigmentation. The purpose this study was to determine the extent of augmentation of hyperreflectivity caused by sodium iodate (SI)-induced retinal degeneration in mice carrying the R345W fib3 mutation.

Methods: Eighteen C57 three-month-old male and female mice were injected with SI dissolved in PBS at 15, 30, 45, or 60 mg/kg. Spectral-domain optic coherence topography (SD-OCT) images were acquired 7 days later (Bioptigen). Frozen vertical retinal cross-sections (10 µm thick) of eyes from wild-type (WT), heterozygous (Fib3^{+/-ki}), and homozygous (Fib3^{ki/ki}) mice were processed for H&E staining.

Results: Hyperreflective foci (HRF) were detected by SD-OCT in the retinas of WT mice given 45 and 60 mg/kg, but not in those given 15 and 30 mg/kg. H&E sections appeared normal in the control mice, and in the WT mice that received 15 and 30 mg/kg of SI. The retinas of WT mice receiving 45 and 60 mg/kg were thinner than the control (31.2% and 27.1%, p<0.001), due to the loss of tissue in the photoreceptor layer. Thinning of the ONL and disorganization of the RPE layer was also noted. Hyperreflective foci were evident in Fib3^{+/-ki} and Fib3^{ki/ki} mice given SI at 30, 45, and 60 mg/kg but were not apparent in mice given 15mg/kg. H&E images followed a similar trend, with the 15mg/kg dose looking similar to the controls, whereas sections from Fib3^{+/-ki} and Fib3^{ki/ki} mice treated with 30, 45, and 60mg/kg presented with pigmented lesions in the neural retina.

Conclusions: The results suggest that SI causes HRF and induces pigment migration into the neural retina in WT mice. Furthermore, presence of the fib3 mutation increases sensitivity to SI exposure, leading to more dramatic retinal degeneration and pigment migration. Our results suggest that the R345W mutation increases susceptibility of the outer retina and RPE to chemical or metabolic insult.

CONTROL ID: 3544479

SUBMITTER (NAME ONLY): Nahrain Putris

TITLE: Activation of p38-MAPK is Required for VEGFA165-induced Migration, but not Proliferation, of Primary Human Retinal Microvascular Endothelial Cells

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Putris, W.A. Dailey, B. Metcalf, M. Deshpande, K.P. Mitton, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|N. Putris, B. Metcalf, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: In addition to the well-known pathological consequences of elevated total VEGFA, reports of isoform switching of VEGFA165b to VEGFA165a in the vitreous of patients with proliferative eye diseases led us to ask whether this isoform shift is a significant contributor to the hyperactivation of primary human retinal microvascular endothelial cells (HRMECs). As part of this investigation, we compared the contributions of MAPK, AKT, and p38-MAPK to proliferation and migration in primary HRMECs using in situ immunofluorescence assays.

Methods: VEGFA165 isoforms were compared for their effects on cell proliferation, measured with infrared-fluorescence Cell-Tag assays. Cell migration was compared using a fluorescent transmembrane migration assay in the multiwell plate format. Relative contribution of the MAPK, AKT, and p38-MAPK pathway to cell proliferation and migration were assessed using pharmacological inhibition of MAPK, AKT, and p38-MAPK activation.

Results: At a saturating activation concentration (5,000pM), VEGFA165b was as good or slightly more potent than VEGFA165a as a stimulator of cell proliferation but was not significantly different between both isoforms. The p38-MAPK inhibitor SB203580 increased HRMEC proliferation but was also found to be a potent activator of MAPK, while blocking p38-MAPK activation. VEGFA165a stimulated cell migration more than 6-fold compared to VEGFA165b at 1000 pM. Inhibition of MAPK with U0126 (MEK inhibitor), did not inhibit VEGFA165-induced migration. Inhibition of AKT activation with MK2206 did not inhibit a VEGFA165-induced cell migration. Inhibition of p38-MAPK with BIRB796 completely blocked VEGFA165-induced cell migration.

Conclusions: VEGFA165b was a poor activator of HRMEC migration at lower, physiological, concentrations where VEGFA165a induced substantial cell migration. This was consistent with our dose-response analysis of their relative activation of intracellular signaling pathways (MAPK, AKT, and p38-MAPK). VEGFA165 driven cell migration was mostly mediated via activation of the p38-MAPK pathway. VEGFA165-induced proliferation of primary HRMECs did not require activation of p38-MAPK in addition to MAPK.

CONTROL ID: 3544484

SUBMITTER (NAME ONLY): Jami Gurley

TITLE: Progressive loss of retinal arteriolar smooth muscle cells (SMCs) with aging and caveolin-1 (Cav1) depletion: Assessing the importance of endothelial cell (EC)-Cav1 in retinal SMC maintenance

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Gurley, Ophthalmology, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|J. Gurley, E.A. Hargis, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|N. Standifer, The University of Oklahoma, Norman, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal vascular disease accounts for the majority of vision loss, and aging and diabetes increase the risk for retinal vascular dysfunction and degeneration. Loss of retinal SMCs has been observed in diabetic humans, and in aged and global Cav1 knockout (KO) mouse retinas. However, the relationships among aging, diabetes, and Cav1 function as it relates to SMC maintenance is unclear. The purpose of this study was 1) to characterize SMC loss that occurs with murine aging, 2) to evaluate potential SMC loss in aged human retinas, and 3) to assess the importance of EC-Cav1 on SMC maintenance.

Methods: Micron IV imaging was used to monitor longitudinal in vivo SMC loss in wild type (WT) animals expressing SMC-GFP driven by the alpha-smooth muscle actin (α SMA) promoter. Aged human retinal punches were stained with α SMA and collagen IV antibodies in order to visualize SMC coverage by immunohistochemistry (IHC). Tie2- and Sm22-Cre recombination of the Cav1 floxed gene were used to generate EC- and SMC-Cav1 KO mice, respectively. SMC coverage area and gap numbers per area along retinal arterioles were determined by ImageJ analysis of confocal laser scanning microscopy images from murine retinal flat mounts stained with α SMA and CD31 (as per Reagan et al. 2018).

Results: Retinal SMC loss occurs in WT mice as early as 10 months of age. We also observed incomplete SMC coverage along aged human arterioles. Tie2-, but not Sm22-, Cav1 KOs exhibited reduced arteriolar SMC coverage compared to WT controls (WT: 0.994 ± 0.002 ; Tie2-KO: 0.979 ± 0.003 ; Sm22-KO: 0.997 ± 0.001 ; $p < 0.0001$ WT vs Tie2-KO). Likewise, Tie2-KO retinas showed increased arteriolar SMC gap numbers per area compared to WT and Sm22-KOs (WT: 0.023 ± 0.006 ; Tie2-KO: 0.129 ± 0.020 ; Sm22-KO: 0.025 ± 0.008 ; $p < 0.0001$ WT vs Tie2-KO).

Conclusions: Our data suggest that aging, as well as loss of EC-Cav1 function, results in reduced SMC coverage along retinal arterioles. Additionally, our data support that EC-, rather than SMC-specific Cav1, is important for arteriolar SMC maintenance in adult murine retinas. Future studies will investigate the importance of EC-Cav1 on SMC maintenance and retinal vascular disease through assessment of: 1) cellular and metabolic EC functions, 2) EC/SMC interactions, and 3) potential EC-Cav1 dysfunction in DR progression.

CONTROL ID: 3544487

SUBMITTER (NAME ONLY): Leslie Wilson

TITLE: Peptidyl Arginine Deiminase 4 (PAD4) inhibition does not prevent neutrophil extracellular traps (NETs) formation or significantly decrease ocular inflammation in two mouse models of uveitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Wilson, V. Wang, K. Pepple, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|R. Kuley, R. Moore, C. Lood, Rheumatology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Determine if NETs form in eyes with experimental uveitis, and measure the impact of inhibiting NET formation on ocular inflammation in Primed Mycobacterial Uveitis (PMU) and Experimental Autoimmune Uveitis (EAU).

Methods: For chemical inhibition of NETs, uveitis was induced with either the PMU or IRBP immunization EAU protocol in C57BL6 mice. Mice were divided into groups treated with either PBS, dexamethasone (Dex), or chloride amidine (CI-Am) a PAD4 inhibitor that significantly reduced NET formation in a mouse model of ANCA vasculitis. For genetic inhibition of NETs, PMU or EAU was induced in C57BL6 and PAD4 deficient animals. Ocular inflammation was scored on the day of peak inflammation in PMU using optical coherence tomography (OCT) or by fundus score in EAU. To detect intraocular NETs, immunohistochemistry (IHC) was performed on ocular sections with antibodies to detect myeloperoxidase (MPO), citrullinated H3, and extracellular DNA. Additionally, intraocular NET concentration was determined using an ELISA that detects extracellular DNA complexed with MPO. Comparisons between treatment groups were made using Kruskal Wallis or unpaired t-test. Differences in NET concentration between right and left eyes in PMU animals were compared using paired t-test. Significant differences were determined as $p < 0.05$.

Results: NETs were detected in inflamed eyes by IHC (A) and ELISA (B). NETs concentrations were significantly elevated in inflamed (right eyes) of PMU animals compared to uninflamed fellow (left eyes) for all treatments. In PMU, no treatment significantly decreased NET concentration compared to PBS. In EAU, treatment with Dex and CI-Am decreased aqueous NET concentration compared to PBS, but not significantly. There was a mild, non-significant decrease in inflammation score in PMU animals treated with CI-Am (C). In EAU, CI-Am treatment also non-significantly decreased inflammation score compared to PBS (D). Only Dex significantly decreased fundus scores in EAU animals. PAD4 deficiency did not impact NET concentration or clinical score in PMU or EAU.

Conclusions: NETs are present in eyes with uveitis, but their formation is not PAD4 dependent. Treatment with CI-Am has a mild anti-inflammatory impact on uveitis, but this effect is likely mediated by inhibition of other protein deiminases and not PAD4

CONTROL ID: 3544490

SUBMITTER (NAME ONLY): Kaori Yamada

TITLE: VEGFR2 trafficking by KIF13B is a novel therapeutic target for wet AMD

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Yamada, C. Zhou, Pharmacology and Regenerative Medicine, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|K. Yamada, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kaori Yamada: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Zhou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Vascular endothelial growth factor (VEGF) and its receptor VEGFR2 are promising therapeutic targets for wet AMD. As a topically applicable option, we developed the peptide KAI to selectively interfere with VEGFR2 trafficking to the cell surface where it receives VEGF. This study sought to determine the efficacy of KAI in the mouse model of choroidal neovascularization (CNV).

Methods: The specificity of KAI was tested by surface plasmon resonance (SPR). The drug delivery was analyzed by cryosection and the ELISA after treatment of KAI eyedrop to the mouse eyes. For the laser-induced CNV model, mice with laser-induced ruptures in Bruch's membrane received daily treatment of KAI eyedrop or control peptide. The other groups of mice received intravitreal injection of anti-VEGF or IgG control. After 2 weeks, CNV was quantified and compared.

Results: First, we showed the specificity and high affinity of KAI to VEGFR2. Next, biodistribution revealed successful delivery of KAI eyedrop to the back of the mouse eyes. KAI significantly reduced the disease progression in laser-induced CNV. The comparison with current therapy suggests that KAI eyedrop is as effective as current therapy to prevent CNV in wet AMD. Moreover, the genetic deletion of a kinesin KIF13B, which mediates VEGFR2 trafficking to the cell surface, confirmed the pivotal role of KIF13B in disease progression of wet AMD and neovascularization from choroidal vessels.

Conclusions: Taken together, pharmacological inhibition and genetic deletion complementarily suggest the therapeutic possibility of targeting VEGFR2 trafficking to inhibit pathological angiogenesis in wet AMD.

CONTROL ID: 3544491

SUBMITTER (NAME ONLY): Sana Arshad

TITLE: A pilot study to characterise the immune response in human Herpes Keratitis

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Arshad, D. Hunter, A.J. White, N.A. Carnt, Centre for Vision Research, The Westmead Institute for Medical Research, Westmead, New South Wales, AUSTRALIA|S. Arshad, D. Hunter, K. Bertram, A.J. White, C. Petsoglou, A. Cunningham, The University of Sydney, Sydney, New South Wales, AUSTRALIA|K. Bertram, A. Cunningham, Centre for Virus Research, The Westmead Institute for Medical Research, Westmead, New South Wales, AUSTRALIA|C. Petsoglou, NSW Tissue Banks, Sydney, New South Wales, AUSTRALIA|N.A. Carnt, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Herpes Keratitis (HK) is a corneal infection causing the highest rate of infectious blindness in developed countries. The immune response to HK in human tissue has not been widely studied to date. This study aims to characterise the different subsets and locations of immune cells in human corneal tissue and compare them between herpetic and cadaver corneas.

Methods: Six corneas from cadavers were collected from NSW Tissue Banks and 1 HK sample was collected from Sydney Eye Hospital. $\frac{3}{4}$ segments of each cornea was incubated with Collagenase Type II for 4 hours to extract cells from the epithelium and stroma in a single suspension before staining with monoclonal anti-human antibodies and analysing them by high parameter flow cytometry. The 23 markers include CD14, CD11c, CD4, CD8 and CD56. Results are presented as mean (\pm SEM).

The remaining $\frac{1}{4}$ segments from each cornea were fixed in 4% paraformaldehyde for 24 hours prior to staining with fluorescently labelled DAPI, langerin, CD3 and CD56. Sections were imaged to assess the locations and morphologies of Langerhans cells, T cells and natural killer cells.

Results: Epithelia of the cadaver samples (time post-enucleation range 0-1 days) showed an increased presence of CD14⁺ macrophages (10.46 ± 2.23) and conventional type 2 dendritic cells (13.94 ± 7.43) compared to the HK corneal sample (1.56 ; 0.28 respectively). However, CD4 cells, CD8 T cells and natural killer cells were shown at higher proportions in the epithelium of the HK sample (21.4 ; 31.5 ; 16.1 respectively) compared to the cadaver control groups (19.74 ± 7.86 ; 26.97 ± 5.11 ; 2.97 ± 1.14). Similar trends were seen in the stroma however, there was no difference between natural killer cell populations.

Immunofluorescence microscopy of the HK cornea showed that there was an accumulation of T cells in the central region of the stroma (59) whereas human cadaver samples showed minimal T cells in this corresponding region (3.33 ± 1.67). Human cadaver samples showed Langerhans' cells, T cells and natural killer cells residing in the limbal epithelium and stroma as previously shown.

Conclusions: Human HK tissue exhibited a decrease in myeloid cells and increase in lymphocytes compared to cadaver samples, which were mainly located in the central stroma. Further investigation is required to better characterise the role of these cell types and the pathway of myeloid cells in human HK.

CONTROL ID: 3544492

SUBMITTER (NAME ONLY): Renato Maccione

TITLE: Comparison of the quality of life between glaucoma and age-related macular degeneration patients living in a middle-income country.

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Maccione, K.S. Tomishige, C.S. Germano, P.A. Ottaiano, N. Kasahara, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, BRAZIL

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ABSTRACT BODY:

Purpose: Health-related quality of life (QoL) has emerged as an essential health outcome in population health, clinical trials, and clinical improvement. Both patients with glaucoma and age-related macular degeneration (AMD) have compromised QoL as compared to their age-matched counterparts with normal vision. This topic has not been extensively assessed in patients with eye diseases living in low-middle income countries. This cross-sectional, case-control study aimed to compare the QoL between primary open-angle glaucoma (POAG) and AMD Brazilian patients.

Methods: Patients with AMD, POAG, and normal controls underwent a complete eye examination including measurement of best-corrected visual acuity, biomicroscopy, tonometry, and eye fundus evaluation; all participants answered the Brazilian-Portuguese version of the Visual Function Questionnaire 25 (VFQ-25). The VFQ-25 consists of a base set of 25 vision-target questions representing 11 vision-related constructs and one additional single-item general health rating question. Each item was scored and an overall composite score was calculated and compared among groups with the ANOVA test.

Results: The sample comprised 48 patients with AMD, 56 with POAG, and 53 controls. All groups were matched for age, gender, ethnic distribution, and comorbidities. VFQ-25 total score was lower in both POAG (61.8 ± 20.4) and AMD (50.7 ± 20.9) as compared to controls (89.3 ± 9.1 , $P < 0.000$); AMD patients' score was lower than POAG patients ($P = 0.04$).

Conclusions: Brazilian patients with POAG and AMD presented significantly lower QoL highlighting the need to improve the care of patients in this middle-income country.

CONTROL ID: 3544496

SUBMITTER (NAME ONLY): Marilyn Schneck

TITLE: Vision Measures as Predictors of Progression to Advanced AMD

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schneck, L. Lott, G. Haegerstrom-Portnoy, S. Hewlett, RERC, Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|G. Haegerstrom-Portnoy, S. Hewlett, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|B.M. Gauer, Bonnie M Gauer, LLC, Roseburg, Oregon, UNITED STATES|A. Zaidi, Pacific Eye Associates, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess whether vision measures are predictive of disease progression to advanced AMD in people with intermediate (I) AMD.

Methods: 125 participants were tested monocularly (best correction) on a test battery described previously (Lott, et al, 2020)¹ and followed over time. All enrolled participants had high contrast acuity better than 20/40 (≤ 0.30 logMAR) at baseline (BL). AMD status was ascertained by dilated eye exam and fundus photos, and each eye was categorized as follows: Control (no drusen or small drusen only), Early (medium drusen), or I-AMD (large drusen and/or pigment abnormalities)². Progression to advanced AMD (neovascularization [NV] or geographic atrophy [GA]) was determined by dilated exam and OCT. General estimating equations (GEE) logistic regression analyses were used to assess the association between vision measures and progression to advanced AMD, taking into account the correlation between the two eyes.

Results: To date, 29 eyes (of 22 participants) progressed to advanced AMD (20 NV, 9 GA) an average of 1.82 +/- 1.05 years after vision data were collected (range 0.08 – 4.52 years). All eyes that progressed had I-AMD at BL vision testing, so age-matched I-AMD eyes that did not develop advanced AMD in either eye were the comparison group (39 eyes of 27 participants). In GEE logistic regression models including age, only shape discrimination hyperacuity (SDH)³ ($p < 0.05$) was a significant predictor of progression to NV. When AMD pigment status (PS; present/absent) was included with age and SDH in the NV model, neither PS nor SDH attained statistical significance due to high shared covariance; PS and SDH were significantly associated in I-AMD⁴. In separate models including age, significant functional predictors of GA were low contrast acuity at low luminance⁵ (LC_LL) ($p < 0.007$) or optotype contrast sensitivity (CS) ($p < 0.04$). When PS was included in the GA model with age and LC_LL, only LC_LL was statistically significant ($p < 0.01$). When PS was included in the model with age and CS, both PS and CS remained significant ($p < 0.05$ and $p < 0.03$, respectively).

Conclusions: Clinically feasible vision function tests may aid the prediction of progression to advanced AMD. Different vision measures predict NV (SDH) vs. GA (LC_LL or CS).

References: ¹ Lott, et al. Ophthalm Epidemiol, 2020; ² Ferris, et al. Ophthalmol. 2013; ³ Wang et al. IOVS, 2013; ⁴ Schneck et al, OVS, 2021; ⁵ Haegerstrom-Portnoy et al. IOVS.1997.

CONTROL ID: 3544499

SUBMITTER (NAME ONLY): Rebecca Chen

TITLE: Electronic clinical decision support tool for hydroxychloroquine dosing guideline adherence

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Chen, B. Kuo, A. Kalur, J. Muste, R.P. Singh, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|A. Kalur, J. Muste, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To implement and assess the impact of an electronic clinical decision support tool (DST) on prescriber adherence to 2016 Academy of Ophthalmology (AAO) recommendations for a hydroxychloroquine maximum daily dose of 5 mg/kg actual body weight.

Methods: A DST was developed to trigger a pop-up alert within the electronic medical record when a prescriber orders hydroxychloroquine exceeding 5 mg/kg actual body weight or >400mg daily. The prescriber may choose to amend the prescription or override the alert. The tool was implemented on April 21, 2020. A chart review was performed of all hydroxychloroquine prescriptions in the 6-month post-intervention period (May – November 2020). Inclusion criteria were patient age ≥ 18 years; availability of dose and frequency; availability of actual body weight; and outpatient prescription status. Only the most recent prescription was used in cases of an individual patient having multiple prescriptions. Prevalence of excess hydroxychloroquine dosing ($>5\text{mg/kg/day}$) and mean daily dose in the post-intervention period was compared to previously collected, pre-intervention data from 2018 (under review for publication), using the chi-squared test and 2-sample t-test, respectively. The odds ratios of excessive dosing was assessed using multivariable logistic regression that included sex, race, weight, and prescriber specialty.

Results: There were 7915 patients with active hydroxychloroquine prescription, of which 7415 (94%) met inclusion criteria. There prevalence of excessive dosing decreased from 27.4% pre-DST to 21.1% post-DST ($P<0.001$). Mean daily dose decreased from 342 ± 94 mg (4.3 ± 1.4 mg/kg/day) pre-DST to 324 ± 93 mg (4.1 ± 1.3 mg/kg/day) post-DST ($P<0.001$). Only 0.2% prescriptions exceeded mean 400mg daily, and 0.1% prescriptions were indicated for COVID-19. In multivariable analysis, a rheumatologist prescriber (in comparison to all other specialties, OR 0.66 [99% CI 0.54-0.80]) and greater weight (OR 0.94 [99% CI 0.93-0.95], equivalent to -0.062 log odds per 1 kg increase in weight) were associated with reduced odds of excessive dosing.

Conclusions: Implementation of a DST significantly improved prescriber adherence with 2016 AAO ophthalmic safety recommendations for hydroxychloroquine dosing. As daily dosage is a strong predictor of retinopathy risk, an electronic DST demonstrates potential to reduce ophthalmic morbidity associated with chronic hydroxychloroquine use.

CONTROL ID: 3544501

SUBMITTER (NAME ONLY): Hadeel Sadek

TITLE: Assessing open angle glaucoma as an independent risk factor for stroke

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Sadek, I.S. Shaikh, S.T. Elsamna, A.S. Khouri, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of vision-threatening disease worldwide and its open-angle variant has previously been explored as a risk factor for stroke. Using a large sample population database, we investigated the possible impact of open-angle glaucoma (OAG) both with and without numerous other clinical and non-clinical factors on the risk of developing stroke.

Methods: Cases of OAG were obtained from the National Inpatient Sample (NIS) database between 2002 and 2013 using ICD-9 codes. Associated morbidities and procedures were assessed in a random sample of cases with a primary hospital admitting diagnosis of stroke, no prior history of stroke, and a history of OAG. Univariate and multivariate logistic regression analyses were carried out in glaucoma cases to determine risk factors for stroke. A second analysis was conducted after propensity matching (1:5 ratio) for other risk factors to determine if glaucoma was independently associated with increased risk of stroke. The Bonferroni correction method was applied.

Results: The random sample consisted of 395,724 cases which were grouped into stroke (n=4,614) and non-stroke (n=391,110) cohorts. History of OAG (n=4,187) was found to be strongly associated with stroke in univariate analysis (OR: 2.26, 95% CI: 2.07-2.46) but this association was found to be weaker (OR: 1.11, 95% CI: 1.04-1.18) in multivariate analysis (Figure 1). When propensity matching (Figure 2) was performed for clinical and non-clinical risk factors found to be significant for stroke (including age, sex, race, insurance status, hypertension, diabetes, alcohol use, congestive heart failure, and valve disease), glaucoma was no longer significantly associated with stroke (p=0.06).

Conclusions: A large patient population was utilized to determine whether OAG is independently associated with stroke. Our findings suggest that prior noted association with stroke is likely based on similar risk factors rather than an independent association. Study limitations include lack of evidence for causal relationships in a retrospective study and limitations in coding of historical diagnoses in patient records.

CONTROL ID: 3544502

SUBMITTER (NAME ONLY): Mahsa Darvishzadeh Varcheie

TITLE: Analysis of agreement of clinical experts to B-scan of interest algorithm

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Darvishzadeh Varcheie, K. Makedonsky, G.C. Lee, V. Kulkarni, H. Ren, L. Tracewell, N. Manivannan, M.K. Durbin, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|A. Lech, ClearVue Eye Care, Roseville, California, UNITED STATES|R.P. Singh, K. Talcott, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mahsa Darvishzadeh Varcheie: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Katherine Makedonsky: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Gary Lee: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Vidya Kulkarni: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Hugang Ren: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Aaron Lech: Commercial Relationship(s);Carl Zeiss Meditec:Code C (Consultant);Carl Zeiss Meditec:Code F (Financial Support) | Laura Tracewell: Commercial Relationship(s);Carl Zeiss Meditec:Code C (Consultant) | Rishi Singh: Commercial Relationship(s);Regeneron:Code C (Consultant);Genentech:Code C (Consultant);Bausch and Lomb:Code C (Consultant);Gyroscope:Code C (Consultant);Apellis:Code F (Financial Support);Graybug:Code F (Financial Support);Aerie:Code F (Financial Support);Alcon:Code C (Consultant);Novartis:Code C (Consultant) | Katherine Talcott: Commercial Relationship(s);Carl Zeiss Meditec:Code F (Financial Support);Roche:Code C (Consultant);Genentech:Code C (Consultant) | Niranchana Manivannan: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment) | Mary Durbin: Commercial Relationship(s);Carl Zeiss Meditec:Code E (Employment)

ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) scans are important for clinical evaluation of the retina, but manual evaluation of each B-scan is time consuming and requires significant expertise. To improve the workflow, a B-scan of interest tool (BSOI) was created using deep learning to indicate B-scans of interest as well as B-scans of poor image quality (IQ). The purpose of this study was to determine if the BSOI tool agreed with doctors' clinical judgement.

Methods: Macular cube 512x128 scans were acquired using CIRRUS™ 6000 (ZEISS, Dublin, CA) on 47 subjects with various pathologies including macular degeneration, diabetic eye disease, epiretinal membranes, macular hole and central serous retinopathy. The BSOI tool first runs an IQ algorithm which flags B-scans with poor IQ then further flags good IQ scans if it finds one of the retinal pathologies as referenced in [1]. The prototype tool was integrated into the macular thickness analysis report, flagging B-scans of interest with a red indicator and poor IQ scans with a yellow indicator.

5 independent expert graders (2 retina specialists (RS) and 3 optometrists (OD)) evaluated the tool results and used a feedback feature to indicate if they agreed (thumbs up) or disagreed (thumbs down) (Fig 1). Intraclass correlation coefficient (ICC) and pair-wise Cohen's kappa between graders were used to assess inter-grader consensus. Graders also answered a survey rating the clinical utility and loading time of the tool.

Results: Mean agreement of an individual grader with the tool was 79% and majority vote agreement between graders and the tool was 81%. Table 1 shows agreement (and 95% confidence interval) of each grader and survey answers. The ICC was 0.44 (0.32, 0.60) indicating poor reliability of agreement between all doctors. Kappas showed fair to moderate agreement between pairwise doctors.

Conclusions: This tool successfully flags B-scans that may have otherwise been missed by doctors. When evaluating agreement between graders on individual cases, differences in inter-clinician's grades were observed, even between retinal specialists. The mean agreement between the B-scan of interest algorithm and the graders were considered clinically acceptable. All graders agreed that the tool increases efficiency with appropriate loading time, can be useful for diagnoses and can be used by both technicians as well as clinicians.

References:

[1] Yu et al. IOVS 2020; 61(9): Abstract PB0085.

CONTROL ID: 3544506

SUBMITTER (NAME ONLY): Richard Artola

TITLE: Retinal nerve fiber layer thickness as a potential marker for macular atrophy in patients with retinitis pigmentosa

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Artola, E. Dawson, University of Florida College of Medicine, Gainesville, Florida, UNITED STATES|J. Yang, K. Fallgatter, J. Chen, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|X. Chen, Epidemiology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The significance of peripapillary retinal nerve fiber layer (RNFL) thickness variations in patients with retinitis pigmentosa (RP) is inconsistent. We performed a retrospective medical record review to investigate whether thickening or thinning of the RNFL in eyes of patients with RP correlated with indications of macular atrophy via spectral-domain optical coherence tomography (SD-OCT) and ocular examination.

Methods: The medical records of 30 eyes from 15 patients with retinitis pigmentosa who are currently enrolled in the University of Florida Health Eye Center database were reviewed. All patients had complete ocular evaluations combined with SD-OCT of both the optic nerve and macula. We analyzed changes to best corrected visual acuity (BCVA), central retinal thickness (CRT), total macular volume (TMV), ellipsoid zone (EZ), and peripapillary RNFL thickness. Data processing was completed using MS excel. The relationship between predictors and outcome variables were assessed using Pearson linear correlation on statistical software SAS.

Results: A total of 15 patients (11 females, 4 males) were included with mean age = 44.7 ± 16.4 years (range, 17-68 years). CRT was significantly correlated with RNFL thickness of the temporal quadrant ($r = -0.41686$, $p = 0.0219$) and EZ foveal sparing ($r = -0.47375$, $p = 0.0082$). Additionally, we found significant correlations between BCVA vs. EZ foveal sparing ($r = 0.56157$, $p = 0.0012$) and CME vs. ERM ($r = 0.43301$, $p = 0.0168$).

Conclusions: The results of our study suggested a possible association between peripapillary RNFL quadrant thickness and central retinal thickness in patients with retinitis pigmentosa. CRT is associated with foveal EZ and temporal thickness of peripapillary RNFL. The eyes with foveal EZ reserved had thicker CRT and thinner temporal peripapillary RNFL. The eyes with damaged EZ under fovea had thinner CRT and thicker temporal peripapillary RNFL due to possible glial cells proliferation. The thickness of temporal peripapillary RNFL can serve as a marker for progressive macular atrophy in patients with retinitis pigmentosa.

CONTROL ID: 3544507

SUBMITTER (NAME ONLY): Andrei Kramerov

TITLE: Validation of nanoconjugates targeting various diabetes-associated protein markers for gene therapy of diabetic keratopathy

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Kramerov, R. Shah, M. Saghizadeh, A.V. Ljubimov, Departments of Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|A.A. Kramerov, R. Shah, M. Saghizadeh, A.V. Ljubimov, Board of Governors Regenerative Medicine Institute, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|H. Ding, J. Ljubimova, Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purposes were to 1) develop nanoconjugates for effective delivery of antisense oligonucleotides (AON) to human stem cell-enriched limbal epithelial cells (LEC) for gene therapy of diabetic keratopathy, and 2) to validate the effect of a novel nanoconjugate with AON to miR-203a suppressing Wnt5a (decreased in diabetes) and to compare it to nanoconjugate with AON to cathepsin F (CF) (increased in diabetes), and miR-409 targeting c-met proto-oncogene (decreased in diabetes), in human diabetic LEC and organ-cultured corneas.

Methods: Stem cell-enriched LEC cultures and corneal organ cultures were obtained from postmortem human donor eyes. Nanoconjugates based on polymalic acid scaffold (1) were synthesized and contained a cell-targeting antibody to LEC transferrin receptor, and morpholino AON to CF and to miR-409 that targets c-met, or to miR-203a (all AON at 10 or 20 μ M). Control nanoconjugate had a scrambled sequence AON (Gene Tools). Healing of scratch-induced (LEC) and heptanol-induced corneal epithelial wounds was monitored microscopically.

Results: Treatment with nanoconjugate bearing AON to miR409+CF caused an increase of its target c-met and a decrease of CF protein levels in diabetic LEC and in organ-cultured diabetic corneas. This treatment also upregulated corneal epithelial stem cell markers and accelerated wound healing of cultured LEC and organ-cultured diabetic corneas, indicating that non-toxic nanoconjugates provide a new tool for gene therapy for normalizing diabetic limbal epithelial cells and organ-cultured corneas. Recently, we found a significantly decreased expression of Wnt5a protein and upregulation of its suppressing miR-203a in diabetic LEC and corneal epithelium. Also, miR-203a antagomir inhibitor increased Wnt5a expression and promoted wound healing in diabetic LEC. We made a nanoconjugate with AON to miR-203a to restore (upregulate) Wnt5a expression and validated its ability to normalize wound healing by diabetic corneal epithelial cells. The data will be presented to support the validity of this approach and possible use for combined treatment with nanoconjugates carrying AON miR409+CF.

Conclusions: Cell-targeting nanoconjugates may be used as a new tool for gene therapy in normalizing diabetic limbal epithelial cells and diabetic corneal wound healing.

1. Proc Natl Acad Sci USA, 2010;107:18143-18148.

CONTROL ID: 3544510

SUBMITTER (NAME ONLY): Geoffrey Chan

TITLE: Glaucoma patient experiences during the COVID-19 pandemic: Changing self-perceived outcomes of care as assessed by the POEM questionnaire

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Chan, R. Pujari, I. Tappley, R. Nitiahpapand, R.R. Bourne, Ophthalmology, Cambridge Eye Research Centre, Addenbrooke's Hospital, Cambridge University Hospital NHS, Cambridge, Cambridgeshire, UNITED KINGDOM|G. Chan, Ophthalmology and Visual Science, Centre for Ophthalmology and Visual Science, The University of Western Australia, Perth, Western Australia, AUSTRALIA|R.R. Bourne, Vision and Eye Research, Vision and Eye Research Institute, School of Medicine, Anglia Ruskin University, Cambridge, Cambridgeshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: COVID-19 continues to disrupt the delivery of ophthalmic care in the third wave of the pandemic. Increased rates of anxiety has been reported in patient cohorts as COVID-19 impacts patients' hospital perceptions and has upended the patient experience. We sought to assess the impacts of COVID-19 on glaucoma patient self-perceived outcomes and experiences as assessed by the POEM questionnaire.

Methods: 126 consecutive patients attending a tertiary clinic over a 2-week period were surveyed with the Patient Reported Outcome and Experience measure (POEM). POEM is an 8-item questionnaire that addresses aspects of outcome (acceptability of treatment, fear of blindness, impact on daily life), and aspects of experience (safety, understanding, organization of care). The questionnaire was modified to determine if each item was more of a concern during the COVID pandemic. Assessments were performed in September 2020 and results were compared to pre-COVID survey results (n= 780). The questionnaires were conducted anonymously with no pairing to clinical data or demographics attempted.

Results: Survey results showed that the items showing the biggest reduction in agreement pertained to the understanding of how glaucoma is treated and patients' perception of their treatment team. There was a a 10-15% decrease in agreement for Q2 (I understand how my eye problem is managed), Q4 (I think my glaucoma is not getting worse), Q7 (I feel safe under the care of my glaucoma team) and Q8 (My glaucoma care is well organized) compared to pre COVID-19 questionnaire findings. Patients identified Q6 (I'm not worried about losing vision from glaucoma), Q7 (I feel safe under the care of my glaucoma team) and Q8 (My glaucoma care is well organized) as the most common aspects of their glaucoma care that COVID has increased concern over with 28.8%, 32.1% and 40.2% giving 'yes' responses respectively.

Conclusions: The COVID-19 pandemic has resulted in an increased uncertainty amongst patients about how their glaucoma is managed. Patients may not feel as safe about their glaucoma care and heightened anxiety about losing vision are issues which need to be addressed. Further studies investigating the patient experience and outcomes are required to fully elucidate the true psychological and physiological impacts of COVID-19.

CONTROL ID: 3544511

SUBMITTER (NAME ONLY): Deborah Stenkamp

TITLE: Flipping the opsin switch: Cis-regulatory elements required for thyroid hormone-mediated differential expression of the tandemly-replicated long wavelength-sensitive (lws) opsin genes of the zebrafish

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.L. Stenkamp, R. Mackin, Biological Sciences, University of Idaho, Moscow, Idaho, UNITED STATES|R. Ashino, S. Kawamura, Integrated Biosciences, University of Tokyo Graduate School of Frontier Sciences, Kashiwa, Chiba, JAPAN|

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ABSTRACT BODY:

Purpose: Human trichromatic color vision requires that the tandemly-replicated LWS/MWS (long- and medium-wavelength sensitive) cone opsin genes are differentially expressed in subsets of cones. We recently reported that the nuclear signaling molecule thyroid hormone (TH) is endogenously involved in differential regulation of the tandemly-replicated lws1/lws2 cone opsin array in zebrafish (Mackin et al., 2019; PNAS). The goal of the current study is to identify cis-regulatory elements residing on the lws locus that are needed for the TH-induced switch from expression of lws2 to lws1.

Methods: We performed stable and transient transgenesis of lws1 and lws2 fluorescent reporter constructs, followed by TH treatment of larvae, confocal imaging of whole eyes, and quantification of cones expressing such reporters (n=9-15 larvae for each condition). Constructs for these assays harbored selected deletions of the lws locus.

Results: Analysis of fluorescent reporter expression within two stable transgenic lines revealed that the same 2.6kb region upstream of lws1 was needed for endogenous patterns of both lws1 and lws2 expression, and for the lws2 to lws1 switch in response to TH. Using transient transgenesis assays, we further dissected this region to identify two, separate ~25bp regions within 0.6kb immediately upstream of lws1. Each of these regions contains a predicted, palindromic TH response element (ppTRE). Deletion of the region containing ppTRE1 resulted in no increase of lws1 in response to TH (# cones expressing lws1 reporter, TH vs. control, p=1.0) and eliminated any expression of lws2. Deletion of the region containing ppTRE2 also resulted in no increase of lws1 in response to TH (p=0.60), and in addition there was no decrease of lws2 in response to TH (p=0.13).

Conclusions: These findings expand our understanding of the mechanisms by which TH differentially regulates the zebrafish lws1/lws2 array. This work contributes to filling in knowledge gaps of visual system development and may also provide insight into how TH regulates other gene arrays including the tandemly replicated LWS/MWS cone opsin array in humans.

CONTROL ID: 3544514

SUBMITTER (NAME ONLY): Franklin Wei

TITLE: Efficient scan pattern and chromatic multiplexing improves performance of low-cost portable confocal scanning laser ophthalmoscopy

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Wei, C. Viehland, A.N. Kuo, J. Izatt, A. Dhalla, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|F. Wei, Department of Electrical and Computer Engineering, Duke University, Durham, North Carolina, UNITED STATES|A.N. Kuo, J. Izatt, Department of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Confocal scanning laser ophthalmoscopy (cSLO) offers improvements over handheld fundus photography in telemedicine applications, such as screening for diabetic retinopathy. Here we report on a portable cSLO design that uses a novel scan pattern to reduce acquisition times over traditional cSLOs and allows widefield color imaging at reduced cost due to its chromatically multiplexed topology.

Methods: A handheld patient interface receives light from a green laser diode and NIR superluminescent diode, operating at 520 and 785nm, respectively. The light is collimated, scanned by galvanometers, and relayed into the patient's pupil using off-the-shelf optics and custom optomechanics. A tunable liquid lens compensates for patient refraction. The two light sources are temporally multiplexed so that only one is active at any time, allowing light collected from the patient eye to be detected on a single photomultiplier tube with no filtering. The optical design achieves diffraction-limited performance over a 50° FOV at a working distance of 16mm. Patient safety is ensured by limiting incident power on the subject eye to <200μW in NIR and <100μW in green, well below ANSI Z80.36-2016 limits. The galvanometers use a novel hybrid spiral scan pattern composed of concentric constant angular velocity (CAV) and constant linear velocity (CLV) portions. The spiral pattern provides a convenient fixation target, and its circular outline is a natural fit for ophthalmic imaging. The CAV/CLV hybridization offers performance advantages over a traditional raster, as well as scan fidelity improvements over CAV or CLV spirals alone. The scan operates at 5.6Hz with 30μm radial resolution. GPU-based algorithms produce contrast-enhanced frames in real time, which are then registered and colorized in post-processing.

Results: Feasibility of the prototype cSLO device in screening applications was demonstrated by imaging a healthy human volunteer under a protocol approved by the Duke University IRB.

Conclusions: We have presented an optimized portable confocal scanning laser ophthalmoscope that offers speed and cost improvements over current designs. Performance of the system was demonstrated by imaging a healthy human volunteer.

CONTROL ID: 3544519

SUBMITTER (NAME ONLY): Radouil Tzekov

TITLE: Spatial averaging effects on multifocal ERG peak times

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.T. Tzekov, S. Bijan, G. Kiri, S. Bhaleeya, Ophthalmology, University of South Florida, Tampa, Florida, UNITED STATES|R.T. Tzekov, Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the effect of spatial averaging on the multifocal electroretinography (mfERG) averaged ring peak times in patients screened for hydroxychloroquine (HCQ) toxicity.

Methods: This was a retrospective review of the records of patients screened for HCQ retinopathy at the USF Eye Institute (University of South Florida) during the period of 2015-2020. Only the records of patients referred internally were used. Patients were tested binocularly with Diagnosys mfERG system (Diagnosys LLC, Lowell, MA) using 61 hexagons grouped in 5 rings. The effects of the lowest level (level 1, or 4%) of spatial averaging on the mfERG N1, P1 and N2 peak times ring averaged values were evaluated.

Results: The records of 40 patients (4 males, 36 females) aged 54.4 ± 14.1 yrs. were selected for analysis. The use of spatial averaging had a differential effect on different rings and mfERG components. Thus, for N1 peak times, only a small, but statistically significant effect was detected for ring #1 (central element): -0.29 ± 0.57 ms right eyes (RE) and -0.54 ± 1.34 ms left eyes (LE) ($p < 0.01$), while the timing for the other rings was unaffected. In contrast, for the P1 component ring #2 peak time was affected (-0.18 ± 0.43 ms / -0.18 ± 0.47 ms RE/LE; $p < 0.05$) and additionally the timing for ring #1 in right eyes (-0.23 ± 0.51 ms; $p < 0.01$) and for ring #4 in left eyes -0.23 ± 0.48 ms; $p < 0.01$, one sample Wilcoxon test). No significant changes were observed for the N2 component timing as a group, although in individual cases the change in timing varied from -20.6 to +18.3 ms. The magnitude of change in timing was strongly correlated with the percent change in timing due to spatial averaging for N1 for rings #1 to #4 (R^2 0.20 to 0.33), while such a correlation was less pronounced for P1 (rings #1 to #3 RE, #1 & #4 LE; R^2 0.11 to 0.44) and for N2 (rings #1, #3, #4 RE, rings #2 & #3 LE; R^2 0.12 to 0.19).

Conclusions: The application of low-level spatial averaging during mfERG analysis can affect the peak times of mfERG components in various ways and given the generally narrow margin of normative values for mfERG peak times, can introduce bias in the results. Therefore, such approach should be strongly discouraged in HCQ toxicity screening mfERG analysis.

CONTROL ID: 3544520

SUBMITTER (NAME ONLY): Matthew Wilson

TITLE: Activation of the STAT3 signaling pathway in Metastatic Uveal Melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.W. Wilson, The University of Tennessee Health Science Center Department of Ophthalmology Hamilton Eye Institute, Memphis, Tennessee, UNITED STATES|M.W. Wilson, Surgery, St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES|S. Parker, M. Sims, Y. Wang, C. Yang, L.M. Pfeffer, Pathology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: Determine whether the metastatic UM cell line OMM2.5 shows high STAT3 activation as compared to non-metastatic UM cell line MEL270 derived from the same UM patient. Does the OM2.5 cell line express more immunosuppressive chemokines/cytokines, and/or less inflammatory cytokines/chemokines.

Methods: Methods: The proliferation of OMM2.5 and MEL270 UM cell lines was determined by IncuCyte Live-Cell Analysis assays. The levels of STAT3 and tyrosine phosphorylated STAT3 in cell lysates was determined by immunoblotting. The expression of STAT3-depedent chemokines and cytokines was compared in MEL270 versus OMM2.5 cells by quantitative real time PCR.

Results: Results: The metastatic UM cell line OMM2.5 cell line showed increased cell proliferation compared to the primary MEL270 UM cells isolated from the same patient. In addition, STAT3 activation was markedly elevated as evidenced by its tyrosine phosphorylation in the metastatic OMM2.5 cell line relative to MEL270 UM cells. Moreover, the gene expression levels of multiple STAT3 regulated genes, such as STAT1, TXNIP, and LIF was significantly increased in metastatic OMM2.5 cells vs. non-metastatic MEL270 UM cells. LIF (leukemia inhibitory factor) is a cytokine that plays a key role in regulating the adaptive immune response. TXNIP (Thioredoxin-interacting protein) is a redox regulator that causes accumulation of reactive oxygen species, and has been associated with tumorigenesis in several cancer. STAT1 is a transcription factor that promotes oncogenesis in various cancer types.

Conclusions: Conclusions: Taken together, these data indicate that the STAT3 signaling pathway is activated in metastatic uveal melanoma cell lines. Thus, STAT3 may be an attractive pharmacological target to treat metastatic uveal melanoma.

CONTROL ID: 3544522

SUBMITTER (NAME ONLY): Kaylin Arpaia

TITLE: A Unique Ophthalmic Presentation Leading to a Diagnostic Dilemma in Wegener's Granulomatosis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Arpaia, K. Hawthorne, Howerton Eye Clinic, Austin, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: A 22-year-old female with a biopsy proven history of Wegener's granulomatosis (WG) maintained on prednisone 40mg daily, presented with a red, painful left eye of 3 weeks duration. She had been cared for in the prior 2 weeks by a referring ophthalmologist with reports of a slow growing, mass in the anterior chamber. Historical manifestations of her disease were sinus related as well as unilateral scleritis to the left eye. Her condition had been quiescent during her recent pregnancy which resulted in her second child three months prior. She had been on cyclophosphamide at the beginning of her diagnosis but after several years, she was taken off the alkylating agent and maintained on oral steroids alone.

Methods: On examination, her visual acuities were 20/70-1 right eye and LP left eye, with the majority of her vision in the left eye lost in 2018 to complications of anterior and posterior scleritis. Anterior segment examination of the left eye showed conjunctival hyperemia localized inferotemporally and a soft, ameboid, white mass in the anterior chamber measuring 7.5 x 5.5mm without corneal involvement. Concern for infectious or fungal etiology was high considering the patient was maintained chronically with 40mg prednisone daily. External photography of the white anterior segment mass was taken. (Figure 1, Figure 2) A preliminary diagnosis of infectious uveitis was made, and the patient was prescribed topical antibiotic and antifungal therapies with a plan for a biopsy/culture of the lesion with concurrent intracameral and subconjunctival antibiotic, antifungal and steroid therapy.

Results: Biopsy results showed that the mass was made entirely of inflammatory material, linking it to WG as opposed to the suspected infectious etiology.

Conclusions: This case shows a unique ophthalmic manifestation of WG in the anterior segment. While there are numerous reports detailing cases of episcleritis, anterior scleritis, ulcerative keratitis, and other inflammatory conditions of the eye associated with WG, to our knowledge there are no such reports of anterior segment masses. This case is interesting in that the inflammatory disease flared with the documented finding while on a high dose of oral steroids, leading to a diagnostic challenge. A review of current treatment recommendations and ophthalmic manifestations of WG accompany this case report as a guide for a challenging ophthalmic and systemic disease.

CONTROL ID: 3544524

SUBMITTER (NAME ONLY): Flavia Leao

TITLE: Dry Eye Disease Results in an Imbalance of Neuropeptides and Neurotrophins in the Cornea and Trigeminal Ganglion

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Leao, V.G. Sendra, B. Kenyon, D.L. Harris, P. Hamrah, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|B. Kenyon, Program in Neuroscience, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|P. Hamrah, Ophthalmology, New England Eye Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has previously been demonstrated that dry eye disease (DED) results in decreased corneal nerve density. The aim of the current study was to evaluate if DED results in alterations of neuropeptides (NPs) and neurotrophins in the cornea and trigeminal ganglia (TG).

Methods: Adult 6-8-week-old C57BL/6N female mice were injected with 0.5mg of scopolamine hydrobromide and kept in a controlled environment chamber for 14 days and compared to control mice. Clinical evaluations included slit-lamp microscopy, tear secretion, corneal esthesiometry and challenge with [5M] saline. Nerve density was assessed by immunohistochemistry of corneal whole-mounts for β III Tubulin and confocal microscopy. mRNA and proteins levels of 11 molecular targets of NPs and neurotrophins were assessed by qRT-PCR and ELISA for corneas and TG. A one-way ANOVA with Tukey's multiple comparison was used to compare effects between groups.

Results: DED mice demonstrated decreased tear secretion ($p \leq 0.0001$) and increased corneal fluorescein staining compared to controls ($p \leq 0.0001$). Decreased corneal nerve density was measured in DED ($78.2 \pm 2.8 \text{ mm/mm}^2$) compared to controls (142.5 ± 13.7 ; $p \leq 0.0001$). A significant increase in paw wipe response was observed with 10 μL of [5M] saline in DED compared to controls 38.6 vs. 17.2 ($p \leq 0.0001$). Corneal qRT-PCR revealed decreased neurotrophin expression in DED compared to controls, with 3.1-fold decrease in NGF, 2.4-fold decrease in BDNF and 2.9-fold decrease in NT3 (all $p < 0.0001$), which was confirmed at the protein level by ELISA (all $p < 0.0001$). In addition, there was an upregulation of corneal Substance P (3.4-fold) and CGRP (2.5-fold) in DED compared to controls ($p < 0.0001$ for both). Interestingly, there was downregulation of VIP (2.5-fold), PACAP (3.3-fold), Neurotensin (5.0-fold), Somatostatin (2.0-fold) and NPY (5.0-fold) (all $p < 0.01$). In contrast TG of DED mice demonstrated 4.5-fold upregulation of NGF and 6.3-fold increase in NT-4/5 vs controls ($p < 0.0001$). However, within the TG, only Substance P and Somatostatin were increased in DED by 1.7-fold and 2.2-fold respectively (both < 0.05).

Conclusions: This study provides evidence of imbalance in corneal and TG neurotrophins and NPs in DED. A deeper understanding of the neurochemistry, trophic factors and nervous system may lead to improved treatments for DED.

CONTROL ID: 3544526

SUBMITTER (NAME ONLY): Niamh Wynne

TITLE: Reproducibility in peak foveal cone density characterization in AOSLO images.

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Wynne, J. Cava, M. Gaffney, A. Schedit, J. Carroll, Department of Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|H. Heitkotter, J. Carroll, Department of Cell Biology, Neurobiology and Anatomy, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|R.F. Cooper, Department of Biomedical Engineering, Marquette University, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the inter-grader reproducibility of characterizing peak foveal cone density in normal subjects.

Methods: 300x300 μm foveal AOSLO images from the right eye of 44 normal volunteers were included. Semi-automated cone identification was performed by three observers, with resulting cone coordinates used to generate cone density maps. Two approaches were employed to estimate the location of peak cone density from these maps: 1) the point of absolute maximum density and 2) the center of an ellipse created by the 95th percentile isodensity contour. Cone density values at these locations were also compared. For each method, the repeatability and measurement error of peak cone density estimates were assessed. The variability in peak cone density location between observers was assessed by calculating confidence ellipses (CE) for each peak density location estimation method described above, and intraclass correlation coefficients (ICCs) were calculated to characterize interobserver variability in density estimates.

Results: The interobserver ICC of the maximum cone density value was 0.805 (95% CI = 0.718-0.893). The ICC using the isodensity contour method was slightly lower (0.748, 95% CI = 0.640-0.856). Accordingly, the measurement error for the maximum cone density method was 21,441 cones/ mm^2 (12.3%) whereas the measurement error for the isodensity contour method was 24,549 cones/ mm^2 (14.4%). Despite this, there was no significant difference between the average peak cone density value extracted using the two methods ($p=0.09$). The location of maximum density was significantly more reproducible between observers when using the isodensity contour method (mean \pm SD CE area = $231.93 \pm 775.15 \mu\text{m}^2$) compared to the maximum density method (mean \pm SD CE area = $905.62 \pm 1214.42 \mu\text{m}^2$, $p<0.0001$).

Conclusions: Peak foveal cone density is important, not only as a quantitative metric of cell packing, but also as an anchor for calculation of retinal eccentricities. Understanding measurement errors, both in peak cone density estimation and in its retinal location is critical, to inform the approach to its identification. The superior reproducibility of the retinal location with the isodensity contour method may best serve comparison of parafoveal metrics, while the maximum density technique could be used to give the best estimate of the highest cone density within the retina, despite variability in the resulting exact retinal location.

CONTROL ID: 3544527

SUBMITTER (NAME ONLY): John Meyer

TITLE: Safety of an Intracanalicular Dexamethasone Insert for the Treatment of Allergic Conjunctivitis: Pooled Post-hoc Analysis of Four Studies

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Meyer, Eye Care Institute, Kentucky, UNITED STATES|K. Kenyon, Tufts University, Medford, Massachusetts, UNITED STATES|M. Sato, East West Eye Institute, California, UNITED STATES|S. Silverstein, Silverstein Eye Centers, Missouri, UNITED STATES|E.J. Meier, Cincinnati Eye Institute, Cincinnati, Ohio, UNITED STATES|K. Dewar, E. Reilly, M. Cheung, M.H. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|P.J. Gomes, Ora, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Though topical ophthalmic steroids are effective in treating allergic conjunctivitis (AC), physicians report infrequent use due to side effects and/or risk of abuse associated with long term use demonstrating the need for a physician administered sustained release steroid with a favorable safety profile. DEXTENZA (dexamethasone ophthalmic insert) 0.4mg is a hydrogel-based intracanalicular insert designed to deliver preservative-free dexamethasone over 30 days. The objective of this study is to evaluate the safety of a steroid insert (DEX) for the treatment of signs and symptoms of chronic AC.

Methods: This was a pooled post-hoc analysis of four prospective, randomized, double-masked, vehicle-controlled, parallel-group studies using a modified Conjunctival Allergen Challenge (CAC) model. In all studies, subjects with a history of ocular allergies were randomized to receive DEX or placebo (PV) inserted into the canaliculus of both eyes on the same day. Safety assessments were performed in each of the four studies which included assessments of adverse events (AEs), visual acuity (VA), and intraocular pressure (IOP).

Results: The safety population from the four trials included 315 subjects (DEX N=154, PV N=161). Overall, 12.3% and 14.3% of DEX and PV subjects reported ocular adverse events, respectively, all of which were mild or moderate in severity. No ocular SAEs were reported and there was a single non-ocular SAE across the four trials (hospitalization due to depression in the DEX group) which was considered unrelated to study treatment. The most common adverse events (>1%) in DEX-treated subjects were increased IOP (3.2%), reduced VA (1.3%), lacrimation increased (1.3%), and eye discharge (1.3%). All AEs of increased IOP were resolved. VA assessments showed no consistent changes over time and all instances of worsening VA were transient. There were no patterns of AEs that would raise concern regarding the safety of DEX.

Conclusions: Overall, findings from the pooled post hoc analysis of four studies demonstrated DEX was generally safe and well tolerated for the treatment of allergic conjunctivitis. Rates of increased IOP following treatment with DEX were low. The physician-administered insert has the potential to be a non-abusable, hands-free, alternative to steroid eye drops.

CONTROL ID: 3544529

SUBMITTER (NAME ONLY): Ryan Larochelle

TITLE: Low Vision Referral Patterns in Intermediate AMD

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Larochelle, J. Patnaik, A. Lynch, N. Mandava, K. Hanson, Dept. of Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Low vision (LV) services are underutilized, but sparse data exist regarding referral patterns. In this retrospective chart review, we examined our institution's intermediate age-related macular degeneration (iAMD) database to determine factors influencing referral.

Methods: We determined which patients in our iAMD registry had been referred to LV, excluding patients with neovascularization or geographic atrophy in either eye. Visual acuity (VA) was collected at the time of LV referral or the most recent visit for patients not referred. Visual Function Questionnaire (VFQ-25) scores (composite and 12 subscales) were collected at enrollment into the iAMD study. We compared patients referred to LV and patients not referred with Chi-square testing and the Wilcoxon rank sum test. Multivariable logistic regression analysis was used to examine each subscale of the VFQ-25 separately ($P < 0.05$).

Results: We found 36 (16%) of the 232 iAMD patients were referred to LV (Table 1). Referred patients were significantly more likely to be older, have worse VA in both eyes, and have lower VFQ-25 composite scores. Univariate analysis of VFQ-25 subscales demonstrated significantly worse scores for LV patients in general vision, near, distance, mental health, role limitations, dependency, and driving (Table 2). In the multivariable analysis, significant subscales included lower scores in general health, general vision, and driving.

Referred patients had a median VA of 20/40 in the better eye and a median VFQ-25 score of 84. We found 46 (48%) of the non-referred patients had VA of 20/40 or worse and/or VFQ-25 score of 84 or lower. Factors identified as reasons for not referring included cataract or posterior capsular opacification amenable to a procedure, fluctuating vision, and extensive comorbidities. However, two thirds of these patients had no documented or discernable reason for not receiving referral.

Conclusions: LV services help AMD patients maximize the function of their remaining vision. This study demonstrates that our institution refers patients with worse objective and functional vision, but that many more patients might benefit from LV services. This study was limited in that VA and VFQ-25 data were not obtained simultaneously. Future studies should aim to identify specific metrics that should prompt LV referral and apply this approach to other diseases.

CONTROL ID: 3544530

SUBMITTER (NAME ONLY): Ermin Dzihic

TITLE: Clinical Comparison of Ophthalmic Ultrasound with a Portable Multipurpose Ultrasound

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Dzihic, D. Horton, School of Medicine, University of California Irvine, Irvine, California, UNITED STATES|J.K. To, A.N. Vu, A.W. Browne, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|A.W. Browne, Institute of Clinical and Translational Science, Department of Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Until recently diagnostic ophthalmic ultrasonography has exclusively utilized piezo-electric transducer technology to visualize ophthalmic anatomy. The purpose of this study was to compare the quality of ultrasonic images from the recent FDA approved handheld Butterfly iQ (BiQ), an Ultrasound-on-a-Chip device, with a standard 10MHz piezo-electric ophthalmic ultrasound.

Methods: A cross-sectional blinded study of sonographic image quality was performed as a comparison between the BiQ portable ultrasound and the 10MHz Accutome B-Scan Pro. Study participants had ultrasound procedures performed on each eye during a typical ophthalmic visit per the standard of care. The BiQ was connected to an iPad for video capture and settings adjustment. Four imaging presets (MSK, MSK-Soft Tissue, Nerve, and Pediatric Lung) with the highest clarity were selected from the BiQ software library. One minute video clips were taken using each ultrasound probe. De-identified still images were cropped, randomized, and presented to three blinded ophthalmologist graders who rated images on a ten-point Likert scale based on four criteria: Resolution, Detail, Image Quality, and Diagnostic Confidence. Resolution was defined as “sharpness of the image and lack of haziness,” detail as “clarity of outlines, how well structures and boundaries are defined,” image quality as “overall image assessment (e.g., absence of noise, contrast between structures),” and diagnostic confidence as “confidence in making clinical decisions based on image.” An ANOVA with post hoc pairwise comparison was performed in SPSS.

Results: The ANOVA results (Table 1) illustrate that 2/3 evaluators reported no statistically significant differences between the BiQ and Accutome in all categories. With respect to image Detail, there was a statistically significant difference for 1/3 graders between the Accutome and two of the BiQ modalities (MSK and Nerve); however, the overall results of the study indicate that there were no statistically significant differences in function of the images generated by the Butterfly iQ ultrasound versus the 10MHz Accutome B-Scan Pro.

Conclusions: These results show promise for the future of portable ultrasound. The benefits of Butterfly iQ are cost-effective, pocket-sized, and versatile, highlighting its potential for clinical utility.

CONTROL ID: 3544532

SUBMITTER (NAME ONLY): Francisco Beltran

TITLE: Sensitivity to netilmicin in infectious keratitis in Mexico in the period 2009 to 2017.

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Beltran, K. Vázquez-Rom, J.A. Oyervides-Alvarado, L.A. González-Dibildox, N. Ramos Betancourt, E. Hernandez-Quintela, Cornea and Refractive Surgery, Asociacion para Evitar la Ceguera IAP Hospital Dr Luis Sanchez Bulnes, Mexico City, Mexico City, MEXICO|M. Garza Leon, Universidad de Monterrey Division de Ciencias de la Salud, San Pedro Garza Garcia, Nuevo León, MEXICO|

Commercial Relationships Disclosure (Abstract): Francisco Beltran: Commercial Relationship(s);SIFI:Code F (Financial Support) | Kristian Vázquez-Rom: Commercial Relationship: Code N (No Commercial Relationship) | José Oyervides-Alvarado: Commercial Relationship: Code N (No Commercial Relationship) | Laura González-Dibildox: Commercial Relationship: Code N (No Commercial Relationship) | Nallely Ramos Betancourt: Commercial Relationship: Code N (No Commercial Relationship) | Manuel Garza Leon: Commercial Relationship(s);Alcon:Code C (Consultant);S4Optik:Code F (Financial Support);SIFI:Code F (Financial Support) | Everardo Hernandez-Quintela: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The 4th generation quinolones are the treatment of choice for infectious bacterial keratitis, however, recent reports suggest an increase in resistance to these drugs, so it is important to recognize the sensitivity of other drugs and compare them with the gold standard

Methods: A cross-sectional study including a consecutive analysis of patients records with a diagnosis of bacterial keratitis with a positive culture and antibiogram report between January 2009 and December 2017 of the Cornea department of the Dr. Luis Sánchez Bulnes Hospital of the Association to Avoid Blindness in Mexico were included. Demographic data, Gram stain, bacterial profile and antimicrobial resistance were analyzed.

Results: In the studied period, a total of 794 (49.53%) cases with a positive culture were included. 27.1% of patients had polymicrobial infections so 1034 cultures were evaluated. 52.3% of the patients were male, the mean age was 48.28 ± 20.43 years (range 1 to 97 years). 81.33% (841) of the cultures were gram positive. The antibiotic with the highest sensitivity for gram positive was Netilmicin (93.23%), followed by Moxifloxacin (92.98%) and Gatifloxacin (92.39%). For gram negative cultures again Netilmicin had the highest sensitivity (88.08%), followed by Gatifloxacin (86.01%) and Moxifloxacin (84.45%).

Conclusions: Gram positive bacterias are the most common cause of infectious keratitis, Staphylococcus and Pseudomonas as the most common isolates. Netilmicine and 4th generation flouroquinolones had a very good sensibility for both types of bacteria.

CONTROL ID: 3544533

SUBMITTER (NAME ONLY): Sarah Powell

TITLE: Elucidating the Role of AMP-activated protein kinase (AMPK) in Human Glaucomatous Lamina Cribrosa (LC) cells

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.K. Powell, M. Irnaten, A. Smyth, C.J. O'Brien, Clinical Research Centre, Mater Misericordiae University Hospital, University College Dublin, Dublin, IRELAND|S.K. Powell, A. Smyth, C.J. O'Brien, Department of Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The Lamina Cribrosa (LC) region of the optic nerve is an important site of damage in glaucoma. AMP-activated protein kinase (AMPK) is the main sensor of cellular energy status in virtually all cells, and is highly conserved across all eukaryotic species. AMPK is upregulated in both cancer and fibrosis. AMPK is activated in response to energy stress by sensing increases in AMP: ATP and ADP: ATP ratios. Here, we investigate the expression of an isoform of AMPK in normal and glaucoma LC cells and examine the possible effect of AMPK on pro-fibrotic gene expression found in glaucoma LC cells.

Methods: LC cells were obtained and cultured from 2 normal non-glaucomatous and 2 confirmed glaucoma age matched eye donors. Expression of an AMPK isoform was measured in both normal and glaucoma LC cells using Quantitative Real Time Polymerase Chain Reaction (qPCR).

Results: The expression level of the AMPK isoform was found to be significantly enhanced in glaucoma LC cells compared to normal control LC cells (1.23 ± 0.083 in glaucoma LC cells versus 0.86 ± 0.067 in normal LC cells; $p < 0.05$; $n=2$). The relative expression of AMPK was calculated using $\Delta\Delta C_t$ method, after being normalized to the housekeeping ribosomal gene 18S.

Conclusions: The data shows that AMPK is significantly elevated in glaucoma LC cells versus normal LC cells. This suggests a role for AMPK as a key driver of underlying fibrotic changes in glaucomatous LC cells, leading to increased proliferation, reduced apoptosis and augmented metabolism. Blockade of AMPK appears to be critically associated with this process of metabolism. Halting the pro-fibrotic activity and metabolism of glaucoma LC cells by restoring AMPK expression and activity to normal levels may lead to a new therapeutic approach targeted at reducing fibrosis in glaucoma. We anticipate that this novel therapeutic approach could ameliorate the ongoing optic nerve cupping, thereby enhancing long-term patient outcomes and quality of life in glaucoma.

CONTROL ID: 3544535

SUBMITTER (NAME ONLY): Padmanabhan Pattabiraman

TITLE: Mechanical Stretch Increases Cholesterol Biosynthesis in Human Trabecular Meshwork

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.P. Pattabiraman, A. Soundararajan, T. Wang, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|P.P. Pattabiraman, A. Wijeratne, A. Mosely, Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Trabecular meshwork (TM) tissue is subjected to constant mechanical stretch due to ocular pulse created by the cardiac cycle. This triggers the modification of various intracellular signaling responses to counter mechanical insults. A loss of such response can lead to elevated intraocular pressure (IOP), a major risk factor for primary open-angle glaucoma. The purpose of this study was to understand the metabolic response of TM cells to mechanical stretch.

Methods: Normal primary human TM cells (n=3) in culture were subjected to 15% mechanical stretch, 1 cycle/second, for 8h and 24h using a computer-controlled Flexcell unit, and unstretched cells were controls. We profiled for mRNA changes in 8h samples using qPCR and protein changes using mass spectrometry-based quantitative proteomics on 24h samples. The data was statistically significant if the $p \leq 0.05$ for mRNA using paired Student's t-test and proteins were screened out using criteria, $p \leq 0.05$ and mean $\pm 2\sigma$ of log2 as confidence fold change limits.

Results: Cyclic mechanical stretch significantly increased 9 proteins and decreased 31 proteins including those involved in metabolism. Among those, were the proteins involved in cholesterol biogenesis, which showed significant changes (Fig 1)- levels of squalene synthase, a critical enzyme in the cholesterol biosynthetic pathway significantly increased ($p=0.04$) with an increasing trend in HMG CoA synthase (HMGCS), and HMG CoA reductase (HMGCR) and a significant decrease in Kelch-like ECH-associated protein 1 (KEAP1) ($p=0.04$), which is a negative regulator of nuclear factor-E2-related factor 2 (Nrf2) involved in sterol metabolism. Further examining the mRNA transcripts of genes involved in cholesterol biosynthesis machinery, there was a significant upregulation of sterol regulatory element-binding protein 2 (SREBP2) ($p=0.05$), a transcription factor and the master regulator of sterol pathway, as well as HMGCS ($p=0.03$), and HMGCR ($p=0.03$) genes.

Conclusions: This is a first-hand report on comparative analysis between changes in mRNA and proteins in response to mechanical stretch. We find that TM cells respond to the changes in biomechanical properties by orchestrating the transcriptional control of cholesterol biosynthesis and tightly regulating the enzymes in the sterol synthesis pathway.

CONTROL ID: 3544536

SUBMITTER (NAME ONLY): Konstantina Sampani

TITLE: Modifiable risk factors for diabetic retinopathy (DR) and macular edema (DME) in children with type 1 diabetes (T1D)

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Sampani, C. Jacoba, C. Gilbert, P.S. Silva, L.P. Aiello, J.K. Sun, Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|K. Sampani, Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|C. Gilbert, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|L. Laffel, Pediatrics, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J. Keady, L. Laffel, Pediatric, Adolescent and Young Adult Section, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although risk factors for DR and DME are well-established in adults with diabetes, they are not as clearly defined in pediatric populations. This study aimed to identify factors associated with DR and DME in a pediatric population with T1D.

Methods: Retrospective chart review was conducted of pediatric (≤ 21 years old) medical records from the Joslin's Beetham Eye Institute from 2005-2020. Data collected included demographic characteristics and DR and DME severity. Body mass index (BMI) and blood pressure (BP) were categorized according to CDC sex and age-adjusted growth curves (BMI: under/normal weight ($< 85^{\text{th}}$ %ile), overweight/obese ($\geq 85^{\text{th}}$ %ile); BP: normal ($< 90^{\text{th}}$ %ile), elevated/high ($\geq 90^{\text{th}}$ %ile). Analyses were adjusted for correlation between eyes of the same person.

Results: In total, 1735 youth (3454 eyes) were included with mean \pm SD age 15.4 \pm 4.6 yrs, T1D duration 7.1 \pm 5.3 yrs, T1D onset 8.3 \pm 5.4 yrs, and A1c 8.4 \pm 1.3%; 50.7% were female, 30.7% were overweight/obese, and 4.1% had elevated/high BP. DR was present in 8.5% and DME in 1.3% of the eyes. Unadjusted analyses found DR presence was associated with higher A1c ($p < .0001$), longer T1D duration ($p < .0001$), younger age of T1D onset ($p = 0.0002$), older attained age ($p < .0001$), female sex ($p = 0.001$), and elevated/high BP ($p < .0001$). After backwards elimination modeling, older age ($p < .0001$), longer T1D duration ($p = 0.002$), and higher A1c ($p = 0.01$) remained significantly associated with DR. In unadjusted analyses, DME was associated with higher A1c ($p = 0.0003$), longer T1D duration ($p < .0001$), younger age of T1D onset ($p = 0.02$), older age ($p < .0001$), female sex ($p = 0.03$), elevated/high BP ($p = 0.002$), and obese/overweight BMI ($p = 0.03$). When adjusting for A1c, T1D duration, age of T1D onset, age, and DR presence, obese/overweight BMI ($p = 0.04$) and elevated/high BP ($p = 0.04$) remained associated with DME.

Conclusions: In this pediatric group with T1D, DR with or without DME was present in 8.5% of eyes. In addition to non-modifiable factors, DR and DME were associated with modifiable systemic risk factors (A1c, BMI, BP). Efforts to optimize these factors in youth from an early age may help reduce adverse ocular outcomes. Future longitudinal studies can assess if early intervention to improve glycemic control, weight, and BP can reduce occurrence of DR and DME in youth with T1D.

CONTROL ID: 3544538

SUBMITTER (NAME ONLY): Kyoung-Hee Kim

TITLE: Toward a Non-Invasive Solution of Wet AMD: Sunitinib, Pazopanib, and Axitinib Eyedrops versus Intraocular Injection of Aflibercept

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kim, J. Oh, D. Cho, M.J. Kim, R&D Center, SCAI Therapeutics, Daejeon, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Wet AMD is a disastrous disease of vision loss where the only medicinal treatment currently available is an intraocular injection of aflibercept or ranibizumab. However, such an intravitreal injection often causes various side-effects and complication. Therefore, we prepared and evaluated eyedrops of three VEGFR tyrosine kinase inhibitors (TKIs) for a safer, non-invasive solution of wet AMD.

Methods: Three TKIs — sunitinib, pazopanib, and axitinib — are aqueously dispersed with our proprietary technology: D-SUT (0.05%), D-PZP (0.2%), and D-AXT (0.01%). C57BL/6 mice were used for a laser-induced choroidal neovascularization (CNV) model. A total of 30 mice were classified into six groups: G1 (PBS), G2 (aflibercept), G3 (SUT solution, 0.05%), G4(D-SUT), G5 (D-PZP), G6 (D-AXT). Aflibercept (1 uL/eye) was given as single intravitreal injection. Test samples and PBS (5 uL/eye each) were instilled twice a day for 10 days. Corrected total fluorescence and volume of CNV lesions were measured after 10 treatment days by FFA and OCT, respectively. The concentration of test samples at the retina was measured.

Results: D-SUT, D-PZP and D-AXT, given as eyedrops, showed statistically significant suppression of the CNV lesion volume by 49%, 26%, and 25%, respectively, compared to the PBS control ($p<0.0001$, $p<0.01$, and $p<0.05$, respectively), whereas SUT solution itself did not. The efficacy of D-SUT is statistically significant compared to that of SUT ($p<0.05$) as well. All three TKI dispersions showed comparable suppression of the area and volume of CNV lesion with the aflibercept injection. Given the concentrations of TKIs in the retina, sufficient amounts of TKIs were delivered to the retina.

Conclusions: We have demonstrated that the eyedrops of three TKI dispersions showed comparable efficacy with the intravitreal injection of aflibercept. Corresponding ocular pharmacokinetic study and tissue distribution analysis of TKI dispersion support the straightforward way of drug delivery through the cornea to the retina. Further efforts to develop the TKI eyedrops for patient-friendly wet AMD treatments are under way.

CONTROL ID: 3544540

SUBMITTER (NAME ONLY): Neha Raparla

TITLE: Internet Search Trends in Refractive Diseases and Interventions During the COVID-19 Pandemic

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gupta, University of Missouri Kansas City School of Medicine, Kansas City, Missouri, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|N. Raparla, H. Pakhchanian, M. Asahi, D. Belyea, Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess national and international internet search trends and public interest in refractive diseases and interventions during the COVID-19 pandemic compared to existing trends prior to the pandemic.

Methods: A Google Trends search for refractive terms was performed between the time periods of January 1, 2016 to November 1, 2020. Refractive terms were divided into two groups: disease terms and procedure/treatment terms. Relative search volume (RSV) indices for refractive terms were assessed in the United States (US) and worldwide from the initial 18-week COVID-19 pandemic period (March 1, 2020 to July 4, 2020) and the subsequent 18-week period. (July 5, 2020 to November 1, 2020) These results were compared to pooled data of overlapping weeks between 2016-2019. A t-test of two independent samples assuming unequal variances was utilized to compare the two groups.

Results: The relative public interest in refractive disease and procedure/treatment terms showed a sharp decline in the initial 18-weeks of the pandemic with a slow increase over the following 18-weeks compared to prior to the pandemic (Figure 1). There was a statistically significant decrease in mean RSV for multiple refractive disease terms (near far sighted/sightedness, keratoconus, hyperopia, cataract, astigmatism, myopia, near sighted/sightedness, blurry/blurred vision) and refractive procedure/treatment terms (intraocular lens, LASIK, cataract surgery/removal/extraction, LASEK, contact lens/lenses) both in the US and worldwide in 2020 compared to 2016-2019.

Conclusions: The onset of the COVID-19 pandemic correlates with declining relative popularity of searches related to refractive disease and elective refractive procedures/treatments. Declining interest in refractive diseases and treatments may lead to poorer health literacy, delay in care, and potentially worse outcomes for these conditions.

CONTROL ID: 3544541

SUBMITTER (NAME ONLY): Jameel Mushtaq

TITLE: Digital profiling and analysis of barriers to teleconsultations among ophthalmic patients in North West London (NWL)

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mushtaq, A. Ghulakhszian, C. Dinah, Central Middlesex Hospital, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Recent advances in technology have allowed remote diagnosis and consultation by medical professionals. The recent COVID-19 outbreak has accelerated this process into widespread adoption. In Ophthalmology, Teleconsultation allows communication between ophthalmic professionals and patients remotely, theoretically increasing efficiency, accessibility and safety of consultations. It is unclear what groups of patients are unable to access this mode of healthcare delivery, putting them at risk of worse outcomes both presently and in the future. Through creation of patient digital profiles, barriers to teleconsultations can be understood, allowing development of tailored interventions at a regional and national level.

Methods: A 28 item survey was administered to patients attending the Macula clinic in NWL involving demographics, current technological access and views towards teleophthalmology.

Results: 106 patients were included (mean age:75.2+/-13.3). The most common device owned was a smartphone (66%), with the most common operating system being Android (55% of smartphone owners). Twenty-one percent of patients did not have access to a suitable device and 25% of patients did not have access to the internet. Those without access to any device were older (82.1vs73.5; $P=0.007$) and those without access to the internet were older (80.8 vs 73.3; $p=0.01$) and less educated ($p=0.04$ [PB1]). Patients without access to help at home had lower confidence (4.1 vs 2.0; $p<0.001$) and perceived usefulness (3.8 vs 2.2; $p<0.001$) of teleconsultations. Number of devices owned correlated with confidence ($r=0.46$; $p<0.001$) and perceived usefulness ($r=0.20$; $p=0.043$).

Conclusions: A significant proportion of ophthalmic patients in NWL are unable to access healthcare via video teleconsultations. These may be older and/or more isolated patients which will require targeted interventions. Digital profiling should be considered to maximise inclusivity of digital health interventions.

CONTROL ID: 3544542

SUBMITTER (NAME ONLY): Brandon Busbee

TITLE: Phase 1 Study of Intravitreal Gene Therapy with ADVIM-022 for neovascular AMD (OPTIC Trial)

SESSION TITLE: AMD: clinical research - new therapies and technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Busbee, Tennessee Retina, Tennessee, UNITED STATES|C. Hoang, A. Turpcu, C. Chung, M. Gasmi, A. Osborne, Adverum Biotechnologies Inc, Redwood City, California, UNITED STATES|D.S. Boyer, Retina-Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|A.M. Khanani, Sierra Eye Associates, Nevada, UNITED STATES|C.J. Danzig, Rand Eye Institute, Florida, UNITED STATES|D.J. Pieramici, California Retina Consultants, California, UNITED STATES|C.C. Wykoff, J. Major, Retina Consultants of Texas, Houston, Texas, UNITED STATES|C. Regillo, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|B.C. Joondeph, Colorado Retina Associates, Colorado, UNITED STATES|S. Kiss, Weill Cornell Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreal gene therapy has the potential to significantly reduce treatment burden and improve vision outcomes in patients with neovascular AMD (nAMD). OPTIC is a phase 1 study designed to assess the safety, tolerability and efficacy of a single intravitreal injection of ADVIM-022 (AAV.7m8-afibercept gene therapy) in patients with nAMD.

Methods: Open-label, multicenter, dose-ranging study in treatment-experienced patients with a previous confirmed response to anti-VEGF therapy. Patients were administered a single intravitreal injection of ADVIM-022 at 6×10^{11} vg/eye (Cohort 1: n=6, Cohort 4: n=9) or at 2×10^{11} vg/eye (Cohort 2: n=6, Cohort 3: n=9). Incidence and severity of adverse events, change in visual acuity (BCVA), change in central retinal thickness (CST), need for and number of supplemental aflibercept injections were evaluated.

Results: As of October 15, 2020, median follow-up was 86 weeks (Cohort 1), 64 weeks (Cohort 2), 48 weeks (Cohort 3) and 16 weeks (Cohort 4). Patients in all 4 cohorts previously received frequent anti-VEGF injections (mean 7.1–9.2 injections in the prior 12 months) to maintain relatively good baseline BCVA (mean 65.0–65.9 ETDRS letters) prior to receiving ADVIM-022. ADVIM-022 continues to be well tolerated with a favorable safety profile. All ADVIM-022-related ocular adverse events were mild (78%) to moderate (22%). Ocular inflammation predominantly affecting the anterior segment, when observed, has been responsive to steroid eye drops. No cases of retinal involvement or vasculitis were reported. A significant reduction in anti-VEGF injection burden was observed with both doses; 14/15 patients receiving high dose and 10/15 patients receiving low dose remained supplemental anti-VEGF injection free while mean annualized anti-VEGF injection frequency was reduced by 99% (high dose) and 85% (low dose) after ADVIM-022. For Cohorts 1–3, data pending for cohort 4, BCVA was maintained with a mean change of -2.5 to +0.2 ETDRS letters, and CST improved with a mean change of -19.7 to -132.7 μ m.

Conclusions: ADVIM-022 is designed to provide continuous expression of aflibercept following a single intravitreal injection. Over 80% of patients with nAMD treated with a single injection of ADVIM-022 in OPTIC have not needed any supplemental anti-VEGF injections up to 92 weeks follow-up. ADVIM-022 has the potential to reduce treatment burden and improve patient vision outcomes.

CONTROL ID: 3544549

SUBMITTER (NAME ONLY): Nehali Nanti

TITLE: Comparison of Virtual Reality Visual Field Testing to Humphrey Visual Field Testing in an Academic Ophthalmology Practice

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.B. Nanti, J. Lenoci, Stony Brook University Hospital, Stony Brook, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nehali Nanti: Commercial Relationship: Code N (No Commercial Relationship) | Jacqueline Lenoci: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Humphrey visual field testing is considered the gold standard. Yet, the machine is expensive and large and the test is time consuming and difficult for patients. Virtual visual field testing is convenient, cost effective and may offer an alternative to Humphrey testing. This study compares a commercially available virtual reality visual field to the Humphrey automated perimetry in a comprehensive academic practice.

Methods: During the COVID-19 pandemic, virtual reality visual field testing was implemented in the Department of Ophthalmology at Stony Brook University. This study retrospectively reviewed patients who underwent virtual visual field testing (VVF) using the BOLT strategy from Virtual Field.io from July 2020 through December 2020. Of these patients, those who had a prior Humphrey 24-2 SITA standard visual field (HVF) performed within 12 months were included. All ocular diagnoses were included. Primary outcome data collected included mean deviation, pattern standard deviation, visual field index, fixation losses, test duration, and false positives and negatives.

Results: A total of 76 patients underwent VVF testing. Of these, 50 eyes of 48 patients had a HVF performed in the prior 12 months and were included in the final analysis (M: 43.75%, F: 56.25%, mean age 55.28). VVF demonstrated no difference in ratio of fixation losses (mean difference -0.08, $p=0.45$) or number of false negatives (mean difference 2.07%, $p=0.05$) but had significantly less false positives (mean difference 5.13%, $p=0.05$). There was no statically significant difference in the mean deviation of the VVF compared to the HVF (mean difference 4.11, $p=0.45$). The VVF had a lower pattern deviation (mean difference -0.23, $p=0.05$) and visual field index (mean difference -2.87, $p=0.05$) compared to the HVF. Test duration was shorter with the VVF by 2.4 minutes (mean difference 2.43, $p=0.05$). Pearson's correlation coefficients for mean deviation, pattern deviation and virtual field index were 0.74 ($p<0.01$), 0.65 ($p<0.01$), and 0.71 ($p<0.01$).

Conclusions: Virtual visual field testing using the BOLT strategy was similar to the Zeiss Humphrey SITA-Standard 24-2. VVF testing provides advantages over HVF in terms of cost effectiveness, portability and efficiency. However, prospective studies are needed to assess virtual field reproducibility and progression analysis.

CONTROL ID: 3544550

SUBMITTER (NAME ONLY): Yichen Bai

TITLE: Accelerated Aging in the Lacrimal Glands of Estrogen-deficient Aromatase (Aro) and Estrogen Receptor (ER) Knockout Mice

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Bai, X. Lu, Ophthalmology, Southern Medical University, Guangzhou, Guangdong, CHINA|Y. Bai, X. Yang, L.W. Reneker, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|D. Lubahn, Biochemistry, University of Missouri, Columbia, Missouri, UNITED STATES|X. Yang, X. Zhong, State Key Laboratory of Ophthalmology, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: The risk of dry eye disease (DED) increases with age in both men and women. Although sex hormones are known to be important for maintaining the ocular surface health, their role in the etiology of DED is still undefined. In this study, age-related changes were investigated in the ocular surface tissues of aromatase (Aro) and estrogen receptor (ER) KO mice.

Methods: The pathology of ocular surface tissues in the aromatase (an estrogen synthase) and estrogen receptor isoform, ER α and ER β , knockout (KO) mice was investigated. The age-related changes in the KO mice were compared to their age- and sex-matched wild type (WT) control mice.

Results: In 6-month old male Aro-KO mice, estrogen deficiency resulted in multiple defects in the lacrimal glands, which can be best characterized as accelerated aging, those including severe acinar atrophy, appearance of Harderian gland-like structures, increase of gland ducts and morphologic dysplasia (cytomegaly, karyomegaly, and cell and nuclear polymorphism) across the gland. Interestingly, the similar phenotype was also seen in the male ER α KO mice as young as 4-month old, suggesting that estrogen's anti-aging effect in the lacrimal gland of male mice is likely mediated through ER α pathway. Deletion of aromatase significantly increased the size and weight of the lacrimal glands in female KO mice. Increase of immune cell infiltration was found in the lacrimal glands of female Aro-KO mice when compared to the age-matched female WT mice. No apparent histopathology was noticed in the meibomian glands and goblet cells between the Aro-KO and WT mice. No significant difference was found in the corneal fluorescein staining score between the one-year old Aro-KO mice and their age- and sex-matched WT control mice.

Conclusions: Estrogen deficiency results in different responses in the lacrimal glands of male and female mice. Our study suggests that estrogen can play an anti-aging role, mediated through ER α , in the lacrimal glands of male mice. The anti-inflammatory function mediated via the estrogen-ER β pathway in female lacrimal glands is under further investigation.

CONTROL ID: 3544552

SUBMITTER (NAME ONLY): Sandra Vermeirsch

TITLE: Mutational profile of the most common genes causing inherited retinal diseases in a large molecularly characterized cohort from the United Kingdom

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Pontikos, S. Malka, M. Michaelides, A. Webster, O.A. Mahroo, G. Arno, Genetics Service, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|N. Pontikos, S. Malka, M. Michaelides, A. Webster, O.A. Mahroo, G. Arno, University College London, London, London, UNITED KINGDOM| S. Vermeirsch, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases are an important cause of blindness, and due to the recent advancement of gene-directed trials it is increasingly important to understand the molecular basis of these disorders. The aim of this study was to examine the mutation spectrum of the 5 most common genes involved in inherited retinal disease in a large molecularly characterized cohort from the United Kingdom.

Methods: We performed a retrospective study of electronic patient records of the Genetics Service of Moorfields Eye Hospital. The 5 most common genes, by persons affected, causing inherited retinal disease in this cohort have previously been reported (Pontikos et al., 2020) as ABCA4, USH2A, RPGR, PRPH2, and BEST1. The electronic records database was interrogated, and all patients with a molecular diagnosis due to one of the above 5 genes were analyzed. A total of 1870 patients from 1720 families were included. For autosomal recessive disorders where 2 or more likely pathogenic or pathogenic changes were reported, all mutant alleles were included.

Results: The most common pathogenic or likely pathogenic mutations in our cohort for ABCA4 were c.5882G>A (p.Gly1961Glu) and c.5461-10T>C (212 and 119 of 2024 mutant ABCA4-alleles, respectively). The five most frequent mutant alleles (c.5882G>A (p.Gly1961Glu), c.5461-10T>C, c.2588G>C (p.Gly863Ala), c.4139C>T (p.Pro1380Leu), c.5714+5G>A) account for more than 25% of disease-associated variants in ABCA4. In USH2A the c.2299del (p.Glu767Serfs*21) mutation was most commonly involved (130/749 mutant USH2A-alleles), c.2405_2406del (p.Glu802Glyfs*32) and c.2426_2427del (p.Glu809Glyfs*25) were most prevalent in RPGR (23 and 21/239 mutant RPGR-alleles, respectively), while c.514C>T (p.Arg172Trp) was the most common in PRPH2 (40/194 mutant PRPH2-alleles). In BEST1 the most commonly observed mutations were c.728C>T (p.Ala243Val) and c.652C>T (p.Arg218Cys) (11 and 10 of 201 mutant BEST1-alleles, respectively).

Conclusions: Our findings provide meaningful population-based data of the mutation spectrum of ABCA4, USH2A, RPGR, PRPH2, and BEST1 from a large cohort of patients with a molecular diagnosis from the United Kingdom.

CONTROL ID: 3544555

SUBMITTER (NAME ONLY): Dinah Chen

TITLE: Quantitative calibration of sensor strip ERG electrodes – Update.

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Chen, S.E. Brodie, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Dinah Chen: Commercial Relationship: Code N (No Commercial Relationship) | Scott Brodie: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: ERGs are traditionally recorded using corneal electrodes, which can be difficult for some patients to tolerate. In the last several years, adhesive skin electrodes have gained in acceptance. We have previously reported on the clinical usefulness of qualitative interpretation of ERG recordings using skin electrodes for a wide spectrum of retinal disorders, as well as a preliminary estimate of the quantitative comparison of simultaneous ERG recordings using contact lens (CL) and adhesive skin electrodes to compare differences in signal strength. In the present report, we update our quantitative findings.

Methods: The study was Institutional Review Board approved. 89 subjects were drawn from the practice of one of the authors who were referred for full-field ERG testing for multiple clinical indications. Informed consent was obtained from patients or accompanying parents. ERGs (obtained according to ISCEV standards) were recorded simultaneously from both eyes with ERG-jet corneal CL electrodes and LKC Technologies Sensor Strip adhesive skin electrodes using multi-channel instrumentation (Diagnosys LLC, Espion3). A- and b-wave amplitudes and implicit times were compared between the two electrode types.

Results: Waveform morphologies were similar for both electrodes. Regression coefficients (conversion factors) for a- and b-wave amplitudes under photopic and scotopic conditions were tightly clustered: DA 0.01 b-wave: 0.368; DA 3 a-wave: 0.343; DA 3 b-wave: 0.360; LA 3 a-wave: 0.256; LA 3 b-wave: 0.325; 30-Hz flicker peak-to-peak: 0.384. Regression coefficients for implicit times were nearly equal to 1.0, indicating comparable latencies for skin and CL electrode recordings: DA 0.01 b-wave: 0.971; DA 3 a-wave: 0.926; DA 3 b-wave: 0.996; LA 3 a-wave: 0.967; LA 3 b-wave: 0.964. The regression coefficient for the entire amplitude data set was 0.336, with an overall correlation between skin and CL electrode amplitudes of 0.799. The regression coefficient for the entire implicit time data set was 0.980, with an overall correlation of 0.96.

Conclusions: Our best estimate for the conversion factor between ERG amplitudes recorded with adhesive skin electrodes and CL electrodes is 0.336 – skin electrode amplitudes are about 1/3 the amplitudes recorded simultaneously using CL electrodes - with a high correlation between skin and CL electrode amplitudes. Implicit times are nearly identical for the two electrode types.

CONTROL ID: 3544556

SUBMITTER (NAME ONLY): E Shepherd

TITLE: Long term visual and neurodevelopmental outcomes in ROP patients treated with laser photocoagulation versus intravitreal anti-VEGF therapy

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.A. Shepherd, K. Hawn, J. Silvestri, J. Cohen, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|A. Patel, P. Meier, R. Kimura, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Over the past 20 years, the mainstay of treatment for retinopathy of prematurity (ROP) has changed from laser photocoagulation therapy to intravitreal injection of anti-vascular endothelial growth factor (antiVEGF). Despite the change in therapy, little is known about the long term outcomes associated with anti-VEGF agents. We performed a retrospective, observational study to determine if there is a difference in the long-term visual and neurodevelopmental outcomes of patients who were treated with laser photocoagulation versus patients treated with an anti-VEGF injection.

Methods: Out of 105 patients who were treated for ROP at Rush University, 24 patients met the inclusion criteria of having at least 1 follow up appointment. 14 were treated using laser photocoagulation, and 10 were treated with an anti-VEGF agent (bevacizumab or ranibizumab). We analyzed visual acuity, ocular alignment, refractive errors, presence of amblyopia, presence of a diagnosed neurodevelopmental disorder, and other notable ocular abnormalities. A student's t-test and a Chi square test were used for statistical analysis.

Results: Analysis of our results showed that patients treated with laser therapy were more likely to be amblyopic than those treated with an anti-VEGF agent (50% versus 10%, $p=0.04$). Additionally, there was a statistically significant difference in the sphere of patients, with laser treatment patients being more myopic (-8 D versus -2.06 D, $p=0.01$). However, the average age at last eye visit has been identified as a possible confounding variable, with the average age being 12 years for patients treated with laser therapy (SD = 2.59) and 2 years for those treated with anti-VEGF (SD = 1.20). Visual acuity could not be analyzed since only one patient in the anti-VEGF group was able to read the eye chart. Analysis of all other categories analyzed revealed no statistically significant differences.

Conclusions: Our results showed a statistically significant difference for two of the outcomes analyzed. Patients treated with laser therapy were more likely to be amblyopic and were more myopic than those treated with an anti-VEGF agent. Further research would include an age-matched, larger sample size. If our results are confirmed, this would suggest a benefit of administering anti-VEGF injections over laser photocoagulation.

CONTROL ID: 3544558

SUBMITTER (NAME ONLY): Tomas Grippo

TITLE: MicroPulse Transscleral Laser Therapy - Fluence as Predictor of IOP Reduction

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Grippo, Grippo Glaucoma & Cataract Center, City of Buenos Aires, Buenos Aires, ARGENTINA|T. Grippo, Ophthalmology, Hospital Aleman, City of Buenos Aires, Buenos Aires, ARGENTINA|F.G. Sanchez, Glaucoma research, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|F.G. Sanchez, Legacy Research Institute, Portland, Oregon, UNITED STATES|J. Stauffer, G. Marcellino, IRIDEX Corp, Mountain View, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether Fluence (F) is a better indicator than Total Energy (TE) in predicting IOP reduction with MicroPulse® Transscleral Laser Therapy (MP-TLT, Iridex Corp., Mountain View, CA) in patients with glaucoma.

Methods: F and TE were calculated from data obtained from published literature. The F formula was adjusted to account for sweep velocity. $F = (\text{power (Watts)} \times \text{duty cycle} \times \text{dwell time (s)}) / \text{fiber area}$. Dwell time is exposure time divided by velocity of the sweep. $TE = \text{power} \times \text{duty cycle} \times \text{exposure time (s)}$. Studies without a description of the treatment parameters (power, exposure time, number of sweeps per procedure) or less than 6 months follow-up were excluded. Boxplots were created to compare the distribution of F and TE, and its relationship with IOP reduction by separating the cohorts into Group A: "equal or lower than the median fluence", and Group B: "above the median fluence"; and mixed effects models were used to compare the parameters between groups. All analyses were performed using R (version 4.0.0, R Foundation for Statistical Computing, Vienna, Austria).

Results: Four of 30 (13.3%) publications included the number of sweeps used to allow for F calculation, yet personal communication with the authors allowed the inclusion of 6 more papers, which yielded a total of 656 eyes from 15 cohorts for analysis (some of the studies included more than one cohort).

Table 1 compares F, TE, baseline IOP, and IOP reduction between group A and group B. Figure 1 shows the distribution of these variables within the groups. Group B had a statistically higher IOP reduction than group A ($p < .001$), and there was no overlap in IOP reduction between the groups (Figure 1, top). TE was not statistically different between group A and group B ($p = .447$), and overlapped in the boxplot (Figure 1, bottom); suggesting that this variable may have less impact on IOP outcomes compared to F. Baseline IOP was not statistically different between the groups ($p = .518$).

Conclusions: Most authors do not report the number of sweeps performed. This fails to account for the impact of sweep velocity on outcomes. In contrary to TE, F combines all the laser parameters including sweep velocity into a single number expressed in Joules/cm². IOP reduction was statistically higher in the high F group (group B), suggesting that F may be a better light-dose metric and a more reliable indicator of IOP reduction than TE.

CONTROL ID: 3544559

SUBMITTER (NAME ONLY): Saagar Pandit

TITLE: Iris Suturing for Posterior Chamber Intraocular Lens Dislocation:

A comparison of In-the-bag versus Out-of-the-bag Dislocations and Development of Uveitis Glaucoma Hyphema Syndrome

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Pandit, V. Paranjpe, H.A. Parikh, K. Wald, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine cases of new onset uveitis-glaucoma-hyphema (UGH) syndrome after posterior chamber intraocular lens (PCIOL) repositioning with iris-sutured IOL, differentiating between in-the-bag versus out-of-the-bag dislocations.

Methods: Retrospective chart review was performed on 99 patients with a posteriorly dislocated IOL operated upon by a single surgeon from 2018-2020. Patients with previously diagnosed UGH, retained lens fragment, early dislocation, or lost-to-follow-up after one month were excluded. Variables of interest included 1-piece versus 3-piece IOL, in-the-bag versus out-of-the bag dislocation, and history of pxeudoexfoliation. UGH was defined as having at least one of the following: elevated intraocular pressure >25 mmHg, anterior uveitis, hyphema, or post-operative cystoid macular edema (CME).

Results: 24 patients were eligible for the study. 18 patients were noted to have in-the-bag dislocations (75%). A total of 12 patients developed UGH (50%). Two of the 12 patients (16.67%) exhibited uveitis, glaucoma, and CME. No patients had hyphema. Among patients with UGH, mean age was 73 years old. 7 of 12 cases were in-the-bag dislocations (58.3%), and 6 of 12 cases (50%) had pre-existing pxeudoexfoliation (PXE). Among in-the-bag dislocations with UGH, 5 out of 7 patients had 1-piece IOLs (71%); whereas among the 5 cases of out-of-the-bag dislocations with UGH, all had 3-piece IOLs. Moreover, none of the patients with out-of-the-bag dislocation had pre-existing PXE. A final logMAR VA of 0.314 for in-the-bag dislocations with UGH ($p = 0.832$) was not found to be statistically significant compared to out-of-the bag UGH patients. Mean follow-up time was 4.5 months. Patients were treated with topical steroids (9 out of 12, 75%), topical nonsteroidal anti-inflammatory (8 out of 12, 67%), and pressure lowering drops (9 out of 12, 75%).

Conclusions: UGH is a notable complication of iris sutured PCIOL repositioning. Pre-existing PXE may be a predisposing factor for in-the-bag dislocations. There was a tendency toward UGH with single-piece in-the-bag dislocations, and three-piece out-of-the-bag dislocations. Moreover, both in-the-bag and out of-the-bag dislocations appear to have similar visual outcomes. However, a larger sample size with longer follow-up time is necessary to draw more definitive conclusions.

CONTROL ID: 3544560

SUBMITTER (NAME ONLY): Yutao Liu

TITLE: The Role of PCSK1 in Keratoconus Pathogenesis in Two Mouse Models

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, H. Yu, S.B. Smith, J. Cai, Cellular Biology and Anatomy, Augusta University, Augusta, Georgia, UNITED STATES|Y. Liu, A. Estes, S.B. Smith, James & Jean Culver Vision Discovery Institute, Augusta University, Augusta, Georgia, UNITED STATES|A.N. Kuo, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|A. Estes, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Keratoconus (KC), a bilateral, asymmetric corneal degeneration, leads to high myopia, irregular astigmatism, and corneal scarring. In a 4-generation KC family, we identified a rare variant rs373951075 (G>A) in a PCSK1 intron co-segregating with KC in an autosomal dominant pattern. Here, we evaluated the genetic contribution of PCSK1 to KC pathogenesis.

Methods: We used two mouse models of human PCSK1 deficiency: ENU-induced Pcsk1^{N222D} & targeted mutation Pcsk1^{tm1Dfs} mice. We examined the thickness and curvature of mouse corneas using anterior segment optical coherence tomography (OCT) with a Bioptigen Envisu R2200 system at 3 & 6 months. We performed histological analysis at 6 months. In addition, we checked the expression of PCSK1 in a RNA-Seq dataset of human corneas. We performed bioinformatics analysis with rs373951075 using the UCSC Human Genome Browser and Ingenuity Pathway Analysis (IPA) to identify its potential function and target genes.

Results: We evaluated 70 (37 male, 33 female, 32 WT, 33 heterozygous, 5 homozygous) Pcsk1^{N222D} & Pcsk1^{tm1Dfs} mice. The average corneal thickness measured by OCT was 110±11µm for WT mice, which did not differ significantly from the mutant mice. No curvature abnormalities were detected in either mutant group. Histologic analyses did not reveal morphologic alterations related to KC in corneas of either mutants at 6 months. The expression of PCSK1 mRNA was limited to background/barely detectable levels in human corneas with RNA-Seq. Bioinformatics analysis indicated that rs373951075 is located in a consensus sequence (TGATGTCAT) binding to JUND, an AP1 transcription factor subunit. This region is predicted to be a distal enhancer to neighboring genes based on ENCODE data. Using IPA Pathway Building, we found that JUND, FOS and estradiol can regulate expression of only 1 of 10 neighboring genes: CAST, which is associated with KC. CAST is also highly expressed in human corneas. Our network analysis connects JUND/CAST/Estradiol with many KC-associated genes, including LOX, IL1B, TGFB1, MMP9, SMAD3, COL5A1, RXRA, COL6A1, FNDC3B, WNT10A, WNT7B, LUM, FBN1, LTBP1, FOXO1, CSNK1E, THBS2, and DCN.

Conclusions: Data from the Pcsk1 mice suggest that Pcsk1 may not contribute to development of KC. Further analyses suggest that the KC-segregating intronic variant rs373951075 in the PCSK1 region may serve as an enhancer for CAST. Future functional experiments will test the role of CAST in KC.

CONTROL ID: 3544562

SUBMITTER (NAME ONLY): Ulisse Bocchero

TITLE: Selective knockout of murine glutamic acid-rich protein 2 (GARP2) alters the photoresponse and significantly decreases photoreceptor dark noise.

SESSION TITLE: Photoreceptors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: U. Bocchero, J. Pahlberg, NEI, National Institutes of Health, Bethesda, Maryland, UNITED STATES|D.A. Stacks, T.W. Kraft, S.J. Pittler, University of Alabama at Birmingham, Optometry and Vision Science, Vision Science Research Center, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Cngb1 gene encodes the β -subunit of the rod photoreceptor cyclic nucleotide-gated (CNG) cation channel. GARP2, a splice variant of the Cngb1 gene, is exclusively expressed in rods and suggested to function as a structural protein, a calcium-binding protein, and a modulator of the basal activity of cGMP phosphodiesterase (PDE). We set out to further assess the structural and functional role of GARP2 within the retina.

Methods: GARP2 knockout mice were generated using ZFN-mediated gene editing. Morphological features were assessed by optical coherence tomography and immunohistochemistry techniques at P180. Functional properties were then assessed by in-vivo electroretinogram (ERG) and whole-cell patch-clamp recordings from retinal slices.

Results: The retina in KO mice exhibited no major alterations, except for occasional longer and bent rod outer segments. The maximum amplitude of the ERG a-waves ($460 \pm 150 \mu\text{V}$ vs. $306 \pm 70 \mu\text{V}$) and b-waves ($1108 \pm 333 \mu\text{V}$ vs. $589 \pm 103 \mu\text{V}$) were reduced in KO mice, with KO mice showing lower than predicted b-wave amplitudes for the measured a-wave. However, single-cell recordings showed no significant differences in the physiological properties of rods and RBCs between the genotypes. Surprisingly, KO rod photoreceptors showed a significant decrease in dark noise levels compared to WT ($0.57 \pm 0.07 \Delta\text{pA}^2/\text{Hz}$ vs. $0.3 \pm 0.04 \Delta\text{pA}^2/\text{Hz}$), $p < 0.01$).

Conclusions: Our morphological analysis suggests that the retina in KO mice develops correctly, with a possible minor role for GARP2 in the structural stability in rod photoreceptors. Importantly, we were able to confirm the modulatory role of GARP2 on the basal activity of PDE, its important role in controlling dark noise levels and implications for regulating visual phototransduction and single-photon sensitivity.

CONTROL ID: 3544563

SUBMITTER (NAME ONLY): Lindsey Morey

TITLE: Functional Physiology of the Regenerated Zebrafish Retina

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Morey, D.M. Mitchell, D.L. Stenkamp, Biological Sciences, University of Idaho, Moscow, Idaho, UNITED STATES|P.C. Meighan, M.D. Varnum, Integrative Physiology and Neuroscience, Washington State University, Pullman, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Zebrafish regenerate their retinas following damage, resulting in restoration of visual function (McGinn et al., 2018 J Neurosci). Behavioral measures of visual function are restored more rapidly following a lesion that destroys only neurons of the inner retina and spares photoreceptors (PR) and glia (=selective lesion), than following a lesion that destroys all retinal neurons and spares only glia (=extensive lesion) (Sherpa et al., 2014 Dev Neurobiol). Here we further evaluate the recovery of visual function through characterization of the electroretinogram (ERG) over time following these two types of retinal damage.

Methods: Right eyes of zebrafish (6mo–1.5yrs, both sexes) were lesioned with intravitreal injection of either 10 μ M (extensive) or 2 μ M (selective) ouabain. Left eyes served as unlesioned controls. Retinal neuronal communication was analyzed at selected recovery times using ERG recordings in intact zebrafish (extensive, n=4-13 per timepoint; selective, n=3-12 per timepoint). Eyes were then harvested and cryosectioned, permitting subsequent histological analysis of bipolar cells (BP), which is currently underway.

Results: A qualitative study of the ERG waveforms focused on the “post-photoreceptor response” (PPR), which in a healthy retina is dominated by the “b-wave” or ON BP response, to assess BP function and connectivity to PRs during regeneration. There was a rapid reduction in the amplitude of the PPR after both extensive and selective lesions, though the reduction was greater for extensively-lesioned fish. During early stages of functional recovery after both types of lesions, we observed a deviated waveform, which was consistent with emergence of a d-wave (OFF BP response) elicited at light termination. After 45 days post-injury (DPI) for extensive and 21 DPI for selective lesions, the PPR waveform amplitude increased and peaked sooner after the light stimulus compared to earlier DPIs, suggesting emergence of the b-wave (ON BP response). By 90 DPI for extensive and 30 DPI for selective lesion, the PPR waveform became more typical of a healthy retina, but did not return to pre-lesion amplitudes.

Conclusions: Consistent with published behavioral results, PPR recovery following an extensive lesion occurred more slowly than PPR recovery following a selective lesion. Interestingly, the ERG waveform topography suggests that PR-OFF BP connectivity may functionally recover before PR-ON BP connectivity.

CONTROL ID: 3544566

SUBMITTER (NAME ONLY): Ann Elsner

TITLE: Retinal vascular changes compared with cone distribution in diabetic subjects

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.E. Elsner, T. Gast, B. Walker, R. Gilbert, S.A. Burns, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: We compared microvascular changes of diabetic subjects in several modes of a custom adaptive optics scanning laser ophthalmoscope (AOSLO) to cone distribution models. We analyzed vascular features that show increasing stages of response to ischemia: 1) microaneurysms of sufficient size to include a build-up of epithelial cells; 2) capillary bends or loops that indicate vessel tubule formation and initial elongation, and 3) doubled or collateral vessels or complex tangles that indicate extensive elongation and alteration of direction of growth.

Methods: Cone density and retinal vessels were imaged for 10 diabetic subjects (29-79 yr, 54.5 +/- 12.7 yr. All subjects were consented and tested in a manner approved by the Indiana University Institutional Review Board, which adhered to the Declaration of Helsinki. We performed OCT and OCTA (Heidelberg Spectralis II), then imaged cones and then retinal microcirculation with AOSLO in about 1.5 hr. We simultaneously acquired confocal and multiply scattered light images, using a roughly 100 micron diameter confocal aperture and 3 offset apertures of about 500 microns diameter and offset by 300 microns that differed in direction or wavelength. We used both reflectance mode and motion (variance) mapping for vessels, montaging images for the 6 x 6 deg central retina and temporal retina to 7 deg. To assess the response to retinal ischemia for stages 1-3, we graded all AOSLO imaging modes. Cone density modelling used a 2 parameter exponential model: $\ln(\text{cone density}) = a * \text{microns eccentricity} + b$ and the deviation from our published norms.

Results: This sample of diabetic subjects had a widely varying response to ischemia. A minimal ischemic response was 1) few microaneurysms, no 2) no capillary bends or 3) doubled vessels. Some eyes with a strong ischemic response had significantly low cone density parameter ($b=10.3$ or 10.4 vs. $10.8 \pm .222$) and 1) many microaneurysms, some overlapping; 2) capillary bends, loops and vessels of varying diameter; and 3) doubled/collateral vessels, some a tangled mass. Vascular lesions differed for imaging modes, e.g. fine gauge tangles better seen in reflectance mode, but some microaneurysms better with motion mapping while others in a reflectance image.

Conclusions: Diabetic subjects have numerous lesions detectably small with clinical means that can be associated with low cone density decrease, which may imply neural damage.

CONTROL ID: 3544570

SUBMITTER (NAME ONLY): Pawan Shahi

TITLE: The Quest for a Safer Alternative to Viral Gene Therapy Continues

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.K. Shahi, M. Kabra, Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|P.K. Shahi, M. Kabra, B.R. Pattnaik, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|B.R. Pattnaik, Pediatrics, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Viral vector-mediated Gene therapy is at the forefront of the treatment for inherited and acquired retinal disorders. The eye provides a tight blood-brain barrier, low antigenicity to the viruses, and ease of surgical access. Retinal Pigment epithelium (RPE) cells are one of the primary targets for gene therapy. A combination of the cell-specific promoter and lentiviruses, adeno-associated virus (AAV)5, or AAV7m8 successfully transduces RPE cells in vivo. We sought to evaluate RPE cells' immune response after viral gene delivery by subretinal injections.

Methods: 6 weeks old C57Bl6 wild type mice were injected with Lentivirus, AAV5, or AAV7m8 carrying GFP reporter gene driven by CMV promoter via subretinal injection. After 7 or 14 days of injection, the mice were sacrificed, and the eyes were enucleated. The RPE florets were imaged for GFP fluorescence expression using the confocal microscope to confirm the transduction. RPE cells were later dissociated, mRNA was isolated and converted to cDNA. These were subjected to qPCR using the primers for IFN γ , IL-1 α , IL-1 β , IL-6, CD-8, and Iba-1 immunogenic markers.

Results: IFN γ , an activator of macrophages, and IL-1 α , an inflammatory cytokine, were not detected in RPE cells after the viral gene delivery. The expression of IL-6, another pro-inflammatory cytokine, was negligible at week 1, being marginally higher in the lentiviral injected eye relative to both AAV7m8 and AAV5. The expression of IL-6 subsequently decreased at week 2. Expression of IL1 β cytokine was profound in the week 1 sample. Its expression in the lentiviral injected eye was 2-fold higher than AAV7m8, or AAV5, which was abolished entirely at week 2. CD-8 transcripts were 2.7-fold higher for lentiviral and 5.2 fold higher for AAV7m8 compared to AAV5 mediated gene delivery. Its expression persisted at week 2. The expression of Iba-1, a microglia marker, was significantly higher with a 2-fold higher presence for AAVs compared to lentivirus. Its upregulation continued in the AAV7m8 injected eye at week 2. We did not detect any of the above cytokines in the PBS injected control eyes.

Conclusions: Our results indicate that transduced RPE cells by subretinal delivery of viruses elicited inflammatory cytokines. The extent of cellular toxicity in the RPE was greater for AAVs compared to lentivirus. It might be beneficial to consider adjunct immune suppressor therapy for the viral-mediated delivery or use non-viral modalities.

CONTROL ID: 3544571

SUBMITTER (NAME ONLY): Damien Goldberg

TITLE: Phase 1 Study of an Intracameral Travoprost Hydrogel-based Implant for the Treatment of POAG and Ocular Hypertension

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Goldberg, Wolstan and Goldberg Eye Associates, California, UNITED STATES|T. Walters, Texan Eye Care, Texas, UNITED STATES|M. Cheung, E. Braun, D. Silva, M.H. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|J. Bacharach, North Bay Eye Associates, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nonadherence to glaucoma drop therapy continues to be an issue in 30-80% of patients and can lead to fluctuations in intraocular pressure (IOP). There remains an unmet need for a therapy with a consistent and durable IOP lowering profile that improves patient compliance. OTX-TIC, an intracameral, bioresorbable, hydrogel-based implant, is designed to deliver travoprost at therapeutic levels in the anterior chamber and can potentially address issues with chronic drop therapy. This study evaluates the safety, tolerability and efficacy of OTX-TIC in subjects with glaucoma.

Methods: Prospective, multicenter, open-label, Phase 1 study in adult subjects with primary open angle glaucoma (POAG) or ocular hypertension (OHT). After washout, subjects were enrolled into 4 cohorts (Cohort 1, 15µg; Cohort 2, 26µg; Cohort 3, fast-degrading hydrogel 15µg; Cohort 4, fast-degrading hydrogel 5µg) and received a single OTX-TIC implant (TIC) in the study eye and topical travoprost (Travatan Z; TZ) in the fellow eye. Diurnal IOP (8am, 10am, 4pm) was assessed at baseline, Days 14, 42, 85, and Months 4, 6, and 4-week follow-up after (8am only). Safety measures include adverse event (AE) collection, endothelial cell count (ECC), and pachymetry.

Results: All cohorts have completed enrollment: Cohort 1 (n=5), Cohort 2 (n=4), Cohort 3 (n=5) and Cohort 4 (n=5). TIC lowered mean IOP levels up to 22, 9, 6 and 6 months in Cohorts 1, 2, 3, and 4, respectively. Eyes treated with TIC had a baseline mean IOP of 21-27 mmHg and all four cohorts showed IOP lowering of 7-11 mmHg which was comparable to TZ-treated eyes. Cohort 2 showed the most consistent and durable response with all subjects going to Month 6 without need for rescue medication in 50% of subjects to Month 9. TIC biodegraded consistently in 5-7 months for Cohorts 1 & 2 and 3-5 months for Cohorts 3 & 4. In all cohorts, no clinically meaningful changes in ECC or corneal thickness were observed. The most common AEs reported were low grade inflammation (all cohorts) and peripheral anterior synechiae (Cohort 1 only).

Conclusions: OTX-TIC showed similar IOP control compared to topical travoprost therapy in subjects with POAG or OHT which was sustained for at least 6 months in many subjects. OTX-TIC was generally well tolerated with a favorable safety profile. Durability of IOP lowering effect was longest and most consistent in Cohort 2.

CONTROL ID: 3544572

SUBMITTER (NAME ONLY): Krithika Iyer

TITLE: Substratum stiffness modulates the proliferation but not the motility of cultured corneal keratocytes in response to PDGF-BB

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Iyer, D. Schmidtke, V. Varner, Bioengineering, The University of Texas at Dallas Erik Jonsson School of Engineering and Computer Science, Richardson, Texas, UNITED STATES|K. Iyer, M. Petroll, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: During corneal wound healing, keratocytes within the corneal stroma are activated into a repair phenotype when soluble growth factors, such as transforming growth factor-beta 1 (TGF- β 1) and platelet-derived growth factor-BB (PDGF-BB), are released into the stromal space. This process is often accompanied by changes in tissue stiffness, and previous work has shown that the TGF- β 1-mediated myofibroblastic activation of these cells is stiffness-dependent. Still, it is unclear if stiffness can also regulate keratocyte behavior in response to other growth factors, such as PDGF-BB. Here, we used a polyacrylamide (PA) gel system to determine whether changes in substratum stiffness can modulate the proliferation and motility of primary corneal keratocytes treated with PDGF-BB.

Methods: Functionalized PA substrata with an elastic modulus of either 1 kPa (soft) or 10 kPa (stiff) were fabricated to mimic the mechanical properties of either normal or fibrotic corneal tissue. The substrates were then plated with primary rabbit corneal keratocytes (NRKs) and cultured in defined serum-free media in either the presence or absence of PDGF-BB. Fixed cells were then stained with either F-actin, to visualize cell morphology, or EdU incorporation, to quantify proliferation. In other experiments, a circular freeze injury was introduced to mimic wound healing, and time-lapse phase-contrast images were captured to quantify keratocyte motility.

Results: In the presence of PDGF-BB, NRKs plated on stiffer substrates exhibited a more elongated morphology, an increased cell area, and a higher rate of proliferation than their counterparts cultured on soft PA gels. To assay changes in keratocyte motility, we also quantified NRK migration into decellularized wounds created on both soft and stiff PA substrata. On all substrata, the NRKs migrated from the densely populated region surrounding the wound into the decellularized area. Keratocytes treated with PDGF-BB traveled further into the wound and exhibited faster migration speeds than cells maintained in serum-free conditions, but we did not observe any stiffness-dependent differences in the PDGF-BB-driven motility of these cells.

Conclusions: Taken together, these results suggest that changes in ECM stiffness can modulate the proliferation and morphology of corneal keratocytes, but not their motility, in response to PDGF-BB.

CONTROL ID: 3544581

SUBMITTER (NAME ONLY): Diane Zheng

TITLE: Correlates of Perceived Vision Loss Impact on Daily Life Functioning among Hispanics/Latinos

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.D. Zheng, Psychiatry & Behavioral Sciences, University of Miami School of Medicine, Miami, Florida, UNITED STATES|D.D. Zheng, L. McClure, D. Lee, Public Health Sciences, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B.L. Lam, C. Mendoza, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|C.E. Joslin, H. Pauls, L. Ulanski, T.S. Vajaranant, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine the relative ranking of perceived vision loss impacts and its association with eye examination recommendation compliance.

Methods: Data were from the Ocular SOL ancillary study to the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) which evaluated ocular health, knowledge, risk factors, and health care use with 1235 HCHS/SOL participants (age ≥ 40 yrs) at the Miami, FL study site. Participants were asked how various conditions would impact their day-to-day life (i.e. loss of memory, hearing, eyesight, speech or an arm or a leg). Each response was rated on a scale of 1 to 10 with 1 having the least impact and 10 having the greatest impact on daily life. Mean responses and corresponding 95% confidence intervals were calculated and compared by paired t-tests. ANOVA was conducted to examine the difference among gender, education, Hispanic heritage, as well as the association with preventive eye care compliance (reported eye examination by an eye care professional in the past 24 months) in the study population and in the subgroup who had diabetes based on American Diabetes Association criteria. All analyses were adjusted for the complex survey design.

Results: Losing eyesight was ranked as #1 condition impacting daily life at 9.74, 95% CI [9.68, 9.80] (paired t-test, $P < .05$), above losing memory (9.61, [9.52, 9.71]), losing hearing (9.14 [9.01, 9.26]), losing speech (9.10 [8.98, 9.22]), or losing an arm or a leg (8.71 [8.56, 8.86]); means not independent. Relative rankings were consistent across gender, education, and Hispanic ethnicity. Females perceived a higher impact of losing eyesight than males (9.81 vs. 9.66, $P < 0.01$). There were no meaningful differences in the perceived impact of losing vision by preventive eye care compliance status (yes vs. no: 9.76 vs. 9.72, $P = 0.5$). However, among the 264 participants who had diabetes, those who had an eye examination within the past 24 months, reported a greater perceived impact of losing vision (9.81 vs. 9.47, $P = 0.04$).

Conclusions: Among Hispanics/Latinos the perceived impact of losing eyesight is consistently ranked #1 among select conditions that would impact daily life. This concern, however, did not appear to result in better preventive ocular care compliance, except possibly for those living with diabetes. Educational campaigns designed to promote better eye care compliance in Hispanics need to be developed and tested.

CONTROL ID: 3544582

SUBMITTER (NAME ONLY): Hannah Yu

TITLE: Real-Time Photographic and Fluorescein Angiographic-Guided Management of Diabetic Retinopathy: Randomized PRIME Trial Outcomes

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yu, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|J.P. Ehlers, D. Sevgi, J. Hach, M. O'Connell, J. Reese, S. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|C.C. Wykoff, Blanton Eye Institute, Houston Methodist, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The optimal approach to utilizing anti-vascular endothelial growth factor (anti-VEGF) pharmacotherapy for the management of diabetic retinopathy (DR) is incompletely defined. Objective metrics such as DR severity scale (DRSS) or panretinal leakage index (PLI) may be able to help guide retreatment among these patients in routine clinical practice. The prospective, randomized PRIME trial compared as needed (PRN) intravitreal aflibercept injections (IAI) guided by real-time DRSS level or PLI for patients with DR.

Methods: Forty eyes with DR (DRSS 47 to 71) without diabetic macular edema (DME) received monthly IAI until ≥ 2 -step DRSS improvement was achieved. Eyes were randomized (1:1): eyes in Arm 1 were retreated according to DRSS level changes and eyes in Arm 2 were retreated according to PLI changes, as graded in real-time by a central reading center (CRC). Main outcome measures included changes in DRSS level and PLI compared to baseline.

Results: Through week 52 (W52), 95% of eyes achieved a ≥ 2 -step DRSS improvement. Following DRSS improvement, 97% of eyes required at least one PRN IAI to maintain anatomic improvements. In eyes requiring PRN IAI and completing W52, 100% and 59% of eyes in Arm 1 and Arm 2 experienced DRSS worsening ($p=0.01$), respectively. Through W52, mean PLI decreased 18.2% ($p=0.49$) and 54.6% ($p<0.0001$) in Arms 1 and 2 respectively. Eyes with NPDR and PDR at baseline achieved the ≥ 2 -step DRSS improvement after a mean 4.9 and 3.6 IAI ($p=0.03$). Two eyes developed a PDR event at W52 following a 5-month quiescent period and a 4- to 5-step DRSS worsening over the preceding one month.

Conclusions: The prospective, randomized PRIME trial utilized CRC-determined criteria to guide retreatment with IAI for DR without DME; most patients required ongoing re-treatment every 3-4 months and recurrence of ultra-widefield fluorescein angiography-determined leakage appeared to precede DRSS level worsening, suggesting PLI as a

potential biomarker for retreatment needs. This data reaffirms that close clinical follow-up is important even among eyes that achieve substantive DRSS-improvements with apparently quiescent disease for months.

CONTROL ID: 3544587

SUBMITTER (NAME ONLY): Benyam Kinde

TITLE: Osteopontin drives retinal ganglion cell resiliency in glaucomatous neuropathy

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) injury and loss in the context of increased intraocular (IOP) are hallmark features of glaucomatous neuropathy. Understanding how different RGC subtypes respond to chronic injury may provide insight into key players involved in neuroprotection and highlight novel therapeutic targets for the treatment of glaucoma.

Methods: Chronic IOP elevation was achieved using the silicone oil (SO)-induced ocular hypertension under-detected (SOHU) model. SO was injected into the anterior chamber of mice 8–10 weeks of age and a saline control into the contralateral eye. IOP was measured using the TonoLab tonometer weekly for up to 6 weeks. AAV-mediated OPN knockdown (KD) or overexpression (OE) in RGCs occurred at 8 weeks of age. Mice were sacrificed at 1 week and 4 weeks post-SOHU surgery for RGC subtype-specific immunohistochemistry (IHC) analysis. OPN expression was also assessed by IHC in post-mortem human retina, as well as an enzyme-linked immunosorbent assay (ELISA) to quantify OPN in the aqueous humor (AH) from patients with glaucoma.

Results: α RGCs and intrinsic photosensitive-RGCs (ipRGCs and M1-RGCs) were found to be uniquely resilient in the setting of chronically-elevated IOP. This increased resiliency was associated with high expression of OPN, a widely-expressed constituent of the central nervous system extracellular matrix, and shown to promote optic nerve regrowth in combination with growth factors in our previous work. KD of OPN in α RGCs in the SOHU model led to a marked decrease in α RGC survival, while OE of OPN in otherwise susceptible RGCs (Foxp2-RGCs) resulted in a dramatic boost in survival after 4 weeks of elevated IOP. In post-mortem human retina, we found that OPN is expressed in large, α -like RGCs and OPN quantification by ELISA from AH of patients with glaucoma demonstrated that the degree of OPN expression is correlated with disease severity.

Conclusions: OPN is thought to play a role tissue repair in response to neuronal injury. Work by others has implicated a neuroprotective role of OPN in ischemic stroke, spinal cord injury, and Alzheimer's disease, and our findings suggest a novel role for OPN in promoting RGC resiliency in mouse models of glaucomatous neuropathy. Our preliminary work with post-mortem human retina, as well as analysis of AH of patients with glaucoma indicate that OPN may be a target for slowing glaucomatous neuropathy in humans.

CONTROL ID: 3544590

SUBMITTER (NAME ONLY): Jiawen Xiang

TITLE: ATF4 is required for both the maintenance of the lens epithelium and late lens fiber cell differentiation

SESSION TITLE: Lens Development and Differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Xiang, A. Faranda, Y. Wang, S.G. Novo, M.K. Duncan, Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|J. Xiang, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: ATF4 is a key transcription factor implicated in diverse biological processes -including the unfolded protein response and regulation of amino acid homeostasis. It was reported over two decades ago that ATF4 null mice have defects in lens development, although there is controversy about whether the primary defect manifested in the lens fiber or epithelial cell. While several reports have found that ATF4 levels upregulate in the lens when the secretory pathway is overloaded with unfolded protein, the function of ATF4 in the healthy lens is largely unknown. Here, we take an unbiased approach to elucidate ATF4 function in the developing lens.

Methods: RNA-seq was performed on E16.5 embryonic lenses obtained from ATF4 knock out homozygous (ATF4^{-/-}) and WT embryos, followed by iPathwayGuide bioinformatics analysis. E16.5 ATF4^{-/-} and WT embryonic lens phenotype was detected by hematoxylin and eosin staining.

Results: The central lens epithelium of E16.5 ATF4^{-/-} mice is disorganized while vacuoles are seen throughout the lens fibers (Figure 1.A). RNAseq revealed that 562 genes were differentially expressed (DEGs) in E16.5 ATF4^{-/-} lenses, with 173 upregulated and 389 downregulated. The downregulated genes included lens epithelium markers like Foxe3 and E-Cadherin (Cdh1) as well as late lens fiber differentiation markers like Crybb2, Birc7 and Dnase2b. Pathway analysis of these DEGs revealed that genes regulating several different metabolic pathways were downregulated, including at least 17 genes known to regulate amino acid synthesis and transport (including Aldoc, Pycr1 and Phgdh) and at least 7 genes known to be involved with glucagon signaling and insulin secretion including Gcg, Pygl, Camk2a and Abcc8(Figure 1.B). Immunostaining has confirmed that E-cadherin downregulates in while α-SMA (Acta2) upregulates in the ATF4^{-/-} lens at the protein level.

Conclusions: Our data demonstrate that ATF4 is required for both lens epithelial cell maintenance and the terminal differentiation of lens fiber cells during late embryonic development. As the downregulated genes are highly enriched in those encoding proteins important for cellular metabolism, we are hypothesizing that ATF4 is required to establish the unique metabolic requirements of the lens.

CONTROL ID: 3544592

SUBMITTER (NAME ONLY): Matthew Pfannenstiel

TITLE: Preoperative versus intraoperative bevacizumab injection in diabetic patients with vitreous hemorrhage

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Pfannenstiel, H. Yu, M. Champion, R. Ajlan, Department of Ophthalmology, University of Kansas School of Medicine, Kansas City, Kansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify vitreous hemorrhage (VH) recurrence rate in diabetic patients during the one-month postoperative visit after pars plana vitrectomy (PPV) with bevacizumab injection either before or during surgery.

Methods: Retrospective chart review was performed for 104 patients that underwent PPV for diabetic VH at the University of Kansas Medical Center during the past three years. Patients who received bevacizumab injection intraoperatively or within 30 days before surgery were included. Patients who were not compliant with postoperative follow-up were excluded. Data collection included LogMAR visual acuity, age, gender, type of diabetes, bevacizumab injection status, vitreous status, and postoperative course. This study was approved by the Institutional Review Board of the University of Kansas School of Medicine.

Results: Forty-eight patients met the study inclusion criteria (27 females, 21 males), with an average age of 52 ± 12.87 years old. The preoperative bevacizumab injection group had 18 patients (53.7 ± 15.43 years old) (9 females, 9 males), including eight patients with tractional retinal detachment (TRD). After one month, four patients (22.2%) had recurrent VH, including one (5.6%) who needed repeat surgery for blood removal. The intraoperative bevacizumab injection group had 30 patients (51 ± 11.22 years old) (18 females, 12 males), including 12 patients with concurrent TRD. After one month, five patients (16.7%) had recurrent VH, including three patients (10%) who needed repeat surgery for blood removal. There was no statistically significant difference between groups regarding size ($p=0.11$), age ($p=0.52$), gender ($p=0.71$), VH recurrence rate at one month ($p=0.92$), or need for repeat surgery ($p=1$).

Conclusions: Early postoperative VH recurrence impacts patients' outcomes and expectations. Our study did not detect a significant difference in VH recurrence at one month after surgery when bevacizumab was injected intraoperatively or within 30 days before surgery. Intraoperative bevacizumab injection may be useful in diabetic patients with VH when bevacizumab cannot be administered preoperatively. Larger prospective trials are needed to further clarify the long-term outcome in similar patients.

CONTROL ID: 3544598

SUBMITTER (NAME ONLY): David Horton

TITLE: Comparing Butterfly IQ vs Conventional Ophthalmic Ultrasonic Imaging

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.K. To, A.N. Vu, A. Browne, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|D. Horton, E. Dzihic, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A. Browne, Institute of Clinical and Translational Science, Department of Biomedical Engineering, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limited reports systematically characterize portable ultrasound devices, such as the Butterfly IQ (BiQ), in ocular imaging. In this study we compare the image resolution of the BiQ portable ultrasound with a conventional piezo-based ophthalmic ultrasound when scanning a phantom model. We hypothesize that the BiQ will perform as well as the conventional B-Scan ophthalmic ultrasound.

Methods: Five BiQ imaging presets (MSK, MSK-Soft Tissue(MSK-ST), Nerve(N), Pediatric Lung(PL), and Ophthalmic(Ophtho)) were chosen and compared against the 10 MHz B-Scan probe on the Ellex Eye Cubed v3 ultrasound unit. Knox gelatin mixed with a gelatin:water ratio of 5:1 cast in a 5cm x 5cm x 2.5cm silicone mold was used as a phantom. Models contained a total of 6 paper stacks made of 3 paper sheets (1mm x 1mm x 0.1mm) with double-sided Scotch tape between layers to increase gap thickness in set increments as in Fig 1 (A, D). The BiQ was held parallel to the ground and scanned in a vertical pattern as in Fig 1 (B, E). The B-scan gain was set to 50 dB and the BiQ gain was set to 0 for MSK, 0 for MSK-ST, 0 for N, 20 for PL, and 0 for Ophtho. Calculated gap length was compared to image-based measurements, which were determined using ImageJ. Resolution was measured in ImageJ using the 1D brightness vs depth plot profile function as in Fig 1 (C, F). The derivative of the plot profile was used to create a slope function in order to determine the local minima, which corresponds to the position of peak brightness. The 1D linear distances were then measured between calculated slope minima of each peak.

Results: The BiQ was less accurate than the Eye Cubed at measuring distances less than 200 microns. The Eye Cubed measured 0.19 +/- 0.00 mm while the butterfly had measurements of 0.39 +/- 0.06 mm(MSK), 0.30 +/- 0.04 mm(MSK-ST), 0.26 +/- 0.39 mm(PL), 0.39 +/- 0.04 mm(N), 0.26 +/- 0.07 mm(Ophtho) for the 1-layer molds. At distances greater than 200 microns (>2 layers of double-sided tape) the BiQ and Eye Cubed performed similarly.

Conclusions: The BiQ demonstrates promising potential as a portable and less costly alternative to conventional piezo-based ophthalmic ultrasound machines in the evaluation of ophthalmic pathologies.

CONTROL ID: 3544599

SUBMITTER (NAME ONLY): Qisheng You

TITLE: Automated central macular fluid volume as a treatment indication for diabetic macular edema

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. You, K. tsuboi, Y. Guo, C.J. Flaxel, S. Bailey, D. Huang, Y. Jia, T.S. Hwang, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the value of automated central macular fluid volume (CMFV) as treatment indication for diabetic macular edema (DME).

Methods: In this retrospective observational study, we consecutively enrolled adult diabetic patients who underwent comprehensive clinical examinations, 6x6-mm horizontal 19-line macular structural optical coherence tomography (OCT) raster scans (Spectralis, Heidelberg), and 6x6-mm macular OCT angiography (OCTA) volumetric scans (Avanti, OptoVue) at the baseline enrollment visit. Two retinal specialists reviewed the baseline raster OCT scans independently and diagnosed center-involved DME if intraretinal or subretinal fluid was detected with 1-mm of the foveal center. A third retinal specialist arbitrated any discrepancy. Mean central macular thickness (CMT) within the 1-mm circle was measured on Spectralis OCT scans using the embedded software. A deep-learning algorithm automatically quantified fluid volumes within the central 1-mm circles (CMFV) on the OCTA scans. All patients with DME were treated per standard of care.

Results: We enrolled one eye for each of 215 diabetic patients (98 men) with a mean age of 60 years. Center-involved DME was diagnosed in 93 eyes. The area under the receiver operating characteristic curve (AROC) of CMFV for diagnosis of center-involved DME was 0.907 with a sensitivity of 78.5% at the specificity of 95%. Forty-eight eyes with center-involved DME underwent anti-VEGF injections at the enrollment visit, among whom 34 (71%) eyes fulfilled the DRCR.net treatment criteria (CMT $\geq 320\mu\text{m}$ in male or CMT $\geq 305\mu\text{m}$ in female). Among the 14 treated eyes who were missed according to DRCR.net criteria, 6 (43%) of them would have been diagnosed as center-involved DME, and indicated a treatment, according to the CMFV. Four of these six eyes underwent focal laser treatment previously. Both CMFV and CMT were significantly correlated with best-corrected visual acuity ($r=-0.303$, $P<0.001$, and $r=-0.339$, $P<0.001$, respectively).

Conclusions: CMFV may be a useful biomarker for DME treatment decisions, particularly for those eyes previously treated with focal laser. A cohort study is indicated to assess the treatment response of CMFV.

CONTROL ID: 3544600

SUBMITTER (NAME ONLY): Xiaofan Jiang

TITLE: The rise-time of the rod-driven electroretinogram a-wave measured in over 200 twins: association with age and estimation of heritability

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The electroretinogram (ERG) response to bright flashes delivered in the dark is driven largely by rod photoreceptors. It has been suggested that the time taken for the a-wave to rise from 10% to 90% of the peak amplitude (termed here the 10-90% rise-time, RT10-90) yields a quantitative measure of rod sensitivity. We investigated associations of this parameter with age and explored heritability in a twin study.

Methods: Healthy adult volunteers from the TwinsUK cohort based at St Thomas' Hospital in London underwent dark-adapted and light-adapted ERG recordings using conductive fibre electrodes following mydriasis. As part of the protocol, white xenon flashes ($67 \text{ photopic cd m}^{-2} \text{ s}$) were delivered in the dark and then later in the presence of a rod-saturating blue background ($1.0 \text{ photopic and } 30 \text{ scotopic cd m}^{-2}$). Subtraction of the latter responses (derived from the cone system) from the former responses (derived from the rod and cone system) yielded the estimated dark-adapted rod system response. RT10-90 measurements were extracted made from these derived responses. We quantified coefficients of intra-pair correlation for monozygotic (MZ) and dizygotic (DZ) twin pairs, and estimated heritability using structural equation modelling. The correlation with age was calculated also.

Results: Recordings were obtained from 208 participants (59 MZ and 45 DZ pairs). Mean (SD) age was 62.8 (10.8) years for the whole cohort. 93% were female. Mean (SD) RT10-90 for the derived rod responses was 3.8 (0.5) ms, with a median of 3.7 ms. The parameter was correlated positively with age (correlation coefficient 0.46). Coefficients of intra-pair correlation were 0.49 and 0.19 for MZ and DZ pairs respectively. Age-adjusted heritability was estimated to be 0.48 (95% CI 0.23-0.66).

Conclusions: The 10-90% rise-time parameter showed a moderate positive correlation with age, indicating that rod system sensitivity declines with age. This might reflect pre-retinal optical factors as well as potential changes at the level of the photoreceptors. The intra-pair correlation was higher for MZ than DZ twins, indicating that genetic factors contribute to the variance of this parameter, and our point estimate of heritability was 48%.

CONTROL ID: 3544601

SUBMITTER (NAME ONLY): Henry Marshall

TITLE: Hypercholestaemia predicts disease progression in primary open-angle glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the association of serum cholesterol with baseline and longitudinal glaucomatous disease progression.

Methods:

A Prospective longitudinal cohort study of 2056 eyes from 1026 pre-perimetric and perimetric glaucoma cases drawn from the Progression Risk of Glaucoma: Relevant SNPs with Significant Association (PROGRESSA) study.

Lipid profiles were measured on serum samples obtained at study enrolment. Mixed effects multivariable linear regression compared lipid parameters to baseline and longitudinal SD-OCT peripapillary retinal nerve fibre layer (pRNFL) and macular ganglion cell-inner plexiform layer (mGCIPL) thickness data, and with longitudinal Humphrey Visual Field data.

Results: After accounting for age, sex, IOP and lipid lowering therapy, a higher serum total cholesterol was associated with a thinner average mGCIPL thickness (Beta: -0.98 [-1.59, -0.37] $P < 0.001$), thinner worst mGCIPL hemisphere (Beta: -1.11 $\mu\text{m}/\text{SD}$ [-1.86, -0.36] $P = 0.004$), and thinner worst pRNFL quadrant thickness (Beta: -1.92 $\mu\text{m}/\text{SD}$ [-3.41, -0.44] $P = 0.011$) at study enrolment. A higher serum LDL-cholesterol concentration was associated with a thinner average mGCIPL thickness (Beta: -0.81 $\mu\text{m}/\text{SD}$ [-1.4, -0.22] $P = 0.007$), a thinner worst mGCIPL hemisphere (Beta: -1.02 $\mu\text{m}/\text{SD}$ [-1.8, -0.29] $P = 0.006$), and a thinner worst pRNFL quadrant (Beta: -1.81 $\mu\text{m}/\text{SD}$ [-3.25, -0.36] $P = 0.014$).

Review of longitudinal progression data (mean follow up: 6.6 ± 1.8 years) showed that a higher total cholesterol was associated with a greater risk of visual field progression (HR: 1.13/SD, [1.02, 1.26] $P = 0.023$). A higher LDL cholesterol was associated with a faster rate of average mGCIPL thinning (Beta: -0.06 $\mu\text{m}/\text{year}/\text{SD}$ [-0.11, -0.001] $P = 0.045$), a faster rate of mGCIPL thinning in the faster progressing hemisphere (Beta: -0.073 $\mu\text{m}/\text{year}/\text{SD}$ [-0.14, -0.001] $P = 0.046$), a faster rate of average pRNFL progression (Beta: -0.06 $\mu\text{m}/\text{year}/\text{SD}$ [-0.12, -0.01] $P = 0.018$), and a faster rate of pRNFL thinning in the faster progressing quadrant (Beta: -0.11 $\mu\text{m}/\text{year}/\text{SD}$ [-0.21, -0.002] $P = 0.045$). Further evaluation identified that a higher genetic risk score for LDL-cholesterol was associated with a thinner average mGCIPL thickness (Beta: -0.95 $\mu\text{m}/\text{SD}$ [-1.75, -0.15] $P = 0.020$), and a thinner worst affected pRNFL quadrant (Beta: -1.87 $\mu\text{m}/\text{SD}$ [-0.02, -3.72] $P = 0.049$).

Conclusions: Hyperlipidaemia is an important risk factor for disease progression in glaucoma.

CONTROL ID: 3544602

SUBMITTER (NAME ONLY): Julia Andrade

TITLE: Perspectives on adherence to glaucoma medical therapy in Brazilian patients.

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Andrade, G.S. Motta, N. Kasahara, Oftalmologia/Glaucoma, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: Poor adherence to glaucoma medication regimens may be associated with subsequent optic nerve damage and irreversible visual loss. Specific barriers to effective patient adherence in low-middle income countries are not fully recognized and new disease-specific instruments to assess adherence have been developed. The purpose of this cross-sectional study was to evaluate adherence of glaucoma patients to treatment and to determine possible associations between medical, demographic/socioeconomic (and other factors) and adherence to topical ocular hypotensive therapy.

Methods: POAG patient were recruited from the Glaucoma Service - ISCMSP, São Paulo, Brazil. Clinical and demographic data were retrieved from participants electronic records. All patients answered the Glaucoma Treatment Compliance Assessment Tool (GTCAT). This questionnaire was designed to evaluate multiple behavioral factors associated with glaucoma medication adherence. It includes 47 statements with a 5-interval Likert-type scale response with anchoring definitions (from 1 = strongly disagree to 5 = strongly agree). The scores were correlated with clinical and sociodemographic parameters.

Results: The sample comprised 96 patients with POAG. The mean age was 63.2 ±8.9 years; 48 were male and 48 female; 55 (57.3%) were white, 36 (37.5%) African-Brazilian, and 5 (5.2 %) were of mixed color; most patients (97.9%) had less than high school degree and all had a family income <USD8,000. The GTCAT identified 69 (71.8%) patients who “sometimes forget to use drops”, 68 (70.8%) patients who “sometimes fall asleep before dosing time”, and 60 (62.5%) patients “whose drops aren’t with them at the time to take them”; 82 (85.4%) patients referred “to use reminders to take medications”; 82 (85.4%) patients agreed that “doctor answers my questions”, and 77 (80.5%) said “they are happy with their eye doctor”.

Conclusions: The GTCAT identified a number of mostly unintentional factors associated with adherence in this cohort of Brazilian patients. The data may impact on how to understand and improve adherence to ocular hypotensive treatment in the Brazilian population and alike.

CONTROL ID: 3544604

SUBMITTER (NAME ONLY): Hunter Angle

TITLE: The potential role of DKK3 in the pathogenesis of posterior capsular opacification

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.L. Angle, A. Faranda, S.G. Novo, A. Krishnan, M.K. Duncan, Biology, University of Delaware, Newark, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Posterior capsular opacification (PCO) is the leading complication of cataract surgery (PCS) While it is established that canonical TGF β /pSMAD3 signaling is a major driver of PCO, we have previously reported that canonical Wnt signaling also upregulates in lens epithelial cells (LECs) PCS. As TGF β and canonical Wnt signaling can synergize to drive fibrosis in other systems, we sought to understand the mechanisms by which Wnt signaling upregulates in LECs PCS.

Methods: The transcriptome of adult mouse LECs was profiled by RNAseq either immediately after lens fiber cell removal or 6, 24, 48, or 120 hours later. The corneal transcriptome of adult mice was also investigated via RNAseq. Mice lacking the DKK3 gene were obtained from the Riken mouse resource, and bred to mice harboring a transgenic canonical Wnt signaling reporter (WntR) whose read out is nuclear localized Green fluorescent protein (GFP). Adult eyes were isolated from mice heterozygous for WntR and either wildtype (WT) or homozygous for the DKK3 null allele. The activity of WntR was assessed by confocal immunofluorescent staining for GFP, which was quantitated using Fiji ImageJ.

Results: The mRNA levels of DKK3, a known Pax6 target gene, are high in naïve LECs and downregulate by 6hrs PCS and remain low in these cells through 120 hours PCS. However, while DKK3 was first described as an inhibitor of canonical Wnt signaling, LECs lacking DKK3 do not upregulate canonical Wnt signaling suggesting that Dkk3 downregulation in LECs PCS is not responsible for the upregulation of canonical Wnt signaling we have previously found to occur in LECs PCS. Notably, DKK3 mRNA levels are also very high in the adult mouse cornea, and DKK3 null mice exhibited a 50% reduction in canonical Wnt reporter activity compared to wildtype (p=0.03) suggesting that DKK3 activates canonical Wnt reporter signaling in the cornea as has been reported in other cell types.

Conclusions: While DKK3 is not essential to keep canonical Wnt signaling low in the lens epithelium, it still may regulate normal lens biology and/or PCO as its high levels in the healthy lens rapidly decrease after cataract surgery and this protein has been reported to modulate both TGF β and NF κ B signaling in other systems. This hypothesis is actively being tested by transcriptome profiling of the DKK3 null lens.

CONTROL ID: 3544606

SUBMITTER (NAME ONLY): Harry Levine

TITLE: Relationships between activated Dendritic Cells and Dry Eye Symptoms and Signs

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Levine, J. Hwang, H. Dermer, A. Galor, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|H. Levine, J. Hwang, H. Dermer, A. Galor, Miami Veterans Administration Medical Center, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry Eye (DE) is a prevalent disease in the US and considerably impacts quality of life. Given its heterogeneous nature, biomarkers are needed in DE that can identify underlying contributors to disease. One potential biomarker is the presence of activated dendritic cells (aDCs) in the central cornea, which can be quantified using In-Vivo Confocal Microscopy (IVCM). The purpose of this study was to examine whether aDCs could serve as a biomarker for DE that is associated with a systemic immune disorder.

Methods: Retrospective chart review of 128 individuals with DE symptoms (DE Questionnaire-5 \geq 6) who underwent IVCM between October 2018- July 2020 at the Miami Veterans Administration Medical Center. Exclusion criteria included corneal scarring and history of previous ocular infections. All individuals underwent a standardized ocular surface examination. IVCM images were analyzed with ACCmetrics software, aDCs were manually quantified based on presence of ≥ 3 dendrites that were of the same size or longer than the body of the cell. A receiver operating curve (ROC) analysis was used to examine relationships between aDCs number and systemic immune disease. Based on this analysis, individuals were grouped into categories by aDCs number (≥ 2 versus < 2) and demographic and DE parameters were examined.

Results: The mean age of the study population was 57.1 ± 15.0 years; 71.1% were male, 53.1% self-identified as white and 24.2% as Hispanic. The mean number of aDCs in the cornea was 1.28 ± 2.16 cells/mm². ROC analysis found that the presence ≥ 2 aDCs in the central cornea had a sensitivity of 60% and specificity of 77% for the diagnosis of a systemic immune disorder. Individuals were thus grouped by aDCs number (≥ 2 versus < 2); those with $\text{aDC} \geq 2$ were more likely to be black, have Secondary Sjogren's, use autologous serum tears, have a higher nerve fiber area, higher nerve fractal dimension, and lower nasal and middle conjunctivochalasis scores.

Conclusions: The presence of ≥ 2 aDC in the central cornea suggests a systemic immune disorder in individuals with DE symptoms. Further longitudinal research is needed to evaluate our finding in more diverse populations and to evaluate if changes in aDC number correlate with changes in clinical symptoms and signs of disease.

CONTROL ID: 3544607

SUBMITTER (NAME ONLY): Kevin Firl

TITLE: Associations between a Strabismus Diagnosis and Subsequent Mental Health Disorders in Children and Adolescents

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Raiker, Ophthalmology, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|K. Firl, H. Pakhchanian, D. Belyea, Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: An association between childhood diagnosis of strabismus and increased risk of diagnosis of several mental health disorders by early adulthood has been demonstrated in previously published literature, however the number and demographics of such studies are limited. To further examine these potential associations, we performed a large, retrospective cohort study using data from multiple large health organizations in the United States.

Methods: Patients 0 to 15 years old with a strabismus diagnosis were identified in TriNetX (Cambridge, MA, USA), a federated electronic health records research network comprising multiple large health organizations in the United States. Relative risk of being diagnosed with any one of several mental health disorders between a patient with a strabismus diagnosis versus one without was calculated using logistic regression to control for primary demographic factors and propensity score matching using a greedy nearest-neighbor matching algorithm.

Results: A total of 131,413 patients with strabismus diagnosed at an average age of 3.7 years old were identified. Patients with a history of strabismus were more likely to be diagnosed with several mental health disorders including generalized anxiety disorder (RR 1.73, 95% CI 1.55-1.93], major depressive disorder (RR 1.22, 95% CI 1.10-1.35), attention deficit hyperactive disorder (RR 1.57, 95% CI 1.51-1.64), substance use disorder (RR 1.60, 95% CI 1.15-2.23), adjustment disorder (RR 1.78, 95% CI 1.63-1.95), obsessive-compulsive disorder (RR 1.63, 95% CI 1.33-1.99), post-traumatic stress disorder (RR 1.21, 95% CI 1.01-1.46), anorexia (RR 1.92, 95% CI 1.73-2.12), conduct disorders (RR 1.75, 95% CI 1.64-1.86), and Tourette's disorder (RR 1.34, 95% CI 1.02-1.77).

Conclusions: In the age group studied (0-15 years old), an association exists between previous diagnosis of strabismus and subsequent diagnosis of several mental health disorders. More research is needed to further elucidate these relationships.

CONTROL ID: 3544609

SUBMITTER (NAME ONLY): Jacky Man Kwong Kwong

TITLE: Quantitative proteomic analysis reveals temporal regulation of aldehyde dehydrogenase 1A1 in the rat retina after partial optic nerve transection

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kwong, J. Caprioli, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|C. To, C.T. Lam, The Hong Kong Polytechnic University, Kowloon, HONG KONG|C. To, C.T. Lam, The Hong Kong Polytechnic University Shenzhen Research Institute, Shenzhen, CHINA|

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ABSTRACT BODY:

Purpose: To explore the retinal proteome profile at times after localized optic nerve injury and compare the protein expressions at the regions characterized by primary and secondary retinal ganglion cell (RGC) degeneration

Methods: Unilateral partial optic nerve transection (pONT) was performed on the temporal side of the optic nerve in adult Wistar rats. The RGC density from 1 to 8 weeks after pONT was topographically quantified with Rbpms antibody. Temporal and nasal retinal samples were collected separately from the eyes after pONT and soluble proteins (n=4; 3 technical replicates) were subjected to profiling with a high resolution hybrid quadrupole time-of-flight MS running on label-free SWATHTM acquisition (SCIEX). An information dependent acquisition ion library was generated from all individual biological replicates for SWATHTM peptides quantification. MS spectra were searched for protein identification with ProteinPilot 5.0 (SCIEX) using the Paragon algorithm. Cellular localization of significantly regulated proteins ($P < 0.05$; FC > 1.4 or < 0.7) using immunohistochemistry was performed.

Results: There was $78.9 \pm 5.8\%$ and $27.7 \pm 6.0\%$ of RGC survival in the temporal quadrant at 1 and 8 weeks respectively indicating primary RGC degeneration. No change in RGC density was observed in the nasal quadrant at 1 week after pONT (n=8) but the percentage loss increased to $43.6 \pm 7.7\%$ at 8 weeks (n=15; $P = 0.0001$) demonstrating secondary RGC degeneration. A total of 3641 proteins ($> 25,000$ peptides) with $FDR < 1\%$ were identified in the rat retinas as an ion library. Compared to nasal retina, 6, 12 and 65 differentially expressed proteins were detected in the temporal retina at 1, 4, and 8 weeks respectively. Approximately 6, 4 and 3 folds upregulation of aldehyde dehydrogenase 1A1 (ALDH1A1) was noted in the temporal retina at 1, 4 and 8 weeks respectively. Immunohistochemistry showed that increased immunoreactivity of ALDH1A1 was predominately localized to Muller cells at the temporal retina at 1 week but not nasal retina, and the upregulation was diminished at 4 and 8 weeks.

Conclusions: The finding demonstrated differential protein expression between primary and secondary RGC degeneration. The temporal change of ALDH1A1 suggests that Muller cells respond to localized injury and may play a role in detoxification during progressive RGC degeneration.

CONTROL ID: 3544611

SUBMITTER (NAME ONLY): Cristian Cartes

TITLE: Outcomes of using topical K2-EDTA as a chelating agent for treatment of band keratopathy in a tertiary hospital in the UK.

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Cartes, S. Pradhan, E. Spowart, F.C. Figueiredo, Ophthalmology, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|F.C. Figueiredo, Biosciences Institute, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Superficial keratectomy with topical disodium ethylenediaminetetraacetic acid (Na₂-EDTA) is an established treatment for band keratopathy (BK). Use of the dipotassium form (K₂-EDTA) acquired from easily available blood collection vacutainer tubes as an alternative to the commercially available Na₂-EDTA was only recently reported in 2018. We report our experience of using K₂-EDTA to treat band keratopathy.

Methods: Retrospective case series of 20 eyes (19 patients) undergoing superficial keratectomy with K₂-EDTA chelation from July 2018 to September 2019. Symptomatic BK patients with visual impairment or discomfort from ocular surface instability were included. 12.3% K₂-EDTA solution was applied topically after superficial keratectomy and chelation was achieved. Followed by placing a bandage contact lens to facilitate epithelial healing/comfort. Outcomes measured were BCVA, resolution of symptoms, time to re-epithelialisation, recurrence, complications, and need for any further treatment.

Results: Mean age was 67.4 years (SD 19.2; range: 24 - 88) and 55% were Males. The indications for the procedure included discomfort 12 eyes (60%), impaired vision in 7 (35%) and improve cosmetic appearance in 1 (5%). The mean operation time was 22 minutes (SD 8) timed from application of the drape and including superficial keratectomy. Effective clearance of the BK was accomplished in all patients. No major complications reported. Post op BCVA improved in 4 but remained the same in 3 eyes undergoing the procedure for visual improvement due to associated corneal scarring (n=2) and age-related macular degeneration (n=1). Corneal surface healing was achieved in all patients except one who developed a persistent epithelial defect due to underlying neurotrophic cornea secondary to past acanthamoeba keratitis resolving with temporary lateral tarsorrhaphy. Recurrence of BSK was noted in none of the patients on mean 150 days (SD 121) follow up time.

Conclusions: Superficial keratectomy with topical 12.3 % K₂-EDTA chelation serves as an efficient and safe surgical technique for band shaped keratopathy clearance and is cheaper as compared to the traditional Na₂-EDTA solution.

CONTROL ID: 3544612

SUBMITTER (NAME ONLY): Vrushali Agashe

TITLE: Role of Extracellular Vesicles in human uveitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Non-infectious uveitis (NIU) is a significant cause of blindness. It is an immune mediated disease however the exact pathogenesis remains elusive. Considerable evidence exists on the immunomodulatory effects of EVs in various diseases; although very little is known regarding EVs in uveitis patients. We have previously shown that cytokine stimulated ARPE19 cells, release Extracellular Vesicles (EVs); these EVs are capable of inhibiting T cell proliferation, inducing pro-inflammatory cytokines from monocytes as well as inducing monocyte cell death, in PBMCs from NIU patients. The purpose of this study is to establish a reliable protocol to isolate EVs from uveitis patients and to determine their immune-modulatory potential in-vitro.

Methods: EVs were isolated from the serum of NIU patients using Size Exclusion Chromatography (SEC), in 500ul fractions. Appropriate fractions were then pooled and concentrated via filtration. Various markers on the surface of isolated EVs were analyzed using the MACSPlex Exosome kit. The EVs were set up in culture with PBMCs or ARPE19 cells; after stimulation the cells were stained to determine cell activation and cytokine production.

Results: The first six SEC fractions contained EVs of appropriate size with very low protein content along with the presence of exosome associated markers CD9, CD63 and CD81. A higher number of EVs were isolated from the sera of patients, as compared to healthy controls. Additionally, EVs from patients expressed increased levels of CD8, CD29, CD44, and importantly HLA-DR/DP/DQ, indicating their potential to activate cells in-vivo. An upregulation of CD69 and CD25 on T cells was observed when the cells were cultured with EVs from patients. Culturing PBMCs, with EVs from patients lead to an increase in IFN γ production from CD4 $^{+}$ T cells as compared to those cultured with EVs from healthy controls. Additionally, incubating ARPE19 cells with the EVs from patients, increased the expression of MCP1 and IL8 in ARPE19 cells.

Conclusions: We observed that SEC, along with filtration, is a reliable and fast method for isolating EVs from low volume samples. Preliminary data indicates that EVs isolated from uveitis patients can induce a robust activation of various cells in-vitro. Future experiments are designed to understand the pro-inflammatory nature of the EVs isolated from NIU patients as well as to further substantiate these results.

CONTROL ID: 3544613

SUBMITTER (NAME ONLY): Karan Tamakuwala

TITLE: COMPARISON OF SERIAL HOME TONOMETRY AND THE WATER DRINKING TEST TO ASSESS PEAK DIURNAL INTRAOCULAR PRESSURE IN NORMAL YOUNG ADULTS

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare peak diurnal intraocular pressure (IOP) assessed by serial home tonometry using the iCare HOME tonometer by the water drinking test (WDT).

Methods: Healthy adults 20-40yrs old with normal ocular health were eligible for inclusion. One eye selected at random was enrolled in the study. All study IOP measurements are the mean of 3 sequential recordings of "Excellent" or "Good" reliability obtained via self-tonometry using an iCare HOME device in an upright seated posture. The WDT was performed after a training session and demonstrated proficiency using the tonometer. Baseline IOP was established, then 1 liter of bottled drinking water was consumed within 5 min. Self-tonometry was performed at 15, 30 and 45 min. The tonometer was then dispensed to the patient for serial home tonometry performed every 2 hrs over a 24 hr period commencing >12 hrs following the WDT. Finally, the subject completed an opinion survey regarding the two procedures.

Results: 11 subjects (5M, 6F; 5 OD, 6 OS; mean \pm SD age: 24.6 \pm 1.8yr) completed the study. Peak IOP achieved during the WDT was significantly correlated with the peak obtain by serial home tonometry ($r = 0.81$, $p = 0.003$). Mean (\pm SD) difference in peak IOP between the two procedures was 0.2 \pm 2.2 mmHg, with \pm 4.3 mmHg 95% CI. Reliability of home tonometry assessed via agreement of the 3 sequential IOP measurements was excellent ($ICC_{(2,1)}: 0.86$; 95%CI: 0.58-0.94). There was no indication that nocturnal measurements (00:00-06:00 hours) were less reliable than those obtained during waking hours (NIGHT $ICC_{(2,1)}: 0.87$; 95%CI: 0.57-0.95, DAY $ICC_{(2,1)}: 0.86$; 95%CI: 0.57-0.94). Survey responses indicated that a majority of subjects (73%-82%) had no difficulty performing either procedure; however, a majority expressed preference for the WDT (64% vs 36%).

Conclusions: There is good agreement between serial home tonometry performed using the iCare HOME tonometer and the WDT in estimating peak diurnal IOP of healthy young adults. These results suggest that both procedures may be useful in the assessment of peak diurnal IOP. Further research in glaucoma patients is warranted.

CONTROL ID: 3544616

SUBMITTER (NAME ONLY): Thamolwan Surakiatchanukul

TITLE: Macular Neovascularization Associated with Central Serous Chorioretinopathy:
Multimodal Imaging-Based Predictors

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate predictors for macular neovascularization (MNV) associated with central serous chorioretinopathy (CSCR) based on multimodal imaging

Methods: Retrospective multi-center chart review study of 134 eyes of 128 consecutive patients with CSCR. Eyes were classified per the multimodal imaging-based classification of CSCR at baseline into i) simple/ complex CSCR & ii) primary episode/ recurrent/ resolved CSCR. Baseline characteristics of MNV and predictors were evaluated with ANOVA.

Results: Of the 134 eyes with CSCR, MNV was present in 32.8% (n=44). Based on severity, those with MNV primarily consisted of complex (72.7%, n=32), followed by simple (22.7%, n=10), and atypical (4.5%, n=2) types. Those without MNV, in contrast, were more commonly simple (55.6%, n=50) than complex (44.4%, n=40). Compared with complex CSCR with MNV cohort, simple CSCR with MNV had a better baseline decimal visual acuity (0.72 vs 0.49, p=0.03) without differences in age (mean 59 vs 59 years, p=0.76), subfoveal choroidal thickness (SFCT 393 vs 390 μ m, p=0.997), and reported duration of symptoms (median 6 vs 18 weeks, p=0.38).

Based on presentation, those with MNV were as likely to be primary (45.5%, n=20) as recurrent (45.5%, n=20), with the rest as resolved cases (9.1%, n=4). No differences between primary, recurrent vs resolved cohorts were found in age (mean 58, 61 vs 52, p=0.27), visual acuity (mean 0.56, 0.50 vs 0.65, p=0.66), SFCT (414, 383 vs 329 μ m, p=0.55), and duration (median 7, 7 vs 30, p=0.42). However, primary CSCR with MNV were older (58 vs 47, p=0.0003), worse visual acuity (0.56 vs 0.75, p=0.01), and of longer duration (median 7 vs 1, p=0.0002) than those without MNV. Similarly, recurrent CSCR with MNV were older (61 vs 52, p=0.004), without differences in visual acuity (0.50 vs 0.61, p=0.31), SFCT (383 vs 424 μ m, p=0.21), and duration (median 7 vs 2, p=0.32) than those without MNV. Further analysis of MNV characteristics in each subgroup and predictive modeling is underway.

Conclusions: Prevalence of MNV associated with CSCR was 32.8% and more likely in complex CSCR and older age. Complex CSCR with MNV also had worse baseline visual acuity than simple CSCR with MNV and complex CSCR without MNV. Primary and recurrent presentations were similarly accounted for nearly half of MNV cases. Multimodal imaging-based classification of CSCR supports detailed analysis of associated MNV.

CONTROL ID: 3544618

SUBMITTER (NAME ONLY): Sophie Lee

TITLE: Utilization and insurance payments for tele-ophthalmology in the United States over 10 years

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Remote eye screening using tele-ophthalmology has the potential to reduce cost and improve rates of retinopathy screening in patients with diabetes. However, lower insurance reimbursements have limited the financial sustainability of many tele-ophthalmology programs. Here, we performed a retrospective claims-based analysis of tele-ophthalmology utilization and insurance payments using the OptumLabs[®] Data Warehouse (OLDW) – a comprehensive database of de-identified administrative claims for commercial enrollees in the U.S.

Methods: We analyzed all healthcare claims in OLDW database from 2010-2019 for tele-ophthalmology using Current Procedural Terminology (CPT) codes for tele-ophthalmology 92227 and 92228 for any providers, as well as fundus photography 92250 by non-eyecare providers. We evaluated the number of administrative claims for tele-ophthalmology codes, rates of insurance claim payments or denials, provider specialty and practice setting, as well as age, sex, race/ethnicity, household income, education level, and rural-urban commuting area (RUCA) codes.

Results: Utilization of tele-ophthalmology increased rapidly over the past 10 years, from 51 claims per 100,000 person-years in 2011 when tele-ophthalmology CPT codes were introduced, to 153 claims per 100,000 person-years in 2019. A majority of administrative claims for tele-ophthalmology include at least one diagnostic code for type 1 or 2 diabetes (59%). The rest include a diagnosis of diabetic eye disease (8%) or any eye condition (41%). However, insurance payments for tele-ophthalmology decreased over the 10-year period, from 88% of claims paid in 2011 to 65% in 2019.

Conclusions: Utilization of tele-ophthalmology has increased rapidly over the past 10 years, but insurance payments have declined. Given the potential cost-savings and reduction of in-person eye screening for diabetic patients, insurance providers should be encouraged to improve coverage for tele-retinal services.

CONTROL ID: 3544619

SUBMITTER (NAME ONLY): Fernanda Abib

TITLE: Types of identified errors of Endothelium Cells segmentation from Corneal Specular Microscopy using a U-Net Network

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.S. Abib, A.D. Britto Jr, Pontificia Universidade Catolica do Parana, Curitiba, PR, BRAZIL|F.C. Abib, Anatomy, Universidade Federal do Parana, Curitiba, PR, BRAZIL|F.C. Abib, Cornea, Prof. Fernando Abib Eye Clinic, Curitiba, PR, BRAZIL|

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ABSTRACT BODY:

Purpose: The traditional segmentation methods for Endothelial Cells in Non-Contact Corneal Specular Microscopy do not identify perfectly these cells, presenting distorted morphometric results, as demonstrated in ARVO 2016 by Ursulino, Hida, Holzchuh & Abib. The purpose of this cross-sectional study is to know the errors in determining the contours of Endothelial Cells (EC) generated by a U-Net network.

Methods: Images from two different contexts were used to train the U-Net: 1) 30 images from the ISBI Challenge: Segmentation of neuronal structures in EM stacks had their labels preprocessed 2) 78 Corneal Specular Microscopy images obtained automatically by Specular Microscopy Tomey EM-4000 in Prof Fernando Abib Eye Clinic, Brazil. A Data Augmentation algorithm using Keras library was used to increase the number of images to train the network. The EC training images were cropped to fit the size of 256x256 pixels, and their respective labels were binarized. The training labels from the ISBI Challenge were pre-processed. The images used to train the network were different from the ones used to test. The metric used to evaluate the training was the binary accuracy. With the endothelial images (30) of the tests performed by the U-Net, the tracing errors were classified as recommended by Ursulino, Hida, Holzchuh & Abib (ARVO 2016):

(Figure 1)

Type I - Non-counted cells;

Type II - Cell cluster;

Type III - Split cell.

Results: During the training phase, the binary accuracy obtained was of 93.14%. Type of Errors by U-Net identifying Endothelial Cells:

(Figure 2)

Type I - No case (0%) of cells not considered in the identified cells area;

Type II - 27 images (90%) didn't have clusters, but the contours in some part of the images were determined in light gray and rarely partially traced; 3 images (10%) had clusters defined only with two cells;

Type III - 4 images (13.3%) presented only one split cell, the other 26 images (86,6%) did not present it;

In all 30 images (100%), in some part of the reticulum, the outline of the cells was in light gray.

Conclusions: The U-Net network showed a small number of errors in determining the contours of the endothelial cells. This technology is promising for clinical use requiring a very high number of images for the network training.

CONTROL ID: 3544621

SUBMITTER (NAME ONLY): Gloria Wu

TITLE: Heidelberg Evaluation of the Iris: New Considerations

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Biometric evaluations of the iris using Heidelberg Spectralis imaging technology.

Background: Infrared (IR) iris scans are used for biometric recognition in airports. However, eyeMDs have not embraced the latest IR technology to evaluate the iris, affected in diabetes, glaucoma, and inherited anterior segment diseases. In 2018, Postalache et al used IR imaging to detect features of the iris not seen in standard light photography. IR imaging could be used to identify crypts, collarettes, ciliary regions, pupillary regions, nevi, contraction furrows, and other features of the iris. Here we describe a novel use of IR imaging for the evaluation of the iris. This work could add to future imaging techniques for new tools for eyeMDs.

Methods: Eyes were imaged using Heidelberg Spectralis, 1081 λ (Heidelberg Engineering HRA + OCT : Heidelberg GE). Crypts were counted and collarettes were measured in each subject. Adobe Photoshop was used to identify and measure crypts and collarettes.

Results: Figure 1.1 - IR image iris in a WM. a) nevi, b) contraction furrows, c) pupillary region, d) ciliary region, e) collarette, f) pupillary boundary

Figure 1.2 - 90° sector IR image iris in WM. a) contraction furrow, b) crypt, c) ridge

Figure 2.1 - IR image iris in a South Asian. a) crypt, b) collarette, c) pupillary region, d) ciliary region, e) pupillary boundary

Figure 2.2 - 90° sector IR image iris in a South Asian. a) five crypts in the iris, b) ridge.

Figure 3.1: IR image iris in a Asian. Collarette outlined in white, arrows point to five crypts

Figure 3.2: 90° sector IR image iris in a Asian. Arrows point to five crypts in the iris

Figure 4.1: IR image iris in a East Asian subject. Collarette is outlined in white, arrows point to five crypts in the iris.

Figure 4.2: 90° sector IR image iris in a East Asian. Arrows point to six crypts in the iris.

Figure 5.1: IR image iris in a East Asian. Collarette is outlined in white.

Figure 5.2: 90° sector IR image iris in a Filipino. Arrows point to six crypts in the iris.

Table 1: total number of crypts identified in a 90° sector IR image and collarette measurements for each subject. There are ethnic differences in the number of crypts in the iris. Collarette measurements differ across ethnic lines as well.

Conclusions: This small pilot study shows that IR photography can document small changes in the iris. We hope other researchers will join us to explore the latest software tools to evaluate the iris.

CONTROL ID: 3544624

SUBMITTER (NAME ONLY): Enoch Peng

TITLE: Risk Factors for the Development of Horseshoe Retinal Tears in Fellow Eyes

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Peng, BioSciences, Rice University, Houston, Texas, UNITED STATES|S. Laswell, H. Yu, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Horseshoe retinal tears (HRT) can progress to retinal detachments (RD) if untreated. While there are known risk factors for HRT development, there is little data related to risk factors for HRT development in the fellow eye (FE) after HRT development in one eye. The purpose of this study was to investigate risk factors associated with HRT development in the FE of patients with HRT in one eye.

Methods: Medical records were reviewed for patients with initial HRT between October 1, 2015 and December 31, 2017 at a large, urban, retina practice. Eyes were excluded if they had prior HRT or RD treatment, a concurrent RD at initial visit, or only 1 visit; eyes with localized RD were included if treatment consisted of cryotherapy or laser demarcation. Vitreous attachment status was graded using presenting macula optical coherence tomography (OCT) images with a four-stage method: 0=fully attached, 1=extra foveally attached, 2=foveally attached, 3=fully detached in view, 4=fully detached out of view. Logistic regression was used to assess factors associated with FE HRT including FE and study eye (SE) posterior vitreous detachment (PVD) status, SE subsequent breaks, SE vitreous hemorrhage (VH), and SE lattice degeneration.

Results: 246 patients presented with an HRT in the SE during the inclusion period with a mean follow up of 68.8 months (median 30.2; IQR 8.0-125.9). Among patients who had an intervention (244, 99.2%), the majority received laser demarcation (239, 98.0). 40 (16.3%) patients developed a FE HRT, and experienced floaters (22, 55%), flashes (8, 20%), blurred vision (5, 12.5%), eye pain (1, 2.5%), light sensitivity (1, 2.5%), and shadow (1, 2.5%), while 7 (17.5%) patients were asymptomatic. Mean time between SE HRT and FE HRT was 6.2 months (median 1, range 0-46). Logistic regression demonstrated an association between occurrence of FE HRT and a stage 3 PVD at the time of initial SE HRT ($p=0.0283$). There was also an association between FE HRT and the development of subsequent breaks in the SE ($p=0.00124$). There were no associations between FE HRT and SE VH ($p=0.86$), SE PVD ($p=0.7719$), or SE lattice degeneration ($p=0.0874$).

Conclusions: The current study found statistically significant associations between development of FE HRT and (1) stage 3 PVD in the FE at the time of SE HRT presentation and (2) subsequent HRT in the SE. These factors may be important to consider in the clinical management of patients with HRT.

CONTROL ID: 3544626

SUBMITTER (NAME ONLY): Peter Heiduschka

TITLE: Anti-VEGF drugs clearly decrease phagocytic ability of retinal microglia.

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Heiduschka, Y. Zhang, T. Plagemann, N. Eter, Ophthalmology, Westfälische Wilhelms-Universität Münster Fachbereich 05 Medizinische Fakultät, Münster, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: While anti-VEGF drugs show high efficacy in the treatment of neovascular AMD, many patients develop geographic atrophy after a longer treatment. We performed an experimental in vitro study to evaluate influence of anti-VEGF drugs on cultivated microglial cells, which are the intrinsic immune cells of the retina and may play a key role in degenerative processes in the retina.

Methods: Microglial cells were isolated and cultivated from pig eyes. Identity of the cells was confirmed by staining against the typical microglial markers Iba1, CD11b and CD68. Microglial cells were exposed to the anti-VEGF drugs aflibercept and bevacizumab of different concentrations ranging from 0.33 to 5.71 mg/ml and ranibizumab at 5 mg/ml. Proliferation was checked by the Click-iT Edu assay, cell viability by ATP viability luciferase assay and phagocytic ability by measuring of the uptake of fluorescent micro beads. Moreover, we looked at the morphology of the cells and investigated influence of simultaneous presence of LPS or microglial inhibitors dexamethasone, minocycline and tripeptide TKP on phagocytosis.

Results: Extent of proliferation was not changed by anti-VEGF drugs. At the highest concentration of the drugs, cells treated with bevacizumab and ranibizumab showed a reduced size, loss of processes and a “foam”-like appearance. Cells treated with aflibercept showed only mild changes of morphology. Cell viability was reduced down to about 70±5% at the highest drug concentrations. Ability to phagocytose decreased clearly already at 0.33 mg/ml bevacizumab (61.0±2.7%) and at 0.66 mg/ml aflibercept (61.4±4.9%). At the highest concentrations of the drugs, ability to phagocytose diminished almost completely (bevacizumab 2.4±0.5%, aflibercept 5.6±0.8%, ranibizumab 5.2±0.8%). LPS or the microglia inhibitors did not change the phenomenon that the drugs reduced phagocytosis, nevertheless, extent of that reduction was smaller depending on the inhibitor and the anti-VEGF drug. When anti-VEGF drug was exchanged by clean medium, ability to phagocytose recovered quickly depending on time and drug concentration.

Conclusions: Anti-VEGF drugs reduce viability moderately and do not show effect on proliferation of microglial cells. In contrast, their ability to phagocytose is reduced dramatically. It may be speculated that reduced microglial phagocytosis allows enhanced accumulation of cellular debris, which in turn may promote progression of dry AMD.

CONTROL ID: 3544628

SUBMITTER (NAME ONLY): Mariana da Palma

TITLE: Phenotypic and genotypic spectrum of HGSNAT-related retinopathy

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. da Palma, J.M. Sallum, Department of Ophthalmology, Universidade Federal de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|M.M. da Palma, A.D. Igelman, A. Burr, C.A. Ku, P. Yang, M.E. Pennesi, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|J.M. Sallum, Instituto de Genética Ocular, São Paulo, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: Heparan-alpha-glucosaminide N-acetyltransferase (HGSNAT) is a lysosomal membrane enzyme that has been historically associated with mucopolysaccharidosis type IIIC (MPS IIIC) or Sanfilippo C syndrome. The variant c.1843G>A (p.Ala615Thr) in HGSNAT has been recently associated with late-onset nonsyndromic pericentral retinitis pigmentosa (RP). The aim of this study is to expand the phenotypic and genotypic spectrum of HGSNAT-related retinopathy.

Methods: This retrospective study from the Casey Eye Institute and the Instituto de Genética Ocular found nine patients with variants in HGSNAT and who presented pericentral retinopathy. We reviewed ophthalmologic data extracted from medical records, color fundus photos, fundus autofluorescence (FAF), and optical coherence tomography (OCT).

Results: Of the nine patients, seven were female, and the median age was 55 (range: 24-77) years. The age of ophthalmologic symptoms onset varied from 15 to 70 (mean 48; median 50) years. The visual acuity varied from 20/20 to 20/80 (mean 20/25; median 20/20), and the plurality of the eyes were 20/20. Color fundus photos varied from normal to the presence of bone spicules in the mid-periphery. FAF showed a pericentral pattern of hypoautofluorescent changes, and two patients presented with hypoautofluorescent spots in the nasal periphery. OCT revealed cystoid macular edema in three patients and outer retinal atrophy surrounding the fovea area in all patients. Genetic testing found four homozygous patients with p.Ala615Thr variant. The remaining patients were compound heterozygous and had the following variants: c.1843G>A (p.Ala615Thr), c.32_46del (p.Leu11_Ser16delinsPro); c.1843G>A (p.Ala615Thr), c.715del (p.Arg239Alafs*37); c.1843G>A (p.Ala615Thr), c.1297A>G (p.Asn433Asp); c.1218G>T (p.Leu406Phe), c.1220C>T (p.Thr407Ile); and c.1726G>T (p.Gly576*), c.525dupT (p.Val176Cysfs*16), c.118G>A (p.Asp40Asn).

Conclusions: There were differences in age of onset between patients; however, all presented with late-onset retinopathy. FAF was more sensitive at demonstrating retinal changes than color fundus photographs. These findings suggest mutations in HGSNAT may cause retinal dystrophy with a late-onset and pericentral pattern.

CONTROL ID: 3544630

SUBMITTER (NAME ONLY): Tanner Ferguson

TITLE: Short-Term OCT Retinal Vessel Diameter Changes Using a Multi-Pressure Dial in Healthy and Glaucomatous Subjects

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the intraocular pressure-lowering effect of the Multi-Pressure Dial (MPD) system on retinal vessel diameter measured by spectral domain optical coherence tomography (SD-OCT, Spectralis, Heidelberg).

Methods: Prospective, randomized, controlled, pilot study. 15 healthy subjects and 15 subjects with open-angle glaucoma were randomized to receive application of 10 mmHg negative pressure to one eye (study eye) with the MPD. Following a baseline evaluation, both the study and control eye of each subject were imaged with OCT at baseline prior to negative pressure and then during the application of negative pressure at the 2, 10 and 30-minute time points. OCT imaging was repeated at 2 and 10 minutes after cessation of negative pressure. The primary outcome measures were retinal vessel parameters. For each patient, the en face OCT image, which is generated from a series of repeated image acquisitions, was used to evaluate the retinal vasculature. In each image, the inferotemporal branch artery and branch vein were utilized for measurement prior to any branching near the peripapillary reference zone.

Results: At baseline, venous diameter (VD) was statistically significantly less in glaucomatous subjects ($121 \pm 15 \mu\text{m}$) compared to healthy subjects ($133 \pm 15 \mu\text{m}$, $P < 0.05$). Arterial diameter (AD) was also less in glaucomatous subjects ($91 \pm 17 \mu\text{m}$) compared to healthy subjects (100 ± 17), but the difference was not statistically significant ($P = 0.20$). In subjects with glaucoma, with negative pressure application, there was a statistically significant increase in both AD and VD compared to baseline at 2 minutes, (A: $99 \pm 16 \mu\text{m}$, V: $127 \pm 16 \mu\text{m}$), 10 minutes (A: $101 \pm 17 \mu\text{m}$, V: $128 \pm 17 \mu\text{m}$), and 30 minutes (A: $103 \pm 17 \mu\text{m}$, V: $128 \pm 17 \mu\text{m}$). There was no statistically significant difference in AD or VD in healthy subjects at any of the time points during negative pressure application in comparison to baseline.

Conclusions: Glaucomatous subjects have diminished venous and arterial diameter compared to healthy subjects. IOP reduction via the MPD has a vasodilatory effect on the retinal vasculature in eyes with a history of glaucoma, suggesting an increase in blood flow occurs during application of negative pressure. Further research will be valuable for assessing the impact of transient IOP reduction on changes in ocular blood flow.

CONTROL ID: 3544632

SUBMITTER (NAME ONLY): Daniela Reyes-Capo

TITLE: Trends in Endophthalmitis Associated with Intravitreal Injection of Anti-VEGF Agents from 2018-2020 at a Tertiary Referral Center

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Reyes-Capo, N.A. Yannuzzi, W.E. Smiddy, T.A. Albini, P.J. Rosenfeld, D. Miller, H.W. Flynn, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the incidence and clinical features of infectious endophthalmitis after intravitreal (IV) injection of vascular endothelial growth factor inhibitors (anti-VEGF) from 2018-2020 and compare the findings to characteristics of endophthalmitis after anti-VEGF injection from prior years.

Methods: Retrospective case series of patients treated at a tertiary referral center between 01/01/2018 – 12/31/2020 with clinically diagnosed endophthalmitis occurring < 4 weeks after IV anti-VEGF injection.

Results: Between 2018-2020, the rate of clinically diagnosed endophthalmitis was 0.013% (9/71,779) and of culture positive endophthalmitis was 0.008% (6/71,779). The endophthalmitis rates per injection were: aflibercept 0.020% (8/40,302); ranibizumab 0.019% (1/5,242); bevacizumab 0% (0/25,548); and brolucizumab 0% (0/687).

The overall rates of endophthalmitis among all injections from 2018-2020 are similar to previously published data of endophthalmitis after IV anti-VEGF from 2005-2017 (0.013% vs 0.013% [p=0.91]). The incidences of endophthalmitis after aflibercept and ranibizumab from 2018-2020 were slightly increased from 2005-2017, though these differences were not significant (aflibercept: 0.020% vs 0.014% [p=0.51]; ranibizumab: 0.019% vs. 0.016% [p=0.87]).

From 2018-2020, a total of 6 eyes had culture positive endophthalmitis. Associations included aflibercept (5/6) and ranibizumab (1/6). All cases of endophthalmitis occurred < 5 days after IV injection. The causative organisms were coagulase negative Staphylococcus (3/6), Streptococcus (2/6), and Abiotrophia defectiva, a nutritionally variant streptococci, (1/6). At final follow up, two eyes had achieved a visual acuity (VA) better than or equal to 20/200 and the two eyes infected with Streptococcus species required enucleation. The 3 eyes with negative cultures had received aflibercept injections and 2/3 achieved their pre-injection VA.

Conclusions: Endophthalmitis rates after IV anti-VEGF remain low. Poor VA outcomes continue being associated with Streptococcus species. Nutritionally variant streptococci may be a rare cause of endophthalmitis after IV anti-VEGF injection.

CONTROL ID: 3544639

SUBMITTER (NAME ONLY): Olga Gkorou

TITLE: The impact of treatment intensity over 3 years of real-world data of neovascular age-related macular degeneration

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Gkorou, H.J. Duncan, J. Hogg, L.G. Stone, M. Blyth, L. Brandes, A. Devenport, L. Timms, J.S. Talks, Ophthalmology, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|J. Hogg, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|O. Gkorou, Manchester Royal Eye Hospital, Manchester University NHS Foundation Trust, Manchester, Greater Manchester, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Neovascular age-related macular degeneration (nAMD) clinical trial data suggest better visual outcomes for patients receiving more intensive aflibercept intravitreal injections (IVIs). Real-world data in nAMD have described more modest outcomes; so it is unclear if there is pragmatic benefit in pursuing greater treatment intensity for individuals, when clinical resources are already limited. This retrospective, observational study aims to describe the effect of IVI frequency on visual outcomes for nAMD patients at different stages of treatment.

Methods: Patients, initiated on treatment for nAMD with 3 years of follow up, were identified through our patients' database. The visual acuity (VA) in early treatment of diabetic retinopathy (ETDRS) letters and IVIs frequency were recorded over a period of 3 years. Age, gender, macula fluid, lens status were recorded. Descriptive and comparative statistics were performed with SPSS v.24.

Results: 175 eyes (89 left, 87 pseudophakic) from 175 patients (109 female, mean age 79.1 years) with 3 years of continuous treatment were identified. Each eye received a mean (95% confidence interval) of 7.6(7.4,7.7), 5.2(4.9,5.5) and 5.4(5.1,5.7) IVIs to achieve mean VAs of 63.7(61.9,65.5), 61.4(59.4,63.5) and 60.6(58.2,62.9) ETDRS letters over their first, second and third years of treatment respectively. 137 eyes (78.3%) received 3 loading IVIs within 9 weeks to gain a mean 5.6(1.1,13.3) ETDRS letters over their first year of treatment. This was statistically equivocal ($p=0.55$) to the 4.2(2.2,13.6) ETDRS letters gained by eyes experiencing loading delays. Univariate logistic regression found that completing loading within 9 weeks had no statistically significant power to predict the absence of retinal fluid 1 year after treatment started($p=0.46$). Univariate linear regression found that annual IVI frequency had statistically significant power to predict VA gain over the first (unstandardised $B=3.8$ (0.2,7.4), $p=0.036$) and second years of treatment (unstandardised $B=0.7$ (0.0-1.3), $p=0.038$), but not the third ($p=0.31$).

Conclusions: A significant increase in visual gain was noted in the first year of treatment for eyes receiving more IVIs in our data. The visual outcomes of second and third years of treatment appear less sensitive to treatment frequency. In a resource limited environment, patients in their first year of treatment should be prioritised.

CONTROL ID: 3544641

SUBMITTER (NAME ONLY): Elisa Cornish

TITLE: Ocular Characteristic in a Cohort of Neuronal Ceroid Lipofuscinoses/ Batten Disease Patients

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Understanding the ocular manifestation of Neuronal Ceroid Lipofuscin (NCL) (Batten disease) is crucial to initiate investigation of the diagnosis as visual decline is often the presenting feature in NCL. This study reports the electrophysiological and multimodal imaging that provides clues to suspect NCL and urgent neurologic and genetic referral.

Methods: Retrospective review of six Batten patients. Visual acuity (VA), electroretinogram (ERG), ultra wide-field (UWF) fundus photography and autofluorescence (FAF), and ocular coherence tomography (OCT) were analyzed.

Results: Six unrelated children, 4 female and 2 male ranging from 4.6 to 11.7 years old with 5 CLN3 mutation and CLN5 mutation. The patients from the cohort had previous diagnosis of speech delay, autism, attention deficit and hyperactivity disorder prior to their first Ophthalmic review. Estimated interval between eye complaint and genetic result was 22.9 ± 14.9 months. VAs ranged from 0.18 to 1.00 logMAR with follow up (FU) obtainable from 3 patients. Two CLN3 patients and 1 CLN5 patient had 0.81 ± 0.35 logMAR and 0.36 ± 0.02 logMAR loss per year during 2.35 and 4.87 years FU respectively.

Electronegative ERGs were identified in each patient. Bull's eye maculopathies were common with hyperAF ring surrounding hypoAF fovea on FAF. Macular OCT findings were schitic changes (1 patients) and ellipsoid zone (EZ) loss at the fovea (4 patients).

Conclusions: While VAs were variable, macular disruption and electronegative ERG were consistent across the NCL cohort. These macular OCT and ERG findings provide strong evidence to initiate further investigations including genetic testing for NCL.

CONTROL ID: 3544643

SUBMITTER (NAME ONLY): Jiayan Wang

TITLE: Mutation of a caveolin binding motif in Na/K-ATPase activates the Nrf2 signaling pathway and attenuates experimental ischemic retinopathy

SESSION TITLE: Blood flow, ischemia, reperfusion

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Increases in oxidative stress is well documented in ischemic retinopathy. The $\alpha 1$ Na/K-ATPase (NKA) has an enzyme independent receptor function through its interaction with signaling proteins such as Src and caveolin-1. Moreover, the $\alpha 1$ NKA/Src receptor complex serves as a reactive oxygen species (ROS) amplifier. In this study, we investigated how the disruption of $\alpha 1$ NKA signaling secondary to a loss of caveolin binding motif (CBM) affects ischemic retinopathy in the mouse model.

Methods: Mice expressing the mutated CBM (mCBM) $\alpha 1$ NKA were obtained by knocking-in of F97A and F100A substitution in $\alpha 1$ NKA. The homozygous mCBM genotype was embryonic lethal, but heterozygous (Het) mice were viable. Oxygen induced retinopathy (OIR) was triggered in mCBM Het neonatal mice and wild-type (Wt) littermates by exposure to 75% oxygen from postnatal day (P) 7 to 12. Eyes were collected and fixed at P12 and P17. Retinas were isolated, stained with lectin, flat-mounted and imaged using fluorescence microscopy. Retinal vascular obliteration and neovascularization (NV) were quantified using SWIFT_NV macro and Image J. Marker genes for angiogenesis, inflammation and the Nrf2 pathway were determined by quantitative RT-PCR. Results were expressed as mean \pm SEM. Data were analyzed using unpaired t-test or one-way ANOVA followed by Tukey's correction for multiple comparisons.

Results: At P12, there was no significant difference of avascular area (AV) between mCBM Het and Wt litter mates. However, at P17, mCBM Het mice had significantly reduced AV and NV compared to the Wt. Consistently, the expression of gene markers for angiogenesis (Vegf, Angpt2 and Epo), inflammation (Tnfa and Cxcl10) was significantly lower in mCBM Het mice. In room air environment, the basal levels of Nrf2-targeted gene markers were increased in mCBM Het mice at P17 compared to Wt. Under OIR conditions, this increase was augmented significantly in mCBM Het mice.

Conclusions: $\alpha 1$ NKA signaling is involved in the mouse model of OIR. The loss of CBM in $\alpha 1$ NKA protects mice from OIR and is associated with increased levels of Nrf2-targeted genes.

CONTROL ID: 3544644

SUBMITTER (NAME ONLY): kim jiramongkolchai

TITLE: Effects of Fetal Hemoglobin on Systemic Oxygenation in Preterm Infants and the Development of Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity/vein occlusion

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To examine fetal hemoglobin levels on systemic oxygenation and development of retinopathy of prematurity (ROP) in preterm infants.

Methods: A prospective study of preterm infants (born < 31 weeks gestational age or <1500 g) with HbF measured at birth (cord blood), 31-, 34-, and 37-weeks post-menstrual age (PMA), complete blood gas and SpO₂ recorded up to 42-weeks PMA, and at least one ROP exam.

Results: From September 1, 2017 through December 31, 2018, 64 preterm infants were enrolled; 3 patients were excluded due to incomplete hemoglobin studies and 1 patient was withdrawn by their parent from the study prior to the first blood sample. Higher HbF was associated with significantly higher SpO₂, lower PCO₂, lower FiO₂ from birth to 31 weeks PMA and 31 to 34 weeks PMA ($r_s=0.51$, $r_s=-0.62$, and $r_s=-0.63$; $p<0.0001$ and $r_s=0.71$, $r_s=-0.58$, and $r_s=-0.79$; $p<0.0001$, respectively). To maintain oxygen saturation goals set by the neonatal intensive care unit, higher median FiO₂ was required for HbF in the lowest tercile from birth compared to HbF in the highest tercile to 31 weeks and 31 to 34 weeks PMA; FiO₂=35 (21-100) vs 21 (21-30) $p<0.006$ and FiO₂=30 (28-100) vs 21 (21-30); $p<0.001$, respectively. Preterm infants with ROP had poorer indices of systemic oxygenation, as measured by median levels of SpO₂ and PCO₂, and lower levels of HbF ($p<0.039$ and $p<0.0001$, respectively) up to 34 weeks PMA).

Conclusions: Low HbF levels correlated with poor oxygenation indices in the preterm infant and were associated with an increased risk for developing ROP. These results show that HbF levels influence systemic oxygenation. Thus, oxygen therapy may need titration that is based on HbF levels to reduce the risk of ROP development.

CONTROL ID: 3544655

SUBMITTER (NAME ONLY): Soojin Lee

TITLE: Epidermal Growth Factor Enhances Exosome-mediated Anti-angiogenic Signals between M1 Macrophages and Human Corneal Endothelial Cells

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kim, Department of Ophthalmology, Chung-Ang University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|S. Lee, K. Kim, CORIA (Chung-Ang Ocular Surface Rehabilitation via Immune-inflammation Alleviation) Laboratory, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Epidermal growth factor (EGF) has been known to alleviate inflammation in atopic dermatitis, but in the field of ophthalmology, its role is limited to the regeneration of corneal epithelial cells and corneal sensory nerves. Antigen-presenting cells such as dendritic cells and macrophages are known to exist in cornea, and in particular, macrophages are located in the deep stromal layer near the corneal endothelial layer. We investigated whether EGF mediates anti-angiogenic signals by the alleviation of inflammation between M1 macrophages and corneal endothelial cells.

Methods: Monocytes (THP-1 cell line) were treated with lipopolysaccharide (LPS) to be transformed into M1 macrophages. EGF protein was treated in M1 macrophages and the changes in the mRNA level of interleukin 1beta (IL-1 β) and IL-6 were analyzed. Then, exosomes were isolated from EGF-treated M1 macrophages and the exosomes were treated in human corneal endothelial cells to evaluate the mRNA expression of vascular cell adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1), vascular endothelial growth factor (VEGF), matrix metalloproteinase 2 (MMP-2), MMP-9, and platelet-derived growth factor (PDGF).

Results: Upon EGF treatment, the expressions of IL-1 β and IL-6 in M1 macrophages significantly decreased compared to before administration. When the exosomes isolated from EGF-treated macrophage cells were treated in cultured human corneal endothelial cells, all of VCAM-1, ICAM-1, VEGF, MMP-2, MMP-9, and PDGF were downregulated in mRNA level.

Conclusions: EGF inhibits IL-1 β and IL-6 in M1 macrophages, and may further mediate the anti-angiogenic signals in human corneal endothelial cells via exosomes
Conflicts of Interest: The authors declare that they have no conflict of interest.

CONTROL ID: 3544656

SUBMITTER (NAME ONLY): Jason Chow

TITLE: Varied gene expression in murine retina after intravitreal injection of human CD34+ stem cells in eyes with retinal degeneration or diabetic retinopathy.

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Previous studies have shown that intravitreal injection of healthy human CD34+ bone marrow stem cells (BMSCs) can result in regenerative or protective effects on the retina in eyes with retinal degeneration or diabetic retinopathy (DR). This study compared the gene expression changes in the retina resulting from intravitreal injection of human CD 34+ BMSCs in eyes with retinal degeneration versus DR to test the hypothesis that CD34+ BMSCs can have regenerative or protective effects on the retina via differing molecular mechanisms depending on retinal pathology.

Methods: Mice with retinal degeneration (rd1 mice) or diabetic retinopathy (streptozotocin-induced diabetic mice) had chronic systemic immunosuppression maintained to avoid rejection of human cells via placement of an Alzet subcutaneous pump to deliver tacrolimus and rapamycin. The right eye received intravitreal injection PBS (control) or healthy human CD34+ BMSC (50k cells) harvested via magnetic beads from bone marrow. These animals were euthanized at week 1, retinas were harvested, total RNA isolated and microarray analysis was performed on RNA samples. Gene expression changes (Fold Change ≤ -1.5 or $\geq +1.5$, ANOVA $P < 0.05$) between CD34+ BMSC injected and PBS injected control eyes were identified and compared between the two different murine models. Ingenuity pathway analysis was then performed on these overlaying genes to identify the pathways involved.

Results: Microarray analysis of the murine retina revealed changes in gene expression of 5275 and 331 genes in eyes with retinal degenerative and DR, respectively, compared to control eyes. Only 38 of these genes were altered in both rd1 and DR murine retina. These common genes include genes involved in pathways regulating photo-transduction, ocular angiogenesis, vascular endothelial growth factor signaling and inflammatory response. The genes uniquely altered in rd1 murine retina included those regulating cell cycle and growth, gene expression and repair, and immune response. The genes uniquely altered in DR murine retina included genes regulating ocular angiogenesis and cell cycle.

Conclusions: The protective effects of human CD34+ BMSCs following intravitreal injection appear to be via multiple molecular pathways that may be common and unique depending on the retinal pathology.

CONTROL ID: 3544659

SUBMITTER (NAME ONLY): Steven Mansberger

TITLE: Clinicians' Use of Global Indices when Assessing Functional Progression in Glaucoma

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Clinicians integrate a wealth of information when assessing the rate of glaucomatous functional progression and they use instrument-derived visual field printouts and global indices to assist this task. We sought to determine the global indices that best correlate with the subjective assessment of the rate of visual field progression by glaucoma experts.

Methods: Expert glaucoma specialists (n=11) reviewed a series of visual field printouts for 5 biannual visits from 100 glaucoma or glaucoma suspect eyes of 51 participants enrolled in the ongoing Portland Progression Project. Each clinician independently scored each series from 1 (improvement) to 7 (very rapid progression). They also scored 20 of those eyes twice to assess intra-clinician repeatability. Generalized estimating equation models were used to predict the average score among the clinicians from the rates of change of each of the available global indices; Mean Deviation (MD), Pattern Standard Deviation (PSD) and Visual Field Index (VFI).

Results: The average MD of study eyes was -2.4dB (range -16.8 to +2.8dB); 18% had average MD < -6dB. When assessing intra-clinician repeatability, 94% of individual clinician scores varied by ≤ 1 point. The mean inter-clinician score was also highly repeatable, with an intraclass correlation coefficient of 0.95. This score was more strongly correlated with the rate of change of VFI ($r=-0.85$) than either MD ($r=-0.80$) or PSD ($r=0.64$); see Figure 1. In bivariable regression models using two global indices, the rate of VFI change was the sole significant predictor. However, among eyes with average VFI>99% (n=25) for which VFI is near its maximum possible value, these correlations were $r=-0.40$ for MD, $r=-0.53$ for VFI, and $r=0.59$ for PSD (Figure 2); and the rate of PSD was the strongest predictor in regression models.

Conclusions: Overall, the mean assessment of functional change from a group of highly experienced glaucoma clinicians correlated better with rates of change of VFI than MD or PSD. However, in early glaucoma or glaucoma suspect eyes, clinician judgment correlated slightly better with changes in PSD, than MD or VFI. This may be related to clinicians identifying localized changes at the earliest stages of the disease. Future studies can use this information to better monitor the rate of progression, and use this data to develop improved quantifications of the rate of functional progression.

CONTROL ID: 3544660

SUBMITTER (NAME ONLY): Maria Kolic

TITLE: A 44 channel suprachoroidal retinal prosthesis: laboratory based visual function and functional vision outcomes.

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The 44 channel (44Ch) suprachoroidal retinal prosthesis is a second-generation bionic eye implant that follows on from a proof of concept study conducted between 2012 and 2014. The 44Ch implant is designed to provide artificial vision (phosphenes) to recipients with end-stage retinitis pigmentosa (RP). We aimed to compare the performance of visual function and functional vision tasks at pre-implantation and post device activation.

Methods: The 44Ch suprachoroidal retinal prosthesis was unilaterally implanted in 4 participants with advanced RP, age range 39 to 66 years, between February and August 2018. After a 16-week period of vision rehabilitation training, participants were assessed on three laboratory-based visual function tasks: moving bar (MB), square localisation (SL) and grating acuity (GA), followed by three functional vision tasks: table-top search (TTS), doorway detection (DWD) and obstacle avoidance (OA). Assessment time points were pre-implantation and from post-device activation at weeks 17 (W17), W20, W32, W44, W56 and W68. Data was pooled across all 4 participants and performance was compared between device on and off.

Results: With device on, three of the four participants could discriminate MB speeds ranging from 7 to 30 degrees per second. Average pointing error for all four participants, across all visits on SL, was $10.3 \pm 3.3^\circ$ (device on) versus $27.7 \pm 8.7^\circ$ (device off), $p < 0.001$. Two of the four participants had measurable GA of 0.033 cycles-per-degree. On average, the device improved participants' ability to locate objects on the TTS, detect and touch the doorway on DWD task and detect and avoid more obstacles during OA, at all-time points post-activation ($p < 0.04$), compared to device off.

Conclusions: The 44Ch second generation suprachoroidal implant improved overall performance on both laboratory-based visual function and functional vision tasks, compared to device off. The device shows the capability to provide visual sensory information, to aid detection of obstacles and improve accuracy when reaching for an object, for people with profound vision loss due to RP.

CONTROL ID: 3544662

SUBMITTER (NAME ONLY): Dylan Freeman

TITLE: Analysis of progression of retinal microvascular ischemia in patients with sickle cell disease using optical coherence tomography angiography

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Freeman, K. Sioufi, E.A. Say, J. Blice, G. Magrath, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate rate of progression and factors affecting retinal microvascular ischemia in patients with sickle cell disease.

Methods: Retrospective review of 40 eyes in 25 patients diagnosed with sickle cell disease and scanned using Zeiss Cirrus-HD. We evaluated 3x3mm optical coherence tomography-angiography (OCT-A) scans at two sequential visits about 1 year apart. Vascular density (VD) was measured at the superficial (sVD) and deep (dVD) plexuses using post capture image processing platform on ImageJ (National Institute of Health). All statistical analyses were performed using SPSS, Version 27 (SPSS, Inc, Chicago, Illinois, USA).

Results: Sickle cell status was sickle cell trait in 1, SS in 14, SC in 6, and Sb in 4 patients. Mean follow-up interval duration was 13.7 months (range: 6-25). Mean logMAR was 0.75 and 0.062 at the first and second visit, respectively. By OCT-A, the mean sVD was 51.33% (range: 41.2-57.3%) and 47.41% (range: 29.31-54.60%) while mean dVD was 46.41% (range: 37.3-53.7) and 46.43% (range: 36.61-53.18) at the first and second visit, respectively. Mean difference in VD between visits was -3.87% for sVD and +0.01% for dVD. There was a statistically significant decrease in sVD ($p<0.001$) but no statistically significant change in dVD ($p=0.984$) or VA. Subgroup analysis showed no significant difference in mean sVD reduction based on sickle cell status, history of prior stroke, and history of avascular necrosis.

Conclusions: Over a follow-up period of 1-year, patients with sickle cell disease demonstrated progression of retinal microvascular ischemia by OCT-A. This reduction in VD appears to affect the superficial plexus more so than the deep plexus.

CONTROL ID: 3544663

SUBMITTER (NAME ONLY): Anuja Java

TITLE: Comprehensive Analysis of Genetic Variants of Uncertain Significance in Complement Factor I (CFI) in Advanced Age Related Macular Degeneration (AAMD)

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Java, J. Atkinson, Department of Medicine, Washington University in St Louis, St Louis, Missouri, UNITED STATES|R. Widjajahakim, J.M. Seddon, Department of Ophthalmology and Visual Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|A. Java, Department of Medicine, VA St Louis Medical Center John Cochran Division, Saint Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Factor I (FI) is a serine protease inhibitor of the alternative pathway of the complement system. This regulation of the complement system is achieved by cleavage of C3b (known as cofactor activity). Heterozygous rare genetic variants in CFI are associated with AAMD. The clinical impact of these variants is unknown since a majority have not been functionally characterized and are classified based on predictive models as 'variants of uncertain significance' (VUS). This study assessed the functional significance of VUS in CFI.

Methods:

Our previous cross-sectional study demonstrated that heterozygous CFI variants in AAMD can be categorized into three major types [Java et al. Trans Vis Sci Tech 2020; 9(9):37]. Type 1 variants caused a quantitative deficiency of FI (decreased FI level with a proportional decrease in function). Type 2 variants demonstrated a qualitative deficiency (normal FI level but decreased function). However, Type 3 variants consisted of VUS that were less dysfunctional than Types 1 and 2 but were not as biologically active as wild-type. In this study we present an in-depth functional assessment of the Type 3 variants. We utilized serum FI antigenic levels, site-directed mutagenesis followed by expression of the recombinant variant and a comprehensive set of functional assays to characterize nine Type 3 variants identified in 34 individuals (R202I, Q217H, S221Y, G263V, G362A, K441R, Q462H, I492L and N536K).

Results: Our study established that the expression of the recombinant protein compared to wild-type by 293T cells was reduced for Q217H, S221Y and G263V. Further, R202I and G362A had significantly reduced cofactor activity. These results led to recategorization of Q217H, S221Y and G263V as Type 1 variants and to reclassification of R202I and G362A as Type 2. The remaining Type 3 variants (K441R, Q462H, I492L and N536K) are best classified as being benign at this time. This study highlights the utility of an in-depth functional analysis in defining the pathologic and clinical implications of complement variants in AAMD and provides further insights relative to the pathogenic mechanisms underlying AMD.

Conclusions: This approach will be a useful model system for guiding more appropriate therapeutic decisions relative to an individualized treatment plan for patients and thereby pave the way for precision medicine in AMD.

CONTROL ID: 3544666

SUBMITTER (NAME ONLY): Alcina Lidder

TITLE: DNA testing for inherited retinal disease (IRD): Initial experience with the SPARK/Invitae 'ID your IRD' genetic testing panel

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lidder, Y. Modi, V.S. Dedania, S.E. Brodie, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the diagnostic yield and clinical impact of the SPARK/Invitae gene panel in patients with known or suspected inherited degenerative retinal disease, in comparison with traditional clinical assessments.

Methods: Patients of the authors' clinical practices obtained genetic screening at no charge via the SPARK/Invitae "ID your IRD" genetic testing panel, which ranged from 248 genes to 293 genes. Over 16 months, tests were submitted for 87 patients and results were available for 70 patients. Clinical diagnoses prior to submitting the gene panel included retinitis pigmentosa; Stargardt disease; Best vitelliform dystrophy; Leber congenital amaurosis; choroideremia; achromatopsia; cone-rod dystrophy; congenital stationary night blindness; occult macular dystrophy; and familial dominant drusen in addition to patients with normal clinical findings and unclear diagnoses.

Results: Of 70 patients, SPARK/Invitae considered the results "Positive" or "Potentially Positive" in 24 cases (34.3%), "Carrier" in 16 cases (22.9%) and "Uncertain" in 30 cases (42.9%). "Uncertain" results comprised patients with only "Variants of Uncertain Significance." Patients categorized as a "Carrier" by SPARK/Invitae but who demonstrated pathogenic genetic changes correlating to the clinical diagnosis were considered to be in agreement with the clinical impression. The genetic diagnosis agreed with the clinical diagnosis in 30/70 (42.9%) total patients. Test results were consistent with the clinical impression in 13/26 (50.0%) retinitis pigmentosa cases, 6/8 (75.0%) Stargardt patients, 3/7 (42.9%) cone-rod dystrophy cases, and 2/4 (50.0%) Best vitelliform dystrophy patients. Gene testing helped elucidate diagnoses in two patients with unclear clinical impressions: one panel showed autosomal recessive achromatopsia and the other showed a carrier state for autosomal recessive retinitis pigmentosa. Of four patients with normal clinical exams, none had diagnostic results: all showed "Uncertain" findings.

Conclusions: The SPARK/Invitae gene panel provided a genetic diagnosis consistent with the clinical impression in about 40 percent of patients. Retinitis pigmentosa and Stargardt disease were the most common clinical diagnoses and the diagnoses most often confirmed by testing. Genetic screening also assisted in clarifying unknown diagnoses for two patients.

CONTROL ID: 3544667

SUBMITTER (NAME ONLY): Nasir Khan

TITLE: Systemic and Ocular Determinants of Macular Vessel Metrics in Optical Coherence Tomography Angiography (OCTA) 6x6 Scans in Healthy African Americans

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine the relationship of various systemic and ocular characteristics with macular vessel density in the African American Eye Disease Study.

Methods: Participants consisted of African Americans 40 years of age and older residing in Inglewood, CA. They underwent 6x6-mm macula eye scans using spectral-domain optical coherence tomography angiography (OCTA; CIRRUS 5000 HD-OCT with AngioPlex; ZEISS, Dublin, CA, USA), a clinical examination, and a clinical questionnaire. Participants with glaucoma, severe non-proliferative diabetic retinopathy, proliferative diabetic retinopathy, and macular edema were excluded. A custom MATLAB based software was used to quantify vessel area density (VAD), vessel skeleton density (VSD), and flux in the superficial retinal layer (SRL) of the macula. Inter-eye correlation was controlled for using generalized estimating equations (GEE). Using SAS, a multivariate regression analysis was performed to determine systemic and ocular determinants of macular vessel metrics using stepwise selection. Candidate variables included: age, gender, body mass index, history of smoking, history of diabetes, diabetes duration, history of stroke or brain hemorrhage (SB), systolic blood pressure (BP), diastolic blood pressure (DBP), pulse pressure (PP), mean arterial pressure (MAP), central subfield thickness (CSFT), visual field mean deviation (MD), intraocular pressure (IOP), axial length (AL), mean ocular perfusion pressure (MOPP), and signal strength (SS). **Results:** A total of 2221 OCTA imaged eyes from 1472 participants remained after excluding eyes for either poor image quality or the presence of an ocular disease. As demonstrated in the table, after controlling for signal strength and age, longer axial length and reduced central subfield thickness were independently associated with reduced VAD, VSD and Flux. Male gender and decreased diastolic blood pressure were also independently associated with reduced flux.

Conclusions: When assessing OCTA images in a clinical setting, it is important to consider the effect axial length, central subfield thickness, gender, and diastolic blood pressure may have on the macular microcirculation.

CONTROL ID: 3544673

SUBMITTER (NAME ONLY): Kyle Marra

TITLE: Differentially expressed microRNAs within extracellular vesicles of a functionally active subpopulation of endothelial colony forming cells demonstrate neurovasculotrophic effects

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.V. Marra, School of Medicine, University of California San Diego, La Jolla, California, UNITED STATES|K.V. Marra, E. Aguilar, A. Ouchi, G. Wei, M. Friedlander, Molecular Medicine, Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endothelial colony forming cells (ECFCs) are endothelial progenitor cells with neurovasculotrophic effects achieved via paracrine action. ECFCs, however, are not functionally homogenous. ECFCs with high expression of CD44 hyaluronan receptor (CD44^{hi}) rescue the oxygen-induced retinopathy (OIR) model of ischemic retinopathy as well as rd10 mice with retinal neurodegeneration; ECFCs with low expression of CD44 (CD44^{lo}) do not. Extracellular vesicles from CD44^{hi} ECFCs (EVs^{hi}) recapitulate this effect while vesicles from CD44^{lo} ECFCs (EVs^{lo}) are ineffective. Here, we investigate the role of EVs^{hi} in mediating the paracrine rescue effects of CD44^{hi} ECFCs and compare their intravesicular small RNA cargo of EVs^{hi} and EVs^{lo} using an -omics based approach to identify microRNA (miR) mediators of their trophic effects.

Methods: Sorted CD44^{hi} ECFCs treated with neutral sphingomyelinase inhibitor GW4869, used to inhibit exosome biogenesis/release, were intravitreally injected into OIR mice. DICER1 knockdown ECFCs (ECFCs-shDICER1) and a control scramble RNA cell line (ECFCs-scrRNA) were generated using lentiviral transfection. Sorted CD44^{hi} ECFCs-shDICER1 and CD44^{hi} ECFCs-scrRNA and their EVs were intravitreally injected into OIR mice. Small RNA of EVs^{hi} and EVs^{lo} were sequenced with Next Generation Sequencing to identify differentially expressed intravesicular miRs. miRs that validated well on RT-qPCR and control scramble miR were injected into OIR.

Results: CD44^{hi} ECFCs rescued OIR and these effects were attenuated after GW4869 treatment. CD44^{hi} ECFCs-shDICER1 and their EVs were significantly less effective in rescuing OIR than CD44^{hi} ECFCs-scrRNA and their EVs, respectively. Small RNA sequencing of EVs^{hi} identified 9 upregulated and 10 downregulated miRs in comparison to EVs^{lo}. On RT-qPCR, 7 of the 9 upregulated miRs validated well. All miRs were functionally tested in OIR and 3 candidate miRs fully rescued the model.

Conclusions: CD44^{hi} ECFCs shed vesicles containing neurovasculotrophic miRs that may contribute to the efficacy of EVs^{hi} treatment in mouse models of ischemic/neurodegenerative retinopathy.

CONTROL ID: 3544675

SUBMITTER (NAME ONLY): Fares Antaki

TITLE: Automated Machine Learning Model For The Classification Of Retinal Diseases From Ultra-Widefield Pseudocolor Fundus Images

SESSION TITLE: AI in the retina: Algorithms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Antaki, R. Duval, Department of Ophthalmology, Hopital Maisonneuve-Rosemont, Montreal, Quebec, CANADA|F. Antaki, K. Hammamji, M. Sebag, Department of Ophthalmology, Centre Hospitalier de l'Universite de Montreal, Montreal, Quebec, CANADA|R. Coussa, Department of Ophthalmology, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Automated machine learning (AutoML) is a new area in artificial intelligence that automates important components in the machine learning design pipeline. It has not been broadly used for retinal disease detection from fundus images. This study aimed to assess the discriminative performance of AutoML in classifying retinal pathologies from ultra-widefield (UWF) fundus pseudocolor images.

Methods: Using Google Cloud AutoML Vision, we developed a deep learning classification model to detect normal fundi, retinal vein occlusion (RVO), retinitis pigmentosa (RP), and retinal detachment (RD) from UWF pseudocolor images. We selected those diseases for the presence of retinal hemorrhage in RVO, retinal pigment epithelial changes in RP, and retinal elevation in RD. We used an open-access dataset provided by the Tsukazaki Optos Public Project (13,047 images) to curate a smaller dataset of training and validation images. Two ophthalmologists (raters) independently graded the images according to consensus criteria. Selected images were then uploaded to the online platform for testing and training through the graphical interface and without any coding. Cohen's kappa coefficient (κ) was used to assess the inter-rater agreement during data labeling. The performance of the AutoML model is reported using the area under the precision-recall curve (AuPRC), precision, and recall.

Results: A total of 2,311 images were relabeled. There was almost perfect agreement between the two raters for normal ($\kappa = 0.82$), RVO ($\kappa = 0.85$) and RD ($\kappa = 0.82$) images, and substantial agreement for RP images ($\kappa = 0.75$). The final dataset included 1,355 images (472 normal, 311 RVO, 187 RP, and 385 RD). The overall AuPRC was 0.95, and the precision and recall were both 91.85%. The per-label precision and recall were as follows: normal (88.46% and 97.87%), RVO (96.43% and 87.1%), RP (100% and 78.95%) and RD (90% and 94.74%).

Conclusions: We demonstrate the feasibility of using AutoML by ophthalmologists without coding experience to create a deep learning disease classification model from UWF images. The model can detect RVO, RP, and RD (three retinal diseases with distinctive clinical features) with excellent precision and recall. With that being established, further research aimed at developing more challenging classification tasks is being carried out by our group (e.g. disease types and stages).

CONTROL ID: 3544677

SUBMITTER (NAME ONLY): Cancan Xue

TITLE: Prevalence of Gunn's Dots and Associated Systematic Factors in an Adult Population

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Xue, L. Gao, Y. Wang, Beijing Tongren Hospital, Beijing, Beijing, CHINA|C. Xue, Peking University Third Hospital, Beijing, CHINA|J. Jonas, Ruprecht Karls Universitat Heidelberg, GERMANY|

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ABSTRACT BODY:

Purpose: To investigate the prevalence of Gunn's dots and associated systemic factors in adult Chinese in a community-based study.

Methods: The Tongren Health Care Study included individuals aged 45+ years and who regularly underwent detailed medical and ophthalmic examinations. Based on the color fundus photographs, Gunn's dots were evaluated by an experienced ophthalmologist. Individuals with eye diseases including age-related macular degeneration, retinal vein occlusion, diabetic retinopathy, myopic retinopathy, glaucoma or non-glaucomatous optic neuropathy, were excluded from the analysis.

Results: Out of 5845 individuals (male: 2461/42.1%), 1670 (27.5%) individuals were excluded due to ocular diseases and 120 (2.1%) individuals were excluded due to unreadable fundus photographs, so that the study eventually included 4118 participants (mean age: 58.3±9.9 years; range: 45-100 years; male: 1699/41.3%). Gunn's dots were found in 931 participants (729/78.3% bilateral and 202/21.7% unilateral), with a prevalence of 22.6±0.07% (95% confidence interval (CI): 21.4 to 23.9%). The prevalence of Gunn's dots decreased from 34.9±1.6 % in participants aged 45-49 years, to 26.0±1.6 % in those aged 55-59 years, and to 2.1±0.6 % in those aged 70+ years. Gunn's dots were more commonly seen in eyes with higher estimated glomerular filtration rate (eGFR), with the presence of 0.0%, 10.7±1.7%, 22.5±1.1 %, and 48.6±8.6 % in those participants with an eGFR of less than 30ml/min/1.73m², 60-74ml/min/1.73m², 90-99 ml/min/1.73m² and higher than 115ml/min/1.73m², respectively. In multivariable analysis, the prevalence of Gunn's dots decreased with older age (odds ratio (OR): 0.92; 95%CI: 0.91 to 0.93; P<0.001), and increased with a higher eGFR (OR: 1.01; 95%CI: 1.001 to 1.02; P=0.02) and higher serum concentration of triglycerides (OR:1.10; 95%CI:1.03 to 1.17; P=0.008). It was not significantly associated with gender (P=0.13).

Conclusions: The prevalence of Gunn's dots decreased with older age, lower eGFR and lower serum triglyceride concentrations. These findings may be of help to elucidate the etiology of Gunn's dots and their clinical meaning.

CONTROL ID: 3544681

SUBMITTER (NAME ONLY): Kenneth Taylor

TITLE: Precursors to Geographic Atrophy in Age-Related Macular Degeneration (AMD)

SESSION TITLE: AMD imaging - GA

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Taylor, S. Cleland, J.W. Pak, M. Banghart, B. Blodi, A. Domalpally, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Incomplete and complete Retinal Pigment Epithelial (RPE) Outer Retinal Atrophy (iRORA and cRORA) are consensus terms published by the Classification of Atrophy Meeting (CAM) group to describe OCT based retinal changes associated with development of atrophy in eyes with Age Related Macular Degeneration (AMD). This is a retrospective cohort study to identify the prevalence of iRORA and the risk of progression to late AMD, particularly cRORA.

Methods: Participants enrolled in the Age-Related Eye Disease Study 2 (AREDS2) at Year 5 and Year 10 study visits from a single center, the University of Wisconsin were included. SDOCT scans (97 B scans each) of 102 eyes of 65 patients with AMD were evaluated by two graders. Disagreements were adjudicated by a senior grader. Year 5 SDOCT scans and color photographs were evaluated to exclude eyes with late AMD (cRORA and neovascular AMD). cRORA was defined using the CAM criteria as follows: choroidal hypertransmission > 250 μ m, attenuation or disruption of RPE, and photoreceptor degeneration, that is, subsidence of the inner nuclear layer (INL) and outer plexiform layer (OPL), presence of a hyporeflective wedge in the Henle fiber layer (HFL), thinning of the outer nuclear layer (ONL), disruption of the external limiting membrane (ELM) or disintegrity of the ellipsoid zone (EZ), and when these criteria do not meet the definition of cRORA or RPE tear. 76 eyes of 48 subjects with intermediate AMD which remained were evaluated for iRORA, which was identified if all three above criteria for cRORA were met but the size was < 250 μ m. Also, the type of photoreceptor degeneration, when present, was documented. Subsequently, 10-year scans were graded and eyes with late AMD were identified.

Results: At year 5, iRORA was present in 11 eyes (14.5%). Absence of the ELM was the most commonly seen feature of photoreceptor disruption (100%). 20 eyes (26.3%) at year 10 follow up had cRORA. Of the eyes with iRORA at year 5, 5 (45.5%) developed cRORA at year 10. For eyes with iRORA, the odds ratio for developing cRORA was 2.17 (95% CI 0.52, 9.08; p=0.28).

Conclusions: iRORA represents a stage before development of irreversible endpoints such as geographic atrophy (GA). Long term studies with larger sample size are required to understand this important new step in AMD classification. It remains to be studied if some OCT related features of iRORA may be more predictive of progression than others.

CONTROL ID: 3544682

SUBMITTER (NAME ONLY): Dawiyat Massoudi

TITLE: The UPR transducer—IRE1 α —is required for photoreceptor health and protection against retinal degeneration

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Several lines of evidence implicate the involvement of endoplasmic reticulum stress (ER stress) and its transducers in neurodegenerative diseases such as retinitis pigmentosa. ER stress triggers an intracellular signaling pathway called the Unfolded Protein Response (UPR). IRE1 α is an ER resident protein that plays a major role in orchestrating the UPR. Here we aim to assess the contribution of IRE1 α to photoreceptor homeostasis and retinal degeneration.

Methods: We selectively deleted IRE1 α in rod photoreceptors of mice and investigated the physiological consequences in photoreceptor homeostasis and function. We also crossed these animals with the rhodopsin Rho P23H mouse model of retinitis pigmentosa in order to evaluate the consequences of IRE1 α loss in an in vivo setting of retinal degenerative disease. We assessed retinal thickness longitudinally using Optical Coherence Topography (OCT) and evaluated the retinal function by electroretinography (ERG) as animals aged.

Results: OCT imaging and histological analysis of IRE1 α deficient mouse retinas did not reveal any abnormalities during early time points (1 and 3 months old). At 6 months and older however, the IRE1 α deficient mice showed a progressive thinning of their outer nuclear layer (ONL) in the retina compared to the controls. ERG recordings during these later time points also showed decreased scotopic responses while photopic responses were unchanged. Analysis performed on IRE1 α deficient mice on the rhodopsin Rho^{P23H} background revealed an exacerbated retinal degeneration in the absence of IRE1 α .

Conclusions: These results suggest that IRE1 α is dispensable for retinal development but important for maintaining photoreceptor homeostasis in aging retinas and for protecting against ER stress-related photoreceptor degeneration. Future work will establish whether there are compensatory changes in the other UPR pathways that could explain the lack of retinal phenotype observed during development.

CONTROL ID: 3544684

SUBMITTER (NAME ONLY): Amanda Piña

TITLE: Objective and Subjective Behavioral Measures in Myopic and Non-Myopic Children during the COVID-19 Pandemic

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Piña, H. Mirhajianmoghadam, L.A. Ostrin, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has dramatically affected children's lifestyle, requiring a shift to electronic device use for education and entertainment, which may ultimately impact eye growth and myopia. Our goal was to assess sleep, time outdoors, physical activity, near work, and electronic device use during the summer COVID-19 pandemic in myopic and non-myopic children. Additionally, behaviors were compared with a typical summer before the pandemic.

Methods: Healthy children (ages 8.3 ± 2.4 years, $n=53$) in Houston, Texas participated. Children wore an Actiwatch for 10 days while quarantine measures were in place for objective measures of light exposure, time outdoors, activity, and sleep. Additionally, parents completed a questionnaire regarding children's demographics, ocular history, and visual activity, including electronic device use, during the COVID-19 pandemic and also for a typical summer before COVID-19. Data were analyzed with repeated measures ANOVA for session (COVID-19 vs pre-COVID-19), day of the week (weekday vs weekend), and refractive error group (myopic vs non-myopic).

Results: Objective measures showed that during the COVID-19 pandemic, myopic children had significantly lower daily light exposure ($P=.04$) and less physical activity ($P=.04$) than non-myopic children, with no significant differences in sleep duration or time outdoors between groups ($P>.05$ for all). Subjective measures showed that children demonstrated increased electronic device use during COVID-19 compared to pre-COVID-19 on weekdays (7.3 ± 0.6 vs 4.9 ± 0.5 hours per day, respectively, $P<0.001$) and weekends (7.9 ± 0.6 vs 6.1 ± 0.5 hours per day, respectively, $P<0.001$). Time spent doing near work was not significantly different during COVID-19, between days of the week, or by refractive error group ($P>.05$ for all).

Conclusions: Children's behaviors during the COVID-19 pandemic varied between myopes and non-myopes. Objective measures showed that during the pandemic, myopic children exhibited lower daily light exposure and physical activity than non-myopes. Additionally, based on parents' report, children's electronic device use increased, and physical activity and time outdoors decreased during the pandemic. Long term follow up is needed to understand if these behavioral changes as a result of the COVID-19 pandemic contribute to increased myopia progression.

CONTROL ID: 3544685

SUBMITTER (NAME ONLY): Kyle Bolo

TITLE: Longitudinal outcomes of Ahmed and Baerveldt implants in neovascular glaucoma in a safety-net patient population

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bolo, S. Mohan, B. Wong, B. Xu, G. Richter, B.J. Song, S. Bedrood, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|J.L. Do, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the longitudinal outcomes of a safety-net patient population with neovascular glaucoma (NVG) treated with glaucoma drainage implants (GDIs).

Methods: We performed a retrospective observational study including eyes that received GDIs for NVG at LAC+USC Medical Center from 2008-2018. Exclusion criteria were an uncertain diagnosis of NVG, history of prior GDI in the study eye, or follow-up of less than one year. Patients were stratified into Ahmed (AGV) and Baerveldt (BGI) groups. The primary outcome was surgical success defined as the preservation of light perception, intraocular pressure (IOP) below 22 mmHg, and no additional glaucoma intervention. Secondary outcomes included visual acuity (VA), intraocular pressure (IOP), and medications prescribed at 1-, 2-, and 3-year intervals postoperatively. Data were compared between groups using Student's t-test for continuous variables and Fisher's exact test for categorical variables.

Results: 162 eyes from 151 patients met inclusion criteria and, of these eyes, all were reported at 1 year, 107 at 2 years, and 66 at 3 years. Mean age was 53.2 and 88% were Hispanic. Age and ethnicity did not vary between groups ($p = 0.49$ and 0.60). Preoperative IOP was 39.4 mmHg in AGVs and 32.7 mmHg in BGIs ($p = 0.0003$), but there was no significant difference in preoperative VA ($p = 0.28$). No significant differences were found in success rate between the groups at 1, 2 and 3 years postoperatively with AGVs reporting success in 75%, 60% and 59% respectively, and BGIs in 82%, 76% and 64%. In the subgroup of successful GDIs, there was not a statistically significant difference in the number of classes of drops used at each follow-up interval, though there was a trend toward a lower drop burden in the BGI group ($p = 0.14, 0.15, 0.41$ at 1, 2 and 3 years); VA and IOP did not vary significantly.

Conclusions: There were no significant differences found in longitudinal outcomes of AGVs and BGIs in the context of NVG.

CONTROL ID: 3544687

SUBMITTER (NAME ONLY): Shuibin Ni

TITLE: Real time ultrahigh speed and widefield handheld swept source OCTA pediatric retinal imaging

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Ni, X. Wei, D. Huang, Y. Jia, J. Campbell, Y. Jian, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S. Ostmo, Department of Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|R. Ng, Department of Engineering Science, Simon Fraser University, Burnaby, British Columbia, CANADA|X. Wei, Y. Jia, Y. Jian, Department of Biomedical Engineering, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Developing a robust handheld OCT system, with ultrahigh speed, widefield, and real-time in vivo OCT/OCTA visualization for clinical imaging of pediatric retina.

Methods: We optimized the optical design for the handheld OCT/OCTA system that achieved a 55-degree field of view and a 1.3 mm beam size on the entrance pupil with low system optical aberrations (Fig. 1). A 11-element lens group was used to relay the imaging beam, and the fast and slow axis of the galvanometer scanner were separated and both conjugated to the pupil plane to reduce the vignetting artifacts. We used a 1060 nm, 400-kHz VCSEL (Thorlabs, Inc.) swept source laser with 100 nm bandwidth that provides an imaging depth of 6 mm and an axial resolution of 4.96 μm in air. A 4-coupler interferometer with an optimum coupling ratio delivered 1.8-mw incident power on the cornea. A motorized reference arm and an electrically tunable lens were rapidly adjusted during the imaging session to match the imaging subject's axial eye length and fine tune focus. Our GPU accelerated OCT acquisition software displayed en face and cross-sectional view of the retina on the imaging probe which enabled direct real-time feedback and facilitated alignment process and navigation. A high-speed alignment mode (10Hz volume rate) and a high-resolution OCTA scanning mode (500 \times 1500 A-scans, 3 B-scans per BM-scan, 5ms interscan time, and 1.875 seconds) were available for the operator to toggle between them.

Results: 3 healthy adult volunteers, 16 awake neonates in neonatal intensive care unit and 7 pediatric patients under general anesthesia in operating room prior to retinal surgery were successfully imaged, all the imaging sessions were completed within 5 minutes. Representative retinal OCT/OCTA images from a patient with X-linked retinoschisis and a patient with retinopathy of prematurity were shown in Fig 2. Vascular network and pathologies were clearly visualized in these images without pronounced motion artifacts.

Conclusions: We have demonstrated a 400-kHz and 55-degree field of view handheld OCT/OCTA system that has overcome many technical challenges in ultrahigh speed OCTA imaging as well as in pediatric retinal imaging in general. The advantages of the system have the potential to improve the diagnosis of retinal diseases and clinical validation.

CONTROL ID: 3544688

SUBMITTER (NAME ONLY): Angela Godinez

TITLE: The neuroprotective effects of exogenous SERPINI1 administration on the retina in chronic glaucomatous conditions

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Godinez, R. Rajput, N. Chitranshi, V. Gupta, S.L. Graham, Clinical Medicine, Macquarie University, Sydney, New South Wales, AUSTRALIA

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ABSTRACT BODY:

Purpose: Primary open angle glaucoma (POAG) is a leading cause of blindness, characterised by optic nerve head excavation and retinal ganglion cell degeneration. Recent studies have shown that inactivation of the serine protease inhibitor neuroserpin (SERPINI1) is associated with plasmin-proteolytic excitotoxicity within the retina, and the protective effects of SERPINI1 overexpression have been previously reported in various neurodegenerative diseases. Here, we examined the protective effects of exogenous intravitreal SERPINI1 administration on inner retinal function and structure in a mouse model of experimental glaucoma.

Methods: Wild-type C57BL/6J mice (n=32) were subject to weekly intracameral microbead injections for eight weeks, to induce a chronic increase in intraocular pressure (glaucoma, n=8). Human recombinant SERPINI1 was injected intravitreally in healthy (SERPINI1, n=8) and experimental glaucoma mice (glaucoma+SERPINI1, n=8; weekly). PBS was administered as a vehicle control (PBS, n=8). Functional changes were assessed using positive scotopic threshold response (pSTR) amplitude measurements. Retinal structural changes were investigated using hematoxylin and eosin staining of tissue sections and quantified by light microscopy.

Results: Exogenous SERPINI1 administration in experimental glaucoma mice demonstrated significant preservation of pSTR amplitudes when compared to glaucoma mice alone ($p<0.02$). Healthy control mice treated with the SERPINI1 protein showed no significant changes in pSTR amplitudes, when compared to untreated and PBS treated mice ($p=0.19$). Histological quantification further revealed no significant changes to GCL density in untreated, PBS and SERPINI1 alone treated groups ($p=0.37$). However, there was significant rescue of the GCL population in glaucoma mice that were administered SERPINI1 protein intravitreally, when compared to the glaucoma control mice ($p<0.01$).

Conclusions: This study establishes a protective effect of exogenous SERPINI1 administration on the retina in chronic glaucoma conditions. The molecule may impart protection by suppressing the excitotoxicity associated with plasmin proteolytic actions. The exact molecular mechanisms of SERPINI1 effects and consequences of its loss however remain undefined. Future proteomics investigations will establish the SERPINI1 signalling networks that are involved in retinal neuroprotection in glaucoma.

CONTROL ID: 3544691

SUBMITTER (NAME ONLY): Lisa Keay

TITLE: Cost-benefit analysis of orientation and mobility programs for adults with vision-related disability: a contingent valuation study

SESSION TITLE: Visual Impairment during a pandemic

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Orientation and Mobility (O&M) programs aim to equip individuals with vision disability with the skills and techniques that optimize their ability for safe, independent travel, and hence foster their social, economic and educational participation. The purpose of this study was to conduct a cost-benefit analysis from three perspectives: the general public, the experienced user and the potential users of O&M programs in Australia.

Methods: Willingness-to-pay, was collected via contingent valuation survey using a double-bound dichotomous choice approach. The survey had three arms: Arm 1, the general public via stratified random sampling, Arm 2, experienced users of O&M programs, and Arm 3, potential users of O&M programs, were drawn from a major O&M service provider's database and two eye clinics via convenience sampling. Willingness-to-pay was estimated using interval regression analyses, accounting for study arm, sex, occupation, income and self-rated health. The cost data, including labour, travel and occupancy costs, were estimated from a service provider's perspective. The Net Present Value, variation if delivered by tele-O&M programs and priority for resource allocation was investigated.

Results: Arm 1 (the general public) included 471 participants (60.7% female) with a mean age of 64.6 years (range 18 - 100); Arm 2 (the experienced user) included 96 participants (59.4% female) with a mean age of 61.9 years (range 19 - 97); and Arm 3 (the potential user) included 137 participants (59.9% female) with a mean age of 74.2 years (range 21 - 97). Overall, the adjusted mean Net Present Value of O&M programs was \$3857 (95%CI: \$3760 - \$3954) per client, with a highest NPV from the general public (\$4289, 95% CI: \$ 4185 - \$4392), followed by the experienced users (\$ 3158, 95% CI: \$ 2897 - \$3419) and the potential users (\$ 2867, 95% CI: \$ 2680 - \$3054). The NPV reached break-even for tele-O&M programs. Priorities for resource allocation were similar between O&M programs, low vision services and care worker assistance.

Conclusions: There was strong community support for investment into O&M programs, including tele-programs. The results of this survey indicated that investment into these programs generates substantial benefits for clients over and above the cost of providing the services.

CONTROL ID: 3544694

SUBMITTER (NAME ONLY): Faruk Orge

TITLE: Reliability of home-based acuity assessment in children with amblyopia: a trial study

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Orge, B. Can, A. Peiffer, M. Kohen, E. Leonard, UH Cleveland Medical Center, Cleveland, Ohio, UNITED STATES|T. Le, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The growing role of telehealth in ophthalmology has only been accelerated by the COVID 19 pandemic. Research has been performed assessing the reliability and utility of remote, web-based visual acuity (VA) measurements, but not to our knowledge in children with amblyopia. We assessed the reliability of parent-obtained, remote visual acuity measurements compared to clinic-obtained values.

Methods: InsideOutMedicine (Seattle, WA) is an online, HIPAA-compliant platform that enhances tracking of amblyopia patient treatment. The platform allows parents to create a virtual "log" in which they record daily treatment and other required values (i.e.VA) for providers to review.

We enrolled eligible patients by creating an account on the platform. Parents were instructed to measure their child's VA within 14 days of the clinic visit at which their child was enrolled. Parents measured their child's VA using the Eyehandbook app (Cloud Nine Development LLC, Overland Park, KS). They then entered the obtained visual acuity values in the platform.

We recorded baseline characteristics of included patients and compared parent-obtained visual acuity measurements to corresponding clinic-obtained measurements, utilizing intraclass correlation (ICC) to assess for correlation.

Results: 14 total patients received 15 parent-obtained VA measurements within 14 days of a clinic visit, for a total of 56 individual VA measurements. The study cohort had an average age of 6.14 years (std = 2.21) and contained 50% females. 8 of the patients had moderate amblyopia, while 5 had mild and 1 had severe amblyopia.

We decided to remove a single set of extreme outlier measurements (20/400 vs 20/50), as no other set of measurements differed by more than 3 lines, with an average difference of .59 lines.

Intraclass correlation coefficient (ICC) comparing clinic-obtained and parent-obtained visual acuity measurements was 0.889 ($p < 0.001$) for amblyopic eyes, .477 ($p = .044$) for healthy eyes, and was .888 ($p < .001$) for the entire sample.

Conclusions: In this small sample size trial, home-based, parent-obtained VA measurements in children with amblyopia correlated significantly with clinic-obtained values in both normal and amblyopic eyes. This small sample size study suggests that home-based visual acuity testing could have utility in this population, especially for tracking changes over time between clinic visits.

CONTROL ID: 3544695

SUBMITTER (NAME ONLY): Vasiliki Gliagias

TITLE: Pattern Electroretinogram Parameters Are Associated With Optic Nerve Head Morphology Abnormalities in Pre-Perimetric Glaucoma After Controlling for Disc Area

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Wide biologic variability and inconclusive Optical Coherence Tomography (OCT) detection of disc margin limit accurate representation of optic nerve head (ONH) disc area (DA). This cross-sectional study assesses the relationship between Pattern Electroretinogram (PERG) and OCT derived ONH measurements after controlling for DA.

Methods: Sixteen pre-perimetric glaucoma (PPG) subjects (thirty eyes) with normal Humphrey 24-2 visual field tests and suspicious ONH were consecutively recruited at Manhattan Eye Ear and Throat Hospital. Participants underwent Diopsys NOVA PERG and Cirrus and Spectralis OCT tests. Partial correlation analysis was conducted between PERG (Magnitude [Mag], MagnitudeD [MagD] and Magnitude D/Magnitude ratio [MagD/Mag ratio]) and ONH measurements (Rim Area and Bruch's Membrane Opening-Minimum Rim Width [MRW]), after controlling for DA. Hierarchical multiple regression analysis was used to determine the ability of PERG to predict variance in rim area and MRW global measurement after controlling for DA.

Results: After controlling for DA, partial correlation analysis showed a significant correlation between Mag, MagD and rim area, ($r>0.503$, $p<0.005$). Similarly, Mag, MagD and MagD/Mag ratio were significantly correlated with MRW temporal superior (MRW-TS) ($r>0.400$, $p<0.039$), and with MRW nasal inferior (MRW-NI) ($r>0.431$, $p<0.025$) sectors. MagD and MagD/Mag ratio significantly correlated with MRW global ($r>0.407$, $p<0.035$).

In two separate hierarchal linear regression models, in the prediction of rim area, after controlling for DA (step 1), Mag then MagD (step 2) explained an additional 26.8% and 25.2 % of variance in rim area ($B=0.174$ [95% CI: 0.065, 0.283], $P<0.005$) and ($B= 0.160$ [95% CI: 0.056, 0.265], $P<0.005$), respectively.

In prediction of MRW global, after controlling for DA (step 1), MagD then MagD/Mag ratio (step 2) explained an additional 13.4% and 12.8% of the variance in MRW global, ($B= 38.921$ [95% CI: 3.872,73.970], $P<0.05$) and ($B=129.024$ [95% CI: 9.589, 248.460], $P<0.05$), respectively.

Conclusions: PERG can predict variance not only in rim area and global MRW, but also in MRW-TS and MRW-NI sectors, after controlling for DA. This highlights the benefit of using PERG in addition to OCT ONH morphology measurements to increase diagnostic accuracy for early glaucoma diagnosis.

CONTROL ID: 3544700

SUBMITTER (NAME ONLY): Baskar Arumugam

TITLE: Modelling Age Effects of Myopia Progression for the MiSight 1 day Clinical Trial

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Arumugam, A. Bradley, D. Hammond, P. Chamberlain, Coopervision Inc, Pleasanton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age has a dominant impact on myopia progression rates within a population (Chua et al 2016). Controlled clinical interventions are, however, routinely constrained by a limited age range of subjects and retaining control cohorts for long study durations is difficult. This study aims to derive estimated annualized elongation (EAnE) models for both Proclear 1 day (omafilcon A, single vision, Coopervision, Inc.; P1d) and MiSight 1 day (omafilcon A, dual focus, CooperVision, Inc.; M1d) soft contact lens wearers over a 10 year age span from a 6-year randomized controlled clinical trial dataset.

Methods: Arumugam et al. (AAO, 2020) found that age also significantly affected axial progression rate in treated eyes, and after accounting for age, number of years in treatment had an insignificant effect, validating cross sectional analysis by age of the clinical trial data. Annualized measured axial elongations (AMAE) were calculated across the full age range (8–18 years) irrespective of treatment years in the study using a cross sectional age analysis. Control group (P1d) AMAE allowed optimization of equation coefficients for the exponential decay function as previously reported by Brennan et al. (AAO, 2018), using an iterative least squared error method. The AMAE rates for subjects treated with the M1d lenses were also plotted by age and the EAnE model was derived based on best fits.

Results: The P1d and M1d datasets consisted of 350 and 888 annualized changes in axial length, respectively. The following univariant (age in years) P1d and M1d EAnE models were derived:

P1d EAnE: $([-0.08135 * e^{-0.1(\text{age})}] / -0.1) - 0.06295$ $R^2: 0.97$

M1d EAnE: $-0.149 \ln(\text{age}) + 0.4659$ $R^2: 0.96$

The P1d EAnE function exhibits a concordant correlation coefficient to the Brennan 'white' ethnicity equation (EAnE = $0.268 * e^{-0.144 * [\text{age} - 9.02]}$ $R^2: 0.97$). A natural logarithm equation was found to be the best fit the M1d dataset. Using these EAnE models, the calculated cumulative axial elongation from 8 to 18 years of age for subjects wearing P1d and M1d lenses are predicted to be 1.84mm and 0.97mm respectively.

Conclusions: EAnE models predict, that if a myope commences M1d lens wear at 8 years of age and continues full time wear until 18, an average myopia control treatment effect of 0.87mm (>2D) would ensue. The findings further support evidence that the greatest impact on eye growth will occur when treatment is started early and sustained longer.

CONTROL ID: 3544702

SUBMITTER (NAME ONLY): Harumasa Yokota

TITLE: Effect of prorenin peptide vaccine on an early phase of diabetic retinopathy in murine model of type 2 diabetes mellitu

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yokota, J. Hanaguri, S. Yamagami, T. Nagaoka, Nihon Daigaku Igakubu Daigakuin Igaku Kenkyuka, Itabashi-ku, Tokyo, JAPAN|H. Hayashi, H. Nakagami, Osaka Daigaku Daigakuin Igakukei Kenkyuka Igakubu, Suita, Osaka, JAPAN|F. Kushiyaama, Meiji Yakka Daigaku, Kiyose, Tokyo, JAPAN|

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ABSTRACT BODY:

Purpose: Prorenin has been viewed as an ideal target molecule in preventing diabetes mellitus (DM)-related microangiopathies. However, none of drugs can specifically inhibit prorenin activation. Here we employed peptide vaccine technique and tested the effect of prorenin peptide vaccine (V_P) in murine models of type 2 diabetes mellitus (DM)

Methods: V_P was prepared by conjugating selected antigen from prorenin prosegment to keyhole limpet hemocyanin (KLH). C57BL/6J underwent 2× injection of KLH only (as control vaccine), peptide E1-conjugated with KLH (E1-KLH), E2-KLH or E3-KLH to optimize V_P . Then, mice underwent 3× vaccination. For three groups; db/db+KLH, db/db+ V_P and db/m+KLH, electroretinogram (ERG) and histological analyses were performed to assess the effect of V_P .

Results: E2-KLH was determined as V_P in subsequent experiments between three candidate vaccines. Specific immunoreactivity of anti-sera from V_P -immunized C57BL/6 mice against prorenin and BSA-conjugated E2, but not renin. Subcutaneous injection of 20 μ g V_P prevented the prolongation of implicit time of b-wave in db/db mice ($p < 0.05$). V_P significantly reduced the number of iba-1 positive activated microglia in the retina of db/db mice compared to db/db+KLH ($p < 0.05$). Furthermore, histological analysis demonstrated that V_P mitigated glomerular and tubular expansion in the kidney and fatty liver. V_P did not affect body weight, glucose levels and blood pressure.

Conclusions: Vaccination against prorenin is effective and safe in protecting the retina from insults due to type 2 DM.

CONTROL ID: 3544704

SUBMITTER (NAME ONLY): Yanjinsuren Otgondemberel

TITLE: Response Characteristics of Direction-Selective Ganglion Cells to Electric Stimulation in Rabbit and Mouse Retinas

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Otgondemberel, H. Roh, M. Im, Brain Science Institute, Korea Institute of Science and Technology, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|Y. Otgondemberel, M. Im, Division of Bio-Medical Science & Technology, University of Science and Technology, Daejeon, KOREA (THE REPUBLIC OF)|H. Roh, Division of Electrical Engineering, Korea University, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|S. Fried, VA Boston Health Care System Jamaica Plain Campus, Boston, Massachusetts, UNITED STATES|S. Fried, Neurosurgery, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: One of the key challenges remaining in the field of retinal prosthetics would be a lack of comprehensive understanding of electrically-evoked responses of various types of retinal ganglion cells (RGCs). For example, directionally selective (DS) RGCs are known to encode motion information from the visual world; interestingly however, no study has been reported regarding characteristics of network-mediated responses arising in those RGCs. In the present work, for the first time, we have explored the electrically-elicited network-mediated responses of ON-OFF DS RGCs in rabbit and mouse retinas.

Methods: Cell-attached patch-clamp technique was used to record spikes from DS RGCs in retinal explants from rabbits (n = 8) and mice (n = 6), both widely-studied species in retinal researches. ON-OFF DS RGCs were identified by their robust spiking at both onsets and offsets of stationary spot flashes and white bars moving in twelve different directions. Their direction selectivity index (DSI) was computed from moving bar responses. A monophasic half-sinusoidal pulse (4 ms duration, -100 μ A amplitude) was delivered from the epiretinal side. The stimulus was repeated at least 5 times.

Results: Unlike network-mediated responses of non-DS RGCs in our previous works, electric pulse evoked remarkably heterogeneous spiking patterns across DS RGCs in each species. Also, Fano Factors (FFs) of their spike counts were quite high in both species (0.84 ± 0.50 and 0.72 ± 0.40 for rabbits and mice), indicating unreliable responses across repeats of electric pulses. Intriguingly, the two species showed a contrasting difference in the relationship between electrically- and light-evoked responses: the peak firing rates of the rabbit DS RGCs were in a strong inverse correlation with their DSIs ($r = -0.839$). On the contrary, the peak firing rates of the mouse DS RGCs appeared to have a weaker correlation with their DSIs ($r = 0.161$).

Conclusions: Given the critical role in the dynamic visual perception, the natural responses of DS RGCs may be crucial for improved artificial vision. However, the heterogeneous and inconsistent network-mediated responses (i.e. high FFs) suggest it may be difficult. Also, the different correlations with light-evoked responses suggest the species-specific DS circuits should be better understood.

CONTROL ID: 3544705

SUBMITTER (NAME ONLY): A Sue Menko

TITLE: Uncovering the Properties of Lens Resident Immune Cells

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Menko, Pathology, Anatomy and Cell Biology, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): A Sue Menko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Our previous studies provided the first evidence that despite the fact that the lens is avascular, it contains a subpopulation of tissue resident immune cells, a typical feature of most other tissues. As the properties of resident immune cells can include many tissue-protective functions, our purpose is to provide a deeper understanding of the properties specific of this unique lens cell population in order to begin to elucidate how they function in the lens.

Methods: This study uses both human and chick embryo post-cataract surgery injury explant cultures. Properties of resident immune cells associated with the lens epithelium on their endogenous basement membrane capsule and after these cells migrate of the capsule and onto the rigid tissue culture plastic surrounding the explant are examined by confocal microscopy imaging following immunofluorescence labeling.

Results: Resident immune cells that we have previously shown populate the lens during development were found to travel to the lens along the ciliary zonules in the absence of a vasculature. These cells were identified based on their expression of a monocyte/macrophage molecule. In the human post-cataract surgery explants CD45+ immune cells interspersed among the cells of the lens epithelium often extend dendritic processes consistent with the morphology of antigen presenting cells. These CD45+ cells migrate to the wound edge of the explant, where the transmembrane glycoprotein CD44, a hyaluronic acid receptor expressed by immune cells, is induced. With the chick post-cataract surgery explants we show that the CD44+ resident immune cells activated to migrate to the wound edge are vimentin-rich cells that express the TLR4 co-receptor CD14, identifying them as monocytes/macrophages and/or dendritic cells. Within 6 days after placing the human post-cataract surgery explants in culture, the CD45+ immune cells present remaining associated with the basement membrane capsule among the lens epithelial cells and those that had migrated onto the rigid substrate surrounding the explant, have acquired a myofibroblast phenotype.

Conclusions: Resident immune cells of the lens function as immediate responders to injury with properties consistent with their function as the liaisons between the innate and adaptive immune response and with the potential to acquire a myofibroblast phenotype, the agents of fibrosis.

CONTROL ID: 3544714

SUBMITTER (NAME ONLY): Kamesh Dhamodaran

TITLE: Decreased levels of Notch signaling in human trabecular meshwork cells cultured on rigid substrate

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Dhamodaran, V. Raghunathan, Department of Basic Sciences, University of Houston College of Optometry, Houston, Texas, UNITED STATES|J. Staverosky, J.A. Vranka, Casey Eye Institute, Oregon Health and Science University Foundation, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) is associated with mechanical changes in the trabecular meshwork, leading to increased aqueous humor (AH) outflow resistance. The role of Notch signaling, an evolutionarily conserved pathway implicated in mechanotransduction, has not been investigated in glaucoma pathogenesis. Here, we determine the expression of Notch pathway molecules in TM cells subjected to cyclical strain or when grown on hydrogels of varying rigidity.

Methods: Primary human total TM (hTM) cells were isolated and validated from donor corneal rings. hTM cells (3-7 passages) were plated on collagen coated 3 kPa or 80 kPa hydrogels for 72hrs with 10% FBS containing Ham's F12 medium. In cyclical strain experiments, hTM cells were cultured on collagen coated PDMS stretch chambers and subjected to uniaxial 20% strain for 24 h at 1Hz. mRNA and protein levels of Notch receptors, ligands, and effectors in the hTM cells was determined by RT-qPCR or western blot.

Results: On stiffer hydrogels, expression of Notch receptors 1(0.6-fold), 2(0.8-fold) 3(0.8-fold) or 4(0.3-fold) was significantly decreased. While expression of Notch ligand Jagged1 was similar on both substrates, expression of Jagged2 (0.4-fold), DLL1 (0.8-fold), 3 (0.8-fold) and 4 (0.3-fold) were all down-regulated. Correspondingly, downstream targets of Notch pathway, Hes3, 5 (0.3, 0.3-fold) or Hey1, 2 (0.4, 0.4-fold) were decreased. In cyclic stretch, expression of Notch receptors 1(0.8-fold), 3(0.9-fold) decreased, whereas Notch2(1.17-fold) increased. While expression of Notch ligands Jagged1 (0.9-fold), Jagged2 (0.8-fold), DLL1 (0.8-fold), 4 (0.8-fold) was down regulated. DLL3 (1.2-fold) was upregulated. Congruently, effectors of Notch pathway, Hes3 (1.2-fold) and 5 (1.2-fold) increased, and Hey1 (0.8-fold) was decreased, compared to non-stretched strains.

Conclusions: Our data demonstrates that Notch signaling in hTM cells differs by mechanical insult. Notably, where substratum stiffness elicited maximal intrinsic differences, cyclical strain did not. These results imply: (i) The different Notch components may have distinct mechanotransduction roles to maintain tissue homeostasis. (ii) Notch signaling may be temporal in cell fate determination. Overall, these findings warrant further studies on the exact role of Notch signal in human trabecular meshwork in health and disease.

CONTROL ID: 3544715

SUBMITTER (NAME ONLY): Paulo Bispo

TITLE: Highly Multiplexed Broad Pathogen Detection Assay for Diagnosis of Ocular Infections

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.J. Bispo, L. Ung, J. Chodosh, L. Sobrin, M.S. Gilmore, Harvard Medical School
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ABSTRACT BODY:

Purpose: Eye infections are among the most common causes of blindness worldwide. The sooner effective therapy can be started, the more vision can be saved. However, current diagnostic modalities are time-consuming, lack sensitivity and inclusiveness, and may result in patients being treated with the wrong drug for long periods. We present a newly developed comprehensive ocular panel designed to improve diagnostic yields and provide a tool for rapid pathogen identification, with potential to improve treatment choices and at earlier stages of the disease

Methods: Using epidemiological information on the etiologies of ocular infections seen at our hospital and in combination with a literature review, we identified 46 pathogens and 2 resistance/virulence markers that are most commonly detected (>90% of cases). Genomic targets were scrutinized for stretches predicted to be specific for a particular species while being conserved across different strains from the same species. Regions of 150 to 300bp in length were selected and a set of primers for pre-enrichment, and two 50mer NanoString compatible probes were designed per target. DNA-DNA hybrids were detected and quantified using the NanoString nCounter SPRINT Profiler

Results: Analytical studies demonstrated highly sensitive detection of a broad spectrum of infectious agents, including bacteria, fungi, viruses and parasites, with limits of detection being as low as 25 femtograms per reaction. We also challenged the diagnostic panel in a pilot clinical study testing samples from infectious keratitis (n=6) and uveitis (n=6) for which the etiologies were confirmed by culture or real-time PCR, and included Gram-positive and -negative bacteria and herpesviruses. The NanoString-based panel correctly identified the causative agent from all clinical specimens. Detection was robust, with probe counts for the targeted pathogen ranging from 5×10^3 to 4×10^5 . For corneal ulcers, higher probe counts seem to correlate with the severity of presentation

Conclusions: This highly multiplexed panel for detection of ocular pathogens offers a sensitive, comprehensive, and uniform assay run directly on ocular specimens, that could significantly improve diagnostics of sight-threatening infections

CONTROL ID: 3544717

SUBMITTER (NAME ONLY): Taylor Shagam

TITLE: Deep learning based binary image quality algorithm for low-cost fundus imaging system in remote care settings

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Shagam, M. Alam, S. Bello, L. Tracewell, B. Rogoff, P. Sha, N. Graves, D. Hitchmoth, M.K. Durbin, N. Manivannan, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: An image quality (IQ) algorithm is important in assisting medical assistants with little to no experience in ophthalmology to judge whether an image is of sufficient quality for clinical diagnosis.

In this study, we developed a binary IQ classification for providing real-time feedback in a remote care or primary care settings.

Methods: Data:

5173 images acquired using VELARA™ 200 (Zeiss, Dublin, CA) camera from a retrospective study were graded by 2 graders and adjudicated by an optometrist). The images were acquired from normal and diseased subjects with various retinal pathologies were graded for quality of readable clinical information in a 1-5 scale (1-very poor and 5-excellent). The ground truth (GT) is determined by converting the gradings to binary: 0- Insufficient if IQ is ≤ 2 (65.6% of 5173 images) and 1-Sufficient if IQ is > 2 (34.4%). Small pupils, incorrect fixation, out of focus and other artifacts were the main causes of insufficient IQ.

Algorithm:

The dataset is split into three: i) training- 3646, ii) validation- 928 and iii) hold-out test – 599. The training set is augmented using flip and brightness adjustments. The deep learning architectures used to train the IQ classification are shown in figure 1. ImageNet weights were preloaded, sigmoid activation with binary cross entropy loss were used. The data was resampled and reweighted to account for the class imbalance. For hyperparameter tuning, all the networks were trained using Adam with cyclic learning rate scheduler and Stochastic Gradient Descent (SGD) with Nesterov momentum. SGD with Nesterov is chosen for the final model as it performed better. Sensitivity, specificity and the execution time were compared to select the final IQ model.

Results: The performance of all networks in hold-out test set is shown in Figure 1. VGG-16 provided high sensitivity, specificity with lower execution time is selected as the final model. It achieved 99% sensitivity, 91% specificity and 220ms execution time in i5-10400H CPU. Figure 2 shows some of the examples results from IQ algorithm.

Conclusions: We developed an image quality algorithm with 99% sensitivity with an execution time to provide real-time feedback to the operator on whether to retake the fundus images.

CONTROL ID: 3544719

SUBMITTER (NAME ONLY): Cameron Czerpak

TITLE: The Curvature and Collagen Network of the Human Lamina Cribrosa in Glaucoma and Control Eyes

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Czerpak, Y. Ling, T.D. Nguyen, Mechanical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|J.L. Jefferys, H.A. Quigley, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure the curvature and features of the collagen beam-network structure of the lamina cribrosa (LC) of post-mortem human glaucoma eyes and analyze for differences between diagnosed glaucoma and age-matched normal eyes.

Methods: The posterior scleral cups of 10 normal eyes and 16 diagnosed glaucoma eyes (Midgett et al. 2020) with axon loss ranging from <10% to >50% were subjected to inflation testing with second harmonic generation (SHG) imaging, and analysis by digital volume correlation (DVC). SHG image Z stacks were analyzed by a custom algorithm (Ling et al. 2019) for ten structural features of the LC beams (Fig 1). The LC curvature was estimated by fitting a 5th order polynomial to the anterior surface of the imaged LC volume (Fig 1d). The structural and strain outcomes were averaged overall and regionally for each specimen. Results will be verified using generalized estimating equation models and linear mixed models.

Results: Preliminary results using unpaired t-tests show mean curvature, Gaussian curvature, and tortuosity averaged over the LC, the central region, and the peripheral region were significantly greater in the LC of diagnosed glaucoma eyes compared to age-matched normal eyes (all $p \leq 0.03$) (Fig 2). The specimen-averaged pore size, and beam aspect ratio (length/width) was significantly smaller in glaucoma eyes than normal eyes ($p \leq 0.04$) (Fig 2).

Conclusions: The smaller average pore size and beam aspect ratio may contribute to a stiffer pressure-induced strain response of the LC. In contrast, the greater curvature and beam tortuosity should produce a more compliant strain response. Computational modeling is needed to estimate the effects of the curvature and LC network structure on the strain response.

CONTROL ID: 3544721

SUBMITTER (NAME ONLY): David Mackey

TITLE: Conjunctival ultraviolet autofluorescence area is predictive of pterygium onset in young adults

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.A. Mackey, G. Lingham, J. Charng, S.S. Lee, S. Yazar, Centre for Ophthalmology and Visual Science, The University of Western Australia, Perth, Western Australia, AUSTRALIA|D.A. Mackey, G. Lingham, J. Charng, S.S. Lee, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|J. Kugelman, D. Alonso-Caneiro, Contact Lens and Visual Optic Laboratory, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|S. Yazar, Garvan Institute of Medical Research, Darlinghurst, New South Wales, AUSTRALIA|M.T. Coroneo, Department of Ophthalmology, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Conjunctival ultraviolet autofluorescence (CUVAF) area has been associated with ocular ultraviolet (UV) radiation exposure and time spent outside. CUVAF area is also associated with greater risk of pterygium on cross-sectional studies; however, longitudinal data is lacking. We investigated the relationship between CUVAF area measured at 20 years of age and incident pterygium over a 7- to 8-year follow-up period.

Methods: Data from the 20-year (age range 19-22 years), 27-year (age range 25-28 years) and 28-year (age range 27-30 years) follow-ups of the Raine Study generation 2 birth cohort were used for this study. CUVAF images were taken at the 20-year follow-up and CUVAF area measured by a single grader using a custom-built software. Pterygium was defined as a wing-shaped fibrovascular growth crossing the limbus and was assessed by a single grader from colour photographs captured at the 20-, 27- and 28-year follow-ups. Participants without CUVAF images taken at the 20-year follow-up or who had a pterygium at the 20-year follow-up were excluded from the analysis. The primary outcome was incident pterygium in either eye. Cox regression was used for statistical analysis.

Results: Of the 1344 participants of the 20-year follow-up, 1313 (97.7%) had CUVAF data and 1298 (96.6%) did not have a pterygium. Of these, 970 (74.7%) had colour photos taken at either the 27- (n=907) or 28-year (n=712) follow-ups and incident pterygia in either eye were present in 13 (1.4%) participants. Of 159 (15%) of participants who reported smoking cigarettes at the 20-year follow-up, none had an incident pterygium. On Cox regression, total CUVAF area (of both eyes) was strongly associated with risk of incident pterygium (per 10mm² increase, hazard ratio [HR]=1.38, 95% confidence interval [CI]: 1.21, 1.57) and remained strongly associated with incident pterygium after adjusting for sex and self-reported time spent outside in summer (HR=1.45, 95% CI: 1.21, 1.73). The area under the ROC curve for total CUVAF area alone was 0.81. Sex, axial length, 25-hydroxyvitamin D concentration and self-reported family history of pterygium were not associated with risk of incident pterygium.

Conclusions: CUVAF area at 20 years was a strong predictor of subsequent development of pterygium and may be useful in identifying patients at high risk of pterygium.

CONTROL ID: 3544722

SUBMITTER (NAME ONLY): Kyle Helms

TITLE: The Tsh transcription factor and the transcriptional co-regulator CtBP interact in *Drosophila melanogaster* eye development

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Helms, J. Curtiss, Biology, New Mexico State University, Las Cruces, New Mexico, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kyle Helms: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Curtiss: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Cell fate determination and proliferation need to be coordinated during development of multicellular organisms, and this requires tissue-specific gene transcription. Transcriptional co-regulators mediate between sequence-specific transcription factors and the transcriptional machinery to promote tissue-specific gene transcription. Current evidence suggests that the sequence-specific transcription factor, Teashirt (Tsh), and the transcriptional co-regulator, C-Terminal Binding Protein (CtBP), have roles in coordinating cell fate determination and proliferation during eye development in the fruit fly, *Drosophila melanogaster*. Whether these proteins interact physically during eye development has yet to be determined.

Methods: We have used genetic and molecular tools to address this question. Over-expressing tsh in proliferating eye precursors results in loss of eye tissue, and loss-of-function mutations in CtBP suppress the effects of over-expressing tsh, suggesting that tsh and CtBP function in the same process during eye development. Furthermore, in vitro Glutathione-S-Transferase (GST)-pulldowns detect direct physical interactions between Tsh and CtBP, and co-immunoprecipitations from lysates of proliferating eye precursors confirm the interaction in vivo.

Results: These results suggest that Tsh and CtBP interact physically during eye development and that their interaction is important for proper eye development.

Conclusions: Future experiments using this GFP-tagged tsh and mass spectrometry will help to identify any proteins complexed with Tsh/CtBP and provide further insight into to how this complex regulates proliferation during the development of the eye.

CONTROL ID: 3544725

SUBMITTER (NAME ONLY): Darrian Kelly

TITLE: Coup and Counter Coup Injury in a Focal Unilateral Ocular Blast Injury in Rats

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kelly, F. Gonzalez-Fernandez, Research Service, Veterans Affairs Medical Center, Jackson, Mississippi, UNITED STATES|M. Harrigill, B. Grayson, University of Mississippi School of Medicine, Jackson, Mississippi, UNITED STATES|R. Chen, H. Zhu, Department of Otolaryngology, University of Mississippi School of Medicine, Jackson, Mississippi, UNITED STATES|D. Kelly, Research Division, PathRD, Inc., Jackson, Mississippi, UNITED STATES|F. Gonzalez-Fernandez, Departments of Ophthalmology and Pathology, University of Mississippi School of Medicine, Jackson, Mississippi, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy is increasingly associated with traumatic brain injury. However, the mechanism(s) behind its often insidious pathology are not understood. Although animal models can provide a means to study this complex process, off target injury can complicate the disease picture. Here, we develop a rat model that provides a reproducible system reminiscent of the coup and counter coup/Commotio Retinae pathology.

Methods: A compressed air driven shock tube delivered 26 psi blast waves from a 3 mm diameter stainless steel nozzle held stereotaxically 2 mm over the cornea of 20 anesthetized age matched adult Sprague-Dawley rats. Body temperature was maintained at 37°C, and heart and breathing rate were monitored. One eye received the blast; sham animals received no blast. After 4 wks under cyclic light: ERGs, electron microscopy, sagittal FFPE sections carefully oriented through the optic nerve and pupil were stained with H&E and PAS. Cell counts of the outer-, inner-nuclear, and ganglion cell layer cell at 400 μ intervals were made from digitized scans with QuPath software.

Results: The animals tolerated the blast without physiological signs of stress, or external evidence of injury to the globe or ocular adnexa. In three animals, hemorrhage over the optic nerve head was noted. Flash intensity plots showed a reduction in ERG a and b wave amplitudes. Cellular morphometrics showed two patterns of degeneration. Pattern 1, Inner Nuclear layer degeneration, or ganglion cell loss with optic nerve degeneration; Pattern 2, Outer Nuclear Layer degeneration with RPE dropout often involving the mid-peripheral retina. EM showed disruption and breaking of rod outer segments, and separation of outer segments from the inner segment compared to controls.

Conclusions: In vivo focused blast injury to a single eye can be accomplished without external trauma or physiological stress, while also avoiding subjecting the body to the blast wave. Coup injury (posterior retinal hemorrhage and optic nerve trauma), and indirect (countercoup) injury (outer segment disruption and outer-inner segment separation, mid-peripheral outer nuclear layer cell degeneration with RPE loss) were readily produced. The focal single-eye blast model provides a valuable system recapitulating human ocular traumatic injury including Coup and Commotio Retinae, and other countercoup pathology.

CONTROL ID: 3544731

SUBMITTER (NAME ONLY): Andrea Vincent

TITLE: Harboyan Syndrome with biallelic SLC4A11 pathogenic variants misdiagnosed as congenital CMV infection

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Vincent, G. Kiray, S. Hull, Eye Department, Auckland City Hospital, Auckland, Auckland, NEW ZEALAND|A.L. Vincent, G. Kiray, S. Hull, Ophthalmology, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|

Commercial Relationships Disclosure (Abstract): Andrea Vincent: Commercial Relationship: Code N (No Commercial Relationship) | Gulunay Kiray: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Hull: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Harboyan syndrome is a rare autosomal recessive disorder characterised by congenital hereditary corneal endothelial dystrophy (CHED) with a later onset of sensorineural hearing loss (SNHL) due to pathogenic variants in the SLC4A11 gene. Congenital cytomegalovirus infection (CMV) may manifest with SNHL and visual impairment. We present a case of a 4 year old girl, diagnosed at birth with congenital CMV infection, but careful phenotyping and genetic testing permitted a definitive diagnosis.

Methods: Case report, clinical ocular and auditory phenotyping, next generation sequencing of corneal genes (Asper Ophthalmics), and parental segregation of variants

Results: A 4 year old female presented with bilateral corneal clouding, and BCVA of 6/19 OD and 6/15 OS. At pregnancy her mother had a 2nd trimester febrile illness and converted from CMV negative to positive, with CMV detected in an umbilical blood sample. Age 2 months a faint corneal haze was noted and normal audiology at 2 months (auditory brain response), and 8 months (otoacoustic emissions). At 18 months of age she developed a right esotropia, and was recorded as having clear corneas. A hypermetropic correction and patching was prescribed. Review at age 3.5 years showed bilateral moderate central corneal oedema, no evidence of bullae, central corneal thicknesses of 980 microns, and a clear periphery, with normal retina and optic nerves. Thought to be consistent with CHED, audiology was repeated demonstrating slight SNHL from 500-2000 Hz, sloping down to moderate SNHL at 8000Hz bilaterally. Genetic testing identified a previously reported pathogenic variant in SLC4A11 c.2609T>C, p.(Leu870Pro) and a second variant c.1318G>C, p.(Gly440Arg) with an allele frequency of 6.57e-6 in gnomAD , and damaging by multiple in silico tools. Parental segregation of these variants was confirmed.

Conclusions: Congenital CMV infection affects 1% of all births although only 15-20% have sequelae. Although progressive SNHL may be a feature, corneal clouding is not described, with the most common ocular features being strabismus, optic atrophy, cortical visual impairment and chorioretinitis. Biallelic mutations in SLC4A11 are more commonly causative of isolated CHED2, but also described in the rarer Harboyan syndrome. The combination of corneal opacification and progressive SNHL should alert the clinicians to alternate diagnoses.

CONTROL ID: 3544732

SUBMITTER (NAME ONLY): Aditya Rali

TITLE: Prospective Analysis of Patient Satisfaction with Inherited Retinal Disease Clinic Visits Conducted via a Hybrid Telemedicine-based Approach

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Rali, J. Yan, N. Jain, Emory Eye Center, Atlanta, Georgia, UNITED STATES|S. Partin, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic adversely impacted patient access to in-person healthcare, bringing telemedicine to the forefront. The Emory Ophthalmic Genetics Service (EOGS) adopted a hybrid model of care, allowing patients to meet the physician via a video telehealth encounter and separately obtain ancillary in-person diagnostic testing. The goal of this study is to evaluate patient satisfaction and completion rate of diagnostic genetic testing with this novel care model for patients with inherited retinal diseases (IRDs).

Methods: Patients age 18 and older who were new to the EOGS and participated in a telemedicine-based IRD clinic appointment after October 1st, 2020, were eligible for this study. After obtaining informed consent, a trained interviewer administered a 14-question survey over the telephone. Each survey item contained 5 Likert-scale response options, assigned a value from 1 to 5. The survey was designed to address two main factors—information exchange and patient comfort. A mean “favorability index” for patient satisfaction was calculated for each item with a score of 5 being most favorable. Completion rate of diagnostic genetic testing was also evaluated. Diagnostic accuracy was determined by comparing the clinical diagnosis to the genetic diagnosis, where available, and results compared to a control group of in-person encounters from July 2019 to December 2019.

Results: Sixteen of 21 eligible patients completed the survey (Figure 1). Of these, 7 (44%) were female, with median age 56.5 (range, 25 to 73 years). Patients lived a median of 29.5 miles (range, 5 to 147 miles) from the Emory Eye Center. Six (37.5%), 6 (37.5%), and 14 (87.5%) patients underwent ancillary in-person testing with electroretinography, perimetry, and fundus imaging, respectively. The median (range) favorability index was 5 (4-5) and 4 (3-5) for information exchange and patient comfort, respectively. Responses were favorable (>3) for telemedicine for all survey items except one. Diagnostic genetic testing was recommended for 12 (75%) patients, and completed in 10 (83%) of those.

Conclusions: Our results suggest high patient satisfaction with a hybrid telemedicine-based approach for care delivery to patients with IRDs. Further study in a larger sample is warranted.

CONTROL ID: 3544738

SUBMITTER (NAME ONLY): Davis Zhou

TITLE: Mitochondrial Dysfunction in Primary Open-angle Glaucoma Characterized by Flavoprotein Fluorescence at the Optic Disc Rim

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Recent studies have implicated mitochondrial dysfunction in the pathophysiology of glaucoma, with in vivo characterization at the macula by Geyman et al. Evaluation of these mitochondrial alterations has been enabled measurement of flavoprotein fluorescence (FPF) through a non-invasive imaging platform. The current study is the first to evaluate FPF at the optic disc rim in primary open-angle glaucoma (POAG) patients compared to healthy controls.

Methods: 50 eyes of 30 POAG patients and 36 eyes of 20 healthy controls were imaged using the OcuMet Beacon (OcuSciences, Ann Arbor, MI; Investigational Device). Infrared and FPF measurements were obtained at the optic nerve head (ONH). Built-in software algorithms identified the optic disc margins on the infrared image and demarcated an elliptical annulus around the ONH rim. FPF was subsequently measured within the annulus boundaries. Averaged FPF of the entire area within the annulus and within anatomical sectors (temporal, superior, nasal, and inferior) were determined for each subject. Distinctions in FPF between POAG and control eyes were evaluated through mixed-effects logistic regression, adjusted for age and interocular pressure. Correlation between FPF and clinical characteristics for glaucoma were also characterized using linear mixed-effects models.

Results: The mean \pm SD of global FPF was significantly higher in POAG eyes compared to control eyes (46.4 \pm 27.9 vs. 28.0 \pm 11.7, $P<0.001$). Differences in FPF between POAG and controls eyes were also present for temporal ($P=0.001$), superior ($P<0.001$), nasal ($P=0.002$), and inferior ($P=0.001$) sectors. FPF exhibited significant correlation to Humphrey 24-2 visual field mean deviation ($P=0.001$). Significant correlation was also present between global FPF and global circumpapillary retinal nerve fiber thickness ($P<0.001$) and at the superior ($P=0.02$), inferior ($P=0.02$), and nasal ($P=0.003$) quadrants.

Conclusions: Measurement of FPF suggests increased mitochondrial dysfunction at the optic disc rim in POAG eyes. FPF may prove useful for evaluation of glaucomatous damage and may permit further exploration of pathophysiology. Future studies on stage-stratified POAG eyes will aim to assess the potential roles for FPF assessment in the detection of early glaucomatous pathology.

CONTROL ID: 3544740

SUBMITTER (NAME ONLY): Patrick Simard

TITLE: THE MONTREAL EXPERIENCE: A RETROSPECTIVE STUDY
PART II- ORTHO-K AND SOFT MULTIFOCAL LENS PERFORMANCES

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Simard, L. Michaud, R. Marcotte-Collard, School of Optometry, Université de Montreal, Montreal, Quebec, CANADA|P. Simard, R. Marcotte-Collard, Clinique d'Optométrie Bélanger, Montreal, Quebec, CANADA|M. OUZZANI, Optometry, université d'Oran, Oran, TUNISIA|

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ABSTRACT BODY:

Purpose: To evaluate the efficacy of different designs of orthokeratology (OK) soft multifocal lenses (SMCL) and low-dose atropine (LAD) to control myopia evolution. The primary outcome relates to axial length (AL) progression during 24 months.

Methods: This is a retrospective study based on data that are extracted from the file of each patient who: (1) consulted EOUM between Jan 2017 and Dec 2018 and (2) were kept under the same MCS (same design/concentration).

Clinical population is composed of 104 SMCL, 140 OK and 42 LDA participants. Elements analyzed include baseline age, gender, ethnicity, spherical equivalent refractive error (SEQ), photopic pupil size, flat and steep K readings. AL was also evaluated at baseline and after 6, 12 and 24 months. To assess whether intervention had a statistically significant effect, a complex statistical model was built. It was developed by first consider all collected parameters. Then, statistically insignificant predictor terms were removed using backward stepwise elimination. In the final model, 5 predictors were retained (month, SEQ, gender, age and age-month interaction).

Results: For OD only, considering SMCL, 4 designs are compared. AL variation at 12/24 months was: 0.14 +/- 0.18 (N=43) and 0.29 +/- 0.29 (N=22) for senofilcon A; 0.07 +/- 0.29 (N=16) and 0.33 +/- 0.66 (N=10) for comfilcon A, 0.18 +/- 0.15 (N=18) and 0.33 +/- 0.25 (N=9) for Omafilcon Toric, 0.13 +/- 0.1 (N=8) and 0.2 +/- 0.06 (N=5) for etafilcon A. About OK lenses, AL results are: 0.18 +/- 0.19 (N=40) and 0.35 +/- 0.27 (N=36) for HDS 5 curves, 0.05 +/- 0.19 (N=44) and 0.17 +/- 0.29 (N=19) for custom 7 curves design; 0.13 +/- 0.17 (N=16) and 0.23 +/- 0.19 (N=11) for custom double-reservoir design, 0.03 +/- 0.18 (N=13) and 0.21 +/- 0.33 (N=15) for a 4 zones VST design. LDA results are 0.21 +/- 0.16 (N=34) and 0.37 +/- 0.25 (N=19). There was no statistical difference between SMCL or OK lenses, within the same category. However, OK led to significant better control after 1 year, which was no longer true after 24 months (see part 1)

Conclusions: When correctly selected at baseline, there is no long term difference between contact lens modalities used to control myopia evolution. OK lenses seem to give better results at the beginning but SMCL becomes as efficient with time. Atropine seems to lead to increased evolution at any time point.

CONTROL ID: 3544745

SUBMITTER (NAME ONLY): Matthew Reilly

TITLE: A quantitative theory linking molecular-level events to changes in lens biomechanical and optical properties

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.A. Reilly, W. Rich, T. Brandt, N. Pennza, Z. Chen, D. Valenzuela, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|M.A. Reilly, Ophthalmology & Visual Science, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related changes in the optical and biomechanical properties of the lens cause presbyopia. However, the molecular origins of these changes remain unknown. In this study, experimental and computational approaches were combined to offer a mechanistic theory of age-related changes in lens material properties.

Methods: Fresh porcine lenses were characterized intact using digital photography and lens compression to determine their macroscopic optical and biomechanical properties. Lenses were then homogenized and fractionated, allowing further characterization using Raman spectroscopy (RS), dynamic light scattering (DLS), and dynamic shear rheometry (DSR). Experiments were conducted at 50°C to simulate “biochemical aging.” The resulting data were used to calibrate a biochemical computational model of lens aging. This model simulated the kinetics of biochemical changes in the lens while predicting changes in optical and mechanical properties.

Results: RS indicated the thermal stability of lens proteins up to ~57°C, suggesting that incubation at 50°C may be a reasonable model for acceleration of biochemical kinetics in the lens. RS, DLS, and DSR measurements suggest that protein structural modifications precede aggregation, which in turn precedes changes in viscoelastic properties of lens protein solutions. At the macroscopic level, lens stiffening occurred at timescales very similar to those found using DSR. Changes to lens transparency occurred later in the process. Multi-scale modeling of these changes demonstrate the feasibility of protein unfolding leading to aggregation, then binding to the lens’ cytoskeleton. This could effectively reinforce the cytoskeleton by decreasing the mobility of its proteins.

Conclusions: While it is unknown whether thermosetting pig lenses recapitulates physiological aging mechanisms, this study offers the first mechanistic theory linking biochemical events to biomechanical and optical changes in lens material properties. Similarities between the ultimate material properties of intact lenses, homogenized lenses, and fractionated homogenates suggest that the simple experimental and theoretical models may capture the key aspects of age-related changes in lens material properties. Future work will require experiments using human donor lenses to ascertain the utility of both the experimental and theoretical models in understanding aging in the human lens.

CONTROL ID: 3544747

SUBMITTER (NAME ONLY): Ahmed Omar

TITLE: Effect of S-Nitrosylation on post-mortem donor cornea endothelial health during hypothermic storage period

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Omar, D. Daroszewski, J.H. Lass, Ophthalmology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|A. Omar, J.H. Lass, Eversight Eye Bank, Cleveland, Ohio, UNITED STATES|O. Sawant, K. Jones, S. How, Center for Vision and Eye Banking Research, Eversight, Cleveland, Ohio, UNITED STATES|J. Reynolds, L. Zhu, Institute for Transformative Molecular Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|J. Reynolds, L. Zhu, Department of Anesthesiology and Perioperative Medicine, University Hospitals, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Protein S-nitrosylation (SNO) is the means by which nitric oxide (NO) bioactivity is conveyed throughout the body to regulate all manners of cellular function. Our previous work has suggested that addition of one or more SNO agents to preservation solutions can extend storage duration and improve the functional status of transplantable organs. This report characterizes the effect of SNO therapy on the corneal endothelial cells (CECs) during hypothermic storage, a key element in keratoplasty success.

Methods: Paired post-mortem human corneas (n=8) from research-consented donors were incubated in the hypothermic corneal storage solution (Life4⁰C, Numedis, Inc.) with SNO agent or without SNO agent. CEC density and corneal thickness were measured at day 0, 7 and 14 using Konan CellChek D+ and OptoVue OCT machine, respectively. Total RNA from CEC layer was isolated using Qiagen MiniKit on day 14 and subjected to RNA-Seq to analyze differential gene expression pattern.

Results: Under normal circumstances during hypothermic storage, CEC density tends to decrease and corneal thickness tends to increase. CEC density was decreased by 8.2% for SNO without donors control group, while it remain unaltered for SNO group between day 7 and day 14. Corneal thickness was increased by 15% in the control group compared to only 8.6% increase in the SNO group between day 7 and 14. RNA-Seq analysis revealed more than 70 genes (transcripts) that were differentially expressed in the SNO group compared to the control group ($P \leq 0.05$, $|\text{Log}_2 \text{Fold Change}| \geq 0.5$).

Conclusions: S-Nitrosylation therapy of hypothermic corneal storage might be beneficial to improve the quality of donated human corneas that are used for keratoplasty. With the significant alteration of transcriptome of the CEC with SNO therapy, these changes might contribute towards programming of the CECs to regulate long-term graft survival.

CONTROL ID: 3544750

SUBMITTER (NAME ONLY): MARIANA AKEMI MATSURA MISAWA

TITLE: Detection of SARS-CoV-2 on conjunctiva by rRT-PCR in patients with severe form of COVID-19

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. MATSURA MISAWA, T. Tanaka, P. Gomes Oliveira Braga, T. Minelli, J. Kato, J.H. Yamamoto, Department of Ophthalmology, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|T. Tanaka, Instituto de Pesquisa e Ensino Santa Cruz - IPESC, Hospital Santa Cruz, Sao Paulo, São Paulo, BRAZIL|M. Soares Gomes Gouvêa, J. Rebello Pinho, Institute of Tropical Medicine and Department of Gastroenterology, Universidade de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has already been detected in ocular samples. However, the role of the eye in Coronavirus disease 2019 (COVID-19) is still unclear. We investigated the presence of SARS-CoV-2 in conjunctival swabs from patients with confirmed severe form of COVID-19 searching for differences in the presentation and assay positivity.

Methods: This cross-sectional study included 50 conjunctival swab samples (one eye per patient) collected from 50 patients with confirmed COVID-19 in Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, Brazil. Samples were collected within 24 hours from the naso/oropharyngeal swab. Inclusion criteria was severe/critical disease and indication for hospitalization according to the Institutional Guideline, which was the presence of Severe Acute Respiratory Syndrome. Conjunctival swab was collected from the inferior fornix, without anesthesia, using a nylon flocked swab. Real-time reverse transcription polymerase chain reaction (rRT-PCR) was performed with primers and probes described in CDC protocol. The study was approved by the Institutional Ethics Committee and informed consent was obtained prior to procedures.

Results: Twenty-four patients were male and twenty-six were female. Median age was 57.38 years (SD 15.23). Mean duration of symptoms before ocular sampling was 7.6 days (SD 3.52). Naso/oropharyngeal swab RT-PCR (within 24 hours from the conjunctival swab) was positive in 34 (68%) patients, negative in 14 (28%) and inconclusive in 2 (4%) patients. All the patients with negative or inconclusive RT-PCR had COVID-19 diagnosis confirmed by another naso/oropharyngeal swab or serology. Five (10%) conjunctival swabs resulted in positive rRT-PCR analysis and two (4%) had inconclusive results. Among the positive patients, 2 patients had a negative naso/oropharyngeal swab and 1 patient had an inconclusive result. None of the patients had ocular symptoms.

Conclusions: The positivity rate of conjunctival swab for SARS-CoV-2 was higher when compared to previous studies and similar to those that evaluated moderate to severe forms of COVID-19, and was not associated with ocular symptoms. This suggests that a greater viral load may be present in the tear film of patients with severe form of COVID-19 and may not be associated with conjunctivitis. Special concern should be taken to healthcare workers.

CONTROL ID: 3544759

SUBMITTER (NAME ONLY): Casey Anthony

TITLE: Clinical Outcomes Following Intravitreal Methotrexate Therapy for Vitreoretinal Lymphoma

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Anthony, C. Bavinger, J. Shantha, A. Voloschin, G. O'Keefe, H.E. Grossniklaus, S. Yeh, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the clinical outcomes of intravitreal methotrexate (MTX) therapy for the treatment of vitreoretinal lymphoma (VRL)

Methods: Single-center retrospective case series of patients with a diagnosis of VRL and treated with intravitreal MTX at Emory University. Patient records were reviewed for demographic information, ocular exam findings, disease course, and treatment regimens including number of MTX injections. Clinical outcomes recorded included final visual acuity (VA), time to partial (PR) or complete response (CR), disease-free survival, time to relapse, number of relapses, and any non-ocular CNS progression.

Results: Ten eyes of 7 patients (4 male, 6 female) were reviewed. The mean age was 70±years (range, 56-85). Five patients had a diagnosis of primary CNS lymphoma with a history of systemic chemotherapy. Three eyes (30%) exhibited vitreous involvement, four (40%) had subretinal lesions, and three (30%) presented with both. Mean initial logMAR VA was 0.38±0.52 (Snellen visual equivalent 20/50), while mean final logMAR VA was 0.34±0.27 (20/40) with a mean follow-up time of 26 months (range, 3-49 months).

Patients received an average of 6 intravitreal MTX injections (range, 1-10) over the course of treatment. Two patients were receiving systemic chemotherapy at the time of injection. Mean time to either PR or CR was 57±37 days, and 6 eyes (60%) exhibited regression with no relapse after local treatment. For the 4 eyes that relapsed, time to first relapse was 193±155 days, and one eye experienced a second relapse. VA remained stable overall between initial treatment and 1, 3, 6, and 12-month follow-up ($P>0.05$ for paired comparisons); however, the largest VA improvement occurred at 3-months, with an average ~2-line improvement to 20/30. One patient with PVRL developed non-ocular CNS lymphoma.

Conclusions: Intravitreal MTX was well-tolerated and led to disease response in the majority of patients at approximately 2 months after initiation of treatment of intraocular lymphoma. Further studies on the efficacy of intravitreal treatment alone versus combined systemic and intravitreal treatment are warranted.

CONTROL ID: 3544760

SUBMITTER (NAME ONLY): Vivek Srinivasan

TITLE: In vivo imaging of inner plexiform layer (IPL) stratification in the human retina with visible light Optical Coherence Tomography (OCT)

SESSION TITLE: Advanced imaging technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.J. Srinivasan, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|V.J. Srinivasan, Ophthalmology and Vision Science, University of California Davis, Davis, California, UNITED STATES|T. Zhang, A.M. Kho, Biomedical Engineering, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Vivek Srinivasan: Commercial Relationship(s);Optovue Inc.:Code P (Patent) | Tingwei Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Aaron Kho: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Employing visible light OCT, we report a stereotyped reflectivity pattern of the inner plexiform layer (IPL) that parallels IPL stratification. We characterize this pattern non-invasively in adult human subjects without ocular pathology.

Methods: Subjects were imaged by a visible light OCT prototype instrument at UC Davis with 1 micron axial resolution. A total of 15 eyes of 15 subjects were analyzed. The inner retinal layer boundaries were demarcated. At each transverse position, the IPL intensity was interpolated onto an IPL thickness percentage abscissa axis. Images were partitioned into transverse segments of 450 microns (1.5 degrees) and IPL intensities were averaged across each segment (Figure 1A-B). To detect salient features of intensity profiles, a 14th order polynomial fit was performed on the intensity profile within the IPL (Figure 1C). The polynomial fit provided access to features such as stratum location and intensity (Figure 1D).

Results: Figure 2A shows subject-by-subject fitting of stratum S5 intensity versus IPL thickness with mixed effects and fixed effects models. The fixed slopes are all greater than zero, pointing to an increase in S5 prominence with IPL thickness (Figure 2B).

Conclusions: The proposed method reveals IPL organization in living human subjects, potentially enabling studies of stratification during development and in diseases.

CONTROL ID: 3544761

SUBMITTER (NAME ONLY): Dominick Canady

TITLE: Functional and Psychosocial Impact of Eye Disease in Pediatric Ebola Survivors, Sierra Leone

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Canady, G. Bastien, Morehouse School of Medicine, Atlanta, Georgia, UNITED STATES|N. Weil, S. Yeh, J. Shantha, Emory Eye Center, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|C. Miller, M.J. Vandy, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|A. Cassedy, S.T. Angeles-Han, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|C. Hartley, Rollins School of Public Health, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the ophthalmic complications in pediatric Ebola virus disease (EVD) survivors and EVD close-contacts, and the impact on quality of life and mental health within Sierra Leone.

Methods: Cross-sectional study. Pediatric EVD survivors and first-degree close contact controls were identified through the Sierra Leone Association of Ebola Survivors and Ministry of Health. EVD survivor status was confirmed by Ebola serum IgG testing. Patients enrolled in this study underwent a medical questionnaire and, ocular examination, and Quality of Life was evaluated with the Pediatric Quality of Life Inventory Version 4.0 (PedsQL). PedsQL assessed holistic quality of life over 4 domains. 1) Physical Functioning 2) Emotional Functioning 3) Social Functioning 4) School function.

Results: A total of 86 Ebola affected pediatric patients were examined which included twenty-three EVD survivors and 63 close contacts. Of EVD survivors, 39.1% were female and mean age was 11.5 years. Among close contacts, 46% were female and mean age was 9.5 years. Higher prevalence of uveitis was observed in the EVD survivor (13.0%) cohort compared to close contacts (1.7%) ($p=0.032$). Overall, 56.5% and 42.9% of EVD survivor eyes and close contact eyes presented with an ocular diagnosis that impaired vision, there was no statistically significant difference. The PedsQL total score showed low overall quality life in both patient populations (60.6 vs 67.0, $p=0.250$). The emotional functioning domain parent report was significantly lower among parents of EVD survivors compared to close contacts (57.4 vs 70.0, $p=0.035$). The main driver was a greater number of parents of EVD survivors affirming the question: "I feel Sad or Blue" (48.21 vs 65.71, $p=0.035$)

Conclusions: We observed a high burden of ocular and psychosocial sequelae in pediatric Ebola survivors in Sierra Leone. While uveitis was observed with a higher prevalence in this cohort of pediatric EVD survivors, non-uveitis eye disease also led to substantial visual acuity impairment in both groups. Psychosocial health burden was also observed within this pediatric population, irrespective of EVD infection. Future studies that examine the relationship between eye health and mental health in pediatric EVD survivors could better define these important relationships, particularly given the current pandemic.

CONTROL ID: 3544762

SUBMITTER (NAME ONLY): Satoshi Shimada

TITLE: The usefulness of a new visual field measurement algorithm “smart Strategy Alpha” using the Variational Bayes Linear Regression in comparing with the conventional algorithm in healthy subjects

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Shimada, Kowa Kabushiki Kaisha, Nagoya, Aichi, JAPAN|R. Asaoka, H. Murata, Y. Fujino, M. Matsuura, Tokyo Daigaku, Bunkyo-ku, Tokyo, JAPAN|R. Asaoka, Y. Fujino, Seirei Hamamatsu Byoin, Hamamatsu, Shizuoka, JAPAN|M. Matsuura, K. Hirasawa, N. Shoji, Kitasato Daigaku Igakubu, Sagamihara, Kanagawa, JAPAN|

Commercial Relationships Disclosure (Abstract): Satoshi Shimada: Commercial Relationship(s);Kowa Company, Ltd.:Code E (Employment) | Ryo Asaoka: Commercial Relationship(s);Kowa Company, Ltd.:Code F (Financial Support) | Hiroshi Murata: Commercial Relationship(s);Kowa Company, Ltd.:Code F (Financial Support) | Yuri Fujino: Commercial Relationship(s);Kowa Company, Ltd.:Code F (Financial Support) | Masato Matsuura: Commercial Relationship(s);Kowa Company, Ltd.:Code F (Financial Support) | Kazunori Hirasawa: Commercial Relationship(s);Kowa Company, Ltd.:Code F (Financial Support) | Nobuyuki Shoji: Commercial Relationship(s);Kowa Company, Ltd.:Code F (Financial Support)

ABSTRACT BODY:

Purpose: We previously reported that a visual field (VF) measurement algorithm, which was named “smart Strategy”, using the Variational Bayes Linear Regression with KOWA AP-7000 (Kowa Company, Ltd., Japan) was useful for saving measurement duration while maintaining the same accuracy as the Swedish Interactive Thresholding Algorithm Standard with Humphrey Field Analyzer (Carl Zeiss Meditec, Dublin, USA) (Br J Ophthalmol in press). We developed a new time-saving algorithm “smart Strategy Alpha”, which was modified the thresholding algorithm from smart Strategy, and assessed its usefulness by comparing with a conventional algorithm “Quick 1” in healthy subjects.

Methods: 22 eyes of 12 healthy subjects were included in the current study. VF measurements were performed using smart Strategy Alpha and the conventional Quick 1 with KOWA AP-7000. The 24-2 tests were conducted in the VF measurements. Measurement duration and visual sensitivities were compared between these algorithms using the linear mixed model where the subjects were treated as random effects.

Results: smart Strategy Alpha measurement duration was significantly 55 % shorter than Quick 1 on average. Mean (standard deviation) measurement duration were 114 (28) seconds for smart Strategy Alpha, and 251 (29) seconds for Quick 1 ($p<0.001$). On the other hand, mean deviation (MD) values were no significant differences between these algorithms. Mean (standard deviation) MD values were 0.03 (0.92) dB for smart Strategy Alpha, and -0.18 (1.09) dB for Quick 1 ($p=0.19$).

Conclusions: smart Strategy Alpha saved measurement duration while maintaining the same accuracy as Quick 1 in healthy subjects.

CONTROL ID: 3544763

SUBMITTER (NAME ONLY): Wilson Luu

TITLE: Age-related changes in the perception of self-motion and presence in virtual reality.

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Luu, B. Zangerl, M. Kalloniatis, J. Kim, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|W. Luu, M. Kalloniatis, Centre for Eye Health, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Visual perception of object-motion and self-motion is critical for safe mobility. However, the risks of accidents and falls during mobility increase with age, presumably due to functional vision loss. We used head-mounted display (HMD) virtual reality (VR) as a tool to understand how the visual perception of self-motion and presence (the feeling of being “there”) varies with age.

Methods: Eighty-six (86) healthy participants aged 18 to 77 (37 females) with normal or corrected to normal visual acuities and normal visual fields were recruited for this study. We measured illusory self-motion perception (vection) and presence when participants viewed radially expanding patterns of optic flow. Optic flow was generated using a HMD VR (Oculus Rift CV1) to simulated different speeds of self-motion. Viewing was performed with the head stationary (passive condition) or with lateral-sway head movements (active conditions).

Results: Presence increased with age ($F_{2,83} = 5.44$, $p < 0.01$). Vection did not significantly change with age ($F_{2,83} = 1.82$, $p = 0.17$). However, head movements had a significant impact on perceived vection ($F_{2,166} = 19.84$, $p < 0.001$). A significant interaction was also found between age and viewing condition ($F_{4,166} = 3.60$, $p < 0.01$). Main effects of simulated speed on perceived vection ($F_{3,249} = 367.89$, $p < 0.001$) and presence ($F_{3,249} = 112.64$, $p < 0.001$) were also found. These results show vection increases with the speed of simulated self-motion, but generally decreases with increasing age (Figure 1).

Conclusions: This study shows there are age-related changes in the perception of self-motion and spatial presence in HMD VR. Our findings suggest that the experience of self-motion perception decreases with age, particularly at slow speeds consistent with normal walking. This may provide further clues to why the elderly have increased risk of accidents and falls.

CONTROL ID: 3544764

SUBMITTER (NAME ONLY): Kaitryn Ronning

TITLE: Monocyte-derived macrophages take up residence in the retina following widespread photoreceptor degeneration

SESSION TITLE: Microglia and other Macrophages in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Ronning, M. Burns, Center for Neuroscience, University of California Davis, Davis, California, UNITED STATES|S.J. Karlen, M. Burns, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: During retinal degeneration, microglia undergo dramatic changes in gene expression and morphology to clear debris and dying cells. Additionally, monocytes from the periphery can infiltrate the retina to join the microglia in the immune response to degeneration. After cell loss is complete a population of resident macrophages re-tile the retina but it remains unclear (1) whether these cells return to a normal “resting” microglial state and (2) whether monocyte-derived macrophages that had infiltrated remain in the retina as part of this population.

Methods: We used in vivo retinal imaging, immunohistochemistry (IHC), flow cytometry, and single-cell mRNA sequencing (scRNAseq) to investigate retinal macrophages before, immediately after, and several weeks after cell loss in a light-inducible model of photoreceptor degeneration ($Arr1^{-/-}$ mice, 0 through 20 days of light exposure). All mice were handled according to ARVO, NIH, and UC Davis IACUC guidelines.

Results: In vivo retinal imaging and IHC revealed that ramified macrophages re-tile the inner retina following the completion of photoreceptor loss. Many macrophages exhibited a normal “resting” microglial morphology, although the degree of complexity varied more than that of cells in the healthy retina. ScRNAseq showed that the population of CD45+CD11b+ cells remained transcriptionally heterogeneous, even as homeostasis was re-established. To clearly distinguish between microglial and monocyte-derived macrophage subpopulations, we used a fluorescent lineage tracing paradigm ($Arr1^{-/-}$ Ai9^{KI/KI} Cx3cr1^{+YFP-CreER}). These fate mapping experiments confirmed that monocyte-derived macrophages take up long-term residence, assume a ramified microglia-like morphology, and comprise approximately half of the population of immune cells in the retina after degeneration.

Conclusions: After photoreceptor degeneration is complete, the remaining inner retina contains a heterogeneous population of ramified macrophages that includes both microglia and monocyte-derived macrophages. These monocyte-derived macrophages adopt a microglia-like phenotype, including gene expression similar to mildly activated microglia and a ramified morphology, persisting for several weeks after recovery and accounting for a substantial portion of the re-established, long-lived resident macrophage population in the retina.

CONTROL ID: 3544765

SUBMITTER (NAME ONLY): Ruslan Grishanin

TITLE: Preclinical Evaluation of ADVN-062, a Novel Intravitreal Gene Therapy for the Treatment of Blue Cone Monochromacy

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Grishanin, D. Cepeda, J. Nieves, C. Dowd, P. Sharma, A. Levinson, K. Hanna, K. Oresic Bender, B. Singh, M. Renz, J. Greengard, M. Gasmi, C. Gelfman, Adverum Biotechnologies Inc, Redwood City, California, UNITED STATES|D. Duffield, R. Veeramachaneni, KCAS Bioanalytical and Biomarker Services, Shawnee, Kansas, UNITED STATES|J. Ver Hoeve, OSOD (Ocular Services on Demand), Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blue cone monochromacy (BCM) is a debilitating, rare X-linked retinal disease resulting from the congenital absence of both L- and M-opsins, that causes severely impaired color discrimination, low vision, nystagmus, and photophobia. We developed ADVN-062, a vector optimized for intravitreal (IVT) delivery aimed at restoring the cone-specific expression of human L-opsin (hL-Opsin). This vector utilizes AAV.7m8 capsid that has been demonstrated to provide efficient transduction of foveal cones in primate retina when delivered intravitreally and uses the opsin LCR and a minimal M-opsin promoter to express human L-opsin in cones. The present study evaluated the dose dependent safety as well as levels and localization of hL-Opsin expression to establish the tolerability and potential efficacy of IVT-delivered ADVN-062 in nonhuman primates (NHPs).

Methods: Cynomolgus monkeys were treated with 5E9, 5E10, or 5E11 vg/eye ADVN-062 or vehicle via bilateral IVT injection, and monitored for ocular and systemic tolerability for 8wk without any steroid treatment. Retinal levels of hL-Opsin in the presence of endogenous NHP opsins were measured using liquid chromatography-tandem mass spectrometry (LC-MS/MS) at 8wk post-treatment. Retinal localization was evaluated by immunofluorescence (IF) analysis by using another AAV.7m8-based vector made to express myc-tagged hLOpsin IVT delivered at the same doses as ADVN-062. Transduction efficiency was determined as a percentage of hL-Opsin.myc-positive foveal cones in a series of histological retinal sections.

Results: IVT administration of ADVN-062 was well tolerated up to the highest dose of 5E11vg/eye and resulted in dose-dependent hL-Opsin expression. Cone specificity was confirmed by colocalization of cone cell markers in IF analyses of retinas expressing myc-tagged hL-opsin. ADVN-062 at lowest dose of 5E9 vg/eye resulted in variable transduction of foveal cones from 4.8% to 49.8%, and doses at 5E10 and 5E11 vg/eye resulted in transduction of foveal cones from 17.7% to 85.3% in the individual animals.

Conclusions: Based on published studies of minimal foveal cone density sufficient to maintain good visual acuity in humans with retinal degenerative diseases or dichromatic vision, our data suggest that IVT ADVN-062 at well tolerated doses may effectively transduce sufficient numbers of foveal cones to potentially achieve clinical efficacy.

CONTROL ID: 3544768

SUBMITTER (NAME ONLY): Milan Shah

TITLE: Post hoc Analysis of Clinical Suprachoroidal Injection Experience for Non-infectious Uveitis

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Shah, Ophthalmology, Midwest Eye Institute, Indianapolis, Indiana, UNITED STATES|C. Wan, B. Kapik, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: To analyze procedural characteristics of suprachoroidal injections (SCIs) using the SCS Microinjector[®] in two uveitis trials. The SCS Microinjector reliably delivers drug to the suprachoroidal space (SCS), an alternative administration route for chorioretinal diseases. SCIs are first attempted with a 900µm length needle and switched to 1100µm length if required. Correlations between needle length, baseline patient characteristics, and physician device experience, via survey, are presented.

Methods: Post hoc analyses were performed to assess the relationship between needle length for baseline SCI and patient characteristics. Univariate analysis was conducted with Pearson chi-square analysis for categorical variables and the biserial correlation for continuous variables. Multivariate logistical regression was run to confirm univariate findings. Furthermore, a user experience survey was completed to evaluate real-world SCI experience.

Results: Of the 133 total baseline SCIs, 74% were completed with the 900µm needle; the remaining with the 1100µm needle. Univariate analysis revealed no relationship between needle length used and gender, lens status, uveitis sub-type, disease course or onset. Disease duration was statistically correlated with needle length: 91% of injections were completed with the 900µm needle for Limited (≤3 months) and 70% for Persistent (>3 months). Age was moderately inversely correlated with needle length. SCI quadrant was statistically related: 82% of supratemporal injections were completed with the 900µm needle compared to 45% of injections administered superonasally. Multivariate logistical regression verified univariate analysis demonstrating the potential impact of age, disease duration and SCI quadrant on needle length. In the user experience survey, over 80% of the physicians responded that SCIs presented no new challenges compared to other types of injections.

Conclusions: While these analyses are retrospective with a small sample size, few patient characteristics were found to correlate with needle length, indicating the procedure can be completed for the majority of patients with the 900µm needle and using a 1100µm needle in remaining patients. This suggests that SCIs with the SCS Microinjector has potential to reliably and repeatably deliver drugs for chorioretinal diseases in an in-office setting.

CONTROL ID: 3544772

SUBMITTER (NAME ONLY): YOICHIRO SHINKAI

TITLE: Evaluation of Müller cell migration on artificial collagen-like polypeptides with various functional amino-acid sequences

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. SHINKAI, K. Kojima, H. Tanaka, C. Sotozono, Kyoto Prefectural University of Medicine, JAPAN|K. Kuroda, S. Ichise, T. Koide, Department of Chemistry and Biochemistry Waseda University of Advanced Science and Engineering, Tokyo, Japan, JAPAN|H. Nose, Kola-Gen Pharma, Kyoto, Japan, JAPAN|

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ABSTRACT BODY:

Purpose: Collagen, an abundantly distributed extracellular matrix protein, is known to maintain the structural integrity of organs and tissues in mammals, and it not only plays a physical function as a structural protein, but also has various biological functions that regulate cell adhesion, migration, and differentiation. In this study, we investigated the migration activity of cells in the human Müller cell line MIO-M1 with certain amino acid sequences displayed on the collagen triple helices, which can control cell adhesion, proliferation, and survival by arbitrarily incorporating collagen-derived functional amino-acid sequences.

Methods: The wells of 48-well plates were coated with a peptide polymer containing four kinds of functional amino-acid sequences (GFOGER, GLOGEN, GVXGFO, and KGHRGF) at the concentrations of 1, 3, 10, 30, and 100%, and 3mm RTV silicones were placed in the center of each well. MIO-M1 cell-line cells (5×10^4 cells/well) were then seeded in the periphery, and the silicones were removed when the cells reached 80% confluence. Photographs were taken immediately after removal and 72 hours later, the cell migration area was measured with ImageJ software, and the migration activity was then compared and evaluated to see if the migration area of the control (0%) was 1. Migration measurements were performed ($n=5$), and the mean value was calculated.

Results: In the GFOGER group, the migration activity was higher in the concentration of 10, 30, and 100% compared to the control, respectively ($p<0.001$, unpaired t test), as well as in the concentration of 3% ($p<0.01$, unpaired t test). In the GLOGEN and KGHRGF groups, the migration activity was higher in the concentration of 30% and 100% compared to the control ($p<0.01$, unpaired t test). In the GVXGFO group, the migration activity was higher in the concentration of 100% compared to the control ($p<0.01$, unpaired t test).

Conclusions: The findings in this study showed that collagen-derived functional amino-acid sequences improved the migration activity of MIO-M1 cell-line cells.

CONTROL ID: 3544774

SUBMITTER (NAME ONLY): Toshihide Kurihara

TITLE: Violet light suppresses lens-induced myopia via neuropsin (OPN5) in mice

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kurihara, X. Jiang, K. Mori, S. Ikeda, H. Torii, K. Tsubota, Keio Gijuku Daigaku Igakubu Daigakuin Igaku Kenkyuka, Shinjuku-ku, Tokyo, JAPAN|M. Pardue, Emory University, Atlanta, Georgia, UNITED STATES|S. D'Souza, R.A. Lang, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|M. Pardue, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myopia has become a major public health concern, particularly across much of Asia. It has been shown in multiple studies that outdoor activity has a protective effect on myopia. It is also known that short-wavelength visible violet light is the component of sunlight that appears to play an important role in preventing myopia progression in the chick and in humans. The mechanism underlying this effect has not been understood.

Methods: Lens defocus-induced myopia (LIM) in mice was performed by attaching 0 diopter (D) lenses on the left eyes and -30 D lenses on the right eyes with a frame on their skull. Combined with 50 lux of white background fluorescent lamp light from 08:00 to 20:00 every day, $400 \mu\text{W}/\text{cm}^2$ (360 nm ~ 400 nm) of violet light was added either 3 hours pre-dawn (05:00~08:00), all daytime exposure (08:00~20:00), continuous violet light, 3 hours of evening (17:00~20:00), or 3 hours of post-dusk (20:00~23:00) for three weeks of the LIM period. The violet light sensitive atypical opsin neuropsin (OPN5) is specifically deleted in the retina by crossing Chx10-Cre⁺ mice with Opn5^{flx/flx} mice (OPN5 cKO).

Results: 3 hours of evening violet light combined with white light significantly suppressed both the refractive shift ($p=0.006$) and axial lengthening ($p=0.045$) compared to white light only in control mice. By contrast, OPN5 cKO mice with violet light showed a refractive shift and an axial length change indistinguishable from the normal white light condition.

Conclusions: These findings identify OPN5 expressing retinal cells as crucial for emmetropization in mice and further suggest a strategy for myopia prevention in humans.

CONTROL ID: 3544775

SUBMITTER (NAME ONLY): Kelleigh Hogan

TITLE: Exposure to bright ambient lighting is not protective if started after induction of experimental myopia in mice

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hogan, P. Mohanty, D. Brown, M. Pardue, Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|M. Pardue, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Increased exposure to bright outdoor lighting protects against myopic development in both animal and human studies. However, the typical experimental paradigm for animal studies starts the bright light exposure prior to or at the time of myopic induction. The objective of this study was to evaluate whether the protective effect of bright light was maintained when exposure occurred after the start of lens-induced myopia (LIM) in C57 mice.

Methods: C57BL/6J mice were housed in bright ambient lighting (10,000 lux, 12:12 cycle) starting on post-natal day 23 (P23, pre-LIM, n = 9) or P30 (post-LIM, n = 7), and compared to mice housed in mesopic lighting (50 lux, 12:12 cycle) for the entirety of the experiment (mesopic, n = 7). On P28, LIM was induced by placing a -10D lens over the right eye (OD) in a subset of animals in each lighting group. Measurements of refractive error using photorefractometry, corneal curvature using keratometry, and ocular axial measurements from SD-OCT were taken at baseline, 1 week, and 2 weeks post-LIM. Three-way repeated measures ANOVA analysis was used to compare the effects of lighting, treatment, and age on each measurement taken.

Results: Mice with lens defocus had significant myopic shifts (OD-OS) compared to naïve controls ($p < 0.05$). The magnitude of the myopic shift was dependent on light exposure group. Mice exposed to bright light pre-LIM had significantly smaller myopia shifts (-3.63 ± 0.50 D) compared to the mesopic group (-4.89 ± 0.80 D, $p < 0.05$). However, this protective effect was not maintained when exposure occurred post-LIM (-4.35 ± 0.80 D, $p > 0.05$). No significant differences were found between groups for corneal curvature or axial ocular parameters.

Conclusions: Pre-LIM exposure to bright ambient lighting resulted in the expected reduction in myopic severity, but post-LIM exposure did not offer any protection against myopia. These results suggest that protective light may be most effective as a prophylactic treatment rather than a therapeutic treatment to slow further myopic development. Future research will focus on the mechanism(s) for the protective effect of photopic lighting and how its effectiveness changes with myopic induction.

CONTROL ID: 3544780

SUBMITTER (NAME ONLY): Eugenia Custo Greig

TITLE: Demographic Characteristics and Clinic No Shows in Patients with Chronic Eye Disease

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Custo Greig, R. Gonzalez-Colaso, K.H. Nwanyanwu, Ophthalmology, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Eugenia Custo Greig: Commercial Relationship: Code N (No Commercial Relationship) | Rosana Gonzalez-Colaso: Commercial Relationship: Code N (No Commercial Relationship) | Kristen Nwanyanwu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patient no shows reduce ophthalmologic clinic efficiency and effective resource allocation. We performed a retrospective cohort study to determine the effect of demographic characteristics on appointment no shows among patients with chronic eye disease.

Methods: A chart abstraction was performed for encounters of patients 18 and older with a diagnosis of glaucoma, diabetic retinopathy (DR), or age-related macular degeneration (AMD) seen in the Yale Ophthalmology Department between January 2013 and December 2018. Only encounters with comprehensive ophthalmologists, retina specialists, and glaucoma specialists were considered in this analysis. Demographic characteristics recorded for each encounter included age, gender, race, ethnicity, language preference, and zip code. Zip code information was utilized to determine median household income according to 2010 census data. Medical diagnostic information included history of diabetes mellitus, hypertension, and history of mental illness. No show encounters were defined as all encounters where the patient failed to cancel their visit and did not sign-in to their scheduled appointment. A multivariate mixed logistic regression model—which clusters data to account for random effects driven by intra-patient correlation—was utilized to determine demographic factors affecting odds of visit no show.

Results: The current study analyzed 90,698 visits for 6,167 unique patients. Demographic characteristics that increased the odds of no show included: Hispanic ethnicity (OR 1.58/ $p < 0.0001$), Black race (OR 1.87/ $p < 0.0001$), and preferred language other than English (OR 1.31/ $p = 0.0004$). Financial factors that increased the odds of no show included Medicare (OR 1.19/ $p = 0.0006$) or Medicaid (OR 1.66/ $p < 0.0001$) as primary insurance and residing in a zip code with reduced median household income (OR 1.68/ $p < 0.0001$). Medical characteristics that increased the odds of no show included a diagnosis of mental illness (OR 1.44/ $p < 0.0001$) or DR (OR 1.21/ $p = 0.01$). Results are displayed in Table 1.

Conclusions: Our results highlight the influence of demographic, ethnic, and racial disparities on proper health care utilization among patients with sight threatening disease. Future interventions aimed at reducing appointment no shows could channel resources to the at risk-populations identified in this analysis, improving access to care and clinic efficiency.

CONTROL ID: 3544781

SUBMITTER (NAME ONLY): Elana Meer

TITLE: Clinical Presentation and Outcomes for Gunshot Wounds to the Orbit

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Meer, B.J. Nguyen, S. Bautista, B. McGeehan, C.A. Briceño, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the clinical presentation, surgical management, long-term complications and outcomes of gunshot wounds to the orbit.

Methods: A retrospective chart review was conducted of all cases of gunshot wounds involving the orbit at an academic institution with a level 1 trauma center. Data included patient demographics, clinical presentation and exam over time, surgical intervention, and long-term outcomes. Descriptive statistics were calculated using mean and standard deviation for continuous measures and frequency and percentage for categorical measures. Tests of associations included Fishers exact tests for categorical data, Kruskal-Wallis rank sum tests, ANOVA, and in the case of repeated measures, generalized estimating equations.

Results: 88 patients with a history of gunshot wound involving the orbit were included with average age of 32.6 years old. Patient were 85.2% male, 75% African-American, 25% Caucasian, and 5.7% Hispanic. Mean follow up was 8.25 years. While injury varied, 53.4% presented with intracranial injury, 21.6% presented with open globe rupture, 80.7% with orbital fracture, 89.8% with lid laceration, 88.6% with vision loss, 92% with pain, and 76.1% with bullet fragments in the orbit on imaging. Surgery occurred for 59.1% of patients, of which 26.9% underwent primary enucleation, 11.5% evisceration, 44.2% fracture repair, and 17.3% another procedure (craniotomy, complex laceration repair, etc). Long-term complications included abnormal lid or globe position in 26.1% of patients, reduced visual acuity in 55.2%, and persistent pain in 50.6%. Predictors on initial presentation for persistent pain included intracranial injury ($p=.003$), pain ($p=.006$), presence of radiographic intraorbital foreign body (bullet/ bullet fragments) ($p=.002$), abnormal CNV2 sensation ($p=.041$), and corneal abrasion ($p=.031$) on clinical exam. Visual acuity improvement over time in individuals who did not receive enucleation or evisceration on presentation was not significant ($p = .09$). Worsening visual acuity was significantly associated with hyphema, vision loss, and presence of intraorbital foreign body on presentation ($p<.05$)

Conclusions: To our knowledge, this represents the first, largest clinical epidemiologic study that serves to provide insight into the clinical presentation, surgical intervention, and long-term outcomes of gunshot wounds to the orbit, which will guide both ophthalmologists and trauma physicians

CONTROL ID: 3544782

SUBMITTER (NAME ONLY): Ninani Kombo

TITLE: Prevalence of psychiatric comorbidities in patients with scleritis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Kombo, Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|A. Abdel-Aty, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ninani Kombo: Commercial Relationship: Code N (No Commercial Relationship) | Ahmad Abdel-Aty: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We performed a retrospective, observational clinical study to identify the prevalence of psychiatric comorbidities among patients with acute scleritis.

Methods: The records of 256 patients with scleritis who presented to the Yale New Haven Health System between January 1, 2013 to January 1, 2018 were retrospectively reviewed. Data was collected on patient comorbidities. The study was approved by the Institutional Review Board (IRB).

Results: We identified 256 patients with a diagnosis of scleritis, 232 (90.6%) had diffuse anterior scleritis, 10 (3.9%) had nodular anterior scleritis, 5 (2%) had necrotizing scleritis, and 9 (3.5%) had posterior scleritis. At least one psychiatric comorbidity was present in 61 patients (23.8%), and 38 patients (14.8%) had at least two psychiatric comorbidities. The most common was major depression (16.8%) followed by an anxiety disorder (12.5%). 14 patients (5.6%) had a substance use disorder. The prevalence of psychiatric comorbidities in our sample was significantly higher than population averages as reported by the National Institutes of Mental Health (23.8% compared to 18.9%, $p < 0.05$).

Conclusions: A high percentage of scleritis patients have a comorbid mental health disorder. Similar to other chronic illnesses, scleritis may be a significant psychosocial stressor for these patients. Mental health disorders may affect treatment compliance and patient outcomes. Future prospective studies will further elucidate the relationship between scleritis and mental health.

CONTROL ID: 3544788

SUBMITTER (NAME ONLY): Ying Li

TITLE: Oral supplementary nicotinamide riboside protects function in a model of inherited mouse glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Li, N. Zhang, X. Zhang, M.A. Chrenek, J. Wang, J.T. Sellers, E. Geisert, J.H.

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ABSTRACT BODY:

Purpose: Purpose: To test whether oral administration of nicotinamide riboside (NR), a nicotinamide adenine dinucleotide (NAD⁺) precursor, protects retina ganglion cells (RGCs) from neurodegeneration in the DBA/2J (D2) mouse model of age-related inherited glaucoma.

Methods: Method: NR administration in drinking water (4000mg/kg of body weight per day) started when DBA/2J mice were 9 months old. NR was dissolved in drinking water and changed twice per week, continuing to 13 months old. Control cohort identically received water with no added NR. Intraocular pressure (IOP) was measured every month until experiment completion. Pattern electroretinography (PERG) using a Celeris system (Diagnosys LLC, MA) was recorded before euthanizing mice at 12-13 months old. Retinas were harvested for whole mount immunofluorescence staining with RGC marker Brn3a and imaged by fluorescent confocal microscopy. Retinal NAD⁺ levels were enzymatically assayed (Abcam, CA).

Results: Results: 13-month-old D2 retinas showed diminished NAD⁺ concentration compared to 4 months old ones. Our data showed that aged D2 mouse retinal NAD⁺ level with NR oral supplementary treatment was significantly higher than which from vehicle treatment group. (9.69 ± 1.72 pmol/ul vs 4.24 ± 1.06 pmol/ul, $p < 0.05$, $n = 6$, Mann-Whitney-U test). The amplitude of PERG in NR treatment group (5.05 ± 0.33 uV, $n = 44$) was also significantly higher than in vehicle group (3.22 ± 0.27 uV, $n = 34$) ($p < 0.05$, t-test). Retinal immunofluorescent Brn3a⁺ cell counts were significantly higher in NR treatment group than age matched vehicle group (27016.50 ± 3721.17 vs 15114.92 ± 4387.32 , $n = 24$, $p < 0.05$, t-test). There was no significant difference in IOP between NR-treated and non-treated eyes at all observation time points from 9 months old up to 12 months old.

Conclusions: Conclusion: NR oral supplementation aids more RGC survival in aged DBA/2J mice, and potentially preserves retinal function via preventing age-dependent NAD⁺ level decline. The effect of rendering RGCs more resilient to glaucomatous damage in a glaucoma model suggests that NR is worth exploring as a therapeutic candidate in treatment of glaucoma.

CONTROL ID: 3544791

SUBMITTER (NAME ONLY): Basil Williams

TITLE: Uveal Melanoma Patient Attitudes Towards Prognostic Testing Using Gene Expression Profiling

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.K. Williams, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|J.J. Siegel, K.M. Alsina, Castle Biosciences Inc, Friendswood, Texas, UNITED STATES|L. Johnston, K. LiPira, S.M. Selig, CURE OM, Melanoma Research Foundation, Washington, District of Columbia, UNITED STATES|A. Cisco, P.G. Hovland, Colorado Retina Associates, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: A prognostic 15-gene expression profiling (GEP) test is widely used for risk stratification in patients with uveal melanoma (UM). The goal of this cross-sectional survey study was to understand patient experiences following 15-GEP testing compared to alternative or no prognostic testing.

Methods: An online questionnaire was distributed by the Melanoma Research Foundation's CURE OM initiative that captured anonymous information regarding patient-reported experiences. Patients were asked validated series of questions regarding the decision to undergo prognostic testing and the extent to which they felt decision regret.

Results: Of the 177 survey participants, 159 (90%) reported wanting prognostic information at diagnosis, but only 124 (70%) remembered the doctor discussing prognostic testing with them. Of all respondents, 91 (51%) had 15-GEP testing, 33 (19%) had alternative prognostic tests, 48 (27%) did not have any prognostic testing, and 19 (11%) did not know (10% of respondents reported having multiple tests). Interestingly, 15-GEP patients reported feeling more involved in their health care decisions regarding testing than those receiving alternative testing only (WilcoxRS, n=85 and 21 respondents, respectively; p=0.0006). Of 15-GEP-tested patients, the vast majority (80/81 respondents, 99%) reported gaining value from their test result, including increased knowledge and understanding, more personalized treatment options, information relevant to life planning, and a sense of relief from uncertainty about the future. Patients who received prognostic testing experienced lower levels of decision regret than those who opted out of testing, independent of which prognostic tests were used (K-W, p=0.001; WilcoxRS post-hoc, n=85, 16 and 5 for GEP, other tests and no GEP; GEP vs. other tests: p=0.89, GEP vs. no GEP: p=0.0002, other test vs. no GEP: p=0.003). Importantly, decision regret levels did not differ depending on 15-GEP Class result (K-W; n=28, 23, 30 for 1A, 1B, 2; p=0.13).

Conclusions: The majority of newly diagnosed UM patients desired prognostic information, though testing options were not always introduced by the doctor. Prognostic testing with 15-GEP had considerable value to UM patients, independent of Class result, and having this test offered at the time of diagnosis was associated with an increased sense of shared decision making.

CONTROL ID: 3544794

SUBMITTER (NAME ONLY): Sally McFadden

TITLE: L-Arginine inhibits myopia in the mammalian eye

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. McFadden, School of Psychology and HMRI, College of Engineering, Science and Environment, The University of Newcastle, Callaghan, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Ocular growth is regulated by the sign of imposed defocus and likely involves amacrine cells. We have previously reported that one particular class of amacrine cell changes its expression of nNOS in a bidirectional manner, being upregulated in myopic eyes, and down regulated in hyperopic eyes in the guinea pig retina. We manipulated the expression of nNOS by administering L-arginine and show here that myopia was also inhibited.

Methods: Two groups of guinea pigs (n=20) were raised with a -6D lens on one eye from 5-12 days of age and twice daily were administered eye drops containing either 0.9% Saline or 1.7% L-Arginine (LA). Drops were given 1 hr after lights on and 6 hrs later in the middle of their day cycle. Lenses were removed during the drop administration which occurred under dim red light or in darkness. At 12 days of age, animals were cyclopleged and refractive error measured. Eye length was subsequently measured in anaesthetised animals using high frequency ultrasound.

Results: At the end of lens wear period, the mean refractive error in untreated eyes did not differ between the two groups (LA: $+5.2 \pm 0.5$ D; Saline: $+5.1 \pm 0.8$ D, $p = .88$). Significant relative myopia developed in 10/10 animals given saline eye drops sufficient to compensate for the -6D of imposed defocus (Saline: -6.7 ± 0.5 D, $p = 0.000$). In contrast, 7/10 animals administered LA eye drops did not develop myopia in the lens-wearing eye and the relative myopia in these 7 animals (LA: -2.5 ± 0.7 D) or the mean across all 10 animals (LA: -3.6 ± 0.8 D) was significantly less than that in the saline treated animals ($p = .000$ and $p = .007$ respectively). The myopia induced by -6D lens wear was caused by a longer eye. Control eyes given saline eye grew by 115 ± 18 μm ; while in animals given LA, the mean growth in ocular length was only 42 ± 17 μm . This reduction in ocular growth caused by LA was highly significant ($p = .01$), and no relative growth occurred in the 70% of animals which failed to develop myopia.

Conclusions: LA eye drops protect the eye from developing myopia in 70% of animals, where the mean myopia was 37% of that in control animals, and completely eliminated the excessive growth normally associated with myopia.

CONTROL ID: 3544795

SUBMITTER (NAME ONLY): Evguenia Ivakhnitskaia

TITLE: Differential Effects of Two Ocular Surface Injury Models on the Functional Properties of Regenerated Corneal Sensory Nerves

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Ivakhnitskaia, T. Nguyen, Q. Zhou, J. Sarkar, V.H. Guaiquil, H. Hirata, M. Rosenblatt, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|K.Y. Tseng, College of Medicine, Department of Anatomy and Cell Biology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dysfunction of corneal sensory nerves can manifest in a wide range of sensory alterations, spanning from insufficient sensation as found in neurotrophic keratopathy to dysesthesia observed in Dry Eye Disease, an ocular surface disorder estimated to affect 5% of the global population. Changes in corneal sensory nerve function after recovery from injury are not well understood. This study tested the hypothesis that corneal sensory nerves regenerated from ocular surface injury display alterations in their activity profiles.

Methods: The impact of regeneration from injury on corneal nerve properties was tested using two models of nerve injury—Corneal Epithelial Debridement (CED) and Benzalkonium chloride (BAK) chemical injury, in adult Sprague Dawley rats of both sexes. CED is one of the most common corneal injury models and was induced using a rotary burr tool, with the entire corneal epithelium removed while sparing the corneal limbus. BAK injury was administered as a prolonged (30min+) ocular instillation with 0.01% Benzalkonium chloride, a common preservative found in eye drops that can damage corneal epithelium and nerves. At 14 and 28 days post injury, corneal nerve functional profiles were assessed in anesthetized rats using in vivo electrophysiological recordings of the trigeminal ganglion, which houses the cell bodies of corneal nerves, while the cornea was exposed to a range of stimuli that activate ion channels responsible for corneal nerve sensation.

Results: Our preliminary data indicate that the two injury models lead to differential response profiles of regenerated nerves that can be observed at both 14 and 28 days post injury. Compared to injury-naïve rats (n=25), CED animals (n=10) showed signs of decreased responsiveness, with blunted responses to stimuli like ocular dryness, hyperosmolar stress, and temperature decreases of the ocular surface. Conversely, BAK-treated animals (n=13) displayed activity shifts toward increased responsiveness compared to injury-naïve animals, with augmented responsiveness to cooling and heating of the ocular surface.

Conclusions: Our findings suggest that corneal sensory nerves that regenerate from injury show long-lasting and differential alterations in their functional activity profiles that are dependent on the model used for ocular surface injury.

CONTROL ID: 3544796

SUBMITTER (NAME ONLY): Gareth Lingham

TITLE: Risk factors for the development of keratoconus in young adults

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report the incidence and investigate risk factors for the development of keratoconus in a young adult cohort with consecutive Scheimpflug imaging over an 8-year period.

Methods: Participants of the Raine Study generation 2 (Gen2) birth cohort underwent an eye examination at the 20-year (age range 19-22 years) and 28-year follow-ups. Scheimpflug imaging (Pentacam, Oculus, Wetzlar, Germany) was performed at each follow-up. Keratoconus was defined as a Belin/Ambrósio Enhanced Ectasia Display D (BAD-D) score >2.6 in either eye. Data from the worst eye was used for analysis, except for conjunctival ultraviolet autofluorescence (CUVAF, a marker of ocular sun exposure) data where the sum area of both eyes was used. Participants were excluded if they had keratoconus at the 20-year follow-up, had a history of significant eye trauma, wore orthokeratology lenses or did not have Scheimpflug imaging at both follow-ups. Logistic regression was used to investigate potential risk factors for keratoconus incidence over 8 years of follow-up.

Results: Of the 1295 participants who had Scheimpflug imaging at the 20-year follow-up, 685 (53%) had Scheimpflug imaging at the 28-year follow-up and 677 (52%) were eligible for analysis (52% female). There were 20 (3.0%) new cases of keratoconus. The mean (range) worst eye BAD-D score in the incident keratoconus group was 1.70 (0.20 to 2.57) and 3.45 (2.63 to 6.15) at the 20- and 28-year follow-ups, respectively. Keratoconus incidence was not associated with spherical refraction, visual acuity or self-reported history of asthma, eczema or asthma ($p>0.05$) on univariable analysis. Greater astigmatism, steeper corneal curvature and a thinner central cornea at the 20-year follow-up were associated with higher risk of keratoconus, but we focused on the BAD-D score as a derivative of these variables. In a multivariable model including sex, CUVAF area and BAD-D score at the 20-year follow-up, male sex (odds ratio [OR]=3.84, 95% confidence interval [95%CI]: 1.30, 11.29) and higher BAD-D score (OR=14.7, 95%CI: 5.93, 36.6), but not CUVAF area (OR=0.98, 95%CI: 0.96, 1.00), were significantly associated with higher risk of keratoconus.

Conclusions: The incidence of keratoconus was 3% over 8 years in this, predominantly Caucasian, young adult cohort in Perth, Australia. Sex and BAD-D score at the 20-year follow-up were significantly associated with greater risk of keratoconus.

CONTROL ID: 3544804

SUBMITTER (NAME ONLY): Cason Robbins

TITLE: Analyzing the Retinal and Choroidal Vasculature and Structure in Cognitively Healthy Individuals at Higher Genetic Risk for Alzheimer's Disease using a Convolutional Neural Network

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Robbins, D.S. Grewal, C. Wisely, S. Soundararajan, A.C. Thompson, E.M. Lad, H. Whitson, S. Fekrat, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|D. Wang, L. Carin, Electrical and Computer Engineering, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|R. Henao, Biostatistics and Bioinformatics, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|J.M. Lee, R.V. Agrawal, Tan Tock Seng Hospital, Singapore, SINGAPORE|B. Plassman, Psychiatry and Behavioral Sciences, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|H. Whitson, Medicine, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate differences in retinal and choroidal vasculature and structure in cognitively healthy individuals with at least one APOE e4 allele (who are at a greater risk for Alzheimer's disease than those without an APOE e4 allele) compared to those without an APOE e4 allele using retinal and choroidal quantitative parameters as well as a convolutional neural network (CNN).

Methods: In this cross-sectional study, 188 eyes of 98 cognitively healthy individuals with at least one APOE e4 allele and 225 eyes of 117 individuals without an APOE e4 allele were imaged. Of these, 150 eyes of 84 APOE e4 participants and 169 eyes of 98 participants without APOE e4 were used to develop a CNN. Zeiss Cirrus HD-5000 with AngioPlex (Carl Zeiss Meditec, Dublin, CA) was utilized to acquire OCT and OCTA images; enhanced depth imaging foveal OCT scans were acquired and underwent image binarization to determine choroidal area and vascularity index. Generalized estimating equations (GEE) adjusted for age and sex were used to compare parameters between groups.

Results: The two groups were matched with regards to age, sex, and Mini-Mental State Examination score (all $p > 0.05$). After adjustment for covariates in a multivariable GEE model, the two groups did not significantly differ in superficial capillary plexus vessel density or perfusion density, foveal avascular zone area, ganglion cell layer thickness, retinal nerve fiber layer thickness, central subfield thickness, subfoveal choroidal thickness, total choroidal area, choroid luminal area, or choroidal vascularity index (all $p > 0.05$). A CNN was unable to discriminate between the two groups (area under the receiver operating characteristic value = 0.526).

Conclusions: Retinal thickness, retinal microvasculature, and choroidal vasculature in cognitively healthy individuals with APOE e4-based predisposition to Alzheimer's disease do not significantly differ from cognitively healthy individuals without an APOE e4 allele. Longitudinal study may help better identify the onset of retinal microvascular abnormalities in relation to the onset of cognitive impairment.

CONTROL ID: 3544806

SUBMITTER (NAME ONLY): Richard Thompson

TITLE: Evaluation of Improved Tetracycline Stains for Fluorescence Imaging of sub-RPE Calcification

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Previously, we showed that drusen contain microscopic calcium phosphate mineral deposits such as hydroxyapatite (HAP), and proposed that they could initiate the growth of such sub-RPE deposits (PMID: 25605911). Further, we found that larger mineral deposits called nodules are strongly associated with progression to advanced AMD within one year (odds ratio 6.4), suggesting that early detection of mineral deposits might serve as a useful early screen for AMD (PMID: 30404862). While such mineral deposits are readily detectable in vitro with stains such as OsteoSense and BoneTag, these stains have unknown human toxicity, pharmacokinetics, and metabolism and aren't administered orally. By comparison, the tetracycline family of legacy antibiotics have been used safely in humans for decades, are mostly administered orally, and were known as fluorescent mineral stains. We found that chlortetracycline and doxycycline selectively stained retinal HAP with increased quantum yield and lifetime, such that chlortetracycline-stained drusen were readily resolved from the short fluorescence lifetime of the remainder of the retina (PMID 32319262). However, some of their other optical properties are suboptimal, so in this study we tested other tetracyclines and related compounds as fluorescence stains for retinal minerals for suitability in in vivo studies.

Methods: We measured the fluorescence spectra and lifetimes of legacy tetracyclines free in solution and bound to HAP and other minerals, and as stains for unfixed flat-mounted aging human donor retinas by fluorescence lifetime microscopy (FLIM). Of particular interest were stains spectrally compatible with existing fluorescence (lifetime) ophthalmoscopes used for fluorescein angiography and FLIO.

Results: Multiple tetracyclines exhibit useful changes fluorescence upon HAP binding. For example, free anhydrochlortetracycline excites at 473 nm, has peak emission at 587 nm, and exhibits a principal lifetime component (two-component fit) of 0.184 ± 0.006 nsec, fractional intensity 84%. However, when bound to HAP the principal component increases more than 7-fold to 1.42 ± 0.05 nsec, fraction 70%.

Conclusions: These data indicate retinal HAP stained with anhydrochlortetracycline or others will exhibit fluorescence resolved spectrally and in lifetime from the known background of the retina.

CONTROL ID: 3544809

SUBMITTER (NAME ONLY): Fabrice Manns

TITLE: Age-dependent Contribution of the Crystalline Lens to the Retinal Image Field Curvature

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Defocus in the periphery of the retinal image field maybe a factor in refractive development. Peripheral defocus is generally attributed to changes in globe shape or axial length. However, age-related changes in crystalline lens shape and optics may also be a factor. The goal is to quantify the lens contribution to the shape of the retinal image field and its changes with age.

Methods: Data were acquired on 70 isolated human lenses obtained from the Ramayamma International Eye-Bank, Hyderabad, India (age: newborn to 56 years, post-mortem time: 0.3 to 4.4 days). The lenses were placed in a combined Laser-Ray Tracing (LRT) and Optical Coherence Tomography (OCT) system (Ruggeri et al, Biomed Opt Exp, 2018). The LRT measures the slopes of on- and off-axis rays refracted through the lens. OCT images are used to reconstruct the 3D lens shape (Martinez-Enriquez et al, IOVS, 2020). Slopes of 49 rays from a 3 mm x 3 mm raster scan with 0.5 mm spacing were used to find the focus position (axial position that minimizes RMS spot size relative to centroid) for incidence angles ranging from -30° to +30° in 5° increment. The curvature of the measured image field was calculated from the variation of the focus position with the incidence angle. In addition, the radii of curvature of the tangential, sagittal, least confusion and Petzval surfaces were calculated from a model of the lens reconstructed using the lens anterior and posterior radii of curvature, thickness and calculated equivalent refractive index. The age-dependence of the field curvature obtained from the measurements and from the lens model constructed from the OCT images was quantified.

Results: The measured image field and calculated Petzval surface of the lens are concave and progressively flatten with age (shift towards less myopic peripheral defocus) (Figure 1). The measured field curvature is steeper than the curvature predicted using a uniform equivalent index, suggesting that the lens gradient contributes to field curvature.

Conclusions: Lens growth produces changes in the retinal image field curvature, which contribute to age-dependent changes in ocular peripheral defocus that may be a factor in refractive development.

CONTROL ID: 3544814

SUBMITTER (NAME ONLY): Stephanie Aigbe

TITLE: Chief Complaints of Low Vision Patients in 2019 compared to 2020

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Aigbe, N.C. Ross, Low Vision Rehabilitation, New England College of Optometry, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Stephanie Aigbe: Commercial Relationship: Code N (No Commercial Relationship) | Nicole Ross: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The COVID-19 pandemic has been disruptive to daily life, including those living with low vision (LV). We conducted a retrospective chart review to understand how chief complaints(CC) of those presenting for low vision services have changed.

Methods: A random subset of 121 charts from NECO Center for Eye Care LV Clinic between 2019 (group 1, pre-COVID-19, n=61) and 2020 (group 2, during COVID-19, n=60) were reviewed. Eligible charts included: those over 18 years, English-speaking, and without cognitive impairment. Group 1 patients were 19-96 years (mean 65, SD±23) with mean best-corrected visual acuity (BCVA) of 0.95 logMAR (SD±0.73, Snellen equivalent 20/178), and mean contrast sensitivity (CS) of 1.03 logCS (SD±0.48). Group 2 patients were 18-98 years (mean 64, SD±21) with mean BCVA of 0.77 logMAR(SD±0.63, Snellen equivalent 20/117) and mean CS of 1.08 logCS (SD±0.48). CCs were categorized as: reading, driving, technology, general LV exam (i.e no specific complaint), mobility, and watching television. Employment status, onset of LV, prior technology use, and home support were also noted.

Results: We found a significant difference between proportions of CCs reported in 2019 vs. 2020 (Cramer's V=0.32, p=0.028). For group 1, top three CCs were reading(52%), general LV exam(34%), technology(15%). For group 2, the top three CCs were reading(43%), technology(27%), general LV exam(12%). There was no significant difference in age, BCVA, CS between groups.

The proportions of CCs were significantly different for those with prior technology use (Cramer's V=0.42, p=0.001). Patients with prior technology use reported difficulties using technology at a greater frequency.

Employment status also influenced reported CCs (Cramer's V=0.29, p=0.006). Reading was the top CC amongst retirees(64%) and technology amongst the employed(30%).

Logistic regression was performed to further explore predictors of technology CCs. Prior technology use was a significant predictor (OR=6.2; 95% CI, 2.0-19.2). Onset of LV, BCVA, home support, and gender were not significant predictors. There was a trend, with more technology related complaints in Group 2 (Cramer's V=0.15, p=0.11).

Conclusions: When exploring chief complaints in 2019 and 2020, we find that there may be a shift in LV patient needs. We note a trend of increasing technology related complaints in 2020, of which prior technology use was a significant predictor.

CONTROL ID: 3544820

SUBMITTER (NAME ONLY): Damon Wong

TITLE: Evaluating the Structure-Function Relationship using Structural and Vascular Measures in Glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the global structure-relationship with optical coherence tomography (OCT) structural measures and OCT angiography (OCTA) vascular measures in subjects with primary open angle glaucoma (POAG).

Methods: 147 eyes from 101 Chinese subjects with POAG underwent OCT and OCTA scans centered on the optic nerve head, and 24-2 visual field testing using standard automated perimetry. A customized algorithm was applied to remove major vessels from the OCTA scans. For each eye, the mean circumpapillary retinal nerve fiber layer thickness from OCT (MRNFL) and mean binarized capillary density from OCTA (MCD) were calculated. Multi-variate regression analysis was performed with the visual field mean deviation (MD) as the dependent variable, and MRNFL and MCD as the predictor variables. Likelihood ratio testing was used to assess the fit of the model with MRNFL and MCD against univariate models trained using either measures separately.

Results: Mean age of the subjects was 63.48 ± 1.05 years and mean visual field severity was -3.74 ± 0.25 dB. Coefficients of MRNFL and MCD from the multi-variate regression analysis were both significant ($P < .001$). Likelihood ratio testing showed that the multi-variate model was significantly better ($P < .001$) than the univariate models using MCD or MRNFL. Predicted mean deviation from the multi-variate model achieved a Pearson correlation coefficient of 0.48 with MD, compared to 0.40 with MCD and 0.37 with MRNFL.

Conclusions: Structure-function modelling using both structural and vascular measures was better than univariate models using either structural or vascular measures, suggesting that combining both can provide complementary information to improve the structure-function relationship.

CONTROL ID: 3544823

SUBMITTER (NAME ONLY): Mark Christopher

TITLE: Performance of Deep Learning Models to Detect Glaucoma Using Unsegmented Radial and Circle OCT Scans of the Optic Nerve Head

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the accuracy of using unsegmented radial and circle OCT scans of the optic nerve head (ONH) in deep learning (DL) models to detect glaucoma and estimate visual field (VF) mean deviation (MD).

Methods: Spectralis ONH radial circle (ONHRC) scans from 192 healthy subjects (330 eyes) and 441 glaucoma patients [DMC1] (712 eyes) provided 2,601 OCTs with 62,424 radial and 7,803 circular B-scans for analysis. The ONH-centered OCTs consisted of 24 equally-spaced radial B-scans and 3 circular B-scans at diameters of 3.5mm, 4.1mm, 4.7mm. VF data consisted of 24-2 testing collected within 180 days of imaging. Subjects were randomly divided into independent training (85%), validation (5%), and test (10%) sets. Individual DL models were trained to

distinguish healthy vs. glaucoma eyes and predict VF MD based on unsegmented (1) radial and (2) circular B-scans using Resnet50 models. Diagnostic accuracy was evaluated using area under the receiver operating characteristic curve (AUC) and examined as a function of B-scan type (radial vs. circle), diameter, position, and glaucoma severity. VF estimation was evaluated using R^2 and mean absolute error (MAE).

Results: DL models using radial B-scans detected any glaucoma with an AUC (95% CI) of 0.77 (0.63 – 0.87), mild glaucoma (MD \geq -6.0 dB) with 0.69 (0.47 – 0.82), and moderate-to-severe glaucoma (MD $<$ -6.0 dB) with 0.86 (0.72 – 0.94). DL models using circular B-scans detected glaucoma with an AUC (95% CI) of 0.84 (0.76 – 0.89), mild glaucoma with 0.75 (0.66 – 0.83), and moderate-to-severe glaucoma with 0.97 (0.94 – 0.98). In detecting glaucoma, circular B-scan diameter had relatively little impact on performance, while radial B-scan position had a larger impact on performance (Figure 1). For predicting VF MD, DL models using circle scans performed better ($R^2 = 0.83$, MAE = 1.8 dB) than models using radial scans ($R^2 = 0.77$, MAE = 1.8 dB).

Conclusions: Circular B-scans outperformed radial in detecting glaucoma and performed comparably in estimating VF damage. However, radial orientation had a substantial impact on glaucoma detection accuracy. DL models that better exploit positional information could help increase accuracy.

CONTROL ID: 3544824

SUBMITTER (NAME ONLY): Lacey Haines

TITLE: Factors associated with central corneal thickness changes after crosslinking combined with photorefractive keratectomy

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The purpose of this study is to investigate changes in epithelial thickness (ET) and total corneal thickness (TCT) one year after crosslinking surgery combined with photorefractive keratectomy (CXL+PRK) and whether these changes are related to post-operative visual and refractive outcomes.

Methods: 10 eyes with keratoconus from 10 subjects were imaged with a Scheimpflug topographer and a research grade swept-source optical coherence tomographer (SS-OCT) no more than one month prior to receiving CXL+PRK surgery and again one year later. The pre-operative thicknesses of the cornea and epithelial layer at the point of minimum total corneal thickness were acquired from the SS-OCT images using custom processing software. Regression analysis was used to explore associations with corneal thickness changes and visual and refractive outcomes one year after surgery.

Results: The mean pre-operative corneal ET ($54.5 \pm 3.4\mu\text{m}$) was not significantly different than the ET at the one year follow-up ($54.3 \pm 5.0\mu\text{m}$; $p=0.46$). The average pre-operative TCT ($478.0 \pm 33.2\mu\text{m}$) was significantly greater than the same measurement one year later ($438.5 \pm 15.4\mu\text{m}$; $p=0.00065$). Individual data demonstrated both increases and decreases in ET and TCT measurements, with changes up to 17% for some participants. Changes in ET were significantly associated with changes in best corrected spectacle acuity ($R^2=0.42$; $p=0.043$) and coma ($R^2=0.75$; $p=0.0012$), but not changes in refractive error ($p>0.05$). Changes in TCT were not significantly associated with changes in VA, coma or refractive error ($p>0.05$ for all).

Conclusions: Mean central TCT measurements were significantly less at the one year follow up but ET did not show a significant change. Both increases and decreases in individual thickness data were observed. Only changes in ET were significantly correlated with changes in VA and coma such that thickness changes were inversely proportional to VA changes and directly proportional to changes in coma.

CONTROL ID: 3544825

SUBMITTER (NAME ONLY): Lauren Marek

TITLE: Systemic factors associated with diabetic macular edema in a New Mexico population

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Marek, R.N. Mankad, G. Acosta, A. Cabrera, F. Monickaraj, A. Das, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|A. Das, New Mexico VA Health Care System, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: The diagnosis of diabetic macular edema (DME) in Type I and Type II diabetics has been associated with various risk factors that correlate with progression of disease. In order to further understand the multi-factorial nature of this disease, we performed a retrospective cohort study to further examine the role of potential systemic factors associated with the development of center-involving DME among a patient population in New Mexico.

Methods: Data on 24 systemic factors was collected from 121 patients seen between February 1, 2018 and February 1, 2020 with either Type I or Type II diabetes and a known diagnosis of center-involving DME (based on OCT). These patients were then compared to a control of 69 patients with mild non-proliferative diabetic retinopathy (NPDR). Each continuous variable was statistically analyzed with chi-squared or Fisher exact test.

Results: Our analysis revealed a statistically significant difference between DME patients and the control for the following risk factors: elevated systolic blood pressure ($p < 0.016$), insulin use ($p < 0.001$), and macroalbuminuria ($p < 0.001$). There was no correlation to the levels of HbA1c, cholesterol, LDL, HDL, triglycerides, and GFR. The majority of American Indians in our cohort did not have any center-involving DME.

Conclusions: Our results show that there was no correlation between HbA1c level and development of center-involving DME. Similarly, there was lack of correlation between lipid levels and DME. The strongest associations with DME were elevated systolic blood pressure, insulin use, and macroalbuminuria. American Indians in this population appear to be protected from center-involving DME. Our ongoing genomics study using whole exome sequencing will identify the possible genetic factors related to development of DME.

CONTROL ID: 3544827

SUBMITTER (NAME ONLY): Minghao Jin

TITLE: Intense Light Stress Activated Necrosomes in Wild-Type but not RPE65-Null rd12 Mouse Retina

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jin, C. Lu, S. Li, Neuroscience Center of Excellence, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|M. Jin, Department of Ophthalmology, School of Medicine, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptors in wild-type, but not in RPE65-deficient, mouse degenerate in response to intense light damage. The mechanisms resulting in photoreceptor death or survival in these different genotype mice remain largely unknown. The purpose of this study was to know whether necrosome activation contributes to determination of the different fates of photoreceptors in wild-type and rd12 mice exposed to intense light.

Methods: Wild-type 129S2/Sv mice and rd12 mice treated with 9-cis-retinal (a functional iso-chromophore) or vehicle were exposed to 15000 lux light for different times. Photoreceptor degeneration was evaluated by peanut agglutinin (PNA)-staining, immunohistochemistry and immunoblot analysis of opsins. Expression of receptor interacting protein kinase 1 (RIPK1), RIPK3, and mixed lineage kinase domain-like protein (MLKL) in the retinas was analyzed by immunohistochemistry and immunoblot analysis. Activation of MLKL was assessed by detecting its phosphorylation. Correlation between photoreceptor degeneration and RIPK1 expression was determined by Spearman's correlation analysis. Interaction of the necrosome proteins (RIPK1, RIPK3, and MLKL) was analyzed by double-immunostaining and immunoprecipitation.

Results: Intense light induced a time-dependent rod and cone degeneration as well as gradual upregulation of RIPK1 expression in wild-type mice. Spearman's correlation analysis showed a negative correlation between photoreceptor degeneration and RIPK1 expression levels in the light exposed wild-type retinas. Intense light stress induced upregulation of RIPK1 in the retinas of rd12 mice treated with 9-cis-retinal, but not treated with vehicle. Expression of RIPK3 was markedly increased in the wild-type but not rd12 mouse retinas exposed to intense light. Retinal photodamage promoted colocalization and interaction of RIPK1 and RIPK3 in the photoreceptors of wild-type mice. Phosphorylation of MLKL was significantly increased in the wild-type retinas, but not in rd12 retinas, under the same light conditions.

Conclusions: Our results indicate 1. activation of the necrosomes contributed to light-induced photoreceptor degeneration and 2. functional visual pigments are required to activate the necrosomes in the photoreceptors under intense light stress.

CONTROL ID: 3544828

SUBMITTER (NAME ONLY): Youichi Shinozaki

TITLE: Loss of ABCA1 in astrocytes causes normal tension-glaucoma-like optic neuropathy

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Shinozaki, S. Koizumi, Department of Neuropharmacology, Interdisciplinary Graduate School of Medicine, University of Yamanashi, Yamanashi, JAPAN|Y. Shinozaki, S. Koizumi, Interdisciplinary Brain-Immune Research Center (YiBIC), University of Yamanashi, Yamanashi, JAPAN|K. Namekata, T. Harada, Visual Research Project, Tokyo Metropolitan Institute of Medical Science, JAPAN|K. Kashiwagi, Department of Ophthalmology, Interdisciplinary Graduate School of Medicine, University of Yamanashi, JAPAN|N. Ohno, Division of Ultrastructural Research, National Institute of Physiological Sciences, JAPAN|N. Ohno, Department of Anatomy, Jichi Medical University, JAPAN|

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ABSTRACT BODY:

Purpose: To clarify the mechanism of dysregulation in ATP-binding cassette transporter A1 (ABCA1) for the pathogenesis of glaucoma.

Methods: Experiments were performed using DBA/1J (wild type, WT) and ABCA1 deficient (KO) mice. Gfap-Cre::flox/flox ABCA1 and Gfap-Cre mice were used as astrocyte-specific ABCA1KO (Astro-cKO) and control mice, respectively. Intraocular pressure (IOP) was measured using a rebound tonometer. The number of retinal ganglion cells (RGCs) in the whole-mount retina was estimated by labeling them with an anti-Brn3a antibody. TdT-mediated dUTP nick end labeling (TUNEL) was performed to detect apoptotic cells. To investigate the complexity of RGC dendrites, the mice were crossed with Thy1-GFP mice to visualize their morphologies. For a detailed analysis of the optic nerve, we used serial block-face scanning electron microscopy (SBF-SEM). The ocular function was evaluated using a multifocal electroretinogram (mfERG).

Results: ABCA1KO mice showed no IOP elevation, reduction in RGC number, and an increase in apoptotic cells at 12 months old but not at 3 months old. ABCA1 signals were localized at the nerve fiber layer and co-localized with GFAP but not with vimentin signals, indicating predominant expression in astrocytes. Astro-cKO mice showed age-associated RGC degeneration without IOP elevation, atrophy of dendritic arbor of RGCs, thinning of retinal layers, axonal swelling, and impaired ocular function.

Conclusions: These data suggest that loss of function of ABCA1 is essential for glaucoma, especially astrocytic ABCA1 is important and triggers normal-tension glaucoma-like phenotype in mice.

CONTROL ID: 3544829

SUBMITTER (NAME ONLY): Hans Andrews

TITLE: Real World Safety Profile of Fluocinolone Acetonide 0.18mg Injectable intravitreal Implant (FAi) in Chronic Uveitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Andrews, S. Hamdan, S. Gangaputra, S.J. Kim, Ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: FAi is a novel therapeutic agent, and little is known about its safety profile in the real-world setting. A retrospective chart review was performed to assess the safety of long-acting FAi in the management of chronic noninfectious uveitis.

Methods: A retrospective review of 103 eyes that received FAi was completed. Outcome variables included immediate and long-term complications such as intraocular pressure (IOP) events, visual acuity (VA) decrease, and cataract surgery events.

Results: Results are reported as the proportion of eyes with available data at each follow up visit. There were no recorded immediate complications of the injection procedure. Anterior chamber implant migration occurred twice among all 103 eyes during the study period. Median IOP at baseline was 16 (IQR 14-19). 2% of study eyes experienced a 10 mmHg or greater increase in IOP 1 month from baseline (n=2/84), 7% at 3 months (n=5/74), and 4% at 6 months (n=3/61). IOP lowering therapy was necessary for 19% of eyes by 6 months (13/61) with two eyes requiring surgical intervention. A 2-line visual acuity decrease was reported in 6% of eyes at 1 month (5/84), 9% at 3 months (7/74) and 9% of eyes at 6 months (6/61). 4 of the 14 phakic eyes at baseline required cataract surgery by 6 months.

Conclusions: In this series, FAi for chronic uveitis had lower rates of steroid-induced increase in IOP as compared to conventional intravitreal steroids and incidence of cataract surgery consistent with those published in the literature.

CONTROL ID: 3544835

SUBMITTER (NAME ONLY): Michael Singer

TITLE: Time to IOP >25mmHg IOP in the PALADIN 24-month Completer Data

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Singer, Ophthalmology, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|M.A. Singer, Medical Center Ophthalmology Associate, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To better understand the timing of IOP >25 mmHg in the PALADIN Study

Methods: The PALADIN study is a 3-year observational US based prospective trial designed to explore safety signals with FAc when used in a real-world observational setting. A subset of patients' eyes with IOP > 25 mmHg were further analyzed from the PALADIN 24-month completer readout.

Results: Among 115 eyes reported, 37 events of an IOP >25 mmHg were reported. Among this group, there were 9 reported events of IOP > 30 mmHg. The majority of the eyes who experienced an IOP >25mmHg had received additional DME therapies during the follow-up period; they also had a baseline IOP > 15mmHg (76.9%). A small number of eyes with IOP > 25 mmHg were reported at all visits through month 24 with more occurring in year 1 vs year 2. 27% of events of IOP>25 mmHg occurred by 3 months. 49% occurred by 6 months, 62% by 9 months, and 72% occurred by month 12. Through 24 months, there were 9 events of IOP >30mmHg. Of the 9 events of IOP >30mm Hg, 78% were reported within the first 12 months of treatment, with the earliest being reported at month 2.

Conclusions: : A rise in IOP above 25mmHg is reported in a minority of eyes. 70% of eyes who experienced this event had it in year 1. Patients should have their IOP monitored at regular intervals to ensure timely detection of any IOP rise.

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CONTROL ID: 3544837

SUBMITTER (NAME ONLY): Edward Lee

TITLE: Macular and peripapillary ocular coherence tomography angiography findings in patients with uveal melanoma treated with proton beam therapy

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.H. Lee, R. Welch, S.S. Park, Ophthalmology, University of California Davis, Sacramento, California, UNITED STATES|K. Mishra, I. Daftari, Radiation Oncology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Though considerable work has been performed studying the retinal microvasculature in patients with uveal melanoma (UM) after plaque brachytherapy, the effects of proton beam therapy (PBT) on this microvasculature are not as well understood. We performed a cross-sectional study of patients with uveal melanoma who underwent proton beam therapy in order to assess retinal vascular changes at the macula and the peripapillary region using optical coherence tomography angiography (OCTA).

Methods: We analyzed OCTA data from 17 adult patients with UM treated with PBT more than one year ago who returned for follow-up. OCT and OCTA data from the treated eye, including parafoveal capillary density from both superficial and deep plexuses, radial peripapillary capillary (RPC) density, and choriocapillaris flow ratio, were compared to the fellow untreated eye using Student's t-test.

This study was approved by the University of California, Davis Institutional Review Board.

Results: Several OCTA features demonstrated statistically significant differences between the two study groups. Peripapillary retinal nerve fiber layer (RNFL) thickness was decreased in the treated eyes as compared to the fellow eyes (88 μ m vs 102 μ m, $p = 0.01$). RPC density was also decreased in the same manner (42% vs 49%, $p = 0.02$). As previously described, the foveal avascular zone (FAZ) perimeter was increased in treated eyes.

Conclusions: The microvasculature of the macula and notably radial peripapillary capillary density are negatively impacted in eyes which have undergone PBT for UM, even in eyes without clinical signs of radiation maculopathy or papillopathy. This is consistent with existing data showing similar changes with plaque brachytherapy. The susceptibility of this plexus to radiation damage is not fully understood but may be further elucidated with additional study of larger patient populations.

CONTROL ID: 3544838

SUBMITTER (NAME ONLY): Yong Kam

TITLE: Examining the relationship between injector lumen diameter and exposed endothelial surface area and tissue conformation of DMEK tissue scrolls

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Schmidt, M.A. Greiner, J. Ling, C. Sales, Iowa Lions Eye Bank, Iowa City, Iowa, UNITED STATES|Y. Kam, M.A. Greiner, J. Ling, C. Sales, Ophthalmology and Visual Sciences, The University of Iowa Hospitals and Clinics, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: The relationship between Descemet membrane endothelial keratoplasty (DMEK) tissue and injector devices is important to understand, particularly as options for tissue insertion expand. We hypothesize that the outer endothelial surface area of a DMEK scroll, which is exposed to trauma during tissue injection, is reduced when the internal diameter (ID) of the distal tube is narrowed.

Methods: DMEK tissues not suitable for transplantation (n=2, 8.0mm diameter) were loaded into either a Straiko or LEITR modified Jones tube (Gunther Weiss). Tissues were ejected from the proximal to the distal end of each tube, and images were captured using optical coherence tomography (OCT, Optovue RTVue) with the tissue positioned at the distal tube. The ID at the narrowest distal tube, as well as the DMEK scroll diameter as it passed through this point, were measured using ImageJ software. Using the measured diameter of the DMEK scrolls, we calculated the outer scroll surface area assuming that DMEK tissue forms a uniform cylinder.

Results: The narrowest ID measured at the distal end of the Straiko and LEITR tubes was 1,200µm (mean, 1,237µm±35; n=3) and 860µm (mean, 905µm±45; n=3), respectively. The diameter of the DMEK scroll at the narrowest ID of the Straiko and LEITR tubes was 1,122µm (mean, 1,174µm±83; n=3) and 795µm (mean, 884µm±80; n=3), respectively. The calculated DMEK outer scroll surface area was 27.3mm² for the Straiko and 19.7mm² for the LEITR tube, which represents a 27.8% decrease in exposed endothelial surface area for the LEITR compared to the Straiko tube. Qualitatively, DMEK tissues do not always form a uniform cylindrical conformation in either injector and sometimes form irregular corrugations (Figure 1).

Conclusions: In this series, DMEK tissue scroll diameter decreased in order to conform to the smallest luminal diameter of the injector. Reducing the injector's distal lumen size may result in a significant decrease in endothelial cells potentially exposed to trauma from the injector. However, tissue scroll conformation may be increasingly altered as the lumen narrows. Further studies are needed to assess the impact of lumen diameter on scroll conformation and endothelial cell loss.

CONTROL ID: 3544839

SUBMITTER (NAME ONLY): Danit Saks

TITLE: Quantification of Localised Wedge-Shaped Vessel Defects in Glaucoma

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Saks, A. Schulz, S.L. Graham, Faculty of Medicine, Health and Human Sciences, Macquarie University, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure (Abstract): Danit Saks: Commercial Relationship: Code N (No Commercial Relationship) | Angela Schulz: Commercial Relationship: Code N (No Commercial Relationship) | Stuart Graham: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Since vascular factors may be involved in the pathogenesis of glaucoma, the distribution and pattern of vascular dropout may reflect particular phenotypes. Previous optical coherence tomography angiography (OCTA) case reports have described a wedge-shaped vessel defect that projects from the optic nerve head (ONH) around the fovea in an arcuate manner, similar to retinal nerve fibre layer (RNFL) defects. This study investigates the prevalence and quantification of this vessel loss and its relationship to other parameters.

Methods: Spectral domain OCT and OCTA images from 299 subjects with suspect, early or moderate primary open angle glaucoma were reviewed (age: 67.5 ± 10.65 years; mean deviation (MD): $+2.38$ to -11.45 DB, mean = -1.63). Good quality OCTA images from 545 eyes were exported to ImageJ for analysis and to identify defects. Area and vessel density within the defect were quantified at the superficial vascular complex (SVC) level. Focal RNFL thinning was determined as a wedge-shaped defect of multiple confluent points below the 95% confidence interval.

Results: Vessel wedge defects were present in 10.8% of OCTA images (59/545 eyes; 68.9 ± 10.31 years; MD: $+2.11$ to -11.45 DB, mean = -3.27 , $p < 0.001$ compared to total cohort). Of these, 83% were located inferotemporally, including 6 eyes with both superior and inferior involvement. 47 wedge defects were able to be fully quantified due to location of the wedge relative to scanned area. Vessel density within the wedge defect averaged $16.45 \pm 6.08\%$, which was 81% of the global macular SVC density. Wedge area was on average $5.51 \pm 4.54 \text{ mm}^2$, with a width of $0.36 \pm 0.16 \text{ mm}$ at the ONH. In all eyes with wedge vessel loss, wedge-shaped RNFL thinning was identified in the corresponding region of the OCT scan. Those with vessel wedge defects also had, on average, $5 \mu\text{m}$ thinner peripapillary RNFL when compared to the total cohort ($p = 0.001$). However, analysis between global vascular and structural parameters showed only weak or no correlations.

Conclusions: This study quantified wedge-shaped vessel loss in a cross section of glaucoma patients and showed that approximately 11% of subjects have defects, predominantly inferiorly, that correlate with RNFL loss. The association between localised vessel loss and RNFL loss suggests there may be a common physiological cause, yet the temporal relationship between these factors is still to be defined and should be explored in a future longitudinal study.

CONTROL ID: 3544841

SUBMITTER (NAME ONLY): Kique Romero

TITLE: Perimeter bowl disinfection during the COVID-19 pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Romero, R. Bourque, T. Callan, K.G. Foote, E. Larson, R. Sprowl, A. Tamhakar, B. Gilbertson, Carl Zeiss Meditec Inc, Dublin, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Automated bowl perimeters present unique challenges for disinfection between patients during the SARS-CoV-2 (COVID-19) pandemic. International public health guidelines recommend the use of 70% isopropyl alcohol (IPA) or Ultraviolet-C light (UV-C) for disinfection. In this study we evaluated the effect of repeated exposure on the visual field stimulus in Humphrey Field Analyzers.

Methods: We subjected perimeter bowls (HFA3 Model 860, ZEISS, Dublin, CA and HFATM II-i, ZEISS, Dublin, CA) to highly accelerated life tests (HALT) for exposure to IPA or UV-C. For IPA, the device was sanitized with an IPA atomizing spray 15 times, followed by an 84hr IPA deep soak of components integral to the stimulus. For UV-C (Figure 1), materials of concern were irradiated with a 254nm light for a cumulative lifetime exposure of 22.8 kJ/cm². This represents an excess of 75,000 disinfection cycles at above the 1-Log Reduction (D_{90}) dose for COVID-19. The effect on the visual field stimulus (combination of projected stimulus and background illumination) was evaluated either by auto verifying that the correct luminance values were recorded at calibrated positions on the instrument or by manually measuring the chromaticity and luminance of the bowl.

Results: Automatic verification tests on an HFA3 after exposure, showed that the instrument was within tolerance with a reading error spread less than 1dB for an attenuation range of 0-34dB (Table 1). UV-C exposure to the HFA II-i bowl itself resulted in a shift of less than 0.002 in chromaticity and 18fL in luminance. Other plastics (chin rest, cover, and baffle) were visibly affected by UV-C and exhibited a shift in chromaticity (> 0.02) and luminance (> 114fL) but this did not affect the visual field stimulus.

Conclusions: There was no effect on the visual field stimulus in an HFA3 or an HFA II-i after repeated exposure to 70% IPA or UV-C at 254nm for the lifetime of the instrument. There was visible solarization on some plastics, however these did not affect the test performance; they were either outside the bowl or were compensated by the stimulus intensity.

CONTROL ID: 3544844

SUBMITTER (NAME ONLY): Rachel Ka-man Chun

TITLE: Effect of Defocus Incorporated Multiple Segments (DIMS) lenses on choroidal thickness in schoolchildren

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Chun, Z. Liu, W. Tang, D. Tse, C. Lam, C. To, Centre for Myopia Research, School of Optometry, The Hong Kong Polytechnic University, Kowloon, HONG KONG|D. Tse, C. Lam, C. To, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: To investigate the effect of Defocus Incorporated Multiple Segments (DIMS) lenses on choroidal thickness in schoolchildren

Methods: 183 myopic Chinese schoolchildren aged from 8-13 years were recruited in a 2-year double-masked and randomised clinical trial. They were either treated with DIMS lenses (n=93) or single vision (SV) lenses (n=90) in a random allocation for 2 years. Baseline measurements including cycloplegic refraction, axial length and subfoveal choroidal thickness (SFChT) were collected before the lens wear. SFChT were obtained from Ocular Coherence Tomography (OCT) images acquired by Heidelberg Spectral Domain OCT. SFChT were measured at 1 week, 1, 3, 6 months post lens wear. Cycloplegic refraction, axial length and SFChT were monitored in a 6-month interval afterwards.

Results: SFChT significantly increased after 1 week of DIMS lens wear compared to those wearing SV lenses (mean change relative to baseline \pm SD at 1 week; DIMS vs. SV; $6.57 \pm 13.54 \mu\text{m}$ vs. $-3.01 \pm 10.70 \mu\text{m}$; $p < 0.001$, repeated measure two-way ANOVA). The magnitude of the thickening increased in the first 6 months of DIMS lens wear. The choroidal thickening sustained during the 2-year lens wear (mean change relative to baseline \pm SD at 24 months; DIMS vs. SV; $13.45 \pm 26.06 \mu\text{m}$ vs. $-9.54 \pm 23.15 \mu\text{m}$). The changes in SFChT at 1 week showed a significant negative correlation with the changes in axial length at 24 months (Pearson $r = -0.2822$, $p < 0.001$).

Conclusions: Schoolchildren with DIMS lens had a significant thicker choroid at subfoveal region after 1 week of lens wear. The magnitude of choroidal thickening maintained throughout the DIMS lens wear for 2 years. Our results demonstrated that the myopic control effect by incorporating defocus produced a long-term and sustained choroidal thickening.

CONTROL ID: 3544846

SUBMITTER (NAME ONLY): William Myles

TITLE: A-type Horizontal Cell-Coupling is Enhanced in Myopic Guinea Pig Retina

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Myles, S.A. McFadden, Vision Sciences, The University of Newcastle Hunter Medical Research Institute, New Lambton, New South Wales, AUSTRALIA

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ABSTRACT BODY:

Purpose: Myopia (short-sightedness) is caused by excessive ocular growth. Hyperopic defocus can experimentally induce myopia, however the underlying mechanisms are not fully understood. Dopamine, retinoic acid and nitric oxide are intrinsic to eye growth and each helps regulate retinal gap-junction conductance. As such, cell-cell coupling may play an important role in the propagation of ocular growth signals in the retina. We investigated whether coupling between A-type horizontal cells (HC) is altered in myopic guinea pig retina.

Methods: Myopia was induced in guinea pigs from p6 using -6 diopter lenses covering one eye for 14 days. Coupling was assessed using cut-loading. Briefly; whole retinas were sustained in Ames solution (37°C, bubbled with 95% O₂ 5% CO₂) and a cut made with a scalpel blade coated in neurobiotin (3% wt/v in Ames media). Retinas were incubated for 25 minutes to allow dye to transfer, fixed (4% PFA 30 minutes), reacted with streptavidin (1:100 in PBS) and imaged using a confocal microscopy. Dye-transfer through HCs was modelled by measuring the decline in cell fluorescence per distance from the cut. For lighting experiments, animals were either dark or light-adapted for one hour prior to euthanasia and retinas were sustained in these lighting conditions for all subsequent stages.

Results: Lens-wearing Guinea pigs developed -4.95D of relative myopia in the lens-wearing eye compared with the contralateral control (W=-2.521, p=0.012). Across both eyes, A-type HCs were more extensively coupled in the superior retina than the inferior (F=7.684, p=0.024). The lens-wearing eye displayed significantly increased A-type HC coupling within both the superior and inferior retina under dark-adapted conditions relative to the contralateral control (F=6.556, p=0.034).

A-type HC coupling was dependant on the lighting environment, with light-adapted retinas displaying reduced coupling compared to dark-adapted retinas (F=17.587, p=0.001).

Conclusions: A-type HC-coupling is locally higher in superior retina which is naturally more myopic. Myopia development enhances coupling further and is possibly involved in propagating ocular growth signals in response to ocular defocus. Since coupling in A-type HCs is also enhanced by dark adaption, and conversely reduced by the light, it is possible that light stimulation may be used to counteract myopia development.

CONTROL ID: 3544849

SUBMITTER (NAME ONLY): Elizabeth Yeu

TITLE: Psychosocial Impact of Demodex Blepharitis

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Yeu, Virginia Eye Consultants, Virginia, UNITED STATES|M.J. Holdbrook, S.N. Baba, Tarsus Pharmaceuticals, Inc., California, UNITED STATES|P.J. Gomes, Ora Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blepharitis affects approximately 20 million Americans, of whom about 45% have an associated Demodex mite infestation, but the psychosocial effects of Demodex blepharitis are poorly characterized. We retrospectively analyzed a large data set of patients with confirmed Demodex blepharitis to better understand the impact of this condition on quality of life and visual function.

Methods: Adult patients (age ≥ 18) with Demodex blepharitis were examined clinically and asked questions about their daily activities and quality of life. These 311 patients had objective signs of Demodex blepharitis, including the presence of Demodex mites, presence of collarettes (cylindrical dandruff) on the lashes, and lid margin erythema. Questionnaire responses from these 311 patients with confirmed Demodex blepharitis were analyzed.

Results: Among these Demodex blepharitis patients, the majority (80%) said the condition had negatively affected daily life. Women (84%) were more likely than men (72%) to experience a negative impact in one or more areas of daily life. Half of all respondents (47%) said they had difficulty driving at night because of their blepharitis. Nearly one-third (30%) said it added time to their daily hygiene routine. Some patients said that blepharitis had caused them to reduce contact lens wear (8%) or avoid ocular surgery (5%). Patients were emotionally affected, with 47% saying they were conscious of their eyes all day; 23% constantly worrying about their eyes; and 6% saying the condition affected their mental state. Demodex blepharitis also affected respondents' appearance, with about one-quarter saying it gave their eyes or eyelids a negative appearance to others (23%) and made it difficult for women to wear makeup (34%). A smaller percentage of women (5%) noted discomfort when wearing artificial lashes.

Conclusions: Demodex blepharitis has important functional and psychosocial effects on patients. Effective treatments for this condition may have a positive impact on patients' quality of life.

CONTROL ID: 3544850

SUBMITTER (NAME ONLY): Ellen Zhou

TITLE: Long-Term Ophthalmologic Outcome of Young Adults Born Extremely Preterm

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.T. Zhou, P. Hamel, C.X. Qian, Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|P. Kassis, S. Chemtob, A. Nuyt, T. Luu, Pediatrics, Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) remains the dominant cause of severe visual impairment in childhood in North America and Europe. With the salient improvement in neonatal care since the 1980s, more and more very/extreme premature infants survived, whom now reach their adulthood. This study aimed to describe the visual function in a cohort of young adults who were born prematurely.

Methods: This cross-sectional observational study compared visual function of young adults (18-29 years old) born prematurely (< 30 weeks of gestational age [GA]) versus full-term controls. Participants were categorized into three groups: preterm without ROP, preterm with ROP and term. Comprehensive ophthalmologic examination was performed with blinding to preterm and ROP status. Best corrected visual acuity (BCVA) was assessed with a standardized linear Snellen chart and contrast sensitivity (CS) with the Vistech system. When analyzing BCVA, refractive errors and contrast sensitivities, we further grouped data based on the strong eyes (better BCVA) and the weak eyes (worse BCVA). Area-under-the-curve (AUC) analysis was performed to gauge the overall CS. Group comparisons were done using ANOVA.

Results: In this study, 88 individuals born prematurely and 86 individuals born full-term were recruited. Among the strong eyes of the 3 groups, there was no significant difference for BCVA or refractive errors (see image). Among the weak eyes, the preterm with ROP group had the worst BCVA and refractive outcomes compared to the preterm without ROP and term groups. In the strong eyes, the CS AUC of the preterm with ROP group (16.22 ± 2.69 ; $p < 0.0001$) was significantly lower than both the preterm without ROP (18.13 ± 2.01) and term (19.55 ± 2.48) groups. In the weak eyes, the AUC of the 3 groups showed a significant and progressive decline from the term group (18.9 ± 2.84) to the preterm without ROP group (18.29 ± 2.14), then to the preterm with ROP group (15.24 ± 2.21).

Conclusions: In our cohort of young adults born preterm, prematurity alone did not affect their BCVA and refractive errors. However, ROP was independently associated with a lower BCVA, higher refractive errors and a reduced contrast sensitivity. Our data have shown, that prematurity and ROP have independent effects on contrast sensitivity. This study highlights the necessity of long-term ophthalmologic follow-ups for adults who were born prematurely.

CONTROL ID: 3544852

SUBMITTER (NAME ONLY): Joo Young Kim

TITLE: A 12-week, Randomized, Double-blind, Placebo-controlled Study Assessing the Efficacy of EGHB010, a Standardized Extract of Paeoniae radix and Glycyrrhizae radix, in Patients with Early Age-related Macular Degeneration

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kim, M. Kim, R. Kim, W. Park, Y. Park, Ophthalmology, Seoul St. Mary's Hospital, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: EGHB010, a standardized extract of Paeoniae radix and Glycyrrhizae radix, inhibits choroidal neovascularization (CNV). The aim of this study is to evaluate the efficacy and safety of EGHB010 on early age-related macular degeneration (AMD) progression inhibition.

Methods: The study was designed as a randomized, double-blind, single-center, placebo-controlled study. Subjects were 50 years of age or older, and early AMD satisfied the criteria of more than 15 small ($<63\ \mu\text{m}$) drusen, less than 20 intermediate ($\geq 63, <125\ \mu\text{m}$) drusen, or pigment abnormalities. For 12 weeks, the treatment group took EGHB010 and the control took the placebo. The main outcomes were the changes in macular pigment optical density (MPOD), central macular thickness (CMT), and central choroidal thickness (CCT). Subgroup analysis was performed on subjects with MPOD <0.75 at baseline.

Results: Forty-eight subjects out of 94 were assigned to the treatment group, and 46 to the control group. At 12 weeks, mean MPOD of the treatment group increased by 0.04 ± 0.27 (p-value = 0.2730), and that of the control group decreased by 0.03 ± 0.21 (p-value = 0.7240), but there was no significant difference between the two groups (p-value = 0.1234). There were no significant differences between the two groups in mean CMT and CCT (p-value = 0.6718 and 0.6608, respectively). In subgroup analysis, there were 39 subjects with MPOD <0.75 in the treatment group and 36 in the control. Mean MPOD of the treatment group significantly increased by 0.09 ± 0.25 (p-value = 0.0218), and there was a significant difference in mean MPOD at 12 weeks between the two groups (p-value = 0.0248). Adverse reactions were similar in both groups, and no subjects had serious adverse events.

Conclusions: EGHB010 is expected to increase MPOD when administered to subjects with MPOD <0.75 . EGHB010 is worth considering as a substance that inhibits the progression of early AMD.

CONTROL ID: 3544854

SUBMITTER (NAME ONLY): Philippe Gros-Louis

TITLE: Bioprinting of a spherical hydrogel dome containing uveal melanoma cells to test the functionality of custom brachytherapy implants

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Gros-Louis, L. Piquet, C. Bellerive, S. Landreville, Department of Ophthalmology, Université Laval Faculté de médecine, Quebec City, Quebec, CANADA|P. Gros-Louis, S. Lemay, T. Lescot, L. Piquet, M. Fortin, S. Landreville, Division of Regenerative Medicine, CHU de Quebec-Université Laval, Quebec City, Quebec, CANADA|S. Lemay, T. Lescot, M. Fortin, Department of Mining, Metallurgy and Materials Engineering, Université Laval, Quebec City, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The radiation received by patients with uveal melanoma (UM) treated with brachytherapy is often poorly distributed for cases of non-spherical tumors. The manufacture of personalized brachytherapy implants (PBI) would improve patient comfort during treatment and reduce post-irradiation ocular complications. Our objective is to develop an in vitro experimental model reproducing the anatomy of the eye with a choroidal tumor in order to test the efficacy and functionality of PBI.

Methods: Our printed model will include the main elements of the extracellular matrix of the choroid and sclera, as well as choroidal fibroblasts (CF), choroidal melanocytes (CM) and UM cells (92.1, M μ 2 and Mel270). Cell death ratio (CDR) was quantified by fluorescence (LIVE/DEADTM Viability/Cytotoxicity Kit) to observe the response of choroidal and UM cell lines when embedded in a hydrogel for 0, 4 or 7 days (T0, T4 and T7). Surgical evaluation of PBI (N = 5) on freshly enucleated human eyes was done and scored (out of 35) based on mechanical properties and surgical precision (MPSP) for each prototype in order to compare them between each other and to standard brachytherapy implants (SBI).

Results: The cell line with the highest CDR was CF (T0= 23.86 \pm 2.53%) and the UM cell line with the lower CDR was Mel270 (T7= 0.79 \pm 0.42%). The CDR of the three other cell lines varied between 13.75 \pm 1.56% and 0.83 \pm 0.28%. Compared to the SBI MPSP score of 21, the two prototypes with flexible eyelets scored higher with a combined MPSP score of 27 and the resin prototype scored the highest of all prototypes with a MPSP score of 29. Both prototypes (with flexible eyelets or in resin) had higher score mainly in mechanical properties, while both the prototype with rigid eyelets and the prototype with full outline had lower scores in surgical precision, with the same MPSP score of 19.

Conclusions: Our results showed a low CDR with all 5 cell lines embedded in our model of hydrogel and identified two potential prototypes of PBI. However, bioprinting the dome and its irradiation will make it possible to better characterize the cellular structural changes post-irradiation, and to further optimize the prototypes of PBI. This would allow the development of an in vitro 3D model of choroidal melanoma for the validation of new forms of implants personalized according to the geometry of the tumor.

CONTROL ID: 3544857

SUBMITTER (NAME ONLY): Samantha Dando

TITLE: Region-specific cyst localisation and widespread innate immune activation in the retina and brain in a mouse model of toxoplasmosis

SESSION TITLE: Microglia and other Macrophages in Health and Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: *Toxoplasma gondii*, a globally distributed neurotropic parasite, is a leading cause of posterior uveitis and encephalitis. We investigated (i) whether *T. gondii* cysts preferentially localise in different regions of the retina and brain in a mouse model, and (ii) whether resident microglia are activated in a region-dependent manner during acute infection.

Methods: C57Bl/6J mice were intraperitoneally inoculated with *T. gondii* Pru-tdTomato tachyzoites (low-dose [5×10^3] n=5; high-dose [1×10^4] n=5) or PBS (n=5). In vivo multimodal fundus imaging was performed every 7 days to monitor clinical disease and initial retinal parasite invasion. Eyes and brains were collected at day 28 post-infection (or earlier if mice exhibited signs of severe infection); retinal wholemounts and brain sections were then processed for immunostaining (using Tmem119 and MHC class II antibodies) and confocal microscopy. *T. gondii* cyst burden and microglia density, field area and MHC class II expression were quantified using FIJI.

Results: Clinical disease (retinal lesions and perivascular cuffing) and tdTomato+ *T. gondii* parasites were observed in infected mice from day 14 using in vivo fundus imaging. Examination of fixed tissues revealed that cysts were detected only in mice infected with high-dose *T. gondii*. In the retina, *T. gondii* cysts were exclusively localised in the ganglion cell layer (GCL) and inner plexiform layer (IPL); whereas in the brain a predilection for cyst formation in the cortex occurred. Despite the regional specificity of *T. gondii* cysts, Tmem119+ microglia activation occurred throughout the retina and brain, evidenced by MHC class II upregulation and reduced microglia field area in all examined CNS regions (retina: GCL, IPL, and outer plexiform layer; brain: cortex, olfactory bulbs, hippocampus, cerebellum) compared to controls ($p < 0.05$). *T. gondii* infection was also associated with a large increase in Tmem119-MHC class II+ cells in the retinal GCL, and upregulation of MHC class II on brain vasculature.

Conclusions: *T. gondii* preferentially forms cysts in the innermost layers of the neural retina and the cerebral cortex; however, microglia activation is not restricted to these regions. Understanding the role of innate immunity in control of *T. gondii* replication in the CNS may lead to novel immunotherapeutic targets for toxoplasmosis.

CONTROL ID: 3544858

SUBMITTER (NAME ONLY): Sean Mullany

TITLE: A novel gelsolin variant associated with Familial Amyloidosis of the Finnish type in an Australian family

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mullany, E. Souzeau, T. Zhou, L. Knight, A. Qassim, E. Berry, H. Marshall, M. Hassall, R.A. Mills, J.E. Craig, O.M. Siggs, Flinders Centre for Ophthalmology, Eye and Vision Research, Flinders University, Adelaide, South Australia, AUSTRALIA|J. Breen, Faculty of Health and Medical Sciences, University of Adelaide, Adelaide, South Australia, AUSTRALIA|S. Klebe, College of Medicine and Public Health, Flinders University, Adelaide, South Australia, AUSTRALIA|M. Hussey, A. Dubowsky, Department of Pathology, Flinders Medical Centre, Bedford Park, South Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: This study identified and sought to validate the association between a novel gelsolin (GSN) variant and the phenotype of Familial Amyloidosis of the Finnish type (FAF) in three first degree relatives harbouring a previously undocumented variant, and manifesting multiple clinical and ophthalmic features consistent with systemic gelsolin (GSN) amyloidosis.

Methods: Three first degree relatives presenting to a single tertiary ophthalmic outpatient clinic exhibiting clinical features consistent with FAF including cutis laxa and vision-affecting corneal stromal changes were enrolled in a genetic study of corneal disease. DNA extracted from whole blood samples collected from two individuals was subjected to exome sequencing. Genes associated with corneal disease were assessed for rare and potentially deleterious variants. Histopathological and immunohistochemical studies of proband corneal tissue collected at the time of corneal graft surgery were performed to investigate for the presence of GSN within corneal deposits.

Results: A previously undocumented GSN:c.1477T>C variant resulting in a predicted p.(Trp493Arg) missense variant was identified in the two individuals who underwent exome sequencing. This variant was subsequently confirmed in all three affected individuals through Sanger sequencing. This rare variant which was absent from the Genome Aggregation Database (gnomAD), a large population-based database of 125,748 exomes and 15,708 genomes, was predicted to be damaging by in silico tools (Phred scaled CADD score: 20.8). Histopathological studies performed on the proband cornea demonstrated irregular stromal inclusions which manifested classic amyloid features when subjected to Congo red staining, and intense GSN labelling in immunohistochemical studies.

Conclusions: This study is the first to describe an association between the GSN:c.1477T>C,p.(Trp493Arg) variant and FAF. This novel variant which affects a GSN region distant from the classic p.Asp214Asn variant and the gelsolin 2 (G2) domain, may lead to insights into the amyloidogenic mechanisms of FAF-associated GSN variants.

CONTROL ID: 3544859

SUBMITTER (NAME ONLY): Martha Neuringer

TITLE: Early Phenotype in a Nonhuman Primate Model of Bardet-Biedl Syndrome

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Bardet-Biedl syndrome (BBS), a syndromic form of retinitis pigmentosa, is a rare autosomal recessive ciliopathy linked to mutations in over 20 BBS genes. It is characterized by rod-cone degeneration in conjunction with renal dysfunction, polydactyly, obesity, hypogonadism and/or intellectual disability. We recently identified and characterized a pedigree of rhesus monkeys with a spontaneous mutation in BBS7. Three affected homozygotes showed severe degeneration of the macular retina by 3-4 years of age, and one developed kidney failure by 6 years of age (Peterson et al., Exp Eye Res 189, 2019, 1078252). We are now beginning to define the development of the retinal degeneration phenotype from birth.

Methods: Ova and sperm were collected from BBS7 carriers to produce embryos by intracytoplasmic sperm injection. Trophectoderm biopsies were sequenced to select BBS7^{-/-} embryos, which were transferred to surrogate dams. A live infant was confirmed to be homozygous for the BBS7 mutation and was assessed by multimodal retinal imaging at 4, 8, 16 and 24 weeks of age, by electroretinography (ERG) at 6, 12 and 24 weeks, and by preferential looking measures of visual acuity at 2, 4, 8, 12 and 16 weeks.

Results: At the first retinal imaging session at 4 weeks of age, the EZ line was severely attenuated. Segmentation of OCT images from 4 - 24 weeks of age showed that thicknesses of the total retina and outer segment layers were well below the normal range as determined in 8 age-matched normal rhesus monkey infants, while the inner retinal layers were within or close to the normal range. At 6 - 24 weeks, photopic and scotopic electroretinograms were substantially reduced in amplitude and delayed. Visual acuity was half of normal values at all ages, compared with longitudinal values for 22 normal infants.

Conclusions: The first examination of an infant rhesus monkey with BBS7 showed evidence of retinal thinning and dysfunction as early as 4 weeks of age. The rapid onset of degenerative changes in this model will make it particularly valuable for preclinical studies of therapies for vision preservation or restoration. This is the first nonhuman primate model of retinitis pigmentosa with a known genetic cause, and its propagation will provide the foundation for future studies of cell replacement approaches to treatment for this family of blinding disorders.

CONTROL ID: 3544860

SUBMITTER (NAME ONLY): Paris Hanson

TITLE: Use of Dexamethasone Intraocular Suspension 9% in Patients with Glaucoma: Results from a Retrospective Study

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To explore the real-world clinical outcomes in patients with a history of glaucoma treated with sustained-release dexamethasone intraocular suspension 9% for inflammation control following cataract surgery.

Methods: Retrospective data were collected from records of patients at multiple surgical sites who received dexamethasone intraocular suspension at the end of cataract surgery between Mar 12 and Dec 15, 2019. Anterior chamber cell (ACC) and intraocular pressure (IOP) at postop days 1, 8, 14, and 30 were summarized, along with minimally invasive glaucoma surgery (MIGS) procedures and number of concomitant IOP-lowering medications.

Results: 641 eyes of 527 patients treated with dexamethasone intraocular suspension were included in the study; glaucoma history was reported for 80 eyes of 66 patients. 15 of these eyes had a MIGS procedure; mean (SD) IOP-lowering medications per eye was 1.4 (0.53). For those with a record at each visit, mean (SD) IOP was 18.5 (8.50), 14.3 (4.34), 15.3 (3.31), and 14.4 (3.51) mmHg at postop days 1, 8, 14, and 30; ACC clearing at these timepoints was present in 52%, 68%, 82%, and 90% of eyes. In the full study population, IOP at the same timepoints was 18.6 (6.69), 15.2 (4.51), 15.1 (3.86), and 14.1 (3.84) mmHg; and 40%, 65%, 85%, and 90% of eyes had no ACC.

Conclusions: Results in this subset of eyes provide real-world insight into the use of a sustained release intraocular corticosteroid in patients with glaucoma undergoing cataract surgery; antiinflammatory efficacy and safety with regard to IOP elevation were similar to the full study population.

CONTROL ID: 3544864

SUBMITTER (NAME ONLY): Amy Scheffler

TITLE: Design, Methods, and Rationale for the Collaborative Ocular Oncology Group 2 (COOG2) Study

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Scheffler, Ophthalmology, Houston Methodist Hospital, Houston, Texas, UNITED STATES|P. Mruthyunjaya, Stanford Medicine, Stanford, California, UNITED STATES|C. Decatur, Z. Correa, J.W. Harbour, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|M. Materin, K. Semenova, Duke University, Durham, North Carolina, UNITED STATES|T. Aaberg, Michigan State University, East Lansing, Michigan, UNITED STATES|B. Marr, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of the COOG2 study was to conduct a large, multicenter study to prospectively evaluate and optimize the established biomarker gene expression profile (GEP), along with emerging biomarkers PRAME and prognostic driver mutations BAP1, SF3B1 and EIF1AX using a novel next generation sequencing (NGS) panel.

Methods: Institutional Review Board (IRB)/Ethics Committee approval was prospectively obtained. Subjects who met the following inclusion criteria were enrolled prospectively: 18 years and older; diagnosed with a uveal melanoma; undergoing a fine needle aspiration biopsy with treatment of enucleation, I-125 plaque therapy, proton beam therapy, or close observation; able to consent to baseline/ongoing metastatic screening; no previous treatment for UM.

Results: 1756 patients were enrolled from 26 sites across the U.S. and Canada. Mean age at time of enrollment was 62 years. 793 patients were women and 963 were men. 1434 patients identified as non-Hispanic white, 57 self-identified as Hispanic, and the remainder declined to answer. 824 eyes enrolled in the study were right and 932 were left. 587 eyes were identified as blue/green, 240 as brown, and the remainder as mixed/intermediate. 98 (6%), 1356 (83%), 302 (17%), and tumors involved the iris, choroid, and ciliary body primarily, respectively. 83 (5%) had associated congenital ocular melanocytosis. The largest base dimension of the tumors in the study ranged from 1.9 mm to 34 mm (mean, 11.8 mm). The thickness of the tumors ranged from 0.5 to 18 mm (mean, 4.9 mm).

171 (10%) were treated with enucleation, and 1296 (74%) with radioactive plaque therapy with biopsy, 120 (7%) with proton beam therapy with biopsy, and 169 (10%) with biopsy then observation. GEP/Prame status was: 1A/Prame- for 577 (33%), 1A/Prame+ for 157 (9%), 1B/Prame- in 302 (17%), 1B/Prame+ in 104 (6%), 2/Prame- in 287 (16%), and 2/Prame+ in 234 (13%). The remaining 6% had a pending GEP analysis from recent enrollment. NGS results are in process.

Conclusions: The COOG network has prospectively collected clinical, molecular, and outcomes data in a 26-center study resulting in the largest database of information ever collected for this cancer. Forthcoming analyses will define a new, more accurate classification system for metastatic prognostication as well as the gold standard synthetic control arm for future adjuvant therapeutic trials.

CONTROL ID: 3544867

SUBMITTER (NAME ONLY): James Samson

TITLE:

Cataract Surgery Outcomes in Uveitis Patients: Experience at a Single
Tertiary Referral Center

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Samson, C.M. Samson, C.I. Samson, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|J.M. Samson, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose:

To describe the cataract surgery outcomes of a cohort of patients with uveitis at a single tertiary care center

Methods:

Charts of patients seen on the Uveitis Service at the Manhattan Eye, Ear, and Throat Hospital with a diagnosis of uveitis who underwent cataract surgery between 2017 - 2020 were reviewed.

Results:

A total of 104 patient charts were reviewed with 121 eyes undergoing cataract surgery. The most common type of uveitis was anterior (66.9%). The most common etiologies were idiopathic (54.8%), sarcoidosis (5.77%), and birdshot (5.77%). 57.0% of patients had uveitis severe enough to warrant systemic immunomodulatory therapy. The complication rate, when including 'significant postoperative inflammation,' was 17.8%; without it, the rate was 5.0%. Intraoperative complication rate was 0.8%. 71.2% of patients had 20/40 or better vision at 1 year. Only 6.6% eyes had 20/200 or worse vision, all due to structural damage to the optic nerve or retina unrelated to the surgery.

Conclusions:

Uveitis patients undergoing cataract surgery have a high incidence of postoperative complications, despite a low intraoperative complication rate. Long-term outcomes depended more on the uveitis severity and control than incidents of operative or peri-operative complications.

CONTROL ID: 3544870

SUBMITTER (NAME ONLY): Dheo Cahyo

TITLE: Volumetric Choroidal Segmentation with a Novel Deep Learning Approach fusing Spatial Information

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Cahyo, L. Schmetterer, Ocular Imaging, Singapore Eye Research Institute, Singapore, SINGAPORE|A. Yow, D. Wong, Nanyang Technological University, Singapore, Singapore, SINGAPORE|S. Saw, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To evaluate the performance of a novel deep learning-based volumetric choroidal segmentation approach incorporating spatial information on swept source optical coherence tomography (SS-OCT) images in eyes with myopia.

Methods: 126 myopia eyes were acquired using a commercial swept-source OCT (SS-OCT) system, DRI OCT Triton (Topcon Corp., Japan) at a 1050 nm wavelength, scanning speed of 100,000 A-scans/sec and 7 mm × 7 mm scanning protocol, centered at the macula. Each volumetric image contained 256 cross-sectional B-scans with dimensions of 256×128 pixels. Manual annotations of the choroid were used as the ground truth. We implemented a novel multi-task deep convolutional neural network architecture, which we named as SA-Net, that reconstructs and segments a target B-scan with the incorporation of spatial context from neighbouring B-scans. Intersection over Union (IoU) of the volumetric segmentation and Structural Similarity Index (SSIM) of the enface choroidal thickness map were used to assess the accuracy of the detected volume. Results were also compared with choroidal segmentation using U-Net.

Results: For the myopia eyes (spherical equivalent = 5.44 ± 2.11 D), the measured choroidal thickness was 0.204 ± 0.046 mm. SA-Net required a processing time of 1.08s for each volumetric choroidal segmentation, and achieved an average cross-validation segmentation IoU of 0.942 (95% CI: 0.937 to 0.946) compared to an IoU of 0.929 (95% CI: 0.923 to 0.934) with U-Net. The mean absolute difference between the ground truth choroidal volume and volumetric segmentation for SA-Net was 0.191 mm^3 (95% CI: 0.164 mm^3 to 0.218 mm^3) with a mean absolute sub-foveal choroidal thickness difference of 0.010 mm (95% CI: 0.008 mm to 0.012 mm) between the ground truth and segmented. For the choroidal thickness map we obtained SSIM of 0.700 (95% CI: 0.688 to 0.711) compared to the ground truth thickness map.

Conclusions: The novel SA-Net approach showed a high accuracy in detecting the choroid from volumetric OCT cube scans in eyes with myopia. This indicates that spatial information can provide useful context for volumetric segmentation. The results are promising for the automated detection of the choroid for further analysis in myopia and other ocular diseases.

CONTROL ID: 3544872

SUBMITTER (NAME ONLY): Susie Suh

TITLE: Base editing restores retinal and visual function in the mouse model of Leber congenital amaurosis

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: CRISPR-Cas9 genome editing has great potential for the treatment of numerous inherited retinal diseases, but its clinical application has been hampered by low precision and substantial indel formation. Cytosine and adenine base editors (CBEs and ABEs) enable conversion of a point mutation in a predictable manner independent of Cas9-induced double-stranded DNA breaks and homology-directed repair. We hypothesized that base editors can be used to target the mutations associated with inherited retinal diseases. To test our hypothesis, we delivered ABE to the rd12 mouse model, which harbors a de novo mutation in the Rpe65 gene, and evaluated the therapeutic efficacy of ABE.

Methods: We first screened for a sgRNA enabling mutation correction using an rd12 mutation-harboring stable cell line. Next, we packaged the selected sgRNA and ABE into a lentivirus, and subretinally delivered to the rd12 mice at 4 weeks old. After 5 weeks, we assessed the DNA correction and RPE65 rescue by deep targeted amplicon sequencing, off-target analysis, immunoblot and retinoid analysis. Furthermore, we evaluated visual function in treated mice with electroretinography, optomotor response assay and visual cortex recordings. Cone density was examined with retinal wholemount stained with cone opsin-specific antibodies.

Results: A subretinal injection of a lentivirus expressing the ABE and a sgRNA corrected a pathogenic mutation in the Rpe65 gene up to 29% with minimal indel and off-target mutations despite the absence of a canonical "NGG" protospacer-adjacent motif (PAM) sequence. The ABE-treated mice show restored RPE65 expression, retinoid isomerase activity, and retinal and visual function at near-normal levels. Treated mice also revealed a higher cone density on retinal flatmounts compared to untreated mice.

Conclusions: In this proof-of-concept study, we provide evidence of the clinical potential of base editors for the correction of mutations causing inherited retinal diseases and for restoring visual function. Base editing technology can provide an alternative treatment model of gene augmentation therapy to permanently rescue the function of a key vision-related protein disabled by mutations.

CONTROL ID: 3544873

SUBMITTER (NAME ONLY): Mojtaba Moharrer

TITLE: Introduction of a novel low-cost myopia Refraction Kit pilot study

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Uncorrected myopic refractive error affects the lives and wellbeing of more than 500 million persons worldwide, most residing in low/middle-income countries. One of the obstacles to addressing the issue of uncorrected refractive error in rural communities in low/middle-income countries is the implementation of refraction measurement. In 2019, a pilot study was conducted in a remote rural community in India, testing an easy-to-use low-cost Refraction Kit (RK) for measurement of refraction error which can be performed by lay persons.

Methods: The easy-to-use RK was developed in 2019 by two vision science researchers; the RK consists of 16 pages of Tumbling E letter chart and a tape measure. The RK determines refraction error based on viewing distance in lieu of trial lenses; it was first tested in the lab on 8 myopic eyes for proof-of-concept. The RK was then pilot tested by a layperson in the rural village of Venkatapuram in Telangana, India, where there is no access to eye-care professionals. The layperson who conducted the tests was the local postmaster who trained by watching a 10 min tutorial video. The postmaster conducted the test on 30 primary school students (age: 8 -9; 13 girls and 17 boys). The duration of the test for each person was less than 10 minutes.

Results: In the laboratory proof-of-concept test, refraction error measured by RK ($M = 3.94$, $SD = 1.66$) was not significantly different from the eye prescriptions of the patients ($M = 3.56$, $SD = 1.69$) using paired t-test[1] ($t(7) = -1.58$, $p = 0.156$). In the on-site pilot study in India, it was found that 20% of students were nearsighted (2 girls and 4 boys) ranging from -1 to -3 diopters.

Conclusions: There is a dire need for providing low-cost and easy-to-use solutions for measuring refraction error in many remote areas around the world. The new low-cost RK could be potentially used to address this issue because of its low cost, relative accuracy, and ease of use by laypersons.

CONTROL ID: 3544874

SUBMITTER (NAME ONLY): Amee Azad

TITLE: Revisit rates and associated costs after emergency room encounters for ophthalmic conditions

SESSION TITLE: Cornea Trauma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To characterize emergency department (ED) revisit rates related to ophthalmologic conditions, variation by diagnosis, and costs.

Methods: We identified 3- and 30-day ED revisit rates by diagnosis, diagnosis categories and demographic groups. Costs associated with revisits were described as a percentage of index visits and adjusted to 2016 US dollars using the Consumer Price Index. We utilized logistic multivariable regression analysis to identify factors significantly associated with revisits.

Results: Among a total of 828,125 index ED encounters from 2007-2016 with an ophthalmic condition as a primary diagnosis, the 3- and 30-day revisit for the overall cohort was 2.5% and 4.1% respectively. Conditions of the cornea and external disease comprised the majority of index diagnoses (65.2%) but were associated with low rates of 30-day revisit (3.1%). Thirty-day revisits rates were highest for conditions related to cataract and lens disorders (28.3%) as well as glaucoma (15.9%). Nearly all (99%) patients revisiting the ED with cataract and lens disorders had a cataract-related procedure within 30 days of the index encounter. In multivariable analysis, younger adults, those with insurance plans lacking out-of-network coverage and cases involving an ophthalmologist were associated with a significantly higher likelihood of a revisit within 3-days of an index visit. Conversely, patients with higher out-of-pocket costs during an index visit were significantly less likely to revisit in the same period.

Conclusions: Revisit rates for ocular conditions overall are low but varied by diagnosis category. Cataract and lens disorders had the highest 30-day revisit rate (with the vast majority within the 30-day postoperative period) followed by glaucomatous disorders. Younger patients, those with insurance lacking out-of-network coverage, those with lower OOP costs on an index visit and patients with an ophthalmologist participating in their ED care all had higher revisit rates. ED revisits for ocular conditions may be preventable with timely follow-up care, particularly for patients presenting in the acute post-operative period following cataract surgery.

CONTROL ID: 3544877

SUBMITTER (NAME ONLY): Ashish Jith Sreejith Kumar

TITLE: Evaluation of Generative Adversarial Networks for High-Resolution Synthetic Image Generation of Circumpapillary Optical Coherence Tomography Images for Healthy Eyes

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the use of generative adversarial networks for the synthesis of high-resolution circumpapillary optical coherence tomography (OCT) images.

Methods: Cross-sectional circumpapillary OCT images of 1590 Chinese, 1040 Malay, and 1327 Indian healthy eyes from the Singapore Epidemiology of Eye Diseases (SEED) study were obtained from a commercial high resolution OCT system (Cirrus HD-OCT, Carl Zeiss Meditec) using an optic nerve head centered imaging protocol. These images were used to train ethnicity-specific Progressively Growing Generative Adversarial Network (PGGAN) models for the generation of synthetic images. In addition, another PGGAN model was trained using the images from all the three ethnicity datasets (a total of 3957 images). An evaluation dataset was constructed for each model using 25 generated synthetic images and an equal number of actual images from the corresponding training data. Two clinicians were asked to review the authenticity of the images in each dataset and were not provided with prior knowledge of the distributions.

Results: Examples of the generated images are shown in Figure 1. Each clinician reviewed the datasets independently. Between the two clinicians, the average accuracy was 49% for the Chinese evaluation dataset (Precision=49%, Recall=48%), 37% for the Malay evaluation dataset (Precision=31%, Recall=28%), 43% for the Indian evaluation dataset (Precision=28%, Recall =33%), and 37% for the combined evaluation dataset of all three ethnicities (Precision=27%, Recall=26%). There were differing opinions on 52% of the synthetic images generated from the Chinese, Malay, and Indian PGGAN models and 40% of the synthetic images from the combined ethnicity-based PGGAN model. Only 24%, 20%, 32%, and 28% of the images generated from the Chinese, Malay, Indian, and combined PGGAN models respectively, were correctly identified as synthetic images by both the clinicians.

Conclusions: Synthetic circumpapillary OCT images generated using PGGAN approach were difficult to discern from actual images. The results suggest a potential use of deep learning-based generative models for data generation and augmentation.

CONTROL ID: 3544880

SUBMITTER (NAME ONLY): Sandra Hammer

TITLE: Statins and α cyclodextrin treatments prevent cholesterol crystal-induced pathology in human retinal endothelial cells and in db/db mice.

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.S. Hammer, D. McFarland, J.V. Busik, Physiology, Michigan State University, East Lansing, Michigan, UNITED STATES|G. Abela, Medicine, Michigan State University, East Lansing, Michigan, UNITED STATES|S. Li Calzi, M.B. Grant, Department of Ophthalmology and Visual Sciences School of Medicine, University of Alabama at Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous work highlights the detrimental effect elevated retinal cholesterol levels have on diabetic retinopathy (DR) progression. We have shown that downregulation of LXR α /SIRT1 results in dysregulated cholesterol metabolism and increased retinal cholesterol levels. In turn, elevated cholesterol levels lead to the formation of retinal cholesterol crystals (CC), exacerbating the pro-inflammatory and apoptotic milieu present in the diabetic retina. The focus of this study was to investigate the therapeutic potential of cholesterol lowering drugs in preventing CC-induced retinal damage in endothelial cells and in a type 2 diabetic mouse model.

Methods: Human retinal endothelial cells (HREC) were treated with CC (2mg/ml) and/or CC pretreated with Atorvastatin (10mM), Rosuvastatin (10mM), or α cyclodextrin (10mM) for 24hrs. Inflammation was measured via IL6 and IL8 levels by qRT-PCR. Cell survival was determined via trypan blue exclusion assay. Type 2 diabetes was modeled in vivo via the db/db mouse model. Alpha cyclodextrin was administered three times a week for 2 weeks via subcutaneous injections (4g/kg). Cholesterol crystals were visualized using SEM and quantified using ImageJ software analysis.

Results: Pretreatment of CC with Atorvastatin, Rosuvastatin, or α cyclodextrin reduced the amount of crystals when compared to non-treated controls ex vivo. In culture, administration of CC significantly upregulated IL6 and IL8 expression ($p < 0.0001$; $n = 3$) in retinal endothelial cells. Treatment with Atorvastatin ($p < 0.05$), Rosuvastatin ($p < 0.001$), or α cyclodextrin ($p < 0.0001$) significantly prevented CC-induced IL6 and IL8 upregulation ($n = 3$). CC significantly increased cell death ($p < 0.01$) after 24hrs while pretreatment with Atorvastatin, Rosuvastatin, or α cyclodextrin prevented CC-induced cell death ($n = 3$). Lastly, long term type 2 diabetes (6 months) significantly increased the amount of retinal CC ($p < 0.05$; $n = 5$) while treatment with α cyclodextrin significantly reduced crystal formation in diabetic mice ($p < 0.01$; $n = 3$).

Conclusions: Increased retinal cholesterol levels, resulting from long term diabetes, leads to the formation of pro-inflammatory CC formation. Treatment with cholesterol lowering and/or dissolving therapeutics is an effective strategy to reduce retinal inflammation and cell death by preventing CC induced retinal damage.

CONTROL ID: 3544881

SUBMITTER (NAME ONLY): Kwan Wun Tsang

TITLE: Effect of lutein in olive oil in the mouse oxygen-induced retinopathy model

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Tsang, A.C. Lo, Department of Ophthalmology, The University of Hong Kong, Hong Kong, HONG KONG|A.M. Joussen, Ophthalmology, Charité – University Medicine Berlin, Berlin, GERMANY|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP), a proliferative retinopathy in preterm babies, is an oxidative stress associated disease. Lutein as anti-oxidative agent is a potential therapeutic agent for ROP. To improve the bioavailability of lutein, olive oil was used to dissolve lutein. To investigating the effect of lutein in olive oil in ROP progression, retinal vasculature and function were examined in mouse oxygen-induced retinopathy (OIR) model.

Methods: C57Bl/6J mother and their pups were placed into 75% oxygen chamber from postnatal day (P) 7 to P12. DMSO, olive oil alone, lutein in DMSO or lutein in olive oil (0.2mg/kg) were intraperitoneally injected into the pups starting from P12 daily. Retinal vasculature was examined in isolectin-stained retinal flat mounts at P14 and P17. Retinal function was assessed at P17 using scotopic electroretinography (ERG).

Results: Olive oil alone, lutein in DMSO and lutein in olive oil did not affect the body weight under normal room air (RA) condition or after OIR at P14 and 17. Under normal RA, the pups receiving lutein in DMSO have higher a-wave and b-wave amplitudes at P17 without affecting the normal retinal vascular development when compared with DMSO, olive oil alone or lutein in olive oil treated group. After OIR, olive oil or lutein in olive oil treated groups have a larger avascular area (DMSO: 26.4±2.9%; olive oil: 32.3±2.6%; lutein in DMSO: 26.2±2.7%; lutein in olive oil: 32.4±3.4%). At P17, although no significant difference was observed in the size of neovascularization, olive oil alone, lutein in DMSO and lutein in olive oil treated pups have a larger avascular area (DMSO: 13.5± 2.8%; olive oil: 17.3±7.2%; lutein in DMSO: 18.1±1.6%; lutein in olive oil: 16.6±5.0%). Most importantly, lutein in olive oil treated pups have higher a-wave and b-wave amplitudes with shorter implicit times.

Conclusions: Lutein in olive oil treated pups displayed an improvement of retinal function including the function of photoreceptors, bipolar cells and Müller cells after OIR, suggesting that lutein in olive oil may preserve retinal function after OIR despite limited effects in vascular protection.

CONTROL ID: 3544883

SUBMITTER (NAME ONLY): Ann Shue

TITLE: Rare Complications of Selective Laser Trabeculoplasty – Corneal Edema, Thinning and Hyperopic Shift: Incidences in the Optum Data Set

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Villegas, S.Y. Wang, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|A. Shue, Ophthalmology, Lucile Salter Packard Children's Hospital at Stanford, Palo Alto, California, UNITED STATES|A. Shue, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ann Shue: Commercial Relationship: Code N (No Commercial Relationship) | Natacha Villegas: Commercial Relationship: Code N (No Commercial Relationship) | Sophia Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Case reports and series describe post-selective laser trabeculoplasty (SLT) central corneal edema, with subsequent thinning and hyperopic shift, which can permanently affect vision. This study tested the hypothesis that the incidences of these findings post-SLT are low in the United States.

Methods: This is a 16-year retrospective population-based study of glaucoma patients >18 years using a de-identified database of administrative health claims for patients of a large national managed care company affiliated with Optum, the Clinformatics[®] Data Mart (CDM). Included for analysis were patients' first SLT with one year of continuous enrollment pre-SLT without prior corneal pathology including edema, ectasia, keratomalacia, recurrent erosions, endothelial dystrophy, herpes simplex and varicella zoster viral keratitis, corneal transplant and complications, corneal scars and other disorders of cornea. The primary outcome was corneal edema in at least one eye within 30 days post-SLT and secondary outcomes were keratomalacia, ectasia or other specified disorders of cornea in at least one eye within 120 days post-SLT.

Results: From the CDM's medical claims and medical procedures tables, 86,634 patients had undergone SLT in at least one eye. After exclusion of prior corneal pathology, 83,253 remained. The baseline characteristics of this cohort revealed 9,472(11%) had myopia, 3,718(4%) hyperopia, 1,518(2%) irregular astigmatism, 55,002(66%) primary open angle glaucoma, 10,765(13%) ocular hypertension, 5,010(6%) normal tension glaucoma, 2,452(3%) pseudoexfoliative glaucoma, 1,790(2%) pseudoexfoliation syndrome, 1,775(2%) pigmentary glaucoma, 1,409(2%) pigment dispersion syndrome, 1,755(2%) chronic angle closure glaucoma, 498(<1%) steroid response, and 310(<1%) uveitic glaucoma. 36 were found to have corneal edema within 30 days post-SLT, and 21 with keratomalacia, ectasia or other specified disorders of cornea within 120 days post-SLT. None overlapped. The overall incidence of both primary and secondary outcomes in patients without previous corneal pathology was 0.07%.

Conclusions: New corneal edema, keratomalacia, ectasia was found post-SLT at a low rate in a cohort with diverse glaucoma diagnoses. Laterality cannot be determined within the dataset, thus the rate may be even lower. Future studies may reveal risk factors among the baseline characteristics.

CONTROL ID: 3544885

SUBMITTER (NAME ONLY): Shireen Khattak

TITLE: Suprachoroidal space injection of AAV provides widespread gene expression in the mouse eye.

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Khattak, M. Reyad, D. Sun, Y. Liu, C. Romano, Ophthalmology, Regeneron Pharmaceuticals Inc, Tarrytown, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Shireen Khattak: Commercial Relationship(s);Regeneron Pharmaceuticals Inc. :Code E (Employment) | Matthew-Mina Reyad: Commercial Relationship(s);Regeneron Pharmaceuticals Inc.:Code E (Employment) | Duo Sun: Commercial Relationship(s);Regeneron Pharmaceuticals Inc.:Code E (Employment) | Yang Liu: Commercial Relationship(s);Regeneron Pharmaceuticals Inc.:Code E (Employment) | Carmelo Romano: Commercial Relationship(s);Regeneron Pharmaceuticals Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Suprachoroidal space (SCS) injection of adeno-associated virus (AAV) provides widespread transgene expression in rat and monkeys (Ding et al. 2019). Here, we developed a technique to perform SCS injections in mice and tested various AAVs to determine whether similar results could be achieved in mice.

Methods: Adult C57BL/6 mice were injected with 3 uL of AAV9 (n=12 eyes) or AAV8 (n=14) CAG-GFP (1E13 vg/mL). For SCS injections, a 30-gauge needle was used to create a shallow incision in the sclera. A 33-gauge needle with 20-degree bevel attached to a 10 uL Hamilton syringe was advanced under the sclera. Correct localization into the SCS was confirmed by evaluating the bevel, which is observable under the transparent sclera but not the pigmented choroid. Once the bevel was within the SCS, the solution was slowly injected. Two weeks post-injection, fundus autofluorescence (FAF) imaging was performed, mice were sacrificed, and eyes were fixed and prepared for flatmounts (RPE/sclera, retina, cornea) or cryosections. Sections and flatmounts were stained with anti-GFP antibody. HALO software was used to quantify the total area of anti-GFP signal in RPE and retinal flatmounts.

Results: FAF imaging showed widespread GFP signal in the eye with AAV8 & AAV9 injection. Similarly, RPE and retinal flatmounts showed extensive GFP expression with both viral vectors. Cryosections showed that GFP signal in the retina was mostly found in the photoreceptor cell layer. Quantification of the total area of anti-GFP signal in RPE flatmounts revealed the greatest coverage in AAV9 group (59% \pm 25%), followed closely by AAV8 (49% \pm 18%). In the retina, AAV8 & AAV9 provided equal area of GFP expression (55% \pm 27% and 56% \pm 28% coverage, respectively). Lastly, GFP signal was also found in flatmounts of sclera and cornea (stromal layer and endothelial cells) with both vectors.

Conclusions: SCS injection of AAV8 and AAV9 provided widespread transgene expression. Several ocular tissues were transduced, including the sclera, RPE, retina, and cornea. The ability to perform SCS injections in mice allows for the exploration of this delivery method in relevant mouse models of ocular disease.

CONTROL ID: 3544892

SUBMITTER (NAME ONLY): Dong Ho Park

TITLE: Customized Color Settings of Digitally Assisted Vitreoretinal Surgery Enable a 3-Fold Decrease of Indocyanine Green Stain Concentration

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Park, S. Park, J. Do, Department of Ophthalmology, Kyungpook National University, Daegu, Daegu, KOREA (THE REPUBLIC OF)

Commercial Relationships Disclosure (Abstract): Dong Ho Park: Commercial Relationship: Code N (No Commercial Relationship) | Su Jin Park: Commercial Relationship: Code N (No Commercial Relationship) | Jae Rock Do: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the color contrast ratio (CCR) of the internal limiting membrane (ILM) using different color settings of digitally assisted vitreoretinal surgery (DAVS) with different indocyanine green (ICG) concentrations.

Methods: Consecutive patients were enrolled that underwent 25G vitrectomy and ILM peeling using a standard operating microscope (SOM) (25 eyes), DAVS Ver. 1.1 (12 eyes), and DAVS Ver. 1.3 (13 eyes). The SOM and DAVS Ver. 1.1 groups used 0.075% ICG, and DAVS Ver. 1.3 used 0.025% ICG. In DAVS Ver. 1.1, macular CCR was compared between four different presets in the red, green, and blue channels. In DAVS Ver.1.3, macular CCR was evaluated using two different customized settings mainly modifying the hue and saturation. ILM peeling time was compared.

Results: In DAVS Ver. 1.1, macular CCR was the highest in Preset 3 ($P < 0.01$). The CCR of customized Setting 2 of DAVS Ver. 1.3 with 0.025% ICG did not differ from that of Preset 3 of DAVS Ver. 1.1 with 0.075% ICG. ILM peeling time did not differ between the SOM with 0.075% ICG and DAVS Ver. 1.3 groups with 0.025% ICG.

Conclusions: Customized DAVS settings enable surgeons to use a 3-fold lower ICG concentration in ILM peeling.

CONTROL ID: 3544898

SUBMITTER (NAME ONLY): Bradley Gundlach

TITLE: Retinopathy of Prematurity: A Longitudinal Prospective Study of Visual Outcomes in Premature Infants

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.S. Gundlach, M. Altendahl, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|M. Khitri, I. Tsui, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|M. Khitri, I. Tsui, Doheny Eye Institute, Los Angeles, California, UNITED STATES|A. Kokhanov, A. Chu, Pediatrics, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The development of anti-vascular endothelial growth factor (anti-VEGF) therapies has revolutionized the treatment of pediatric retinal disease including retinopathy of prematurity (ROP), however clinical data of long-term visual outcomes surrounding its use in these patients is incomplete. Here, we investigate long-term visual outcomes of infants screened for ROP in the anti-VEGF era.

Methods: We reviewed Stein Eye clinic charts of subjects born at UCLA Medical Centers and screened for ROP as neonates. Data collected included parameters at birth (e.g., gestational age (GA), birth weight (BW)), treatment modalities (e.g., laser, anti-VEGF), and visual outcomes (e.g., visual acuity, refraction, amblyopia, strabismus, poor structural outcomes). The most recent eye exam was used for each age group. Generalized estimating equations were used for analysis to account for inter-eye correlations. A final multivariate model was used, incorporating covariates significant at the univariate stage.

Results: 137 patients were included in the analysis, with average GA 28.03 ± 2.71 weeks and BW 1064.4 ± 368.9 g; 66 (48.1%) were inborn, and 76 (55.45%) were male. 76 (55.45%) did not develop ROP, 39 (28.4%) had Type 2 ROP, and 22 (16.1%) had Type 1 ROP; 23 patients received primary laser treatment, while an additional 4 received primary anti-VEGF followed by delayed laser treatment. Strabismus was associated positively with poor structural outcomes (OR = 1.36, $p=.023$) and negatively to GA (OR=0.97, $p=.017$); primary laser compared to primary anti-VEGF followed by delayed laser was positively associated with amblyopia (OR=1.33, $p=.002$) while controlling for GA. Subgroup analysis for visual acuity was performed on 51 patients who were 4+ years old, with average age at last follow-up 6.04 ± 1.3 years and average refraction -0.08 ± 3.7 D. Primary laser as compared to primary anti-VEGF followed by delayed laser was independently associated with worse visual acuity (OR=1.75, $p<.0001$). No treatment vs. primary anti-VEGF followed by delayed laser was also independently associated with worse VA (OR=1.34, $p=0.009$).

Conclusions: Primary anti-VEGF followed by delayed laser led to better visual outcomes than primary laser, independent of GA, BW, or underlying poor structural outcomes. This supports the concept that anti-VEGF treatment improves visual development in preterm neonates.

CONTROL ID: 3544900

SUBMITTER (NAME ONLY): Jared Chrispell

TITLE: Rod- and Cone-specific Phosphorylation of Retinal GRKs in Mice and Zebrafish

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Chrispell, Y. Xiong, E.R. Weiss, Cell Biology & Physiology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jared Chrispell: Commercial Relationship: Code N (No Commercial Relationship) | Yubin Xiong: Commercial Relationship: Code N (No Commercial Relationship) | Ellen Weiss: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In the vertebrate retina, phosphorylation of photoactivated visual pigments in rods and cones by G protein-coupled receptor kinases is essential for sustained visual function. GRK1 and GRK7 are phosphorylated in a cAMP-dependent manner in vivo in the retinas of dark-adapted vertebrates. We have shown that a phosphomimetic of GRK1 affects the rate of dark adaptation in mouse rods but not in cones, suggesting a role in the disparate dark adaptation rates in these two cell types. The present work evaluates phosphorylation of GRKs in rods and cones of mice and zebrafish.

Methods: Phosphorylation was analyzed by western blot analysis of retinal tissue (mice and adult zebrafish) and isolated eyes (larval zebrafish) using anti-phosphoGrk antibodies. Grk1a was targeted for knockout in zebrafish using CRISPR gene editing. Recovery of the cone photoresponse in zebrafish was evaluated by ERG using a white light dual flash with increasing interstimulus intervals. To evaluate the effect of elevated cAMP on the rate of cone recovery in vivo, zebrafish larvae were incubated with forskolin.

Results: GRK1 was not observed to be phosphorylated in dark-adapted *Nrl*^{-/-} mice, which only have cones. Phosphorylation of Grk1 is detected in dark-adapted *grk1b*^{-/-} zebrafish lacking the cone-specific paralog, suggesting that phosphorylated Grk1 is Grk1a in rods and that cone Grk1b is not phosphorylated. To evaluate this hypothesis, fish lacking the *grk1a* paralog are being generated. F0 mosaic larvae exhibit significant deletion of Grk1a and an absence of Grk1 phosphorylation in the dark. Wildtype larvae treated with forskolin display a significant decrease in the rate of cone recovery compared to vehicle. This decrease is also observed in *grk1b*^{-/-} larvae, which express only *grk7a* in cones. In contrast, forskolin has no effect on the rate of cone recovery in *grk7a*^{-/-} larvae, consistent with our observation that only Grk7 is phosphorylated in zebrafish cones.

Conclusions: These data are consistent with our report of a GRK1 phosphomimetic in mice suggesting a role for GRK1 phosphorylation in rod adaptation. Grk7, but not Grk1, phosphorylation seems to be important in cone adaptation in zebrafish. Further experiments using complete Grk1a knockouts and dark adaptation analyses will be used to determine the roles of GRK phosphorylation in vertebrates that, like humans, express both GRKs in cones.

CONTROL ID: 3544901

SUBMITTER (NAME ONLY): Mollie Woodworth

TITLE: Defining multiplicity of plasmid electroporation in the retina for high-throughput genetic screening

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Woodworth, S. Wang, J.L. Goldberg, L.C. Greig, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mollie Woodworth: Commercial Relationship: Code N (No Commercial Relationship) | Sui Wang: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Goldberg: Commercial Relationship: Code N (No Commercial Relationship) | Luciano Greig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Electroporation of plasmid DNA into mouse retinal progenitor cells (RPCs) has been extensively used to investigate gene function during retinal development. To perform high-throughput genetic screens, it is important to know how many plasmid copies are delivered to individual electroporated RPCs and their progeny. Here we investigate multiplicity of electroporation in the retina based on fluorescent protein expression and high-throughput sequencing of barcoded plasmids.

Methods: CD1 mouse pups were electroporated on postnatal day 1 (P1) with plasmids containing a CMV-beta-actin (CAG) promoter driving expression of one of three fluorescent proteins, EGFP, tdTomato, or mKate. The plasmids were mixed in equimolar concentrations totaling 10, 100, or 1000 ng/ul. DNA was injected subretinally and electroporated using five 80V pulses. Mice were euthanized at postnatal day 21 (P21), and fixed retinas were cryosectioned and imaged on a Zeiss confocal microscope. In separate experiments, pups were electroporated with a library of plasmids containing BFP tagged with random 18-nucleotide barcodes. Individual electroporated cells were FACS-purified, and barcodes were PCR-amplified to perform high-throughput DNA sequencing.

Results:

All plasmid concentrations resulted in most transfected cells being labeled with all three fluorescent proteins, with random variation in expression levels resulting in a rainbow-like range of hues. Modeling suggests that most cells receive at least 6-10 plasmid copies at the lowest concentration and as many as 1000 copies at high concentrations. Experiments in which barcodes were recovered from individual cells by high-throughput sequencing allowed us to more directly estimate multiplicity of electroporation across a range of plasmid concentrations, further supporting our prior estimates.

Conclusions: Our results suggest that gene delivery by plasmid electroporation in the retina results in high plasmid copy numbers in each cell. These data support the premise of using high-throughput screening by electroporating libraries of plasmids, but highlights the importance of titrating the concentration of such libraries in order to avoid simultaneously manipulating thousands of genes in each cell.

CONTROL ID: 3544902

SUBMITTER (NAME ONLY): Suman Adhikari

TITLE: Comparison of microaneurysms (MA) number between early versus late phase fluorescein angiography (FA) and optical coherence tomography angiography (OCTA)

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Adhikari, Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|A.H. Kashani, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Suman Adhikari: Commercial Relationship: Code N (No Commercial Relationship) | Amir Kashani: Commercial Relationship(s); Carl Zeiss Meditec: Code F (Financial Support); Carl Zeiss Meditec: Code R (Recipient)

ABSTRACT BODY:

Purpose: To compare the number of MA in early versus late phase FA with counts from SS-OCTA images in subjects with diabetic retinopathy (DR).

Methods: This was a retrospective, observational study. Subjects were selected based on the availability of the images and the quality of the available images. The FA images were obtained from Spectralis® OCT (Heidelberg Engineering, Germany) and OCTA images were obtained from SS-OCTA (PlexElite™, Carl Zeiss Meditec, Dublin, CA). Early and late phase FA were defined as 30 seconds (range: 30-35 seconds) and 3 minutes (range: 2.71-3.46 minutes) during the transit respectively. MA counts from 6×6 mm OCTA scans were compared with counts from the corresponding area of early and late phase FA images. Statistical analysis was performed using ANOVA and a paired student t-test.

Results: Four eyes of 4 subjects were included in the study. The mean (\pm SD) age of the subjects was 56.5 (\pm 8.4) years. One of the subjects had proliferative DR and three had severe non-proliferative DR. The MA count in each eye on OCTA was 23, 11, 30 and 95 (Mean \pm SD = 39.8 \pm 32.6). The MA count during early and late phase FA for the same eyes was 41, 21, 52 and 140 (Mean \pm SD = 63.5 \pm 45.5) and 46, 27, 54 and 153 (Mean \pm SD = 70 \pm 48.9), respectively. There were significantly more MA detected in late phase FA than in OCTA ($P=0.04$). The difference in MA detected in early phase FA and OCTA did not reach significance ($P=0.49$).

Conclusions: The number of MAs counted on OCTA images is significantly less than on any stage of FA but closer to MA counts in the early phase of the FA. This suggests that patent MA with active blood flow are best represented on OCTA.

CONTROL ID: 3544903

SUBMITTER (NAME ONLY): Ahmed Sayed

TITLE: Measurement of monocular and binocular visual field defects with a virtual reality head mounted display

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Sayed, Biomedical Engineering, Helwan University, Helwan, Cairo, EGYPT|A. Sayed, EECS, Milwaukee School of Engineering, Milwaukee, Wisconsin, UNITED STATES|V. Roongpoovapatr, T. Eleiwa, R. Kashem, R. Parrish, M. Abou Shousha, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|T. Eleiwa, Ophthalmology, Benha University, Benha, EGYPT|M. Abdel-Mottaleb, Electrical and Computer Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|O. Jumbo, Industrial Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe and evaluate a portable visual field (VF) quantification tool for determining monocular and simultaneous binocular VF measurements.

Methods: We used a virtual reality head mounted display (HMD) to quantify VF defects in the central 80 degrees diameter of two groups of patients by applying a fast thresholding strategy with an inverted static stimuli pattern. The first group included 20 patients (30 eyes) with known glaucomatous monocular VF defects. We compared the HMD VF monocular test results with the known full static standard automated perimetric (SAP) values as a reference measurement. In the second group, 20 patients (40 eyes) with binocular neurological and glaucomatous related VF defects, we validated HMD binocular measurements (testing both eyes simultaneously) by comparing the results with the integrated/combined monocular SAP VF tests for both eyes, as a reference test. We determined reproducibility by repeated testing of ten measurements in each group.

Results: The HMD VF measurements were comparable to their corresponding references in each group based on a point by point comparison. Testing points responses in discord with the corresponding SAP thresholds were counted to calculate VF measurement mismatches. These mismatches were 7.08% and 7.38% in the two groups, respectively, calculated as the ratio between the number of mismatched points to the total number of common test points. The HMD VF reliably quantified defects with an intraclass correlation coefficient (ICC) of 0.83 for the first test group and 0.73 for the second binocular test group.

Conclusions: Monocular and binocular HMD VF and SAP VF measurements were comparable in this pilot study.

CONTROL ID: 3544905

SUBMITTER (NAME ONLY): You Zhou

TITLE: Impact of Fornix Based Micro-Trabeculectomy Technique on Astigmatism in Pseudophakic Patients

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhou, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|A. Mazharuddin, B. Hong, G. Vizzeri, Ophthalmology and Visual Sciences, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): You Zhou: Commercial Relationship: Code N (No Commercial Relationship) | Anam Mazharuddin: Commercial Relationship: Code N (No Commercial Relationship) | Bennett Hong: Commercial Relationship: Code N (No Commercial Relationship) | Gianmarco Vizzeri: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Fornix-based micro trabeculectomy with adjunctive mitomycin C is a novel minimally invasive procedure that was first introduced at ARVO 2019 (poster #B0083). This study seeks to assess whether this modified technique induces significant astigmatism in pseudophakic patients.

Methods: This is a retrospective single surgeon case series. Pseudophakic patients who underwent micro trabeculectomy between 1/1/2013 and 1/1/2019 were included. Patients who did not have manifest refraction or demonstrated visual acuity of count fingers or less were excluded. Outcomes included were a change in significant astigmatism, which is defined as 1.0D or more, change in visual acuity (0.2 LogMAR), and shift in axis of astigmatism in the operative eye. Analysis was performed using the Student's T-Test.

Results: 31 patients had refraction before and after procedure available for comparison, and 21 had a second refraction after at least 1 year. Baseline demographics and primary outcomes for included patients are provided in Tables 1 and 2. The patients included were on average 74.9 years old and 42% male and 58% female. On average micro trabeculectomy was performed 4.3 years after cataract surgery. Average baseline astigmatism prior to surgery was 1.36D while post-procedure average astigmatism was 1.23D. 1 eye experienced an increase in astigmatism postoperatively that resolved after 1 year on repeat refraction. 2 eyes experienced a clinically significant decrease that remained stable after 1 year. 2 eyes that did not have astigmatism prior to the procedure developed astigmatism, however this was not significant ($\leq 1D$). 9 eyes experienced no change in astigmatism postoperatively. Analysis showed that there was no statistically significant difference between pre-trab and post-trab astigmatism outcomes (0.620, $p > 0.05$). Similarly, there was no statistically significant difference between baseline astigmatism and astigmatism measured at least one year post-operatively (0.524, $p > 0.05$). Visual acuity remained stable after procedure (0.827, $p > 0.05$). 3 eyes shifted from oblique or no cylindrical astigmatism (sphere only) to against the rule (ATR) astigmatism.

Conclusions: Incisional surgery can induce astigmatism and affect visual acuity. This study demonstrates that the novel micro trabeculectomy technique does not induce significant astigmatism in pseudophakic patients.

CONTROL ID: 3544906

SUBMITTER (NAME ONLY): Homayoun Tabandeh

TITLE: “En face” Imaging of ILM Flap Following Macular Hole Surgery

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Tabandeh, A. Morozov, D.S. Boyer, Retina-Vitreous Associates Medical Group, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Homayoun Tabandeh: Commercial Relationship: Code N (No Commercial Relationship) | Andy Morozov: Commercial Relationship: Code N (No Commercial Relationship) | David Boyer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To visualize and evaluate the internal limiting membrane (ILM) flap following macular hole (MH) surgery.

Methods: Retrospective case series including eyes that underwent pars plana vitrectomy (PPV) and ILM flap for MH. Postoperatively, ICG fluorescence images were obtained using a confocal laser scanning system (Spectralis, Heidelberg Engineering Inc., Heidelberg, Germany) with the 795 nm ICG filter. Optical coherence tomography (OCT) was used to evaluate the status of the MH.

Results: Twenty eyes of 20 patients, mean age 67.2 years, with mean follow-up of 11.1 months were included in the study. Five (25%) eyes were highly myopic, 8 (40%) eyes had chronic MH, and 3 (18%) eyes had history of prior MH surgery and ILM removal. The MH closed in 19 (95%) eyes. Typically the ICG fluorescence imaging showed a well defined area of hypofluorescence corresponding to the harvest site and removed ILM, an area of hyperfluorescence corresponding to the ILM flap and the residual ILM, and an area of increased hyperfluorescence corresponding to the overlap area of ILM flap with the residual ILM. Hyperfluorescence over the MH site, and speckled hyperfluorescence over the macular region were present in most eyes. ICG fluorescence imaging demonstrated coverage of the MH by the ILM flap in 17 (85%) eyes, partial coverage in 1 (5%) eye, and no coverage in 2 (10%) eyes. Folding of the ILM flap was present in 5 (25%) eyes. OCT demonstrated bridging of the fovea by the ILM flap in 4 (20%) eyes.

Conclusions: ICG fluorescence imaging is a non-invasive imaging modality that provides an “en face” image of the ILM flap following MH surgery, allowing study of ILM flap techniques.

CONTROL ID: 3544909

SUBMITTER (NAME ONLY): Chaewon Hwang

TITLE: The Use of Encircling versus Segmental Buckling as Primary Surgery for Retinal Detachment Repair

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Hwang, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES | K. Astafurov, D. Roth, Ophthalmology, Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, UNITED STATES |

Commercial Relationships Disclosure (Abstract): Chaewon Hwang: Commercial Relationship: Code N (No Commercial Relationship) | Konstantin Astafurov: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Roth: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Primary scleral buckling (SB) is a common technique employed to repair rhegmatogenous retinal detachment. This is most commonly accomplished using either encircling or segmental SB approach. However, currently, there is a lack of data comparing these two techniques. Here we present and compare features and outcomes of segmental primary SB versus encircling SB surgical approaches.

Methods: A retrospective chart review of 100 consecutive patients who underwent primary SB surgery between March 2019 and January 2020 for a rhegmatogenous retinal detachment at a single retina practice was performed. Data were collected on patients with greater than 3-month follow up after surgery.

Results: Out of the 100 surgical eyes, 95 were included in the final analysis: 55 of those eyes had encircling and 40 had segmental SB procedure, respectively. The average follow-up time was comparable between the two groups: 10.7 months and 10.6 months for segmental and encircling SB respectively ($P = 0.48$, t-test). The average pre-operative best corrected visual acuity (BCVA) was 20/110 for segmental and 20/68 for encircling SB, respectively. There was no significant difference in the average BCVA at the final follow up which was 20/35 for segmental and 20/38 for encircling SB, respectively ($P = 0.25$, t-test).

There were no significant differences in the lens status (phakic in 85% and 93% for segmental and encircling SB respectively, $P = 0.23$, Chi-square), fovea-on status (60% and 58% for segmental and encircling respectively, $P = 0.86$, Chi-square), and the extent of the retinal detachment (4.4 clock hours and 4.7 clock hours for segmental and encircling respectively, $P = 0.22$, t-test) between the patients in the two groups. Two patients in encircling SB group had recurrent retinal detachment requiring reoperation, while in the segmental SB group, none required reoperation at the final follow up.

Conclusions: Our results suggest that segmental SB technique is not inferior to the encircling SB technique in cases of primary buckling procedure for retinal detachment repair in regard to the anatomical success of single surgery and final visual outcome. Given that segmental scleral buckling technique is associated with less morbidity, it should be considered, when indicated, for the repair of retinal detachments amenable to surgery with primary SB.

CONTROL ID: 3544913

SUBMITTER (NAME ONLY): Ke Cao

TITLE: Novel, high-performance machine learning model for detection of subclinical keratoconus

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Cao, E. Chan, M. Daniell, S. Sahebjada, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|K. Cao, S. Sahebjada, P.N. Baird, Department of Surgery, Ophthalmology, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|K. Verspoor, Department of Computing and Information System, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|E. Chan, M. Daniell, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|

Commercial Relationships Disclosure (Abstract): Ke Cao: Commercial Relationship: Code N (No Commercial Relationship) | Karin Verspoor: Commercial Relationship: Code N (No Commercial Relationship) | Elsie Chan: Commercial Relationship: Code N (No Commercial Relationship) | Mark Daniell: Commercial Relationship: Code N (No Commercial Relationship) | Srujana Sahebjada: Commercial Relationship: Code N (No Commercial Relationship) | Paul Baird: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Keratoconus (KC) represents one of the leading causes for corneal transplantation. Early detection of KC is important due to its early age of onset and impact on quality of life of the patients. The aim of the study was to develop a simple, automatic machine learning model to detect subclinical KC from control (non-KC) using key parameters obtained from the entire Pentacam parameter set.

Methods: Complete Pentacam output (1692 parameters) and clinical data of 145 subclinical KC and 122 control eyes were collected and analysed. A random forest method was applied to these data to build models using different parameter combinations, and a best performing parameter set was identified. A final model was built using the key Pentacam parameter set, along with other clinical data, and validated using a separate test data.

Results: 3 novel Pentacam parameters were identified, consisting of eccentricity value at an angle of 30 degrees of the front cornea, eccentricity in the 9 mm diameter zone of the cornea and inferior versus superior corneal asymmetry, that were widely available in other commonly used imaging systems to achieve an accuracy of 94%, sensitivity of 97% and specificity of 91% that was comparable with previously reported models built using more parameters. The utility of this combination was further enhanced with the inclusion of clinical parameters (i.e. vision and refraction) to reach an accuracy of 97%, a sensitivity of 99%, and a specificity of 96% in detecting subclinical KC.

Conclusions: The use of the identified key Pentacam parameters along with important clinical parameters, achieved a high level of differentiation between subclinical KC and control eyes. The compact model proposed in this study could be incorporated into the diagnosis of subclinical keratoconus.

CONTROL ID: 3544915

SUBMITTER (NAME ONLY): Srilekha Sundaramurthy

TITLE: Complete mitochondrial genome sequencing in individuals with Leber hereditary optic neuropathy negative for the common pathogenic mitochondrial DNA mutations

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sundaramurthy, S. Mathavan, S. Sarangapani, SNONGC Department of Genetics & Molecular Biology, Vision Research Foundation, Chennai, Tamil Nadu, INDIA|P. Yu-Wai-Man, Cambridge University Hospitals, Cambridge Eye Unit, Addenbrooke's Hospital, Cambridge, UNITED KINGDOM|P. Yu-Wai-Man, Department of Clinical Neurosciences, John Van Geest Centre for Brain Repair, Cambridge, University of Cambridge, UNITED KINGDOM|A. Selvakumar, V. Dharani, Department of Neuro-Ophthalmology, Medical Research Foundation, Chennai, TamilNadu, INDIA|

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ABSTRACT BODY:

Purpose: Reports from populations of different geographic backgrounds show that about 90% percent of individuals with Leber hereditary optic neuropathy (LHON) harbour one of the three (primary) mitochondrial DNA (mtDNA) point mutations: m.3460G>A (MT-ND1), m.11778G>A (MT-ND4) or m.14484T>C (MT-ND6). The purpose of this study was to screen the whole mitochondrial genome of LHON patients negative for these three common mtDNA mutations to investigate the role of other mtDNA variants in the pathogenesis of this blinding optic neuropathy.

Methods: Forty-one individuals who were clinically suspected to have LHON were recruited from the Neuro-Ophthalmology Clinic (Medical Research Foundation, Sankara Nethralaya, Chennai, Tamil Nadu, India). A comprehensive neuro-ophthalmic examination, including slit lamp examination, indirect ophthalmoscopy and visual field perimetry was performed. Targeted re-sequencing using next-generation sequencing (NGS) on the HiSeqX Ten platform (Illumina, San Diego, California) was performed using a 2×150bp paired-end setting. The reads were aligned to the human mitochondrial genome sequence (hg19). The variants were filtered using VARIMAT tool (v.2.3.9) and haplogroup analysis was performed using haplogrep 2 tool (v2.0).

Results: Whole mitochondrial genome sequencing of 41 clinically suspected cases of LHON revealed a total of 1,594 variants of which 869 variants were present in the coding region, and 582 were synonymous and 287 were non-synonymous variants. We have identified secondary mtDNA variants reported in mitomap in 12 individuals (12/41, 29%) with variants in MTND1 being the most common (7/41, 17%). Control screening for the m.4216T>C and m.9966G>A variants was conducted on 25 unrelated healthy individuals. The majority of individuals belonged to haplogroup M (n= 23). None of the controls were positive for m.9966G>A, but m.4216 T>C was identified in 2 controls. We plan to screen additional controls in order to further investigate the pathogenic status of the m.4216T>C and m.9966G>A variants.

Conclusions: Our study of a well-characterized Indian LHON cohort negative for the three primary mtDNA mutations has revealed a number of secondary mtDNA variants that should be considered in the evaluation of optic atrophy cases. The MTND1 subunit gene could be a mutational hotspot for LHON in the Indian population.

CONTROL ID: 3544916

SUBMITTER (NAME ONLY): Yiqin Du

TITLE: Intracamerally transplanted stem cells changed the segmental outflow pattern and reduced intraocular pressure in a mouse glaucoma model

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Du, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yiqin Du: Commercial Relationship(s);University of Pittsburgh:Code P (Patent)

ABSTRACT BODY:

Purpose: Primary open-angle glaucoma is associated with pathological changes of the trabecular meshwork (TM). TM stem cells (TMSCs) preferentially home to the injured TM tissue for regeneration (Yun et al. Communi Biol. 2018; 1: 216). The hypothesis of this study was that intracamerally transplanted TMSCs can change the segmental outflow pattern for IOP regulation in a glaucoma mouse model.

Methods: Human TMSCs were labeled with Vybrant dye DiO and 5×10^4 cells were intracamerally transplanted into a primary open-angle glaucoma model of mice with transgenic myocilin (Myoc) Y437H mutation (Tg-MyocY437H, a kind gift from Dr. Gulab Zode, UNTHSC) as well as wildtype mice as controls. Human corneal fibroblasts were injected as a control. Mouse IOP was measured before cell injection and at 3 weeks after injection. At 3 weeks, anterior segment optical coherence tomography (OCT) was performed to evaluate central corneal thickness (CCT) and the anterior chamber angle. Then microbead perfusion was performed and mice were sacrificed. Wholemount staining on the TM was evaluated on a confocal microscope for quantifying the high-flow, low-flow, and no-flow region. Statistical analysis was done by one-way ANOVA followed by the Tukey posttest to assess the significance.

Results: TMSC injected mice showed similar CCT and anterior angle to the control groups (both $p > 0.05$), which indicates there was no effect on the CCT and the angle of TMSC injection, and the IOP measurement was not affected by CCT. With TMSC transplantation, Tg-MyocY437H mice had reduced IOP, increased high-flow length, and lowered no-flow length than controls (no injection, sham injection, and fibroblast inject) (all $p < 0.05$). The same change was observed in wildtype mice and there was no statistical difference between Tg-MyocY437H and wildtype mice. TMSCs distributed to the TM high-flow, low-flow, and no-flow regions.

Conclusions: TMSC intracameral transplantation can upregulate aqueous humor outflow and reduce IOP which is partially by increasing the high-flow region and reducing the no-flow region in mice

CONTROL ID: 3544917

SUBMITTER (NAME ONLY): Miriam Ramos-Hernández

TITLE: Could a Nootropic Formulation Benefit Patients with End-Stage Glaucoma?

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Ramos-Hernández, J.A. Paczka, Research, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Research, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|M.Y. Guzmán Ornelas, M.A. Ibañez Sandoval, Lamar Universidad, Guadalajara, MEXICO|M.A. Ibañez Sandoval, L.A. Giorgi-Sandoval, Research and Development, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: End-stage glaucoma is a challenging clinical situation that required very low IOP to control it. Diverse non-dependent IOP factors are involved in visual function stability and neuroprotective compounds have been proposed as potentially helpful. Nootropic supplements such as Neuro Optimizer (Jarrow Formulas) have been purportedly used due to their neuroprotective effects. The objective of this study is to evaluate the benefit of orally administered Neuro Optimizer in patients with end-stage glaucoma in a real-world setting.

Methods: A retrospective assessment of data from 132 consecutive patients with end-stage glaucoma under oral treatment with Neuro Optimizer was performed. Clinical data including BCVA, IOP, number of glaucoma medications, visual field indexes evaluated by applanation tonometry, cup-to-disc (CD) ratio, peripapillary retinal nerve fiber layer (RNFL) and perimacular ganglion cell complex (GCC) thickness by OCT. Tolerability and safety issues were also assessed.

Results: One hundred and thirty-two patients were under oral Neuro Optimizer treatment, from which 31 were excluded. Therefore, 197 eyes of 101 patients (61 females, 40 males; mean age of 64.8 ± 17.6 years) were included. This population showed a greater proportion of POAG (59.4%), and usage of ≥ 2 glaucoma medications (81.1%). Mean time of Neuro Optimizer administration was 9.4 ± 3.3 months. Baseline IOP was 14.5 ± 5.8 mmHg (RE) and 14.7 ± 5.2 mmHg ($P=0.79$) and no difference was noted with the last visit values (RE, 14.8 ± 6.0 mmHg; LE, 14.4 ± 5.7 mmHg; $P=0.63$). BCVA, MD, DSM, CD ratio, CFNR and GCC were not statistically different when the two moments were compared ($p>0.05$). Mean pre-treatment VFI in both eyes (RE, 43.7 ± 32.4 %; LE, 39.8 ± 33.6 %) was higher as compared to the post-treatment period (RE, 37.5 ± 31.8 mmHg; $p=0.001$; LE, 34.1 ± 29.2 mmHg; $p=0.02$). Heartburn (9.9%), minor headache (7.9%) and a transient cutaneous rash (1.9%) were the side-effects recorded. Two patients (1.9%) interrupted supplement administration because of persistent headache. Eighteen patients (17.8%) claimed to have a subjective improvement in their vision.

Conclusions: The current results of this retrospective "real world" study of end-stage glaucoma patients showed no improvement but a reduced VFI when Neuro Optimizer was orally administered during a short-term period. No relevant safety/tolerability issues were relevant. Subjective perception of improvement was infrequent.

CONTROL ID: 3544918

SUBMITTER (NAME ONLY): Neesurg Mehta

TITLE: Effect of Vitrectomy Surgery with Internal Limiting Membrane Peeling on Macular Morphology and Perfusion: Optical Coherence Tomography Analysis. A Retrospective Study

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Mehta, G. Yiu, A. Morshiri, S.S. Park, Ophthalmology, University of California Davis, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Internal limiting membrane peeling (ILMP) is a common part of vitrectomy surgery for epiretinal membrane (ERM) or macular hole (MH). However, safety concerns remain since changes in macular thickness and vascular flow have been reported following ILMP. This retrospective study compared the macular morphology and flow following surgical ILMP when compared to the contralateral normal eye.

Methods: We identified 62 patients who had undergone ERM or MH surgery in one eye with normal contralateral eye and follow-up of at six months postoperatively. Optical coherence tomography (OCT) was used to measure central subfield thickness (CST), mean cube thickness (MCT) and macular volume (MV) in both eyes at pre and post-operative visits. In a subset of eyes with OCT angiography (OCTA) performed postoperatively, vascular density (VD) in the 3x3mm foveal and parafoveal regions of the superficial, deep and full vascular slabs was obtained from the most recent image. Paired Student t test was used to compare means (p-value<0.05 statistically significant).

Results: Among 62 patients, 44 had ERM surgery (35 with ILMP) and 18 had MH surgery (all with ILMP). Mean follow-up was 106.7 weeks (range 46.8-266.4 weeks). All operated eyes had significant reduction in CST, MCT and MV postoperatively. Among eyes that had ERM surgery with ILMP, mean CST, MCT and MV were 355um, 305um, and 9.6 mm³ respectively, while that for the contralateral eyes were 267um, 252um, and 9.0mm³ respectively (p value=2.33E-9, 1.82E-4, 0.01 respectively) at last postoperative visit. Among MH eyes, the operated eyes had mean CST, MCT and MV of 312um, 274um, and MV 9.05 mm³ respectively, while that for the contralateral eyes were 236um, 252um, and 9.1mm³, respectively (p value=0.01E-1, 0.03, 0.43 respectively). Postoperative OCTA was available in 10 eyes that had ILMP. No statistically significant difference was noted in the VD between the operated and contralateral eyes in the superficial, deep and full vascular slabs at the parafoveal and foveal regions.

Conclusions: Although eyes with ERM and MH had reduction in macular thickness and volume following vitrectomy, ILMP was not associated with reduction in macular thickness, volume or perfusion when compared to the contralateral normal eye in this limited retrospective study.

CONTROL ID: 3544925

SUBMITTER (NAME ONLY): Madhu Nath

TITLE: α A-Crystallin modulates neuroinflammation in retina via stress specific inflammatory pathways

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Nath, Y. Shan, A.M. Myers, P.E. Fort, Kellogg Eye Centre, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The α -crystallins molecular chaperones are involved in the pathophysiology of diabetic retinopathy (DR), however, the role and regulation of these proteins remained unclear. We recently demonstrated that the α A-crystallin exerts its intrinsic neuroprotective role during diabetes, by its phosphorylation on residue 148. We also reported that α A-crystallin is highly expressed by glial cells. Because of the growing interest of the potential causative role of low-grade inflammation in the DR pathophysiology, this study was carried out to delineate the regulatory function of α A-crystallin in the inflammatory response associated with metabolic stresses.

Methods: Primary Müller glial cells (MGCs) isolated from Ko- α A-crystallin mice were transfected with plasmids encoding either wild-type (WT), phosphomimetic (T148D), or non phosphorylatable mutants (T148A) of α A-crystallin. The cells were then exposed to multiple metabolic stress including serum starvation (SS) or high glucose with TNF- α (HG+T) before being evaluated for the expression of inflammatory markers by qPCR and protein expression of NF κ B1 & NLRP3 components by western blot.

Results: Elevated levels of inflammatory markers in SS were diminished in MGCs overexpressing WT (IL-6-97%; IL-1 β - 88%; MCP-1-89%; IL-18-72%) and further in T148D (IL-6-87%; IL-1 β - 86%; MCP-1-28%; IL-18-64%) as compared to EV. The HG+T induced increase in IL-6, IL-1 β , MCP-1 & IL-18 were dampened by WT (55%, 36%, 85% & 93% respectively) and even more significantly by T148D (IL-6- 92%; IL-1 β -54%; MCP-1-98%; IL-18-55%) overexpression, whereas T148A was ineffective in either stress. Further, overexpression of WT or the T148D, also lead to a significant reduction of Nlrp3 (85%), Asc (61%) and caspase-1 (68%) expression in serum deprived MGCs and nearly abolished the NF- κ B induction (α A-WT-97%; α A-T148D-95%) in HG+T stress. The protein levels of NLRP3 components and NF- κ B were consistent with the transcriptomic data in a metabolic stress specific manner.

Conclusions: The data gathered in this study demonstrate the central regulatory role of α A-crystallin and its modulation by phosphorylation on T148 in retinal MGC. This study demonstrates that α A-crystallin can dampen sustained expression of pro-inflammatory cytokines through modulation of multiple key inflammatory pathways, therefore, suggesting its potential as therapeutic target for modulation of chronic neuroinflammation.

CONTROL ID: 3544928

SUBMITTER (NAME ONLY): Rujuta Gore

TITLE: Virtual Vision Outreach Program: Give Kids Sight Day (GKSD) 2020

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gore, B. Wasserman, Wills Eye Hospital Department of Pediatric Ophthalmology, Philadelphia, Pennsylvania, UNITED STATES|C. Wu, R. Elias, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|M. Lai, Rowan University Cooper Medical School, Camden, New Jersey, UNITED STATES|C. Green, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Give Kids Sight Day is an annual free outreach program in Philadelphia region, targeting low-income and underinsured communities. In 2020, a novel virtual screening program was conducted to face the challenges presented by the COVID19 pandemic. Continual innovation in vision screening methods is necessary to help reduce rates of blindness and visual impairment in children and adolescents. We performed a retrospective chart review to describe the outcomes of this new program.

Methods: Families to be screened were sent a packet with an eye chart and a 5-foot string, as well as instructions. On GKSD, screeners called the families and instructed the adults through screening the children over the phone. Results were collected and children who failed screening were sent to Wills Eye Hospital for an in-person appointment for re-screening and evaluation. After the Wills Eye Hospital Institutional Review Board approved this study, registration forms and clinical charts of all patients who attended GKSD 2020 were reviewed retrospectively. Demographic characteristics and ophthalmic findings were analyzed. Visual acuity on virtual screening was compared with in-person vision testing using Pearson correlation coefficient. Further subgroup analysis is being conducted at the time of abstract submission.

Results: Four hundred and seventy five children registered for virtual vision screening. Consequently, 151 children (43% female; 27% speaking languages other than English) with median age 11 years (age range 5-17 years) who failed screening received in-person evaluation. Out of these, 19% children underwent an eye exam for the first time. Refractive errors correctable with glasses were seen in 88%; 30 children with other diagnoses were referred to pediatric ophthalmology for further evaluation and management. There was a moderate correlation between screening and in-person visual acuity without refractive correction ($R=0.66$ OD, 0.58 OS); and a strong correlation between screening and in-person visual acuity with refractive correction ($R=0.76$ OD, 0.91 OS).

Conclusions: The GKSD virtual visual acuity testing demonstrated good correlation with in-person visual acuity testing, supporting the virtual screening approach as a useful tool for future applications in vision outreach programs.

CONTROL ID: 3544929

SUBMITTER (NAME ONLY): Rajiv Mohan

TITLE: Long-term tolerability profiling of BMP7+HGF overexpression on rabbit cornea in vivo

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.R. Mohan, S. Gupta, N.R. Sinha, L. Martin, N. Hesemann, S. Kamil, P.R. Sinha, P. Balne, R. Tripathi, S.S. Chaurasia, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES| R.R. Mohan, S. Gupta, L. Martin, N. Hesemann, S. Kamil, P. Balne, R. Tripathi, S.S. Chaurasia, Harry S Truman VA Hospital, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recently, we found targeted BMP7+HGF dual gene therapy applied to stroma via PEI2-GNP effectively treated preformed corneal scar and restored transparency in vivo in rabbit with minimal acute toxicity (Invest Ophthalmol Vis Sci. 2018;59:1045-57). The goal of this study was to evaluate long-term in vivo tolerability of this BMP7+HGF therapy using a rabbit model.

Methods: Eighteen New Zealand White rabbits were used and divided into three groups. One eye of rabbit received BSS (n=6), naked-vector (n=6) or BMP7+HGF genes (n=6) via PEI2-GNP nanoparticles using published method (Invest Ophthalmol Vis Sci. 2018;59:1045-57). Rabbits were treated following ARVO guidelines under approved ACUC protocol. Clinical eye exams and diagnostic tools (Slit lamp, HRT3-RCM, Spectralis, and Specular microscopes; and pachymetry, tonometry, Schirmer, fluorescein and MacDonald-Shadduck tests) were employed in live rabbits in a time-dependent manner for 7 months for safety profiling. Thereafter, rabbits were humanely euthanized, corneal tissues were collected, and used for histological, immunofluorescence, and qRT-PCR analyses.

Results: Clinical eye exams detected no signs of chemosis, erythema, blepharospasm, or epiphora in all 3 groups until 7-month. HRT3-RCM, Spectralis and Specular biomicroscopy noted healthy corneal epithelium, stroma, and endothelium; and normal stromal and endothelial cell counts in all groups. No significant changes in intraocular pressure and MacDonald-Shadduck parameters in BMP7+HGF-delivered versus control eyes were observed ($p=0.9989$, $p=0.9876$). Histology and molecular investigations revealed no significant differences in cellular phenotype and levels of tested proinflammatory and fibrotic markers in BMP7+HGF-delivered versus control eyes ($p=0.9992$, $p=0.9619$; $p=0.9646$ $p=0.98379$).

Conclusions: Nanoparticle-mediated BMP7+HGF nanomedicine modality appears tolerable to the eye long-term in vivo.

CONTROL ID: 3544930

SUBMITTER (NAME ONLY): Benton Chuter

TITLE: A deep learning model to assess fundus photograph image quality and improve predictive value of deep learning models of glaucoma detection.

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop a deep learning model to appraise fundus photograph image quality, and to determine how the quality of photography influences the predictive value of separate glaucomatous optic neuropathy (GON) detection deep learning (DL) models.

Methods: A training dataset of 2,815 optics disc photographs acquired from healthy and GON patients as part of the Diagnostic Innovations in Glaucoma Study (DIGS) and African Descent and Glaucoma Evaluation Study (ADAGES) was used to develop a DL model to quantify the quality of photographs (0=good, 1=poor). Image quality ground truth was determined by two reviewers, with high quality images defined as sufficient to detect GON. The DL quality model was then applied to an independent test dataset of 11,350 photographs from the Ocular Hypertension Treatment Study (OHTS). A previously published DL model to detect GON in fundus photos was also applied to the OHTS data. To determine the impact of DL predicted quality on automated review of fundus photos, area under the receiver operating characteristic curve (AUC) was calculated for both good quality OHTS photographs (score 0.0-0.1) and poorer quality photographs (score > 0.1).

Results: All OHTS photographs were considered good quality by the OHTS graders. In this dataset, 68 eyes reached OHTS primary open angle glaucoma (POAG) endpoint based on the development of visual field (41 eyes) or optic disc changes (55 eyes). The diagnostic accuracy of the DL model for POAG detection performed better in good quality compared to poorer quality photographs (AUROC: (95% CI)) of 0.86 (0.79, 0.91) and 0.81 (0.73, 0.88), respectively, though the differences did not reach statistical significance. Sensitivity at 90% specificity was also higher in the good quality (0.67) compared to poorer quality (0.44) photographs. Similar trends were found when the quality score was used to evaluate the DL glaucoma detection model separately on eyes that reached a visual field endpoint or an optic disc endpoint.

Conclusions: In the OHTS data, DL models for GON detection performed better in photos with DL predicted good quality, suggesting that DL based photograph quality assessment can be used to automatically identify low quality photos for removal. Incorporating quality assessment into automated review of fundus photos may thus improve GON detection model performance

CONTROL ID: 3544932

SUBMITTER (NAME ONLY): Xiao Lin

TITLE: Mapping of label retaining cells and hyaluronan in the mouse cornea

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Lin, M. Sun, K.N. Mutoji, V.J. Coulson-Thomas, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Xiao Lin: Commercial Relationship: Code N (No Commercial Relationship) | Mingxia Sun: Commercial Relationship: Code N (No Commercial Relationship) | Kazadi Mutoji: Commercial Relationship: Code N (No Commercial Relationship) | Vivien Coulson-Thomas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Limbal epithelial stem cells (LSCs) are vital for maintaining corneal epithelium homeostasis and for resurfacing the cornea after injury. The LSC niche is composed of a specialized hyaluronan (HA) matrix that is necessary for maintaining viable LSCs. In the cornea, HA has been shown to be almost exclusively expressed in the limbal region. Our preliminary data show HA rich clusters also exist in the peripheral cornea. Herein we characterize these HA clusters.

Methods: The distribution of LSCs, corneal epithelial progenitor cells (CEPCs), transient amplifying cells (TACs), and HA were analyzed in whole mounted corneas of wt (n=3) and HAS2^{Δ/ΔCorEpi} mice (n=3) using label-retaining techniques. For label retaining, mice were pulsed with 5-ethynyl-2'-deoxyuridine (EdU) via daily intraperitoneal injections from P7-P14 and thereafter chased for 8-weeks. LRCs were detected using Click-iT™ EdU Alexa Fluor™ 488 Imaging Kit. 1.0 mm central debridement wounds were used to trigger the influx of TACs into the peripheral cornea 24 or 48 hours prior to euthanasia. Corneas were stained for HA using biotinylated HA binding protein and analyzed under the LSM 800 confocal microscope (Carl Zeiss Microscopy LLC).

Results: After 8w chase, LRCs were mainly located in the limbal region, however, a small population LRCs were found within the corneal epithelium of all mice. HAS2^{Δ/ΔCorEpi} mice, which have previously been shown to be LSC deficient, presented limited LRCs in the limbal region, and, significantly fewer LRCs in the cornea when compared to wt mice. Wt mice present a rich HA network throughout the limbal epithelium and HA clusters within the peripheral cornea. In contrast, HAS2^{Δ/ΔCorEpi} mice presented limited HA expression within the limbal epithelium and few HA clusters within the peripheral cornea. A positive relationship was found between LRCs and HA clusters in naïve and wounded wt corneas 24h after wounding.

Conclusions: A positive relationship was found between HA clusters and LRCs (including TACs), within the wt limbal and peripheral corneal epithelium in vivo. Thus, our preliminary data indicate TACs could exist in the peripheral cornea within HA clusters.

CONTROL ID: 3544934

SUBMITTER (NAME ONLY): Annabelle Gallois-Bernos

TITLE: Development of a Meibomian Gland Dysfunction Model in the Rabbit

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gallois-Bernos, C. Blackie, Johnson & Johnson Vision Care Research & Development, Johnson and Johnson Medical Devices, Jacksonville, Florida, UNITED STATES|S. Vasanth, L. Zhong, Toxikon Corp, Bedford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Create a model of evaporative dry eye or meibomian gland dysfunction in the rabbit via closure of meibomian glands, building on the Gilbard et al.'s previous work.

Methods: Six (6) New Zealand White rabbits were divided into two equal groups. Meibomian gland closure was achieved by cauterization of either alternating (Group 1) or all (Group 2) meibomian glands orifices in upper and lower eyelid of right eyes (OD), while left eyes (OS) were left untreated. Two (2) animals served as a control (no cauterization in either eye). Tear break-up time (TBUT) and tear production were measured on Day -2 and Day -1 (baseline), and slit lamp evaluations were performed prior to cauterization. Animals were followed for five weeks, with daily clinical observations (Draize score), weekly measurements of TBUT, tear production, and slit lamp evaluation prior to termination at Day 35.

Results: Clinical observations revealed eschar formation and swelling of the eyelids post cauterization that completely resolved at three weeks. Fluorescein staining did not reveal any corneal epithelial defect. There were no consistent differences in tear production between eyes or between time points in either group during the study. Cauterization of all meibomian gland orifices (Group 2) resulted in a consistent decrease in TBUT relative to baseline or untreated eye (Baseline Day -1 TBUT: 10.3 ± 1.5 sec in OD and 12.7 ± 2.1 sec in OS), which was significant at Day 14 (TBUT: 8.7 ± 1.5 sec in OD and 16.3 ± 2.1 sec in OS), Day 21 (TBUT: 7.7 ± 1.5 sec in OD and 15.7 ± 1.5 sec in OS) and Day 28 (TBUT: 8.7 ± 4.2 sec in OD and 16.7 ± 0.6 sec in OS), $p = 0.039$. Histopathological evaluation of eyes (sacrificed at Day 35) including eyelids, lacrimal, harderian, and meibomian glands did not reveal any significant findings.

Conclusions: Cauterization of all meibomian glands of rabbits yielded a significant reduction in tear film stability after 2 weeks and through 28 days. This model may be further optimized to serve as a tool to screen formulations for their ability to restore tear film stability and alleviate evaporative dry eye condition.

CONTROL ID: 3544937

SUBMITTER (NAME ONLY): Nicholas Chan

TITLE: Does Ocular Biometry in Adults Change Over Time?

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.K. Chan, R. Gulati, S. Basti, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nicholas Chan: Commercial Relationship: Code N (No Commercial Relationship) | Reeti Gulati: Commercial Relationship: Code N (No Commercial Relationship) | Surendra Basti: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: It is standard practice to repeat biometry every 1-2 years prior to cataract surgery. The goal of this study was to assess if axial length (AL) and average keratometry (KER) (vital in lens calculation) change over time and question the clinical necessity of regularly repeating biometry.

Methods: Retrospective study of biometry data collected via IOL Master 700 (Zeiss, Germany) at Northwestern Memorial Hospital from January 1, 2016 through September 15, 2020. Inclusion criteria were patients over 35 years old, with two biometry measurements over 6 months apart. Patients were excluded if they had any other intraocular surgery, other than cataract. This analysis focused on AL and KER variables. To compare AL measurements among timepoints, a paired t-test was used. P-values were adjusted using the Bonferroni correction. Data was also stratified into four groups by axial length: hyperopia (<22mm), average (22 – 24.5mm), mild myopia (24.5 – 26.0mm), and high myopia (>26.0mm).

Results: A total of 201 patients (402 eyes) were included (average age 73.3, 59.3% female). Average time between biometry measurements was 21.5 months, average AL was 24.08 mm, and average KER was 43.73 D. The mean change in AL was 0.04 mm (95% CI: 0.03 to 0.05). The mean change in KER was 0.10 D (95% CI: -0.10 to 0.30, p=0.33). At the 6mo to 1 year interval (n=73), mean change in AL was 0.04 mm. Mean change in AL did not increase at the 1 to 2 year interval (n=204, Δ AL=0.05), the 2 to 3 year interval (n=87, Δ AL=0.03) or the 3 to 4 year interval (n=38, Δ AL=0.04). Using a linear regression model, there was no correlation between time and change in AL (p=0.06), nor between time and KER (p=0.15).

Eyes with high myopia showed a Δ AL of 0.07 (n=23; 95% CI: 0 to 0.15, p=0.06). This subgroup had the highest mean change in AL; compared to hyperopia (Δ AL = 0.04), average length eyes (Δ AL = 0.04) and moderate myopia (Δ AL of 0.03).

Conclusions: AL and KER change minimally over time between biometry readings. The mean change in AL was 0.04 mm (95% CI: 0.03 to 0.05). Change in AL did not increase with longer intervals of time between measurements. High myopes had a larger change in AL compared to shorter eyes, however, Δ AL was still low at 0.07 mm. These results suggest repeating biometry at a 1 to 2-year interval during surgical workup may not be a necessity, rather can be used selectively – for example, in high myopes.

CONTROL ID: 3544938

SUBMITTER (NAME ONLY): Ayesha Karamat

TITLE: Sensitivity and Specificity of Reticular Pseudodrusen detection using multimodal imaging in Amish Population

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Karamat, S. Srinivas, M. Nittala, S. Velaga, S.R. Sadda, Doheny Eye Institute, Los Angeles, California, UNITED STATES|A.N. Karamat, S. Srinivas, M. Nittala, S. Velaga, S.R. Sadda, University of California Los Angeles, Los Angeles, California, UNITED STATES|J.L. Haines, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|D. Stambolian, Penn Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare sensitivity and specificity for the detection of reticular pseudodrusen (RPD) associated with age-related macular degeneration using multiple imaging modalities.

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Methods: A post-hoc analysis was performed on images collected from a family-based prospective cohort study of 1320 elderly Amish subjects (age range 50–99 years) (2,640 eyes) who had a family history of at least 1 individual with AMD. All subjects underwent complete ophthalmic examination, spectral domain optical coherence tomography (SDOCT; 6x6mm ~ 20°), blue-light fundus autofluorescence (FAF), infrared reflectance (IR), and flash color fundus photography (CFP). Both eyes were included in this analysis. Individual imaging modalities were assessed separately in a masked fashion by expert human graders for the presence of RPD, also termed subretinal drusenoid deposits (SDD). To be deemed to be present, a minimum of three discrete lesions were required. Ground truth was established based on the presence of RPD on at least two modalities. Sensitivity and specificity were computed for each individual modality against the ground truth. As SDOCT images covered a smaller region (20° vs 30°) compared to other imaging analyses, SDOCT sensitivity and specificity was recomputed after cropping the other modalities to a similar region of interest.

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Results: RPD were noted to be present on at least one modality in 140 (6.3%) of the 2640 eyes, and in 132 eyes (of 66 subjects; 5%) they were noted in at least two modalities (ground truth or reference determination). Overall, RPD were observed in 133 (5 %), 126 (4.8%), 115 (4.4%), 35 (1.3 %) eyes by IR, FAF, SDOCT and CFP respectively. Sensitivity and specificity for identification of RPD for each imaging modality is shown in Table 1. IR demonstrated the highest sensitivity, and CFP showed the lowest sensitivity. When cropping to a similar region, sensitivity and specificity of SDOCT improved to 93% and 95%, respectively.

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Conclusions: IR imaging appears to be the most sensitive modality for detection of RPD, with a high specificity. SDOCT imaging can also show high sensitivity but may require the scan field to be enlarged beyond the dimensions commonly acquired in clinical practice.

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CONTROL ID: 3544939

SUBMITTER (NAME ONLY): Omar Moinuddin

TITLE: Quantitative Analysis of VEGF in Infant Tears as a Biomarker for ROP

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Moinuddin, S. Sathrasala, M. Pawar, C.G. Besirli, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|J. Magnani, R. Vartanian, Pediatrics, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if VEGF can be safely and effectively be obtained and detected in adequate quantities in the tears of premature infants to serve as a potential adjunct biomarker to indirect ophthalmoscopy for ROP disease screening, as well as to monitor disease progression and response to treatment.

Methods: Tear and saliva samples were collected from 20 infants born <28 weeks gestation or with a birth weight <900 g. Tear samples were collected using Schirmer strips placed in both eyes for 5 minutes. Saliva samples, acting as a surrogate for systemic VEGF, were collected using salivette cotton swabs placed in the infant's mouth for 3 minutes. Samples were diluted and analyzed using microfluidic platform detection antibodies directed against VEGF.

Results: Infants with ROP requiring treatment (n=4) and ROP not requiring treatment (n=5) were younger and smaller than infants without ROP (n=9). An increase tear to saliva ratio between 31-33 and 37-39 weeks gestation was found in infants without ROP and with ROP not requiring treatment but was persistently low in infants with ROP requiring treatment.

Conclusions: Adequate tear and saliva samples can be safely obtained from premature infants for analysis of VEGF. Infants with ROP requiring treatment have no increase in tear to saliva VEGF levels except following laser treatment. VEGF analysis may be an effective adjunct to ophthalmologic examination or may serve as a surrogate for ophthalmologic examination in resource-poor areas.

CONTROL ID: 3544940

SUBMITTER (NAME ONLY): Xuan Wu

TITLE: Evaluation of different OCT systems in quantitative imaging of Schlemm's Canal in human

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Wu, J. Chua, D. Wong, L. Schmetterer, Ocular Imaging, Singapore Eye Research Institute, Singapore, SINGAPORE|X. Wu, D. Wong, B. Tan, L. Schmetterer, X. Yao, SERI-NTU Advanced Ocular Engineering (STANCE), Nanyang Technological University, Singapore, Singapore, SINGAPORE|J. Gan, A. Lam, J. Chua, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: The morphology of SC is believed to be closely related to glaucoma and accurate assessment on the dimension of Schlemm's Canal (SC) is vital. Optical coherence tomography (OCT) enables high-resolution, three-dimensional (3D) imaging of SC in living humans. This study quantitatively compares the performance of three commercial OCT systems in SC imaging and analyzes the impact factors that may affect the image quality as well as the morphological analysis of SC therefrom. Our study provides a guideline to choose an optimized OCT system for better visualization of SC.

Methods: Ten healthy subjects were imaged using three OCT machines: ZEISS Cirrus 5000 (840nm, spectral-domain (SD)-OCT), ZEISS Plex Elite 9000 (1060nm, swept-source (SS)-OCT) and Tomey Casia (1310nm, SS-OCT). For each subject, both eyes underwent two cubic scans by each machine, one on the nasal quadrant and the other temporal. The B-scan showing the largest SC was chosen and processed to obtain SC dimensional metrics. The SC contrast was investigated by quantitative comparison. Four morphological metrics, including the cross-sectional area (CSA), the perimeter, the longest, and shortest diameters of SC, were extracted via manual segmentation. The difference between the three OCT systems were analyzed.

Results: The CSAs were significantly different between different machines (Cirrus - Casia: $\Delta=1763.89\mu\text{m}^2$, $p < 0.001$; Plex - Casia: $\Delta=1026.21\mu\text{m}^2$, $p < 0.001$; Cirrus - Plex: $\Delta=737.68\mu\text{m}^2$, $p=0.003$), as well as the longest diameters (Cirrus - Casia: $\Delta=56.50\mu\text{m}$, $p < 0.001$; Plex - Casia: $\Delta=39.29\mu\text{m}$, $p < 0.001$; Cirrus - Plex: $\Delta=17.21\mu\text{m}$, $p=0.031$). The SC perimeter measured from Casia was significantly different compared to that from Cirrus or Plex (Cirrus - Casia: $\Delta=100.90\mu\text{m}$, $p < 0.001$; Plex - Casia: $\Delta=39.29\mu\text{m}$, $p < 0.001$). The shortest diameter measured from Cirrus and Casia was significantly different ($\Delta=-3.9\mu\text{m}$, $p=0.039$). The Michelson contrast was seen highest in Cirrus (0.63 ± 0.05), mediocre in Plex (0.57 ± 0.06), while lowest in Casia (0.40 ± 0.07). Based on visual assessment, the 1060nm system showed a good balance in angle delineation and SC visualization. Conversely, the 840nm system displayed good performance in SC visualization while the 1310nm system excelled in angle delineation.

Conclusions: The wavelength and resolution of the anterior segment OCT system may affect the visualization as well as the quantitative assessment of SC morphology.

CONTROL ID: 3544942

SUBMITTER (NAME ONLY): Weiwei Wang

TITLE: Miniaturization of Usher Syndrome Type 2A gene for AAV mediated gene therapy

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Wang, L.H. Vandenberghe, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|W. Wang, L.H. Vandenberghe, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Weiwei Wang: Commercial Relationship: Code N (No Commercial Relationship) | Luk Vandenberghe: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Usher Syndrome (USH), an inherited disorder, is the leading cause of deaf-blindness. USH2A, one of the genes that causes Usher syndrome, encodes protein Usherin with an open reading frame of 15.6kb. Our goal is to engineer minigenes with reduced size and yet sufficient function, to meet the AAV volumetric constraints (<~5kb) for gene augmentation to rescue vision.

Methods: Full length Usherin consists of many motif repeats. We hypothesize that some of the repeats are redundant and aim to miniaturize USH2A through rational design of several exploratory minigenes and then high-throughput screening of combinatorial libraries with variant minigenes. We chose Oc-k1 cell line as our in vitro model as it displays the characteristic periciliary localization of Usherin and is originated from mouse organ of Corti. Our immunocytochemistry data showed that upon transfection, full length human USH2A expressed and localized at the periciliary region of Oc-k1 cell line (USH2A -/-). We observed that wild type Oc-k1 cells proliferate significantly faster than USH2A -/- cells, and full length USH2A can rescue cell proliferation. This yet to be explained feature is currently used as our in vitro screening platform.

Results: We designed 7 minigenes to interrogate the motif repeats and screened them by proliferation rate. Three minigenes achieved >60% rescue effect of the full USH2A, two displayed >30% increase and two had no effect compared to control group (vehicle vector). Four of the positive minigenes also demonstrated periciliary localization. Our result showed that deletion among the FN3 repeats affects cell proliferation less than the other motifs. Based on above results, we designed 3 independent libraries: Lib614 targets FN3 repeats #6~14, Lib1625 for #16~25, Lib2734 for #27~34. Each variant contains a unique barcode for batched screening through NGS. We have completed the assembly of Lib614, with Lib2734 assembly in progress. These libraries will be subject to cell proliferation assay and NGS for functionality screening.

Conclusions: We conclude that the FN3 repeats region, occupying almost 2/3 of the entire USH2A gene, bears redundant motifs that may be deleted for USH2A miniaturization. The proliferation assay with Oc-k1 cells revealed potential physiological role of USH2A, though it calls for further investigation on the mechanism to justify the correlation between in vitro proliferation and in vivo photoreceptor rescue.

CONTROL ID: 3544943

SUBMITTER (NAME ONLY): Tetsuju Sekiryu

TITLE: ARMS2 and CFH polymorphism and aqueous humor complement activation products in Japanese patients with age-related choroidal neovascularization

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Sekiryu, Y. Kato, K. Tanaka, Y. Oguchi, K. Itagaki, O. Masashi, Ophthalmology, Fukushima Kenritsu Ika Daigaku Igakubu, Fukushima, JAPAN|T. Omori, Y. Ishida, T. Machida, H. Sekine, Immunology, Fukushima Kenritsu Ika Daigaku Igakubu, Fukushima, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate the relationship between genetic polymorphisms in Japanese patients with age-related macular choroidal neovascularization (CNV) and complement activation products in the aqueous humor.

Methods: We enrolled 248 eyes of 248 patients; 60 patients with neovascular age-related macular degeneration (nAMD), 62 patients with Pachychoroid neovasculopathy (PNV), 57 patients with polypoid choroidal angiopathy (PCV), 25 patients with retinal hemangiomatous proliferation (RAP), and 52 patients with cataract who received surgery as controls. Genotyping of ARMS2 A69S and CFH I62V, which was reported as the major susceptibility genes in Japanese nAMD patients, was performed by the TaqMan method. Aqueous humor was collected immediately before the first vitreous injection of anti-VEGF therapy or before cataract surgery. Complement activation products (C3a, C4a) concentrations were measured using a bead array system (Cytometric Bead Array, The BD-TM).

Results: In the patients with CNV, the allele frequency of ARMS2 A69S was TT: TG: GG = 4.1: 4.0: 1.9, and the C3a concentration (median, ng / mL) was 3.02: 3.00: 2.27, respectively. The C3a concentrations in the patients with TT (P = 0.001) and TG (P = 0.002) were significantly higher than those with GG. The allele frequency of CFH I62V was GG: GA: AA = 5.1: 4.0: 0.9, and the C3a concentration was 3.00: 2.93: 2.69, respectively. There were no significant relations between the CFH I62V allele and C3a concentration. The C4a concentration in the aqueous humor showed allele-specific changes in neither ARMS2 A69S nor CFH I62V genotypes. Neither ARMS 2 A69S nor CFH I62V was associated with C3a and C4a concentrations in the control group.

Conclusions: ARMS2 A69S may activate the intraocular complement system in association with the alternative pathway.

CONTROL ID: 3544944

SUBMITTER (NAME ONLY): Yao Wang

TITLE: Teprotumumab for the Treatment of Thyroid Eye Disease: Clinical Experience from Expanded Access Program (EAP)

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Wang, T. Mester, R. Douglas, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|S. Ugradar, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Teprotumumab was approved in January of 2020 for the treatment of thyroid eye disease (TED). The purpose of this study was to evaluate additional efficacy parameters in patients receiving teprotumumab in the EAP (NCT04040894), which was initiated prior to the drug's approval by the US. Food and Drug Administration.

Methods: This was a retrospective cohort study of patients who received teprotumumab at one study center. Eligible patients included those who were at least 18 years old with a clinical diagnosis of active, moderate-to-severe TED with a clinical activity score (CAS) equal to/greater than 4 with onset of TED within 12 months. Patients were provided 8 infusions (10 mg/kg first infusion, 20 mg/kg thereafter) every 3 weeks over course of 21 weeks. End points included changes in proptosis, intraocular pressure (IOP), extraocular motility deficit, CAS, photophobia score (visual light sensitivity questionnaire-8 [VLSQ-8]), basic secretion test, volumetric analysis of facial compartments (Canfield Vectra H2 camera). Paired t-tests were used to evaluate statistical significance from baseline. Results are presented for the more severe (study) eye.

Results: 13 patients (4 males, 9 females) were included in the analysis. 10/13 patients were Caucasian. Average age was 46.5 ± 15.9 years with a mean TED duration of 7.1 ± 3.0 months. 10/13 (77%) received the complete set of 8 infusions (3 discontinued due to COVID-19, personal choice, and hyperglycemia). At week 21, the change from baseline (CFB) was -4.6 ± 2.1 mm (n=11) for proptosis and -4.0 ± 1.6 (n=11) for CAS (both $p < 0.001$), -9.1 ± 5.0 (n=11; $p < 0.001$) for light sensitivity, and -3.6 ± 3.4 mmHg (n=9; $p < 0.05$) for IOP. 6 patients (n=12) had abnormal wetting test at eligibility visit, compared to 3 at week 21 (n=10). 6 patients had manifest strabismus, 5 of who had complete data. Out of the 5 patients, all but one patient had improvements in either extraocular motility or strabismus measurements. Facial volumetric analysis demonstrated reductions in both upper (CFB: -1.4 ± 0.7 cc; n=4; $p = 0.03$) and lower lid volume (CFB: -2.2 ± 1.3 cc; n=4; $p = 0.04$).

Conclusions: These results support previously reported teprotumumab improvements in proptosis and CAS. Data from this cohort of patients suggest that teprotumumab may also be effective in improving light sensitivity, IOP, motility deficit, dry eyes, and periorbital edema.

CONTROL ID: 3544946

SUBMITTER (NAME ONLY): Terri Young

TITLE: Missense mutations in LRP2 as causal for autosomal dominant primary congenital glaucoma

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.L. Young, K.N. Whisenhunt, S. LaMartina, S. Martin, S.W. Tompson, Ophthalmology and Visual Sciences, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|V. Limviphuvadh, S. Maurer-Stroh, Agency for Science Technology and Research, Bioinformatics Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Primary congenital glaucoma (PCG) is a rare genetic disorder and accounts for 5% of childhood blindness worldwide. Increased intraocular pressure (IOP) leads to corneal clouding, globe size expansion, and optic nerve damage. Genetic studies to date only explain approximately 60% of the mutation etiology. We sought to find the causal mutation in a collection of PCG families prescreened and determined to be negative for mutations in known PCG genes CYP1B1, MYOC, and TEK.

Methods: After consent was obtained, medical histories and blood samples for DNA extraction were acquired from available members of 4 non-consanguineous families (African and European descent) with non-syndromic PCG. Exome sequencing was performed on the 4 affected probands utilizing either a Sure Select Human All Exon capture kit or a Roche/Nimblegen SeqCap EZ v2.0 capture kit, and an Illumina HiSeq platform. Golden Helix SVS software was used to remove variants that were outside of coding/splice site regions, synonymous, or with an allele frequency greater than 0.002 (gnomAD global data). Sanger sequencing validated the candidate variants and the genotypes of additional family members. Gene expression in ocular tissues was interrogated using the Iowa Ocular Tissue Database.

Results: Exome sequencing identified 4 rare heterozygous missense variants within either the extracellular LDL-receptor class A repeat domain (p.Gln1025His), B repeat domain (p.Arg2276His and p.Arg2577His) or linker region (p.Asp2101Gly) of the low density lipoprotein receptor 2 gene LRP2. Global and ethnically matched population allele counts were low for all variants (gnomAD database). FATHMM, SIFT, Polyphen2, and CADD algorithms predicted variants to be functionally detrimental. Vertebrate protein sequence alignments showed strong conservation of the reference residues at all 4 missense variant locations. LRP2 ocular gene expression was identified as high in the optic nerve, retina, and ciliary body.

Conclusions: We provide evidence for autosomal dominant PCG with reduced penetrance caused by heterozygous missense mutations in LRP2. Human LRP2 mutations residing in the same protein domains as our variants have been associated with high myopia with normal IOP. Our findings suggest that LRP2 may also play a role in early-onset glaucoma. Increased suspicion for glaucoma is advised with clinical inspection of individuals with high myopia.

CONTROL ID: 3544948

SUBMITTER (NAME ONLY): Christopher Griffis

TITLE: Rod bipolar cell contributions to changes in response sensitivity during light adaptation

SESSION TITLE: Inner retinal function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Griffis, A.P. Sampath, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|C. Griffis, MC&IP, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mammalian rod bipolar cells desensitize with increases in mean luminance. This process of light adaptation reflects the sum of presynaptic gain changes in rods and postsynaptic changes in the mGluR6 signaling cascade. Here we dissect these contributions and study their underlying mechanism by measuring the properties of light-evoked signals in both rods and rod bipolar cells using patch electrodes.

Methods: Whole-cell voltage clamp recordings were made from rod photoreceptors and rod bipolar cells in dark-adapted mouse retinal slices. Light-evoked responses were recorded for a series of flashes in darkness and during the presentation of background light up to 400 Rh^* (activated rhodopsins) $\text{rod}^{-1} \text{ sec}^{-1}$. A Hill equation with three free parameters was fit to the rod bipolar cell response-intensity relationship - including the maximum photocurrent (R_{max}), the half-maximal flash strength (k), and the extent of nonlinearity in response amplitude as a function of flash strength (n).

Results: Rod photoreceptors exhibited a 2-fold loss of sensitivity at light intensities that cause $\sim 50 \text{ Rh}^* \text{ sec}^{-1}$. Downstream rod bipolar cells exhibit a more complicated sensitivity change. In dim backgrounds, n was reduced from a value of 1.6 in darkness to 1.0 by approximately $10 \text{ Rh}^* \text{ rod}^{-1} \text{ sec}^{-1}$. At brighter light intensities, k began to shift, reflecting the decline in rod sensitivity. R_{max} was also reduced by up to 60% at the brightest backgrounds tested. Dialysis of 10mM BAPTA during recordings, or holding the membrane potential at +50mV, reduced this modulation. Nonstationary noise analysis of the falling phase of light-evoked responses elicited in darkness and in background light reveal that the reduction in R_{max} does not arise from a reduced TRPM1 single-channel current. Instead, it must result from a reduction in the coupling between the mGluR6 receptors and TRPM1 channels.

Conclusions: Measurements in mouse rod bipolar cells reveal that the loss in sensitivity as a function of background light is a combination of the loss in sensitivity due to rod phototransduction, along with mechanisms intrinsic to the rod bipolar cell dendrites. These collectively allow rod bipolar cells to respond robustly to single photon absorptions in a minority of the rods, while continuing the signal at brighter lights that also cause rod adaptation.

CONTROL ID: 3544949

SUBMITTER (NAME ONLY): Zelun Wang

TITLE: Metabolic capacity regulates retinal ganglion cell survival in neurodegeneration

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Wang, P. Williams, Department of Ophthalmology & Visual Sciences, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|Z. Wang, Graduate Program in Neuroscience, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|P. Williams, Department of Neuroscience, Washington University in St Louis School of Medicine, St Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) death underlies vision loss during glaucoma. RGCs exhibit differential resilience to glaucomatous neurodegeneration, but it is unclear what cellular characteristics underlie this heterogeneous survival. Since survival in degenerative conditions likely requires high energy expenditure, we set out to test whether metabolic fitness influences survival of resilient RGC subsets.

Methods: We measured cellular ATP by 2-photon in vivo imaging of the FRET biosensor ATeam1.03 expressed specifically in RGCs. This method allows us to assess variance in ATP levels across the RGC population at the resolution of individual cells. We examined ATP dynamics in RGCs following pharmacologic challenge, correlating their differential response to survival following axon injury by optic nerve crush.

Results: At baseline, mouse RGCs maintain normally distributed cellular ATP levels. Intravitreal injection of sodium azide (NaN_3), a mitochondrial respiration inhibitor, revealed three RGC populations with distinct energetic behavior: a population resistant to ATP decline; a susceptible population with early decline and prolonged ATP depletion; and an intermediate population exhibiting delayed onset of ATP decrease followed quickly by recovery. Individual ATP responses in RGCs were reproducible across repeat NaN_3 challenge injections. Further, NaN_3 was not toxic as no RGC loss was observed up to 8 weeks after injection, allowing correlation of ATP dynamics with survival after optic nerve injury. Preliminary analysis suggests that the ATP-stable population have increased survival 14 days after optic nerve crush (32% survival) compared to RGCs that exhibited transient or prolonged ATP decline (17% survival).

Conclusions: We can directly examine energetic characteristics of individual RGCs in vivo and match energetic signatures with survival potential. We have found three cohorts of RGCs differentiated by their susceptibility to mitochondrial inhibition. Our preliminary data suggest that this heterogeneity in the ability to sustain cellular ATP may influence RGC survival after axotomy. Future experiments will examine other energetic pathways using appropriate pharmacologic inhibitors, in addition to more relevant glaucoma models.

CONTROL ID: 3544953

SUBMITTER (NAME ONLY): Irving Domínguez Varela

TITLE: Ophthalmological care during COVID-19 times. Perspectives from a Mexican eye healthcare system

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: I.A. Domínguez Varela, G. Ortiz-Morales, D. Gomez-Elizondo, A. Bustamante Arias, J.A. Nava García, J. Valdez-Garcia, Ophthalmology, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO]

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ABSTRACT BODY:

Purpose: To report the ophthalmological care management of cataract patients during the COVID-19 pandemic in an eye healthcare system in Mexico.

Methods: A retrospective observational study was designed to review the surgical management of cataract patients from March 1st to December 31, 2020, compared to the same period from 2019. We classified surgical management in three categories: urgent, emergent, and elective procedures, based on the the Mexican Society of Ophthalmology (SMO) and our Epidemiological Surveillance Unit (UVEH). Three eyecare centers participated in this study. The main outcome measure was the rate of reduction in urgent and elective surgeries performed. Priority was given to patients with retinal disease, glaucoma, brunescant cataracts, pediatric patients, and patients with visual acuity ($\leq 20/200$). Routine preoperative RT-PCR testing for SARS-COV-2 was required for all patients.

Results: 240 cataract surgeries were performed in the 2020 period compared to the 643 surgeries performed in the same period of the previous year (-62.7% in 2020 compared to 2019, $p < 0.0001$). (Fig. 1) The mean age of operated patients was 66.5 ± 11.81 years in 2019 and 66.2 ± 12.06 y in 2020. During the studied period, thirteen cataract surgeries (5.4%) were suspended in our healthcare system due to positive preoperative results for SARS-CoV-2 by nasopharyngeal PCR.

Conclusions: The implementation of strict protocols in our non-COVID-19 units allowed for surgical management of cataract patients. As expected, a significant reduction in the amount of cataract surgeries was recorded during the SARS-COV-2 outbreak. Preoperative PCR testing for all patients who undergo cataract surgery in conjunction with strict hospital protocols might allow for safe surgical management of cataracts.

From our healthcare university system, a tertiary referral hospital was converted into a COVID-19 unit in order to tackle the challenges of the pandemic. A second tertiary hospital increased its capacity to attend to the needs of all surgical and clinical necessities of non-COVID-19 patients. Lastly, the specialized ophthalmological unit (CAM) reopened in August, with restricted capacity, restructuration of areas, staff rotation, COVID-19 testing of staff and strict sanitary precautions.

CONTROL ID: 3544960

SUBMITTER (NAME ONLY): Marcus Altman

TITLE: 5-Year Results of a Home Monitoring Device in Study Participants at High Risk for Neovascular Age-related Macular Degeneration

SESSION TITLE: AMD: clinical research - new therapies and technologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.T. Altman, M. Thomas, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|V. Chaikitmongkol, Department of Ophthalmology, Chiang Mai University, Suthep, Chiang Mai, THAILAND|N.M. Bressler, Department of Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) with choroidal neovascularization (CNV) is a leading cause of blindness, necessitating early treatment before significant vision loss occurs. The ForeseeHomeTM Preferential Hyperacuity Perimeter (PHP) is FDA-approved to aid in home monitoring for CNV related to AMD. A prospective cohort study evaluated how often home monitoring detects conversion to CNV in patients with intermediate AMD over a relatively long follow-up.

Methods: Patients were ≥55 years-old and had intermediate AMD with visual acuity ≥20/63 in the study eye. A previous study determined that an in-office qualifying test could identify patients most likely to use the PHP device successfully. Patients who qualified were then required to establish a baseline score at home with the device. If successful, the patient proceeded with daily home use. Patients were monitored for 5 years and could trigger an in-office visit by either a device alert or by reporting a visual symptom. If no CNV was detected at the visit, the patient could then re-establish a baseline with the device to continue home testing.

Results: 91 patients qualified for device use, with mean age of 73.1 years and visual acuity of 20/28. Of these, 132 study eyes established a baseline to begin home testing, with 54 eyes (41%, 95% CI 32%-50%) having at least one alert (by symptom and/or device) over 5 years of testing. Among 90 device-triggered visits, 83 (92%) were false positive, while 7 (8%, 95% CI 3%-15%) resulted in detection of CNV at mean 2.1 years following enrollment. Two eyes that developed CNV were diagnosed by symptom only without a device alert (2 of 9 total CNV cases; 22% false negatives, 95% CI 3%-60%). Mean visual acuity at time of CNV detection was ~20/32. 23 eyes that had a false-positive alert withdrew from the study due to a failure to re-establish baseline—of these, 6 (26%) developed CNV on average 2.7 years later. Mean monthly device usage was 15 times per month and was higher in the first year of an eye's enrollment versus the fifth year (18.5 vs 12.8 uses per month, difference = 5.7, 95% CI: 3.5-7.9; P<.001).

Conclusions: These data over 5 years suggest a large proportion of incident neovascular AMD cases were detected by home monitoring, and eyes monitored by the device had good visual acuity at time of CNV detection. In this study, the device showed a 22% false negative rate.

CONTROL ID: 3544962

SUBMITTER (NAME ONLY): Mary Flokis

TITLE: Fibroblast growth factor (FGF) potentiates transforming growth factor-beta (TGF- β)-induced EMT of lens epithelial cells in a spatially dependent manner

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Flokis, F.J. Lovicu, The University of Sydney School of Medical Sciences, Sydney, New South Wales, AUSTRALIA|F.J. Lovicu, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Epithelial-to-mesenchymal transition (EMT) of lens epithelial cells is involved in the development of fibrotic cataract. Ocular growth factors and cytokines such as fibroblast growth factor (FGF) and transforming growth factor-beta (TGF- β) have been shown to regulate and/or dysregulate lens epithelial cell (LEC) regulatory processes, including proliferation, fibre differentiation and EMT. Here we tested the hypothesis that FGF-2 differentially potentiates lens epithelial TGF- β -induced EMT in the rodent lens.

Methods: Postnatal 21-day-old rat LEC explants treated with TGF- β 2 (50 pg/ml) to induce EMT, and/or co-treated with FGF-2 (150 ng/ml), were monitored over a 5-day culture period, comparing central and peripheral regions. Changes in levels of EMT marker α -SMA and fibre differentiation/elongation markers including β -crystallin were examined using immunolabeling, as well as canonical TGF- β signaling (Smads 2/3) at 2 hours. Western blotting was also used to compare LEC protein expression levels.

Results: Compared to LECs treated with only TGF- β 2, we show that the addition of a high fibre differentiating dose of FGF-2 differentially impacted TGF- β 2-treated LECs after 5 days of culture; with central LECs undergoing TGF- β 2-induced EMT, whereas peripheral LECs primarily undergoing lens fibre-cell elongation in place of EMT. This co-treatment with FGF-2 and TGF- β 2 retained labelling for α -SMA in central LECs with little to no β -crystallin; however, β -crystallin was most prominent in peripheral LECs. Interestingly, FGF did not potentiate nuclear translocation of Smad2/3 in TGF- β -treated LECs by 2 hours of culture.

Conclusions: The current study showed an important role for FGF-2 in potentiating EMT in TGF- β 2-treated LECs, in a spatially dependent manner. This provides a new perspective for the role of FGF-2 in lens, in particular its role in the modulation of TGF- β 2-induced EMT leading to cataract.

CONTROL ID: 3544971

SUBMITTER (NAME ONLY): Liang Liu

TITLE: Comparing the Speed of Glaucoma Progression at Various Stages as Measured by Function, Structure, and Perfusion

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare the speed of glaucoma progression as measured by visual field (VF), optical coherence tomography (OCT), and OCT angiography (OCTA).

Methods: This is a prospective, observational study. Pre-perimetric glaucoma (PPG) and perimetric glaucoma (PG) patients are followed up every 6 months for at least 18 months (average: 30.4 ± 11.0 months). One eye of each participant was scanned using 4.5x4.5-mm OCTA centered on the disc with the AngioVue system (Optovue). The nerve fiber layer plexus capillary density (NFLP CD) was defined as the percentage area occupied by flow pixels excluding large vessels. The nerve fiber layer (NFL) thickness was measured from ONH scan. The NFLP mean deviation (NFLP MD) and NFL MD were visual field (VF)-equivalent dB-scale quantities based on sectorwise nonlinear regression of NFLP CD and NFL thickness with VF deviation. The speed of glaucoma progression was measured by linear regression trend slope over time. A linear mixed model was used to calculate the P values of the slopes.

Results: Forty-one patients were analyzed. Twelve had PPG (average VF MD -0.55 dB), 29 had PG (average VF MD -5.13 dB; range -0.84 ~ -18.35 dB). Reproducibility, on dB scale, was best for NFL MD, followed by NFLP MD and VF MD (Table 1). The trend slope in VF MD was not significantly different from zero in either group. In the PPG group, progression as measured by NFL MD was significantly ($P < 0.007$, Wilcoxon test) faster compared to NFLP MD and VF MD. In the PG group, NFLP MD progression was significantly ($P < 0.001$) faster than NFL MD and VF MD. NFLP CD and NFLP MD had significant decrease only in the PG stage, not the PPG stage. While NFL thickness loss was twice faster ($P < 0.001$, Mann-Whitney test) in the PPG stage compared to the PG stage.

Conclusions: VF MD is not suitable for measuring progression over such a short follow-up period due to the high measurement variability of this functional parameter. NFL thickness and its derivative NFL MD may be useful in monitoring progression in PPG patients as these structural parameters decreased faster in this early stage. NFLP CD and its derivative NFLP MD may be useful in monitoring PG patients as these perfusion parameters decreased faster in this later stage.

CONTROL ID: 3544978

SUBMITTER (NAME ONLY): Philip DeSouza

TITLE: Effect of intravitreal steroid injection or implant on visual and imaging outcomes in patients with non-infectious uveitis

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. DeSouza, A. Moshiri, G. Yiu, S.S. Park, P. Emami-Naeini, Department of Ophthalmology, University of California Davis, Sacramento, California, UNITED STATES|D. Nidamarthi, Athens High School, Athens, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the efficacy of intravitreal triamcinolone acetonide (Triesence®, IVT) and intravitreal dexamethasone implants (Ozurdex®, OZD) for cases of non-infectious posterior uveitis.

Methods: A clinical database was queried to identify all eyes treated with IVT or OZD from 2018 through 2020 at the University of California, Davis Health System. Clinical and imaging data, including visual acuity (VA), intraocular pressure (IOP), use of systemic immunomodulatory therapy (IMT), and central macular thickness (CMT) on optical coherence tomography were analyzed before and after their most recent IVT or OZD treatment. Eyes were excluded if there was a concurrent diagnosis of other fundus pathology (e.g. diabetic retinopathy, retinal vein occlusion), a lack of follow-up after treatment, or no light perception VA.

Results: 22 eyes from 16 patients (4 men, 12 women) were identified that met inclusion criteria. The average age at time of treatment was 67.3 years (range 37.7-98.4). The distribution of non-infectious uveitis amongst the eyes were: 15 idiopathic, 4 sarcoid, 2 tubulointerstitial nephritis and uveitis syndrome, and 1 Vogt-Koyanagi-Harada. 12 eyes received IVT (54.5%) and 10 eyes received OZD (45.5%). Only four eyes (three patients) were on systemic IMT at the time of injection. The patients were followed for a mean of 145.5+/-31.7 days for IVT and 160.5+/-34.7 days for OZD. Overall, there was a statistically significant improvement in LogMAR VA (-0.17, p=0.03), and reduction in CMT (-70.1 microns, p=0.01) after treatment, while there was no difference in IOP compared to baseline (p=0.26). The change in LogMAR VA after IVT treatment was -0.105+/-0.06 and after OZD treatment was -0.245+/-0.14, which was not statistically significant between groups (p=0.37). The change in CMT was -81.33 microns after IVT treatment, and -56.6 microns after OZD treatment, which was not significantly different between groups (p=0.6370).

Conclusions: The use of intravitreal steroid resulted in a significant improvement in VA, and CMT on OCT without significantly affecting IOP in eyes with non-infectious uveitis. No significant difference was noted in visual acuity and CMT change in following OZD when compared to IVT in this small retrospective study. While there was a trend towards better visual and imaging outcomes in eyes treated with OZD, it was not statistically significant.

CONTROL ID: 3544982

SUBMITTER (NAME ONLY): Steven Morrison

TITLE: Cost-Effectiveness of Artificial Intelligence-Based Retinopathy of Prematurity Screening

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Morrison, J. Campbell, Department of Ophthalmology, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|R. Chan, Department of Ophthalmology and Visual Sciences, Illinois Eye and Ear Infirmary, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|M.F. Chiang, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Studies have shown that artificial intelligence (AI) algorithms can help screen for treatment-requiring retinopathy of prematurity (ROP), though it is unknown how cost-effective this is versus standard methods. This study evaluated the cost-effectiveness of autonomous and assistive AI-based ROP screening compared to telemedicine and ophthalmoscopic screening over a range of probabilities, costs, and outcomes.

Methods: Decision trees created and analyzed in TreeAge Pro modeled outcomes and costs of four possible ROP screening strategies: ophthalmoscopy, telemedicine, assistive AI with telemedicine review, and autonomous AI with only positive screens reviewed. We assumed similar sensitivity for detection of severe ROP with a wide sensitivity analysis, but a higher specificity for ophthalmoscopy. Screening and treatment costs were based on Current Procedural Terminology codes, and opportunity costs to physicians were modeled. AI cost was assumed to be \$30. Outcomes were based on the Early Treatment of ROP study, defined as timely treatment, late treatment, or correctly untreated. Incremental cost-effectiveness ratios were calculated at a willingness-to-pay threshold of \$100,000. One- and two-way sensitivity analyses were performed comparing AI strategies to telemedicine and ophthalmoscopy, as was a probabilistic sensitivity analysis.

Results: Autonomous AI was as effective and less costly than each other screening modality (Table 1). Cost of AI evaluation was the most important factor in the sensitivity analysis. AI-based ROP screening was cost-effective up to \$17 for assistive and \$43 for autonomous screening compared to telemedicine, and \$51 and \$73 compared to ophthalmoscopy. In the probabilistic sensitivity analysis, both AI screening modalities were cost-effective in over half of trials in all but one comparison (Figure 1).

Conclusions: We demonstrate that AI-based screening strategies may be more cost-effective than traditional screening modalities across a range of parameters, and cost-effectiveness depends significantly on what cost is assigned to AI.

CONTROL ID: 3544984

SUBMITTER (NAME ONLY): Hon Shing Ong

TITLE: The Effects of Donor-Recipient Age and Sex Compatibility in the Outcomes of Anterior Lamellar Keratoplasties

SESSION TITLE: Corneal transplantation and surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Htoon, Singapore Eye Research Institute, Singapore, SINGAPORE|N. Chiam, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|H. Ong, A. Arundhati, J.S. Mehta, Corneal and External Diseases, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|H. Ong, J.S. Mehta, Tissue Engineering and Cell Therapy, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Corneal transplantations are the commonest allogenic transplant surgeries performed worldwide. Transplantable grade donor cornea is a finite resource. There is thus an impetus for eye banks to optimise the use of each harvested cornea, and clinicians to minimise risks of graft rejection and failure.

Studies on donor-recipient (D-R) age or sex compatibility have mainly been focused on penetrating keratoplasty (PK) and endothelial keratoplasty (EK) procedures. Although studies have reported beneficial effects of sex or H-Y matching in lowering risks of PK or EK rejection and failure, current evidence is still equivocal.

With better survival and lower rejection rates, anterior lamellar keratoplasty (ALK) has gained popularity as an alternative to PK, to treat corneal stromal diseases. We evaluated the effects of D-R age- and sex-matching on the outcomes of eyes that had undergone ALK surgeries.

Methods: ALK surgeries performed in an ophthalmic hospital over an 11-year period were identified (graft registry data). To analyse the effects of sex-matching, transplants were classified as 'presumed H-Y incompatible' (male donor to female recipient) or 'presumed H-Y compatible' (all other D-R sex combinations). For age-matching, differences in donor and recipient ages were calculated. Cox proportional hazards regressions were used to assess the influence of D-R sex- and age-matching on graft failure and rejection.

Results: 359 eyes (322 patients) were included. 246 (68.5%) grafts were presumed H-Y compatible. 14 (3.9%) grafts failed and 8 (2.2%) rejected. There were trends of lower hazard ratios (HRs) in graft failure and rejection in the presumed H-Y compatible group (0.59[95% CI 0.20-1.77] and 0.93[95% CI 0.22-3.89], respectively). Median difference in age between recipients and donors was 14.9 years (IQR 2.8-33.2). HRs of graft failure and rejection were not influenced by D-R age (HRs per 1-year increase in age difference: 1.00[95% CI 0.98-1.02] and 1.01[95% CI 0.99-1.03], respectively).

Conclusions: Sex- or age-matching had no significant effect on ALK rejection and failure. Although trends of fewer graft rejection and failure in presumed H-Y compatible grafts were observed, over 500,000 ALK surgeries would be required to achieve adequate power to show significant effects of matching, if any. Routine sex- and age-matching during graft allocation for ALK surgeries thus cannot be recommended.

CONTROL ID: 3544986

SUBMITTER (NAME ONLY): Sherin Lajevardi

TITLE: Posterior segment manifestations in patients with HLA-B27 associated uveitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Posterior segment involvement in patients with HLA-B27 associated uveitis is a relatively uncommon condition, with a prevalence of 17.4 to 23.1%. This retrospective cohort study investigated the prevalence and characterized the posterior segment involvement in eyes with HLA-B27 associated uveitis. We also aimed to assess the patient characteristics which are associated with posterior segment involvement.

Methods: Medical records of 65 patients (130 eyes) with HLA-B27 associated uveitis, from two university uveitis clinics (United States and Turkey) were reviewed. Posterior segment findings were identified based on medical records and optical imaging including color fundus photography, fluorescein angiography and optical coherence tomography. Findings identified were vitreous haze, vasculitis, optic disc leakage and macular edema. Clinical course of anterior uveitis was described as acute, recurrent, or chronic according to the standardization of uveitis nomenclature (SUN) classification. Recurrent uveitis was defined as repeated episodes separated by periods of inactivity without treatment ≥ 3 months in duration, and chronic uveitis was persistence or relapse of symptoms within 3 months after discontinuation of treatment. Patients who had significant systemic and ocular comorbidities were excluded from the study.

Data was collected using REDCap and analyzed using Stata ver. 16.1.

Results: Forty-four patients were included from US while 21 patients were included from Turkey. The mean age at presentation was 41 ± 15.1 years with a majority being male [42 (65%)] and non-Hispanic Caucasian [34 (53%)]. Overall, 26 patients (36 eyes) demonstrated posterior segment findings; 15 (34%) belonged to US while 11 (52.4%) patients belonged to Turkey. Among eyes with posterior segment involvement, most common findings were peripheral vasculitis and vitreous haze [13 (36.11%) each] followed by macular edema and disc leakage [6 (16.67%) each]. Patients with chronic uveitis (5/7) presented with more posterior segment involvement in US while patients with recurrent uveitis (5/6) presented with more posterior segment findings in Turkish cohort.

Conclusions: Posterior ocular findings can be seen in up to 40% of patients with HLA-B27-associated uveitis. Patients with chronic or recurrent uveitis are more likely to have posterior segment involvement and therefore should warrant more comprehensive evaluation for posterior disease.

CONTROL ID: 3545001

SUBMITTER (NAME ONLY): Amir Hejri

TITLE: Reliable suprachoroidal delivery in rodents using a high-precision microneedle injector

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Hejri, I.I. Bowland, M.R. Prausnitz, School of Chemical & Biomolecular Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|J.M. Nickerson, Department of Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: While robust methods exist for suprachoroidal space (SCS) delivery in larger animals (e.g. rabbits, primates), reliable SCS injection in rodents has yet to be achieved given their substantially smaller eye size. We hypothesize that liquid formulations can be successfully deposited in the SCS when 1) a microneedle injector is properly scaled to ascertain the complete and precise penetration of the needle length across the extremely thin rodents' sclera, and 2) the eye is stabilized while injecting to reduce the probability of failure due to stochastic movements.

Methods: Glass microneedles were fabricated out of glass pipettes, tapering to a tip diameter of 110 μm . 3D-printing was utilized to fabricate different injector designs, and each design was tested to find the optimal configuration. Wistar rats (N=12) and guinea pigs (N=6) were each injected suprachoroidally in one eye with nanoparticle suspensions, while the contralateral eye remained naïve. A custom-made 3D-printed probe was constructed and used to secure the eye firmly in position while injecting. Fundoscopy, slit lamp examination and post-mortem analysis including histological and immunohistochemical staining were performed on all eyes post-procedure.

Results: An optimum injector was achieved with design features fit for miniscule dimensions of rodents' eyes and was used henceforth. Fundoscopy together with confocal imaging of the histology sections confirmed the targeted delivery of nanoparticles to the SCS in all eyes. The optimum microneedle length was found to be $160 \pm 10 \mu\text{m}$ and $260 \pm 10 \mu\text{m}$ for rats and guinea pigs, respectively. Immunohistochemistry and histopathological analysis further revealed no evidence of retinal/RPE abnormalities or choroidal complications in the injected eyes compared to the control eyes.

Conclusions: The ability to reliably deliver to the SCS of rodents facilitates pre-clinical testing of a variety of novel therapeutics and accelerates the development of new ocular therapies. Rodents are an ideal model for pre-clinical investigations given their low cost and availability of various ocular disease models. Here, we highlight the ability of a robust microneedle delivery technique for SCS injection in rodents. The proposed method accomplished SCS delivery with 100% success rate in a simple, minimally-invasive procedure that takes less than one minute for each injection and requires no surgical microscope.

CONTROL ID: 3545002

SUBMITTER (NAME ONLY): Jay Lusk

TITLE: Real-world practice patterns of diabetic retinopathy screening in primary care: direct ophthalmoscopy and screening exam documentation

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) screening is critical to prevent vision loss, but how screening is conducted and documented in the real-world primary care setting has not been reported. We performed a retrospective, observational study to determine the practice patterns for preventative eye care for patients with diabetes seen in a large single-institution primary care network.

Methods: All adult patients with diabetes mellitus who were seen at least once at one of the practices within a large primary care network in the year of 2019 were identified (n=7449). A subset of patients was randomly selected for chart review (n=171), and all primary care encounters for diabetes care or general wellness within the year were reviewed for each patient. Within each encounter, we examined whether the primary care provider (PCP) documented: 1) a direct ophthalmoscope examination; and 2) if the patient's screening eye exam was up to date. The ophthalmology visit closest in date to each primary care encounter, if within 2 years of the encounter, was also reviewed for diagnoses and examination findings, and findings were compared to the PCP's direct ophthalmoscopy results. Statistics were calculated in R.

Results: 414 primary care encounters from 171 patients were reviewed, 38% (159) for an annual physical examination and 62% (255) for diabetes care. PCPs documented a direct ophthalmoscope examination in 14% (24) of the patients; all results were documented as normal (Table 1). PCPs also documented whether the ophthalmology exam was up to date for 79% (165) of patients; 42% (71) were up to date, and 37% (64) were not up to date. There was no documentation of ophthalmology exam status for the remaining 21% (36) of patients. 50% (85) of patients had an ophthalmology visit within 2 years. For the encounters where both direct ophthalmoscopy results and ophthalmology clinical diagnosis were available (n=18), the rate of agreement was 33% (13%, 59%); sensitivity of direct ophthalmoscopy for detecting posterior eye pathology was 0% (0%, 27%).

Conclusions: This study is one of the first to document the real-world practice patterns for DR screening in primary care, demonstrating the challenges associated with DR screening in that setting. Systems-level approaches are needed to improve preventative eye care for patients with diabetes.

CONTROL ID: 3545003

SUBMITTER (NAME ONLY): Takeru Nishikawa

TITLE: Deep neural network for the analysis of guttae via semi-supervised learning in a Fuchs endothelial corneal dystrophy mouse model

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Nishikawa, N. Okumura, K. Narimoto, S. Yamada, K. Okamura, N. Koizumi, Department of Biomedical Engineering, Doshisha University, Kyotanabe, JAPAN|A. Izumi, ActualEyes Inc., Kyotanabe, JAPAN|

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ABSTRACT BODY:

Purpose: Although numerous numbers of accurately annotated data as grand truth is necessary for deep learning, the preparation of grand truth can create a bottleneck. In this study, we prepared a small number of annotated corneal endothelial images in a early-stage Fuchs endothelial corneal dystrophy (FECD) model mouse, and tested the feasibility of semi-supervised learning to widen the indication of AI to late-stage FECD.

Methods: Corneal endothelial images were obtained from FECD mouse-model eyes via contact specular microscopy. A trained model (AI 1) was created via the use of 28 manually annotated images (ground truth) of early-stage FECD mouse eyes. Supervised data 1 (n=250) of late-stage FECD was generated via AI 1, and AI 2 was generated via the use of supervised data 1. Then, supervised data 2 was generated by AI 2, and AI 3 was generated by using supervised data 2. Subsequently, those learning processes were repeated up to AI 12. Finally, AI was used to analyze the 25 test data images of late-stage FECD.

Results: AI 1 was generated via the 28 annotated image data of early-stage FECD. The guttae area detected by AI 1 was strongly associated with ground truth in early-stage FECD ($r=0.97$, $p=3.83 \times 10^{-27}$), however, AI 1 underestimated the guttae area by a mean systematic error (i.e., between the guttae area detected by AI and ground truth) of $-2.2 \pm 1.3\%$ ($r=0.86$, $p=2.83 \times 10^{-8}$) in late-stage FECD. After semi-supervised learning, systematic error tended to decrease throughout AI 2-9, though it increased slightly due to overestimation in AI 10-12. The mean systematic error of AI 9 was $-0.1 \pm 0.9\%$, and the guttae area detected by AI 9 was strongly associated with the manually annotated test data of late-stage FECD ($r=0.94$, $p=5.84 \times 10^{-12}$).

Conclusions: Semi-supervised learning by the use of limited numbers of annotated data of early-stage FECD enables the generation of a deep neural network for analyzing different disease phases of late-stage FECD. Our data suggests that semi-supervised learning can be applicable to multiple clinical settings; e.g., reduction of the time and cost of preparing annotated data and expanded indication (to very early or late stages) of a deep neural network.

CONTROL ID: 3545011

SUBMITTER (NAME ONLY): Jodi So

TITLE: Geographic and Socioeconomic Disparities in Uveal Melanoma Treatment, 2004-2016

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate patient-level disparities in uveal melanoma (UM), the most common primary intraocular tumor in adults.

Methods: We analyzed 14,674 UM cases from 2004-2016 National Cancer Database records. Enucleation, brachytherapy, and proton beam utilization were analyzed over time. We performed logistic regression analyses to assess odds of worse stage at diagnosis, use of brachytherapy or proton beam versus enucleation, and use of proton beam versus other radiation. Patient-level variables included diagnosis year, tumor stage and location, age, sex, comorbidities, insurance, income, metropolitan residence, distance to hospital, hospital type and location (by census division), and treatment at multiple hospitals.

Results: Brachytherapy and proton beam use increased from 2004-2016, while enucleations declined. Patients who were nonwhite (OR=1.2, $p<0.01$), uninsured (OR=1.7, $p<0.01$), and who were treated at academic centers had higher odds of presenting with worse-stage disease. By contrast, those in the highest income quartile had lower odds of worse stage at presentation (OR=0.9, $p<0.05$). Patients with public (OR=0.7, $p<0.01$) or no insurance (OR=0.4, $p<0.01$), or who were treated at community cancer programs (annual caseload<500, OR=0.2, $p<0.01$) were less likely to receive radiation over enucleation, while those with higher incomes, metropolitan residence, treatment at academic centers, or treatment at facilities on the East and West coasts were significantly more likely to be treated via radiation. Metropolitan and high-income patients, and those treated at academic centers or facilities in the Pacific region were significantly more likely to receive proton beam over other types of radiation, while those treated at hospitals in the Middle Atlantic were less likely to receive proton beam (OR=0.2, $p<0.05$). Enucleation was predominant in Central US regions, brachytherapy in the Middle Atlantic, and proton beam in the Pacific (Figure 1).

Conclusions: Although utilization of enucleations for UM has decreased over time and utilization of brachytherapy and proton beam has increased, substantial treatment differences persist based on factors such as patient income, insurance status, and—especially—geography, with radiation therapies most common in Coastal regions. Further work is needed to evaluate treatment availability and ensure equitable access to UM care.

CONTROL ID: 3545012

SUBMITTER (NAME ONLY): Nafisa Nuzhat

TITLE: Investigating how a novel mutation in the distal-end centriolar protein, CEP162, alters ciliogenesis and results in retinal dystrophy

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Willer, J.N. Pearring, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|N. Nuzhat, Cell and Developmental Biology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|H. Truong, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary cilia are thin microtubule-based projections that extend from the plasma membrane of quiescent cells. Photoreceptor cells contain a specialized primary cilium called the outer segment, which is responsible for light capture. In general, human mutations present in core ciliary components cause syndromic diseases collectively termed ciliopathies. Interestingly, a subset of these mutations leads to non-syndromic retinal dystrophy. In this study, we identified a human patient with late-onset retinitis pigmentosa caused by a novel frameshift mutation resulting in early truncation of the CEP162 protein. CEP162 is localized to the distal-end of centrioles and required for ciliogenesis. To understand its underlying role in retinal dystrophy, we investigate how the human CEP162 mutation affects protein localization and cilia formation in patient derived human fibroblasts and mouse photoreceptors.

Methods: Control and patient derived human fibroblasts were analyzed for CEP162 mRNA expression, non-sense mediated decay, CEP162 protein stability and localization, and primary cilia formation and structure. Additionally, CEP162 staining was performed on mouse retinal cross-sections.

Results: Our analysis of the patient's fibroblast revealed that while truncated mutant CEP162 protein was expressed, it was not localized to the centrosomes. Absence of CEP162 from the basal bodies resulted in reduced ciliation in the patient fibroblasts compared to control. Interestingly, in patient fibroblasts CP110, a negative regulator of ciliogenesis, accumulated at the basal body. Further analysis revealed that although CEP290 was recruited to the basal body polyglutamylated tubulin was absent suggesting that ciliogenesis was halted at the stage of axoneme extension prior to transition zone assembly. Correlative light and scanning electron microscopy (CL-SEM) also showed stalled ciliary structures in the patient fibroblast compared to the control. Immunohistochemistry from mouse retinal cross-sections revealed endogenous CEP162 is localized to the distal end of the basal bodies at the base of the outer segment.

Conclusions: Our results indicate a novel role for CEP162 mediated axoneme extension, prior to transition zone assembly, as well as establish CEP162 as a retinal dystrophy gene.

CONTROL ID: 3545014

SUBMITTER (NAME ONLY): Fidelle Chahine Karam

TITLE: A novel intronic RPGR variant in patient-derived iPSC retinal pigment epithelium and retinal organoids reveals abnormal splicing and protein expression

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Novel variants found in the retinal dystrophies require definitive pathogenicity classification for informed patient dialogue and access to current and future clinical trials and therapies. We use patient-derived induced pluripotent stem cells (iPSCs) differentiated to retinal pigment epithelium (iPSC-RPE) and retinal organoids (iPSC-RO) to contribute to pathogenicity determination in these cases, and as a platform to test novel therapies. Here, this approach was undertaken in a family with a novel intronic variant in RPGR, which was reported by the diagnostic laboratory as a variant of uncertain significance.

Methods: iPSC patient clonal lines, formed from fibroblast samples, were used to culture iPSC-RPE and iPSC-RO, through proneural induction methods. Fibroblast and iPSC-RPE cells were used to determine presence of aberrant splicing through cDNA sequencing. RPGR gene and protein expression studies were undertaken using qRT-PCR, and immunofluorescence in iPSC-RPE and ROs was utilised to explore protein interactions and localisation.

Results: The novel intronic RPGR variant was shown to alter typical exon 12 splice acceptor site function. Gene expression of RPGR in patient iPSC-RPE and iPSC-ROs was decreased. RPGR protein analysis revealed decreased expression and mislocalisation in primary cilia and the photoreceptor cilium. Additionally, iPSC-ROs showed other photoreceptor protein mislocalisation.

Conclusions: Investigation of this novel patient RPGR variant in iPSC-RPE and ROs has revealed abnormal splicing, with decreased gene and protein expression, and abnormal photoreceptor protein localisations. This work has aided in variant classification to likely pathogenic, providing genetic information and eligibility for future treatments for the affected individuals.

CONTROL ID: 3545023

SUBMITTER (NAME ONLY): Ping-Yen Huang

TITLE: Topical BRM421 Ophthalmic Solution improves signs and symptoms of moderate to severe dry eye patients in clinical trials

SESSION TITLE: Dry eye clinical treatments

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: BRM421 is a synthetic peptide comprising 29 amino acids derived from Pigment Epithelium-Derived Factor (PEDF) with neurotrophic and anti-inflammation properties. We performed two clinical studies to confirm the early onset of efficacy in subjects with different dry eye severities.

Methods: The first-in-human (FIH) study and second-in-human (SIH) study were multi-center, double-masked, randomized, vehicle-controlled, Ora CAE® screened studies. The FIH study evaluated 157 subjects. It comprised 5 visits in approximately 5 weeks. Based on the FIH study results, the SIH study evaluated 220 subjects in 4 visits in approximately 3 weeks.

Results: The FIH study showed that BRM421 treatment significantly improved sign in corneal sum (Ora Calibra® scale) in moderate to severe patients (higher baseline fluorescence corneal stain and central corneal staining score) at Visit 4 on Day 14 (BRM421 n=18, Placebo n=13, p=0.02). Significant improvement was also observed in symptom (ODS dryness, Ora Calibra® scale) on Day 14 (BRM421 n=22, Placebo n=22, p=0.01). In addition, the BRM421 group had superior Tear Film Break-Up Time at Visit 5 on Day 29 (p=0.03). The data suggest that BRM421 has an early onset of action; hence, the SIH study was designed for 4 visits. In the SIH study, BRM421 showed trending efficacy in sign (BRM421 n=81, Placebo n=83, p=0.11). Significant improvement was observed in the secondary endpoint of symptom in VAS–Eye Dryness (BRM421 n=108, Placebo n=111, p=0.02) and VAS-Burning (p=0.003) at Visit 3 on Day 8. Significant improvement was also observed in the Ora Calibra® Ocular Discomfort & 4-Symptom Burning/Stinging (BRM421 n=108, Placebo n=110, p=0.02) and Dryness (p= 0.03) in patient diary records on Day 8.

Conclusions: Both clinical studies confirmed consistent early onset of BRM421 treatment effects of sign and symptoms. The post hoc analyses showed improved efficacy in favor of BRM421 in a more severe patient population. The findings warrant further study of BRM421 Ophthalmic Solution in subjects suffering from dry eye syndrome.

CONTROL ID: 3545026

SUBMITTER (NAME ONLY): Alisa Prager

TITLE: 3D-printing and Computer Aided Design (CAD) technology to create a prototype prosthetic iris

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There are limited treatment options for aniridia. 3D-printing may provide cost-effective, cosmetically acceptable iris implants for individuals with aniridia. The purpose of this study was to develop a proof-of-concept workflow for the fabrication of prosthetic irises using slit lamp photography, computer aided design (CAD) and 3D-printing.

Methods: High resolution external ocular slit lamp photographs taken from healthy volunteers who had primarily green, blue, or brown irises to be representative of the overall population. Images were transferred to Photoshop Software Suite where the irises were isolated for additional processing. The isolated image of the iris was then transferred to Computer Aided Design (Auto CAD) software where it underwent additional processing into a vector file, followed by subsequent extrusion of iris detail. This extruded design was then sliced and used for 3D-printing. To match the color of inks used in the 3D-printed design, photos of the eye were white balanced in Photoshop in order to derive Cyan-Magenta-Yellow-Black (CMYK) values. A matrix of pigment concentrations was created to develop silicone inks (OOMOO 30 Smooth ON silicone rubber) with CMYK values that matched those derived from high resolution photos. 3D-printing of iris prototypes was accomplished with Envisiontec 3D-Bioblotter, which is designed for high resolution and automated bio-fabrication. A disc with a diameter of 34mm and circular pupil opening diameter of 3.5mm was printed. After partial curing, the additional detail of the design for the prototype was printed onto this disc. For the prototype, a simplified human-derived iris design was printed in black (iris detail) and white (base disc) but moving forward color of the disc will be matched to the most common secondary color of the healthy volunteer's iris image.

Results: Using images of six volunteer irises (3 brown, 2 green, 1 blue) we identified 9 shades for brown in tandem with 3 different shades that are used to calibrate the color matrix. We have four brown variations (dark, light, yellow, and red) that are within this color matrix. Our workflow produced a prototype iris (currently in black and white) with abovementioned dimensions derived from an external ocular slit lamp photograph.

Conclusions: Future work will focus on miniaturization, use of color-matched inks, expansion of human iris matching, and tests for biocompatibility and safety.

CONTROL ID: 3545027

SUBMITTER (NAME ONLY): Aamir Aziz

TITLE: Real World Efficacy and Safety of Brolucizumab in Neovascular AMD: The REBEL Study

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Brolucizumab was FDA approved for the treatment of neovascular age-related macular degeneration (nAMD) in 2019. This multi-center real-world retrospective study evaluated the safety and efficacy of brolucizumab in patients diagnosed with nAMD.

Methods: In this multi-center retrospective study, both treatment-naïve patients and patients switched to brolucizumab from other anti-VEGF agents were evaluated. Information collected included demographics, number of previous treatments or if treatment naïve, ETDRS visual acuity, central retinal thickness (CRT) and changes in pigment epithelial detachments (PED), if applicable. Improvements in PED height and retinal fluid are evaluated as a proportion of patients. Improvements in visual acuity, CRT and PED height are evaluated as averages. Observed and calculated data is reported.

Results: A total of 282 eyes were evaluated after treatment with brolucizumab for nAMD. The mean [SEM] age of patients was 81.2 [0.51] years. The majority of patients were switched from other anti-VEGF agents after persistent disease activity (63.9%), followed by a desire to elongate treatment intervals (32.3%). Patients received an average of 2.4 [0.06] injections. Over half of the patients treated with brolucizumab discontinued the agent (54.4%), with 86% of these doing so out of caution after reports of intraocular inflammation (IOI) or occlusive vasculitis. A total of 14 patients experienced an adverse event: 10 cases of IOI, one case of occlusive vasculitis and 3 cases of pain. In patients who received at least three treatments of brolucizumab, the proportion of patients with intraretinal fluid (IRF), subretinal fluid (SRF), and PEDs decreased, (34.5% to 27.2%), (49.8% to 31.6%), (59.8% to 54.6%), respectively. Improvements in visual acuity (62.4 [0.94] letters to 64.5 [1.25] letters), CRT (312.4 [6.32] mm to 269.8 [7.31] mm) and PED height (236.0 [15.98] mm to 206.7 [12.9] mm) were also calculated.

Conclusions: Brolucizumab demonstrated efficacy in naïve as well as previously treated patients with nAMD through various measures, by achieving improvements in the proportion of patients without IRF, SRF and PEDs, and improving visual acuity, CRT and PED height. Overall, 10 patients had IOI and one patient had occlusive vasculitis. Further studies are needed to continue evaluating real-world safety and efficacy outcomes of patients treated with brolucizumab.

CONTROL ID: 3545029

SUBMITTER (NAME ONLY): Eileen Wang

TITLE: Immune Homeostasis and Aging Lipid Mediator Circuits

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Aging is a primary risk factor for dysregulated routine ocular surface immune responses, which can lead to autoimmune diseases, such as Dry Eye. Our knowledge of how aging impacts the delicate regulation of healthy and essential immune responses is very limited. Lipid mediators, such as the lipoxin circuit, have emerged as important resident pathways that regulate leukocyte and T cell functions and homeostasis in the retina and ocular surface. The goal of this study was to characterize how aging impacts lipid mediator circuits that regulate immune response in the ocular surface and eye.

Methods: Healthy 3-5 months old and 20-27 months old C57BL/6J male and female mice were housed under standard conditions. Eyes, lacrimal glands, draining lymph nodes, spleen, serum and bone marrow were collected for HPLC/LC/MS/MS-based lipidomic analysis. Gene expression of cyclooxygenase, lipoxygenase and lipoxin receptors in tissues was assessed by QPCR. Leukocytes were isolated from zymosan-induced peritonitis in young and aged mice to define leukocyte lipidome and expression of lipid mediator pathways and receptors.

Results: Lipidomic and QPCR analyses identified marked sex- and tissue-specific changes in aged mice. Specifically, 5-LOX and 15-LOX pathways, the lipoxin circuit and levels of prostaglandins were markedly altered in aged mice and showed sex-specific differences. Impaired 5-LOX activity and capacity to generate LXA₄ was a phenotype of leukocytes from aged mice.

Conclusions: Execution of healthy routine innate and adaptive immune responses depend on tight regulation of effector cells and return to immune homeostasis. Lipid mediator circuits, such as lipoxins and prostaglandins, are important local signals that control the threshold of activation, amplitude and duration of an immune response. Their formation and receptors are dynamically and tightly regulated. The data indicates that in healthy mice, aging alters the balance of lipid mediator circuits in leukocytes, lymph nodes, lacrimal glands and eye, which may set the stage to initiate dysregulated immune responses.

CONTROL ID: 3545031

SUBMITTER (NAME ONLY): James Tian

TITLE: Impact of the COVID-19 pandemic and a regional stay-at-home order on Emergency Department and inpatient consults for ocular complaints at a tertiary hospital

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tian, H. Gabr, G. Andrew, S. Hsu, D.S. Grewal, D. Gupta, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|H. Gabr, Department of Ophthalmology, Ain Shams University, Cairo, EGYPT|

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ABSTRACT BODY:

Purpose: Coronavirus disease 2019 (COVID-19) has impacted individuals seeking preventative, follow-up, and emergent ophthalmic care. In this retrospective study, we assessed the impact of COVID-19 on inpatient and emergency department (ED) ophthalmology care at a large tertiary academic hospital in the United States.

Methods: We analyzed 570 ED and inpatient ophthalmology consults from March 13th to May 15th in 2020 and over the same period in 2019. Our primary endpoints were the number of consults and the percentage of consults that were 'vision-threatening' between the time periods. Our secondary endpoints were the demographics of the patients, relation to trauma, relation to an exacerbation of a chronic ocular condition, if the consult required surgical intervention, and time to surgery.

Results: The total number of ED and inpatient consults decreased by 35.2% in 2020 compared to 2019. The total number of visually threatening diagnoses decreased, 97 in 2019 to 83 in 2020. The proportion of presentations with visually threatening diagnosis increased from 28.0% to 37.1% ($p=0.0237$). In 2020, there were a higher proportion of consults related to trauma (31.7% compared to 23.4%, $p=0.0289$), and consults requiring surgical intervention (19.6% compared to 12.4%, $p=0.0192$). The time to surgery was similar between time periods studied ($p=0.902$). There was not a significant difference in proportion of consults resulting from exacerbations of chronic ocular conditions ($p=0.554$).

Conclusions: The volume of ophthalmic consults to our tertiary eye center and ED declined during the COVID-19 pandemic. There was an increase in the proportion of visually threatening diseases indicating a higher overall acuity seen by the consulting service. There was a total decrease in visually threatening diseases (despite an increase in numbers of consults from trauma), suggesting that some patients may have avoided urgent ophthalmic care due to fear of COVID-19 and the lockdown. Further research is needed to characterize the effect of COVID-19 and the regional stay-at-home order on emergent ophthalmic care delivery so we can better prepare for later stages of the pandemic and also for future pandemics.

CONTROL ID: 3545037

SUBMITTER (NAME ONLY): Yoon Lee

TITLE: Repeat Ranibizumab Injections in Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.H. Lee, A.J. Weiner, I. Tsui, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The objective of this case series is to discuss the role of repeat intravitreal ranibizumab (IVR) in treating posterior retinopathy of prematurity (ROP). To our knowledge, there are only 2 other reported cases using repeat intravitreal injections (IVI) for ROP.

Methods: We report 2 cases of premature infants born at gestational age (GA) 23-24 weeks (w) with birthweight (BW) of 540-601g at university neonatal intensive care units who were treated with IVR (0.25 mg/0.025 mL) for recurrent posterior ROP followed by delayed laser for anterior recurrence.

Results: First case is a female (GA = 23-2/7w, BW = 540 g) with bronchopulmonary dysplasia (BPD) and sepsis. Exam at post-menstrual age (PMA) 31-3/7w showed zone 1, stage 3, no plus in both eyes (OU) and was treated with IVR OU. Repeat IVR was given OU at 38-0/7w for recurrence (zone 1-2, stage 2, pre-plus OU). Laser was performed OU at 47-4/7w for zone 2, stage 3 with pre-plus OU. The following week, patient had worsening plus OU and was treated with additional laser. ROP regressed OU at follow up.

Second case is a female (GA = 23 4/7w, BW = 601 g) with BPD, sepsis, and hypotension. IVR OU were given at 34-1/7w for vitreous hemorrhages (VH) OU and zone 1, stage 3 with plus OU. OS was reinjected at 39-1/7w for worsening VH and zone 1, stage 2, pre-plus and OD at 40-1/7w for zone 1, stage 2, pre-plus. At 51-1/7w, ROP reactivated (anterior zone 2, stage 3 without plus) and laser was performed. ROP regressed OU at follow up.

Conclusions: Repeat IVI was selected over laser because of posterior recurrence. A second IVI was performed to allow further peripheral vascularization of the retina, with the added benefit of avoiding general anesthesia in critically ill infants until they are older. IVR was chosen because it has a shorter systemic half-life compared to bevacizumab, theoretically causing less side effects. However, ranibizumab has been associated with earlier ROP recurrence compared to bevacizumab.

In conclusion, this case series demonstrates the use of repeat IVR in posterior recurrence of ROP. As advances in neonatal care continue to evolve and infant viability extends to younger GA, the use of repeat IVI for ROP may be increasingly necessary. Future studies could seek to determine the safest and most effective agent, dose, and interval for repeat IVI.

CONTROL ID: 3545038

SUBMITTER (NAME ONLY): Ted Maddess

TITLE: Diagnostic power of rapid ETDRS-grid matched objective perimetry in early- to late-stage AMD

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Maddess, B.B. Rai, C. Carle, E. Rohan, J. van Kleef, F. Sabeti, John Curtin School of Medical Research, Australian National University, Canberra, Australian Capital Territory, AUSTRALIA|F. Sabeti, Optometry and Vision Science, University of Canberra, Canberra, Australian Capital Territory, AUSTRALIA|R.W. Essex, Ophthalmology, Canberra Hospital, Canberra, Australian Capital Territory, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To examine the diagnostic power of a new version of multifocal pupillographic objective perimetry. The new test has 18 test-regions per eye, which match the ETDRS retinal thickness grid used in OCTs, and tests both eyes concurrently in 80-seconds.

Methods: We recruited 34 AMD patients and 26 normal control subjects, mean ages (\pm SD) of 72.6 ± 7.06 and 73.1 ± 8.17 years respectively. Among our 68 patient eyes the distribution of eyes per AREDS step was: AREDS1: 28, AREDS2: 18, AREDS3: 13 and AREDS4: 9. The 9 AREDS4 eyes were all neovascular-AMD. Given that the severity was often different between eyes the Receiver Operator Characteristic plot analysis was done by eye rather than by subject. We also estimated Effect-sizes as Hedge's g. The new M18 test matches the pattern of the of the ETDRS grid with two stimuli that bi-sect each grid sector. The 18 stimuli/eye thus assess the central 6 mm (20 deg). We used an FD-cleared prototype of the Konan Objectified Analyser (OFA). Both eyes are tested concurrently in 80 s. We obtained % Areas under the Curve (%AUC) for ROC plots for diagnosis of AREDS group vs. controls. Separate %AUCs were calculated for the mean of the worst 3, and the worst 9, per-region response delays. %AUCs are also done for Best Corrected Visual Acuity (BCVA).

Results: BCVA showed no diagnostic power for AREDS1 and 2 (Table 1), whereas M18 per-region delays provide values in the range of 72.8 ± 6.65 to 84.3 ± 4.21 (mean \pm SE) (Table 2). AREDS3 and 4 were diagnosed at 86.8 ± 5.33 to 92.9 ± 3.93 . Effect-sizes (right two columns of Table 2) up to 2.48 were found.

Conclusions: The M18 test provided superior %AUC performance compared to BCVA. Reasonable diagnostic power was found, even for AREDS 1. M18 stimuli are easily compared with retinal thickness data obtained for the ETDRS grid pattern given that pairs of M18 stimuli exactly match each of the ETDRS grid regions popular with OCT manufacturers, thus allowing simple structure-function comparisons.

CONTROL ID: 3545042

SUBMITTER (NAME ONLY): Siyan Zhu

TITLE: RPE utilizes proline to enhance nutrient availability to the retina

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: We reported that the retinal pigment epithelium (RPE) preferentially metabolizes proline to support the retina. RPE could also use lactate released by the retina, which spares glucose for the retina. In this study, we aim to understand the relationship of proline with lactate and glucose in RPE metabolism, and the metabolic communications between RPE and the retina using ^{15}N labeled proline.

Methods: To study how RPE uses glucose, lactate and proline, we incubated mature human RPE cells with 5.5 mM glucose, 5 mM ^{13}C lactate or 5 mM proline in DMEM. After incubation for 24 and 48 hours, we compared the metabolites in the remaining medium. We also incubated freshly isolated mouse retina and RPE/choroid with ^{15}N labeled proline and other amino acids. To study the proline utilization in vivo, we retro-orbitally injected 150 mg/kg ^{15}N proline in mice and collected retina and RPE at 15, 30 and 60 min to trace ^{15}N proline and its derived metabolites.

Results: Lactate supplementation increases ~40% more glucose remaining in the medium compared to glucose alone group at 24 hours. The addition of proline further increases the amount of leftover glucose (~63%). The RPE consumes similar amounts of proline and lactate when they are provided in the same concentration. Unlike lactate, proline supplementation significantly increases non-essential amino acids (NEAAs) such as aspartate and glutamate in the medium. Incubation of RPE/choroid with ^{15}N proline confirms that ^{15}N is rapidly incorporated into NEAAs to release into the medium. Retina could not utilize ^{15}N proline directly but consumes ^{15}N proline derived NEAAs from the medium. Tracing in vivo shows the concentrations of ^{15}N proline derived NEAAs peak at 30 min and quickly drop afterwards in RPE. However, in the retina, the concentrations of NEAAs were gradually elevated or maintained after 30 min, supporting that RPE uses proline to generate NEAAs for the retina.

Conclusions: Proline enhances glucose sparing by the RPE in the presence of lactate. In addition, RPE uses proline to synthesize NEAAs, thereby increasing the nutrients available to the retina.

CONTROL ID: 3545043

SUBMITTER (NAME ONLY): Eung Suk Kim

TITLE: OCTA biomarkers of CNV secondary to aged-related macular degeneration following intravitreal aflibercept

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kim, J. Park, K. Kim, S. Yu, Kyung Hee University Medical Center, Dongdaemun-gu, Seoul, KOREA (THE REPUBLIC OF)

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ABSTRACT BODY:

Purpose: To investigate prospectively long-term functional and anatomical outcomes for fixed regimen of intravitreal aflibercept in patients with CNV by quantitative analysis based on OCT and swept-source OCT angiography.

Methods: 33 patients who are diagnosed as CNV are enrolled for prospective, single arm, interventional study. At first, 3 intravitreal aflibercept injections by monthly and 5 intravitreal aflibercept injections by fixed every 2 months regimen were done. Investigation of functional and anatomical outcomes were performed every 1 week later after intravitreal aflibercept injection. Analysis of 33 eyes with follow-up for 49 weeks were done for BCVA(ETDRS), CST, PED volume, CNV area, vessel density and vessel length density prospectively.

Results: Average baseline of age was 72.38 ± 8.82 and BCVA(ETDRS) was 50.27 ± 23.57 . There were significant correlation between last vessel length density and last BCVA($r = -0.765$, $p = 0.006$), last CNV area and last CST($r = -0.743$, $p = 0.009$), total change of vessel density and last CST($r = -0.651$, $p = 0.030$), total change of vessel density and first change of CST($r = 0.709$, $p = 0.022$). As a result of multiple regression analysis, the dependent variable, last CST, was statistically significant with a variable as total change of CNV vessel density in the independent variable.

Conclusions: Fixed 2-months regimen of aflibercept improved both visual and anatomical outcomes in patients with neovascular AMD at 49 weeks. Also OCTA biomarkers can be used for evaluating neovascular AMD.

CONTROL ID: 3545048

SUBMITTER (NAME ONLY): Ghazal Narimanfar

TITLE: Identification of diagnostic and prognostic indicators of hypercoagulability in patients with pseudoexfoliation syndrome

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kesim, A. Sahin, Department of Ophthalmology, Medical School, Koc Universitesi, Istanbul, Istanbul, TURKEY|G. Narimanfar, E. Uğurel, N. Zibandeh, Ö. Albayrak, A. Sahin, O. Yalcin, Koc University Research Center for Translational Medicine, Koc Universitesi, Istanbul, Istanbul, TURKEY|O. Yalcin, Department of Physiology, School of Medicine, Koc Universitesi, Istanbul, Istanbul, TURKEY|

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ABSTRACT BODY:

Purpose: Pseudoexfoliation (PEX) syndrome is an age-related disease that may affect all vascular structures of the body due to the accumulation of degraded abnormal fibrillar deposits in the intraocular and extraocular tissues. This vascular structure may generate the inflammation environment and alter the morphological or functional protein structure of platelets. In this study, we tested the relationship between clot dynamics and platelet activation markers. The aim of our study is to find specific biomarkers with a diagnostic and prognostic value that will independently predict the PEX syndrome.

Methods: Two groups were included in this study, 1- Patients with ocular PEX syndrome (n=19) 2- Sex-matched individuals without ocular PEX syndrome (n=19). Ophthalmological examination and complete blood count measurements were performed in all participants aged between (40-75) years. Patients with von Willebrand disease, platelet dysfunction, diabetes, and ones using anticoagulant drugs were excluded. Peripheral blood was collected, analyzed by ROTEM (EXTEM, INTEM, and FIBTEM) tests, and flow cytometry was performed to analyze the expression of CD 41a, CD42b, CD61, CD62p, and PAC-1. A one-tailed Mann-Whitney test was used for statistical analysis.

Results: Analysis of the ROTEM data showed that the FIBTEM coagulation time (67.4 vs 60.3s; $P < 0.05$) and the FIBTEM alpha angle (73.3 vs 70.0; $P < 0.05$) increased in the PEX patients compared to the control group. Flow cytometry findings showed that there was a significant difference in the CD62p surface expression ($P < 0.0001$) and PAC-1 surface expression ($p=0.018$) between the PEX patients and the control group. Furthermore, analysis of antigen-binding capacity showed a significant difference only in the CD62p marker ($P=0.0178$).

Conclusions: To the best of our knowledge, this study is the first to examine clot dynamics and platelet activation markers in PEX patients. ROTEM results illustrated the higher contribution of functional fibrinogen in clot formation in the PEX patients. Flow cytometry data show that platelet activation markers are significantly elevated in PEX patients, suggesting the presence of a prothrombotic state. Further studies are recommended to investigate the exact role of platelets and functional fibrinogen in the initiation or development of PEX syndrome.

CONTROL ID: 3545054

SUBMITTER (NAME ONLY): Zeinab Ghassabi

TITLE: Retinal Oximetry Revealed Glaucomatous Eyes Had Lower Retinal Metabolism Using Visible Light Optical Coherence Tomography (vis-OCT)

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Ghassabi, B. Tayebi, M. Wu, S. Palmer, R. Zambrano, J. Li, G. Wollstein, J.S. Schuman, H. Ishikawa, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|B. Tayebi, Neuroscience Institute, NYU Langone Health, New York, New York, UNITED STATES|M. Wu, Division of Biostatistics, Departments of Population Health and Environmental Medicine, NYU Langone Health, New York, New York, UNITED STATES|I. Rubinoff, R. Kuranov, H. Zhang, Department of biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|R. Kuranov, Y. Wang, Opticent Inc., Evanston, Illinois, UNITED STATES|G. Wollstein, J.S. Schuman, H. Ishikawa, Department of Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare in vivo measurements of oxygen saturation (sO_2) between healthy and glaucomatous eyes using visible-light optical coherence tomography (vis-OCT).

Methods: Eight eyes of 8 healthy volunteers and five eyes of 5 glaucoma age-matched patients were enrolled into our pilot study. For each eye, one pair of retinal major artery and vein in superior and inferior regions near the optic nerve head (Figure) were scanned during the same session with our prototype vis-OCT (8192 x 16 samplings in $1 \times 1 \text{ mm}^2$). Spectroscopic analysis was performed using short-time Fourier transformation (STFT). Wavelength-dependent OCT amplitudes from the same depth location across adjacent A-lines, all within the blood vessels, were averaged and then fitted to hemoglobin absorption profile based on Beer-Lambert's law. Highest artery and vein sO_2 values in superior or inferior regions were recorded as the sO_2 measurements for each eye. Wilcoxon's paired signed rank test was used to compare the age-matched healthy and glaucomatous subjects. Correlation between vein sO_2 and visual field mean deviation (MD) recorded at the same visits was calculated using Spearman correlation coefficient (r). Results were compared with conventional structural OCT measurements, retinal nerve fiber layer (RNFL) and ganglion cell inner plexiform layer (GCIPL) thickness measured using Cirrus HD-OCT (Zeiss, Dublin, CA).

Results: Table 1 and Table 2 show demographics and measurements on 5 age-matched pairs of healthy and glaucomatous eyes. Artery sO_2 showed no difference between healthy and glaucomatous eyes, while vein sO_2 was marginally higher in glaucomatous eyes than healthy eyes (Table 2). Vein sO_2 and RNFL and GCIPL thicknesses all showed statistically significant correlation with MD (Table 3). When comparing the correlation between vein sO_2 , RNFL and GCIPL, no statistical difference was detected between any combination (Fisher's paired test).

Conclusions: Glaucomatous eyes had marginally higher oxygen saturation in the veins compared to healthy eyes, while there was no difference in oxygen saturation in the arteries, suggesting less oxygen consumption in the retina with glaucomatous damage. Vis-OCT sO_2 measurement may have a potential as a clinical glaucoma biomarker in parallel with RNFL and GCIPL thickness. Further study with a larger sample size is warranted.

CONTROL ID: 3545058

SUBMITTER (NAME ONLY): Pradeep Ramulu

TITLE: Association of OCT imaging parameters with longitudinal changes in cognition in older adults participating in the Atherosclerosis Risk in Communities (ARIC) study

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.Y. Ramulu, X. Guo, A. Mihailovic, L.T. Arsiwala, Ophthalmology, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|R.A. Sharrett, Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, UNITED STATES|A. Abraham, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous cross-sectional studies have demonstrated a thinner retinal nerve fiber layer (rNFL) and macular ganglion cell complex (GCC) in persons with Alzheimer's Disease/cognitive impairment. Here, we examine the association of these OCT parameters with longitudinal changes in cognition in a biracial population-based sample of older adults participating in the Atherosclerosis Risk in Communities (ARIC) study.

Methods: Non-demented Black ARIC participants from Jackson, MS, and White ARIC participants from Washington County, MD, were enrolled in the Eye Determinants of Cognition (EyeDOC) study, in which peripapillary and macular OCT imaging was performed on a randomly selected eye between 2017 and 2019. Changes in cognition were derived from a 10-test neurocognitive battery administered to each participant three times between 2011 and 2020. Primary analyses examined the association of rNFL and GCC thickness with longitudinal changes in global cognition in the full cohort, using linear mixed effect models incorporating spline terms, adjusting for age, sex, education, smoking history, hypertension, diabetes, physical activity, and intraocular pressure. Additional analyses examined change within cognitive domains (memory, executive function and language) and were stratified for participants at each study site.

Results: A total of 914 participants (407 from Jackson; 507 from Washington County) had adequate OCT imaging and complete cognitive data. Mean participant age was 74 years at the initial cognitive examination and 64% were female. Neither GCC thickness ($p=0.53$) nor rNFL thickness ($p=0.76$) was associated with a greater rate of decline in global cognition scores. Likewise, neither GCC nor rNFL thickness were associated with the rate of decline in the memory, executive function, or language domains ($p>0.4$ for all). Similar results were observed when analyses were stratified for Jackson and Washington County participants.

Conclusions: In this biracial cohort of non-demented older adults, lower rNFL and GCC thickness was not associated with declines in cognition. These results suggest that OCT parameters may not have utility in predicting the risk of future cognitive decline in all populations.

CONTROL ID: 3545061

SUBMITTER (NAME ONLY): Lakshminarayanan Gowtham

TITLE: Elevated Histamine Levels in the Aqueous Humor of the Patients with Primary Open Angle Glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Gowtham, T. Velpandian, N. Halder, T. Dada, D. Angmo, Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|R. Jayasundar, Department of NMR, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|S. Singh, Department of Biophysics, All India Institute of Medical Sciences, New Delhi, Delhi, INDIA|

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ABSTRACT BODY:

Purpose: To determine variations in the levels of both excitatory (L-glutamate) & inhibitory (GABA) neurotransmitters (NTs), Histaminergic NTs (histamine and 1-methyl histamine), Adrenergic (noradrenaline, adrenaline, DOPA & dopamine), Cholinergic (acetylcholine) and Serotonergic (serotonin and N-acetyl serotonin) NTs in primary glaucomatous versus cataract patients.

Methods: This preliminary case-control study involved the three age-matched groups of patients with primary open angle glaucoma (POAG, n=14), primary angle closure glaucoma (PACG, n=21) and cataract patients (control, n=19). Patient's aqueous humor (70 to 100 µL) was collected by paracentesis during the trabeculectomy and cataract surgery and the plasma (2 ml) of the same patients was collected one hour before the surgery, stored at -80 degree. Aqueous humor and plasma were subjected for ultrasensitive LC-MS/MS analysis for the quantification of neurotransmitters.

Results: Baseline intraocular pressure and cup-to-disc ratio was found significantly elevated in both the glaucomatous groups as compared to the control group. In aqueous humor, histamine was found to be significantly elevated (5-fold, $p<0.0001$) whereas 1-methyl histamine was significantly decreased ($p<0.05$) in POAG as compared to the control. Significant increase in L-glutamate and GABA has been observed among both the glaucomatous patient groups as compared to the cataract control. Adrenaline was found to be elevated only in the PACG group (2.7-fold, $p<0.05$). Significant difference was observed among the compared plasma NT levels between the groups.

Conclusions: This study demonstrated the prominent role of histaminergic system apart from autonomic mechanisms in the progression of glaucoma. Elevated L-glutamate and GABA showed their release could be the result of the retinal ganglionic cell death. Further studies are required to evaluate the effects of histamine on Müller cell dysfunction.

CONTROL ID: 3545068

SUBMITTER (NAME ONLY): Kaitlyn Rutter

TITLE: Chronic stress induces mitochondrial movement and turnover in zebrafish cone photoreceptors

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.M. Rutter, S.E. Brouckerhoff, R. Hutto, Biochemistry, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite chronic stress and high metabolic demands, photoreceptors remain viable to perform their essential function throughout a lifetime. Maintaining healthy pools of mitochondria is crucial in photoreceptor health and identifying mitochondrial quality control and turnover mechanisms can yield insight into photoreceptor robustness. Photoreceptors may have specialized adaptations in response to mitochondrial stress.

Methods: We generated zebrafish lines that expressed mitochondrially-targeted fluorophores specifically in cone photoreceptors: Tg(gnat2:Su9-mKate2) and Tg(gnat2:Su9-TagBFP). To visualize Müller glia cells, we used the Tg(GFAP:TdTomato) zebrafish line and cone cell bodies were visualized with the Tg(gnat2:eGFP) zebrafish line. Zebrafish larvae were imaged on a Leica SP8 confocal microscope at 6dpf following 48 hours of being maintained at 16°C (cold stress) or 28°C (normal temperature). To assess if mitochondria were within acidic compartments, zebrafish larvae were incubated in 10µM LysoTracker Green for 2 hours prior to imaging. Results are reported as mean ± SEM.

Results: Mitochondria in zebrafish cone photoreceptors are found in a dense cluster in the ellipsoid of the cell. Rarely, photoreceptor mitochondria can move away from the mitochondrial cluster towards the synapse, and this is observed much more frequently following cold stress. These mislocalized photoreceptor mitochondria are typically observed in the photoreceptor layer but can also be observed in other areas of the retina. We found that 23.3% ± 5.1% (n = 7 zebrafish) of photoreceptor mislocalized mitochondria colocalized with Müller glia. Mislocalized mitochondria are more likely to colocalize with LysoTracker Green (8.4% ± 0.6% of ellipsoid mitochondria vs 28.3% ± 4.2% of mislocalized mitochondria (n = 7 zebrafish)) suggesting increased mitochondrial turnover upon movement away from the ellipsoid.

Conclusions: Zebrafish photoreceptors can traffic some mitochondria away from the ellipsoid in response to stress, and these mislocalized mitochondria are more likely to be acidic, which suggests they may be in lysosomes. This may be a protective mechanism in response to mitochondrial stress that aids photoreceptor health and longevity.

CONTROL ID: 3545070

SUBMITTER (NAME ONLY): Thomas Volatier

TITLE: Autophagy in the limbal epithelium during UV-induced stem cell damage

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Volatier, C. Cursiefen, M. Notara, Experimentelle Augenheilkunde, Uniklinik Köln, Köln, Nordrhein-Westfalen, GERMANY]

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ABSTRACT BODY:

Purpose: To characterise autophagy in the limbal and conjunctival epithelium as well as in pterygium.

Methods: Limbal sections from healthy donor corneas and excised pterygium were immunostained for autophagy markers ATG5, ATG7, ATG12, mTOR, and LC3B as well as stem cell marker p63a. Cells were also extracted from each of the aforementioned tissues to compare conjunctival, limbal epithelial, and pterygium cell behaviour in culture.

Results: The mean age of pterygium donors was 60 ± 21 ; all were males. The mean age and sex of healthy donors is unknown. p63a+ epithelial cells have a high concentration of mTOR both in vitro and in vivo. Pterygium in comparison showed an absence of mTOR both in vivo and in vitro. Further investigation via immunofluorescent microscopy of the downstream components of the autophagy pathway showed that ATG7 was absent in the limbal epithelial cells while present in pterygium. LC3B was absent in pterygium but present in limbal epithelia. When comparing both pterygium and limbal epithelium to conjunctiva, it was found that the distribution of autophagy-related proteins in conjunctival epithelium did not resemble either tissue.

Conclusions: The autophagy response is usually inhibited by mTORC1 and this inhibition is normally removed when low cellular energy is detected by AMPK. The absence of mTOR in pterygium confirms that autophagy is dysregulated in the corneal tumour. The absence of ATG7 in healthy p63a+ limbal epithelial suggests that therapeutic strategies could aim to restore healthy epithelial autophagy by targeting either mTOR or ATG7.

CONTROL ID: 3545073

SUBMITTER (NAME ONLY): Zhiming Li

TITLE: Characterization of Ultrasound-mediated Trans-corneal Delivery of Riboflavin by Modified Fluorotron™ Master

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Li, M. Aresdhayana, L. Lau, J. Chung, Y. Chau, Chemical and Biological Engineering, The Hong Kong University of Science and Technology, Kowloon, HONG KONG|B.M. Ishimoto, OcuMetrics, Inc., Mountain View, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The corneal drug penetration is commonly detected by measuring fluorescence profile of labelled drug in corneal tissues by cryosection. However, such method requires sacrificing animals and the data is often debased by artefacts. Although ocular fluorophotometer may provide a better alternative, problems of Inner Filter Effect (IFE) and low resolution have been reported. This study reports a modified Fluorotron to circumvent this issue to allow quantitative measurement of both the absorption and penetration of riboflavin into the cornea. Using the new approach, the penetration depth of riboflavin by ultrasound-mediated delivery was characterized.

Methods: The objective lens of ocular fluorophotometer was stabilised with plexiglass and the angle was increased between excitation and emission paths from 28 degree to 53 degrees that resulted in decreasing depth of focus to about 85 microns. The modified fluorophotometer was used to detect porcine eyes (Epi-on) which were soaked in 0.5% riboflavin for 30 minutes followed by washing and 0.025% riboflavin solution for 15 minutes by dropping different concentration riboflavin separately. The cryosection method was employed after ultrasound-mediated riboflavin delivery with different operating parameters of sonification which will be used to validate the result in modified fluorophotometer.

Results: The riboflavin penetration profile of cornea which detected by the modified fluorophotometer can have a higher resolution and minimized IFE (Fig.1). We anticipate that the modified fluorophotometer will expedite the optimization of new modalities, such as mediation by ultrasound, in corneal drug delivery.

Conclusions: This modified Fluorotron fluorophotometer can detect the riboflavin penetration depth and concentration across the corneal sections with higher resolution and minimized IFE. The absorption and penetration of riboflavin in cornea by ultrasound-mediated delivery is distinguishable in cryosection fluorescence microscope image.

CONTROL ID: 3545084

SUBMITTER (NAME ONLY): Xiao Zhou

TITLE: En face area quantification of choroidal mass lesions using swept source optical coherence tomography

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhou, A.T. Legocki, Z. Chu, K. McKay, R.K. Wang, K.L. Pepple, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the feasibility of using en face OCT images to reliably delineate choroidal lesion boundary and measure total choroidal lesion area.

Methods: Pigmented and amelanotic lesions of the choroid were imaged with a PLEX Elite 9000 SS-OCTA device. The full thickness choroidal en-face image was generated using the minimum projection of the region between the RPE/BM complex and the choroidal-scleral interface. Lesion boundaries were defined by a masked human grader and lesion area calculated in MATLAB. Clinical determination of en face lesion area was made by the treating physician on color fundus images or at the time of dilated exam and recorded in disc diameters. Clinical ultrasound measurements of maximal transverse and longitudinal base diameter were used to calculate the en face lesion area using the formula for an ellipse. Agreement in lesion area determined by each method was evaluated by intraclass correlation coefficient (ICC).

Results: Seventeen lesions were imaged by OCT: 8 choroidal melanomas, 4 choroidal nevi, 5 choroidal hemangiomas. In the en-face image, all lesions appeared as homogeneous white regions without characteristic pattern of large choroidal vessels. 3 lesions had borders extending beyond the SS-OCT image window and were not included in area analysis. The agreement between OCT and fundus exam area was poor (ICC=0.03). The agreement between US and fundus exam was moderate (ICC =0.51). The agreement between US and OCT on the 4 lesions with same day imaging was excellent (ICC=0.99). Three lesions with mixed pigmentary components measured much smaller by fundus exam than by OCT or US.

Conclusions: Pigmented and amelanotic fundus lesions can be identified in the SS-OCT choroidal en face projection. The resulting image provides a new method for lesion area measurement with excellent agreement to US measurements and could be useful for longitudinal monitoring. Larger studies with same day exam, SS-OCT, and ultrasound measurements will be required to verify the extent of agreement suggested by this pilot study.

CONTROL ID: 3545085

SUBMITTER (NAME ONLY): Tatsuya Nakagawa

TITLE: Proteomic analysis of TCF4 knock-out corneal endothelial cells derived from the patients with Fuchs endothelial corneal dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Nakagawa, N. Okumura, N. Hanada, N. Koizumi, Department of Biomedical Engineering, Doshisha University, Kyotanabe, Kyoto, JAPAN|P. Padmanabhan, Department of Cornea and Refractive Surgery, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|S. Elchuri, A. Chatterjee, N. Janakiraman, Department of Nanobiotechnology, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|G. Sathe, V. Ghose, Institute of Bioinformatics, Bangalore, Karnataka, INDIA|T. Tourtas, U. Schlötzer-Schrehardt, F.E. Kruse, Department of Ophthalmology, University of Erlangen-Nuremberg, Erlangen, GERMANY|

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ABSTRACT BODY:

Purpose: Patients with Fuchs endothelial corneal dystrophy (FECD) often harbor expansion of a trinucleotide CTG repeat in the TCF4 gene, thus suggesting that TCF4 is a potential causative gene for FECD. We previously reported that the expression of TCF4 is upregulated in the corneal endothelium of FECD patients. The purpose of this present study was to elucidate the involvement of TCF4 in the pathophysiology of FECD via proteomic analysis of an FECD cell model.

Methods: Corneal endothelial cells (CECs) isolated from FECD patients were immortalized using both SV40 and hTERT to produce an immortalized FECD cellular model (iFECD). TCF4 was knocked out using CRISPR/Cas9 in iFECD (TCF4^{-/-} iFECD). Total proteins were isolated, detected by mass spectrometry, and analyzed by use of the SEQUEST[™] search algorithm through Proteome Discoverer software against Human RefSeq protein database. For functional enrichment analysis, the gene ontology (GO), KEGG, and Reactome pathways were investigated. In addition, the GeneMANIA Cytoscape plug-in was used to clarify protein-protein interaction (PPI) and hub proteins, which are involved in the knockout of TCF4.

Results: Ninety differentially expressed proteins (DEPs) ($|\log_2$ fold change| > 0.5 and P value < 0.05) were identified among a total of 6510 identified proteins, including 52 upregulated and 38 downregulated proteins. GO pathway analysis revealed enrichment of extracellular matrix (ECM) organization, response to oxidative stress, and cell motility, KEGG pathway analysis revealed enrichment of ECM-receptor interaction, and Reactome pathway analysis demonstrated that multiple proteins related to collagen, integrin, and glycosaminoglycan were downregulated by loss of TCF4. Finally, GeneMANIA identified 20 hub proteins and showed that 5 of those 20 proteins were related to ECM.

Conclusions: Functional and pathway enrichment analyses revealed that TCF4 is involved in ECM-related pathways in the corneal endothelium of FECD. Our findings indicate that TCF4 plays an important role in the pathophysiology of FECD, probably by inducing excessive production of ECM proteins.

CONTROL ID: 3545093

SUBMITTER (NAME ONLY): Yan Zhang

TITLE: Dynamic BMP Gene Expression Regulation in Chick RPE During Recovery from Lens-Induced Defocus and Form-Deprivation

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Zhang, G. Chuang, D. Sun, K. Cheung, A. Chou, A. He, C.F. Wildsoet, School of Optometry, University of California, Berkeley, California, UNITED STATES|Q. Zhu, School of Optometry and Vision Science, West China Hospital of Sichuan University, Sichuan, CHINA|W. Song, Department of Ophthalmology, the 2nd Affiliated Hospital, Harbin Medical University, Harbin, Heilongjiang, CHINA|

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ABSTRACT BODY:

Purpose: This study investigated the differential gene expression of BMPs in chick retinal pigment epithelium (RPE) during recovery from lens-induced defocus and form-deprivation treatments.

Methods: 14-day old White-Leghorn chicks wore monocular +10 or -10 D lenses or diffusers for 2 or 48 h. The lenses and diffusers were then removed and eyes allowed to recover for 0, 15 min, 2, 24, 48, or 96 h, after which RPE was collected from sacrificed birds. RPE gene expression of BMP2, 4, and 7 was examined using real-time PCR and expression levels in treated and their contralateral control eyes compared.

Results: BMP2 gene expression was up-regulated with the +10 D lens treatment, after both 2 and 48 h. For the 2 h treatment groups, gene expression up-regulation was maintained 15 min into the recovery period, but decreased rapidly thereafter to reach the same level as in contralateral control eyes, with the exception of a short term rebound (up-regulation), 24 h into the recovery period. Meanwhile, for the 48 h treatment groups, BMP2 gene expression decreased gradually from up-regulation at $739 \pm 121\%$ to down-regulation at $72 \pm 14\%$ over the recovery period. BMP2 gene expression was down-regulated with both -10 D lens and FD treatments, after both 2 and 48 h. BMP2 gene expression continued to be down-regulated 15 min into the recovery period, changing to up-regulation after 2 h of recovery, with the time required for gene expression to return to the same level as in the contralateral control eyes varying with the initial treatment duration. Similar gene expression patterns were observed for BMP4 and BMP7, although the changes were generally smaller.

Conclusions: The dynamic changes in BMP gene expression in chick RPE during recovery from three visual manipulations widely used in studies of eye growth tend to follow similar trends in induced refractive error and/or choroidal thickness changes. Thus this study provides further evidence for the role of the RPE as an important signal relay, and RPE-derived BMPs as critical signaling molecules in eye growth regulation.

CONTROL ID: 3545094

SUBMITTER (NAME ONLY): Ashley Polski

TITLE: Comprehensive somatic copy number analysis using the aqueous humor liquid biopsy for retinoblastoma

SESSION TITLE: Advances in Diagnosis and Management of Retinoblastoma and Congenital Eye Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Polski, M.E. Kim, L. Xu, J. Kim, J.L. Berry, The Vision Center, Children's Hospital Los Angeles, Los Angeles, California, UNITED STATES|A. Polski, M.E. Kim, J. Kim, J.L. Berry, Ophthalmology, USC Roski Eye Institute, Los Angeles, California, UNITED STATES|R. Prabakar, Molecular and Computational Biology, University of Southern California, Los Angeles, California, UNITED STATES|R. Shah, R. Jubran, Cancer and Blood Disease Institute, Children's Hospital Los Angeles, Los Angeles, California, UNITED STATES|P. Kuhn, J. Hicks, Biological Sciences, University of Southern California, Los Angeles, California, UNITED STATES|P. Kuhn, J. Hicks, Norris Comprehensive Cancer Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The aqueous humor (AH) liquid biopsy has been established as an enriched source of tumor-derived cell-free DNA (cfDNA) for retinoblastoma (RB). Use of this AH liquid biopsy allows for genomic analysis of eyes throughout treatment and at enucleation. Previous AH studies have focused on highly recurrent RB somatic copy number alterations (SCNAs) including gain of 1q, 2p, 6p, and loss of 13q and 16q; in this retrospective study, we provide a comprehensive, whole-genome analysis of RB SCNAs and their associated clinical features.

Methods: Patients diagnosed with RB between 12/2014-10/2020 from whom AH was obtained via clear corneal paracentesis were included. Shallow whole-genome sequencing of AH cfDNA was performed to assess for SCNAs. Mann-Whitney U and Fisher's exact tests were used to examine the relationship between SCNAs and clinical findings.

Results: 68 eyes of 64 patients were included. 33 eyes were enucleated (16 primarily; 17 secondarily after chemotherapy) and 35 were salvaged. The most common non-highly recurrent RB SCNAs were 12p loss (8 eyes; 11.8%), 16p loss (8 eyes; 11.8%), 5p gain (7 eyes; 10.3%), 17q gain (6 eyes; 8.8%), 18q gain (6 eyes; 8.8%), 17p loss (5 eyes; 7.4%), 20q gain (5 eyes; 7.4%), and 22p gain (5 eyes; 7.4%). The prevalence of specific non-highly recurrent SCNAs differed between primarily and secondarily enucleated eyes (Fig 1). Focal MYCN amplification was present in 3 eyes, and all were enucleated (2 primarily, 1 secondarily). Of secondarily enucleated eyes, 6 eyes had AH sampled during conservative management and immediately following enucleation; 4 eyes demonstrated new SCNAs at secondary enucleation that were not present in earlier AH samples. Eyes with sphere or cloud seeding had significantly more SCNAs (4.64 ± 4.76) than eyes with dust or no vitreous seeding (2.70 ± 3.72 ; $P=0.022$). Eyes with an endophytic tumor growth pattern (without retinal detachment; RD) were significantly more likely to have one or more SCNA (84.6%) than eyes with an exophytic tumor growth pattern (with RD) (57.5%; $P=0.030$).

Conclusions: The AH liquid biopsy platform is an efficient method of whole-genome RB SCNA analysis, and SCNAs are associated with numerous clinical findings in RB eyes. Prospective analyses are encouraged to further elucidate the clinical relevance of specific SCNAs in RB.

CONTROL ID: 3545101

SUBMITTER (NAME ONLY): Deniz Hos

TITLE: Corneal Crosslinking to Regress Pathological Corneal Neovascularization Before High-Risk Keratoplasty

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hos, F. Schaub, Y. Hou, W. Zhang, F. Bock, C. Cursiefen, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Corneal neovascularization is the main risk factor for graft rejection after high-risk penetrating keratoplasty (PK). Corneal crosslinking (CXL) has been shown to regress pathological corneal neovascularization and to reduce the risk of graft rejection after high-risk PK in mice. The aim of this work was to analyze whether CXL of the corneal periphery sparing the limbus ("peripheral CXL") is also able to regress corneal neovascularization in patients.

Methods: This case series included 5 patients with progressive corneal neovascularization and the need for high-risk PK because of graft rejection and/or keratitis. Peripheral CXL was performed prior to or directly in combination with PK, and corneal neovascularization was assessed morphometrically on slit-lamp images. Patients were followed up to determine the incidence of adverse effects and graft rejection.

Results: No intraoperative or postoperative complications were observed. Peripheral CXL resulted in a significant reduction of corneal neovascularization (mean reduction of $70.5\% \pm 22.7\%$). Revascularization was not observed. All transplants remained clear and without immune reactions (mean follow-up 16.4 ± 14.9 weeks, range 4-42 weeks).

Conclusions: Peripheral CXL is able to reduce pathological corneal neovascularization in patients and might therefore be a novel treatment option to reduce graft rejection rates after high-risk PK.

CONTROL ID: 3545103

SUBMITTER (NAME ONLY): Jose A. Fernández-Albarral

TITLE: Changes in cytokine and growth factor levels at different time points after experimental glaucoma induction.

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fernández-Albarral, A. Ramirez, R. de Hoz, E. Salobar-García, I. López Cuenca, J. Salazar, J. Ramirez, Universidad Complutense de Madrid, Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, Madrid, Madrid, SPAIN|J. Fernández-Albarral, I. López Cuenca, J. Ramirez, Universidad Complutense de Madrid, Facultad de Medicina. Departamento de Inmunología, Oftalmología y ORL, Madrid, Madrid, SPAIN|A. Ramirez, R. de Hoz, E. Salobar-García, J. Salazar, Universidad Complutense de Madrid, Facultad de Óptica y Optometría. Departamento de Inmunología, Oftalmología y ORL, Madrid, Madrid, SPAIN|M. López-Gallardo, B. Martín-Sánchez, E. Flores-Salguero, Universidad Complutense de Madrid, Facultad de Medicina. Departamento de Fisiología, Madrid, Madrid, SPAIN|E. Marco, Universidad Complutense de Madrid, Facultad de Ciencias Biológicas. Departamento de Genética, Fisiología y microbiología, Madrid, Madrid, SPAIN|M. Avilés-Trigueros, M.A. Vidal-Sanz, Universidad de Murcia and Instituto Murciano de Investigación Biosanitaria Virgen de la Arrixaca, Facultad de Medicina, Departamento de Oftalmología, Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To quantify the expression of different cytokines (IL-1 β , IL-4, IL-6, IL-10, IL-17, IFN- γ), neurotrophic factors (BDNF, VEGF) and Fractalkine (CX3CL), released by retinal glial cells, at different times after unilateral laser-induced ocular hypertension (OHT), both in OHT eyes and their contralateral eyes respect to naïve eyes.

Methods: Six groups of albino Swiss mice (a naïve group and five OHT groups) were analyzed. Animals were sacrificed at different time-points after OHT laser induction (1, 3, 5, 7 and 15 days) and both treated OHT eye and contralateral untreated eye were studied. The samples obtained were processed in two different ways: i) multiarray kits (MILLIPLEX MAP Mouse Cytokine/Myokine Magnetic Bead Panel) were used to quantify the expression of cytokines, and ii) Double immunolabelling were performed in retinal sections to determinate which cells expressed the different molecules analyzed. In multiplexed study 12 animals per group were used and 5 animals in each group for immunohistochemistry study.

Results: Compared to naïve, in OHT eyes, were observed a significant increase in the expression of : i) IFN- γ at 3, 5 and 15 days; ii) IL-4 at 1, 3, 5 and 7 and IL-10 at 3 and 5 days (which coincided with the downregulation of IL-1 β at days 1, 5, and 7); iii) IL-6 at 1, 3 and 5 days; iv) VEGF and Fractalkine at 1 day; and v) BDNF at 1, 3, 7 and 15 days. In contralateral eyes, the significant changes were: i) increase of IL-1 β at 1 and 3 days and decrease at 7 day (which coincided with the downregulation of IL-4 at 3 and 5 days and the upregulation at 15 days); ii) increase of IL-6 at 1, 5 and 7 days and decrease at 15 days; iii) increase of IL-10 at 3 and 7 days; and iv) increase of IL-17 at 15 days. Immunohistochemical study shown that microglia expressed IL-1 β , IFN- γ , IL-4, IL-6, IL-17 and fractalkine, and that the macroglia (astrocytes and Müller) expressed IL-1 β , BDNF and VEGF. IL-10 were expressed by retinal ganglion cells axons.

Conclusions: Unilateral laser-induced ocular hypertension causes changes in the expression of anti- and pro-inflammatory molecules associated with inflammatory process, mainly 3 days after OHT induction, both in OHT eyes and in contralateral eyes, which may confirm the implication of the immune system in glaucoma.

CONTROL ID: 3545105

SUBMITTER (NAME ONLY): Marta Zola

TITLE: Galectin 3 and Central Serous Chorioretinopathy: a promising new biomarker

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Galectin 3 (Gal3) is a galactosidase-binding protein acting on different aspects of inflammation related to the response to stress stimuli, which expression is highly sensitive to corticoids. It has been recognized as a biomarker for cardiovascular diseases. It mediates the vascular pro fibrotic effect of aldosterone. In the human eye, we found it localized in retinal Muller glial cells, the retinal pigment epithelium and in the choroid. In this multicentre retrospective case-control study we measured Gal3 levels in the serum of patients with central serous chorioretinopathy (CSCR).

Methods: Serum levels of Gal3 were measured in CSCR patients (N= 155) with acute (N=76) and chronic (N=79) disease and in age and sex-matched controls (N=153). Presence of epitheliopathy on multimodal imaging approach allowed to differentiate chronic from acute CSCR. All patients had active disease defined by the presence of subretinal fluid at the time of the blood sample. Patients with concomitant ocular pathologies were excluded, as were samples with CRP > 5 mg/L, creatinine > 100 µmol/L, and/or urea > 7.5 mmol/L. Human Gal3 was measured with a specific Elisa Kit (BGM Galectin-3 Assay, BG Medicine Galectin-3 Kit – RUO Product n°:12727). Descriptive, comparative and correlative statistics were performed on Prism (Graphpad; San Diego), using Dunn test for quantitative values.

Results: Gal3 serum levels were significantly reduced in patients with CSCR compared to the control group (mean difference 1,250; IC 95% 0,06-2,43; p=0,03), and this level was even lower in patients with acute CSCR compared to controls (mean difference 2,063; IC 95% 0,74-3,18; p=0,004). Gal3 was significantly lower in the population younger than 45 years compared those older than 45 years, irrespectively of the group (mean difference 14,02; IC 95% 11.23-16.82; p<0,0001). Acute CSCR patients showed lower levels of Gal3 compared to chronic CSCR (mean difference 2,602; IC 95% 1,08-4,11; p<0,0001), independently from the age group.

Conclusions: Galectin 3 serum levels are reduced in patients with CSCR, similarly to what has been recently observed for lipocalin 2. This reduction is particularly important in patients with acute CSCR and could be an important biomarker for diagnosis and follow up of these patients. Age was an important factor in analyzing the variations of this protein, as with other inflammation markers commonly used in medicine.

CONTROL ID: 3545107

SUBMITTER (NAME ONLY): Gereon Huttmann

TITLE: Improved SELFF-OCT using motion correction and artifact detection

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Self-examination low-cost full-field optical coherence tomography (SELFF-OCT) can place the control of ophthalmic therapies into the hand of the patient. Regular self-examination by volumetric OCT imaging of the retina can detect retinal changes in age-related macular degeneration (AMD) and other diseases in such early stages that optimal treatment is possible. First clinical studies showed that 77% [1] to 86% [2] of all self-examined eyes resulted in interpretable retinal OCT volume scans. Necessity for anti-VEGF treatment of AMD could be determined with 94% sensitivity and 95% specificity [2]. During the recording time of 1.3 seconds, motion of the eye can considerably degrade image quality. Depending on severeness, planes in the volume will be shifted laterally or axially, SNR will be reduced or en-face planes are completely missing.

[1] von der Burchard C, et al. Graefes Arch Clin Exp Ophthalmol, 2020, DOI: 10.1007/s00417-020-05035-6.

[2] von der Burchard C, et al. Ophthalmology, 2021, submitted

Methods: SELFF-OCT records interferograms of en-face plane, which contain not only information on the retinal structure but also on the iris position. The imaging process and the possibility to detect ocular motion from a recorded volume were analyzed theoretically and experimentally in a phantom and in self-measurements of patients.

Results: The SELFF-OCT data contained accurate position information. Accuracies better than 4 µm laterally and 30 µm axially were demonstrated. An algorithm quantified both lateral and axial changes of the retina position in the recorded images. The accuracy is on par with modern eye-trackers, but was achieved without any additional optical components. A complete loss of the OCT signal was also successfully identified.

Conclusions: Due its special technology and the intended hand-held use, SELFF-OCT is more sensitive to motion artifacts than clinical OCT devices. Currently, 20% of the recorded volumes cannot be analyzed, and part of them contain motion artifacts. Automated detection can identify invalid volumes. Since acquisition of a volume takes only 1.3 seconds, remeasuring is possible in these cases. Integrated into the self-measurement process (i.e. repeat measurement until a valid scan was obtained) will increase success rate. Furthermore, automated artifact correction in postprocessing in cases of light and especially lateral movement will improve image quality and diagnostic accuracy.

CONTROL ID: 3545108

SUBMITTER (NAME ONLY): Muneeswar Gupta Nittala

TITLE: Risk factors for progression of Age-related Macular Degeneration: Amish Eye Study

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate optical coherence tomography (OCT)-based risk factors for progression to late Age-related macular degeneration (AMD) in a population-based of the elderly Amish.

Methods: A total of 1339 subjects (2668 eyes) were enrolled in this multicenter, prospective, longitudinal, observational study as part of the population-based Amish eye study. 666 subjects (49.7%) returned for a two-year follow-up visit and underwent complete ophthalmic exam, OCT (Spectralis 20°X20°), infrared reflectance images (IR) & color fundus photography. Baseline OCT images were reviewed for presence of drusen volume $> 0.03 \text{ mm}^3$ in the central 3mm ring, intraretinal hyperreflective foci (IHRF), hyporeflective drusen core (hDC), subretinal drusenoid deposits (SDD), drusenoid pigment epithelium detachment (PED), subfoveal choroidal thickness, drusen area, volume within 3, 5-mm circles centered on ova. Presence of SDD/reticular pseudodrusen (RPD) were also evaluated on IR images, including in regions outside the OCT scan field. Two year follow-up images were evaluated for presence of late AMD (geographic atrophy/macular neovascularization). These features at baseline were correlated with 2-year incidence of late AMD development by logistic regression.

Results: Twenty-one (1.5%) of 1332 eyes progressed to late AMD at 2 years. Mean age of study subjects was 65 ± 10.17 (\pm SD) years and 410 were female. Univariate logistic regression showed drusen area, volume in 3 & 5-mm circles, subfoveal choroidal thickness, drusen volume $\geq 0.03 \text{ mm}^3$ in 3-mm ring, SDD, IHRF, and hDC were all associated with an increased risk for development of late AMD (odds ratios (OR) and 95% confidence intervals shown in table 1). Multivariate regression model identified that drusen volume in the 3-mm circle (OR:2.59, $p=0.049$) & presence of IHRF (OR:57.06, $p<0.001$) remained as independent and significant risk factors for progression to late AMD.

Conclusions: This population-based study confirms previous findings from clinic-based studies that high central drusen volume and IHRF are associated with an increased risk of progression to late AMD. These findings may of value in risk stratifying patients in clinical practice or identifying subjects for early intervention clinical trials.

CONTROL ID: 3545110

SUBMITTER (NAME ONLY): Alvaro Meana

TITLE: Oral mucosa culture system for ocular surface treatment avoiding the use of xenogeneic components

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Meana, M. Persinal-Medina, N. Vázquez, M. Chacon, S. Alonso-Alonso, C. Fernández-Vega-González, J.I. Blazquez, S. Llamas, J. Merayo-Llves, Instituto Universitario Fernández-Vega - Fundación de Investigación Oftalmológica - Universidad de Oviedo, Oviedo, Asturias, SPAIN|S. Llamas, U714, Centro de Investigación Biomedica en Red de Enfermedades Raras, Valencia, Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: To develop an easy and xenogeneic free culture system of oral mucosa stem cells

Methods: Tissue and blood collection. Oral mucosa biopsies were obtained from deceased organ donors following Spanish laws. Platelet Rich in Growth Factors (PRFG) used for media supplementation and PRGF fibrin membranes were obtained from voluntary donors and processed using a commercial kit (Endoret®)

Cell culture. 3-4 mm² biopsies were cut in fragments and cultured as explants in a 12 well culture plate

Culture media. Cells were expanded in two different media: DMEM/F12 (2:1), 5 µg/ml insulin, 8.33 ng/ml cholerich toxin, 24 µg/ml adenine, 1.3 ng/ml triiodothyronine, 0.4 µg/ml hydrocortisone, 40 µg/ml vancomycin-amikacin, 0.5 µg/ml amphotericin B and either 10% SBF or 10% PRGF

Data analysis. Expansion efficiency of SBF and PRGF cultures were compared quantitatively and qualitatively PRGF membrane in vivo assay. Confluent cultures of epithelial cells expanded in PRGF were subcultured on 4 cm² PRGF fibrin membranes (2.5 x 10⁵ cells/cm²), cultured for 72h and grafted in the subcutaneous space of nude mice. After 21 days, animals were euthanized and tissue samples were subjected to immunohistochemical analysis Immunofluorescence. Cultures and tissues were fixed with 4% paraformaldehyde and immunofluorescence studies were performed using anti-p63, anti-CK5 and anti-CK14 monoclonal antibodies

Results: Cell culture. 93±5% and 91±9% of cultures were successfully expanded from initial biopsies cultured in SBF and PRGF, respectively. The expanded cells showed epithelial cells, fibroblast or a mix of both. Pure epithelial cell cultures without contaminant fibroblasts were observed in 61±6% of SBF cultures and in 69±13% of PRGF cultures.

Data analysis showed that there were no statistically significant differences between the media

Immunofluorescence. Oral mucosal epithelial cells were positive against CK5, CK14, and p63 either cultured with SBF or PRGF. Cells cultured on the PRGF membrane still retained their morphological and phenotypic markers

In vivo assay. Oral mucosal epithelial cells remained viable and retained its characteristic morphology and phenotypic markers without any apparent tissue defect in the in vivo model

Conclusions: It is possible to isolate oral mucosal epithelial stem cells without the need of xenogenic factors. These cells could be grafted and represent a potential alternative for ocular tissue engineering

CONTROL ID: 3545111

SUBMITTER (NAME ONLY): Faran Sabeti

TITLE: Correlation between macular structure and function with multifocal pupillographic objective perimetry in early-stage type 2 diabetic macular oedema

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To correlate regional macular thickness, with per-region macular sensitivities and delays as measured by multifocal pupillographic objective perimetry (mfPOP), commercially known as ObjectiveField Analyser (OFA), in Type-2 diabetes (T2D) patients without and with off-centre mild diabetic macular oedema (DMO).

Methods: We recruited 33 T2D patients (59.2 ± 10.5 y, 17 males). Mean OFA values within inner and outer macular regions were sorted according to retinal thickness. This allowed structure-function correlations to be computed relative to the degree of DMO, wherever it was. A generalised linear mixed-effects model determined which variables contribute to clinical diagnosis of DMO.

Results: The mean sensitivity difference compared to normal in T2D patients was negative and the mean delay difference positive indicating declining sensitivity and prolonged delay relative to normal. Peripheral OFA hypersensitivity and shorter delays than normal were seen with shorter diabetes duration. For DMO patients outer macular thickness was correlated significantly with inner- and outer-macular OFA sensitivity and delay, all $p < 0.0012$, but inner thickness was not correlated. The same was true for diabetic patients without DMO (median p-value was 0.001). A Mixed-effects logistic regression model determined outer thickness and OFA sensitivity ($p = 0.043$), male gender ($p = 0.313$) and time in the study ($p = 0.001$), contributed independently to the odds of a clinical diagnosis of DMO.

Conclusions: The mean sensitivity difference decreased, and mean delay difference increased in diabetic patients compared to normal in later-stage disease. Outer macular thickness correlated significantly with inner and outer OFA sensitivity and delay, while the inner macular thickness did not. As a clinical end-point outer thickness and functional measures may be a better indication of eye health in diabetic eye disease than is provided by visual acuity or other central functional measures.

CONTROL ID: 3545113

SUBMITTER (NAME ONLY): Félix Sauvage

TITLE: Gold nanoparticles for the treatment of eye floaters by light-induced vapor nanobubbles

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Vitreous opacities are collagen aggregates that form in the vitreous body due to myopia and/or age-related structural changes (i.e. fibrous liquefaction) which cast shadows on the retina, impacting vision. Current therapies are based on laser treatment with an yttrium garnet laser (YAG) or vitrectomy. The efficacy of YAG laser vitreolysis is unproven and vitrectomy remains invasive with associated side effects).

We propose a nanotechnology-based treatment of floaters using the plasmon properties of gold nanoparticles (AuNPs). AuNPs bind to vitreous opacities, and when exposed to pulsed-laser light (typically a nanosecond laser), heat up and generate vapour nanobubbles (VNBs) due to the evaporation of the surrounding water. These VNBs then burst, providing sufficient mechanical energy to fragment and destroy the opacities.

Methods: In Vitro: Type I collagen fibers were prepared as artificial floaters and human vitreous opacities were obtained from patients after vitrectomy. Samples were mixed with Hyaluronic (HA) coated AuNPs (10 nm) and irradiated with a pulsed laser (<7ns; 561 nm) at different fluences. Dark field imaging was performed to assess effects. In Vivo: Type I collagen fibers were injected intravitreally in rabbits so that they were located close to the retina (<500 µm). 5 days later, HA-AuNPs were injected. Three days after the injection of AuNPs, fibers were irradiated with a nanosecond laser (<7ns; 530 nm). Photoacoustic imaging was performed to assess binding of gold on the injected fibers, and optical coherence tomography was performed to assess destruction of the fibers.

Results: HA-AuNPs can diffuse in the vitreous and bind to collagen fibers and vitreous opacities.

Type I collagen fibers and vitreous opacities could be completely destroyed in vitro and ex vivo at a fluence of 4.5 J/cm². In vivo, collagen fibers could be destroyed after 7 scans at a fluence of 1.9 J/cm². Preliminary retinal toxicity assessment (TUNEL and H&E staining) did not reveal significant changes compared to untreated rabbits.

Conclusions: This approach can effectively and rapidly destroy vitreous opacities ex vivo and collagen fibers in vivo, using lower energy levels than YAG therapy and paves the way for the vitreolysis with pulsed-lasers and nanotechnologies

CONTROL ID: 3545116

SUBMITTER (NAME ONLY): Swetha Bindu Velaga

TITLE: Alterations of the Ganglion Cell Complex in Age-Related Macular Degeneration: an AMISH Eye Study Analysis

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although the outer retina is the primary area affected in age-related macular degeneration (AMD), secondary alterations in the inner retina have been suggested. To test this hypothesis, we evaluated the Ganglion Cell Complex (GCC) thickness in subjects with AMD.

Methods: A total of 620 eyes of 310 elderly (>age 50) Amish individuals who were enrolled in a population-based study were included in this post-hoc analysis. All subjects underwent complete ophthalmic examination, optical coherence tomography (Cirrus OCT, 6x6mm, 512 x 128) and flash color fundus photography. Foveal central subfield retinal thickness, mean retinal thickness, mean macular volume, and mean thickness of the GCC were obtained using the instrument software. The color fundus images were graded according to the Beckman classification as: Stage 0 (normal), Stage 1 (normal aging), Stage 2 (early AMD), Stage 3 (intermediate AMD), and Stage 4 (late AMD). The GCC thickness between groups were compared in a pairwise fashion using t tests.

Results: Among the 620 eyes, 408 eyes were normal, 67 eyes had early AMD, 101 eyes had intermediate AMD, and 44 eyes had late AMD. The mean age was significantly (<0.0001) lower in the normal group (62.43 years) compared to the AMD group as a whole (71.88 years). After adjusting for age, there was no significant difference in retinal thickness ($p = 0.16$) or retinal volume ($p = 0.14$) between the study groups. However, the mean GCC thickness was significantly ($p < 0.05$) lower in all AMD groups [early AMD: 73.94 μ m; intermediate AMD: 76.55 μ m; late AMD: 58.80 μ m] compared to normals (78.22 microns).

Conclusions: Eyes with AMD show lower GCC thickness compared to normal eyes, with the most severe reduction observed in eyes with late AMD. Alterations in the inner retina during the progression of AMD warrant further study.

CONTROL ID: 3545117

SUBMITTER (NAME ONLY): Muhammad Hassan

TITLE: Effect of Photodynamic Therapy on Choroidal Indices in Patients with Central Serous Chorioretinopathy

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To report the effect of photodynamic therapy (PDT) on choroidal indices in patients with central serous chorioretinopathy (CSC).

Methods: Patients with a confirmed diagnosis of CSC managed at a tertiary care center, who underwent PDT with subsequent resolution of the subretinal fluid were analyzed. The PDT procedure was performed by the same physician. Enhanced depth imaging optical coherence tomography (EDI-OCT) scans of the study population were captured and analyzed before and after the resolution of the subretinal fluid. 5-line high definition scans centered on the foveal center were utilized. Image J (Version 1.52a, NIH) was utilized to segment the choroidal layer in each of the b-scan to evaluate: 1) Subfoveal Choroidal Thickness (SFCT); 2) Choroidal Volume (CV); and 3) Choroidal Vascularity Index (CVI). Multiple linear regression was used to compare the choroidal indices at the two time points.

Results: Six patients with a confirmed diagnosis of CSC that demonstrated resolution of subretinal fluid after receiving PDT were analyzed. The mean age of the study population was 62 (Range: 45-68 years). Five (83.33%) patients were male. The mean (SD) SFCT, CV, and CVI before the PDT of the study population was 310.35 (97.84), 1.64 (0.35), and 0.648 (0.009), respectively. Following the resolution of the subretinal fluid, the mean (SD) SFCT, CV, and CVI of the study population were 240.43 (95.25), 1.61 (0.31), and 0.649 (0.008), respectively. Multiple linear regression demonstrated a statistically significant decrease in SFCT ($R^2=91$, $p=0.045$), CV ($R^2=97$, $p=0.021$) and increase in CVI ($R^2=98$, $p=0.015$) after PDT.

Conclusions: PDT is associated with significant changes in the choroidal structure in CSC patients. Choroidal indices may be employed to monitor disease progression.

CONTROL ID: 3545121

SUBMITTER (NAME ONLY): Yu Jeong Kim

TITLE: Investigation of MicroRNA Expression in Anterior Lens Capsules of Senile Cataract Patients and MicroRNA Differences According to the Cataract Type

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Kim, W. Lee, Y. Yeon, H. Lim, Hanyang University College of Medicine, Seongdong-gu, Seoul, KOREA (THE REPUBLIC OF)|B. Ko, Apgujeong Eye Center, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: We investigated the microRNAs (miRNAs) expression in the anterior lens capsules of patients with senile cataract and compared it to that in the anterior lens capsules of healthy controls. Moreover, we compared the differences in miRNAs expression according to the types of cataracts.

Methods: Individual lens epithelium samples were collected from 33 senile patients and 10 controls. The cataract patients were classified into cortical, nuclear, posterior and anterior subcapsular and mixed. The expression of 12 different miRNAs in lens epithelium was measured using real-time polymerase chain reaction, and compared between the senile cataract patients and controls. The differences of miRNA levels according to cataract type were analyzed.

Results: The expression levels of let-7g-5p, miR-23a-3p, miR-23b-3p, and miR-125a-5p were significantly upregulated in patients with senile cataract when compared with those in the control group ($P < 0.05$). The expressions of let-7a-5p, let-7d-5p, miR-16-5p and miR-22-3p were significantly downregulated in the senile cataracts ($P < 0.05$). Let-7a-5p, let-7d-5p, let-7g-5p and miR-23b-3p had significant difference in expression between nuclear and anterior subcapsular cataracts.

Conclusions: The 8 differentially expressed miRNAs may be involved in the pathogenesis of senile cataract, in particular, related to oxidative stress and autophagy.

CONTROL ID: 3545129

SUBMITTER (NAME ONLY): Rosa de Hoz

TITLE: Retinal thickness changes over time by SD-OCT in a AD mouse model (APP^{NL-F/NL-F})

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. de Hoz, E. Salobar-García, I. López Cuenca, L. Sanchez-Puebla, J. Fernández-Albarral, P. Rojas, J. Salazar, A. Ramirez, J. Ramirez, Instituto de Investigaciones Oftalmológicas Ramon Castroviejo. Universidad Complutense de Madrid, Madrid, SPAIN|R. de Hoz, E. Salobar-García, J. Salazar, A. Ramirez, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|P. Rojas, Instituto Oftálmico, Hospital General Universitario Gregorio Marañon, Madrid, Madrid, SPAIN|I. Bravo-Ferrer, UK Dementia Research Institute, Edinburgh Medical School, University of Edinburgh, Edinburgh, UNITED KINGDOM|I. Bravo-Ferrer, Department of Pharmacology and Toxicology, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|V. Medina, M. Moro, Spanish National Cardiovascular Research Centre, Carlos III Health Institute, SPAIN|T. Saido, Laboratory for Proteolytic Neuroscience, Brain Science Institute, RIKEN, JAPAN|T. Saito, Department of Neurocognitive Science, Institute of Brain Science, Nagoya City University Graduate School of Medical Sciences, JAPAN|J. Ramirez, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Alzheimer's disease (AD) presents retinal neurodegenerative changes even before they appear in the brain, suggesting the retina as an accessible biomarker of AD. The present work is a diachronic study using spectral domain optical coherence tomography (SD-OCT) to determine the total retinal thickness and retinal nerve fiber layer (RNFL) thickness at 6, 9, 12, 15, 17, and 20 months old, in an APP^{NL-F/NL-F} mouse model of AD compared to wild type (WT) animals.

Methods: Total retinal thickness and RNFL thickness were determined in male APP^{NL-F/NL-F} (n=55) and WT (n=41) animals. The mean total retinal thickness was analyzed following the Early Treatment Diabetic Retinopathy Study sectors. RNFL was measured in six sectors of axonal ring scans around the optic nerve. Microglial and astroglial activation was evaluated at 17-months-old, by analyzing vertical retinal sections immunostained with Iba-1 and GFAP.

Results: In the APP^{NL-F/NL-F} group compared to WT animals, for total retinal thickness was observed: i) At 6-months-old, a significant thinning in the outer temporal sector; ii) at 15-months-old a significant thinning in the inner temporal and in the inner and outer inferior retinal sectors; iii) at 17-months-old, a significant thickening in the inferior and nasal sectors in both inner and outer rings; and iv) at 20-months-old, a significant thinning in the inner ring of nasal, temporal and inferior retina and in the outer ring of superior and temporal retina. In RNFL thickness, a significant thinning in the global analysis and in nasal and inner-temporal sectors at 6 months old were observed. In addition, in the APP^{NL-F/NL-F} group we found activation of microglial cells (thicker somas and processes and amoeboid forms) and astroglial cells (higher GFAP+ immunostaining with astrocyte clusters in certain areas).

Conclusions: In the APP^{NL-F/NL-F} model, the thickness of the retina over time exhibited a thinning, probably produced by neurodegeneration alternating with the thickening possibly caused in addition to the deposits by neuroinflammation observed in some areas of the retina in this model. These changes over time are similar to those found in the human retina and could constitute a biomarker of AD. The APP^{NL-F/NL-F} AD model can provide us a

better understanding of the different retinal alterations during the progression of AD.

CONTROL ID: 3545130

SUBMITTER (NAME ONLY): Inken Becker

TITLE: Non-invasive Treatment of Early Diabetic Macular Edema by Multi-Wavelength Photobiomodulation with the Valeda Light Delivery System

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.S. Becker, H. Schwahn, H. Kaymak, I.I.O. Breyer Kaymak Klabe, Düsseldorf, GERMANY|M.R. Munk, Department of Ophthalmology, Inselspital Universitätsspital Bern, Bern, BE, SWITZERLAND|S. Tedford, C. Croissant, R. Rückert, C.E. Tedford, LumiThera, Inc, Poulsbro, Washington, UNITED STATES|R. Rückert, eye.gnos consulting, Bern, BE, SWITZERLAND|H. Kaymak, Experimental Ophthalmology, Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Homburg/Saar, Saarland, GERMANY|

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ABSTRACT BODY:

Purpose: The complex pathophysiology of DME results in extracellular fluid accumulation and in decreased visual function. Light-based Photobiomodulation (PBM) provides a non-invasive treatment strategy that directly targets the underlying pathology through light-sensitive cellular cascades. The Valeda Light Delivery System is successful in the treatment of AMD (cf. LIGHTSITE I & II). We here present an observation of novel PBM therapy in early DME patients with the Valeda System.

Methods: A total of 28 eyes from 18 DME patients (67% male; 57.3±14.0 yrs) with good vision but OCT evidence of macula edema were assessed for functional (BCVA), anatomical (CRT, RV, presence of IRF, SRF and HE), and safety outcomes (integrity of EZ, IZ, ELM and RPE) following one series of PBM treatments (3x per week for 3-4 weeks) with the Valeda Light Delivery System. Assessments were conducted at baseline (BL), immediately following the final (9th) treatment and at follow up visits out to approx. 6 months. Presence of ERM, VMT and DRIL in the OCT and patients' subjective evaluations (via questionnaire) were recorded as well.

Results: After initial treatment with PBM, 28.6 % and 40 % eyes showed a resolution of inner retinal fluid and hard exudates, respectively. Retinal thickness (CRT) remained stable, from 302±58 µm at BL to 296±47 µm after 9th treatment. In all eyes, photoreceptors and RPE remained intact during the treatment and up to 6 months follow-up. At the same time, visual acuity remained stable at 0.1±0.1 logMAR. Most patients noted a considerable improvement in their subjective vision and reported less problems in everyday life and were more confident and more positively biased towards the development of the disease even up to 6 months.

Conclusions: Anatomical benefits suggest disease-modifying effect with PBM treatment with the Valeda in early DME patients. These study subjects typically had good vision and nearly normal CRT and RV but clear evidence of macular edema. PBM treatment demonstrates potential as a novel, non-invasive, cost-effective and well-tolerated approach for treatment of early DME patients. Moreover, the early treatment may provide a viable option to stabilize the functional and anatomical parameters and prevent the progression of the DME disease.

CONTROL ID: 3545132

SUBMITTER (NAME ONLY): Chen-Ching Peng

TITLE: Single particle analysis of extracellular vesicles in aqueous humor from pediatric diseased eyes: a pilot study

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Peng, L. Xu, J.L. Berry, The Vision Center, Children's Hospital of Los Angeles, Los Angeles, California, UNITED STATES|C. Peng, L. Xu, Department of Biological Sciences, Dornsife College of Letters, Arts, and Sciences, University of Southern California, Los Angeles, California, UNITED STATES|J.L. Berry, Roski Eye Institute, Keck School of Medicine, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Extracellular vesicles (EV) are detectable in aqueous humor (AH) from adult patients in previous studies. However, the presence of EVs in AH from pediatric diseased eyes has not been explored. Also, the expression profile of exosomal tetraspanins (CD9, CD63 and CD81) on AH EVs remains unclear. Herein, we measure the concentration of the pediatric diseased eye-derived AH EVs and analyze their size distribution and the phenotypic expression levels of exosomal tetraspanins of AH EV at single vesicle resolution.

Methods: AH samples were obtained from 3 congenital cataract, 3 congenital glaucoma and 5 retinoblastoma (RB) eyes. Plasma samples were obtained from 2 RB patients. Unprocessed, enrichment-free 10uL AH samples or 1uL plasma samples were subjected to Nanoparticle Tracking Analysis (NTA) (Nanosight NS300, Malvern Panalytical) for size distribution and concentration, and to Single Particle-Interferometric Reflectance Imaging Sensor (SP-IRIS) (Exoview R100, Nanoview Biosciences), for interferometric sizing and fluorescent-based immunophenotyping of exosomal marker expression (CD81, CD9, and CD63, including CD41a, which detects platelet derived vesicles).

Results: By NTA, the concentration of AH EVs is within $2.65E+09$ - $1.58E+10$ particles/mL with a major population in a mean modal size of 93.3 ± 19.8 nm across diseases in contrast to the $1.55E+11$ - $2.56E+12$ particles/mL with a mean modal size of 60.2 ± 2.1 nm detected in plasma samples. SP-IRIS analysis revealed that CD9+, CD63+ and CD81+ EVs were detected across all AH samples using the Exoview R100 platform. Platelet-derived CD41a+ EVs could only be detected in the plasma EVs. In addition, we identified an enrichment of a single-positive CD63+ EV population in AH across all disease groups (50.9% and 13.6% CD63⁺ EV among all fluorescent positive EVs in AH and plasma, respectively) suggesting a unique phenotypic exosomal tetraspanin expression pattern in AH.

Conclusions: Exosome size ranged-EVs are readily detectable in unprocessed AH with a dominant mono-CD63+ EV in AH regardless of pediatric eye disease types. These novel findings uncover a new path on AH exosomal biomarker research focusing on CD63+ EVs.

CONTROL ID: 3545142

SUBMITTER (NAME ONLY): Corinne Carle

TITLE: Diagnostic power of rapid objective visual testing of multiple sclerosis patients

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Carle, T. Maddess, E. Rohan, J. van Kleef, John Curtin School of Medical Research, Australian National University, Canberra, Australian Capital Territory, AUSTRALIA|J. Baird-Gunning, C.J. Lueck, Canberra Hospital Neurology Department, Woden, Australian Capital Territory, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To examine the diagnostic power of two new forms of rapid objective perimetry in patients with multiple sclerosis (MS).

Methods: We tested 44 MS patients aged 60.7 ± 10.1 y (mean \pm SD), 13 of them with progressive disease, the remaining 31 with relapsing remitting. The 40 normal control patients were aged 60.2 ± 12.5 y. EDSS scores were assessed by J B-G who is a neurologist. We used two variants of multifocal pupillographic objective perimetry: W12 and W20, which had 12 or 20 stimuli/eye that sampled the central 60 degrees of each visual field. Both eyes were tested concurrently in 80 seconds. We used an FD-cleared prototype of the Konan objectiveFIELD Analyser (OFA). The main variable of interest was the asymmetry between eyes in the per-region response delays. We calculated % Areas under Curve (%AUC) for Receiver Operating Characteristic (ROC) plots. Separate %AUCs were calculated for the mean of the worst 4, and worst 12, per-region response delay asymmetries for each of 3 EDSS groups: < 2.5 ; 2.5 to < 4.5 ; and ≥ 4.5 , compared to controls. We also estimated Effect-sizes as Hedge's g.

Results: The measured %AUCs increased with disease severity, reaching 94.4 ± 3.16 for EDSS3 (Table). Both methods had similar performance although W20 was better for the less severe EDSS1 patients. The Hedge's g values indicated 'large' to 'huge' Effect-sizes. An interesting sub-analysis compared subjects who had experienced Optic Neuritis (ON, N=30) and those who had not (no-ON, N=14). The resulting %AUCs were very similar for both tests. For No-ON and ON, W12: 86.9 ± 5.24 vs 86.0 ± 4.46 ; and W20: 87.2 ± 5.45 vs 86.8 ± 4.36 .

Conclusions: The relatively large %AUCs and Effect-sizes for the EDSS 1 group possibly indicates an ability to diagnose and monitor disease condition in early-stage disease. The results for ON vs. no-ON suggest that the tests are more biased towards disease progression rather than the history of acute inflammation. This is similar to our earlier multifocal VEP data that used related stimuli [Annals Neurology, 57, 904-913].

CONTROL ID: 3545147

SUBMITTER (NAME ONLY): Aveen Kadhum

TITLE: The effect of patching and gaming therapy on visual acuity in children with amblyopia and influence on quality of life

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kadhum, E. Tan, H.J. Simonsz, S.E. Loudon, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Bruijning, Optometry & Orthoptics, Hogeschool Utrecht, Utrecht, Utrecht, NETHERLANDS|M.V. Joosse, Ophthalmology, Haaglanden Medical Center Westeinde Hospital, The Hague, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To make a valid comparison between the effect of patching therapy and dichoptic video gaming in children with amblyopia: preliminary results after 24 weeks of treatment.

Methods: In this prospective Randomized Clinical Trial all newly diagnosed children with amblyopia were recruited by ten treating orthoptists in four clinics. Exclusion criteria were previous amblyopia treatment, strabismus angle >30PD, neurological disorder, nystagmus and other eye disorders. The research orthoptist examined the child according to the study protocol using the crowded tumbling E-chart to measure visual acuity (VA). If necessary, a refractive adaptation period of 16 weeks was carried out prior to randomization. After informed consent they were randomized to patching therapy: 2 hrs/day; compliance was monitored electronically using the Occlusion Dose Monitor; or dichoptic video game therapy: 1 hr/wk under direct supervision at the outpatient clinic. VA was assessed every 6 weeks by the research orthoptist during the study period of 24 weeks. Main outcome measure was improvement in VA (logMAR units/time period). In addition, quality of life data was collected using the adjusted Child Amblyopia Treatment Questionnaire (CAT-QoL).

Results: One-hundred children were recruited; 29 subjects refused participation, 2 were excluded. After refractive adaptation period, 27 subjects attained interocular VA <0.2 logMAR. Thirty-five children were included for randomization; 18 were boys (51%). During the study 3 children dropped out of the patching group and 10 out of the gaming group, resulting in 22 (22%) children completing the full study period. Mean age was 6.4±2.8 years. These children had mean VA at start of treatment of 0.43±0.31 logMAR in the amblyopic eye and 0.07±0.15 logMAR in the fellow eye. Mean VA after 24 weeks of treatment improved to 0.20±0.29 logMAR in the amblyopic eye and 0.03±0.13 logMAR in the fellow eye. Nineteen children were interviewed for the CAT-QoL and 18 parents filled out the same questionnaire independently.

Conclusions: After 24 weeks of patching or gaming treatment mean VA improved with 2.3 logMAR lines in the amblyopic eye. Depending on the results from the CAT-QoL, in-depth interviews will be conducted investigating experiences of parents whose child had either received occlusion therapy or gaming therapy.

CONTROL ID: 3545151

SUBMITTER (NAME ONLY): Sergio Alonso-Alonso

TITLE: Development of a new xeno-free human corneal endothelial cells culture system based on Platelet Rich in Growth Factors.

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Alonso-Alonso, J. Alfonso, B. Alfonso, Instituto Oftalmológico Fernandez Vega, Oviedo, Asturias, SPAIN|N. Vázquez, C. Suarez-Barrio, S. del Olmo Aguado, M. Chacon, E. Garcia-Perez, M. Persinal-Medina, J. Merayo-Llves, A. Meana, instituto universitario Fernández-vega - Fundación de investigación Oftalmológica - Universidad de Oviedo, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: The purpose of the present study is to develop a culture system for human corneal endothelial cells (hCEC) replacing the use of xenogeneic components by a standardized kit in Ophthalmology to obtain human Platelet Rich in Growth Factors (PRGF) and to evaluate the adequacy of this culture system by the study of functionality markers, Transendothelial electrical resistance (TER) and gene expression.

Methods: 12 corneas discarded for transplantation were used for this study 6 per each group. Corneal endothelium was dissected following the Schwalbe line and was conditioned for 2-7 days at 37 °C in a culture plate with 4 mL of PRGF or SBF culture medium:

PRGF Medium: Optimum I, 10 v/v% PRGF, 200 mg/L CaCl₂ and 10 U/mL penicillin, 10 µg/mL streptomycin.

SBF Medium: Optimum I, 8 v/v% fetal bovine serum (FBS), 200 mg/L CaCl₂, 0.3 mM ascorbic acid 2-phosphate, 0.04% chondroitin sulfate, 20 ng/mL nerve growth factor, 5 ng/mL epidermal growth factor and 10 U/mL penicillin, 10 µg/mL streptomycin.

Conditioned endothelium was digested with TrypLE for 90 min at 37 °C. After that, the loosened cells were centrifuged at 0.4 g for 10 min, the supernatant was removed and the cells were seeded on a culture plate previously treated with FNC coating mix®.

Cellular growth was assessed by phase contrast microscopy until confluence. Both hCECs cultured with basal or conventional medium were used for TER evaluation. Confluent cultures were fixed using ice-cold methanol for 10 min. Then, immunocytochemistry of major corneal endothelial markers (Na⁺/K⁺ ATPase, ZO-1, connexin-43 and vimentin) were performed. Additionally confluent cultures of hCECs were loosened with accutase and used for gene expression analysis for the same expression markers.

Results: hCECs obtained from both PRGF and SBF supplemented cultures proliferated until confluence showing positive staining for connexin-43, vimentin, ZO-1 and Na⁺/K⁺ ATPase, responsible these last two for endothelial barrier and pump functions, respectively. In addition, similar gene expression levels and TER values were observed in PRGF and SBF hCECs cultures.

Conclusions: hCECs can be obtained using a PRGF culture medium avoiding the use of animal derived substances.

CONTROL ID: 3545153

SUBMITTER (NAME ONLY): Elena Salobar-García

TITLE: Choroidal changes as a biomarker of cerebral amyloid angiopathy in mild Alzheimer's disease patients.

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Salobar-García, I. López Cuenca, R. de Hoz, J. Fernández-Albarral, A. Ramirez, P. Rojas, J. Garcia-Feijoo, J. Salazar, J. Ramirez, Instituto de Investigaciones Oftalmológicas Ramón Castroviejo. School of Medicine, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|E. Salobar-García, R. de Hoz, A. Ramirez, J. Salazar, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|P. Rojas, Instituto Oftálmico de Madrid, Hospital General Universitario Gregorio Marañon, Madrid, Madrid, SPAIN|C. Mendez-Hernandez, S. Wang, J. Garcia-Feijoo, Instituto de Investigación Sanitaria del Hospital Clínico San Carlos (IdISSC), Hospital Clinico Universitario San Carlos, Madrid, Madrid, SPAIN|J. Ramirez, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|P. Gil, Servicio de Geriátria, Hospital Clinico Universitario San Carlos, Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Alzheimer's disease (AD) is a progressive neurodegeneration in which cerebral amyloid angiopathy develops, resulting in vascular changes. In recent works, alterations and deposits in the choroids and retinas of patients with AD have been observed that correlate with the disease's progression. Novel techniques for the study of ocular vascularization, such as the Laguna ONhE and the angio-optical coherence tomography (OCTA), tests that can be performed in these patients (non-invasive and without contrast), will allow the study of ocular vascular changes caused by AD

Methods: Seventeen patients with mild AD (mAD) and 49 healthy controls, which after a complete eye examination did not present any ophthalmological diseases, were studied for the coefficient of hemoglobin (Hb) in the optic nerve head by Laguna ONhE, and for thickness of the choroid and foveal avascular zone (FAZ) of the retina by the OCTA. For the statistical study, the Mann-Whitney test was used.

Results: The Mini Mental State Examination of the mAD patients was 24.00 ± 5.32 , while the control group was 29.40 ± 1.83 , with a significant difference ($p < 0.001$) between them. In the Hb coefficient of the optic nerve head there was no significant difference when comparing both groups, although in the papillomacular bundle there was a slight increase in the Hb coefficient in mAD patients. However compared to the control, the choroid in the mAD patients showed a significant thinning ($p < 0.05$), while the FAZ did not change.

Conclusions: In patients with mAD, a significant decrease in the choroidal vascular system was found, while the retinal system and the Hb of the optic nerve head did not exhibit any changes in the mild stages of AD. These results are showing that choroidal changes potentially could be an early biomarker of amyloid angiopathy which may be used for the diagnosis and follow-up of AD.

CONTROL ID: 3545164

SUBMITTER (NAME ONLY): Xiaolin Wang

TITLE: In vivo longitudinal assessment of cone photoreceptor density in age-related macular degeneration

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess cone photoreceptor survival in the human eye with age-related macular degeneration (AMD), using adaptive optics scanning laser ophthalmoscopy (AOSLO) and spectral-domain optical coherence tomography (SDOCT).

Methods: AOSLO was performed to image cones in central 20° of the retinae. A 2-dimensional normative macular cone density map was obtained in 29 eyes of 18 subjects aged 67.1 ± 10.8 years without evidence of any macular disease. In 10 eyes of 7 patients with intermediate stage AMD including 5 eyes with predominantly subretinal drusenoid deposits (SDD) and 5 eyes with classical drusen but without SDD, AOSLO and SDOCT were acquired 4 times over 39.6 ± 3.3 months. Retinal regions absent of AMD lesions were ascertained by reflectivity and packing structure of the cones imaged by AOSLO, and by the integrity of the cross-sectional structure in SDOCT. Cone density change was evaluated using linear regression at 1174 loci in these regions. The change of the proportion of retinal loci with cone density lower than normal values was estimated among the locations where cone density could be measured at both the baseline and the 4th visit, including 197 loci in eyes with SDD and 268 in eyes with drusen but without SDD.

Results: Cone density decreased over time at 98.3% (1154/1174) of the examined locations. In eyes with SDD, cone density declined with a slope of -160 ± 75 cones/degree²/year in the central 5° of the retina and with a slope of -59 ± 24 cones/degree²/year in the 5°-10° surrounding annular zone. In eyes with drusen but without SDD, cone density reduction slopes were -98 ± 48 cones/degree²/year in the central 5° and -27 ± 18 cones/degree²/year in the 5°-10° annular zone, respectively. Over the follow-up period, the percentage of retinal locations with cone density lower than normal (Z-score < -2) in eyes with SDD increased from 16% (32/197) to 59% (117/197). In contrast, in eyes with drusen but without SDD, this number changed from 1.5% (4/268) to 16.4% (44/268).

Conclusions: AOSLO revealed cone density reduction over time in retinal regions that were not clinically impacted by AMD lesions. Eyes with SDD showed an accelerated rate of cone density decrease compared with eyes with only classical drusen, suggesting a different natural history of photoreceptor degeneration in AMD of different phenotypes, and implying more severely impaired visual function.

CONTROL ID: 3545165

SUBMITTER (NAME ONLY): Christoph Grechenig

TITLE: Impact of Residual Subretinal Fluid Volumes on Treatment Outcomes in a SRF-tolerant Treat & Extend Regimen

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Grechenig, G.S. Reiter, S. Riedl, B. Gerendas, H. Bogunovic, U. Schmidt-Erfurth, Department of Ophthalmology and Optometry, Medizinische Universität Wien, Wien, Wien, AUSTRIA|J. Arnold, Marsden Eye Specialists, Parramatta, New South Wales, AUSTRALIA|R.H. Guymer, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To investigate associations between residual subretinal fluid (SRF) volumes, quantified using artificial intelligence (AI) and treatment outcomes in a SRF-tolerant treat and extend (T&E) anti-VEGF regimen in neovascular age-related macular degeneration (nAMD).

Methods: In this post-hoc analysis, patients enrolled in the prospective, multicenter FLUID study and randomized in a SRF-tolerant T&E regimen were examined by spectral-domain optical coherence tomography (SD-OCT) imaging and tested for best-corrected visual acuity (BCVA) over a 24 months follow-up. Validated AI-based image analysis tools were used to quantify SRF and intraretinal fluid (IRF) volumes on SD-OCT. 375 visits of 98 patients of the SRF tolerant arm were divided into two subgroups: Extended intervals despite residual SRF, and visits with extension without fluid. BCVA change at the follow-up visit was compared between the groups. The associations of SRF volumes in the central 1mm and 6mm as well as treatment intervals with BCVA change were estimated using generalized linear mixed models.

Results: At visits with extended intervals despite residual SRF an increase in SRF was associated with a significant BCVA reduction at the next visit in the central 1mm (-0.138 letters/nl SRF; $p=0.014$) and the total 6mm (-0.024 letters/nl SRF; $p=0.049$). Visits with extended intervals despite residual SRF had significantly higher SRF volumes in the central 6mm ($p=0.002$) at the following visit, and showed a trend in the central 1mm ($p=0.061$). A statistically significantly negative association between increased treatment interval and change in BCVA was found for residual SRF in 1 and 6mm (-0.250 and -0.233 letter/week interval, respectively, both $p<0.001$).

Conclusions: A fully automated quantitative analysis of extended visits despite residual SRF demonstrated increasing SRF volumes associated with BCVA loss at the following visit. This association contributes to our understanding of the quantitative impact of residual SRF volumes on visual function and highlights the importance of precise and quantitative measurements of fluid volumes as the field determines the most efficacious regimens for individualizing treatment for nAMD with anti-VEGF therapies.

CONTROL ID: 3545166

SUBMITTER (NAME ONLY): Anna Nowinska

TITLE: Objective Ocular Surface Assessment in Patients with Dry Eye Disease coexisting with Demodex Mite Infestation

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nowinska, E. Chlasta-Twardzik, E. Wylegala, Ophthalmology, Slaski Uniwersytet Medyczny w Katowicach, Katowice, Slaskie, POLAND|

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ABSTRACT BODY:

Purpose: The presence of Demodex species can be associated with DED, but the precise relationship remains unclear. The purpose of this prospective, observational, cross-sectional study was to assess the objective ocular surface abnormalities in patients with DED coexisting with Demodex infestation

Methods: This study was performed in accordance to the Declaration of Helsinki after approval by the Bioethics Committee. 180 eyes of 90 patients with DED diagnosed according to TFOS guidelines were recruited for the study. The study group (SG) consisted of 76 eyes of 38 patients with DED and coexisting Demodex infestation confirmed on sampled eyelashes. The control group (CG) consisted of 106 eyes of 53 DED patients. The groups were gender and age matched. Analysed ocular surface parameters included NITBUT, TMH, Meibomian gland drop-out, Bulbar redness were assessed by Keratograph 5M (Oculus). Measurements were performed twice in the morning and in the afternoon.

Results: Distribution of OSDI scores were comparable between groups, as well the results of NITBUT and TMH. Mild DED was the most prevalent among groups (SG: 85,18%; CG: 77,35%). The groups differed significantly in the MG drop out (SG: $0,51 \pm 0,23$; CG: $0,29 \pm 0,12$ $p < 0,001$) and conjunctival and limbal redness in the morning (SG: $1,2 \pm 0,43$; $1,1 \pm 0,53$ vs CG: $0,8 \pm 0,26$, $0,7 \pm 0,2$ $p < 0,0001$; $p < 0,01$ respectively). Parameters which were characterized by significant daily variability were NITBUT ($p < 0,001$), TMH ($p < 0,0001$) in both groups and conjunctival and limbal hyperaemia in the study group.

Conclusions: The infestation of the eyelids with Demodex species is associated with changes of the bulbar redness and anatomic changes of Meibomian gland in patients with DED, which confirm the role of the MGD and inflammation in the disease pathogenesis. Daily variability in NIBUT, TMH and ocular redness should be taken into consideration in DED studies.

CONTROL ID: 3545172

SUBMITTER (NAME ONLY): Omar Shareef

TITLE: Corneal collagen cross-linking in children and developmentally delayed populations

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the results of corneal collagen cross-linking (CXL) in developmentally delayed and pediatric patients with keratoconus (KCN) under both general and topical anesthesia.

Methods: Data of individuals with KCN who underwent CXL under both general anesthesia as well as topical anesthesia were analyzed retrospectively by examining patient charts. This study is comprised of individuals who had CXL between January 2019 and November 2020. Differences between patients with and without developmental delay (DD) as well as changes in disease characteristics before and after surgeries were compared using the Pearson χ^2 and t-test.

Results: This study tracked 35 eyes of 22 patients with a mean follow-up of 7.2 ± 6.2 months. Of these 22 patients, 9 (40.9%) had DD. Patients with DD underwent CXL at an older age compared to patients without DD (mean age: 22.1 years vs 17.8 years), although this difference was not statistically significant. The nine DD patients were administered general anesthesia, and the remaining 13 patients without DD were given topical anesthesia. Regarding preoperative characteristics, patients with DD had a BCVA in LogMAR of 0.829 vs. 0.325 ($p = 0.005$). Corneal thickness (CT), sphere, cylinder, K1, K2, and K_m were not significantly different between the two groups. Postoperatively, BCVA in LogMAR for patients with DD was 0.739 and 0.222 in non-developmentally delayed ($p = 0.012$). Sphere, cylinder, K1, K2, K_m , and CT were not significantly different between the two groups.

There was no significant postoperative change in BCVA, K1, K2, K_m , sphere, cylinder, and CT compared to preoperative for the entire cohort of patients. No complications were observed during the procedures. Two patients needed retreatment at 1 and 11 months after initial crosslinking.

Conclusions: CXL under general anesthesia for developmentally delayed patients gives equivalent outcomes in halting progression of topographic parameters as compared to CXL under topical anesthesia for non-developmentally delayed patients. Pre and postoperative BCVA was not equivalent between the groups because of the inability of patients with DD to wear glasses or contact lenses. Early intervention should be considered in DD so that vision can be preserved to the greatest degree possible.

CONTROL ID: 3545179

SUBMITTER (NAME ONLY): Jose Rivera

TITLE: Retinal Degeneration Associated with Mutations in the KIZ Gene

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Rivera, I. Erdinst, A. Onala, S. Idan, A. Shemesh, D. Sharon, E. Banin, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|

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ABSTRACT BODY:

Purpose: The Kizuna (KIZ) gene encodes a centrosomal protein and was first reported to be associated with inherited retinal dystrophy (IRD) in 2014. Since then only six cases have been reported worldwide. Here we aimed to characterize genotype and phenotype in what to our knowledge is the biggest cohort of patients with KIZ-associated IRD reported to date.

Methods: Medical records of KIZ patients were retrospectively reviewed, and genetic, clinical, imaging, and electrophysiological data were analyzed.

Results: We identified 18 patients with KIZ mutations: 16 (ages 13-66) have a homozygous p.R76* mutation and 2 (ages 42&50) were compound heterozygous for p.R76* and c.3G>A (p.M1?). From the homozygous group, 13/16 were of Ashkenazi Jewish (AJ) descent, 2 from Morocco and 1 from Turkey. Both compound heterozygous patients were from a mixed background (Bulgaria-Macedonia & Poland-Iraq).

Clinical data was available for 14 patients: 8/14 patients (ages 21-66) had good visual acuity ($\geq 20/40$) in at least one eye up until the last examination and 8/12 patients (ages 25-66) manifested cataracts, commonly posterior subcapsular.

Fundus imaging, available in 11 patients, showed two main phenotypes: 6 patients (5 Homo & 1 het, ages 13-66) manifested relatively mild disease with minimal fundusoscopic changes even at advanced age, although FAF revealed hypoautofluorescent spots and a macular hyperautofluorescent ring. Five other homozygous patients showed more aggressive disease with fundusoscopic features of classic RP, including bone spicule-like pigmentation, attenuation of retinal vessels and optic disc pallor.

On OCT, 4/8 patients (2 mild and 2 with RP-like phenotype) showed a mild ERM, and only one (in the mild group) had cystoid changes. Visual fields showed progressive constriction, reduced to less than 10 degrees by the age of 30 in 7/9 patients. FFERG was still recordable in patients up until 62 years of age, with a rod>cone dystrophy pattern. Interestingly, the Arden ratio on EOG testing was reduced in all 6 patients who performed this test to values lower than predicted by the extent of FFERG loss.

Conclusions: KIZ mutations are an uncommon cause of IRD worldwide, but are not rare among AJ, with a 1:79 carrier rate for the p.R76* mutation. Fundus findings are often mild and can be missed. In an AJ patient, FFERG testing showing a rod>cone pattern of injury and an EOG Arden ratio that is lower than expected may suggest KIZ as the cause of disease.

CONTROL ID: 3545183

SUBMITTER (NAME ONLY): Linda Lundstrom

TITLE: Peripheral optical errors and hazard perception

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Lundstrom, Kungliga Tekniska Hogskolan, Stockholm, SWEDEN|A. Venkataraman, Karolinska Institutet, Stockholm, SWEDEN|R. Rosén, A. Alarcon, P. Piers, C. Canovas, Johnson & Johnson Surgical Vision Inc, NETHERLANDS|

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ABSTRACT BODY:

Purpose: While driving, hazards might appear in the periphery. It is known that peripheral optical errors decrease peripheral contrast sensitivity. This study evaluates how the elevated peripheral optical errors affect hazard perception in the peripheral visual field.

Methods: We evaluated hazard perception, as well as resolution acuity and contrast sensitivity in the 20° nasal visual field of 11 healthy eyes. Two optical conditions were tested with an adaptive optics vision simulator designed for peripheral vision evaluation: 1) Simulated average optical errors in 20° nasal visual field (-0.60 D in spherical equivalent, -0.50 D in cross-cylinder J0 and 0.09 µm horizontal coma for a 4 mm pupil); 2) Simulated elevated optical errors in 20° nasal visual field (-1.20 D in spherical equivalent, -1.45 D in cross-cylinder J0 and 0.09 µm horizontal coma for a 4 mm pupil). Peripheral resolution acuity and contrast sensitivity were evaluated with Gabor gratings. A hazard perception test was developed, wherein the subjects fixated foveally at a moving road scene while peripheral test stimuli were presented 20° nasally. The test stimuli consisted of hazards that were animals, and non-hazards that were plants and rocks. The subjects' task was to respond when a hazard was seen. The test conditions were randomized, and each measurement was performed twice.

Results: The elevated condition significantly reduced the peripheral grating resolution acuity and contrast sensitivity at 1 cycle per degree compared to the phakic condition: on average 0.08 logMAR and 0.25 logCS, respectively. In the hazard perception test, all subjects also showed worse performance with the elevated condition, resulted in increased false positives by 8 % and misses by 13 % together with 0.3 seconds longer reaction time.

Conclusions: This study tested the visual and functional aspects of peripheral optical errors. Improving the peripheral optics increases resolution acuity, contrast and hazard perception in the nasal visual field. Therefore, reducing peripheral optical errors produces visual and functional improvements that may have safety implications.

CONTROL ID: 3545189

SUBMITTER (NAME ONLY): Pablo Artal

TITLE: Less astigmatism and better contrast sensitivity in the periphery of pseudophakic patients implanted with a new intraocular lens

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Artal, E.A. Villegas, P. Prieto, Laboratorio de Optica, Universidad de Murcia, Murcia, SPAIN|J. Marin, E. Alcon, Oftalvist, Murcia, SPAIN|H.S. Ginis, Athens Ete Hospital, Athens, GREECE|C. Robles, Voptica SL, Murcia, SPAIN|P. Taña-Rivero, Oftalvist, Alicante, SPAIN|

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ABSTRACT BODY:

Purpose: The optical quality in the periphery of the retina in pseudophakic patients implanted with standard intraocular lenses (IOLs) is worse than those in the normal phakic eye (Jaeken et al., IOVS, 2013). This may affect specific visual tasks impacting patient's orientation in space and therefore may pose a hazard to their safety. We have evaluated peripheral astigmatism and contrast sensitivity in a group of patients implanted with a new type of IOL that was designed to provide better peripheral optics and compared results with a group of patients implanted with a standard IOL.

Methods: A new type of IOL (ArtIOLs, Voptica SL, Murcia, Spain) with an inverted meniscus shape designed to improve the optical quality of the pseudophakic eye in the periphery was evaluated. These lenses were implanted in a group of 87 patients undergoing cataract surgery. A control group of 38 patients were implanted with a standard monofocal IOL as reference. Peripheral refraction in the horizontal meridian was obtained using a scanning Hartmann-Shack wavefront sensor. Contrast detection threshold at 45 degrees of visual angle (both horizontally and vertically) was measured psychophysically by means of an adaptive staircase technique, using a 30-arcmin round stimulus 1 m in front of the patient's eyes and a green LED for foveal fixation.

Results: Patients implanted with ArtIOLs presented a reduced amount of peripheral astigmatism as compared with the control group. At 30 degrees, the average cylinder in the control group was 3 D, dropping to 2 D in the ArtIOL's group. At 45 degrees, cylinder mean values were 6 D and 3.5 D respectively. This reduction in astigmatism had a positive impact in contrast sensitivity. In the horizontal meridian, average sensitivity values were 0.07 (SD=0.04) and 0.10 (SD=0.05) for the control and ArtIOL groups respectively. In the vertical meridian, average sensitivity values were 0.06 (SD=0.03) and 0.08 (SD=0.03) for the control and ArtIOL groups respectively.

Conclusions: Patients implanted with a new meniscus-shaped IOL present a reduced amount of peripheral astigmatism compared to patients implanted with standard lenses. This improvement in optical quality leads to a better contrast sensitivity measured at 45 degrees of eccentricity. Further research would be required to evaluate how this IOL may have also an impact in the patient's functional vision.

CONTROL ID: 3545191

SUBMITTER (NAME ONLY): Ana Ramirez

TITLE: Microglial activation in healthy retina and experimental glaucoma during aging.

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To quantify morphological signs of microglial cell activation and P2RY12, MHC-II and CD68 expression in aged mice (15 month) compared to young adult mice (3 month) and after unilateral laser-induced ocular hypertension (OHT).

Methods: Albino Swiss mice were divided in four groups: young naïve (YN, n=6), aged naïve (AN, n=6), young OHT (YG, n=6), and aged OHT (AG, n=6). In OHT groups both eyes (OHT and contralateral) were studied. Retinal whole-mounts were immunolabeled with anti Iba-1 to quantify: i) Iba-1 + cells number (Ibacn) in outer segments (OS), outer plexiform layer (OPL) and inner plexiform layer (IPL); ii) area of retina occupied by Iba-1 + cells (Iba-1 RA) in the nerve fiber layer- ganglion cell layer (NFL-GCL); iii) cell body area of Iba-1+ cells (Cblbac) in OPL, IPL and NFL-GCL; iv) arbor area of Iba-1+ cells (AAlbac) in OPL and IPL; and v) vertical processes number of Iba-1+ cells (VPIbac) between OS and OPL. Antibodies against P2RY12 (resident microglia), CD68 (phagocytic activity) and MHC-II (microglial activation marker) were also used.

Results: In AN respect to YN the quantitative analysis showed a significant increase in the Cblbac in OPL, IPL and NFL-GCL and a significant increase in the VPIbac. Both OHT eyes and contralateral eyes of YG and AG showed significant increase of Ibacn, Iba-1 RA, Cblbac and VPIbac and decrease of AAlbac, more pronounced in OHT eyes, compared to their respective naïve groups. Comparing AG vs YG showed: i) a significant decrease of Iba-1 RA and VPIbac in OHT eyes; ii) a significant increase of Ibacn (OS) and a significant decrease of Cblbac and AAlbac (IPL), in contralateral eyes. Analyzing the P2RY12, CD68 and MHC-II expression we observed: i) in YN and in YG all Iba-1+ cells were P2RY12+, except perivascular and dendritic cells, but in AG most cells were Iba-1+/P2RY12- and some cells in AN; ii) in AN, AG and YG numerous amoeboid-like CD68+ cells were found but in AG CD68+ cells with ramified appearance were also observed. In YG practically all Iba-1+ cells were MHC-II+, while in GA only some Iba-1+ cells were MHC-II+. However, in YN and AN Iba-1+ cells were MHCII-.

Conclusions: The morphological and expression differences of P2RY12, CD68 and MHC-II found in the microglial cells of AN and AG compared to those of YN and YG show that aging can increase the inflammatory process in glaucoma.

CONTROL ID: 3545205

SUBMITTER (NAME ONLY): Janika Nättinen

TITLE: Ocular surface characteristics in Finnish elderly population

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The prevalence of many ocular surface diseases (OSDs) increases with age, which together with population ageing, create a need for better understanding of OSD among the elderly. The aim of this study was to describe the clinical characteristics of OSD in a well-defined Finnish elderly population.

Methods: This cross-sectional study included subjects born between years 1933-1956 and living in Savitaipale, Finland. Various ocular surface health parameters were evaluated, including Schirmer's I test, fluorescein tear break-up time (FTBUT), corneal and conjunctival staining, conjunctival redness, blepharitis, Meibomian gland dysfunction (MGD) and Ocular Surface Disease Index (OSDI). The prevalence of various forms dry eye (DE) and their clinical characteristics were evaluated based on adjusting different OSD criteria and comparing them statistically using Wilcoxon rank sum test and two-sample t-test.

Results: The study included 590 subjects (328 women and 262 men), with mean age of 72.1 years (SD=6.3). Lid and tear lipid dysregulation characteristics were following; 16% of subjects had signs of blepharitis (Efron scale ≥ 2), 15% had signs of MGD (Efron scale ≥ 2) and 38% had FTBUT below 10 sec. Over half of all subjects (54%) had signs of conjunctival redness (SILK-HU ≥ 2), while conjunctival (Lissamine) staining and corneal (fluorescein) staining showed signs of epithelium damage for 12% and 29% of subjects, respectively (Oxford scale ≥ 1). Altogether 32% of subjects had Schirmer I test below 10 mm indicating lowered tear flow. OSDI scores suggested that 13% of subjects had mild, 6% moderate and 3% severe DE. Prior to the study, DE had been diagnosed for 30% subjects and 36% used a DE medication of some form. Based on the clinical signs observed, 10% of all subjects suffered from DE and 38% from OSD. When aforementioned groups were compared to subjects with healthy ocular surface, conjunctival and corneal staining as well as OSDI were increased (all $p < 0.001$) while FTBUT was decreased (all $p < 0.001$) among all groups.

Conclusions: DE and OSD are common among the old adult population. Their prevalence is, however, strongly dependent on the criteria and cut-off values of independent parameters. Comparison of the patients' awareness of their disease and the use of artificial tear substitutes with the clinical signs and symptom scores indicates unmet needs for better understanding of factors related to OSD and improved biomarkers in their analyses.

CONTROL ID: 3545216

SUBMITTER (NAME ONLY): Siegfried Wagner

TITLE: Risk of myocardial infarction following diagnosis of a common ophthalmic disease: analysis of a longitudinal record-linkage study of over 350,000 patients from the UK.

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To characterize the incidence rate of myocardial infarction (MI) in patients following a new diagnosis of cataract, glaucoma, neovascular age-related macular degeneration (AMD) or proliferative diabetic retinopathy (PDR).

Methods: A retrospective cohort study of all patients aged ≥ 40 years attending a large ophthalmic hospital of ten separate sites across London, United Kingdom linked with secondary care Hospital Episodes Statistics Admissions data between January 1st 2008 and June 1st 2018. Myocardial infarction (MI) was defined by diagnostic code I21 or I22 using the International Classification of Diseases, 10th revision and ophthalmic disease through the local electronic health record system. Crude MI incidence rates and those stratified by age, sex, ethnicity and socioeconomic deprivation (through the Index of Multiple Deprivation 2015) per ophthalmic disease were estimated with 95% Poisson intervals. Adjusted cause-specific and subdistribution hazard ratios (HR) were estimated from Cox proportional hazard and Fine-Gray competing risks regression models respectively.

Results: Of 353,191 patients, 59102 had cataract, 31060 glaucoma, 7262 AMD and 2494 PDR. Crude MI incidence rates were 494.6 (461.2-529.5), 297.7 (270.7-326.5), 528.5 (451.4-613.8) and 1449.8 (1173.3-1766.5) per 100,000 person-years at risk (PYAR) for cataract, glaucoma, AMD and PDR respectively. Patients with PDR had the highest incidence rate of MI across all strata. Incidence of MI rose sharply in young patients with cataract from 35.3 (5.0-108.8) for those aged 40-49 years to 368.8 (288.0-463.6) for those aged 50-59 years per 100,000 PYAR with a corresponding HR of 1.54 (1.43-1.66) per decade of age. Those of Asian ethnicity had increased hazards of MI following cataract diagnosis (cause-specific HR 2.67, 1.98-3.61), glaucoma (2.40, 1.69-3.40) and PDR (3.32, 1.41-7.84). Less deprivation was significantly associated with slightly reduced incidence of MI for those with cataract (HR 0.95, 0.92-0.97 per decile) and AMD (0.92, 0.87-0.97).

Conclusions: In accordance with the cardiovascular consequences of diabetes mellitus, MI incidence rate among patients with newly diagnosed PDR was highest. However, a particularly steep rise was noted in younger patients newly diagnosed with cataract supporting a role for cardiovascular risk-stratification in this group.

CONTROL ID: 3545222

SUBMITTER (NAME ONLY): Richard Zhang

TITLE: Development of a thermosensitive hydrogel for sustained drug release and in situ bleb support

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zhang, J.J. Armstrong, C.M. Hutnik, Western University Schulich School of Medicine & Dentistry, London, Ontario, CANADA|C.M. Hutnik, Ivey Eye Institute, London, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Anti-scarring agents are integral to glaucoma filtration surgery success. When injected as a solution or applied via sponge, rapid washout from the subconjunctival tissues limits long-term efficacy. Chitosan-based thermosensitive hydrogels (ThermoGels) are injectable liquids at room temperature that solidify into gels at temperatures approximating the subconjunctival space. In this study, we evaluate ThermoGels' thermosensitive properties, resistance to outflow, and biocompatibility with human Tenon's capsule fibroblasts (hTCFs) with the goal to develop an injectable sustained-release anti-fibrotic drug depot and in situ bleb scaffold.

Methods: Hydrogels were prepared by dissolving chitosan in 2% acetic acid, dialyzing to remove the acid, and adding beta-glycerophosphate (β -gp). Various recipes were tested for gelation time vs temperature using the tube inversion test. Biocompatibility was tested by culturing hTCFs on chitosan gels at 37°C. Resistance to flow was tested by measuring afferent pressure when perfusing a gel-filled flow chamber with saline at the rate of aqueous humor production (2.6 μ L/min). Drug release was tested by measuring acetylsalicylic acid (ASA) or bovine serum albumin (BSA) in the effluent when perfusing drug-loaded gels with saline at 2.6 μ L/min.

Results: Gelation time of chitosan/ β -gp solutions is inversely related to temperature and the concentration of β -gp used. 5% and 6% β -gp mixtures gelled the quickest at 37°C. MTT and LDH assays showed that chitosan hydrogels have no significant effect on cellular metabolic activity or necrosis compared to vehicle controls. Perfusion of the hydrogel demonstrated a reproducible, transient increase in afferent pressure of 5.0 ± 1.5 (SD) mmHg compared to no gel. However, this was transient and fully resolved by 9 hours. ASA and BSA were successfully loaded into chitosan gels and perfusion with saline elicited a delayed release of ASA/BSA.

Conclusions: Chitosan/ β -gp hydrogels solidify at eye-surface temperatures or higher, are biocompatible with ocular fibroblasts, do not substantially affect outflow capacity, and can be loaded with small molecules or proteins to act as a delayed-release drug depot. These properties support the potential subconjunctival injection of ThermoGel to provide sustained drug-release and structural support for the bleb.

CONTROL ID: 3545226

SUBMITTER (NAME ONLY): Leopold Schmetterer

TITLE: Compensation of anatomical confounders improves the diagnostic ability of retinal nerve fiber layer thickness to detect glaucoma

SESSION TITLE: Imaging in Glaucoma I: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Schmetterer, D. Wong, C. Cheng, T. Aung, J. Chua, Singapore Eye Research Institute, Singapore, SINGAPORE|L. Schmetterer, D. Wong, Nanyang Technological University, Singapore, Singapore, SINGAPORE|F. Schwarzhans, G. Fischer, C. Vass, Medizinische Universität Wien, Wien, Wien, AUSTRIA|C. Cheng, T. Aung, J. Chua, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To determine the diagnostic ability of retinal nerve fiber layer (RNFL) thickness to detect glaucoma after compensating the RNFL thickness for demographic and anatomical factors.

Methods: This case-control study enrolled 2699 healthy participants, including Chinese, Indians and Malays to construct an Asian-specific compensation model, which was then tested in 738 eyes without glaucoma and 386 eyes with glaucoma (early, n = 231; moderate, n = 90; and, advanced, n = 65). Participants underwent Cirrus spectral-domain optical coherence tomography (SD-OCT; Carl Zeiss Meditec) imaging of the optic disc and macular cubes. Compensated RNFL thickness was generated based on ethnicity, age, refractive error, optic disc (ratio, orientation and area), fovea (distance and angle), and retinal vessel density. RNFL thickness measurements and their corresponding areas under the receiver operating characteristic curves (AUCs) were obtained.

Results: After applying the Asian-specific compensation model, the standard deviation (SD) of RNFL thickness reduced, where the effect was greatest for Chinese (16.8%), followed by Malays (13.4%) and then Indians (11.7%). Compensated RNFL outperformed measured RNFL for discrimination of early glaucoma (AUC = 0.89 vs 0.85; $P < 0.001$), moderate glaucoma (AUC = 0.94 vs 0.91; $P < 0.001$) and advanced glaucoma (AUC = 0.98 vs 0.96; $P < 0.001$).

Conclusions: Compensated RNFL showed better glaucoma discrimination capability than measured RNFL thickness in a multi-ethnic Asian group. This finding suggests there may be utility in accounting for demographic and anatomical variance in RNFL thickness to improve glaucoma detection.

CONTROL ID: 3545227

SUBMITTER (NAME ONLY): Manuel Chacon

TITLE: Evaluation of ocular irritancy based on cell membrane capacitance on a cruelty-free in vitro corneal model

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Animal testing remains as the gold standard for the evaluation of potential damages on the ocular surface of topical products. Although alternative methods are currently available via in vitro reconstructed epithelia, these methods base its prediction on destructive test. In this study, we use a cruelty-free in vitro corneal model (CFreeCM) previously developed by our laboratory, and analysed the changes in cell membrane capacitance using the Standardized Operational Procedures detailed in OECD TG 492 for identifying chemicals not requiring classification and labelling for eye irritation. Cell membranes display the ultrastructure of a natural capacitor due to the dielectric properties of the phospholipid bilayer, meaning that cell capacitance can be related to the cell membrane integrity which could be altered after chemical exposure and might lead to ocular irritation

Methods: CFreeCMs were prepared from limbal cells isolated from human normal corneoescleral rims discarded after corneal keratoplasty using animal component-free culture media. Limbal cells were cultured on 1.12cm² Transwell insert and differentiated for 7 days under air-lift conditions. Cell membrane capacitance was evaluated using coupled electrodes connected to a EUCOL U2817A Precision LCR Meter prior to chemical exposure at different frequencies (from 50Hz to 100kHz). Next, 26 chemicals (12 irritants and 14 non-irritants) including liquids and solids were applied in duplicates for 30 minutes or 6 hours respectively. After PBS rinse, CFreeCMs were incubated at 37C for 2 hours for liquids or 18 hours for solids. Finally, cell capacitance was evaluated again and cell viability was assessed using the MTT assay

Results: A prediction model was developed based on changes of cell membrane capacitance and compared to standard classification obtained by the MTT assay. Standard classification according to MTT resulted in 91.6% sensibility (11/12), 64.2% specificity (9/14) and 76.9% accuracy (20/26). Cell capacitance prediction model at 1kHz resulted in 91.6% sensibility (11/12), 78.5% sensibility (11/14) and 88% accuracy (22/26)

Conclusions: Although standard classification based on cell viability is in accordance with OECD TG 492 requirements, classification using cell capacitance resulted in higher specificity and overall accuracy, leading to an optimized non-invasive and non-destructive prediction model of ocular irritancy

CONTROL ID: 3545228

SUBMITTER (NAME ONLY): Bonnie He

TITLE: Outcomes of scleral buckle after failed pneumatic retinopexy

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. He, H. Chen, D. Albiani, A. Kirker, A. Merkur, D. Maberley, Z. Mammo, Ophthalmology and Visual Sciences, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: To evaluate the visual and anatomic outcomes of patients who underwent a scleral buckle (SB) as a secondary procedure for failed primary pneumatic retinopexy (PR) in the repair of rhegmatogenous retinal detachments (RRD).

Methods: This is a retrospective, single-center, consecutive case series of patients from 2009 to 2020 with a RRD who failed a primary PR and underwent a secondary SB repair. Patients with at least six months of post-operative follow-up were included in the study. Demographic information, pre-operative characteristics, parameters of the failed PR, parameters of the subsequent SB procedure, and serial optical coherence tomography (OCT) imaging data were recorded. The data was analyzed using ANOVA with statistical significance level set at 0.05.

Results: A total of 57 patients (59.7% male, mean age of 47 ± 15 years old) were included in our study, with a mean follow-up was 48.6 ± 31.8 months. 26 right eyes and 31 left eyes were identified, and all eyes were phakic. The mean total number of clock hours in the initial RRD was 4.1 ± 1.6 , and 45.6% of patients had macula-off RRD, with over 36% having more than one retinal break. The average time to PR failure was 7.6 ± 11.2 days, and 61% had the secondary SB procedure within a week. Visual acuity (VA) in (LogMar [Snellen equivalent]) at presentation (0.72 ± 0.82 [20/70]) and at time of PR failure (0.51 ± 0.47 [20/65]) were not significantly different ($p=0.487$).

At six months post-SB repair, VA was (0.42 ± 0.37 [20/53]). VA at twelve months and at final follow-up were (0.35 ± 0.34 [20/45]) and (0.27 ± 0.30 [20/37]) respectively, both of which were significantly better than the initial visual acuity ($p=0.032$ and $p=0.002$, respectively). Thirteen patients (13/57, 23%) required at least one additional surgery. Reasons for additional surgery included: non-resolving subretinal fluid on serial OCT (6/13, 46.1%), new breaks (5/13, 38.5%) or proliferative vitreoretinopathy (2/13, 15.4%). The average time to secondary surgery was $84. \pm 201$ days.

Conclusions: Among phakic patients who fail PR for RRD, SB remains a viable alternative with acceptable anatomical and functional outcomes at six months and one year follow-up respectively.

CONTROL ID: 3545232

SUBMITTER (NAME ONLY): Thanadet Chuangsuwanich

TITLE: Adduction Induces Large Anterior Displacement of the Pre-lamina Tissue in Normal Tension Glaucoma Subjects

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Chuangsuwanich, T. Aung Tin, D. Milea, T. Aung, M.J. Girard, Singapore Eye Research Institute, Singapore, SINGAPORE|T. Chuangsuwanich, Biomedical Engineering, National University of Singapore, Singapore, SINGAPORE|X. Wang, School of Biological Science and Medical Engineering, Beihang University, Beijing Advanced Innovation Center for Biomedical Engineering, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: To assess the changes in anterior prelaminar depth (PLD) following adduction, abduction and IOP elevation in high tension glaucoma (HTG), normal tension glaucoma (NTG), and ocular hypertensive (OHT) subjects.

Methods: We recruited 221 subjects (Chinese ethnicity and more than 60 years old) which comprised of 93 HTG, 87 NTG, and 41 OHT subjects. For each subject, we imaged the ONH using Spectral-domain optical coherence tomography (OCT) under the following conditions: (1) primary gaze, (2) 20° adduction, (3) 20° abduction and (4) primary gaze with acute IOP elevation (to ~40 mmHg) achieved through ophthalmodynamometry. For each OCT volume, we automatically segmented the prelaminar tissue (PLT) using deep learning. We calculated the PLD for each volume with respect to the Bruch's membrane opening (BMO) reference plane and calculated the change in PLD of each subject under loads (2)-(4) with respect to the baseline primary gaze (1).

Results: Under IOP elevation, we observed an increase in PLD (posterior displacement) with an average change of (+12.8 ± 30.1 micron) across all subjects (Figure 1). Additionally, we found that PLD of HTG eyes were significantly more sensitive to IOP elevation (+17.24 ± 29.2 microns) as compared to PLD of NTG eyes (+7.4 ± 28.8 microns, p<0.05, Figure 2a) and OHT eyes (+7.9 ± 35.3 micron, p<0.1). Under adduction, we observed a decrease in PLD (anterior displacement) with an average change of (-15.5 ± 32.3 micron) across all subjects (Figure 1). Additionally, we found that PLD of NTG and OHT eyes were more sensitive to adduction (NTG: -18.8 ± 38.2 micron, OHT: -15.0 ± 40.3 micron) as compared to PLD of HTG eyes (-8.0 ± 29.8 micron, p<0.05, Figure 2b). Abduction did not result in significant changes in PLD (Figure 1).

Conclusions: Using PLD changes as the mode of measurement, we found that NTG and OHT subjects were more sensitive to adduction as compared to IOP elevation and HTG subjects were more sensitive to IOP elevation as compared to adduction. These preliminary results could provide clues to the different pathophysiology of between NTG and HTG which warrants further investigation.

CONTROL ID: 3545233

SUBMITTER (NAME ONLY): Carol Cheung

TITLE: A Multi-Task Deep-Learning System to Classify Diabetic Macular Edema for Different Optical Coherence Tomography Devices: A Multi-Center Analysis

SESSION TITLE: Deep learning for classification and segmentation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.Y. Cheung, F. Tang, A. Ran, Ophthalmology and Visual Sciences, The Chinese University of Hong Kong Faculty of Medicine, Hong Kong, HONG KONG|G. Tan, D.S. Ting, T.Y. Wong, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|H. Chen, Joint Shantou International Eye Center of Shantou University and The Chinese University of Hong Kong, Shantou, Guangdong, CHINA|H. Ma, S. Tang, Aier School of Ophthalmology, CHINA|T. Leng, S. Kakavand, S.S. Mannil, R. Chang, Byers Eye Institute at Stanford, Stanford University, Stanford, California, UNITED STATES|G. Liew, Department of Ophthalmology, Westmead Institute for Medical Research, University of Sydney, New South Wales, AUSTRALIA|B. Gopinath, Macquarie University Hearing, Department of Linguistics, Macquarie University, New South Wales, AUSTRALIA|X. Wang, Computer Science and Engineering, The Chinese University of Hong Kong Faculty of Engineering, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Diabetic macular edema (DME) is the primary cause of irreversible vision loss among individuals with diabetes mellitus (DM). We developed, validated, and tested a deep-learning (DL) system for classifying DME and for retinal abnormalities other than DME simultaneously using images from three common commercially available optical coherence tomography (OCT) devices.

Methods: We trained and validated two versions of a multi-task network, one based on three-dimensional (3D) ResNet-34 and another based on two-dimensional (2D) ResNet-18, to classify DME (center-involved DME [CI-DME], non-CI-DME, or absence of DME) and other retinal abnormalities (their presence or absence) using 3D volume-scans and 2D B-scans respectively. A total of 73,746 OCT images, representing 2,444 eyes from 1,238 subjects with DM, were used for training and primary validation. These images include 3,788 3D volume-scans from Cirrus OCT, 30,515 2D B-scans from Spectralis OCT, and 39,443 2D B-scans from Triton OCT. External testing was performed using 3,218 volume-scans from Cirrus OCT, 18,295 B-scans from Spectralis OCT, and 5,468 B-scans from Triton OCT across seven independent datasets under different clinical settings.

Results: In classifying the presence or absence of DME, the DL system achieved AUROCs of 0.937 (95% CI 0.920–0.954), 0.958 (0.930–0.977), and 0.965 (0.948–0.977) for primary datasets obtained from Cirrus, Spectralis, and Triton OCTs respectively, in addition to AUROCs greater than 0.906 for the external datasets. For the further classification of the CI-DME and non-CI-DME subgroups, the AUROCs were 0.968 (0.940–0.995), 0.951 (0.898–0.982), and 0.975 (0.947–0.991) for the primary datasets and greater than 0.894 for the external datasets. In classifying the presence or absence of other retinal abnormalities, the AUROCs were 0.948 (0.930–0.963) 0.949 (0.901–0.996), and 0.938 (0.915–0.960) among images obtained from the Cirrus, Spectralis, and Triton OCTs, respectively, in primary datasets. The performance in external datasets remained excellent, with the ranges for AUROCs being 0.901–0.969.

Conclusions: We demonstrated excellent performance with a DL system for the automated classification of DME, highlighting its potential as a promising second-line screening tool for patients with DM, which will create a more effective triaging mechanism to tertiary eye clinics.

CONTROL ID: 3545234

SUBMITTER (NAME ONLY): Ioannis Pallikaris

TITLE: Intraocular Lens Stabilisation with a novel implant: Our experience with a cohort of 72 patients

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Pallikaris, O. Sahin, L. Leonidou, H.S. Ginis, EYEPCR BV, NETHERLANDS|I. Pallikaris, O. Sahin, D. Liakopoulos, School of Medicine, Panepistemio Kretes, Rethimno, Crete, GREECE|A. Elmassry, Medicine, Alexandria University, Alexandria, EGYPT|

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ABSTRACT BODY:

Purpose: To analyze postoperative refraction and postoperative anterior chamber depth (pACD) in a cohort of patients implanted with the fixOflex intraocular ring in conjunction with a monofocal intraocular lens (IOL). Moreover, to analyze the intraoperative time for the ring implantation and to report on the intraoperative complications.

Methods: The fix-O-flex (EYE-PCR B.V, The Netherlands) intracapsular ring is implanted prior to the intraocular lens to facilitate its centration while maintaining the anatomical shape of the peripheral capsule. It has an external diameter of 9.8 mm, axial thickness of 1.7mm and retainers to fasten the optical part of the IOL. In a prospective clinical trial to assess the safety and efficacy of the fix-O-flex ring, seventy two (72) patients were randomly enrolled. Patients were selected randomly from the patients that presented with cataract at the Elnour Eye Center (Alexandria, Egypt). An informed consent was obtained from all patients. The patients received the ring through a 2.4 mm incision and the IOL (Tecnis ZCB00, J&J, NJ) was implanted after the ring had expanded in the capsule and its optical part was secured in the ring's retainers. Both the IOL calculation (Haigis formula) and postoperative lens position (pACD) were obtained from the Lenstar 900 optical biometer (Haag Streit AG, Germany). Patients were followed at the 1 day, 1 week, 1, 3, 6 and 12 months postoperatively. We report on the interim results following the 1-month postoperative follow up.

Results: Mean Best Spectacle corrected Visual Acuity at the 1-month postoperative interval was 0.82 (SD 0.18). Mean spherical equivalent refraction was -0.94D (SD 0.88). Mean pACD was 4.65 mm (SD 0.73). The difference between pACD at 1 month and day 1 was not statistically significant ($p=0.021$) indicating a stable postoperative lens position. Mean time duration for ring implantation was 1.29 minutes (SD 0.31) (1min 17 sec). In 5 patients (6.9%) the ring required additional manipulations for centration after injection. In one case the IOL was implanted behind the ring. No serious adverse events were reported.

Conclusions: The Fix-o-flex ring provides an open capsule space for IOL implantation. Biometry and refraction were stable postoperatively. Implantation was fast and safe. Intraoperative complications involved the position of the ring and the IOL after implantation and were controlled by surgical manipulations.

CONTROL ID: 3545236

SUBMITTER (NAME ONLY): Soyoung Choi

TITLE: Automated Characterisation of Retinal Microglia in a Multiple Sclerosis Mouse Model and Age-Matched Controls

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Choi, D. Hill, L. Guo, V. Luong, M. Cordeiro, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|R. Nicholas, Institute of Ophthalmology, Imperial College London, London, London, UNITED KINGDOM|M. Cordeiro, Imperial College Ophthalmology Research Group, Imperial College London, London, London, UNITED KINGDOM|D. Papadopoulos, Laboratory of Molecular Genetics, Hellenic Pasteur Institute, Athens, GREECE|

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ABSTRACT BODY:

Purpose: A common hallmark of Multiple Sclerosis (MS) is the thinning of retinal layers that contain retinal microglia. Microglia are the immune cells of the central nervous system which carry out their dynamic age- and disease-related neuromodulatory functions by dynamically shifting between five distinctive morphotypes (ramified, hyper-ramified, activated, rod and amoeboid). Here, we sought to develop automated algorithms to identify differences in the total and distinct microglia morphotype densities between experimental MS induced by cuprizone (CPZ) treatment, and untreated controls.

Methods: The MS-modelled male C57 mice were given CPZ (0.2%w/w) mixed with chow for 4 months (m) until their sacrifice at 6m or 28m. Age-matched controls (Ctrl) were fed standard chow. Post-sacrifice, mouse eyes were enucleated, the retinas dissected, immunostained, whole-mounted and then imaged. Automated cell counting and morphotyping methods including supervised machine learning algorithms (SVM-C) were developed to quantify densitometric differences. Non-parametric statistical analyses were performed on the collected data (n: 6mCPZ=7; 6mCtrl=15; 28mCPZ=10; 28mCtrl=7).

Results: The SVM-C produced performance accuracies of 87.9-100% for each morphotype with AUC >0.99. Experimental groups did not significantly affect the total retinal microglia densities. However, there were more ramified ($p<0.05$) and amoeboid (ns) cells in old diseased (28mCPZ) retinas compared to young diseased (6mCPZ) and old healthy (28mCtrl) retinas. Also, there were significantly more rod microglia ($p<0.01$) in young animals (6mCtrl and 6mCPZ) compared to old animals (28mCtrl and 28mCPZ). There were no significant differences between the densities of young animal groups whilst there were between the old, with significantly less activated, hyper-ramified and rod cells ($p<0.05$) in 28mCPZ.

Conclusions: The SVM-C worked with a high accuracy and discriminative power. No differences in the total densities suggest that age- and CPZ-induced morphotype density differences might occur as a result of morphological changes rather than proliferation. The current study did not investigate the functional associations, although ramified and amoeboid morphotype trends may suggest increases in debris detection and phagocytosis with the increase of age and CPZ-induced experimental MS.

CONTROL ID: 3545237

SUBMITTER (NAME ONLY): Kseniya Palchunova

TITLE: Relationship between OCT retinal shape and peripheral refractive error.

SESSION TITLE: Refractive Error, Emmetropization and Ocular Development

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To study the relationship between the retinal shape measured using OCT and the off-axis refractive error in adults.

Methods: A prospective clinical study was performed including the 32 eyes of 16 adult subjects at the age of 23-62 years old (age 39.00 ± 13.22 ; mean \pm SD, SE = -3.15 ± 2.38 D) have been examined using an OCT with auto-alignment (3D-OCT-1 Maestro, Topcon, Tokyo) and retinal shape modeling (prototype software, Topcon, Tokyo) functions. The RPE position in horizontal 12mm scans centered on the fovea was used to represent retinal shape after alignment correction considering corneal curvature, axial length, and eye movement. The off-axis refraction data were obtained from an open-view auto refractometer (Grand Seiko, Japan) by measurements from 5 angles in the horizontal plane (-30° , -15° , 0° , 15° , 30°). Both retinal shape profiles and the refraction levels were then fitted into curves, and the first order (slope) and the second order (curvature) coefficients were used for the analysis.

Results: We found strong correlations between the slopes of left and right eye in the OCT retinal shape data between left and right eye in slopes (CC = -0.903 p-value < 0.001), in curvatures (CC = 0.893 , p-value < 0.001). In the off-axis refraction data fitting the slopes (CC = -0.511 , p-value = 0.061) relation was not significant, while curvatures (CC = 0.736 , p-value = 0.003) correlated strong between left and right eyes, conforming the expected properties. In relations between the retinal shape model and the levels of refraction fitting we discovered significant correlations of the curvatures in the right eyes (CC = 0.657 , p-value = 0.045) and the left (CC = 0.774 , p-value = 0.001).

Conclusions: Both OCT retinal shape model fitting and off-axis refraction error fitting confirm the expected properties, such as contralateral reflective symmetry in slopes and symmetry in the curvatures, therefore confirming the accuracy of the measurements. Significant correlations between two models in the curvatures allow us to assume that the OCT retinal shape can be used for the assessment of the off-axis refraction.

CONTROL ID: 3545240

SUBMITTER (NAME ONLY): Uwe Hansen

TITLE: Organization of lamellae in the corneal stroma: Mouse models for better understanding of the pathomechanism of keratoconus

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Hansen, M. Timmen, R. Stange, T. Pap, Institute for Musculoskeletal Medicine, University Hospital Munster, Universitätsklinikum Munster, Munster, Nordrhein-Westfalen, DE, academic/hospital, Muenster, GERMANY|M. Schannne-Klein, M. Schmeltz, C. Raoux, M. Bied, G. Latour, Laboratory for Optics and Biosciences, Ecole Polytechnique, Palaiseau, Île-de-France, FRANCE|G. Latour, Université Paris-Saclay, Saint-Aubin, Île-de-France, FRANCE|M. Goette, Department for Gynaecology and Obstetrics, University Hospital Munster, Universitätsklinikum Munster, Munster, Nordrhein-Westfalen, DE, academic/hospital, Muenster, GERMANY|N. Eter, M. Alnawaiseh, Department for Ophthalmology, University Hospital Munster, Universitätsklinikum Munster, Munster, Nordrhein-Westfalen, DE, academic/hospital, Muenster, GERMANY|

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ABSTRACT BODY:

Purpose: In keratoconus (KC), structural and compositional changes lead to disruptions of the lamellar organization with thinning and scarring of the cornea. Both genetic and environmental factors have been associated with KC and recent studies suggest that inflammation (e.g. high TNF α levels) could trigger the onset of KC. Therefore, we analyzed human corneas as well as corneas of hTNFtg mice and syndecan-1 and -4 deficient mice.

Methods: Human and mouse corneas were analyzed by TEM and stromal collagen degradation was visualized by the collagen hybridizing peptide B-CHP. Moreover, 3D-cell cultures of human keratocytes were analyzed by TEM and for activity of the cross-linking enzyme tissue transglutaminase (TG). Furthermore, collagenous structures of healthy and KC corneas were analyzed by P-SHG microscopy and OCT analysis was used for 3D imaging of hTNFtg and wt corneas.

Results: Sheets of orthogonally arranged collagen fibrils were found in the stroma of wt mice and human controls. In contrast, lamellae were disrupted and fibril diameter increased in hTNFtg and in both syndecan-deficient mice. Interestingly, stromal morphology of hTNFtg mice was similar to that of KC patients. We found an invasion of macrophages and apoptotic keratocytes. 3D-cell cultures of KC keratocytes generated a structurally altered ECM with reduced TG-activity. Moreover, binding of B-CHP was significantly stronger in KC and hTNFtg mice. In addition, OCT analysis revealed a slightly altered shape of the cornea of hTNFtg mice. Alterations in the Bowman's membrane together with disrupted cell-cell-contacts were found in all mouse models. P-SHG analysis revealed changes in lamellae orientation in KC. The entropy was higher and the orientation index was lower demonstrating a disorganization of stromal lamellae compared to controls.

Conclusions: Disruptions of the lamellar organization of collagen fibrils in hTNFtg and syndecan-1 and -4 deficient mice are similar to KC patients. Thus, inflammation and altered cross-links could be crucial factors for the onset of KC. The strong binding of B-CHP supports our hypothesis of enhanced collagen degradation in the stroma. Thus, hTNFtg mice as model for KC will help to better understand the pathomechanism of KC and P-SHG analysis provides new parameters for characterization of lamellar changes in KC.

CONTROL ID: 3545241

SUBMITTER (NAME ONLY): Hartmut Schwahn

TITLE: Therapeutic Effects of Low-Dose Atropine on Myopia Progression in a Real-Life Clinical Setting in Germany

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Schwahn, B. Graff, H. Kaymak, I.I.O. Breyer Kaymak Klabe, Düsseldorf, GERMANY|F. Schaeffel, Institute for Ophthalmic Research, Eberhard-Karls-Universität Tübingen Medizinische Fakultät, Tübingen, GERMANY|H. Kaymak, Experimental Ophthalmology, Universitätsklinikum des Saarlandes und Medizinische Fakultät der Universität des Saarlandes, Homburg/Saar, Saarland, GERMANY|

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ABSTRACT BODY:

Purpose: Several randomized clinical studies (RCTs) have demonstrated the beneficial effects of low dose (0.01%) atropine eye drops on myopia progression in children. However, treatment effects may be different in a routine clinical setting.

Methods: We performed a retrospective analysis of our clinical data from 80 atropine treated and 103 untreated children of white population in Germany with a wide range of myopic refractive errors and ages. Objective refraction and ocular biometry (anterior chamber depth, lens thickness, axial length) were determined at the initial and at later visits. As requested by the parents, children in the treatment group were asked to instill one drop of 0.01% atropine solution in each eye every evening at five days a week. Myopic children who did not undergo atropine treatment served as controls. All children were re-examined about one year later.

Results: Myopic refractions (spherical equivalents) at baseline ranged from -0.625 to -15.25 D (-4.21 ± 2.90 D) in atropine treated children and from -0.125 to -9.375 D (-2.92 ± 1.77 D) in untreated children. Ages at the initial visits ranged from 3.2 to 15.5 years (10.1 ± 2.7 years) in the treated group and from 3.4 to 15.5 years (11.2 ± 3.0 years) in the untreated group. Myopia progression continued in both atropine treated and untreated children. Variability of progression rates was high. A two-factor ANOVA for age and atropine effects on axial length growth confirmed that eye growth rates generally declined with age ($p < 0.0001$). Atropine had a significant inhibitory effect on axial eye growth ($p < 0.0015$) which was independent of age. On average we observed 0.08 mm inhibition per year, equivalent to 28% less compared to average growth rate in untreated children. Interestingly, effects of atropine on refractive states were not significant.

Conclusions: In this real-life clinical setting, the effects of 0.01% atropine were not very distinctive. Myopic progression in individuals did not show obvious differences between atropine treated and untreated children. A statistical analysis over the whole sample confirmed that atropine reduced axial length growth, but to an extent which is of minor clinical relevance. Under the given conditions, the beneficial effects of 0.01% atropine eye drops on myopia may not be obvious in each single child which should be communicated to parents and residents.

CONTROL ID: 3545243

SUBMITTER (NAME ONLY): Bo Lei

TITLE: Autosomal recessive rod-cone dystrophy associated with compound heterozygous variants in ARL3 gene

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Fu, Ophthalmology, Henan University People's Hospital, Zhengzhou, Henan, CHINA|

B. Lei, Ophthalmology, Henan Provincial People's Hospital, ZHENGZHOU, Henan, CHINA|

Commercial Relationships Disclosure (Abstract): Bo Lei: Commercial Relationship: Code N (No Commercial Relationship) | Leming Fu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: ARL3 (ADP-ribosylation factor-like 3) variants cause autosomal dominant retinitis pigmentosa or autosomal recessive Joubert syndrome. A recent report showed a homozygous variant in ARL3 caused cone-rod dystrophy. We found a family with rod-cone dystrophy and confirmed it was associated with compound heterozygous variants in ARL3 gene.

Methods: Ophthalmic examinations including optical coherence tomography and electroretinogram (ERG) were performed in the 18-year-old male proband and the family members. DNA was extracted from peripheral blood. Targeted next generation sequencing (NGS) was performed for the proband using a custom designed panel containing genes associated with inherited retinal diseases. Sanger sequencing and co-segregation were conducted in the family members. The pathogenic prediction was performed with ACMG guideline. Changes of protein structure mediated by the variants were studied in vitro. ARL3 protein stability and its interaction with RP2 protein were assessed by cycloheximide chase assay and co-immunoprecipitation (Co-IP) assay.

Results: Visual acuity of the proband was 0.25 in the right and 0.20 in the left eye, while his mother and sister was normal. Fundus photography showed peripheral bone spicule pigmentation and ERG revealed severe reduction in scotopic responses and to less extent in photopic responses bilaterally. The proband also had tunnel visual field and dyserythrochloropsia. But he did not have hearing abnormality, mental dysplasia or gait instability. Targeted NGS identified two novel compound heterozygous variants (c.91A>G, p.T31A; c.353G>T, p.C118F) in ARL3. Bioinformatics analysis indicated that the amino acid positions of the two variants are highly conserved among species. LRT, Mutation Taster, SIFT, FATHMM and CADD predicted the variants to be harmful. Protein structure analysis showed the two variants had potential to alter the protein structure. According to the ACMG guidelines, the two variants were likely pathogenic, supported by evidences: PS2, PM1, PM2, PP1 and PP3. In addition, the ARL3 mutations destabilized ARL3 protein, and disrupted the interaction between ARL3 and RP2 in HEK293T cells.

Conclusions: We showed two novel compound heterozygous variants in ARL3 were associated with autosomal recessive rod-cone dystrophy. The two variants in ARL3 could be causative by destabilizing ARL3 protein and impairing its interaction with RP2 protein.

CONTROL ID: 3545247

SUBMITTER (NAME ONLY): Alex Goldbach

TITLE: Visual field measurements using Heru Visual Field Multi-platform application downloaded on two different commercially available augmented reality devices

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.H. Goldbach, M. Abou Shousha, C. Duque, R. Kashem, F. Mohder, A.R. Shaheen, S. Bonyadi, M. Sharma, W.J. Feuer, R. Parrish, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: 1- To evaluate the comparability of visual field measurements between Heru visual field application (Heru, Miami, FL) as a multiplatform visual field-testing application downloaded on two different commercially available augmented reality devices and the standard automated perimetry in both normal patients and those with visual field defects. 2- Evaluate the reproducibility of Heru VF measurements in normal and pathologic patients.

Methods: This prospective comparative clinical study included 81 eyes, 40 normal eyes and 41 eyes of patients with glaucoma and neuro-ophthalmic diseases (hemianopic, altitudinal and ring scotomas). VF results were obtained using Heru VF software downloaded on Magic Leap 1 (Magic Leap, Plantation, FL; 41 eyes) headset, on Hololens 2 (Microsoft Inc, Redmond, WA; 40 eyes) and Humphrey Field Analyzer (HFA) 800 series perimeter (Carl Zeiss Meditec, Inc, Dublin, CA, USA; 81 eyes). All patients underwent 24-2 test pattern with all 3 testing devices. Correlations of threshold values and mean deviations (MD) obtained using Heru VF and HFA were calculated to determine agreements between them. To evaluate the reproducibility of Heru VF, 39 eyes (27 normal and 12 pathological eyes) were tested twice on the same day with 5-minutes in between, and the intraclass correlation coefficient was calculated.

Results: Mean deviation (MD) and Threshold values obtained using Heru VF software application downloaded on the two different platforms showed strong correlations with those of Humphrey Field Analyzer (HFA) ($R=0.91$ and $R=0.8$, $P < 0.001$, respectively). The Heru VF software was reproducible with ICC of 0.974 (95%CI 0.94-0.987) for MD and 0.8 (95%CI 0.813-0.845) for threshold values in normal eyes and in patients with glaucoma and neuro-ophthalmic diseases.

Conclusions: Central visual field measurements obtained using Heru VF as a multi-platform application downloaded on two different commercially available augmented reality devices were comparable to HFA in normal, glaucoma, and neuro-ophthalmology patients. Heru VF measurements are reproducible in normal and pathologic patients.

CONTROL ID: 3545248

SUBMITTER (NAME ONLY): Sue Fletcher

TITLE: RNA therapeutics in the treatment of retinal disease - delivering the potential

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Fletcher, C. Hall, M. Anastasas, A. Martin, T. Chai, K. Priebatsch, A. Stirnweiss, R.W. Francis, S.M. Juraja, A.D. Mills, F. Ong, L. Florez, M. Kerfoot, J. Nicholls, D. Champain, P. Cunningham, PYC Therapeutics, Nedlands, Western Australia, AUSTRALIA|S. Fletcher, Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Murdoch, Western Australia, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Treatment options for inherited retinal diseases (IRD), the leading cause of vision loss in persons aged 15 - 45 years have been limited, however, novel gene and molecular therapeutics are now demonstrating significant potential in the treatment of IRDs. RNA therapeutics hold unique promise in these diseases; although achieving safe and efficient delivery of molecular drugs to the retina and the retinal pigmented epithelium in particular, remains a significant obstacle to clinical application. Antisense oligomers (AO) are a well-established class of RNA therapeutic whose potential is yet to be fully realised due to this delivery challenge. We report an AO conjugate that traffics through the vitreous after intravitreal administration, reaching the deepest layers of the retina and localising to the nuclei to modulate gene expression. This class of therapeutic holds substantial promise in the treatment of IRDs.

Methods: We exploit peptide libraries derived from 82 microorganism genomes and 118 synthetic viral genes to identify cell penetrating peptides (CPP) to deliver AO cargos to cells in vitro and to tissues and organs in vivo. The CPPs were screened initially against mammalian cells using a cytosolic extraction method, followed by next generation sequencing and selection using a combination of algorithms known to produce a favourable toxicology and efficacy profile in the eye.

Results: The CPPs were conjugated to an antisense morpholino oligomer designed to mediate exon selection in a reporter mRNA. Standout performance in the latter assay, when administered via intravitreal injection, and a clean toxicology profile identified a lead peptide for our retinal disease program. CPP conjugation to our candidate AO therapeutic and evaluation in IRD patient-derived retinal pigmented epithelium rescued target gene expression and improved cell function.

Conclusions: Notable CPPs in pre-clinical and clinical development include chemical stabilisation or poly-arginine that can limit efficacy or increase toxicity. Our discovery peptides are derived from nature, lack chemical modifications, and yield optimal amino acid sequences with enhanced efficacy and toxicity performance. The lead CPP, HPG_0031, traffics the AO through the vitreous, into the retinal pigment epithelium with no evidence of retinal damage, resulting in enhanced exon skipping and 6-fold lower cytotoxicity than the competitor CPP.

CONTROL ID: 3545250

SUBMITTER (NAME ONLY): Josselin Gautier

TITLE: Measurement of retinal sensitivity and directionality in myopes with modified microperimetry and multimodal imaging approach

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Gautier, K. Grieve, M. Paques, Paris Eye Imaging, INSERM, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Nasal misalignment of cones toward the optic nerve head (ONH) in myopic eyes is believed to be associated with the greater length of the eyeball. However, both physiological explanations at the retinal level and functional evaluation of the practical, visual impact of this photoreceptor misalignment in the daily lives of myopic individuals are limited.

Methods: We developed two microperimetry multi-angle methods to measure the peak location and directionality known as the Stiles Crawford Effect type I (SCE-I). A clinical grade MAIA microperimeter presented Maxwellian-view background and test (Goldman size III) stimuli at various eccentricities, while compensating for eye movements. SCE-I functions were obtained from directional sensitivity measurements, either by controlled translation of the instrument or rotation of the eye, without and with background illumination, respectively. Displacement of the peak of the SCE-I function was compared to objective measurement of foveal axis alignment in relation to pupil entry point with Directional OCT.

Results: Myopic subjects (N = 4) unlike emmetropes (N=3) appeared to show irregular nasal contrast sensitivity, and nasal misalignment of the SCE-I peak toward the ONH. SCE-I functions were corroborated by directional OCT based foveal axis measurements.

Conclusions: The methods described here provide a rather fast and accessible way to measure photoreceptor alignment at various retinal locations, which could be important to characterize - and potentially better treat - functional visual losses experienced by individuals with myopia. Our next step will be to determine alignment of individual photoreceptors using high resolution imaging modalities.

CONTROL ID: 3545257

SUBMITTER (NAME ONLY): Juleke Majoor

TITLE: Comparing test-retest variability of Compass perimetry with the Humphrey Field Analyzer at the edges of glaucomatous scotomas.

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Majoor, K.A. Vermeer, H.G. Lemij, Het Rotterdams Oogheelkundig Instituut, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The commonly used Humphrey Field Analyser (HFA) shows high measurement variability in glaucoma patients, notably at the borders of scotomas, making it difficult to determine if a scotoma is stable or shows progression. It has previously been suggested that this variability may in part be due to gaze instability. By using an eye tracker that compensates for gaze instability, the Compass fundus perimeter (CMP) might lower the variability at scotoma borders. We therefore aimed to determine the test-retest variability of the CMP at the edges of glaucomatous scotomas and compare it with that of the HFA.

Methods: One eye from each included glaucoma patient was tested with the CMP (24-2 ZEST) and the HFA (24-2 SITA standard) at each of three study days (screening, baseline and follow-up visit) and stratified by mean deviation (MD) into a mild ($-6 \text{ dB} \leq \text{MD}$), moderate ($-12 \text{ dB} \leq \text{MD} < -6 \text{ dB}$) or advanced glaucoma stage ($\text{MD} < -12 \text{ dB}$). Two CMP VF tests were performed at the screening visit for learning purposes. To identify the scotoma borders for each eye, the total deviation plot of the HFA test from the screening visit was used (Figure 1). To assess test-retest variability, the mean absolute difference of the scotoma border points (SBP, i.e., the test points on either side of the scotoma edges) between the baseline and follow-up VF test (3-10 days between tests) was calculated.

Results: 29 eyes (31% women, median (IQR) age 64 (56-72) years) were included for analysis. Median (IQR) time between baseline and follow-up visit was 7 (5-7) days. There were no statistically significant differences in mean absolute SBP difference between the CMP and HFA for all stages combined (1.8 vs 1.9 dB, $P = 0.42$, Wilcoxon signed ranks test) nor for each glaucoma stage separately (mild: 1.6 vs 1.7 dB, $P = 0.70$, moderate: 1.8 vs 1.9 dB, $P = 0.55$, advanced: 1.9 vs 2.2 dB, $P = 0.051$, Wilcoxon signed ranks test). Figure 2 shows a scatter and density plot of the absolute SBP differences between CMP and HFA.

Conclusions: CMP and HFA are equally variable at the edges of scotomas with 24-2 VF testing, suggesting that fixation stability with the CMP eye tracker has no advantage over the HFA for detecting progressing scotomas in glaucoma patients by 24-2 VF testing. Studies are warranted to further evaluate the added value of fixation stability on lowering VF test-retest variability in glaucoma patients.

CONTROL ID: 3545261

SUBMITTER (NAME ONLY): David Li

TITLE: CREB Positively Regulates Multiple Acetylation Transferases to Control p53-Bak/Bax Signal Axis and Mediate Stress-Induced Apoptosis

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.W. Li, L. Wang, Y. Gan, Y. Liu, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou City, Guangdong Province, CHINA|

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ABSTRACT BODY:

Purpose: The general transcription factor, CREB has been shown to play an essential role in promoting cell proliferation, neuronal survival and synaptic plasticity in the nervous system. However, its function in stress response remains to be elusive. Here, we present first evidence to show that CREB can positively regulates multiple acetylation transferase to activate p53-Bak/Bax signal axis and mediate stress-induced apoptosis of lens epithelial cells.

Methods: RNA-seq, qRT-PCR, automated western immunoblotting, classic western blot analysis and immunocytochemistry were used to analyze expression patterns of the genes including CREB, p53, Bax, Bak, p300, Gcn5 and Pcaf, Co-IP and immunocytochemistry were used to determine protein-protein interaction. CRISPR/Cas9 technology was used to knockout gene function, Over-expressing vector was used to analyze the effect of gene dose. Gel mobility shifting (EMSA) and ChIP assay were used to determine the CREB control of the acetylation transferases p300, Gcn5 and Pcaf. CellTiter-Glo® luminescent cell viability assay and live/dead viability/cytotoxicity were used to examine apoptosis.

Results: EMSA and ChIP assays reveal that CREB directly controls expression of p300, Gcn5 and Pcaf genes in lens epithelial cells, which enhanced the transcriptional activities of p53. The enhanced p53 activity upregulates two downstream genes: Bax and Bak to mediate CREB-controlled stress response and promotes apoptosis of lens epithelial cells. Dephosphorylation of CREB significantly downregulates its ability to control the above acetylation transferase genes, and as a result attenuates CREB-mediated stress response.

Conclusions: CREB, an important transcription factor mediates stress response in the ocular lens through two major pathways: negative regulation of α B-crystallin but positive regulation of p300/Gcn5/Pcaf-p53 signal axis. This function is important in ensuring normal lens development (Supported by grants from National Natural Science Foundation of China, 81770910, 81970787, 81700821, 81970784, 81900842), the grant from Guangdong province (2019B1515120014) and the Fundamental Funds from the State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University (3030901010110).

CONTROL ID: 3545262

SUBMITTER (NAME ONLY): Hyeonhee Roh

TITLE: Neural information of artificial vision varies depending on the level of spiking heterogeneity across retinal ganglion cells

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Roh, E. Kim, S. Chung, J. Kang, T. Kim, M. Im, Brain Science Institute, Korea Institute of Science and Technology, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|H. Roh, Division of Electrical Engineering, Korea University, Seongbuk-gu, Seoul, KOREA (THE REPUBLIC OF)|E. Kim, Department of Electronic and IT Media Engineering, Seoul National University of Science and Technology, Nowon-gu, Seoul, KOREA (THE REPUBLIC OF)|S. Chung, Department of Mechanical and Biomedical Engineering, Ewha Womans University, Seoul, KOREA (THE REPUBLIC OF)|M. Im, Division of Bio-Medical Science & Technology, University of Science and Technology, Seoul, Seongbuk-gu, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Retinal prostheses electrically activate surviving retinal ganglion cells (RGCs) to create artificial vision. Given the incredible neural information transmission from the retina during natural viewing, it is critical to consider how much information RGCs would carry for the prosthetic vision. Recently, we reported ON RGCs transmit richer neural information than OFF RGCs by more heterogeneous spiking responses arising from the same electric stimulus. Here, we quantified neural information changes depending on the levels of heterogeneity across simulated spike trains.

Methods: We used neural computational methods to generate correlated spike trains and calculate the amount of information of those simulated spiking activities. First, we created five groups of 1-sec-long spike trains using a modified version of 'Brian 2', an open-source simulator for spiking neural networks. All groups had the same range of mean firing rate (80 ± 20 Hz) and peak firing rate (200 ± 50 Hz) but different levels of correlations across spike trains in each group. Second, 50 spike trains were randomly chosen until their spike time tiling coefficient (STTC) average reached specific values (i.e., 0.1, 0.3, 0.5, 0.7, and 0.9). Then, the neural information was computed for 200 of random combinations of 15 spike trains.

Results: The average STTCs of the five groups were 0.09 ± 0.07 , 0.31 ± 0.08 , 0.50 ± 0.07 , 0.69 ± 0.06 , and 0.90 ± 0.04 (mean \pm std). The amounts of neural information transmitted by 15 cells of each group were 7.59 ± 0.06 , 7.06 ± 0.09 , 6.14 ± 0.11 , 4.84 ± 0.12 , and 2.33 ± 0.15 bits, respectively. Consistent with our work, more homogeneous spike trains resulted in more reduced information. However, it is notable similar increments in STTCs produced different information reductions. For example, the neural information was slightly decreased by 0.53 bits ($p < 0.001$) for the STTC change from 0.09 to 0.31. In contrast, the information was substantially decreased by 2.51 bits ($p < 0.001$) for the STTC change from 0.69 to 0.90.

Conclusions: Our results showed the level of cell-to-cell spiking heterogeneities significantly impacts on the information transmission: increase in the correlation level leads to decrease in the quantity of neural information. This suggests optimization of spiking correlation in RGC populations may enhance the performance of the prosthetic vision.

CONTROL ID: 3545269

SUBMITTER (NAME ONLY): Daire Hurley

TITLE: Bioenergetics Assessment and ECM gene expression in Glaucoma Lamina Cribrosa cells: Role of Metformin

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hurley, M. Imnaten, C.J. O'Brien, Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|S. Millington-Ward, G. Farrar, Genetics, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The Lamina Cribrosa (LC) is a key site of retinal ganglion cell axonal injury in Open Angle Glaucoma (OAG). Our lab has previously shown human glaucoma LC cells have pro-fibrotic altered gene expression and mitochondrial dysfunction. Metformin has been shown to have anti-fibrotic effects in numerous organ systems. In this study, we aim to assess Metformin's effect on mitochondrial function in glaucomatous LC cells by carrying out a systematic mitochondrial bioenergetic assessment.

Methods: Human LC cells from age matched normal and confirmed glaucoma donors were assessed using a Seahorse XFe96 Analyzer. Glaucoma LC cells were treated with Metformin at different doses: 10mM, 5mM, 2mM, 1mM, 0.5mM, 0.1mM and 0.05mM. Adenosine Triphosphate (ATP) production, Basal Oxygen Consumption Rate (OCR), Maximal OCR and Spare Respiratory Capacity were measured and normalized to total protein content using the Bradford method. In addition, the effect of Metformin on extracellular matrix (ECM) gene expression (Col1A1, α -SMA, and vitronectin) was assessed by real time RT-PCR.

Results: Glaucoma LC cells have lower basal and maximal OCR, lower spare respiratory capacity and lower ATP production than the normal cells. Treatment with Metformin, however, significantly improves Maximal OCR (0.473 ± 0.026 pmol/min vs 0.398 ± 0.083 pmol/min) ($p < 0.05$) and spare respiratory capacity (0.193 ± 0.035 pmol/min vs 0.168 ± 0.046 pmol/min) ($p < 0.05$) in glaucoma cells. Additionally, there is a trend towards improvement of basal OCR and ATP production in treated glaucoma LC cells versus untreated glaucoma LC cells ($p=0.1076$ and $p=0.0655$ respectively). The most effective Metformin dose was 0.1 mM. In addition, Metformin treatment (0.1mM) resulted in a significant ($p < 0.05$) reduction of the ECM gene expression seen in glaucoma LC cells.

Conclusions: We demonstrate evidence of mitochondrial dysfunction and enhanced ECM gene expression in glaucoma LC cells and subsequent improvement with Metformin treatment. These results may provide some explanation as to the reduced OAG glaucoma incidence in those taking Metformin. A better understanding of Metformin's effect on mitochondrial dysfunction and fibrosis may aid the development of a disease modifying agent in OAG.

CONTROL ID: 3545274

SUBMITTER (NAME ONLY): Marika Zuanon

TITLE: Developing P2X7 antagonists for the treatment of inflammatory eye disease

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zuanon, M.T. Young, School of Bioscience, Cardiff University, Cardiff, Wales, UNITED KINGDOM|A. Brancale, School of Pharmacy, Cardiff University, Cardiff, Wales, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Age-related Macular Degeneration (AMD), glaucoma and Diabetic Retinopathy (DR) are the most common cause of blindness worldwide, with few effective treatments available. All are characterized by a state of chronic inflammation, thought to be at least in part mediated by the P2X7 receptor, an ion channel widely expressed in the eye, which is activated by high concentrations of extracellular ATP present during inflammation. P2X7 activation promotes the release of pro-inflammatory cytokines and cell death, contributing to disease progression and leading to loss of cells critical for vision. Blocking P2X7 activation may present a valid therapeutic strategy to treat chronic inflammation in eye disease.

This study has two main aims; (1) to confirm the involvement of P2X7 activation and signalling in the progression of AMD using retinal pigment epithelial (RPE) cells, and (2) to use structure-based virtual screening methods to develop novel-small molecule P2X7 antagonists.

Methods: For Aim 1, P2X7 expression and function have been evaluated in a human RPE cell line (ARPE-19) using Western blotting and ATP-stimulated fluorescent dye uptake (YO-PRO1). For Aim 2, structure-based screening was performed on human P2X7 molecular models to identify potential hit molecules (from commercially available libraries) likely to bind to orthosteric and allosteric pockets. Potential hits were purchased and tested on 1321N1 astrocytoma cells stably transfected with human P2X7 using ATP-stimulated YO-PRO 1 uptake and the Membrane Potential Red assay (MPR), to assess their ability to inhibit P2X7 activation.

Results: ATP-stimulated YO-PRO1 uptake was observed in non-polarised ARPE-19 cells (EC_{50} in the low millimolar range), consistent with P2X7 expression, but Western blot analysis failed to detect protein, suggesting low expression levels. A total of 30 potential hit molecules were selected and their activity was assessed by YO-PRO 1 and MPR assays. A number of compounds showed a reduction in the response to ATP compared to control when pre-applied at either 10 μ M or 30 μ M.

Conclusions: This work demonstrates that ATP-stimulated activity consistent with that of P2X7 is observed in ARPE-19 cells, despite no protein being detected by Western blot. In addition, this study demonstrates the identification of P2X7 antagonist hit compounds, which have the potential to be developed into novel anti-inflammatory therapeutics.

CONTROL ID: 3545280

SUBMITTER (NAME ONLY): Agata Mosinska

TITLE: Longitudinal analysis of Retinal Pigment Epithelium Atrophy progression using automated segmentation algorithm

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mosinska, M. Stadelmann, S. Apostolopoulos, C. Ciller, S. De Zanet, RetinAI Medical AG, SWITZERLAND|A. Montesel, A. Gigon, I. Mantel, Hopital ophtalmique Jules-Gonin, Lausanne, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To study atrophy growth rate, its dependence on area, time and retinal regions, using an automated segmentation method in retinal SD-OCT scans.

Methods: 589 SD-OCT volumes of 97 patients (99 eyes) with nonexudative atrophic AMD and at least 1 year follow-up were selected and segmented using an automated atrophy detection algorithm. Total en face atrophic area was calculated for each scan using the segmentation output.

The square root atrophy areas were used to compute the growth rate [mm/year] by fitting a linear model to each patient and averaging across all subjects and patient subgroups: those with small ($<5\text{mm}^2$) and large ($>5\text{mm}^2$) baseline areas as well as those with foveal and extrafoveal atrophy at the baseline. A time-normalized growth map was constructed for each patient and averaged across the whole dataset to obtain progression growth rate with respect to retinal location.

Results: The mean follow-up time was 43 months and the mean area at the baseline was $4.6 \pm 4.2 \text{ mm}^2$. The average growth rate was $0.31 \pm 0.21 \text{ mm/year}$. Despite square root transformation, the growth rate was significantly higher for patients with smaller baseline atrophies and amounted to $0.35 \pm 0.22 \text{ mm/year}$, than for larger ones ($0.26 \pm 0.17 \text{ mm/year}$, $p=0.042$). Baseline atrophy area and the square root area growth rate were correlated ($R^2=0.083$, $p=0.005$). The growth rate decreased both as a function of progressing atrophy area and time since the baseline (Figure 1). Out of 99 eyes, 37 (37%) had foveal involvement at the baseline. The growth was slower for them ($0.22 \pm 0.16 \text{ mm/year}$) than for the eyes with extrafoveal atrophy ($0.38 \pm 0.22 \text{ mm/year}$, $p=0.0002$).

The topological analysis of the growth rate revealed that the atrophy progresses faster in a ring around the fovea, towards the nasal and inferior area relative to the fovea (Figure 2).

Conclusions: The automated atrophy segmentation method enabled analysis of atrophy progression of a large patient dataset. It has shown that growth rate varies significantly across retinal regions, depending on the lesion area and time elapsed since the baseline.

CONTROL ID: 3545285

SUBMITTER (NAME ONLY): Lawrence Chan

TITLE: Variability in high resolution cone spacing measures in eyes with retinitis pigmentosa

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Chan, J. Wong, J.L. Duncan, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|S. Griffin, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|A.J. Roorda, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|S.K. Lynch, Eye Specialists of Georgia, Atlanta, Georgia, UNITED STATES|T.C. Porco, Francis I. Proctor Foundation, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate inter-visit, intragrader, inter-grader, and inter-ocular variability in cone spacing measures at baseline in a clinical trial of sustained-release ciliary neurotrophic factor (CNTF) treatment in retinitis pigmentosa using confocal adaptive optics scanning laser ophthalmoscopy (AOSLO) images.

Methods: A single-center, double-masked clinical trial (NCT01530659) of patients with retinitis pigmentosa or Usher syndrome type 2 or 3 randomly assigned 1 eye in each patient to receive a high- or low-dose (20 or 5 ng/day) CNTF-secreting implant and the contralateral eye to receive sham surgery. AOSLO was used to image the macula in each eye at 2 baseline visits separated by no more than 1 month to identify regions of interest (ROIs) of 100 arcmin² with at least 50 contiguous, unambiguous cones. Cones were marked by 2 independent, trained graders at baseline. Cone spacing Z-scores (standard deviations from the mean of 37 normal subjects) were reported to account for the known relationship between cone spacing and eccentricity from the fovea. Cone spacing Z-scores from all ROIs in each eye were averaged and compared to the contralateral eye of each patient. We computed the agreement intraclass correlation coefficient (ICC) between mean Z-scores of sham- and CNTF-treated eyes.

Results: 22 participants were enrolled ranging in age from 19-66 (mean 39.8±11.9) years, and 13 were male. Intragrader repeatability of measurements for the same visit showed ICC=0.88 and 0.86 for the 2 graders. Intragrader agreement ICC of cone spacing measurements between 2 baseline visits was excellent (0.82, 95% CI=0.80 to 0.83), as was agreement ICC of cone spacing scores between the graders at the baseline visit (ICC=0.78, 95% CI=0.76 to 0.80). The agreement ICC between the mean Z-scores for each of the 2 eyes at baseline was excellent (ICC=0.94, 95% CI=0.86 to 0.97).

Conclusions: Cone spacing measures were repeatable within a single grader at the same visit and between visits separated by no greater than 1 month, and were repeatable between graders. Cone spacing measures were also similar between contralateral eyes of patients with retinitis pigmentosa. Interocular agreement of cone spacing measures suggests the contralateral eye may serve as a control for uniocular treatments. AOSLO cone spacing measurements may be a reliable and sensitive means of monitoring disease progression in patients with retinitis pigmentosa.

CONTROL ID: 3545287

SUBMITTER (NAME ONLY): Moon Jung Back

TITLE: The efficacy evaluation study of the clinical eye drop formulation of the NOX inhibitor, SJP1804 and the design of a phase 1 clinical trial for the treatment of wet AMD.

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Back, N. Jung, D. Jeong, D. Lee, E. Jo, M. Choi, J. Kim, H. Kim, M. Ki, Samjin Pharmaceuticals Co Ltd, Seoul, Seoul, KOREA (THE REPUBLIC OF)|S. Lee, S. Moon, Aptabio Therapeutics Inc., Yongin, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: The repeated invasive intravitreal (IVT) injections and the presence of poor responders of the VEGF blocking agent, the currently only available treatment for wAMD, have raised the need for less invasive dosage and drugs of new mechanism. We previously showed the superior/equivalent efficacy of the non-invasive eye drop of the NOX inhibitor compared to aflibercept (IVT) in CNV animal models. In this study, the eye drop SJP1804 containing 0.25% API was optimized for clinical application and the efficacy of the clinical formulation of SJP1804 for wAMD was evaluated using the mouse and rabbit CNV models.

Methods: SJP1804 (0.25% API) was administered (3 or 6 times/day, which corresponds to 1~3 times/day in human based on human equivalent dose and intraocular PK of the experimental animals) via eye drop for 15 days and 56 days, respectively, in mouse and rabbit CNV models. Additionally, combination therapy of SJP1804 (3 or 6 time/day) and aflibercept (2 mg/eye IVT) was also treated in rabbits. The CNV lesions in both animal models were measured by angiography. And the concentration of API in the rabbit retina/choroid after administration of the SJP1804 was determined by LC-MS/MS.

Results: In both mouse and rabbit CNV models, 3 or 6 times daily eye drops of SJP1804 (0.25% API) significantly reduced the CNV lesions. In details, 3 times daily eye drop of SJP1804 showed equivalent efficacy and 6 times daily eye drop of SJP1804 showed superior CNV lesion reduction compared to 2 mg/eye aflibercept in the rabbit CNV models. Moreover, 3 or 6 times daily eye drops of SJP1804 complemented the weak therapeutic effects of 2 mg of aflibercept in this model. And the data from LC-MS/MS suggested that the drug in eye drop reached to the target region through the trans-sclera pathway.

Conclusions: Taken together, the results showed that excellent efficacy of the clinical eye drop formulation of SJP1804 (0.25% API) in CNV. Considering the fact that the intraocular half-life of various drugs in human is about 2.5 times longer than that in rabbit, it is supposed that 1~3 times/day administration of SJP1804 eye drop is sufficient to exert clinical efficacy. Based on the results, we further designed phase 1 clinical trial of SJP1804 (0.25% API) eye drop in health Korean and Caucasian male subjects for investigating PK, safety and local tolerability.

CONTROL ID: 3545292

SUBMITTER (NAME ONLY): Pilar Rojas

TITLE: Retinal neuroinflammation in an ALS mouse model (SOD1G93A)

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Rojas, J. Fernández-Albarral, I. López Cuenca, E. Salobar-García, R. de Hoz, J. Salazar, J. Ramirez, A. Ramirez, Instituto de Investigaciones Oftalmológicas Ramón Castroviejo, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|P. Rojas, M. Cadena, J.L. Urcelay, Ophthalmology, Hospital General Universitario Gregorio Marañon, Madrid, Madrid, SPAIN|E. Salobar-García, J. Salazar, A. Ramirez, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Optica y Optometria, Madrid, Comunidad de Madrid, SPAIN|R. de Hoz, J.L. Urcelay, J. Ramirez, Departamento de Inmunología, Oftalmología y ORL, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|I. Santos, E. Lago, Instituto Universitario de Investigación en Neuroquímica, Departamento de Bioquímica y Biología Molecular, Universidad Complutense de Madrid Facultad de Medicina, Madrid, Comunidad de Madrid, SPAIN|I. Santos, E. Lago, Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED) and Instituto Ramón y Cajal de investigación Sanitaria (IRYCIS), Madrid, Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: To determine the differences in retinal microglial and ganglion cell behaviour in a SOD1G93A mouse model (SOD) of amyotrophic lateral sclerosis (ALS) compared to the wild type (WT).

Methods: In retinal whole-mounts labelled with anti-Iba-1 (microglial marker) from two experimental groups WT (n=6) and SOD ALS (n=6), were quantified the number of retinal ganglion cells (RGCs) Brn3a+ and the signs of microglial activation in different retinal layers: i) Iba-1 + cells number in outer segments (OS), outer plexiform layer (OPL) and inner complex layer (ICL) constituted by inner plexiform layer (IPL), ganglion cell layer (GCL) and retinal nerve fiber layer (RNFL); ii) area occupied by Iba-1+ cells in OPL and IPL; and iii) arbor area of Iba-1+ cells in OPL and IPL. In addition, the expression of anti-IFN- γ and anti-IL-1 β (pro-inflammatory M1 phenotype) and anti-arginase-I and anti-IL-10 (anti-inflammatory M2 phenotype) were analysed. Animals were sacrificed with 120 days old (advanced stage of the disease).

Results: Compared to WT, the retina of SOD1 ALS mice showed: i) Migrations and reorientation processes of some Iba-1 + cells; ii) a significant increase in the area occupied by each microglial cell in the total area of the retina; iii) a significant increase in arbor area in the outer plexiform layer (OPL) inferior sector; iv) presence of cells with retracted processes; v) areas of cell groupings in some sectors; vi) no significant increase in the number of microglial cells, vii) expression of IFN- γ and IL-1 β ; viii) non-expression of IL-10 and arginase-I; ix) A decrease in number of RGCs.

Conclusions: In the SOD1G93A ALS model at 120 days (advanced stage of the disease), retinal microglial activation occurs, taking a pro-inflammatory M1 phenotype, which affected OPL and inner retinal layers and could be related to the RGCs loss. Although ALS is a disease of motor neurons, it can also affect retinal tissue, where an inflammatory process and death of retinal neurons occurs.

CONTROL ID: 3545299

SUBMITTER (NAME ONLY): Emmanuelle Clerin

TITLE: A mouse model with specific inactivation of the thioredoxin-like protein encoded by the nucleoredoxin-like1 reveals its role in the prevention of secondary cone death in retinitis pigmentosa

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The loss of rods in retinitis pigmentosa (RP) results in the loss of expression of rod-derived cone viability factor (RdCVF) encoded by the nucleoredoxin-like 1 (NXNL1) gene which triggers to the loss of cone function. The second product of the NXNL1 gene, the thioredoxin-like protein RdCVFL, expressed by rods and cones repairs oxidative damages. Since the redox power of RdCVFL on cones relies on the metabolism of glucose, we hypothesize that the death of cones results ultimately from a deficit of RdCVFL activity. So, we constructed the RdCVFL^{-/-} mouse that carries specific inactivation of RdCVFL.

Methods: A stop codon was knocked-in to the RdCVFL-specific part of the coding sequence of NXNL1. We quantified the level of malondialdehyde acid (MDA), a marker of lipid peroxidation, in the retinas of RdCVFL^{-/-} compared to RdCVFL^{+/+} (n=9) mice. We also exacerbated the visual phenotype by light damage (LD) during 3 hours with 10,000 lux after light calibration with pigmented animal control. Ten days after the exposure, the thickness of outer nuclear layer (ONL) was measured by optical coherence tomography (OCT), followed by electroretinogram (ERG) recording. After sacrifice of the animals, retinas were collected, followed by cone density measurement using an automated counting platform, e-conome.

Results: The expression of RdCVF mRNA is not affected by the presence of a stop codon in the RdCVFL sequence in RdCVFL^{-/-} mice whereas the retina does not produce the RdCVFL protein as seen by western blotting. The RdCVFL^{-/-} retina displays a 38% increase of MDA and a reduction of 13.5% of cone density compared to RdCVFL^{+/+}. LD reduces the thickness of the ONL by 90% for the RdCVFL^{-/-} retina and only by 10% for the RdCVFL^{+/+} retina. LD reduces both scotopic and photopic ERG by 70%-50% respectively for RdCVFL^{-/-} mouse and only by 20%-0% respectively for the RdCVFL^{+/+} mice. LD reduces cone density by 28% in the RdCVFL^{-/-} retina but not in the RdCVFL^{+/+} retina.

Conclusions: The RdCVFL^{-/-} mouse is highly susceptible to photo-oxidative damage to rods and cones. The reduction of cone density in the RdCVFL^{-/-} retina demonstrates that RdCVFL is essential for cone survival. The RdCVFL^{-/-} model offers an essential model to study the mechanisms of cone cell death in RP.

CONTROL ID: 3545300

SUBMITTER (NAME ONLY): Thomas Ach

TITLE: Near infrared autofluorescence (NIR-AF) of the human retinal pigment epithelium (RPE)

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ach, L. von der Emde, L. Bourauel, Department of Ophthalmology, University Hospital Bonn, Bonn, GERMANY|C.A. Curcio, A. Berlin, Department of Ophthalmology, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using super-resolution microscopy, NIR autofluorescence (AF) signals of the RPE were attributed to melanin and melanolipofuscin granules in RPE cell bodies (Ach et al., ARVO 2020). In human RPE cell bodies, melanolipofuscin are more frequent than melanosomes (PMID: 32433758) which also impacts clinical NIR-AF image interpretation. Here, we report the NIR-AF signal of RPE cells including apical processes to further evaluate its contribution to clinical NIR-AF imaging.

Methods: Retinal tissue cross-sections (10 µm thick) from five human donors (age range: 64-86 years) with normal maculas determined by ex vivo imaging by optical coherence tomography and confirmed by histology were imaged using a confocal microscope (white light laser source [excitation wavelengths in nm: 488, 635, 750, 780]; hybrid detector for optimized imaging in the NIR range; plan-apochromatic 40X 1.46 oil immersion objective; z-stacks in ~0.5µm steps). In addition, bright field images were taken to capture optically dense melanin pigment. RPE cells within areas of attached neurosensory retina at the fovea and perifovea were scanned. Finally, images were post-processed using FIJI.

Results: Both 750 nm and 780 nm excitation, lead to NIR-AF emission from the RPE cell body, though very weak compared to short wavelength excitation from the same areas. In addition, individual spindle-shaped melanosomes are visible in the apical processes of the RPE cells, exhibiting a bright NIR-AF signal, but clearly lacking AF in the short and mid wavelength range (480 – 635 nm).

Conclusions: There are probably two sources of RPE NIR-AF signals: spindle-shaped melanosomes in the apical processes as well as melanolipofuscin granules and more roundish melanosomes within the RPE cell bodies. The numerical predominance of melanolipofuscin granules within the cell bodies suggests that this signal is the leading source of NIR-AF imaging. These histological findings should be considered in the interpretation of future clinical NIR-AF imaging studies.

CONTROL ID: 3545301

SUBMITTER (NAME ONLY): Sarah Eivers

TITLE: Retinoblastoma signalling pathway inhibitor CDKN2B is regulated by promoter methylation in the lamina cribrosa region in primary open angle glaucoma

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Primary open angle glaucoma (POAG) is characterized by a loss of retinal ganglion cells and structural changes at the optic nerve head (ONH). Fibrosis in the form of extracellular matrix (ECM) deposition occurs at the lamina cribrosa (LC) region of the ONH and glaucomatous LC cells exhibit an increase in ECM and profibrotic factors, along with dysregulation of cellular growth and responses. Genome wide association studies have identified several single nucleotide polymorphisms within the 9p21 gene locus that are associated with glaucoma risk. The cyclin D Kinase inhibitor (CDKN)2B gene is located within this locus and encodes a key cell cycle regulator involved in inhibiting the Retinoblastoma (Rb) signalling pathway. Alterations in this pathway are typically associated with dysregulation of the cell cycle. In particular, gene silencing of CDKN2B by promoter hypermethylation is observed in several cancers and has been reported in fibrotic diseases. The aim of this study is to investigate if CDKN2B is regulated by promoter methylation in the LC in POAG.

Methods: LC cells were cultured from age-matched control and confirmed glaucomatous donors (GLC). Promoter methylation was analysed using a methylated DNA immunoprecipitation (MeDIP) assay. Gene expression was quantified using quantitative real-time PCR. GLC cells were treated with the methylation inhibitor 5-azacytidine (0.3 μ M) for 24 hours.

Results: The promoter region of CDKN2B was found to be significantly methylated in GLC cells ($P < 0.05$) compared to controls following MeDIP analysis. Expression of CDKN2B was decreased in GLC cells compared to controls, in concurrence with increased promoter methylation observed in GLC cells. Treatment of GLC cells with 5-azacytidine upregulated CDKN2B and decreased expression of the ECM gene collagen (COL)1A1. Additionally, gene expression of Rb pathway components cyclin (CCN)D1, cyclin D kinase (CDK)4, CDK6 and the transcription factor E2F1 were found to be increased in GLC cells compared to controls.

Conclusions: These results show that the promoter of CDKN2B is methylated in the LC in POAG, resulting in downregulation of a key cell cycle regulator within the Rb pathway. Coupled with an increase in expression of the other main players in this pathway, this may explain, at least in part, dysregulated cell cycle control observed in fibrotic GLC cells.

CONTROL ID: 3545302

SUBMITTER (NAME ONLY): Anran RAN

TITLE: Association Between Alzheimer's Disease and Artificial Intelligence-based Glaucomatous Optic Neuropathy Score

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The associations between Alzheimer's disease (AD) and glaucoma are inconsistent in the current literature. We aim to assess the association between AD and glaucomatous optic neuropathy (GON) using artificial intelligence (AI) predicted continuous scores from optical coherence tomography (OCT) volumetric scans.

Methods: This study included 2,269 volumetric optic disc OCT scans measured with Cirrus HD-OCT (Carl Zeiss Meditec, Dublin, CA) from 440 eyes of 233 AD subjects and 1,158 OCT scans from 271 eyes of 136 cognitively normal subjects. GON score was calculated from each OCT scan using a validated AI deep-learning algorithm. GON score was a continuous variable ranged from 0 to 1, and a more significant score represented a higher probability of GON. In addition, average and quadratic retinal nerve fiber layer (RNFL) thicknesses were also extracted from the OCT device.

Results: There was no significant difference in AI-based GON scores between AD and cognitively normal subjects (0.28 ± 0.31 vs. 0.30 ± 0.33 , $p = 0.20$). However, AD subjects had significant thinner RNFL average ($85.97 \pm 17.65 \mu\text{m}$ vs. $90.35 \pm 13.71 \mu\text{m}$, $p < 0.001$), temporal ($67.39 \pm 17.02 \mu\text{m}$ vs. $74.31 \pm 21.35 \mu\text{m}$, $p < 0.001$), nasal ($66.06 \pm 15.28 \mu\text{m}$ vs. $67.68 \pm 12.12 \mu\text{m}$, $p = 0.002$), inferior ($106.46 \pm 29.58 \mu\text{m}$ vs. $112.54 \pm 23.91 \mu\text{m}$, $p < 0.001$) and superior ($103.96 \pm 25.79 \mu\text{m}$ vs. $106.86 \pm 21.31 \mu\text{m}$, $p = 0.001$) thicknesses. A simple linear regression test showed that the association between AD and AI-based GON scores was insignificant ($p = 0.199$). GON score is equal to $0.297 - 0.015 \times (\text{diagnosis})$ when diagnosis is 1 (AD) or 0 (normal). Pearson's correlation showed that GON scores had moderate and inverse correlation with RNFL average ($R = -0.524$, $p < 0.001$), superior ($R = -0.495$, $p < 0.001$), and inferior ($R = -0.556$, $p < 0.001$) thickness, as well as weak and inverse correlation with RNFL temporal ($R = -0.210$, $p = 0.001$) and nasal ($R = -0.220$, $p < 0.001$) thickness. AD was only weakly and inversely associated with RNFL average ($R = -0.125$, $p < 0.001$), temporal ($R = -0.174$, $p < 0.001$), and inferior ($R = -0.103$, $p < 0.001$) thicknesses.

Conclusions: Although AD subjects had thinner RNFL thickness than cognitively normal subjects, AD is not associated with AI-based GON score. Further research is still warranted to confirm the null association between AD and GON.

CONTROL ID: 3545305

SUBMITTER (NAME ONLY): Justino Rodrigues

TITLE: Automated machine learning detection of transcellular pores in Schlemm's canal endothelial cells exposed to stretch

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Rodrigues, A. Bharath, D.R. Overby, Bioengineering, Imperial College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To drain from the eye, aqueous humor (AH) passes through micron-sized pores in the inner wall endothelium of Schlemm's canal (SC). SC pores are reduced in glaucoma, which may contribute to increased AH outflow resistance and elevated IOP. To investigate pore formation mechanisms, we previously developed a fluorescent assay to label pores in SC cells (Braakman et al. ARVO, 2014). The cells are stretched, which triggers pore formation, and exposed to fluorescent avidin that crosses the cell body at pore locations to create a fluorescent "hotspot" on the substrate that can be imaged by confocal microscopy. This technique produces high volumes of image data that must be examined by a trained human observer to identify individual pores. Because cultured SC cells form immature intercellular junctions, pores are often difficult to discern from noisy junctional labelling, and pores themselves are relatively sparse. These difficulties make pore labeling time consuming and labor-intensive. To increase efficiency, we developed an automated machine learning algorithm to detect SC pores in fluorescent images.

Methods: The algorithm consisted of a custom pre-processing block for interest point detection, a Histogram of Oriented Gradients feature extractor and a RUSBoost classifier (Seiffert et al. IEEE, 2008). This architecture was trained and tested on separate datasets derived from ~1,500 manually labelled pores and ~65,000 non-pore objects, obtained from 300 previously analyzed images of two SC cell strains, one normal (SC67) & one glaucomatous (SC57g).

Results: Our trained algorithm significantly accelerates SC pore detection relative to identification by a human observer (0.2 s vs. ~8 min per 0.2mm² image containing ~60 cells). Based on a testing set of 100 pores and 20,000 non-pores, our algorithm achieves 80% recall, 16% precision and 4% false positive rate (FPR) on SC pores.

Conclusions: Machine learning algorithms maximize the value of fluorescent pore detection in SC cells. The high recall indicates that the algorithm can successfully identify most pores. The low FPR indicates that the algorithm has high discriminative capacity, but the low precision prevents the algorithm from being used as a stand-alone pore detection tool. However, our algorithm can be used to rapidly identify candidate pores to pass to a human observer, accelerating the process of pore detection in SC cells.

CONTROL ID: 3545309

SUBMITTER (NAME ONLY): Ahmed Hagag

TITLE: The significance of double layer sign in eyes with choroidal neovascularization secondary to central serous chorioretinopathy

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To identify the OCT characteristics of eyes with double layer sign (DLS) that are associated with the presence of OCT angiography (OCTA)-confirmed choroidal neovascularization (CNV) in eyes with central serous chorioretinopathy (CSCR)

Methods: In this retrospective study, consecutive patients with a clinical diagnosis of CSCR with available OCT and OCTA scans were included. The presence or absence of DLS on OCT defined as a shallow RPE elevation with a minimum length of 1000µm and a maximum height of 100µm in the same frame were recorded. In eyes with DLS, further qualitative characteristic features on OCT including sub-RPE reflectivity and homogeneity, RPE layer irregularity, photoreceptor layers disruption, and subretinal hyperreflective material (SHRM) were graded and analyzed to explore whether one or more of these features can accurately identify CNV. The presence of CNV was confirmed by OCTA. Logistic regression was used to determine the OCT associations of CNV in cases with DLS.

Results: One hundred and sixty-three eyes with CSCR (age, 55.1±12.2 years) from 132 patients were included in this analysis. DLS was identified in 94 eyes (57.7%) and CNV was detected in 54 eyes (33.1%). Within the DLS group, 46 eyes (48.9%) had CNV. None of the dimensional parameters of the DLS were significantly associated with CNV on univariable regression. However, hyperreflectivity and nonhomogeneity of the sub-RPE space in the DLS were strong predictors of CNV (Table 1). The presence of SHRM and the absence of serous pigment epithelial detachment (PED) in the OCT scan were also significantly correlated (Table 1) with the detection of CNV on OCTA. Although RPE irregularity and photoreceptor disruption were commonly present in the CSCR eyes, they were not associated with CNV. On multivariable model, only hyperreflectivity (OR, 12.2, p=0.001) and nonhomogeneity (OR, 22.2, p=0.005) of the sub-RPE space, and absence of serous PED (OR, 8.2, p=0.02) were identified as independent OCT predictors of the presence of CNV on OCTA in eyes with DLS (Table 1). The combined significant OCT features had a sensitivity and specificity of 96% and 67%, respectively.

Conclusions: Double-layer sign with nonhomogeneous hyperreflective sub-RPE space indicated higher probability of the presence of CNV. Interestingly, serous PED seemed to be a protective sign against the development of CNV in CSCR.

CONTROL ID: 3545322

SUBMITTER (NAME ONLY): eyal gal

TITLE: Validation of a Novel Test for Detection of Astigmatism in Participants with Keratoconus, Astigmatism and Simulated Astigmatism

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Astigmatism blurs the retinal image of a spot along a particular orientation rendering an elliptical shape. The Wilkins Egg and Ball Test (WEBT) was created based on the hypothesis that astigmatic patients encounter difficulty differentiating between oval and circular targets. In WEBT, patients are asked to identify a circle hidden in a row with nine ovals. This study examined the utility of WEBT in identifying patients requiring astigmatic correction in three cohorts; participants with astigmatism, participants with keratoconus and normal participants with induced astigmatism.

Methods: Non-astigmatic participants (N=27, mean age:27±5, range:20-36, 8 male), participants with astigmatism (N=28, mean age:36±10, range:18-36, 9 male) with mean spherical equivalent (SE) corrections of -4.16±4.25, and mean cylindrical corrections of 2.80±0.76 DC (range: -2.00 DC to -4.00 DC), and keratoconic participants (N= 7 eyes, mean age:37±13, range:26-54, 2 female) with mean SE corrections of 0.27±2.20 DS, mean cylindrical corrections of -3.32±3.33 DC (range: -0.75 DC to -10.70 DC), were recruited. Participants detected the circle in each of the ten rows of each page, while the search time (sT) and number of errors(noE) were recorded. Non-stigmatic participants were examined under five conditions (baseline, and induced cylinder at four primary meridians) and participants with keratoconus and astigmatism were examined under corrected and uncorrected conditions, in random order. The sT and noE of varying conditions were compared using the Friedman test.

Results: In non-astigmatic participants, sT was significantly quicker and the noE was significantly lower in the baseline condition (38±9 sec, 0.97±1.5 errors) compared with all induced cylinder conditions (approximately 54±19 sec, 2.35±2.2 errors, p<0.05 for all except for the induced 90 deg astigmatism condition). Astigmatic participants were 6 sec faster and had one less error on average in the corrected condition. Keratoconic participants were 12 sec faster and had three less errors on average in the corrected condition. However, these differences were non-significant.

Conclusions: The potential of WEBT for detection of uncorrected astigmatism remains uncertain, though preliminary results in the clinical population are promising. More participants are being recruited to draw definitive conclusions.

CONTROL ID: 3545324

SUBMITTER (NAME ONLY): Alexandra Miere

TITLE: Deep learning-based classification of retinal atrophy using fundus autofluorescence imaging

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To automatically classify retinal atrophy according to its etiology, using fundus autofluorescence (FAF) images, using a deep learning model.

Methods: In this study, FAF images of patients with advanced dry age-related macular degeneration (AMD), also called geographic atrophy (GA), and genetically confirmed inherited retinal diseases (IRDs) in late atrophic stages [Stargardt disease (STGD1) and Pseudo-Stargardt Pattern Dystrophy (PSPD)] were included. The FAF images were used to train a multi-layer deep convolutional neural network (CNN) to differentiate on FAF between atrophy in the context of AMD (GA) and atrophy secondary to IRDs. Three-hundred fourteen FAF images were included, of which 110 images were of GA eyes and 204 were eyes with genetically confirmed STGD1 or PSPD. In the first approach, the CNN was trained and validated with 251 FAF images. Established augmentation techniques were used and an Adam optimizer was used for training. For the subsequent testing, the built classifiers were then tested with 63 untrained FAF images. The visualization method was integrated gradient visualization. In the second approach, 10-fold cross-validation was used to determine the model's performance.

Results: In the first approach, the best performance of the model was obtained using 10 epochs, with an accuracy of 0.92 and an area under the curve for Receiver Operating Characteristic (AUC-ROC) of 0.981. Mean accuracy was 87.30 +/- 2.96. In the second approach, a mean accuracy of 0.79 +/-0.06 was obtained.

Conclusions: This study describes the use of a deep learning-based algorithm to automatically classify atrophy on FAF imaging according to its etiology. Accurate differential diagnosis between GA and late-onset IRDs masquerading as GA on FAF can be performed with good accuracy and AUC-ROC values.

CONTROL ID: 3545328

SUBMITTER (NAME ONLY): TING SHEN

TITLE: Multifocal VEP measurements in healthy aging subjects reveal correlations with RNFL changes in OCT and cognitive assessment

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The cortex and the retina share many characteristics, including embryologic origin, biochemistry, neurotransmitter communication and microvasculature. To better understand whether visual pathway changes reflect a relationship with cognitive function, we evaluated correlation between retinal structural (OCT), neuropsychological (trail making test, TMT; digit span) and visual functional (multifocal visual evoked potentials, mfVEP) measurements in healthy aging subjects.

Methods: In this cross-sectional, observational clinical study, 74 healthy participants with a mean (SD) age of 67.5 (9.0) years were enrolled from the Optic Nerve and Cognitive Decline (ONDC) study. All participants underwent OCT peripapillary ring scan protocol for RNFL analysis and mfVEP for amplitude and latency assessment. They were also subjected to TMT testing for attention and executive function and digit span neuropsychological examination for working memory assessment. A total of 148 eyes were included for correlation analysis between OCT and mfVEP. Averaged mfVEP measures were used to analyze the relationship with TMT. Correlations between OCT, TMT and mfVEP parameters were analyzed using partial correlation and controlled for age and gender ($P < 0.05$).

Results: At study entry, a significant correlation between digit span total score and mfVEP latency ($r = 0.39$, $P = 0.001$) was observed. The mfVEP amplitude showed mild but significant correlations with global ($r = 0.25$, $P = 0.005$), temporal superior ($r = 0.18$, $P = 0.05$), temporal inferior ($r = 0.23$, $P = 0.01$) and nasal inferior ($r = 0.3$, $P = 0.001$) sectoral RNFL thickness. The TMT-test A also demonstrated negative correlation with mfVEP amplitude ($r = -0.26$, $P = 0.04$).

Conclusions: Our results suggested a significant correlation between mfVEP latency and working memory. MfVEP amplitude was also significantly correlated with global and sectoral RNFL thickness changes as measured by OCT as well as cognitive function characterized by the attention and executive function assessments. These findings indicate that the mfVEP measurements may parallel cognitive decline in the aging population. Further studies are planned in confirmed cognitively impaired subjects.

CONTROL ID: 3545334

SUBMITTER (NAME ONLY): Clara Mestre

TITLE: Vergence and accommodation responses in the control of intermittent exotropia

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Mestre, S. Neupane, T. Candy, School of Optometry, Indiana University, Bloomington, Indiana, UNITED STATES|V. Manh, K. Tarczy-Hornoch, Division of Ophthalmology, Seattle Children's Hospital, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine how young patients with intermittent exotropia (IXT) use vergence and accommodation when controlling their deviation.

Methods: Vergence and accommodation responses of 25 subjects with IXT (5-31 years) and 17 age-matched typical participants were recorded using simultaneous Purkinje image eye tracking and eccentric photorefractometry (PowerRef3). They watched a movie on a 7x7 cm screen, moving between 80 and 33 cm, in binocular and monocular viewing. Data were averaged over 2s windows of stable gaze and refraction during the 8s periods at each viewing distance. Periods of deviation were identified objectively using gaze position in monocular viewing. Fusional ranges were measured at the 80cm distance with a Risley prism. Fusional limits were defined objectively as the last prism for which subjects maintained alignment. Accommodative change during this test was assessed as the difference in refractive state between no prism and the fusional limit prism.

Results: 18 IXT participants were aligned throughout the binocular periods at distance and near viewing. Across all participants, vergence and accommodative responses to the change in binocular viewing distance were 10.20 ± 1.96 pd and 1.52 ± 0.51 D for IXTs, and 10.25 ± 1.75 pd and 1.44 ± 0.38 D for controls. Responses in monocular viewing were reduced to 6.95 ± 5.23 pd and 1.00 ± 0.51 D for IXTs, and 4.79 ± 2.13 pd and 1.03 ± 0.34 D for controls. For participants who deviated spontaneously in binocular viewing at 80cm and had uncorrected hyperopia of <1 D, the mean change in eye alignment was 18.39 ± 8.15 pd, accompanied by 0.09 ± 0.23 D of accommodative change. This was similar to the change in refractive state during monocular viewing at 80cm of control subjects (-0.01 ± 0.12 D). 12 IXT patients and 9 controls had fusional divergence limits of 10.12 ± 6.35 PD and 8.62 ± 3.80 PD, respectively, beyond their dissociated position with refractive changes <0.64 D. Fusional convergence limits from the dissociated position were 32.60 ± 10.41 PD for IXTs and 21.93 ± 9.52 PD for controls (3 reached the maximum prism), typically with <1.00 D increase of accommodation.

Conclusions: Most emmetropic or optically corrected IXTs were aligned in binocular conditions with wide fusional ranges, accompanied by only small changes in refraction. This suggests accommodative convergence is not uniquely responsible for control of the deviation in IXT and alignment is not achieved at the expense of focus.

CONTROL ID: 3545337

SUBMITTER (NAME ONLY): Bin Sun

TITLE: Contribution of ^{99m}Tc -DTPA SPECT/CT in the evaluation of thyroid-associated ophthalmopathy in patients with thyroid carcinoma

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Sun, Z. Zhang, C. Yan, Shanxi Eye Hospital, Taiyuan, Shanxi, CHINA|

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ABSTRACT BODY:

Purpose: Thyroid-associated ophthalmopathy (TAO) is most often seen in patients with autoimmune thyroid disease. But thyroid carcinoma with concurrent TAO is rare. The aim of this study was to evaluate ^{99m}Tc -DTPA SPECT/CT in pre-existing TAO in the patients with thyroid carcinoma.

Methods: 12 thyroid carcinoma patients (40~50 years) presented with ophthalmopathy. All patients received thyroidectomy and/or radioiodine (RAI) with the pathological characteristics of papillary thyroid carcinoma. Levothyroxine substitutive therapy was used after thyroidectomy to keep euthyroid. The activity of TAO was determined by means of the clinical activity score (CAS) and ^{99m}Tc -DTPA SPECT/CT. All active TAO patients received periocular injection of triamcinolone acetonide (TA, 20mg 3 weeks intervals, 5 times total) and support treatment (Selenium Yeast 25 μg Bid; Aescuvén forte 150mg, Bid). Data were obtained from a follow-up survey. GO-QOL surveys were used in all patients with TAO.

Results: All 12 patients with thyroid carcinoma accompanied with moderate-severe active TAO (CAS \geq 4). The clinical manifestations of 8 patients worsened after thyroidectomy and/or RAI treatment. Main symptoms were eyelid retraction (100%), exophthalmos (100%) and restricted ocular motility (80%). Compared with the normative values, obvious enlargement of multi-rectus muscles was involved in all patients. ^{99m}Tc -DTPA SPECT/CT were positive in all patients and ^{99m}Tc -DTPA accumulated intensively in site of rectus muscles involved. Thus, TAO substantially reduced QOL of the patients. After periocular injection of TA, the symptoms of TAO were improved. With the stabilization of ophthalmopathy, CAS and the uptake ration (UR) of ^{99m}Tc -DTPA scintigraphy were decreased accordingly in all patients (P<0.05). QOL of the patients with TAO was improved.

Conclusions: ^{99m}Tc -DTPA SPECT/CT played a critical role in the evaluation of the clinical activity of these middle-aged TAO patients with papillary thyroid carcinoma, who presented more severe and more active signs compared with age-matched TAO patients with Graves' Disease (GD). Prominent extraocular muscles involvement, rather than expansion of the orbital fat compartment should be the main subtype. Periocular injection of TA was suggested to provide improvement of ophthalmologic symptoms and QOL in thyroid carcinoma patients with TAO.

CONTROL ID: 3545345

SUBMITTER (NAME ONLY): Xinyu Liu

TITLE: In-vivo posterior retinal fibrillary structure visualized under triple input PS-OCT on a non-human primate

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: In the eye, fibrillary structures play vital roles for the eye functioning. Polarization sensitive optical coherence tomography (PS-OCT) is an in-vivo fibrillary tissue imaging tool. We developed a novel scheme of PS-OCT, named as triple input PS-OCT (TIPS-OCT), and investigated the fibrillary structures in the posterior eye of a non-human primate.

Methods: A Rhesus Macaque was anaesthetized and scanned using the proposed TIPS-OCT.

Results: In the peripapillary region of the sclera, we observed that a thin layer of radial fiber structure was distributed from the inner side and transited to thicker, multi-directional, interweaving circumferential fiber structure. The transition boundary can be clearly seen around the ONH.

In the macular region, we observed that the sclera was significantly thicker and primarily contained two orthogonally interweaving fibrillary structure. Fibrils from different directions were observed to entangle under the fovea spot, probably thickening and strengthening the sclera around the macular region.

Conclusions: TIPS-OCT provides new insight to understand the retinal fibrillary structure in vivo.

CONTROL ID: 3545347

SUBMITTER (NAME ONLY): Seung-Young Yu

TITLE: Retinal Microvascular Changes following Internal Limiting Membrane Peeling Surgery for Epiretinal Membrane versus Macular Hole

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yu, K. Yoon, E. Kim, K. Kim, Kyunghee University medical center, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To evaluate macular microvascular changes following Internal Limiting Membrane (ILM)-peeling surgery for Epiretinal Membrane (ERM) or Macular Hole (MH).

Methods: A retrospective study, total of 30 patients (30 eyes), 20 patients diagnosed with epiretinal membrane and 10 with macular hole, were evaluated with SS-OCTA after ILM peeling during PPV. Perifoveal microvascular change and nonperfusion area were measured by Matlab from the 6mmx6mm and 12mmx12mm SS-OCTA images excluding FAZ and optic discs. The presence of Dissociated Optic Nerve Fiber Layer (DONFL) was evaluated using en-face SS-OCTA images.

Results: Total of 30 eyes, the best corrected visual acuity after surgery was significantly improved from 0.56 ± 0.36 (logMAR) to 0.32 ± 0.31 (logMAR). In epiretinal membrane, superficial layer nonperfusion area was significantly decreased ($p=0.047$). In macular hole, the perifoveal vessel density in superficial layer after surgery showed a significant decrease ($p=0.045$), and the deep perifoveal vessel density and the deep nonperfusion zone showed a tendency to decrease, but not statistically significant. DONFL was observed in 7 out of 10 patients diagnosed with macular hole, but in 4 out of 20 patients diagnosed with epiretinal membrane. The correlation between perifoveal microvascular change and DONFL was not statistically significant.

Conclusions: Perifoveal vessel density after ILM peeling surgery tend to decrease in macular hole and epiretinal membrane. It was observed more significant in macular hole.

CONTROL ID: 3545351

SUBMITTER (NAME ONLY): Seong Joon Ahn

TITLE: Predictive Features of Future Progression of Hydroxychloroquine Retinopathy on Recommended Imaging Modalities for Retinopathy Screening

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Lee, Ophthalmology, Hanyang University, Seoul, KOREA (THE REPUBLIC OF)|S. Ahn, Ophthalmology, Hanyang University, Seoul, KOREA (THE REPUBLIC OF)|K. Kim, Eulji Hospital, Seoul, KOREA (THE REPUBLIC OF)|J. Lee, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To investigate predictors on optical coherence tomography (OCT) and fundus autofluorescence (FAF) for future progression of hydroxychloroquine (HCQ) retinopathy after drug cessation

Methods: Among the 80 eyes of 41 Korean patients with HCQ retinopathy with follow-up period over than 2 years, progression of HCQ retinopathy was judged as increase in photoreceptor defect size on OCT and increased or newly appeared hypo- or hyperautofluorescence on FAF. Several characteristic features on OCT and FAF were assessed and compared between those without and with progression in the eyes with HCQ retinopathy.

Results: Eyes with newly developed retinal pigment epithelium (RPE) defects or those with expanded RPE defects showed choroidal hypertransmission, without definite defective RPE/Bruch's membrane complex line, compared to the area without such change in the same eye or those without such progression. Complete photoreceptor loss, including the outer nuclear layer, external limiting membrane and ellipsoid zone, was significantly associated with future appearance of adjacent RPE defects. On FAF, double hyperautofluorescent rings on FAF was noted in those with progression, which was significantly different between those with and without progression to severe stage. The eyes with these signs showed continuous progression over the follow-up period following drug cessation.

Conclusions: Choroidal hypertransmission and complete photoreceptor loss on OCT and double hyperautofluorescent rings on FAF might indicate subclinical damage of the RPE in eyes with HCQ retinopathy, which later becomes overt in subsequent periods. These signs may be clinically useful for prediction of future behavior, continuous progression, in HCQ retinopathy.

CONTROL ID: 3545355

SUBMITTER (NAME ONLY): Natalia Porporato

TITLE: Towards 'Automated Gonioscopy': A Deep Learning Algorithm for 360° Angle Assessment by Swept-Source Optical Coherence Tomography

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Porporato, T.A. Tun, B. Mani, D. Wong, R. Husain, S. Perera, L. Schmetterer, T. Aung, Glaucoma, Singapore Eye Research Institute, Singapore, SINGAPORE|H. Fu, Inception Institute of Artificial Intelligence, Abu Dhabi, UNITED ARAB EMIRATES|R. Sultana, Duke-NUS Medical School, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To validate a deep learning algorithm (DLA) for 360° angle assessment on swept source OCT (SS-OCT, CASIA-1000, Tomey Corporation, Nagoya, Japan).

Methods: This was a reliability analysis from a cross-sectional study. An independent test set of 39,936 SS-OCT scans from 312 phakic subjects (128 SS-OCT meridional scans per eye) was analyzed. Participants above 50 years old with no previous history of intraocular surgery were consecutively recruited from glaucoma clinics. Indentation gonioscopy and dark room SS-OCT were performed. Gonioscopic angle closure was defined as non-visibility of the posterior trabecular meshwork in $\geq 180^\circ$ of the angle. For each subject, all images were analyzed by a deep learning-based network based on the VGG-16 architecture, for gonioscopic angle-closure detection. Area under receiver operating characteristic curves (AUC) and other diagnostic performance indicators were calculated for the deep learning algorithm (index test) against gonioscopy (reference standard).

Results: Approximately 80% of the participants were Chinese, and more than half were women (57.4%). The prevalence of gonioscopic angle closure in this hospital-based sample was 20.2%. After analyzing a total of 39,936 SS-OCT scans, the AUC of the DLA was 0.85 (95CI%:0.80-0.90, with sensitivity of 83% and a specificity of 87%) to classify gonioscopic angle closure with the optimal cut-off value of $>35\%$ of circumferential angle closure.

Conclusions: The DLA exhibited good diagnostic performance for detection of gonioscopic angle closure on 360° SS-OCT scans in a glaucoma clinic setting. Such an algorithm, independent of the identification of the scleral spur, may be the foundation for a non-contact, fast and reproducible 'automated gonioscopy' in future.

CONTROL ID: 3545360

SUBMITTER (NAME ONLY): Jacques Bertrand

TITLE: Calcium-Dependent Transcellular Pore Formation in Schlemm's Canal Endothelial Cells

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Bertrand, D.R. Overby, Department of Bioengineering, Imperial College London, London, UNITED KINGDOM|D.W. Stamer, Duke Eye Center, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Micron-sized pores are conduits for aqueous humor flow across Schlemm's Canal (SC) endothelium. SC pore reduction in glaucoma contributes to increased outflow resistance and elevated IOP. SC pore formation is triggered by mechanical stretch (Braakman, EER 2014) and stretch increases intracellular $[Ca^{2+}]_i$ by opening stretch-activated Ca^{2+} channels. Ca^{2+} regulates vesicle exocytosis and membrane fusion in neurons and other cell types. As membrane fusion is necessary for transcellular "I" pore formation, we hypothesize that stretch-induced Ca^{2+} influx promotes I-pore formation in SC cells.

Methods: In this study, we compare I-pore formation between SC cells depleted of $[Ca^{2+}]_i$ using BAPTA vs. vehicle treated SC cells exposed to the same level of mechanical stretch. Human SC cells were isolated from 2 non-glaucomatous donors (SC69 and SC75) and characterized following established protocols (Perkumas & Stamer, EER 2012). SC cells were seeded (8×10^3 cells/cm²) onto 6mm \varnothing islands of biotinylated gelatin on elastic PDMS membranes and cultured for 24hrs. Test samples were incubated with 5 μ M BAPTA-AM (30 min) and 1 mM EGTA (5min) in Ca^{2+} free PBS at 37°C. Samples were exposed to 0% or 20% equibiaxial stretch for 2 mins followed by incubation with streptavidin (SA) for 2 mins and then fixed. I-pores were identified based on transcellular movement of SA across the cell body where it binds to the underlying biotinylated substrate. SA labelling patterns were imaged at 20x by epifluorescence microscopy. One masked observer (JB) identified I-pores and measured the area of SA labelling within the perimeter ("pore area") normalized by total cell area (N = 229 and 206 cells in SC69 and SC75). Statistical significance was determined by 3-way ANOVA.

Results: Without BAPTA, increasing stretch from 0% to 20% led to doubling of pore area (0.0025 ± 0.007 vs. 0.0041 ± 0.008 ; $p = 0.004$). BAPTA decreased pore area at both 0% and 20% stretch (0.0021 ± 0.001 and 0.0035 ± 0.002 ; $p < 0.001$) relative to vehicle. BAPTA eliminated the increase in pore area in response to stretch ($p > 0.7$).

Conclusions: Transcellular pore formation is mechanosensitive in SC cells and is triggered by stretch. Ca^{2+} is a necessary component of pore formation, such that depletion of $[Ca^{2+}]_i$ inhibits formation of transcellular pores in SC cells exposed to stretch. This suggests that alterations in $[Ca^{2+}]_i$ may contribute to impaired pore formation in glaucomatous SC cells.

CONTROL ID: 3545361

SUBMITTER (NAME ONLY): Sophie Ginton

TITLE: Machine Learning for Classification of Functional Phenotypes in Stargardt Disease from Full-Field Electroretinography

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Ginton, A. Calcagni, G. Zhang, N. Pontikos, S. Wagner, M. Michaelides, P. Keane, A. Webster, A.G. Robson, O.A. Mahroo, Institute of Ophthalmology, University College London, London, UNITED KINGDOM|S.L. Ginton, G. Zhang, N. Pontikos, S. Patel, S. Wagner, M. Michaelides, P. Keane, A. Webster, O.A. Mahroo, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|A. Calcagni, A.G. Robson, Department of Electrophysiology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|W. Lilaonitkul, Institute of Health Informatics, University College London, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: This study aims to test the applicability of machine learning (ML) to the analysis of full-field electroretinography (ERG) for the identification of clinically relevant phenotypic subtypes in patients diagnosed with ABCA4-retinopathy (Stargardt disease).

Methods: Patients with ABCA4-retinopathy who had undergone full-field were ascertained. All patients had a molecularly confirmed, likely-disease causing, genotype in the ABCA4 gene and a clinical presentation consistent with ABCA4-retinopathy. All ERGs adhered to the International Society for Clinical Electrophysiology of Vision (ISCEV) standard. Based on interpretation of the dark-adapted strong flash (DA 10.0) ERG, light-adapted single flash cone (LA 3.0) ERG and 30Hz flicker (LA 30Hz) ERG, data were subdivided into three groups by two experienced electrophysiologists: normal (group 1 n=344), consistent with cone dystrophy (group 2 n=45) or cone-rod dystrophy (group 3 n=210). For model development, ERG data were divided 80/20 at patient level into training and test datasets. Individual ERG traces, their derivatives, patient age, and pupil size were input into three logistic regression models corresponding to each of the above stimuli. The collated probabilities from an individual patient's ERG traces were input into a further model generating one phenotype prediction.

Results: Expert analysis and ML methods predicted phenotypic subtypes with 88.2% to 94.2% concordance in the unseen ERG data. In a 5-fold cross validation average test group accuracy was 91.1% with a kappa value of 0.83. Combining phenotypes 2 and 3 in a binary classification gave an average accuracy of 93.8%, sensitivity of 0.93, and specificity of 0.94.

Conclusions: Machine learning classification and human analysis of ERG phenotypes in ABCA4-retinopathy show a high degree of concordance. Machine learning methods have the potential to deepen understanding of retinal dysfunction and disease, previously dependent on specialist expertise and extensive training.

CONTROL ID: 3545367

SUBMITTER (NAME ONLY): Dong Hyun Kim

TITLE: Therapeutic Effects of Topical RCI001 on Environmental and Inflammation-related Dry eye mouse Models

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kim, Ophthalmology, Gil Medical Center, Gachon University College of Medicine, Incheon, KOREA (THE REPUBLIC OF)|D. Kim, S. Kim, Y. Ku, H. Jeon, Y. Jang, RudaCure Co., Ltd, Incheon, KOREA (THE REPUBLIC OF)|Y. Jung, J. Moon, C. Yoon, M. Kim, Ophthalmology, Seoul National University College of Medicine, Seoul, KOREA (THE REPUBLIC OF)|K. Lee, J. Ryu, C. Yoon, M. Kim, Laboratory of Ocular Regenerative Medicine and Immunology, Seoul Artificial Eye Center, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To evaluate the therapeutic effects of topical RCI001 on mouse models of environmental and inflammation-mediated dry eye disease (DED).

Methods: We used a scopolamine-induced environmental dry eye model in a dry chamber with 8-week-old BALB/c mice and 12-week-old NOD.B10.H2b mice, a model for primary Sjogren syndrome. The eyes of mice were topically treated with RCI001 and phosphate-buffered saline (PBS) twice a day for a week. Clinical findings such as ocular surface staining and tear production were assessed. Conjunctival goblet cell densities and inflammatory cytokines in the ocular surface and lacrimal gland were also analyzed.

Results: Topical application of RCI001 eyedrops resulted in a significant improvement of ocular surface staining and tear secretion in two mouse models, compared to the PBS-treated group. Although conjunctival goblet cell densities were not different between RCI001-treated and PBS-treated group, the expression of proinflammatory cytokines in the ocular surface and lacrimal gland of NOD.B10.H2b mice were repressed by RCI001, compared to PBS.

Conclusions: Topical RCI001 application showed significant therapeutic effects in two DED models via stimulating tear secretion and modulating inflammation.

CONTROL ID: 3545368

SUBMITTER (NAME ONLY): Benedetto Falsini

TITLE:

USH2A-related Retinitis Pigmentosa: staging of disease severity and morpho-functional studies.

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Usher syndrome type 2A (USH2A) is a genetic disease characterized by bilateral neuro-sensory hypoacusia and retinitis pigmentosa (RP). While several methods including electroretinogram (ERG) describe retinal function in USH2A patients, structural alterations can be assessed by Optical Coherence Tomography (OCT). According to a recent collaborative study, RP can be staged considering visual acuity, visual field area and ellipsoid zone (EZ) width (Iftikhar et al., 2019). The aim of this study was to retrospectively determine RP stage in a cohort of patients with USH2A gene variants and to correlate the results with age, as well as additional functional and morphological parameters.

Methods: In 26 patients with established USH2A genotype, RP was staged according to recent international standards (Iftikhar et al., 2019). The cumulative staging score and the grade were correlated with patients' age, amplitude of full-field and focal flicker ERGs, and the OCT-measured area of Sub-RPE illumination (SRI, Figure 1).

Results: RP cumulative score and grade were positively correlated ($r = 0.6$) with patient age. Both parameters were negatively ($r = -0.45$) correlated with log10 ERG amplitudes and positively correlated ($r = 0.50$) with SRI.

Conclusions:

RP severity score is correlated with age and additional morpho-functional parameters not included in the international staging system, and can reliably predict their abnormality at different stages of disease.

References

Iftikhar M, Lemus M, Usmani B, Campochiaro PA, Sahel JA, Scholl HPN, Shah SMA. Classification of disease severity in retinitis pigmentosa. Br J Ophthalmol. 2019 Nov;103(11):1595-1599.

CONTROL ID: 3545370

SUBMITTER (NAME ONLY): Sophie Riedl

TITLE: Correlation of AI-quantified retinal morphology with topographic function in neovascular AMD

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Riedl, M. Schranz, O. Leingang, G.S. Reiter, C. Grechenig, W. Vogl, M. Arikan, P.K. Roberts, H. Bogunovic, U. Schmidt-Erfurth, Department of Ophthalmology, Medizinische Universität Wien, Wien, Wien, AUSTRIA | I. Steiner, Center for Medical Statistics, Informatics and Intelligent Systems, Section for Medical Statistics, Medizinische Universität Wien, Wien, Wien, AUSTRIA |

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ABSTRACT BODY:

Purpose: To establish precise topographic structure-function relation in neovascular age-related macular degeneration (nAMD) by correlating AI-quantified fluid and photoreceptor (PR) alteration with retinal sensitivity (RS) as assessed by microperimetry (MP).

Methods: Morphology and function of n=38 eyes of 38 consecutive patients with nAMD were analyzed at the treatment-naïve stage and one month following an aflibercept loading dose. SD-OCT data was acquired using Spectralis OCT. Intraretinal fluid (IRF), subretinal fluid (SRF) and PR volumes were quantified using fully automated segmentations based on deep learning. RS was measured using a fovea-centered grid of 45 locations on the Nidek MP-3. Locations were registered to OCT volumes to precisely assess co-located morphology, which we report as nanoliters (nl) within a cuboid volume corresponding to MP-locations (Figure 1). Mixed models were computed to analyze the effect of IRF, SRF and PR volumes on RS at the corresponding location.

Results: RS and morphology at MP-locations are summarized in Table 1. Results of mixed models are reported per nl of fluid/PR. At baseline RS increased with PR volume (fovea: +5.73 dB; parafovea: +6.13 dB; perifovea: +2.95 dB, all $p < 0.001$). IRF corresponded to decreased RS by -1.51 dB ($p < 0.001$) and -1.13 dB ($p = 0.002$) in the fovea and parafovea. For SRF, a decrease in RS by -1.88 dB ($p < 0.001$) and -2.15 dB ($p < 0.001$) was revealed in the para- and perifovea. By month 3 the positive association of RS with PR was even stronger in the fovea, parafovea and perifovea (+11.34 dB; +8.94 dB; +8.32 dB, all $p < 0.001$). A significant effect of fluid remained for IRF in the parafovea (-7.86 dB, $p = 0.023$) and SRF in the fovea (-1.65 dB, $p = 0.012$). Reduction of foveal fluid expectedly corresponded to significantly increased RS by +0.59 dB ($p = 0.011$) for IRF and +0.53 dB ($p = 0.028$) for SRF. Furthermore, reduction of parafoveal SRF resulted in a RS gain of +0.82 dB ($p = 0.012$). Interestingly, increase in PR corresponded to increased RS in the fovea (+1.88 dB, $p = 0.003$), but decreased RS in the para- and perifovea (-1.61 dB and -2.01 dB, $p = 0.022$ and $p = 0.008$).

Conclusions: PR integrity is essential for topographic function. Resolution of foveal fluid and SRF in the parafovea corresponds to RS gains. In summary, retinal morphology, assessed by automated methods, shows meaningful correspondence with precise topographically corresponding RS.

CONTROL ID: 3545371

SUBMITTER (NAME ONLY): Ralf Brinkmann

TITLE: Automatic Temperature Control for Retinal Laser Exposures

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal laser treatments lack an objective dosing control, particularly for sub visible irradiations becoming more and more popular. However, laser effects vary largely due to inter and intraocular variations of light scattering and pigmentation at the fundus, leading to strong variations of the induced temperatures. We developed an optoacoustic method to determine the temperature rise during laser irradiation and demonstrated the technique in a clinical trial. The method was now been extended with an automatic closed-loop feedback control system in order to automatically obtain a desired target temperature preselected by the ophthalmologist.

Methods:

A commercial treatment laser (532nm) is used. The laser fiber is coupled to a control unit containing a pulsed probe laser (523 nm, 75 ns, 3 kHz) to excite thermoelastic pressure waves at the retina, and a fast modulator to modify the power of the therapy laser with a frequency of 3 kHz. Both beams are transmitted by the same fiber to a laser slitlamp. The acoustic amplitudes contain the current retinal temperatures and are recorded by an ultrasonic transducer embedded in a standard contact lens. A control software calculates the required laser power in real-time in such a way that the desired temperature rise is reached. Experiments were performed on freshly enucleated pig eye globes and RPE-choroid-sclera explants. Target temperatures between 40°C and 70°C were selected for irradiation times between 50 and 200 ms and a spot diameter of 200 µm.

Results: Depending on the control settings, the aim temperature was reached within 10-100 ms. Thereafter it is kept constant until the end of the irradiation period. For an irradiation time of 100 ms for example, target temperatures of 40, 50 and 60 °C were achieved with accuracies of 1.6 +/- 1.4 % after 78 +/- 9 ms, 2.1 +/- 1.1 % after 74 +/- 12 ms and 5.0 +/- 2.6 % after 41 +/- 20 ms, respectively. When adjusting the controller towards a fast temperature rise, target temperatures were reliably reached within 30 ms with fluctuations thereafter of about +/- 1 °C around the target temperature.

Conclusions: A device automatically controlling the temperature rise during retinal laser therapies has been developed and demonstrated. It can be adapted to every commercially available continuous wave retinal laser. The method allows a reliable thermal impact for visible or subvisible coagulations and especially for sublethal hyperthermia.

CONTROL ID: 3545379

SUBMITTER (NAME ONLY): Adam Dubis

TITLE: Democratizing Deep Learning Research Through Large Publicly Available Datasets and Tools

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Deep learning technologies hold great potential to transform and optimize decision support systems in healthcare. As we advance deep learning research and its applications in ophthalmology, massive amounts of high-quality pre-labelled data will be required for model training. Yet, publicly available large databanks for this purpose are limited and the process of generating such datasets can be prohibitively costly both in time and effort. To ease this challenge and to support the democratization of deep learning research, we built and make publicly available a large data set of high-quality labelled optical coherence tomography images along with a repository of supporting analytical toolkits.

Methods: One-hundred and fifty volumes split evenly between intermediate age-related macular degeneration (AMD), diabetes[MVC1] retinopathy, and normal controls were obtained using the Heidelberg Spectralis. From this dataset, 20 volumes (19-69 B-scans/volume; 1668 total scans) from each disease class were labeled for the location of the ILM, INL/OPL boundary, top of the IS/OS, the inner and the outer boundary of the RPE using a custom-built image labelling platform. All images were graded independently three times by a team of experienced graders. A subset of 200 images were graded twice for presence/location of fluid and classes of drusen. All images were adjudicated and corrected if needed to ensure all grades match layer definitions. Agreement between graders was determined using DICE, Intersection over Union (IoU) and Interclass Correlation Coefficients (ICC).

Results: A total of 5004 grades were produced for the presence and location of 5 retinal interfaces and corresponding 6 layers. The agreement between graders for the retinal layers is shown in Table 1, separated by disease. Labels for fluid presence at the B-scan and bounding box tags are also generated and available.

Conclusions: This dataset and subsequent web listing (AI4eyes.org) serve as the beginning of a providing a common database by which to benchmark novel tool development. The platform also provides tools for uniform labelling, thereby lowering the burden on new entrants. The hope is that this platform will continue to expand through our work and others to provide an ever growing depository of images and labels for groups looking to develop artificial intelligence tools, as well as a source for tools to help new groups begin.

CONTROL ID: 3545388

SUBMITTER (NAME ONLY): Emilie Picard

TITLE: Exposures to low-dose of bisphenol A during perinatal retinal development

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Our environment is continuously enriched in pollutants that contribute to increase the prevalence of diseases or even the emergence of new pathologies. The effects of chronic low-doses exposure to endocrine disruptors (EDs) on the retina remain unclear. Bisphenol A (BPA) is an ED widely used in the production of polycarbonate plastics leading to organ dysfunction and/or cancers. The aim of this study is to assess the effect of BPA on retina following low-dose perinatal exposure and to elucidate underlying mechanism of action.

Methods: Five µg/kg of BPA was administered to 5-day-pregnant rats 3 times a week. At weaning day 21, newborns received the same dose of BPA until post-natal day 30. Eyes were collected for histology, immunohistochemistry and transcriptomic analysis.

Results: No alteration in the retina structure was noticed by histology. However, a statistically significant modification in the thickness of the inner plexiform layer and the outer nuclear layer were noted (respectively -24% and +12%). Quantification of retinal cells using specific markers demonstrated a statistically significant increase in the number of cones (11.7 %) and a decrease in the number of bipolar cells and retinal ganglion cells (respectively, 21.3% and 10.4%). The number of amacrine and horizontal cells were unmodified. Pre-synaptic dendrites of bipolar cells displaying length reduction with BPA treatment, all synaptic vesicles were stained with synaptophysin. The vesicles distribution in the ONL increased up to 57.2% in BPA condition. Transcripts analysis revealed 1,395 genes significantly regulated in BPA retina compared to control ($p \geq 0.05$; $FD \pm 1.2$). Canonical ingenuity pathways analysis showed significantly regulation of pathways involved in cell-cell junctions, neurogenesis, hormones signaling, protein G signaling, visual cycle, responses to neurotransmitters and to hypoxia. Androgen signaling, G beta Gamma signaling and dopamine receptor signaling pathways were significantly activated (Z -score > 2).

Conclusions: Our results show that low-dose perinatal exposure of BPA induce slight modifications of the cones-bipolar-retinal ganglion cells ways network, corroborated by the wide transcriptional pathways variations. In conclusion, BPA induces slight retinal cell modifications which may contribute to increase the prevalence of neurodegenerative diseases.

CONTROL ID: 3545394

SUBMITTER (NAME ONLY): Berbang Meshko

TITLE: Epithelial-mesenchymal transition markers upregulation in corneal epithelial cells after UV-B irradiation which is irreversible with Resveratrol

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Meshko, M. Domday, S. Brosig, C. Cursiefen, M. Notara, ophthalmology, Uniklinik Köln, Köln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: Epithelial-mesenchymal transition (EMT) is a common feature for fibrotic eye disease including pterygium. UVB irradiation mediates EMT through upregulation of TGF β 1 and 2 but Resveratrol inhibits this later one. We aim to assess UVB radiation's effect in transforming limbal epithelial cells into myofibroblastic cells. And investigate whether the Resveratrol can inhibit limbal cells EMT induced by UVB or not In Vitro.

Methods: HCE-T cell line was cultured at the density of 2×10^4 cells /cm². When cells reached around 80-90% confluence, they were irradiated at a wavelength of 0.03 J/cm² UVB on two consecutive days or not irradiated. Two days after the irradiation, the protein was isolated, and immunoblotting was performed. Western Blot signals were quantified using ImageJ, and significance was calculated by two-tailed student t-test in Excel using the two-sample unequal variance setting.

For resveratrol experiment the same process was repeated, before 3 hours of irradiation cells incubated in 2% serum media and 0 or 50 or 100 μ M of Resveratrol. After 2 cells were fixed with PFA4% and Immunocytochemistry staining with aSMA, vimentin and β -Catenin was performed.

Results: Western Blot data showed that β -Catenin was significantly down-regulated in irradiated cells. The β -Catenin/Actin ratio of 1 ± 0.04 in non-irradiated cells was decreased to 0.060 ± 0.004 and 0.08 ± 0.04 in irradiated cells 2 days and 3 days after irradiation, respectively (2d post irr. $p=0.0006$ and 3d post irr. $p=0.00001$), while two and three days after irradiation, vimentin expression was 22- and 20-fold increased, respectively. Changes were significant ($p=0.007$ (2d post irr.) and $p=0.0016$ (3d post irr.)).

Immunocytochemistry showed increased aSMA and vimentin expression after irradiation versus non irradiated cells, but Resveratrol did not prevent the expression of aSMA, vimentin. The β -Catenin expression was unchanged.

Conclusions: UV-B irradiation of corneal epithelial cells induced EMT-related events by downregulation of β -catenin and upregulation of vimentin in HCE-T In Vitro. Resveratrol did not affect the UV induced changes related to EMT.

CONTROL ID: 3545395

SUBMITTER (NAME ONLY): Víctor López-Soriano

TITLE: Mapping the cis-regulatory landscape of ABCA4 in adult human retina

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Stargardt disease (STGD1) is a frequent inherited retinal disease (IRD) affecting ~1/8,000 people. Significant advances have been made over the recent years in elucidating the molecular basis of STGD1, with over 600 pathogenic coding variants and with a substantial number of deep-intronic splicing variants in the disease gene ABCA4. The cis-regulatory domain of ABCA4 is unexplored so far and may represent an attractive target for non-coding disease-causing or modifying variants. By mapping and functionally validating ABCA4 putative cis-regulatory elements (CREs), we aimed to gain more insights into ABCA4 expression regulation.

Methods: In order to identify candidate CREs, we integrated published and in-house human retinal epigenomics datasets. CRE predictions were based on chromatin accessibility (ATAC-seq), chromosome conformation capture combined with ChIP-seq (Hi-ChIP), histone modifications (ChIP-seq) and transcriptomics data (RNA-seq), all generated on human donor retina. To functionally validate in silico predicted CREs, dual luciferase reporter assays using pGL4.23 vectors were performed in hTERT RPE-1 cells. A chromatin interaction profile of the ABCA4 locus was obtained via UMI-4C experiments on neural retina and RPE from human donors.

Results: A total of 21 predicted CREs were cloned both in their native and reverse orientation in order to assess their regulatory effect in vitro. Five regions showed an increase of reporter activity, three of which display active enhancer marks (H3K4me1 and H3K27ac) in photoreceptors, and three regions showed a significant decrease in luciferase activity. The UMI-4C data showed a decrease in background compared to previously generated 4C-seq data (Gómez-Skarmeta et al., unpublished data) and an improved sensitivity and resolution. The generation of replicates and reverse experiments to confirm the interactions are currently ongoing.

Conclusions: Using an integrated approach based on data mining of retinal datasets, in vitro functional validation of putative retinal CREs and targeted chromosome conformation capture (UMI-4C), we have gained insight into the cis-regulatory landscape of ABCA4. The CREs identified and validated here can represent targets of non-coding pathogenic and modifying variants in cases with unsolved ABCA4-associated disease. An improved annotation of tissue-specific cis-regulatory domains of IRD genes may advance the interpretation of non-coding variants.

CONTROL ID: 3545401

SUBMITTER (NAME ONLY): Bianca S Gerendas

TITLE: Deep learning-based automated fluid quantification in clinical routine OCT images in neovascular AMD over 5 years

SESSION TITLE: AI in the retina: Clinical Applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Gerendas, A. Sadeghipour, M. Michl, F. Goldbach, G. Mylonas, T. Alten, O. Leingang, S. Sacu, H. Bogunovic, U. Schmidt-Erfurth, Department of Ophthalmology, Medical University of Vienna, Vienna, AUSTRIA|

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ABSTRACT BODY:

Purpose: To demonstrate the benefit of objectively quantifying intra- (IRF) and subretinal fluid (SRF) in real-world clinical routine OCT monitoring in eyes with nAMD using an automated deep learning-based algorithm.

Methods: Data from five databases of the Vienna Imaging Biomarker Eye Study (VIBES) registry from 2007-2018 (electronic patient records, treatment database and 2 OCT devices) were analyzed using the Vienna Fluid Monitor. Matching all entries and filtering for active nAMD by baseline (BSL) OCT of suitable quality for automated IRF, SRF and CST segmentation led to inclusion of 1127 eyes. Visual acuity (VA) and OCT data at BSL, month (M) 1-3 and years (Y) 1-5, age, gender and number of treatments were included in the analysis. Subanalyses compared the performance of the algorithm to manual analysis of the Vienna Reading Center in a subset of 20% of eyes.

Results: Mean CST was 358µm at BSL and decreased to 280-303µm over the entire follow-up. IRF/SRF volumes were highest at BSL (IRF: 22/77/107nl in 1/3/6mm area; SRF 14/86/263nl in the 1/3/6mm area). IRF decreased to a mean of 4-5nl at M1-M3 in the 1mm area and increased to 11nl at Y1 and to 16nl at Y5. SRF decreased to a mean of 3-5nl at M1-M3 in the 1mm area and remained below 7nl until Y5. IRF was the strongest parameter to reflect the course of visual acuity over time (Figure). When compared to manual expert analysis the Vienna Fluid Monitor found large amounts of fluid (IRF/SRF=39/23nl 1mm; 186/350nl total volume) in reading center determined presence and almost no fluid (IRF/SRF=2/1nl 1mm; 16/21nl total volume) in determined absence of both IRF and SRF (accuracy/sensitivity/specificity ~0.80).

Conclusions: Deep learning-based automated fluid quantification in clinical routine images is well-suited to objectively, reliably and rapidly measure treatment response and may guide clinical management in nAMD. The Vienna Fluid Monitor introduces expertise at reading-center level to a clinical routine setting while saving valuable time of the examiner. Automated volume measurements of retinal fluid compartments in a real-world dataset over a period of 5 years suggests IRF volume as the most practical parameter for treatment decisions.

CONTROL ID: 3545402

SUBMITTER (NAME ONLY): Kealan McElhinney

TITLE: Elucidating the role of p53 and MDM2 in glaucomatous lamina cribrosa cells.

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) is an age-related fibrotic condition and a leading cause of irreversible blindness worldwide. POAG-related damage is initiated within the lamina cribrosa (LC) region of the optic nerve head, driven by the pathological activation of resident LC cells. LC cells bear striking similarities to proliferative, apoptotic-resistant myofibroblasts known to be responsible for organ fibrosis. Myofibroblast dysregulation is linked to targeted proteasomal degradation of p53 by the E3 ubiquitin-protein ligase MDM2 (mouse-double-minute-2) thus negating p53's important regulatory role in cell-cycle/apoptosis. This project aims to evaluate the role of p53, MDM2, and the ubiquitin-proteasomal pathway in glaucomatous LC cells.

Methods: Primary human normal LC (NLC) and glaucoma LC (GLC) cells (n=3 donors) were cultured under standard conditions and treated for 48 hours with RG-7112 (p53-MDM2 interaction inhibitor, Abcam). The p53-MDM2 ubiquitin-proteasomal pathway was analysed by real-time polymerase chain reaction (qRT-PCR) for gene expression and protein levels via western blotting.

Results: MDM2 gene expression levels were significantly elevated ($p=0.006$) in GLC cells (1.00 ± 0.12) versus NLC cells (0.89 ± 0.08). p53-MDM2 inhibitor RG-7112 treatment caused a further significant ($p=0.001$) increase in MDM2 transcription levels in GLC cells (1.17 ± 0.04). p53 transcription levels were equivocal between GLC cells (0.88 ± 0.09) and NLC cells (0.87 ± 0.08), with RG-7112 treatment leading to a significant increase ($p=0.028$) in p53 transcription levels in GLC cells (0.95 ± 0.06). Western blot analysis showed significant decreased protein expression levels of p53 (0.76 ± 0.09) ($p=0.047$) and increased protein expression of MDM2 (1.57 ± 0.33) ($p=0.042$) in GLC cells compared to NLC. Interestingly, p53-MDM2 inhibitor RG-7112 treatment increased p53 (1.14 ± 0.43) ($p=0.267$) and decreased MDM2 protein expression levels (0.92 ± 0.25) ($p=0.06$) in GLC cells.

Conclusions: Our data suggests the ubiquitin-proteasomal pathway is significantly dysregulated in GLC cells with MDM2 led p53 protein degradation negatively impacting its key role as "guardian of the genome". Targeting the p53 ubiquitin-proteasomal pathway in lamina cribrosa fibrosis may lead to future novel therapeutic interventions.

CONTROL ID: 3545412

SUBMITTER (NAME ONLY): Daniela Santos

TITLE: ACE2-overexpression protects RPE cells from inflammation and oxidative stress

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.F. Santos, D.B. Bitoque, R.L. Sequeira, B. Cabrita, G.A. Silva, iNOVA4Health, CEDOC, NOVA Medical School, NMS, Universidade Nova de Lisboa, 1169-056 Lisboa, Portugal, PORTUGAL|D.F. Santos, ProRegeM PhD Programme NOVA Medical School | Faculdade de Ciências Médicas, Universidade Nova de Lisboa, Lisboa, Portugal, PORTUGAL|G.A. Silva, NOVA Medical School. Universidade Nova de Lisboa, Lisboa, Portugal, PORTUGAL|S. Simão, Centre for Biomedical Research, CBMR, University of Algarve, 8005-139, Faro, Portugal, PORTUGAL|S. Simão, Algarve Biomedical Center, University of Algarve, 8005-139, Faro, Portugal, PORTUGAL|

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ABSTRACT BODY:

Purpose: Treatment options for Diabetic Retinopathy (DR) are limited making research into alternative therapeutics of utmost need. The finding that the deregulation of the retinal Renin-Angiotensin System (RAS) triggers hallmarks of DR, support a role for RAS in this pathology.

We have previously characterized the ACE/AngII/AT1R axis and found it to be over-activated in retinal pigmented cells (RPE) cells (Simão et al., 2016; 2017). We aim to investigate the potential benefit for DR of a gene therapy approach promoting the activation of the protective axis of the RAS, the ACE2/Ang (1-7)/Mas.

Methods: A plasmid containing the human gene of ACE2 (pEPito-hCMV-ACE2) was used to transfect RPE cells (D407), with pEPito-hCMV-eGFP used as control. The cellular localization and expression of ACE2 in RPE cells was analyzed by immunocytochemistry and Western blot. The expression of components from the protective axis of RAS, PEDF, VEGF, and pro-inflammatory markers TNF- α and IL1- β were evaluated by Western blot or ELISA, and the levels of ROS were assessed using an oxidative stress indicator.

Results: The transfection of RPE cells with pEPito-hCMV-ACE2 significantly increased the expression of ACE2 and Mas receptor. Moreover, ACE2 localized in both the perinuclear and cytoplasmatic compartments of RPE cells. We found no differences in the levels of Ang (1-7) or expression of PEDF, VEGF or IL1- β when ACE2 is overexpressed in RPE cells. However, the levels of TNF- α in RPE cells transfected with pEPito-hCMV-ACE2 are much lower than those observed in cells transfected with the control (pEPito-hCMV-eGFP), which can be attributed to a protective effect from the ACE2 overexpression. A similar result has been observed for oxidative stress, with a significantly decrease in the levels of ROS in cells overexpressing ACE2.

Conclusions: Overexpression of ACE2 significantly increases the expression of the Mas receptor in RPE cells, with no effect on the levels of Ang (1-7). TNF- α and ROS levels are decreased in RPE cells overexpressing ACE2. Altogether these results point to a protective effect regarding inflammation and oxidative stress by ACE2 overexpression in RPE cells, and suggest a promising gene therapy approach towards the halting progression of retinal damage.

CONTROL ID: 3545413

SUBMITTER (NAME ONLY): Sukanya Jaiswal

TITLE: A doubling in the occurrence of dry eye symptoms during extreme smoke from wildfires surrounding Sydney, Australia

SESSION TITLE: Dry eye and microbiome clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Jaiswal, B. Golebiowski, N. Tein, S. Wang, I. Jalbert, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA

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ABSTRACT BODY:

Purpose: Wildfires are increasingly frequent and severe and release pollutants which can adversely impact the ocular surface. The Australian fires of 2019-2020 released extreme amounts of smoke, affecting half the Australian population. This pilot study compared ocular surface symptoms, signs and management strategies used in an optometry practice during the wildfires and during a control period.

Methods: Records of patients examined at the optometry clinic at UNSW in Sydney, Australia between October 2019 and February 2020 (fire period when extreme smoke severely reduced air quality) and from same months in 2018-2019 (control) were audited. Records containing ocular surface examinations of patients who had provided prior research consent were included. Ocular surface symptoms, signs and management were extracted from records and compared between the fire period and control period using Chi Square and Mann-Whitney U test. Associations with ambient air quality (PM2.5 level, NSW Department of Planning, Industry and Environment) were examined using Spearman's correlation ($p < 0.05$).

Results: 104 records in the fire period and 74 in the control period were audited. Patient age and sex did not differ between fire and control periods (35 ± 15 years; 44% male). The most common reason for presentation was for general check-up in both the fire (28%) and control period (26%). The symptom of 'dry eyes' was recorded more frequently during the fire (22%) than the control (11%) period ($p = 0.04$), but there were no significant differences in the occurrence of other ocular surface symptoms or clinical signs (Table). There were no differences in the recommended management such as lubricants, lid hygiene or warm compress (Table). Out of the 123 days in each fire and control period, ambient air PM2.5 levels exceeded national air quality standards on 23 days in fire period and zero days in control period, but no associations were evident between PM2.5 level on the date of eye examination and recorded ocular surface symptoms, signs management.

Conclusions: There was more frequent reporting of symptoms of dry eyes during wildfire period than during control (non-fire) period. This was not associated with a clear pattern of exposure and did not lead to increased diagnosis of chronic dry eye disease. Confirmation of these findings using optometry practices from other regions impacted by wildfires is warranted.

CONTROL ID: 3545414

SUBMITTER (NAME ONLY): Thomas Ciulla

TITLE: Longer term Visual Acuity Outcomes and Anti-Vascular Endothelial Growth Factor Therapy Intensity in Neovascular AMD, Diabetic Macular Edema and Retina Vein Occlusion–Related Macular Edema: A Real World Analysis of 130,247 Patient Eyes

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.A. Ciulla, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|T.A. Ciulla, Retina, Midwest Eye Institute, Indianapolis, Indiana, UNITED STATES|J. Pollack, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|D. Williams, Ophthalmology, University of Minnesota Academic Health Center, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Longer term “Real-world” visual acuity (VA) outcomes of anti-vascular endothelial growth factor (anti-VEGF) therapy were assessed in neovascular AMD (nAMD), diabetic macular edema (DME), branch and central retinal vein occlusion (BRVO, CRVO)-related macula edema (ME).

Methods: A retrospective analysis was performed on a large database of aggregated, longitudinal, deidentified electronic medical records from a geographically and demographically diverse sample of patients of United States retina specialists (Vestrum Health Retina Database). Treatment naïve nAMD, DME, BRVO-ME and CRVO-ME patients who underwent anti-VEGF injections between 2014 and 2019 were eligible if follow up data was available through at least 12 months.

Results: At 1, 3 and 5 years, in those 67,666, 21,305 and 5,208 eyes with nAMD, after a mean of 7.6, 19.5 and 32 injections, there was a mean change of +3.1, -0.2 and -2.2 letters respectively. At 1, 3 and 5 years, in those 40,832, 7,728 and 1,192 eyes with DME, after a mean of 6.2, 15.4 and 26.0 injections, there was a mean change of +4.7, +3.3 and +3.1 letters respectively. At 1 and 3 years, in those 12,451 and 3,027 eyes with BRVO-ME, after a mean of 7.1 and 18.2 injections, there was a mean change of +9.5 and +7.7 letters respectively. At 1 and 3 years, in those 9,298 and 2,264 eyes with CRVO-ME, after a mean of 7.3 and 18.8 injections, there was a mean change of +8.3 and +6.0 letters respectively. In all 4 conditions, mean letters gained increased with mean number of anti-VEGF injections at each of the aforementioned time periods. In all 4 conditions, patient eyes with baseline VA of 20/40 or better tended to lose VA, and those with progressively worse baseline VA experienced progressive greater gain in VA at 3 years.

Conclusions: Real-world nAMD, DME, BRVO-ME and CRVO-ME patients experience meaningfully worse visual outcomes compared with patients in randomized controlled trials, with nAMD patients tending to lose VA at 3 and 5 years. Across all 4 disorders, mean change in VA correlates with treatment intensity at 1, 3 and 5 years. Patients with better VA at presentation tend to be particularly vulnerable to vision loss. There remains unmet need for more effective therapy with durability to address treatment burden.

CONTROL ID: 3545417

SUBMITTER (NAME ONLY): Theodore Spaide

TITLE: Analysis of numerical feature extraction from automated geographic atrophy segmentation

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Spaide, J. Patil, J. Jiang, N. Anegondi, M. Kawczynski, V. Steffen, S.S. Gao, Genentech, Inc., South San Francisco, California, UNITED STATES|J. Jiang, University of California, Santa Barbara, Santa Barbara, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To examine deep learning-based segmentation of geographic atrophy (GA) lesions and the reliability of derived features.

Methods: Nine hundred and forty pairs of images were taken from 194 patients, with each pair comprising a fundus autofluorescence (FAF) and near-infrared (NIR) image from 1 eye (Proxima B, NCT02399072). Lesions were annotated on the FAF by a grader, and the data were split at the patient level into training (n=155) and validation (n=39) sets. A test set comprising 90 FAF-NIR pairs from 90 patients (Proxima A, NCT02479386) was annotated by 2 graders (G1 and G2). Two multimodal deep learning networks (UNet and YNet) were trained on the training set and tuned on the validation set. The final network was applied to the test set. For each segmentation mask, the lesion area, perimeter, circularity, Feret diameters, and number of lesions were extracted. As a numerical proxy for the FAF pattern, the excess rim intensity (ERI), equal to the mean FAF intensity in a 0.5-mm rim around the lesion minus the mean FAF intensity in a 0.5- to 1-mm rim around the lesion, was also extracted. For all measures except for number of lesions, the relevant metric was computed for the whole segmented area without separating it into different components.

Results: The average Dice score between the network and G1 on the test set was 0.92. The Pearson correlation (r) of area, perimeter, circularity, major Feret diameters, minor Feret diameters, ERI, and number of lesions between the YNet and G1 was 0.98, 0.93, 0.86, 0.87, 0.93, 1.00, and 0.46, respectively. Analogous statistics for the network and G2 and for G1 and G2 are given in Table 1.

Conclusions: Networks trained to segment GA lesions could produce accurate segmentations. When the segmentations were used to obtain the values of area and ERI, the agreement between the networks and human graders was similar to the agreement between two graders. Inferred values of perimeter, circularity, and Feret diameters were less similar, and often varied between models despite similar Dice scores. The inferred number of lesions matched human grading poorly. The variable accuracy of the examined features could be an important factor for their use in predictive models of GA growth.

CONTROL ID: 3545419

SUBMITTER (NAME ONLY): Kate Leahy

TITLE: Optic atrophy and inner retinal thinning in CACNA1F-related congenital stationary night blindness

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.E. Leahy, M.K. Grudzinska Pechhacker, A. Tumber, H. MacDonald, J. Locke, C. VandenHoven, E. Heon, J.R. Buncic, A. Vincent, Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, Toronto, Ontario, CANADA|K.E. Leahy, T. Wright, M.K. Grudzinska Pechhacker, E. Heon, J.R. Buncic, A. Vincent, Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|T. Wright, Kensington Eye Institute, Toronto, Ontario, CANADA|I. Audo, C. Zeitz, INSERM, CNRS, Institut de la Vision, Sorbonne Universite, Paris, Île-de-France, FRANCE|I. Audo, DHU Sight Restore, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts Centre d'investigation clinique, Paris, Île-de-France, FRANCE|E. Tavares, Program in Genetics and Genome Biology, The Hospital for Sick Children, Toronto, Ontario, CANADA|H. MacDonald, Department of Molecular Genetics, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Hemizygous pathogenic variants in CACNA1F lead to defective signal transmission from photoreceptors to bipolar cells and cause incomplete congenital stationary night blindness (iCSNB). Knowledge of inner retinal changes in iCSNB is limited. This study measured macular ganglion cell layer-inner plexiform layer (GCL-IPL) thickness and optic disc pallor to assess if subjects carrying pathogenic variants in CACNA1F have inner retinal thinning and optic atrophy in excess of the expected degree of disc pallor seen in myopia.

Methods: Ocular phenotypic data including distance and color vision, refraction, optical coherence tomography (OCT) GCL-IPL thickness and electroretinogram (ERG) were collected from 22 subjects with molecularly confirmed CACNA1F-iCSNB. OCT data was collected from an age-matched control population (n=87) without organic ocular pathology, subdivided into 3 groups based on spherical equivalent (SE) refractive error: (1) emmetropia or hyperopia: SE $\geq 0D$, (2) low myopia: SE ≤ -0.5 and $> -6.00D$, and (3) high myopia: SE $\leq -6.00D$. ERG parameters were correlated against GCL-IPL thickness. Optic disc photos were evaluated by a pediatric neuro-ophthalmologist noting the presence and extent of disc pallor in clock hours.

Results: Mean patient age was 14.3 years (range 6-58 years); mean refractive error was -6.32D (range -20.50 to +2.50D); 68% (15 of 22) were myopic. Distance vision was universally reduced (mean 0.42 LogMAR) and six had abnormal color vision. Mean GCL-IPL thickness in patients was significantly lower (55.00 μm) compared to controls (84.57 μm) as well as compared to emmetropia or hyperopia (88.25 μm), low myopia (83.07 μm) and high myopia (78.59 μm) control sub-groups ($p < 0.001$). The GCL-IPL thickness correlated with scotopic standard ($p = 0.04$) and bright-flash ($p = 0.014$) ERG b/a ratios, and photopic b-wave amplitude ($p = 0.05$). Twenty-one patients had some degree of disc pallor (bilateral in 19). There was no correlation between GCL-IPL thickness and extent of disc pallor or mutation class. Fifteen putative disease-causing variants were identified: 5 missense, 4 nonsense, 3 frameshift, 2 splice site and 1 silent variant predicted to affect splicing; 5 variants were novel.

Conclusions: This study establishes macular inner retinal thinning and optic atrophy as features of CACNA1F-related iCSNB which are independent of myopia and could impact potential future treatment strategies.

CONTROL ID: 3545421

SUBMITTER (NAME ONLY): Benjamin Mc Clinton

TITLE: Using Oxford Nanopore long-range sequencing to phase ABCA4

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Mc Clinton, L. Crinnion, M. Ali, C. Inglehearn, C.M. Watson, C. Toomes, University of Leeds Leeds Institute of Medical Research at St James's, Leeds, West Yorkshire, UNITED KINGDOM|L. Crinnion, C.M. Watson, Yorkshire and North East Genomic Laboratory Hub, Leeds, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mutations in ABCA4 are the most prevalent cause of monogenic retinal disease and are responsible for a range of phenotypes including Stargardt disease and cone-rod dystrophy. ABCA4-disease is caused by biallelic variants and recent studies have revealed pathogenic hypomorphic common variants and complex alleles (two or more variants in cis). The ability to cheaply and efficiently phase ABCA4 variants is therefore important to establish the biallelic status of variants when diagnosing singleton cases and to facilitate the further investigation of complex alleles. The goal of this study was to develop a cost-effective long-range sequencing method to phase ABCA4.

Methods: Long-range PCR primers encompassing the entire 130kb ABCA4 locus in overlapping blocks of 6-12kb were used to amplify genomic DNA using the Sequel Prep Long-Range PCR Kit. Samples were purified using AxyPrep Mag PCR Clean Up Kit and equimolar concentrations of each amplicon were combined and run on an Oxford Nanopore MinION with a flongle adaptor. Fast5 files were converted to Fastq files using Guppy, trimmed using Porechop and aligned using Minimap. Variants were called using Nanopolish and haplotypes assembled using WhatsHap.

Results: A pilot test involved amplifying 2 previously phased cases (eg. CEPH NA12878) and 2 Stargardt patients with two unphased variants. Initially 23 amplicons ranging between 6kb and 12kb in size and overlapping by a minimum of 2.5kb were used. One sample per flongle achieved an average read depth of ~7500, reducing stochastic effects. This method could be used to successfully phase the ABCA4 gene into 4 phase blocks which confirmed the phasing of previously identified variants in the control samples. The gaps were caused by a lack of variants in the overlap regions so amplicons were redesigned for these regions after analysing WGS datasets to ensure the capture of maximum variation.

Conclusions: This study has designed and tested a long-range, low-cost sequencing strategy to phase ABCA4. This will increase the accuracy of diagnosing individuals which is becoming increasingly important with the advent of therapies. It also has far reaching implications for the investigation into the contribution of complex alleles in ABCA4 related disease.

CONTROL ID: 3545428

SUBMITTER (NAME ONLY): Naïg Chenais

TITLE: Epiretinal photovoltaic prosthesis with high pixel density

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Chenais, M. Airaghi Leccardi, D. Ghezzi, Medtronic Chair in Neuroengineering, Center for Neuroprosthetics and Institute of Bioengineering, School of Engineering, École Polytechnique Fédérale de Lausanne, Geneva, SWITZERLAND|

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ABSTRACT BODY:

Purpose: The theoretical visual acuity offered by retinal prostheses is limited by the use of implantable pulse generators and feedlines on the array. In parallel, the visual angle restored by most prostheses is limited to at best 20 degrees, primarily by reason of low conformability materials and subretinal placement. The combination of these limitations prevents implanted blind patients to benefit from artificial vision in their day-to-day life, as navigation in complex spaces and most of the daily visually-guided manipulation activities require both visual acuity and visual field together.

Methods: Conjugated polymers allow for photovoltaic retinal stimulation with flexible and large arrays, thus opening the possibility for wide-field and high-density arrays freed from external power generator. In this work, we designed a photovoltaic epiretinal implant embedding 10'498 physically and electrically independent miniaturised photovoltaic pixels. Such implant combines a large visual angle, thanks to the flexibility of the organic materials used, and a high pixel density, possible through the patterning of the organic polymer films. Using single-pixel stimulation, minimum separable and grating visual acuity paradigms, we evaluated the spatial resolution of the prosthetic response elicited by this high-density photovoltaic implant in explanted retinal degeneration 10 mouse retinas.

Results: Each of the discrete photovoltaic pixels could elicit reproducible network-mediated response in light-insensitive retinal ganglion cells from $80 \mu\text{W} \cdot \text{mm}^{-2}$. Moreover, the high-density arrangement of the pixels allowed retinal ganglion cells to be stimulated with a 0.3-degree resolution, what corresponds to a 20/480 visual acuity. During both two-points discrimination test and decreasing gratings tests, retinal ganglion cells exhibited desensitized response to repeated stimulation patterns, but marked response to pattern reversals. Such response resolution was observed in ganglion cells whose receptive field diameter exceeded the pixel pitch, suggesting that spatial discrimination can be achieved at the inner retinal level with epiretinal network-mediated stimulation.

Conclusions: In view of the large visual angle (43°) covered by the photovoltaic epiretinal implant, this device could provide artificial vision with high peripheral resolution to retinitis pigmentosa patients, a valuable improvement for obstacle recognition, ambulation, and independence.

CONTROL ID: 3545430

SUBMITTER (NAME ONLY): Arvind Chandna

TITLE: Characterization of Higher Visual Function Deficits (HVFDs) with a Question Inventory in children with Cerebral Visual Impairment (CVI) and good visual acuity (VA)

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chandna, S. Foster, Alder Hey Children's NHS Foundation Trust, Liverpool, Merseyside, UNITED KINGDOM|A. Chandna, S. Ghahghaei, Smith Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: CVI, the commonest cause of visual loss in children in the developed world with prevalence rising worldwide; manifests with variable VA loss and diverse HVFDs such as difficulty with motion perception and visual environmental clutter. Visual behaviorisms suggestive of HVFDs even in CVI children with good VA, are observed by parents and teachers with adverse effects on daily activities at school and home. Good VA in CVI children often precludes further investigation for HVFDs. We investigated HVFDs in children with CVI and good VA through structured history-taking with HVF Question Inventory (HVFQI) and develop an abbreviated QI for rapid screening.

Methods: Parents of 33 children with CVI (7.0 +/- 2.7 yrs.) with good VA (≥ 0.2 LogMar) and 111 typical children (8.7 +/- 2.8 yrs.) participated. CVI diagnosis was based on integrated assessment of history, eye and neurologic examination and brain imaging. Parents responded to the 51 questions choosing from a 5-point Likert scale: Never, Rarely, Sometimes, Often, Always. 'Not Applicable' (NA) option was available. Initial analysis tested the ability of HVFQI to differentiate between CVI and typicals by calculating average score for each question adjusted for NA responses. Next, the questions that offered best discriminability as a screening tool were determined by scoring across a series of binary divisions along the Likert scale followed by area-under-curve (AUC) analysis for each question and each binary-scoring method.

Results: Children with CVI scored significantly higher than typical children in overall scores and in all binary scoring methods (p-values < 0.001). Three binary-scoring methods gave us the highest AUC values (>0.87) and revealed 11 questions that contributed most to an affirmative result for presence of HVFD. These related to problems with clutter, lower visual field, motion perception and multi-tasking and termed HVFQI-Top11.

Conclusions: Our results confirm the presence of HVFDs and that HVFQI-51 is a sensitive tool able to differentiate children with CVI despite good VA and characterize the spectrum of HVFDs for each child. HVFQI-51 has the potential for; longitudinal studies to document the natural history, effects of habilitative measures and use in other conditions where HVFDs are suspected. We recommend a subset, the HVFQI-Top11, for screening for HVFDs.

CONTROL ID: 3545437

SUBMITTER (NAME ONLY): Diogo Bitoque

TITLE: PAEMA nonviral vectors display enhanced gene transfer ability in retinal cells

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.B. Bitoque, R.L. Sequeira, G.A. Silva, NOVA Medical School, NMS, Universidade Nova de Lisboa, iNOVA4Health, CEDOC, Lisbon, Lisbon, PORTUGAL|A.M. Rosa da Costa, Faculty of Science and Technology, Universidade do Algarve, CIQA – Algarve Chemistry Research Centre, Faro, Algarve, PORTUGAL|

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ABSTRACT BODY:

Purpose: Non-viral vectors present several advantages for retinal gene therapy, in particular by carrying genes above 4.5 kb; however, these still need to be optimized to achieve higher transfection efficiencies. Previous results from our group revealed that entering the nucleus was the bottleneck for our nonviral vectors (Bitoque, et al. Materials Science and Engineering: C, 2018; Bitoque, et al. Bioscience Reports, 2021). Therefore, we aimed to increase the efficiency of a polymeric nonviral vector by conjugating nuclear localization signals (NLSs), which are short amino acid sequences capable of directing molecules to the nucleus.

Methods: To test our hypothesis, we have produced and characterized a nonviral vector by combining a plasmid encoding a reference gene with our NLS-conjugated PAEMA (poly(2-aminoethyl methacrylate polymer). We further tested it in vitro using a human pigment epithelial cell line (D407) to assess its effect on cell viability and transfection efficiency and in vivo in the rd10 mouse. All experimental procedures were carried out according to the Portuguese, European Union, FELASA, and the Association for Research in Vision and Ophthalmology (ARVO) regulations for the use of animals in ophthalmic and vision research.

Results: We have found that PAEMA can be efficiently modified to incorporate NLSs, and this modified polymer efficiently complexes plasmid-based expression systems, with size and charge adequate for cell entry. We have further confirmed this polymer to be capable of protecting its load from degradation but adequately releasing it 24 hours after cell entry. Furthermore, in RPE cells, the qualitative (fluorescence microscopy) and quantitative (flow cytometry) analysis of the transfection efficiency show that PAEMA conjugated with NLSs is able to increase the expression of the gene of interest by 63%. Lastly, intravitreal injection of PAEMA-NLSs polyplexes in the retina of rd10 mice has shown in vivo compatibility, and negligible, fast-resolving, inflammatory response. Further studies are focused on the capacity of the optimized polymer to deliver the β subunit of PDE6 gene to the nucleus of retinal cells.

Conclusions: Overall, these results demonstrate the potential of PAEMA nonviral vectors for retinal gene therapy, in particular for overcoming the nuclear bottleneck for an efficient delivery.

CONTROL ID: 3545438

SUBMITTER (NAME ONLY): Oudy Semoun

TITLE: Adaptation of practices during the pandemic period of Covid-19 among French Ophthalmologists

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Semoun, M. Srour, A. Miere, F. Amoroso, E.H. Souied, Ophthalmology, Creteil Retina, Creteil, FRANCE|

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ABSTRACT BODY:

Purpose: We aim to better understand the practices of ophthalmologists during the COVID-19 pandemic period in France, and particularly in the management of patients with exudative AMD

Methods:

During the months of June and July 2020, French ophthalmologists were invited to answer an online questionnaire evaluating the adaptation of their practice during the pandemic period (March to May 2020) and more particularly the management of exudative AMD . The questionnaire consisted of 40 questions.

Results: 107 ophthalmologists responded to the online questionnaire. Ophthalmologists treated an average of 146 participants with exudative AMD per month (median: 80). 89.5% of participants maintained their activity during this period. 90.2% selected the patients to be called, on the basis of their medical reports. 9.8% saw only emergencies. All ophthalmologists adapted their practices and 43.5% systematically took patients' temperatures. 91.8% spaced the intervals between appointments to 15 minutes or more. 49% did not check visual acuity. 41.8% only controlled OCT when absolutely necessary. 80% of ophthalmologists adapted the therapeutic regimens to fixed or Treat-and-Extend regimens based on the last treatment interval. For 25%, pharmacological and / or pharmacokinetic properties were important for the choice of the molecule used. 82.5% of practitioners observed a significant worsening of exudative AMD due to a lack of follow-up during the confinement period

Conclusions: This survey allowed us to better understand the practices of ophthalmologists for patients with exudative AMD during the beginning of the pandemic period of Covid-19 in France. Health conditions have prompted all ophthalmologists to quickly change their reception and care practices

CONTROL ID: 3545441

SUBMITTER (NAME ONLY): Manar Salameh

TITLE: ABCA4 c.859-25A>G, a frequent Palestinian founder mutation associated with retinal dystrophy, results in multiple splice defects

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Salameh, Y. AlSwaiti, A. AlTalbish, Saint John Eye Hospital, Jerusalem, PALESTINE, STATE OF|Z. Corradi, M. Khan, R. Hitti-Malin, F.P. Cremers, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|Z. Corradi, R. Hitti-Malin, F.P. Cremers, Radboud Universiteit Donders Institute for Brain Cognition and Behaviour, Nijmegen, Gelderland, NETHERLANDS|M. Salameh, E. Banin, D. Sharon, Hadassah Medical Center Department of Ophthalmology, Jerusalem, Jerusalem, ISRAEL|A. Vincent, E. Heon, Ophthalmology and Vision Sciences, The Hospital for Sick Children, Toronto, Ontario, CANADA|E. Heon, Program of Genetics and Genome Biology, The Hospital for Sick Children, Toronto, Ontario, CANADA|M. Khan, Pathology and Medical Biology, Universitair Medisch Centrum Groningen, Groningen, Groningen, NETHERLANDS|C. Dhaenens, Lille Neuroscience & Cognition, Centre Hospitalier Universitaire de Lille, Lille, Hauts-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The effect of noncoding variants is often unknown in the absence of functional tests. The purpose of this study was to characterize an ABCA4 intron 7 variant, c.859-25A>G, identified in Palestinian probands with a clinical diagnosis of Stargardt disease (STGD) or cone-rod dystrophy (CRD). We assessed the effect of this variant on the ABCA4 mRNA and retinal phenotype, and investigated its prevalence in inherited retinal dystrophy (IRD) cases from Palestine.

Methods: Molecular inversion probe (MIP)-based sequencing of ABCA4 was performed in 876 probands with STGD or CRD collected worldwide. In silico analysis of DNA variants was performed using SpliceAI. The effect of variant c.859-25A>G was investigated using in vitro splice assays in HEK293T cells using ABCA4 exon 7-11 midgenes. ABCA4 sequencing data was obtained or re-analyzed from another 890 Palestinian IRD cases using MIPs-based sequencing, whole exome sequencing, and targeted Sanger sequencing. The ophthalmologic characteristics were examined using retinal imaging techniques, including optical coherence tomography and also full field electroretinography.

Results: smMIPs-based ABCA4 sequencing revealed the c.859-25A>G variant in three Palestinian probands living in, or originating from, the city of Hebron. SpliceAI predicted a significant effect on the nearby splice acceptor site, and splice assays revealed an exon 8 deletion and two upstream elongations in mRNA. None of these products yields a functional ABCA4 protein. ABCA4 genotyping in 890 Palestinian cases revealed another 48 affected persons carrying this variant, all living in or originating from the Hebron area. Haplotype analysis in 22 of 38 homozygotes revealed a shared genomic segment. Homozygotes for variant c.859-25A>G show an average age at onset of 5.4 years confirming that this is a severe variant. The mean logmar best corrected visual acuity for these cases was 1.1. Of the 38 homozygotes 25, 7, and 6 cases had a clinical picture compatible with CRD, STGD1 and retinitis pigmentosa (RP) respectively.

Conclusions: ABCA4 variant c.859-25A>G results in multiple severe splice defects and CRD, RP or early-onset STGD1 in homozygotes. It was found in 50/892 IRD cases in Palestine and represents the most frequent IRD-causing variant to date in Palestine.

CONTROL ID: 3545447

SUBMITTER (NAME ONLY): Sumeia Elkazza

TITLE: Random Forest model matches clinician performance in forecasting visual outcomes from anti-VEGF treatment in retinal vein occlusion.

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinal vein occlusion (RVO) is often complicated by sight limiting macular oedema (MO). Intravitreal injections (IVIs) of anti-vascular endothelial growth factor (anti-VEGF) carry some clinical risk to patients but improve MO and vision for many. A significant minority show partial or no response despite many IVIs. If treatment outcomes could be forecast at RVO presentation, such patients may decline anti-VEGF treatment. This prognostic accuracy study aimed to test the feasibility of such forecasts using Random Forest technique (RF).

Methods: A retrospective dataset of RVO treated with anti-VEGF IVIs for MO was assembled from the electronic medical record (EMR) of a large provincial UK ophthalmology centre. 412 eligible eyes were identified (212 left eye, 194 CRVO, 205 male, mean age 72.6, mean delay between diagnosis and treatment 110.9 days) with a mean visual acuity (VA) at treatment initiation of 50.3 early treatment diabetic retinopathy study (ETDRS) letters and a mean VA of 58.8 letters following 1 year of treatment. Fovea centred optical coherence tomography slices, taken at treatment initiation, were included. The dataset was divided 80:20 for training and testing. Features of the images were extracted using Histogram Oriented Gradient feature descriptor. To evaluate the performance of the RF model, 11 different ophthalmology doctors provided similar VA forecasts for two subsets (n=41) of the RF test set (n=82).

Results: The mean absolute error (MAE) of the RF model is 14.3 (SD=16.2), which was not significantly different to the pooled MAE of 16.7 (SD=22.4) from all clinicians' forecasts (p=0.42). The root mean squared errors were 19.55 and 23.53 for the RF model and pooled clinician forecasts respectively. The best performing clinician achieved a MAE of 14.8, which was not significantly different to the RF model's MAE of 12.9 on the same subset (p=0.35).

Conclusions: Such a RF model can match ophthalmologists in their ability to forecast VA outcomes for RVO complicated by MO undergoing 1 year of anti-VEGF treatment. The error reported here is too great to be of clinical use, but further work is required to establish if larger datasets and more powerful techniques could help to support patients' treatment decisions.

CONTROL ID: 3545449

SUBMITTER (NAME ONLY): Isabel Fabelo Hidalgo

TITLE: Normal values of mesopic and scotopic retinal sensitivity using microperimetry in a healthy reference population.

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Fabelo Hidalgo, C. Fernández-Nuñez, N. Pérez-Llombet Quintana, O. Duran Carrasco, M.M. Alberto-Pestano, M. Alonso Plasencia, R. Abreu-Gonzalez, Ophthalmology, University Hospital of La Candelaria, Santa Cruz de Tenerife, Tenerife, SPAIN|

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ABSTRACT BODY:

Purpose: To determine normal values of mesopic and scotopic retinal sensitivity obtained by microperimetry , using MP3s microperimeter (Nidek, Gamagori, Japan), in a healthy population. Secondly, to assess the association among retinal sensitivity, gender and age.

Methods: Microperimetry was performed using the Nidek MP3s system (Nidek, Gamagori, Japan) with a 13-point fovea-centered pattern in mesopic and scotopic mode in volunteers which did not present fundoscopic alteration or structural OCT changes compatible with maculopathy. All of them presented a corrected visual acuity of 1.0 on a decimal scale (0.00 Log Mar) and a spherical equivalent less than +/- 5.0 D. A intraclass correlation coefficient (ICC) was performed to evaluate mesopic and scotopic microperimetry reliability.

Results: We analyzed 102 eyes of 54 patients (62.7% male and 37.3% female) with a mean age of 49.8 +/- 15 years old (p=.14) The mesopic and scotopic mean retinal sensitivity (MRS) was 28.55 ± 3.3 dB (95% CI=[27.87-29.23]) and 15.72 ± 1.9 dB (95% CI=[15.35-16.09]) respectively, showing a significant statistical difference (p <0.05).

There were no statistical significant differences related to gender and MRS in both microperimetry modes. Regarding to age we divided the patients into quartiles (<39 y; 40-53 y; 54-67 y; >67 y). MRS was higher in the <35 years old group (mesopic: 30.3 ± 1.7 dB and scotopic: 16.3 ± 1.3 dB) and lower in the >67 years old group (mesopic: 26.7 ± 2.2 dB and scotopic: 13.8 ± 1.8 dB (p= .0001).

The reliability analysis of both tests, using the intraclass correlation coefficient (ICC), revealed an excellent reliability of the mesopic microperimetry with a Crombach alpha of 0.958 (ICC = 0.958, f = 23.893, p <0.0001) and a good reliability of 0.841 (ICC = 0.841, f = 6.305, p <0.00) in scotopic microperimetry.

Conclusions: With the results of our study, we may conclude that there is no difference in mean retinal sensitivity related to gender, in the mesopic and scotopic tests, and that it decreases with age.

CONTROL ID: 3545452

SUBMITTER (NAME ONLY): Danah Albuainain

TITLE: Myocilin mutations account for 5% of POAG in a West Yorkshire clinic

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To investigate the frequency of myocilin (MYOC) mutations in patients diagnosed with Primary Open Angle Glaucoma (POAG) from a West Yorkshire clinic.

Methods: Patients were diagnosed with POAG by an experienced ophthalmologist. Genomic DNA was extracted from peripheral blood. PCR and direct Sanger Sequencing was used to analyse the coding exons and splice recognition sites of the MYOC gene. The frequency of the variants in the general population was investigated using the gnomAD database and their pathogenicity assessed using prediction programs PolyPhen2, SIFT, PROVEAN, CADD, BLOSUM62, MutationTaster and Human Splicing Finder.

Results: 12 out of 219 patients (5%) analysed had a MYOC mutation that was predicted to be pathogenic and could possibly account for their disease phenotype. The patients between them had 8 MYOC mutations including a novel frameshift (p.Lys484Argfs), previously identified nonsense (p.Gln368Stop) and non-synonymous (p.Glu352Lys, p.Lys398Arg and p.Thr419Ala) mutations as well as synonymous variants (p.Thr204Thr, p.Thr285Thr and p.Glu396Glu) that are predicted to affect splicing.

Conclusions: MYOC mutations are likely to account for 5% of the POAG cohort studied, which is consistent with findings in previously published studies. This leaves an enriched cohort of cases for systematic screening of the other known genes that cause POAG.

CONTROL ID: 3545456

SUBMITTER (NAME ONLY): Lupe Villegas

TITLE: Biomechanical effects of Scleral crosslinking using Rose Bengal/Green-light and Rivoflavin/UVA

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Villegas, J. Germann, S. Marcos, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|

Commercial Relationships Disclosure (Abstract): Lupe Villegas: Commercial Relationship: Code N (No Commercial Relationship) | James Germann: Commercial Relationship: Code N (No Commercial Relationship) | Susana Marcos: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Scleral collagen crosslinking (SXL) has been proposed as a therapeutic treatment for prevention of progressive myopia. In this study, we compare the effects of Rose Bengal-Green Light (RGX) and Rivoflavin-UVA (UVX) crosslinking in scleral stiffening through a hydration-stiffness correlation.

Methods: 35 eyes from adult New Zealand white rabbits (2.5-3.5 kg) were treated with either RGX (523nm 0.25W/cm², 400s) or UVX (370nm, 3mW/cm², 30min). Posterior nasal (NR) and temporal (TR) regions were crosslinked (24-48h post-mortem). One side of the globe was SXL and the other kept as control. Strips (3mmx20mm) were extracted and brought under hydration-tensile and tensile tests. In hydration-tensile tests, strips from control and treated regions were dehydrated (24h, room temperature), re-hydrated using 10uL/min phosphate-buffered saline solution (PBS) and mounted in a uniaxial stretcher (CellScale, Canada). In tensile tests, samples were mounted after extraction. Part of the specimens were immersed in PBS (n=54) and the rest kept in air (n=24) while subjected to a stress-recover test. The Young's modulus (YM) was calculated between 0% and 12% strain and stress-strain curves were plotted as a derivative marker for SXL strength. T-test was used to test treatment and hydration-induced differences in scleral biomechanics.

Results: RGX and UVX produced an increase in stiffness (115% and 296% (TR), respectively) compared with untreated sclera. At 8% strain, the YM of UVX samples was significantly higher than the untreated ones (16.11±0.94 vs 3.36±0.69MPa (TR), and 15.76±1.28 vs 3.15±0.49MPa (NR) P<0.001), and significantly higher than RGX samples (7.24±0.70MPa (TR) and 10.44±0.96MPa (NR) P<0.001). Tensile behavior is influenced by PBS immersion during the mechanical test. Control samples processed in air were twice (TR) and 1.5 times (NR) stiffer than ones in PBS (P<0.05). Hydration and stiffness are inversely correlated in TR (r=-0.6, P< 0.05) and directly correlated in NR (r=0.7, P< 0.05) for untreated and treated samples.

Conclusions: Posterior scleral stiffening with RGX and UVX treatment in rabbit is affected by a combination of treatment, region, and hydration. These results provide a method for in vivo studies to determine the efficacy of SXL-induced stiffening to help treat myopia.

CONTROL ID: 3545460

SUBMITTER (NAME ONLY): Satoshi Yasuhara

TITLE: Predictors of retinal pigment epithelium tear development after treatment for neovascular age-related macular degeneration using swept source optical coherence tomography angiography

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Yasuhara, M. Miyata, S. Ooto, H. Tamura, N. Ueda, A. Uji, Y. Muraoka, M. Miyake, A. Takahashi, T. Wakazono, K. Yamashiro, A. Tsujikawa, Department of Ophthalmology and Visual Sciences, Kyoto Daigaku, Kyoto, JAPAN|K. Yamashiro, Department of Ophthalmology, Otsu Sekijoji Byoin, Otsu, Shiga, JAPAN|

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ABSTRACT BODY:

Purpose: To investigate predictors of retinal pigment epithelium (RPE) tear development after anti-vascular endothelial growth factor (VEGF) therapy or photodynamic therapy (PDT) for neovascular age-related macular degeneration (AMD) using swept source optical coherence tomography angiography (SS-OCTA)

Methods: This prospective, observational study included treatment-naïve eyes with neovascular AMD in consecutive patients who were followed for 1 year after receiving the initial treatment at Kyoto University Hospital between June 2017 and June 2019 and who underwent SS-OCTA examinations (PLEX Elite 9000, Dublin, California) prior to the treatment. Eligible eyes were classified into eyes with or without RPE tear development during 1-year observation period. They were matched for 1:2 ratio using propensity scores. The area of choroidal neovascularization (CNV) and RPE detachment (PED) were measured from OCTA and optical coherence tomography (OCT) en face images, respectively. Specific OCTA-derived parameters, which represent vessel caliber and complexity of CNV, were also analyzed.

Results: In 8 of 164 eyes (4.9%), RPE tear developed (RPE tear group). After matching, 16 eyes without RPE tear were analyzed (no RPE tear group). The ratio of CNV/PED area was significantly lower in the RPE tear group than in the no RPE tear group (0.24 ± 0.13 vs. 0.52 ± 0.26 , $P = 0.01$). The PED area was broader (9.07 ± 5.79 mm² vs. 4.29 ± 5.47 mm², $P = 0.01$), and PED height was greater in the RPE tear group (413.6 ± 224.4 μm vs. 231.8 ± 218.3 μm, $P = 0.02$). There were no significant differences in specific OCTA-derived parameters between the two groups.

Conclusions: Neovascular AMD with pre-treatment broad PED, high PED, and small CNV area relative to PED area may have a high risk of RPE tear development after the therapy. Vessel caliber or complexity of CNV may not be associated with RPE tear development.

CONTROL ID: 3545461

SUBMITTER (NAME ONLY): Louise Mesentier-Louro

TITLE: Immunoprofiling of Nonarteritic Anterior Ischemic Optic Neuropathy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Mesentier-Louro, Y. Yan, A. Montague, Y.J. Liao, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|L. Stell, Biomedical Data Science, Stanford University, Stanford, California, UNITED STATES|Y. Yan, Ophthalmology, Shanghai Jiao Tong University, Shanghai, CHINA|V. De Jesus Perez, Pulmonary Medicine, Stanford University, Stanford, California, UNITED STATES|Y.J. Liao, Neurology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in those older than 50. There is no blood diagnostic test or effective treatment for NAION, and the etiology for progression of vision loss in some patients remains unclear. We investigated the suitability of blood inflammatory proteins as biomarkers and potential therapeutic targets of NAION.

Methods: We conducted a prospective case-control study including 18 patients with NAION (n=5 acute, n=13 chronic) and 9 age-matched controls. NAION was confirmed by clinical exam and optical coherence tomography. Subjects underwent peripheral blood collection; plasma was isolated within 2h and analyzed using a 76-plex array of cytokines, chemokines and growth factors.

Results: In acute NAION, there was increased peripapillary retinal thickness on optical coherence tomography consistent with optic disc edema. Plasma profiling revealed significant changes of the levels of 20 inflammatory proteins in NAION. Analysis of these 20 proteins using principal component analysis (PCA), hierarchical clustering and Spearman correlation generally segregated controls and NAION. In acute NAION, Eotaxin-3, MCP-2, TPO and TRAIL were the top biomarker candidates. In chronic NAION, out of 10 top-ranked molecules, IL-1a and CXCL10 emerged as the strongest therapeutic targets. Statistical analysis of the 20 top-ranked molecules in NAION revealed that there was only 15% overlap in acute and chronic NAION. Longitudinal data from one patient demonstrated an evolving inflammatory pattern from acute to chronic NAION matching that of the PCA.

Conclusions: Profiling of 76 immune molecules in plasma of NAION patients revealed significant inflammation in acute NAION. Surprisingly, there was even more inflammation in chronic NAION, which may be related to neurodegeneration. Of the 20 significantly changed molecules, there was little overlap between the acute and chronic NAION groups, so a larger study to better delineate immune changes over time in the same NAION patients can help elucidate potential therapeutic targets for treatment of patients with visual deterioration.

CONTROL ID: 3545462

SUBMITTER (NAME ONLY): Shruti Chandra

TITLE: Long-term incidence and risk factors for Atrophy in Acquired Vitelliform Lesions (AVL)

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chandra, S. Sivaprasad, National Institute of Health Research Moorfields Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|S. Chandra, S. Gurudas, S. Sivaprasad, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: AVL are infrequent manifestations of multiple disorders with undetermined risk for progression to advanced disease. We performed a retrospective, observational clinical study to determine the time to atrophy and baseline predictors for atrophy in eyes with AVL.

Methods: Both eyes of consecutive patients registered between Jan 2009 to Jan 2014 with diagnosis of AVL confirmed by multimodal imaging and minimum follow-up of 5 years were included. AVL secondary to cuticular drusen, tractional maculopathy, paraneoplastic, infectious, and inflammatory pathologies were excluded. Serial optical coherence tomography (OCT) scans and fundus autofluorescence were graded and analysed. Main outcome measure was time to the first OCT evidence of MA stratified by presenting visual acuity (VA) and AVL lesion subtypes. Secondary outcome included risk factors for incident MA. Turnbull's estimator was employed, and time censored at 5 years. Multivariable Weibull parametric proportional hazards models was used to assess association of risk factors with MA, following adjustment for baseline lesion type. Hazard ratios were reported with 95% CI's.

Results: Total 188 eyes (100 patients) met the inclusion criteria. A further 19 eyes were excluded due to atrophy or choroidal neovascularization at baseline. Incident MA was detected in 35/169 (20.7%) eyes by 5 years. Stratified by baseline VA, 42.9% eyes with VA \leq 54 letters developed atrophy within 2 years and 78.6% within 5 years of first diagnosis by multimodal imaging. In contrast, only 26.9% and 8.6% eyes with VA 55-70 and >70 letters developed atrophy by 5 years, respectively. For eyes in pseudohypopyon and vitelliruptive stage, 35.9% and 36% eyes developed MA by 5 years. In adjusted analysis, baseline factors associated with increased risk of atrophy included VA ≤ 70 letters (HR 4.87; 95% CI 1.82-13.04), log-maximum lesion area (HR 4.59; 95% CI 2.53-8.34), presence of subretinal drusenoid deposit (HR 2.71; 95% CI 1.16 -6.32) and disrupted external limiting membrane (HR 2.34; 95% CI 1.07-5.10).

Conclusions: Baseline VA ≤ 70 letters attributes higher risk for atrophy and VA ≤ 54 accelerates time to incident MA. Baseline presence of SDD, disrupted ELM and larger lesion area led to higher risk of MA. These results provide prognostic indicators for MA in patients with AVL.

CONTROL ID: 3545467

SUBMITTER (NAME ONLY): Orla Galvin

TITLE: The Genetic Testing Landscape in Europe 2020

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Galvin, P. Stratieva, A. Daly, Retina International, IRELAND|

Commercial Relationships Disclosure (Abstract): Orla Galvin: Commercial Relationship(s);The Allergan Foundation:Code F (Financial Support) | Petia Stratieva: Commercial Relationship(s);The Allergan Foundation:Code F (Financial Support) | Avril Daly: Commercial Relationship(s);The Allergan Foundation:Code F (Financial Support)

ABSTRACT BODY:

Purpose:

While potential treatments are emerging for Inherited Retinal Diseases (IRDs), the genetic characteristics of IRDs mean a genetic diagnosis is a prerequisite for inclusion in clinical trials. For many however, treatment options are only one element. Patients are very concerned about inheritance patterns, and disease progression, and can take action on these points. Yet, there are a number of barriers to accessing genetic testing services for IRDs which can vary from region to region. To advocate effectively for equitable, affordable, accessible and timely genetic testing for IRDs it was first necessary to investigate the genetic testing landscape from a processes and systems perspective.

Methods: A dual approach of desktop research supplemented by a survey of ophthalmic and/or genetic specialists across 18 countries was employed. A survey was conducted in an interview style via zoom. Information was provided by: Medical Geneticists, Clinical Laboratory Geneticists, Ophthalmologists/Retinal Specialists – Clinical Researchers.

Results: Genetic services (testing and counselling) for IRDs vary substantially among countries from an awareness, accessibility and affordability perspective. Methods of genetic testing vary and can include cerebral MRI, Sanger sequencing or Next Generation Sequencing, Whole Exome Sequencing or Whole Genome Sequencing and for some genes SNP array or MLPA. Affordability is a barrier for patients in countries without any payment scheme (e.g., Poland) and in countries where only a targeted population is covered (e.g., Bulgaria). Where genetic testing is not covered by healthcare systems or insurance, participation of research projects is in some regions an alternative, however usually the number of patients who could benefit is limited, with patients often advised to send their samples for examination abroad, or travel themselves for full examination outside their country of origin.

Conclusions: There is huge disparity in the approach to genetic testing for IRDs. Greater awareness of genetic testing services is required among the health sector as a whole, and among the eye care professional community. A revised approach to the provision of genetic testing services is required to ensure equitable access and reimbursement, which will empower patients through knowledge, aid discovery, improve access to clinical trials, expedite innovation, improve access to therapy and the delivery of care.

CONTROL ID: 3545479

SUBMITTER (NAME ONLY): Connor Brown

TITLE: Investigating the metabolic effects of basal mineral calcification on human RPE cell culture

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.N. Brown, E. Emri, I. Lengyel, Queen's University Belfast School of Medicine Dentistry and Biomedical Sciences, Belfast, Belfast, UNITED KINGDOM|E. Emri, Roche Diagnostics International AG, Rotkreuz, Zug, SWITZERLAND|

Commercial Relationships Disclosure (Abstract): Connor Brown: Commercial Relationship: Code N (No Commercial Relationship) | Eszter Emri: Commercial Relationship(s);Roche:Code E (Employment) | Imre Lengyel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Calcification is increasingly becoming recognized as an important contributor to the clinical appearance of age-related macular degeneration (AMD). In this study, we studied the effects of various calcium minerals on human retinal pigment epithelial (RPE) cell.

Methods: Human RPE cells (hRPE; 85,000 or 125,000 cells/cm² seeding density) were cultured in the presence or absence of 25 µg/cm² hydroxyapatite (HAP) or whitlockite (WHT), embedded in the Geltrex coating of 0.33cm² Transwell membrane inserts, and were maintained in culture for up to 4 weeks. Cell phenotype was assessed by qualitative monitoring of cell pigmentation and measuring trans-epithelial electrical resistance (TEER). Metabolic alterations were assessed using the Seahorse XF Cell Energy Phenotyping Kit to determine the mitochondrial (oxygen consumption rate (OCR)) and glycolytic (extracellular acidification rate (ECAR)) respiratory capacity of the hRPE cells.

Results: Based on visual assessment of pigmentation, control cells began to differentiate earlier than cells cultured on any of the seeded minerals (2 vs 3 weeks, respectively). TEER for HAP and WHT was significantly lower than that of control cells at both 2 weeks and 4 weeks (45.7±0.9 and 49.6±0.8; 44.6±1.6 and 46.9±0.4 vs 53.1±0.9 and 63.5±2.7 Ω*cm², respectively; p<0.05). Cells cultured on HAP and WHT had significantly higher ECAR values at baseline compared to control cells at 2 and 4 weeks (36.6±3.6 and 39.4±2.1; 35.4±2.3 and 36.9±1.8; vs 24.9±1.7 and 28.7±1.1 mpH/min/10,000 cells, respectively; p<0.05). After stress induction the cells grown on HAP and WHT had significantly lower OCR values compared to control cells, at 4 weeks only (219.0±22.2; 203.3±11.6 vs 299.2±9.2 pmol/min/10,000 cells, respectively; p < 0.05) with no significant difference observed at 2 weeks.

Conclusions: When sub-RPE minerals are present, the RPE appears to utilise the glycolytic respiratory pathway under resting conditions, and continues to do so after differentiation is initiated. Cells grown in the presence of calcium-phosphate minerals also show reduced mitochondrial respiration under stress compared to cells grown naturally, but only after differentiation appears to have started. These indicate that the mitochondrial respiration pathway is detrimentally affected by the presence of calcification in vivo, which is consistent with the notion that mitochondrial changes are involved in AMD.

CONTROL ID: 3545482

SUBMITTER (NAME ONLY): James Germann

TITLE: Collagen Organization in the Posterior Rabbit Sclera Post Cross-Linking

SESSION TITLE: Role of choroid and sclera in myopia development

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Germann, L. Villegas, E. Martinez-Enriquez, S. Marcos, VIOBIO, Instituto de Optica Daza de Valdes, Madrid, Comunidad de Madrid, SPAIN|L. Revuelta, Departamento de Fisiologia. Facultad de Veterinaria, Universidad Complutense de Madrid, Madrid, Comunidad de Madrid, SPAIN|B. Cómitre, D. Sanderson, V. Llorente, M. Desco, M. Gómez-Gavero, Biomedical Imaging and Instrumentation Group, Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Comunidad de Madrid, SPAIN|

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ABSTRACT BODY:

Purpose: Myopia is a growing global ophthalmological concern. One preventative treatment of myopia under development is scleral cross-linking (SXL), where the posterior sclera is stiffened to retard axial length growth. The optimal location and microscopic effects of SXL are still under investigation.

Methods: A total of 18 freshly enucleated rabbit eyes were treated ex vivo with one of two treatments on either the nasal (N) or temporal (T) posterior sclera: (1) Rose Bengal/green irradiation (RGX, 0.25 W/cm^2 , 6.6 min 532nm irradiation, 2.5 min installation) (N, n=6; T, n=6); (2) Riboflavin/UVA irradiation (UVX, 3 mW/cm^2 , 30 min 370nm irradiation, 1 hr installation) (N, n=3; T, n=3). The untreated N or T side of the globe was used as a control. After treatment, scleral pieces ($1.25 \text{ cm} \times 2.5 \text{ cm}$) were extracted from the globe and optically cleared with Murray's clear (1:2 Benzyl Alcohol-Benzyl Benzoate mix). Images were taken of the collagen fibers through the depth of the tissue ($150 \mu\text{m} \times 150 \mu\text{m}$ en face, 250-300 μm depth) with a custom-built, second harmonic generation microscope and analyzed with an order coefficient (OC), which quantized how uniform the direction of the fibers was (1 for uniform direction and 0 for even distribution).

Results: The average OC values were 0.400 ± 0.008 (N) and 0.413 ± 0.007 (T) in untreated tissue, 0.421 ± 0.007 (N) and 0.407 ± 0.014 (T) in RGX-treated tissue and 0.417 ± 0.012 (N) and 0.422 ± 0.010 (T) in UVX-treated tissue. On average, in untreated sclera, OC was 3.2% larger in the temporal than in the nasal side ($p < 0.01$, student t-test). In the nasal sclera, RGX and UVX treatments produced a statistically significant increase in OC ($p < 0.01$), by 5.1% and 3.9% respectively ($p < 0.01$, t-test) and in the temporal sclera, RGX decreased OC by 1.5% and UVX increased by 2.2% ($p < 0.05$, t-test), compared to untreated tissue. UVX produced a significantly larger increase in OC than RGX (by 3.4%, $p < 0.05$) on the temporal side ($p < 0.05$, t-test), but there were no significant differences between UVX and RGX treatments on the nasal side.

Conclusions: Scleral collagen organization varies geographically, with the posterior temporal sclera exhibiting higher order than the nasal sclera. Both RGX and UVX SXL treatments further significantly increased collagen order in the temporal sclera, but not consistently in the nasal sclera. These findings indicate that selecting the treatment area may be critical to optimize the efficiency of SXL.

CONTROL ID: 3545484

SUBMITTER (NAME ONLY): Yashan Bu

TITLE: Sustained hyperglycemia impairs corneal re-epithelialization after alkaline injury through modulation of the ocular surface, systemic Immunity and intestinal microbiome

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Bu, Y. Chan, A.C. Lo, K.C. Shih, The University of Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose:

- 1) To compare corneal re-epithelialization rates, ocular surface and systemic immune response after corneal alkali burn injury between Akita (diabetic) and wild type (WT) mice.
- 2) To compare gut microbial diversity patterns between diabetic and WT mice at baseline and 72 hours after alkaline burn injury and to correlate this with ocular surface findings.

Methods: Heterozygous $Ins2^{Akita}$ mice were used as a mouse model of Type I diabetes, with WT C57Bl6/J mice serving as controls. Alkaline burn injury was induced on the right eye of mice under general anesthesia. The cornea was examined with slit lamp with fluorescein stain under cobalt blue light. Tear samples were collected using Schirmer's strip paper to determine ocular surface cytokine secretion by protein microarray assay. T cell profile on the ocular surface, in the peripheral blood and intestine were analyzed by flow cytometry. Intestinal microbiome diversity pattern was characterized using shot gun sequencing technique.

Results: Sustained hyperglycemia was associated with prolonged corneal wound healing after cornea alkali burn injury. Furthermore, diabetic mice had significantly lower tear angiopoietin-2(Ang-2), insulin growth factor-1(IGF-1) and vascular endothelial growth factor A (VEGF-A) levels after injury compared to controls. In the peripheral blood, significantly elevated levels of CD4+ T cells was seen in WT mice at day 3 after injury, but not in Akita mice.

Meanwhile, significantly higher levels immature CD4+CD8+ T cells were found on the ocular surface of Akita mice compared to controls after injury. Regarding microbial diversity, Akita mice were found to have higher abundance of microbiota composition as compared to WT mice from the CHAO1 index of alpha diversity at day 3 after the injury.

Conclusions: Diabetic mice have shown significantly impaired corneal wound healing response after injury compared to controls. This is associated with the altered ocular surface immunity in diabetic mice. Baseline and post-injury differences in intestinal microbiome composition and diversity may play a role in the altered immune response in diabetes. The presence of systemic chronic inflammation and immature T cell population on the ocular surface of diabetic mice may lead to attenuated post-injury T cell response in diabetic mice.

CONTROL ID: 3545485

SUBMITTER (NAME ONLY): Zachary Sluzala

TITLE: T148 Phosphorylation on α A-crystallin Controls Functional and Structural Biochemical Properties

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z.B. Sluzala, P.E. Fort, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|Z.B. Sluzala, P.E. Fort, Neuroscience Graduate Program, University of Michigan, Ann Arbor, Michigan, UNITED STATES|A. Phadte, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Earlier studies from our lab have shown that the molecular chaperone protein α A-crystallin demonstrates neuroprotective properties that are regulated by S/T148 phosphorylation. While this phosphorylation has been implicated in the anti-apoptotic activity of α A-crystallin, its influence on the structural and functional biochemistry of the protein remains unclear. The present study sought to characterize the effects of S/T148 phosphorylation on the biochemical properties of α A-crystallin, with emphasis on its solubility, oligomeric structure, and chaperone function.

Methods: Differentiated R28 retinal neurons were transfected with plasmids encoding expression of either Wild-type (WT), phosphomimetic (148D), or non-phosphorylatable (148A) mutants of α A-crystallin. Protein solubility was then assessed under normal or metabolic stress (serum starvation) conditions using the triton solubility method. Additionally, purified recombinant α A-crystallin proteins (WT, 148D, and 148A) were used to assess the impact of the phosphorylation on the oligomerization and chaperone function using Native gel electrophoresis and chaperone activity assays.

Results: Protein solubility was measured as a ratio of insoluble α A-crystallin relative to the total content for each construct and condition, and normalized to WT. While no differences were observed under normal and short metabolic stress conditions, longer stress duration revealed differences in solubility, with 148A becoming dramatically more insoluble than 148D ($p < 0.01$, $n = 6$), and 148D becoming slightly (though not significantly) more soluble than WT α A-crystallin. Consistent with changes in solubility, analysis of the recombinant proteins using native gel analysis revealed a shift towards smaller-size oligomers for the 148D mutant, and towards larger-size oligomers for the 148A mutant respectively. Chaperone function analysis of the recombinant proteins also confirmed a significantly increased chaperone activity of the phosphomimetic mutant compared to the WT and non-phosphorylatable mutant ($IC_{50} = 4.4 \mu g$ (148D) vs $8 \mu g$ (WT) and $7.1 \mu g$ (148A)).

Conclusions: The results of this study strongly support a critical role for T148 phosphorylation on the structural and functional biochemistry of α A-crystallin, shedding light on the mechanisms of regulation of the anti-apoptotic role of α A-crystallin.

CONTROL ID: 3545487

SUBMITTER (NAME ONLY): Vivian Summers

TITLE: Age-Related Ocular Changes in the RPE of C57/BL6J Mice

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Summers, S. Ferdous, K. Liao, K. Donaldson, I. Gefke, Y. Kim, D. Shelton, J.T. Sellers, S. Markand, J.H. Boatright, J.M. Nickerson, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|J.H. Boatright, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age is usually examined in a young versus old group in research. We looked at the gradual changes of retinal pigmented epithelium (RPE) over time in wild type C57/BL6J mice to examine when changes take place. The goal of this is to expand upon established knowledge of aging effects on the RPE.

Methods: We looked at both male and female wildtype C57/BL6J mice. They were split up into four groups: G1 (<0.5 years), G2 (1.0 – 1.5 years), G3 (1.5 – 2.0 years), G4 (>2.0 years). We used electroretinogram (ERG) to collect c-wave data which looks at the visual function of the RPE. We also hand counted the number of Ionized calcium binding adaptor molecule 1 (IBA-1) in concentric circles that divided the flatmount into five zones. Imaris was used to determine the amount of alpha catenin within cells to be used as an indicator of change across the groups. We looked at the number of total nuclei across groups. All results were analyzed by using one or two-way ANOVAs with Tukey's posthoc test, n's were between 3-10.

Results: The data that we have analyzed show that there is an increase in the number of IBA-1 cells between groups 1 and 4 in the two outermost zones. There was also an increase in the number of IBA-1 cells across all groups from our most central zones to our most outer zones. There were no significant increases in the total number of IBA-1 positive cells across groups. Cytosolic alpha-catenin increased between groups 1 and 4, and groups 3 and 4. Total number of nuclei in RPE cells, and RPE morphometrics, and c-wave data were not significantly different.

Conclusions: The lack of statistical difference in c-wave data between groups 1 through 3 would be indicative that the RPE visual function does not change with age. While we don't see an increase in the total number of IBA-1 positive cells with age, we do see an increase in the number of IBA-1 positive cells with age in the outer zones of the flatmount. This could be indicative of where these cells where damage is occurring. The change in the outermost zones could be indicative of where the RPE begins to break down first with age. The cytosolic alpha-catenin increased between groups 1 and 4, and groups 3 and 4. Alpha catenin in the cytosol could be attributed to the breakdown of RPE-cell borders with age. Total number of nuclei in RPE cells, and RPE morphometrics show cells remain relatively unchanged with age.

CONTROL ID: 3545490

SUBMITTER (NAME ONLY): IKRAM ISSARTI

TITLE: Mechanical analysis of an ocular globe, a required complexity during inflation test?

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. ISSARTI, C. Koppen, J.J. Rozema, Department of Ophthalmology, Antwerp University Hospital, Antwerp, BELGIUM|I. ISSARTI, C. Koppen, J.J. Rozema, Antwerp University Faculty of Medicine and Health Sciences, Antwerp, BELGIUM|

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ABSTRACT BODY:

Purpose: To describe the effect of varying the structure of biomechanical models on corneal deformation under progressing intraocular pressure (IOP).

Methods: A 3-D finite element model of an ocular globe was implemented to evaluate corneal deformation under various mechanical conditions during inflation testing. The eye model includes the cornea, limbus, sclera, iris, lens, muscles, anterior chamber and vitreous. The Ogden hyper-elastic model ($\mu=0.458$ kPa, $\alpha=136.14$) was suggested for the corneo-limbal structure, the Yeoh isotropic ($C_1=0.81$, $C_2=56.05$, $C_3=2332.26$ (MPa)) model for the sclera, the anterior chamber was modeled as a fluid cavity with progressing pressure [0-25 mmHg], while other eye components were incorporated as linear elastic material, each with different density and viscosity. This study investigates the interplay between several cases, including: Case 0 : restrained limbus; Case 1: unrestrained limbus with restrained sclera, Case 2 (Reference): unrestrained limbus and restrained sclera; Case 3: unrestrained limbus with restrained posterior sclera and free anterior sclera; Case 4: unrestrained limbus with restrained anterior sclera and free posterior pole; Case 5: effect of anterior chamber; Case 6: effect of vitreous; Case 7: effect of anterior chamber and vitreous; Case 8: effect of iris; Case 9: effect of Lens; Case 10: effect of muscle.

Results: The maximum apical displacement and maximum stress under IOP=15 mmHg was 0.22 mm, 0.013 MPa, the cornea underwent an increased stiffness above IOP>7 mmHg (Figure 1.a, Figure 2.a)). Cases 1,2 & 4 resulted in nearly similar displacements, with a slight increase when the limbus is unrestrained. Case 3 leads to reduced stiffness (25%), with increased displacement. Adding individual eye components (Cases 5-7), results were nearly similar to the reference. The presence of the iris slightly decreases the displacement, but leads to higher stress on corneal periphery. Meanwhile, the contribution of the muscles and lens together cannot be neglected as it reduces the corneal displacement with 50% (Figure 1.c-d, Figure 2.b)).

Conclusions: As the lens, iris and muscles each provide major contributions to the corneal deformation model, it is highly recommended to account for such internal eye contributions during ex vivo experiments.

CONTROL ID: 3545491

SUBMITTER (NAME ONLY): Hannah Levis

TITLE: Biosynthetic corneal endothelial graft functions in a rabbit model of corneal endothelial damage

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.J. Levis, C. Carserides, V. Romano, R. Williams, Eye and Vision Science, University of Liverpool Faculty of Health and Life Sciences, Liverpool, Liverpool, UNITED KINGDOM|V. Romano, St Paul's Eye Unit, Liverpool University Hospitals NHS Foundation Trust, Liverpool, Liverpool, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Corneal endothelial dysfunction leads to visual impairment and a requirement for corneal endothelial transplant. There is a worldwide donor cornea shortage, so biosynthetic graft alternatives are being developed using in vitro expanded corneal endothelial cells. Our poly-ε-lysine (pεK) hydrogel is highly tunable and its properties can be controlled by the nature and percentage of the cross-links and the density of the peptide to produce a panel of hydrogels with different properties. We have chosen a hydrogel with excellent optical and mechanical properties for this application and here we investigate the functionality of the biosynthetic graft using porcine corneal endothelial cells in a rabbit model of endothelial damage.

Methods: Hydrogels were synthesised from pεK crosslinked 60% with nonanedioic acid and then punched into 8mm circles. Gels were seeded with primary porcine corneal endothelial cells at a density of 1×10^5 cells/gel and cultured for 3 weeks. Immunocytochemical staining (ZO-1 and Na+K+ATPase) was performed to assess the phenotype of cells on gels. PεK hydrogels (+ and – cells) were transplanted into the right eyes of New Zealand white rabbits with Descemet's membrane and endothelial layer removed. A group with no gel acted as control. Optical coherence tomography (OCT) imaging and pachymetry was used to measure corneal thickness for the experimental period (3 weeks). Photographs of rabbit corneas were taken to assess corneal clarity and eyes were dissected for histological analysis.

Results: Porcine corneal endothelial cells adhered to the pεK hydrogels and formed monolayers expressing ZO-1 and Na+K+ATPase. OCT imaging showed control unoperated corneas had a mean thickness of 399.5mm (SD27.6) and the corneas with Descemet's membrane and endothelial layer removed (no gel) had a mean thickness of 1052mm (SD77.1). Corneas with attached gels (no cells) were 583.5mm (SD 251.0) and attached gels with cells were 451mm (SD37.4).

Conclusions: Cellular pεK grafts show good cell compatibility, handleability and are able to function to thin the cornea to near control levels after 3 weeks in a rabbit in vivo model of endothelial damage.

CONTROL ID: 3545494

SUBMITTER (NAME ONLY): Benjamin Nash

TITLE: Aberrant splicing caused by a novel synonymous RPE65 variant, demonstrated in iPSC-derived retinal pigment epithelial cells and on minigene assay

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Nash, T. Loi, A. Sabri, S. Eamegdool, J.R. Grigg, R. Jamieson, Eye Genetics Research Unit, Children's Medical Research Institute, University of Sydney, Sydney, New South Wales, AUSTRALIA|T. Loi, A. Sabri, R. Jamieson, Specialty of Genomic Medicine, Children's Hospital at Westmead Clinical School, Faculty of Medicine and Health, University of Sydney, Sydney, New South Wales, AUSTRALIA|M. Fernando, A. Gonzalez-Cordero, Stem Cell Medicine Group, Children's Medical Research Institute, University of Sydney, Sydney, New South Wales, AUSTRALIA|J.R. Grigg, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|S. Chung, Translational Neurogenomics Group, Kids Research, Sydney Children's Hospital Network, Sydney, New South Wales, AUSTRALIA|B. Nash, Sydney Genome Diagnostics, Western Sydney Genetics Program, Sydney Children's Hospital Network, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Genomic studies of our Australian retinal dystrophy cohort are providing molecular diagnoses in >60% of families examined. However, curation can often be challenging when assessing novel variants. This is especially relevant where there are strict inclusion criteria for gene therapy, such as voretigene neparvovec recently approved for use in Australia for retinal dystrophy due to RPE65 mutations. Patient-derived iPSC-RPE cells provide a valuable resource for investigation of genes with retinal-specific expression. This study investigates the pathogenicity of a novel RPE65 synonymous variant detected in trans with a previously reported pathogenic variant on clinical genomic testing in two affected siblings with early onset retinal degeneration.

Methods: iPSC cells were generated from the peripheral blood of a carrier of the RPE65 synonymous variant, and cells were differentiated to RPE. Pluripotency and RPE differentiation were examined with gene expression markers using qRT-PCR (ThermoFisher, USA) and immunohistochemistry. Minigene studies were performed with cloning of the genomic region of interest into a p.ExonTrap vector (MoBiTec, Germany), before transfection into HEK293 cells. RNA was extracted from iPSC-RPE cells and transfected HEK293 cells, and RT-PCR and Sanger sequencing were performed to investigate aberrant transcripts.

Results: Analysis of iPSC and subsequent RPE lines showed gene expression consistent with pluripotency and presence of RPE-specific markers respectively. Studies of iPSCs using SNP microarrays confirmed genomic stability. Analysis of RNA from both patient-derived iPSC-RPE and minigene studies demonstrated exon skipping from the RPE65 transcript, resulting in a mutant RPE65 allele of only 22 amino acids. There was concomitant reduction in RPE65 expression.

Conclusions: Modelling of the RPE65 synonymous variant in both iPSC-RPE and minigene assays demonstrated a RPE65 loss of function allele. These findings facilitate the reclassification of the novel synonymous variant from a variant of uncertain significance to a likely pathogenic variant, in turn providing eligibility for access to voretigene neparvovec gene therapy. This study demonstrates the importance of synergistic stem cell research and diagnostic genomics, especially in the era of gene therapies.

CONTROL ID: 3545495

SUBMITTER (NAME ONLY): Mirella Barboni

TITLE: Biofeedback fixation training in amblyopia

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.T. Barboni, O.A. Maneschg, Z.Z. Nagy, J. Németh, Ophthalmology, Semmelweis Egyetem, Budapest, HUNGARY|M.T. Barboni, O.A. Maneschg, J. Németh, Bionic Innovation Center, Budapest, HUNGARY|

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ABSTRACT BODY:

Purpose: Patients with strabismic amblyopia referred to surgical treatment of strabismus often show disturbed visual fixation. The purpose of the present study was to investigate fixation stability before and after surgical treatment of strabismus and the effects of biofeedback fixation training on fixation stability of amblyopic adult eyes.

Methods: Participants were 12 patients with strabismus (mean age = 29.6 ± 8.5 years; 6 females) and 12 healthy volunteers (mean age = 23.8 ± 1.5 years; 9 females). The protocol included ophthalmological and microperimetric follow-ups. Biofeedback fixation training (MAIA; CenterVue, Padova, Italy) was delivered monocularly to the amblyopic eye once per week for six months. Trained retinal locus was selected as either the spontaneous preferential retinal locus or as a fixation point closer to the anatomical fovea after the surgical treatment of strabismus. Group differences were evaluated using ANOVA. Paired comparisons between amblyopic, fellow, and control eyes were performed using Bonferroni post-hoc analyses.

Results: Baseline measurements showed significantly altered fixation stability ($p < 0.001$) in amblyopic eyes compared to control eyes. Fixation stability did not significantly change after the surgical treatment of strabismus ($p = 0.622$). On the contrast, biofeedback fixation training applied to operated amblyopic eyes resulted in more stable fixation for all four subjects trained so far with 50% of average improvement.

Conclusions: Fixation stability is impaired in amblyopic adult eyes, also after the surgical treatment of strabismus. The present report highlights the beneficial use of biofeedback fixation training as a therapeutic option to improve fixation stability in amblyopic eyes after the surgical treatment of strabismus. Alternatively, this method could be associated with standardized treatments to improve monocular and binocular vision in patients with amblyopia as an attempt to enhance the treatment effect.

CONTROL ID: 3545497

SUBMITTER (NAME ONLY): Bingyao Tan

TITLE: Distortion-corrected retinal curvature using a Fourier domain mode locking (FDML) laser ultrawide-field optical coherence tomography (OCT)

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tan, F. Zheng, J. Chua, L. Schmetterer, Singapore Eye Research Institute, Singapore, SINGAPORE|R.P. McNabb, A.N. Kuo, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure the distortion-corrected retinal curvature with a ultrawide-field OCT system using an ultrafast Fourier domain mode locking (FDML) laser.

Methods: An ultrafast swept-source OCT system (OptoRes, Germany) using a 1.6MHz FDML laser (central wavelength: 1060nm) was used for dense imaging of an ultrawide field of view (FOV, ~65 degree) of the posterior eye. The imaging FOV was calibrated with a custom-built phantom eye. A total of 13 eyes from 11 healthy volunteers, with spherical equivalent (SE) refraction from -1D to -7D, and axial length (AL) from 23.1 mm to 26.8 mm, were imaged thrice without mydriasis. Retinal pigment epithelium (RPE) was segmented automatically using MATLAB. Ocular biometrics, including AL, central corneal thickness and corneal curvature were acquired with the IOL Master700. Ocular biometrics and system parameters were fed into a ray tracing algorithm using ZEMAX and MATLAB, for correction of the optical and display distortions and mapping the RPE segmentation into spatial location. The radius of curvature (Rc) of the retina was calculated by finding the best sphere fit to the corrected RPE.

Results: The mean \pm standard deviation (SD) of Rc in 13 eyes was 12.86 ± 0.19 mm. A high repeatability was obtained for Rc measurements (intraclass correlation coefficient, ICC = 0.96). Rc was correlated with the AL ($r = -0.389$), but not correlated with the SE ($r = -0.015$) (Figure 1). Figure 2 shows the original RPE elevation maps and their corrected retinal shapes in eyes with mild (SE=-2.25D) and moderate (SE=-4.25D) myopia.

Conclusions: The distortion-corrected measurements of Rc using an ultra-fast widefield OCT can provide the true retinal curvature with high repeatability. This suggests that wide-field OCT may be used to monitor retinal curvature changes in myopia over time.

CONTROL ID: 3545498

SUBMITTER (NAME ONLY): Huibert Simonsz

TITLE: EUSCREEN APP calculates the cost-effectiveness of vision screening programs, taking local circumstances into account

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.J. Simonsz, E. Heijnsdijk, J. Kik, M. Nordmann, H. de Koning, Erasmus Medical Center, Rotterdam, NETHERLANDS|H.J. Simonsz, Netherlands Institute for Neuroscience, Amsterdam, NETHERLANDS|H. Hoeve, A. Horwood, University of Reading, Reading, UNITED KINGDOM|I. Úhlen, Karolinska Institutet, Stockholm, SWEDEN|G. Carr, Independent consultant in Early Hearing Detection, Intervention and Family Centered Practice, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Vision screening programs vary in organization, location, screening tests, screening professionals, referral criteria and coverage, which makes comparison of their cost-effectiveness difficult. We develop a web-based application that calculates their cost-effectiveness.

Methods: The EUSCREEN APP at www.euscreen.org simulates the path followed by a child within a vision screening program consisting of several screening steps. Users enter demographic data like birth figures, tests used, screening location, screening professionals etc. The model simulates this screening program and calculates the number of tests, number of referrals to diagnostics, number of cases detected, costs of screening until referral, costs of diagnostic assessment, total costs, costs per test and costs per case detected. Then the user adjusts variables to see what effect a change of age of screening, screening test, number of screening steps, screening professional etcetera has.

Results: The accuracy of the prediction depends upon the quality of the input data. Notably, the sensitivity and specificity of a screening test at a specific age, performed by a given professional with a given training and a given experience are difficult to estimate and are the most critical component of the model. Costs of screening, diagnostic assessment and treatment are calculated from salaries, overhead, visual acuity charts and other material, housing etc. Combination of vision screening with other screening or with school attendance reduces cost components. Photorefractive and prescription of glasses at age 1 or 2 may precede measurement of visual acuity at age 4-6. As the model is also intended for use in Low-Income Countries, questions check if lack of healthcare infrastructure, competing healthcare priorities, lack of awareness of advantages of prevention and long travel distances render vision screening unacceptable, inappropriate or unsustainable.

Conclusions: The EUSCREEN APP for cost-effectiveness of vision screening programs will assist professionals in their decisions to introduce, modify or disinvest childhood vision screening programs. Utility and quality of life, effectiveness of treatment, newborn vision screening, type and severity of amblyopia and orthoptic training need to be added. Ubiquitous lack of data collection in vision screening makes it difficult for the user to know the correct input values.

CONTROL ID: 3545509

SUBMITTER (NAME ONLY): Kyle Fallgatter

TITLE: Correlations between Spectral-Domain OCT Measurements and Visual Acuity Change after One Year Follow-up in Patients with Retinitis Pigmentosa

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Fallgatter, J.F. Yang, J. Chen, Ophthalmology, University of Florida Health, Gainesville, Florida, UNITED STATES|E. Dawson, R. Artola, College of Medicine, University of Florida Health, Gainesville, Florida, UNITED STATES|X. Chen, Epidemiology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cystoid macular edema is a known cause of central vision loss in retinitis pigmentosa (RP) patients as the disease progresses. A retrospective chart review was performed to investigate whether clinical and/or spectral-domain optical coherence tomography (SD-OCT) data could be used to correlate with visual acuity outcomes.

Methods: The medical records of 60 eyes from 30 patients from the University of Florida Eye Center database were reviewed. Best corrected visual acuity (BCVA), central retinal thickness (CRT), total macular volume (TMV), presence or absence of epiretinal membrane, and presence or absence of ellipsoid zone in the fovea and in the macula (EZ) at the first visit and one year follow up were collected and analyzed. The relationship between predictors and outcome variables were assessed using simple correlation analysis.

Results: The mean age of the 30 patients (9 male, 21 female) included in the study was 46.8 ± 18.9 (range, 10-80 years). Sex does not correlate with measurements. Aging has a negative effect on BCVA and EZ fovea. BCVA at 1st visit was significantly correlated with CRT ($r = -0.38437$, $p = 0.0024$) and EZ foveal sparing at the 1st visit ($r = 0.65218$, $p < 0.0001$). CRT is an indicator of CME and has a negative effect on EZ fovea. ERM has no correlation with BCVA, CME, CRT, TMV or EZ. Multiple regression analysis showed that TMV at the first visit is significantly correlated with BCVA changes at one year visit ($r = -0.31972$, $p = 0.0128$).

Conclusions: The results of our study suggest that in patients with retinitis pigmentosa, visual acuity outcomes are correlated with CRT and the condition of the EZ fovea. Thinner retina has EZ fovea depleted and worse BCVA. The baseline TMV can serve as a predictor of BCVA change at the end of one year. Eyes with higher baseline TMV end up with worse BCVA after one year. Aging is correlated with decreasing BCVA and disruption/disappearance of EZ fovea.

CONTROL ID: 3545510

SUBMITTER (NAME ONLY): Joost Brinks

TITLE: Genome-wide transcriptional responses of human choroidal endothelial cells to corticosteroids as a model for central serous chorioretinopathy

SESSION TITLE: Advances in intra and extra ocular pathologies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Corticosteroids are a strong risk factor for central serous chorioretinopathy (CSC). However, the underlying pathophysiological mechanisms are unclear. CSC has been proposed to result from choroidal hyperpermeability. Therefore, choroidal endothelial cells (CECs), which are important for barrier function, are of particular interest. This study describes the effect of cortisol on human CECs, in order to identify potential target genes involved in CEC hyperpermeability as seen in CSC patients.

Methods: Human CECs from 10 individuals (5 males, 5 females) were isolated from cadaveric anonymous donor eyes by magnetic-activated cell sorting. Cells were treated with either cortisol (10^{-6} M) or vehicle (0.01% ethanol) medium, and subsequently whole transcriptome analysis was performed on a Novaseq Illumina platform.

Results: Bioinformatic analysis showed upregulation of 153 genes and downregulation of 169 genes. Classical corticosteroid target genes were upregulated in human CECs and included FKBP5 (log2 fold change 6.8) and TSC22D3 (log2 fold change 4.5). The strongest induced gene by cortisol was ZBTB16 (log2 fold change 7.0).

Conclusions: In summary, this study describes 322 genes regulated by cortisol in primary human CECs. This includes classical corticosteroid target genes, but also a subset of these genes that has been previously linked to endothelial cell dysfunction. Functional assays based on genes of interest found in this study may help to expand the understanding of mechanisms behind the induction of CEC hyperpermeability by corticosteroids, as observed in CSC patients.

CONTROL ID: 3545513

SUBMITTER (NAME ONLY): Nabil HERDA

TITLE: The impact of 1st wave COVID-19 on macular diseases' management in a referral hospital in FRANCE

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To analyze the impact of the 1st wave COVID-19 on macular diseases' management in ophthalmology department of "Centre hospitalier intercommunal de Créteil (CHIC)" and correlate it with patients' demographic and clinical features

Methods: Retrospective cross-sectional study. During the lockdown period from March 17th to May 11th, 2020, we analyzed the activity in the medical retina and more specifically intra-vitreous injections (IVIs) and compared it to that of the same period in 2019. The impact of patients' demographic and clinical features (age, sex, visual acuity (VA), retinal disease, therapeutic strategy) on this activity was evaluated

Results: In 2019, the number of IVIs carried out between March 17th and May 11th, combining all indications was 2189. In 2020, this number was 953 corresponding to a decrease of 56.46 %, statistically significant ($p < 0.05$). During the 1st wave, 767 patients (1020 eyes) were scheduled for at least one IVI. 833 eyes of 615 patients received 1 or 2 scheduled IVIs (Group 1). 187 eyes of 152 patients did not receive any IVIs (Group 2). 83.06% out of the patients in group 1 received all the scheduled IVIs (1 or 2). 16.94% received only a single IVI when they were scheduled to receive a 2nd injection. In group 1, the average age is 76 y. Female patients represent 59.67%. Average VA before lockdown was 63.52 letters. This remained stable after, at 63.15 letters. The therapeutic strategy used before lockdown was Pro re nata (PRN) in 62.46% and Treat and extend (TAE) in 30.56%. Age related macular degeneration (AMD) was the most common disease (61.13%). In group 2, the average age is 76 y. Female patients represent 58.55%. Average VA before lockdown was 60.77 letters. It was reduced to 50.63 letters after. The predominant therapeutic strategy was PRN (47.05%) followed by TAE (32.62%). AMD was the most common disease (56.68%)

Conclusions: The COVID-19 lockdown severely impacted management of macular diseases by IVIs at CHIC. The short-term impact on VA is significant in the absence of treatment. The impact is not statistically different with respect to age, gender, and retinal disease. However, regarding therapeutic strategy, PRN seems to have enabled a better observance. These results underline the importance of sensitizing patients to treatment observance. They can also contribute to develop effective management strategies for macular diseases during times of crisis

CONTROL ID: 3545516

SUBMITTER (NAME ONLY): Nada Alfahad

TITLE: Optimising outcomes for cataract surgery in ocular mucous membrane pemphigoid

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mucous membrane pemphigoid (MMP) is a heterogenous group of immunobullous disorders affecting the orificial mucous membranes including the ocular (OcMMP), oral and aerodigestive regions. MMP is associated with significant ocular morbidity due to conjunctival shrinkage where visual loss is secondary to ocular surface failure, secondary glaucoma and complex cataract. Cataract surgery is challenging due to difficult access, poor visualisation and risk of postoperative epithelial breakdown and disease progression. We describe an ocular surface optimising protocol that aims to minimise post-operative complications and improve patient outcomes.

Methods: Cataract surgery was performed on 73 consecutive eyes (47 OcMMP patients, aged (50-87) years, 25 (53%) Female, 35 (74.5%) biopsy-positive) presenting to a regional tertiary centre between 2005 and 2019. Optimisation was achieved by ensuring all patients were free of inflammation for a minimum of 3 months prior to surgery, followed by preconditioning of the ocular surface with topical non-preserved dexamethasone eyedrops for 2 weeks, intravenous methylprednisolone on the day of surgery, intra-operative hydroxypropylmethylcellulose corneal protection, amniotic membrane to the corneal surface, and post-operative topical non-preserved dexamethasone, chloramphenicol, and lubricants. Six-month outcomes are reported using generalised linear models adjusted for longitudinal and inter-eye correlations

Results: Of the 47 patients, 34 (72.3%) required systemic immunosuppression. At the time of surgery, >50% forniceal foreshortening was observed in 44 (60%) eyes with 35 (74%) eyes requiring intraoperative lid sutures. There was significant improvement in visual acuity by >0.7 LogMar (P=0.000). While there were no statistically significant differences between pre- and postoperative inflammation, scarring, morbidity and dryness scores (all p>0.05), one patient demonstrated progressive scarring at 6-months follow-up and 14(19%) eyes required serum eyedrops for increased ocular surface staining. No cases of corneal perforation, microbial keratitis or endophthalmitis were recorded.

Conclusions: Cataract surgery can be safely performed in OcMMP patients with advanced conjunctival scarring but requires careful preoperative optimisation and post-operative ocular surface management for good patient outcomes. Good vision may be temporary due to the progressive nature of the underlying disease.

CONTROL ID: 3545517

SUBMITTER (NAME ONLY): Anupama C

TITLE: Impact of oxidative stress on the cytoskeleton and barrier integrity of the corneal endothelium

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Oxidative stress (OS) is implicated in the pathophysiology of Fuchs Endothelial Corneal Dystrophy (FECD). It is known to induce microtubule disassembly in other cell types, leading to remodelling of the apical junctional complex via actomyosin contraction and eventually to barrier failure (Srinivas; EER, 2012). This study aims to investigate the impact of experimental oxidative stress on the barrier properties of the corneal endothelium (CE).

Methods: All experiments were carried out with primary cultured cells of porcine/bovine CE. For oxidative stress, cells were exposed to H_2O_2 (100 μ M, 1 h) after holding the cells in a culture medium containing 2% serum for 24 hrs. Immunocytochemical techniques were employed to assess the disassembly of the microtubules and the organization of ZO-1. The loss of barrier function was assessed by TER, which was measured by electric cell-substrate impedance sensing with bovine CE grown on gold electrodes that were coated with an ECM cocktail. In these experiments, the culture medium was supplemented with 50 μ M Riboflavin (Rf) and exposed to UV-A (365 nm; 30 min, 0.5 mW/cm²) to induce the Type-1 photochemical reactions and thereby cause an in situ release of H_2O_2 .

Results: Exposure to H_2O_2 for 1 h led to microtubule disassembly (immunocytochemistry with α -tubulin), which could be inhibited by pre-treatment with 10 μ M of SB-203580 (a p38 MAPK inhibitor; 1 h). In independent experiments, exposure to H_2O_2 led to a loss of the contiguous appearance of ZO-1 (Fig. 1B), which marks the breakdown of tight junctions. Accordingly, a sustained loss of TER (over 10-12 h) was induced when cells on gold electrodes, bathed in Rf-supplemented medium, were exposed to UV-A. Inclusion of catalase (7000 U/mL), which prevents the accumulation of H_2O_2 , abolished the loss in TER induced by UV-A.

Conclusions: We have demonstrated that acute oxidative stress induces microtubule disassembly, leading to a destruction of apical junctional complex and barrier integrity in cultured CE. The effects of p38 MAPK confirms a role for the stress kinase downstream of oxidative stress. Thus, the response to oxidative stress is reminiscent of the TNF- α -induced breakdown of barrier failure reported in CE (Srinivas; EER, 2012).

CONTROL ID: 3545518

SUBMITTER (NAME ONLY): Eliza Barnwell

TITLE: Endophthalmitis Associated with Intravenous Drug Use Compared with Other Endogenous Etiologies

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare endogenous endophthalmitis characteristics among patients who inject drugs with endogenous endophthalmitis from other causes.

Methods: This retrospective study included all cases of endogenous endophthalmitis diagnosed and treated at a single academic institution over a seven-year period, from February 2013 until February 2020. 62 eyes of 52 patients were included, with a mean follow-up time of 8.6 months. 23 cases were related to intravenous drug use (IVDU) and 29 cases were due to other endogenous etiologies. The primary outcome was final visual acuity (VA).

Results: Overall, mean presenting VA on presentation was logMAR 1.81 (Snellen 20/1291) and at final follow-up was logMAR 1.60 (Snellen 20/796). IVDU-related cases were more likely to have improvement in VA following treatment compared with cases due other etiologies (OR=2.85, p=0.049). Patients with IVDU-related endophthalmitis were significantly younger at time of diagnosis (mean 39 years) than those with other etiologies (mean 60 years, p<0.00001) and had significantly longer duration of symptoms before diagnosis (mean 28 days) compared to other etiologies (mean 8 days, p=0.005). Out of the IVDU-related cases, only 30% had a known infectious site in addition to ophthalmic findings, while 86% of cases due to other etiologies had a known infectious site. Overall, Staphylococcus aureus was the most commonly isolated pathogen in vitreous cultures (n=6) as well as in blood cultures (n=13). Confirmed or suspected fungal etiology was more likely in the IVDU-related cases (OR=5.96, p=0.003).

Conclusions: In this case series, patients with endogenous endophthalmitis have high ocular morbidity despite appropriate treatment. Patients with endogenous endophthalmitis due to IVDU are significantly younger with longer duration of symptoms prior to diagnosis compared to patients with endophthalmitis from other etiologies. In many cases, patients with IVDU-associated endophthalmitis have ophthalmic findings only; therefore, it is important to have a high index of suspicion in a young, otherwise healthy patient.

CONTROL ID: 3545521

SUBMITTER (NAME ONLY): Keegan Mechels

TITLE: Clinical profile of patients with necrotizing scleritis and the risk of surgical intervention

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Mechels, T.J. Ferguson, S. Srivastava, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Necrotizing scleritis is an uncommon, destructive inflammatory condition that often has a systemic association. We performed a retrospective case-series to observe the demographics, clinical features, and disease associations of a group of patients identified with necrotizing scleritis.

Methods: This is a retrospective review of all necrotizing scleritis documented as a diagnosis in the EMR of a single tertiary referral center (n=17) between July 2014 and September 2020. Demographic data, clinical exam findings, operative reports, and clinic notes from rheumatology at the same center were reviewed by the authors of this study.

Results: A total of twenty-two eyes of seventeen patients (22/17) were included in this study. 9 of the 17 patients were female (52.9%). The average age of the patients was 70.1 years with 6/17 over the age of 70. 12/17 patients (70.6%) had a systemic disease association, the most common of which was rheumatoid arthritis (7/12) followed by granulomatosis with polyangiitis (4/12). 3/17 patients (5/22 eyes) had an infectious cause of scleritis. Best-corrected visual acuity was worse than 20/200 in 7/22 eyes at presentation. Anterior uveitis was noted in 4/22 eyes at presentation, and panuveitis was also noted in 4/22 eyes at presentation. At the time of presentation, 4/22 eyes required surgical repair. The average age of these patients was 71.3 years. Of these patients, three had a diagnosis of rheumatoid arthritis (RA) and one had infectious scleritis secondary to *Pseudomonas aeruginosa*. Two of the three surgical RA patients were not on steroid-sparing agent prior to surgical intervention. Of the 18 eyes that at presentation did not require surgery, none of these eyes warranted repair after starting immune suppression.

Conclusions: Necrotizing scleritis can be a devastating diagnosis with a host of ocular complications that can accompany it, including perforation requiring patch grafting. Aggressive immune suppression is often warranted to avoid perforation necessitating surgical intervention.

CONTROL ID: 3545522

SUBMITTER (NAME ONLY): Ailis Moran

TITLE: Deciphering the role of Rab28 in cone vision and outer segment phagocytosis

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rab28 is a small farnesylated G-protein associated with human autosomal recessive cone-rod dystrophy (CRD). Rab28 localises to cone photoreceptor outer segments (OS) which are modified cilia. Knockout of murine or zebrafish Rab28 diminishes OS phagocytosis (OSP) by the retinal pigment epithelium (RPE). As Rab28 function and regulation of cone OSP are poorly understood, this study further investigates the molecular mechanism by which Rab28 functions in zebrafish cone photoreceptors and its role in OSP.

Methods: Genetic, biochemical, behavioural and imaging approaches interrogated the function of Rab28 in zebrafish cone photoreceptors using a rab28 knockout (KO) model and transgenic strains overexpressing gnat2:egfp-rab28. Visual behaviour was analysed using optokinetic response, contrast sensitivity and visual acuity assays. For TEM analysis of shed OS, phagosomes were manually counted, and the density calculated as phagosomes per μm of RPE. Proteomic profiling of rab28 knockout and sibling eyes collected at ZT 4, ZT 9 and ZT 17 was performed by mass spectrometry (MS). Retinoid profiling was carried out by HPLC.

Results: At 15 days post fertilisation (dpf), rab28 KO zebrafish display a 55% reduction ($N=3$, $p<0.001$) of shed OS material at morning (ZT 4) and evening (ZT 17) OSP peaks. Overexpression of Rab28 specifically in cones rescues the OS shedding defect in rab28 KO fish ($N=3$, $p<0.001$). Real-time PCR identified *cerkl*, *mertka* and *abcf1* genes to maximise expression prior to one or both OSP peaks. Proteomic analysis demonstrates loss of zebrafish Rab28 leads to reduced levels of phototransduction cascade components and core ciliary BBsome proteins ($N=3$, $p<0.05$). Visual cycle retinoid levels are also reduced ($N=3$, $p<0.03$) in larval and adult rab28 KO retinae inferring a direct or indirect role of Rab28 in the visual cycle. We observed no visual impairment in juvenile rab28 KO fish.

Conclusions: Our findings indicate that Rab28 regulates phagocytic processes at the ciliary/OS membrane, thereby providing insight into the mechanisms of RAB28-associated cone-rod dystrophy and cone OSP regulation.

CONTROL ID: 3545526

SUBMITTER (NAME ONLY): Stuart McKeown

TITLE: Regenerating the ocular retinal vasculature using endothelial progenitors is modulated by miR-130

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. McKeown, J. Guduric-Fuchs, R.J. Medina, A. Stitt, Queen's University Belfast, Queen's University Belfast, Belfast, Belfast, GB, academic, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Ischemic retinopathies are significant causes of vision loss. A strategy to repair damaged vasculature and reperfuse the hypoxic retina is a valid and important goal. Many groups have sought to harness the reparative potential of endothelial progenitors in a cell therapy strategy. In the current study, we have built upon our previous work showing that endothelial colony forming cells (ECFCs) can integrate into the murine vasculature and drive a regrowth of patent vessels in the ischaemic retina. Based on transcriptomics of hypoxia-exposed ECFCs we have identified that miR-130 regulates angiogenesis-related gene expression events. The current study has sought to determine the role of miR-130 in ECFCs and whether this miRNA can be manipulated to improve vascular repair.

Methods: ECFCs were isolated from umbilical cord blood and categorised via flow cytometry, as well as cellular morphology. Cells were fixed and stained for vinculin to identify focal adhesions (FA). FA were then enumerated, and the cells adhesion assessed via a modified MTT assay. Overexpression (OE) of miR-130 or a control-mimic (c-mim) was then induced in ECFCs, the effect of this OE was then assessed. These, miR-130 OE ECFCs were applied to the ex vivo choroidal explant model to assess their ability to interact with, and possibly improve, sprouting choroidal vasculature. Explants were imaged daily to determine total sprouting distance. In the murine oxygen-induced retinopathy (OIR) model miR-130 OE or c-mim OE ECFCs were administered intravitreally and the impact on ischemic retinopathy assessed.

Results: Cells OE miR-130 had a greater number of FA compared to untreated cells and C-mim OE cells ($P<0.001$) as well as greater adhesion ($P<0.05$). In the ex vivo choroid angiogenesis model, explants exposed to miR-130 OE cells had a significantly greater sprouting distance ($P=<0.001$) than explants grown in co-culture with C-mim OE cells, non-transfected cells or no cell controls. In the murine OIR model, administration of miR-130 OE cells led to a reduction in the avascular area of retinas that was significantly greater than that achieved by non-transfected control cells ($P<0.05$).

Conclusions: Whilst ECFCs have previously demonstrated vasoreparative potential in the eye, an ability to improve their function in the ischaemic retina would be valuable. Augmentation of ECFCs via miR-130 OE enhances the efficacy of this cell therapy.

CONTROL ID: 3545532

SUBMITTER (NAME ONLY): Titus Ovik

TITLE: Foveal thickness and vascular parameters in adolescents born moderate-to-late preterm

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Ovik, A. Lind, Z. Popovic, E. Aring, M.A. Gronlund, Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg,, Gothenburg, SWEDEN|A. Lind, Z. Popovic, E. Aring, M.A. Gronlund, Department of Ophthalmology, Sahlgrenska University Hospital, Gothenburg, SWEDEN|J. Dahlgren, Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden., Gothenburg, SWEDEN|

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ABSTRACT BODY:

Purpose: It is well established that children born preterm are at increased risk for ophthalmologic complications including altered fundus morphology. However, there is a lack of knowledge how children born moderate-to-late preterm (MLP, gestational age 32-36 weeks) with no retinopathy of prematurity (ROP) are affected later in life. This study intends to evaluate foveal parameters such as foveal avascular zone (FAZ) area, vascular density (VD) of a determined area surrounding the fovea and foveal thickness of adolescents born MLP and compare the results with age-matched controls born full-term.

Methods: In an ongoing, prospective population-based cohort study, 37 adolescents born MLP (19 female, 18 male; mean age 15.9 years) were examined with optical coherence tomography (OCT) and OCT angiography (OCT-A) (Topcon DRI OCT-1Triton Plus, Tokyo, Japan). Exclusion criteria were the following: children with chromosomal abnormalities, syndromes, severe malformations, ROP and mothers with severe chronic disease. FAZ and VD were obtained by OCT-A scans and measured using Fiji image processing software. All these foveal measurements were adjusted for the axial length related ocular magnification by usage of the Littmann formula. Foveal thickness was obtained from the OCT scan. The results of the foveal parameters from the MLP individuals were compared with the results from 25 healthy controls (mean age 16.1 years). Statistical analyses (Mann-Whitney's U-test and Spearman's rank correlation coefficient analysis) were made using the software IBM SPSS Statistics 26 (IBM Corp., Armonk, NY, USA).

Results: There were significant differences in size of FAZ and foveal thickness between the two study groups; FAZ area (mm^2) MLP group (mean \pm standard deviation (SD)) $0.21 \pm 0.10 \text{ mm}^2$ compared with controls (mean \pm SD) $0.27 \pm 0.09 \text{ mm}^2$, foveal thickness (μm) MLP group (mean \pm SD) $251.89 \pm 19.03 \mu\text{m}$, controls (mean \pm SD) $240.60 \pm 17.77 \mu\text{m}$ ($p=0.025$ and $p=0.032$, respectively). A strong correlation between FAZ area and foveal thickness was found in the MLP group ($r=-0.782$, $p<0.0001$). The VD measurements showed no significant differences.

Conclusions: Our results show that adolescents born MLP, without having ROP as infants, have a smaller FAZ area and an increased foveal thickness compared with age-matched full-term controls. Additionally, FAZ area and foveal thickness were negatively correlated within the MLP group.

CONTROL ID: 3545534

SUBMITTER (NAME ONLY): Marius Ader

TITLE: Endogenous cone and rod photoreceptors exchange cytoplasmic material via direct cell-cell connections

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Cell transplantation into the mouse retina has been shown to result in the transfer of cytoplasmic material between donor and host photoreceptors. Here we assessed whether material transfer can also occur between endogenous photoreceptors in a horizontal fashion under normal physiological conditions.

Methods: Retinal wholemounts and sections of cone-specific GFP reporter mice, wild-type mice and primary human retinas were used for immunohistochemistry using cone- (cone arrestin; PNA) and rod- (Nr2e3) specific antibodies. GFP signals and immunostainings were imaged using structured illumination-, spinning disc-, confocal- or stochastic optical reconstruction (STORM) microscopy. By computational estimation the distance between cone axonal processes and rod cell bodies was assessed.

Results: In retinas of cone-GFP mice, approximately 2000 GFP⁺ cells/retina with rod-specific morphology, location and marker expression were detected in close proximity to GFP⁺ cone axons. Quantification of the distance between the cell bodies of GFP⁺ rods and GFP⁺ cone axons revealed an average distance of approximately 1.1µm, which is significantly lower than the distance that would be expected given a random distribution of rods in relation to cones (ca. 4.24 µm). Indications for thin protrusions formed between the cell body of GFP⁺ rods and GFP⁺ cone axons were observed by spinning disk microscopy within retinal wholemounts. The presence of GFP⁺ nanotube-like connections between rods and cones could be confirmed on retinal sections by STORM super resolution microscopy. Expression of cone-specific markers could be further observed in distinct rod cell-bodies in wild-type mice and human retinal sections.

Conclusions: Using cone-specific reporter mice and super-resolution microscopy, we identified previously undescribed direct cell-cell connections presumably mediating the horizontal transfer of cytoplasmic material between rod and cone photoreceptors. The extent of cellular material exchange and its biological significance remains to be explored in further studies.

CONTROL ID: 3545536

SUBMITTER (NAME ONLY): Sarah Weber

TITLE: A Validated Analysis Pipeline for Vitreous Proteomics

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Weber, Y. Zhao, J.M. Sundstrom, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|S. Weber, T.W. Gardner, J.M. Sundstrom, Kellogg Eye Center, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|V. Basrur, F. Da Veiga Leprevost, A. Nesvizhskii, Pathology, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|A. Nesvizhskii, Computational Medicine and Bioinformatics, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|C. Gates, Bioinformatics Core, Biomedical Research Core Facilities, University of Michigan, Ann Arbor, Michigan, UNITED STATES|J. Ma, Pathology, St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proteomic analysis of vitreous is capable of identifying proteins and pathways known to play critical roles in retinal disease. However, the number of samples required to generate statistically meaningful comparisons across groups remains unknown. In addition, the methods used to merge data from multiplex tandem mass tag mass spectrometry (TMT-MS) studies remains to be assessed and validated. The purpose of this study was to determine the proper algorithm to merge data across multiple 10-plexes and to identify the number of samples required to produce statistically reliable differential expression and pathway analyses.

Methods: Vitreous was derived from patients undergoing repair of epiretinal membrane or non-clearing vitreous hemorrhage secondary to proliferative diabetic retinopathy (PDR). Samples were processed according to protocols previously developed by our group. Samples were analyzed either individually (biological replicates) or as a pooled mixture of multiple samples, which was then aliquoted into smaller volumes (technical replicates). Samples were then distributed across five total 10-plexes in two TMT-MS experiments. Multiple algorithms were used to normalize the data across plexes. Validation of the normalization algorithm, differential expression, and power analyses were performed using the single normalized data matrix. This study was approved by the University of Michigan and Penn State College of Medicine institutional review boards and adhered to the tenets of the Declaration of Helsinki.

Results: The total number of unique proteins was 1,152 in experiment 1 and 1,191 in experiment 2. The average coefficient of variation (CV) across technical replicates was 4.2%. The average CV across patients was 36.9%. Power analysis revealed that 6 samples are required to achieve a power level of approximately 0.80 for proteins with log2 fold change of at least 1.194. As expected, differential expression and pathway analyses demonstrated significant activation of metabolic pathways and inhibition of neuroprotective pathways in PDR samples.

Conclusions: These data demonstrate minimal technical variability and low biological variability using TMT-MS to interrogate of human vitreous samples. In addition, methods to merge data across multiple 10-plex runs have been validated. As such, this vitreous proteomic analysis pipeline has been validated and allows for quantitative, cost-effective, and scalable analysis.

CONTROL ID: 3545538

SUBMITTER (NAME ONLY): Stephanie Poon

TITLE: A Living Biological Bandage for management of corneal injuries

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Poon, K.C. Shih, Y. Chan, Ophthalmology, University of Hong Kong, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: A large percentage of corneal opacifications are caused by chemical injuries, for which current conventional treatment strategies are costly, and may even result in complications, including immunological rejection after transplantation or glaucoma. Cell sheet engineering via an Aqueous-Two-Phase-System (ATPS) is an emerging technique which may act as a more economical alternative to construct an epithelial bandage for healing of corneal epithelial wounds. The purpose of this study is to increase the rate of re-epithelialisation in corneal epithelial defects, using a cellular construct that is delivered to the injured ocular surface with the help of a contact lens. We investigate the properties of the corneal epithelial cell sheet, and quantify the efficacy of the cell sheet therapy via an in vitro chemical injury model and an ex vivo porcine cornea model.

Methods: A primary human corneal epithelial cell line was used for in vitro experiments. The cell sheet was formed between a liquid-liquid interface, which was formed with a Poly(ethylene glycol)(PEG)-rich layer on top and a Dextran(DEX)-rich layer at the bottom. The cell density used for constructing the cell sheet, as well as the time for incubation, were optimised. We carried out in vitro tests to investigate the properties of the cell sheet as well as its viability in the ATPS components. We also measured the efficacy of cell sheet transplantation in healing a chemical injury wound on a Transwell model. In addition, an ex vivo porcine cornea model was adopted to examine the integration, proliferation properties, and retention of the cell sheet on a de-epithelialised cornea.

Results: Upon measuring the percentage area of defect on the in vitro chemical injury model on set time points throughout a 7 day observation period, we found the cell sheet to significantly reduce the time required for wound healing compared to the control group without transplantation performed. In addition, our ex vivo model illustrated strong adherence of the transplanted cell sheet on the de-epithelialised porcine cornea.

Conclusions: Our current results illustrate potential for the ATPS cell sheet engineering technique to be used as a management strategy for ocular injuries. Future work points towards the conducting in vivo experiments to assess the efficacy and physiological outcomes of the cell sheet transplant method for wound repair.

CONTROL ID: 3545540

SUBMITTER (NAME ONLY): Xiaorong Xin

TITLE: Proteomic alterations in the rat retina responding to the hypobaric hypoxic stress

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Xin, Department of Ophthalmology, Sichuan Provincial People's Hospital, Chengdu, Sichuan, CHINA|

Commercial Relationships Disclosure (Abstract): Xiaorong Xin: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: High-altitude retinopathy (HAR) is initiated by hypobaric hypoxia and characterized by retinal function deficits. However, the exact molecular mechanisms involved in HAR remain incompletely understood. Our current investigation is to utilize the proteomic analysis to profile the proteomic changes in rat retina exposed to hypobaric hypoxia and evaluated the protective efficacy of hesperidin (HSD) on the hypobaric hypoxia-induced impairment to the retina.

Methods: In the present study, we undertook an approach to mimic 5000m altitude with a low-pressure oxygen cabin. SD rats were randomized into control group, hypobaric hypoxia (HH), and HSD intervention group. Retinas were dissected following different treatments for 7 days. A quantitative comparison of the proteome in the retina was performed through TMT labeling, HPLC fractionation, LC-MS/MS and PRM analysis.

Results: A total of 154 and 259 proteins were upregulated, 216 and 54 proteins were downregulated when compared the HH group with the control, HSD with HH group respectively. Subcellular distribution of deferentially expressed proteins were mostly localized in the cytoplasm, nucleus, followed by extracellular, plasma membrane and mitochondrion. Hypobaric hypoxia-triggered down-regulation of proteins in the retina were mainly related with cellular process, biologic regulation, stimulus response, multicellular-organismal process, metabolic and developmental process. HSD dramatically inhibited the hypobaric hypoxia-induced stress by upregulation of proteins mainly associated with the above-mentioned biological activities. Proteins including glial fibrillary acidic protein(GFAP), aldehyde dehydrogenase,dimeric NADP-preferring (ALDH3A1), neurofilament light polypeptide (NEFL), collagen alpha-1(Colla1) were downregulated in the hypobaric hypoxic condition but enhanced by HSD intervention, which were validated by PRM assay. ECM-receptor interaction and PI3K-Akt signaling pathway were identified to be the most relevant pathways related with retina affected by either hypobaric hypoxia or HSD intervention through the KEGG pathway enrichment analysis.

Conclusions: Our proteomic analysis suggests that hypobaric hypoxia exerts a pathological impact on the rat retina through affecting protein function. The intervention of HSD elicits a protective response to the hypobaric hypoxia-induced stress on the rat retina.

CONTROL ID: 3545544

SUBMITTER (NAME ONLY): Diego Paredes Jalil

TITLE: Frequency of co-existing ocular surface neoplasms in pterygium biopsies: Experience from a South American country

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.I. Paredes Jalil, C. Aravena, C. Cartes Pinto, A. Cruzat, R. Garretón Cárcamo, M. Ibañez Bruron, P. Liberman, Ophthalmology, Pontificia Universidad Catolica de Chile, Santiago, CHILE|P. Zoroquiain, Pathology, Pontificia Universidad Catolica de Chile, Santiago, CHILE|

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ABSTRACT BODY:

Purpose:

Pterygium is a frequent benign condition, and the standard medical practice is to discard the sample when excised. Ocular surface squamous neoplasia (OSSN) co-existence in pterygium biopsies is variable between cross-sectional studies. A higher correlation is observed amongst people from lower latitudes and Caucasians. Data on the association of OSSN and pterygium in Latinos are sparse. The purpose of this study is to estimate the frequency of coexisting OSSN in pterygium biopsies in people from Chile.

Methods: Samples from adult patients who underwent a pterygium removal surgery during the first semester of 2018 were prospectively collected and sent for pathological examination. Patients with clinical suspicion of OSSN were excluded. All biopsies were evaluated by an ocular pathologist. Co-existence of OSSN was compared between central (33°S, similar distance from equator to Los Angeles, CA, USA) and southern latitudes (41°S, similar to Chicago, IL, USA). This investigation was approved by the Ethics Review Board.

Results: A total of 55 surgeries from 54 patients were performed. The average age was 55±12 years and 50.91% were women. Grade one conjunctival intraepithelial neoplasia was found in two cases (both female, 53 and 54 years-old), corresponding to 3.63% of excised lesions. OSSN was found in two patients from central Chile and in none from southern Chile (p=0.54).

Conclusions: To the best of our knowledge, this is the first study reporting association of OSSN and pterygium in a Latino population, with 3.63% prevalence in the study sample. This data suggests that excised pterygium from Chile should be submitted for pathology evaluation. We note the additional observation that a higher proportion of OSSN was observed in central Chile compared to southern Chile, although this was not a statistically significant finding and a larger cohort of patients is needed to be able to further study this hypothesis. Aside from increasing the number of patients, future studies could include data from a third distinct latitude in northern Chile.

CONTROL ID: 3545546

SUBMITTER (NAME ONLY): Andras Komaromy

TITLE: Four-year follow up of intraocular pressure (IOP) control in a canine model of open-angle glaucoma (OAG) treated with adeno-associated virus (AAV)-mediated modification of gene expression within the aqueous humor outflow pathways (AHOP)

SESSION TITLE: Pharmacological intervention or cellular mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.M. Komaromy, C. Harman, K. Koehl, A. Anderson, Small Animal Clinical Sciences, Michigan State University, East Lansing, Michigan, UNITED STATES|S.L. Boye, Department of Pediatrics and the Powell Gene Therapy Center, University of Florida, Gainesville, Florida, UNITED STATES|J. Steibel, Department of Animal Science & Department of Fisheries and Wildlife, Michigan State University, East Lansing, Michigan, UNITED STATES|L. Teixeira, Pathobiological Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|C.B. Toris, Ophthalmology & Visual Sciences, University of Nebraska Medical Center College of Medicine, Omaha, Nebraska, UNITED STATES|C.B. Toris, S.E. Moroi, Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|S.E. Boye, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To demonstrate that gene enhancement therapy of the AHOP following a single intracameral AAV injection results in long-term stable IOP control by preventing extracellular plaque formation in the trabecular meshwork (TM) of a well-established canine OAG model.

Methods: Six ADAMTS10-mutant dogs with early stages of OAG were injected unilaterally with a 75-100µL volume of single-stranded AAV2(Y444F)-smCBA-hADAMTS10 vector ($1.25-1.61 \times 10^{12}$ vector genomes). Clinical outcome measures were monitored for 24-48 months, including weekly diurnal IOP, repeated aqueous humor (AH) flow measurements, and high-resolution imaging of retina and optic nerve head (ONH) by optical coherence tomography (OCT). IOP analysis consisted of pairwise comparisons of treated vs. fellow control eyes while accounting for dog-to-dog variation. Safety monitoring included routine clinical ophthalmic examinations and AH analyses (protein concentrations, cell counts, and neutralizing AAV antibody titers). Ocular tissues were examined by routine light and transmission electron microscopy (TEM).

Results: IOP decreased significantly and was less variable for the entire 24- to 48-month observation period in 5/6 ADAMTS10-mutant dogs in treated vs. fellow control eyes (16.6 ± 7.5 vs. 29.7 ± 8.7 mmHg; $p < 0.0001$). Outflow facility was significantly higher and more variable in treated (0.34 ± 0.15) vs. untreated (0.23 ± 0.08) eyes ($p < 0.01$). OCT imaging showed that ONH morphology remained unchanged over time in successfully treated eyes, but degeneration/cupping progressed in untreated controls. Mild anterior uveitis with positive neutralizing antibody titers developed in the serum of all dogs as well as in the AH of AAV-treated but not untreated fellow eyes. TEM examination of the TM revealed almost complete prevention of extracellular plaque formation in treated vs. untreated eyes.

Conclusions: Long-term, stable IOP control can be achieved for at least 4 years following a single intracameral injection of AAV in a clinically relevant canine OAG model. These findings are consistent with reduced extracellular TM plaque formation and increased AH outflow facility.

CONTROL ID: 3545558

SUBMITTER (NAME ONLY): Chiao Yu Wang

TITLE: Association between myopiogenic factors and emmetropia in a Taiwan preschool population

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Emmetropia has been reported as a predictor of myopia onset. But the distribution of myopiogenic factors among emmetropic children has not been well understood. This study aimed to investigate the factors for myopia among preschoolers and the associations with emmetropia.

Methods: Since launch of the Yilan Myopia Prevention and Vision Improvement Program (YMVIP) in August 2014, we have promoted outdoor activities and conducted a countywide population-based, annual cross-sectional study in all kindergartens in Yilan County, Taiwan. Eye examinations, including cycloplegic autorefraction, have been provided for all preschoolers aged 5-6 years. Demographics, medical history, parental history, near work habits, screen time and outdoor activity was collected by questionnaire. Refractive status was determined according to the cycloplegic spherical equivalent (SE) of the eye with less SE and classified into myopia ($SE \leq -0.5D$), emmetropia ($0.5D > SE > -0.5D$), or hyperopia ($SE \geq 0.5D$).

Results: Among 20,419 preschoolers from 2014 through 2019, a total of 18,621 (9,715 [52.2%] boys) were finally included. Of those, 2,003 (10.8%), 5,057 (27.2%) and 11,561 (62.0%) were myopic, emmetropic and hyperopic. Most of association factors for myopia identified by multinomial logistic regression, including male (odds ratio [OR], 1.25; 95% CI, 1.13-1.37), caregiver myopia (OR, 1.76; 95% CI, 1.58-1.96), screen time ≥ 1 hour/weekday (OR, 1.20; 95% CI, 1.09-1.32), exposure to the YMVIP promoting outdoor activity (one-year exposure: OR, 0.80; 95% CI, 0.69-0.94; two-year exposure: OR, 0.46; 95% CI, 0.41-0.52), and higher education level of caregiver (OR, 0.79; 95% CI, 0.72-0.88), were also significantly associated with emmetropia (male [OR, 1.22; 95% CI, 1.14-1.30], caregiver myopia [OR, 1.42; 95% CI, 1.32-1.53], screen time ≥ 1 hour/weekday [OR, 1.15; 95% CI, 1.07-1.23], exposure to the YMVIP promoting outdoor activity [one-year exposure: OR, 0.84; 95% CI, 0.74-0.94; two-year exposure: OR, 0.62; 95% CI, 0.56-0.68], and higher education level of caregiver [OR, 0.87; 95% CI, 0.81-0.94]).

Conclusions: Emmetropia and myopia share similar risk factors in a preschooler population and the associations of these myopiogenic factors with emmetropia are weaker than with myopia, which may indicate the tendency of emmetropia toward myopia among preschoolers.

CONTROL ID: 3545573

SUBMITTER (NAME ONLY): Jenny Youale

TITLE: Human apo-Transferrin confers neuroprotection in ex vivo glaucoma rat models

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Youale, K. Bigot, T. Bordet, Eyevensys, Paris, FRANCE|J. Youale, T. Javorsky, E. Picard, F.F. Behar-Cohen, UMRS 1138 Team Behar-Cohen, INSERM, Paris, FRANCE|F.F. Behar-Cohen, Ophtalmopole, Cochin Hospital, Paris, FRANCE|

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ABSTRACT BODY:

Purpose: Even though iron is essential for retinal homeostasis, its overload is involved in most of pathogenic mechanisms associated with many retinal diseases¹. In glaucoma, progressive retinal ganglion cell (RGC) death has been associated with dysregulation of iron homeostasis. Apo-Transferrin (apo-TF) is an endogenous iron transporter that neutralizes free toxic iron (III) in biological fluids and also delivers iron to cells by binding to its receptors. In various models of retinal degeneration, we previously demonstrated that local administration of apo-TF is neuroprotective, controlling iron-induced oxidative stress and regulating other iron unrelated pathways without undesirable side-effects unlike chemicals iron chelators¹. The purpose of this study was to evaluate the effects of apo-TF on RGCs death induced by various stresses that mimic glaucoma pathogenesis.

Methods: Retinas from adult rats were harvested and placed on polycarbonate membrane with RGCs facing up. Retinal explants were then subjected for 24 hours to hypoxia (CoCl_2 100-500 μM) or excitotoxicity (NMDA 100-500 μM). Apo-TF (50 mg/mL) was added to the medium during the 24-hour stress induction period. RGC survival was quantified by Brn3a immunolabeling on flat-mounted retinas and quantification of LDH release at 24 to 96 hours post exposure. Markers for necrosis (RIP3) or apoptosis (Cas-8, Apaf-1, Cas-3, Bcl2) were evaluated by western blot at 6 to 96 hours post exposure.

Results: Both CoCl_2 and NMDA induced a dose-dependent reduction in RGCs density with LD50 around 100 μM . CoCl_2 induced a gradual increase of Apaf-1- and activated caspases along with a parallel reduction in Bcl2 and a necrosis activation peak at 24 hours. Conversely, NMDA induced a rapid increased in RIP3 and Apaf-1 in the very first hours of intoxication followed by a delayed activation of Cas-8 and Cas-3 with maximal activation at 72 hours. Incubation with apo-TF prevented CoCl_2 -induced RGC hypoxia (+109% RGCs; -33% LDH release) reducing Cas-3 activation. Similarly, apo-TF partly preserved RGCs against NMDA-induced excitotoxicity (+35% RGCs; -26% LDH release) reducing levels of necrotic and apoptotic markers to normal.

Conclusions: These results indicate that apo-TF can promote RGC survival by interfering with cell death mechanisms involved in glaucoma pathogenesis.

1. Picard, E. et al. From Rust to Quantum Biology: The Role of Iron in Retina Physiopathology. Cells 9, 705 (2020).

CONTROL ID: 3545574

SUBMITTER (NAME ONLY): Alecia Gross

TITLE: The cytoskeletal network in photoreceptors is dependent upon NUDC expression

SESSION TITLE: Ocular disease models: molecular mechanisms and therapeutic approaches

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: We have shown Nuclear distribution protein C (NUDC) has a critical role in the maintenance of post-mitotic rod photoreceptors by regulating outer segment (OS) disk diameter through interactions with actin. Here we test the hypothesis that NUDC is critical in microtubule cargo movement by examining the localization of rhodopsin and arrangement of mitochondria in the inner segment in the absence of NUDC mouse photoreceptors.

Methods: We have previously generated the NUDC floxed mouse and bred them with the rod-cell specific Cre recombinase (iCre75) mouse to produce NudC^{+/-} or NudC^{-/-} in rod photoreceptors. The retinas of the resulting mice were isolated and examined by electroretinography (ERG), transmission electron microscopy (TEM), immunohistochemistry (IHC), and quantitative PCR (qPCR) of mRNAs involved in fission and fusion of mitochondria.

Results: ERG analysis uncovered very low a- and b-wave amplitudes in 3wk-old NudC^{-/-} mice under scotopic conditions. IHC staining of retinal cryosections taken from NudC^{-/-} mice demonstrate disorganized microtubules in the inner segment (IS) of rod photoreceptor cells along with rhodopsin mislocalization in the IS, outer nuclear layer and synapse. Instead of long, fused mitochondria that align to the IS plasma membrane, TEM images of ultrathin NudC^{-/-} mouse retinal sections show mitochondria localized throughout the entire IS cytoplasm instead of adjacent to the plasma membrane as in wild type rods. Differences in expression of key genes critical for mitochondrial fission and fusion as measured by qPCR were statistically insignificant.

Conclusions: We have found that the protein NUDC is critical in rod photoreceptor OS disk formation and for mitochondrial localization in the IS. Our data are consistent with the hypothesis that NUDC governs disk dimension through actin regulation and mitochondrial localization through microtubule regulation, stressing the key importance of this protein in the cytoskeleton of photoreceptors in development and during homeostasis.

CONTROL ID: 3545581

SUBMITTER (NAME ONLY): Sergio Crespo-Garcia

TITLE: Inhibition of BCL-xL with the small molecule UBX1967 targets Col1a1-positive endothelial cells in ischemic retinopathy

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Crespo-Garcia, A. Dejda, F. Fournier, F. Pilon, R. Juneau, F.A. Mallette, P. Sapieha, Hopital Maisonneuve-Rosemont Centre de Recherche, Montreal, Quebec, CANADA|P. Tsuruda, R. Ryan, C. Yohn, R. O'Brien, D. Marquess, P.J. Beltran, UNITY Biotechnology, California, UNITED STATES|J. Joyal, Centre Hospitalier Universitaire Ste-Justine Research Center, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Pathological neovascularization (NV) remains one of the main challenges in the treatment of proliferative diabetic retinopathy (PDR). Current therapies for PDR target NV yet often lead to off-target effects on healthy blood vessels. We previously demonstrated that pathological vasculature in the retina selectively engages programs of cellular senescence. This study aims to understand the molecular signatures of diseased vessels in order to elucidate new drug targets.

Methods: Ischemic retinopathy was studied in the proxy mouse model for PDR, oxygen-induced retinopathy (OIR) using C57Bl/6J mice. Pups were exposed to 75% O₂ from post-natal day (P)7-P12 and 21%O₂ P12-P17. The BCL-xL small molecule inhibitor, UBX1967, was administered intravitreally at P12. In vitro studies were performed using human retinal microvascular endothelial cells. Quantitative PCR, single-cell (sc) and bulk RNA-Seq were used for transcriptomic analyses. Protein expression was studied by means of Western blot or tissue immunolabelling. All animal studies complied with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research and were approved by institutional ethical committees.

Results: Pathological neovascularization is associated with expression of the anti-apoptotic BCL-2 protein family members. Senolysis via inhibition of BCL-xL suppresses neovascularization, accelerates the recovery of ischemic regions and is accompanied by a decrease of the senescence-associated secretory phenotype. Using scRNA-Seq, we observe an OIR-specific subpopulation of Col1a1-positive endothelial cells that localizes to regions of pathological NV and that is not present after BCL-xL inhibition.

Conclusions: Inhibition of BCL-xL with UBX1967 suppresses retinal pathological NV and targets Col1a1-positive subpopulations of endothelial cells. These data highlight the use of senolytics as potential therapies for PDR.

CONTROL ID: 3545583

SUBMITTER (NAME ONLY): Riccardo Sacco

TITLE: Paracellular and intracellular transport in aqueous humor production: theoretical modeling and simulation

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is an established risk factor for glaucoma. Steady-state IOP stems from a balance between aqueous humor (AH) production (AHp) and drainage. AHp results from the interaction among hydrostatic, osmotic and oncotic pressure differences determining a net fluid motion across ciliary epithelium (CE) bilayer from the stroma (S) to the aqueous side (AQ). The role of transcellular and paracellular (P) transport in AHp is difficult to disentangle experimentally, thus, we propose a mathematical model to investigate the contribution of each mechanism to AHp

Methods: AHp is described by a compartment model solving iteratively the coupled interaction between ion electrodiffusion and AH fluid motion until convergence. The model includes S, a cell cytoplasm (C) representing the CE bilayer, P and AQ sides. A tight junction separates S from P to prevent large size proteins from flowing into the AQ. Ion transport is modeled through active and passive membrane transporters and carbonic anhydrase (CA)-mediated intracellular CO₂ hydrolysis. Cell electroneutrality is ensured by a fixed intracellular negative charge. Simulations are performed under a transepithelial potential difference of 1mV (AQ negative) and hydrostatic pressures of 20 and 15 mmHg in S and AQ

Results: Fig. 1 shows a scheme of AHp including membrane protein transporters driving primary active, secondary and passive ion transport. Transporters are not evenly distributed according to membrane diverse functional roles. Fig. 2 shows the scheme on which arrows represent the AH velocity vector across membranes. Model seems to indicate a much higher P velocity than C velocity. Results also indicate a flow of water from C into P and water recirculation from AQ into C. Model predicts a total AH volumetric flow rate (VFR) of 2.74 μ L/min, in accordance with physiological data

Conclusions: Simulations suggest that P transport significantly contributes to total AH VFR. They also indicate that osmotic pressure gradients determine a passive water flow from C into P and a water back flow from AQ into the cell. Results support the use of the proposed model as a mathematical virtual laboratory, noninvasively complementing the animal model, to test the efficacy of IOP lowering medications to decrease AHp

CONTROL ID: 3545585

SUBMITTER (NAME ONLY): Liying Low

TITLE: Gut dysbiosis in Ocular Mucous Membrane Pemphigoid

SESSION TITLE: Dry eye and microbiome clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Low, K. Suleiman, M. Murad, K. Tsang, M. Davidson, K. Bassilious, M. Shamdas, N. Poonit, P.I. Murray, G.R. Wallace, S. Rauz, Academic Unit of Ophthalmology, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, West Midlands, UNITED KINGDOM|L. Low, K. Bassilious, N. Poonit, P.I. Murray, G.R. Wallace, S. Rauz, Birmingham and Midland Eye Centre, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, West Midlands, UNITED KINGDOM|A. Rossiter, Institute of Microbiology and Infection, University of Birmingham, Birmingham, West Midlands, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Mucous Membrane Pemphigoid is a multi-system autoimmune scarring disease involving mucosal sites, including the ocular surface (OcMMP) and gastrointestinal tract. Loss of tolerance to epithelial basement membrane proteins (BMP), and generation of autoreactive T cell and/or autoantibodies to BMP are central to the disease process. Mechanisms on how and where the T cells first become autoreactive is unknown.

The gut microbiome plays a critical role in the development of the immune system and has been shown to activate ocular autoimmune T cells. The aims of this study were to 1) compare the gut microbiome profiles of OcMMP patients with age- and gender-matched controls, and to 2) examine the relationship between the gut microbiome diversity and ocular inflammation in OcMMP.

Methods: Faecal samples were collected from 50 OcMMP patients attending a tertiary referral centre and 40 healthy controls and DNA extracted, amplified for the V4 region of the 16S rRNA gene and sequenced using Illumina Miseq platform. Sequencing reads were processed using bioinformatics pipeline available in the mothur v.1.44.1 software.

Results: OcMMP patients had lower alpha diversity compared to healthy controls (HC) [Median observed OTUs in OcMMP: 214 (IQR: 173 – 276) vs HC: 317 (277 – 549), $p < 0.0001$; Median Shannon Index in OcMMP: 3.05 (2.54 – 3.45) vs HC: 3.60 (3.18 – 4.01), $p < 0.0001$]. Reduced number of observed OTUs were correlated with conjunctival inflammation (R^2 : 0.1, $p = 0.03$). Alpha-diversity was not significantly associated with duration of disease, treatment, clinical scoring of scarring and morbidity, or immunofluorescence results. The linear discriminant analysis effect size scores indicated that Streptococcus, Lachnospiraceae, and Eggerthella were enriched in OcMMP patients whilst Oxalobacter, Clostridia, uncultured genus-level group (UCG) 014, Christensenellaceae R-7 group, UCG 002, 003, 005, NK4A214 group and butyrate-producing bacteria such as Ruminococcus, Lachnospiraceae, Oscillospiraceae, Coprococcus, Roseburia were enriched in healthy controls (\log_{10} LDA score < 2 , FDR-adjusted $p < 0.05$).

Conclusions: OcMMP patients have gut dysbiosis correlating with ocular inflammation, providing the framework for future causative studies on the role of the gut microbiome in OcMMP.

CONTROL ID: 3545588

SUBMITTER (NAME ONLY): Juan J. Salazar

TITLE: Retinal microglial activation in the triple-transgenic Alzheimer's Disease mouse model (3xTg-AD).

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Alzheimer's disease (AD) is a neurodegeneration that constitutes the most common type of dementia in the world. The main features associated with AD are amyloid protein plaques β ($A\beta$) and tau protein neurofibrillary tangles, which lead to a microglial cell-mediated neuroinflammation in the brain. The retina as a window to the brain can also be affected in AD, presenting some molecular and cellular changes such as microglial activation. The aim of the present study was to analyze microglial changes in retinal whole-mounts in the triple-transgenic AD mouse model (3xTg-AD).

Methods: Whole retinal mounts were processed with anti Iba-1 to perform a quantitative morphometric analysis of microglia activation in the 3xTg-AD mice and wild-type mice (n=8 in both group), which allows the visualization of the whole microglial cell, as well as its location along the extension of the retina in different layers. A quantification of Iba-1+ cells and of the cell body area in the outer plexiform layer and in the inner retinal layer complex, constituted by the inner plexiform layer and the nerve fiber layer-ganglion cell layer were performed.

Results: Compared to wild animals, the retina of 3xTg-AD mice shows a thicker microglial cell body area and a higher number of microglial cells. In addition, the microglial retract, migrate, and reorient their processes, changing their location from a parallel position to one that is perpendicular to the surface of the retina as well as well as forming groups in rows or circular clusters.

Conclusions: In the 3xTg-AD model, microglial cells showed several signs of activation, such as increased number and soma size, and retraction and reorientation of their processes, and changes in the cell's location. These morphological changes could represent that in this model of AD a neuroinflammatory process is taking place.

CONTROL ID: 3545590

SUBMITTER (NAME ONLY): qin ke

TITLE: p53 plays a regulatory role in DNA damage response of mono- and multi-nucleated retinal pigment epithelial cells

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. ke, L. Gong, M. Zou, R. Qi, D.W. Li, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Existence of multi-nucleated (MN)retinal pigment epithelial cells(RPE) has been demonstrated inboth human and mouse.In human, specific macular distribution ofMN RPE, and the positive correlation between MN RPE and rod photoreceptors has been reported, suggesting MN RPE reflect physiological functions. Because damaged DNA is detected in RPE from patients with age-related macular degeneration (AMD), here we analyzed the DNA damage response in mono-nucleated (MO) and MN RPE, and explored the regulatory effects of p53, the key DNA damage player, in this process.

Methods: Immunofluorescence (IF) was performed to measure the percentage and distribution of MO and MN RPE cells in 2-month C57BL/6J mice (n=4). To induce DNA damage, 2-month wild-type (n=8) and p53+/- (n=8) mice were exposed to 1 GyX-ray irradiation.The DNA damage repair efficiencywas evaluated by comet assay and immunofluorescence with anti-γ H2Ax (DNA damage marker) at 1- or 3-day post irradiation.

Results: MN RPE cells show higher distribution in the center region of retina (75.4%) as compared with peripheral retina (40.8%). Irradiation-induced DNA damage occurs in both MO and MN RPE cells.IF analysis shows more γH2Ax signals in MN as compared with MO RPE at both 1- (41.2% vs. 27.7%) and 3-day post irradiation (9.2% vs. 6.1%). Comet assay shows that the overall DNA double strand breaks were repaired with less efficiency in p53+/- RPEas compared with wild type mice at 3-day after irradiation, but the MO and MN RPE cells exhibited similar repair efficiency in both WT and p53+/- mice.

Conclusions: MN RPE appears to repair DNA less efficiently than MO RPE cells upon X-ray irradiation, and p53 is required for DNA damage repair in both MO and MN RPE. (Supported by National Natural Science Foundation of China (#82070969, #81770910, #81970787) and the Fundamental Research Funds for the Central Universities (#19ykpy153)).

CONTROL ID: 3545591

SUBMITTER (NAME ONLY): Ming Zhang

TITLE: Ocular murine cytomegalovirus (MCMV) gene expression in aged BALB/c mice following systemic MCMV neonatal infection

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zhang, X. Zhang, J. Xu, B. Marshall, Department of Cellular Biology and Anatomy, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our previous studies have shown that systemic neonatal murine cytomegalovirus (MCMV) infection of BALB/c mice can spread to the eye with subsequent establishment of latency in the choroid and RPE. MCMV latency in the choroid/RPE was associated with the upregulation of several inflammatory/angiogenic factors, and the development of AMD-like pathology in a progressive manner, including loss of choroidal capillaries, deposits in basal aspects of the RPE, degeneration of RPE and photoreceptors and eventually, choroidal neovascularization (CNV) in later life. The purpose of this study was to determine if the development of AMD-like pathology is associated with reactivation of viral gene expression.

Methods: MCMV (50 pfu per mouse) or medium as control were injected intra-peritoneally (i.p.) into BALB/c mice at <3 days after birth. At 8 and 18 months p.i., optical coherence tomography (OCT) examinations were performed to monitor the integrity of retinal structure using an Envisu R2210 system. MCMV or medium injected mice were sacrificed and eyes were collected and examined by realtime-RT-PCR for expression of 26 virus genes related to latency.

Results: The mean retinal thickness in MCMV latently infected aged mice was significantly lower than in eyes of age matched controls at both 8 and 18 months p.i. Severe photoreceptor degeneration (including disappearance of the entire outer nuclear layer in some areas) and CNV lesions (average 2 per eye) were observed in 7 and 4 eyes respectively of 26 total eyes. Among 26 genes studied, 17 were expressed in some eyes from MCMV infected mice at both 8 and 18 months p.i. These included immediate early genes (IE1 and IE3) and genes functioning in anti-apoptotic (M37, M38.5, MM41 and M45) and immune evasion (M04, M138, M152). In addition, 2 genes (M18 and M82) were expressed only in aged eyes at 18 months p.i.

Conclusions: Virus gene expression during MCMV ocular latent infection may significantly alter homeostasis of the latently infected cell and the surrounding cellular environment and therefore induce the development of AMD-like pathology.

CONTROL ID: 3545593

SUBMITTER (NAME ONLY): xiaodong gong

TITLE: Differentiation Expression of GAP Junction Proteins in Senile Cataract Patients and Aging Mice

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. gong, Z. Shuyu, J. Fu, Y. Wang, L. Wang, Q. Nie, M. hou, J. Xiang, Y. xiao, D.W. Li, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: GAP junction channels are formed from connexin protein subunits. Three major connexin protein subunits (Cx43, Cx46 and Cx50) have been shown to play important roles in lens growth, differentiation and maintenance of lens transparency through biochemical and genetic studies using transgenic animals and cell lines. However, aging dependent changes of these proteins in normal and cataract patients have not been individually analyzed. In this study, we report the aging-dependent changes in cataract patients of ages from 50s to 80s, and also compared the expression patterns of these proteins in young and aged mice.

Methods: Automated western immunoblotting was used to analyze the changes of connexin protein subunits (Cx43, Cx46 and Cx50) in individual cataract patients aged from 50-years to 89-years. Over 120 cataract patients were divided into 4 groups: 50-59 years old (50s), 60-69 years old (60s), 70-79 years old (70s) and 80-89 years old (80s). The capsular epithelia isolated during surgical operation were frozen immediately and then used for extraction of total proteins.

Results: From transparent lenses to cataract lenses, Cx43 level is significantly upregulated. In contrast, Cx46 and Cx50 are distinctly downregulated. From 50s to 70s, three types of connexin proteins remain relative stable. However, from 70s to 80s, the levels of the connexin proteins are significantly downregulated. Differences between male and female individually are not statistically significant.

Conclusions: The three types of connexin proteins display distinct changes from transparent lens to cataract lenses, and also age-dependent changes from 50s to 80s. These changes are closely associated with their function alterations which contribute to cataractogenesis (Supported by the grants, #81770910, #81970787, #81900842 and #81970784 from the National Natural Science Foundation of China, the grant, 2019B1515120014 from the Natural Science Foundation of Guangdong Province and the Fundamental Funds,3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center, and the Graduate Scholarship from Sun Yat-sen University).

CONTROL ID: 3545595

SUBMITTER (NAME ONLY): Jay Chhablani

TITLE: Sectorial Choroidal Assessment between Two Eyes of Healthy Subjects

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chhablani, G. Nkrumah, M.A. Rasheed, O. Beale, F. Tatti, C. Iovino, K.K.

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ABSTRACT BODY:

Purpose: Choroidal vascularity index (CVI) and choroidal thickness (CT) are novel biomarkers for the evaluation of choroidal vasculature. Although well established, comparative analysis of CT and CVI at different choroidal sectors in healthy eyes have not been performed. Aim of this study was to compare the sectorial choroidal vascularity index and thickness of the macula between two eyes in healthy subjects

Methods: This prospective study included 50 eyes of 25 healthy subjects who underwent a comprehensive ophthalmic examination and enhanced-depth spectral-domain optical coherence tomography for both eyes. CVI and CT measurements were obtained using a validated algorithm for each sector using an early treatment diabetic retinopathy study map. A comparison of corresponding sectors between two eyes and multivariate analysis was performed.

Results: The mean age was 50.4 ± 13.2 years with 13 females and 12 males. There was no statistical difference in mean CVI and CT values between corresponding sectors of both eyes (central CVI $P=0.74$, CT $P=0.77$; inner superior CVI $P=0.74$, CT $P=0.87$; inner temporal CVI $P=0.87$, CT $P=0.80$; inner nasal CVI $P=0.16$, CT $P=0.74$; inner inferior CVI $P=0.84$, CT $P=0.55$ outer superior $P=0.87$, CT $P=0.83$; outer inferior $P=0.89$, CT $P=0.68$; outer temporal $P=0.72$, CT $P=0.83$; outer nasal $P=0.66$ CT $P=0.90$). Age was the only significant factor on multivariate regression ($R^2=0.31$) Example of CVI maps of two eyes of the same subject has been uploaded as figure.

Conclusions: We report a significant positive relationship between age and sectoral values, whereas gender remained insignificant in both groups. Intra-sectoral (within the same eye) and inter- sectoral (between right and left eye) analysis of CT and CVI values yielded no significant difference. These results would be applicable to explore various chorioretinal diseases to evaluate sectoral choroidal changes.

CONTROL ID: 3545599

SUBMITTER (NAME ONLY): David Friedman

TITLE: Predictors of long-term intraocular pressure control after clear lens extraction in primary angle closure glaucoma: results from the EAGLE

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The EAGLE trial provides evidence supporting the use of initial early lens extraction (ELE) as a first-line intervention for patients with primary angle closure glaucoma (PACG) or primary angle closure (PAC) with high intraocular pressure (IOP). We assess baseline parameters associated with better long-term IOP control using data from the EAGLE trial.

Methods: The EAGLE trial was a multicenter randomized controlled study comparing ELE with laser peripheral iridotomy (LPI) in patients who did not have cataract and had newly diagnosed PAC with IOP \geq 30mmHg or PACG. Good responders were defined as IOP $<$ 21mmHg at 36-month follow up without using any medications and requiring no additional surgery.

Results: A total of 369 patients (182 in ELE arm and 187 in LPI arm) who completed the 36-month follow up visit were included in this study. Among 419 randomized participants, only one study eye randomized to ELE underwent trabeculectomy (0.5%) while six had trabeculectomy in the LPI arm (2.8%). After ELE, 66% met our pre-defined good response criterion at 36 months with significantly longer drops/surgery-free survival time as compared to only 18% in the LPI arm ($p < 0.05$). Using a multi-variate Cox proportional hazards model, patients randomized to LPI [Hazard ratio (HR) (95% CI)=2.52 (1.92-3.31)], non-Chinese [HR=1.52 (1.14-2.05)], those who used glaucoma drops before [HR=1.48 (1.12-1.95)] and those who had higher baseline IOP [HR=1.02 (1.00-1.03) per 1mmHg] were less likely to maintain long-term good IOP control over 36 months. Other baseline characteristics such as age, gender, diagnosis (PACG versus PAC), presence of peripheral anterior synechiae, anterior chamber depth, baseline visual field and visual acuity were not associated with long-term IOP control.

Conclusions: Patients with PACG/PAC are more likely to maintain drops-free good IOP control with initial ELE surgery than LPI. Chinese ethnicity, higher baseline IOP and using glaucoma drops prior to randomization are predictors of worse long-term IOP response.

CONTROL ID: 3545600

SUBMITTER (NAME ONLY): Daniela Castro Farías

TITLE:

Neurovascular coupling in the human retina evaluated by adaptive optics ophthalmoscopy

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Neurovascular coupling (NVC) is the capability of vessels in neural tissue to adapt to neuronal demand. Here we report the results of flicker-induced dilation of retinal arterioles in normal subjects using adaptive optics ophthalmoscopy (AOO).

Methods:

The command program of the internal fixation light of a commercially available flood-illumination adaptive optics camera (rtx1, Imagine Eyes, Orsay, France) was modified to accommodate a 28°x20° flickering yellow light emitting diode, which is the light used for fixation target. The clinical procedure comprises 3 basal images before stimulation (taken within ± 60 seconds), followed by 3 periods of flickering stimulation at 15Hz during 20 seconds each; the image was captured during the last 2 seconds of the stimulation cycle. AOO images of arterial segments of at least 250 μm long in the posterior pole were segmented offline using a custom software (AOV image, developed by Florence Rossant). The protocol was approved by an ethical committee (Comité de Protection des Personnes).

Results:

21 eyes of 21 controls (10 females and 11 males; mean age \pm SD 38.4 years \pm 12.7) were examined. The average diameter of the arteries lumen was 85.1 μm (\pm 20.4). The difference between the basal measurements ranged from -2.22% to +2.86% with an average of +0.17%. Flicker-elicited dilation ranged from +0.83% to +6.63% with an average of +2.98%. The average wall to lumen-ratio of the vessels was of 0.24. Dilation was independent from age and size of vessel, but was inversely correlated with WLR ($p < 0.05$) (Figure 1).

Conclusions:

AOO-based NVC analysis offers a novel approach of the evaluation of the vasomotricity of retinal vessels. The vasodilation was found comparable to that reported using other methods, with the additional advantage of analyzing local changes and the concomitant measurement of the WLR. The latter was found to be inversely correlated to flicker-induced vasodilation. This may be an indication that microvascular tone may influence flicker response.

CONTROL ID: 3545601

SUBMITTER (NAME ONLY): Chenna Sugali

TITLE: Activation of canonical Wnt signaling pathway inhibits dexamethasone-induced glucocorticoid receptor signaling in the trabecular meshwork

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.K. Sugali, N.P. Rayana, J. dai, M. Peng, S.L. Harris, S. Liu, S. Dixon, P. Parekh, E. Martin, L.B. Cantor, W. Mao, Ophthalmology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|H.C. Webber, A.F. Clark, Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|V. Raghunathan, Basic Sciences, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dexamethasone (Dex) is frequently used to treat inflammation. Though Dex has many advantages, it has side effects including elevated intraocular pressure (IOP) and glaucoma. About 40% of general population may develop ocular hypertension (OHT) upon prolonged glucocorticoid treatment which is due to damages in the trabecular meshwork (TM). This type of secondary glaucoma is called glucocorticoid-induced glaucoma (GIG). Identifying the key molecules responsible for glucocorticoid-induced OHT and GIG is crucial since they can be used to develop novel glucocorticoids without causing side effects. Our published studies using perfusion cultured bovine eyes suggested that inhibition of the canonical Wnt signaling pathway promotes glucocorticoid-induced OHT and glucocorticoid responsiveness. Therefore, we hypothesize that activation of canonical Wnt signaling prevents the side effects of glucocorticoids.

Methods: Aqueous humor and TM tissues were collected from patients and donor eyes for analyzing DKK1 expression using ELISA and immunofluorescence, respectively. Luciferase assays were performed in GTM3 and NTM5 cells using the GRE or TCF reporter kit to study the activity of the glucocorticoid receptor (GR) signaling or Wnt signaling pathway. Primary human TM (HTM) cells were treated with or without Dex, Wnt3a and/or GSK3 β inhibitors, and whole cell lysates and conditional medium were used for western immunoblotting (WB).

Results: We found elevated canonical Wnt signaling inhibitor Dkk1 in the aqueous humor and TM of glaucoma patients. At signaling level, we found that Dkk1 positively regulated GR signaling. We also observed that Wnt signaling activators decreased GR signaling in HTM cells using luciferase assays. Similarly, activation of GR signaling inhibited Wnt signaling. At protein level, Dex-induced extracellular matrix (ECM) was inhibited by Wnt activation using Wnt activators or Dkk1 knockdown in primary HTM cells. In contrast, inhibition of canonical Wnt signaling by β -catenin knockdown increased Dex-induced ECM proteins. At physiological level, we found that adenovirus-mediated Wnt3a expression decreased Dex-induced OHT in mouse eyes.

Conclusions: Wnt and GR signaling inhibit each other in the TM, and canonical Wnt signaling activators have the potential to prevent the side effect of glucocorticoids.

CONTROL ID: 3545602

SUBMITTER (NAME ONLY): Valerie Kuan

TITLE: Effects of smoking, alcohol, blood pressure, body mass index and glycaemic risk factors on advanced age-related macular degeneration: a mendelian randomisation study

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess whether smoking, alcohol consumption, body mass index (BMI), blood pressure (BP) and glycaemic traits have a causal role in the risk of advanced age-related macular degeneration (AMD).

Methods: We used two-sample inverse-variance weighted, MR-Egger and weighted median mendelian randomisation methods to investigate the association between modifiable risk factors (smoking, alcohol consumption, BMI, BP and glycaemic traits) and the risk of advanced AMD (neovascular AMD or geographic atrophy). Summary level genetic association data for advanced AMD (n=16,144) were obtained from the International AMD Genomics Consortium (IAMDGC) genome-wide association study (GWAS). Genetic instruments composed of single nucleotide polymorphisms associated with modifiable risk factors at genome-wide significance ($P < 5 \times 10^{-8}$) were obtained from published GWASs.

Results: Genetically predicted lifetime smoking was associated with increased advanced AMD risk (odds ratio (OR) per unit increase of the lifetime smoking index 1.49; 95% CI 1.13-1.95; $P=0.004$). Specifically, a one-standard deviation (SD) increase in log odds of ever smoking was associated with higher risk (OR 1.26; 95% CI 1.13-1.40; $P<0.001$), while a one-SD increase in log odds of smoking cessation (former versus current smoking) was associated with lower risk (OR 0.66; 95% CI 0.50-0.87; $P=0.003$). A one-SD increase of log-transformed alcoholic drinks per week was suggestive of an association with higher risk of advanced AMD (OR 1.57; 95% CI 1.03-2.40; $P=0.04$). There was insufficient evidence to suggest associations with genetically predicted BP, BMI and glycaemic traits (figure).

Conclusions: This study provides genetic evidence that ever smoking is causal for advanced AMD risk, while smoking cessation is protective. The evidence also suggests that increased alcohol intake is a causal risk factor. Public health messages regarding the adverse consequences of smoking and excessive alcohol consumption should include warnings about the risk of blindness.

CONTROL ID: 3545604

SUBMITTER (NAME ONLY): Bhim Rai

TITLE: Per-region visual field sensitivities and delays in AMD

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To compare central vs. peripheral visual field sensitivities and delays in neovascular AMD (nAMD) and earlier-stage fellow eyes using FDA-cleared multifocal pupillographic objective perimetry (mfPOP).

Methods: We recruited 18 nAMD patients testing both eyes concurrently. Practitioner directed intravitreal anti-VEGF injection was administered monthly for 14 to 28 visits. Diagnostic procedures included mfPOP, Matrix 10-2 perimetry, and OCT. The macular mfPOP variant had 44 interleaved stimuli/eye presented from fixation to 15^o eccentricity. We examined correlations between central and peripheral mfPOP per-region sensitivities and delays within eyes, and between nAMD eyes and untreated fellow eyes.

Results: Twenty-three eyes of 18 patients were tested (14 females, 77.8%). In treated eyes central sensitivity decreased over time by -2.23 ± 0.051 dB/month ($p < 0.0002$). Untreated fellow central sensitivity declined at -0.17 ± 0.07 dB/month ($p = 0.033$). Treated eyes showed quicker central responses by 13.08 ± 3.77 ms than untreated eyes ($p = 0.001$). Based on peripheral sensitivities and delays we have identified two patient categories: positive types with hypersensitivity and longer delays, and negative types with hyposensitivity and shorter delays compared to normal controls. When analysed separately mfPOP data showed an ability to predict the need for anti-VEGF injection. Among the positive eyes peripheral sensitivity increased by 9.88 ± 4.41 dB ($p = 0.042$) before treatment, and delays increased by 3.49 ± 1.75 ms/month ($p = 0.049$). For the negative eyes, the peripheral sensitivity dropped, and the delay was shorter a month before the treatment by 9.38 ± 3.59 ($p = 0.013$), and a month following treatment it improved towards normal values (shorter by 8.50 ± 2.71 ms, $p = 0.004$).

Conclusions: We observed decreased central sensitivity, and coincident peripheral hypersensitivity. In the untreated fellow eyes, the central sensitivity decreased and delay increased progressively until treatment was needed. Based on peripheral responses the eyes could be divided into positive and negative groups. The predictive value of mfPOP improved after the positive and negative eyes were analysed separately. Diagnostic sensitivity and delay changes could precede active disease by 1 to 3 months. We conclude that mfPOP may be a potential biomarker to predict the need for anti-VEGF injections in nAMD.

CONTROL ID: 3545605

SUBMITTER (NAME ONLY): Siyang Chaili

TITLE: Purposeful Pneumatic Induced Resorption of Submacular Fluid in Macula-off Retinal Detachments

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chaili, J. Fitzpatrick, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|A. Pirouz, S. Grant, S. Adrean, Retina Consultants of Orange County, Fullerton, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate visual outcomes in eyes with macula-off retinal detachments (RD) with purposeful submacular fluid retention after vitrectomy to allow for slow pneumatic macular flattening.

Methods: Retrospective study of 139 patients with macula-off RD. Patients were included if repaired with primary vitrectomy (VIT) or VIT with scleral buckle (SB). Patients were excluded if they had >6 wks to surgery, prior vitreous surgery, SB alone, drainage retinotomy or perfluorocarbon, development of proliferative vitreoretinopathy (PVR), <6 mon follow up, or other macular pathology. Patients underwent 3-port pars plana VIT with SB. Subretinal fluid was aspirated from pre-existing retinal breaks during air-fluid exchange (AFX). At the end of surgery fluid remained in the posterior pole and SF6 or C3F8 gas was then introduced with proper head positioning.

Results: Subretinal fluid was reabsorbed and gas fill was observed at post-op day 1. Mean baseline vision was 20.0±24.4 ETDRS letters (20/400) for 127/198 included patients. Of 71 excluded patients, 12 developed PVR. Primary repair success rate was 91.4% (127/139). Mean time to surgery was 8.6±7.9 days. At 6 months post-op, mean vision improved to 62.9±17.9 letters (20/60), an increase of 43.1±28.0 letters (8.6 lines) which was better than baseline ($p<0.001$). Best achieved vision averaged 72.6±13.2 letters (20/30-2), an increase of 52.8±25.1 letters (9.5 lines), at an average of 14.1±11.0 months later ($p<0.001$ vs baseline & 6 months post-op). Mean time to final follow-up was 25.8±26.5 months. Patients with $\geq 20/40$ vision increased from 3.1% at baseline to 44.9% at 6 months post-op to 74.8% at best achieved vision. Conversely, patients with $\leq 20/200$ vision decreased from 78.7% at baseline to 14.2% at 6 months post-op to 4.7% at best achieved vision.

Conclusions: Good visual outcomes may be achieved and maintained even if the duration of the macular detachment is longer than several weeks. Leaving fluid in the macula at the end of the surgery may allow the RPE pump to more physiologically remove submacular fluid, and for the photoreceptor/RPE microvilli interdigitation to anneal with better retinotopic organization, promoting visual recovery.

CONTROL ID: 3545606

SUBMITTER (NAME ONLY): Alex Gonzalez

TITLE: Development of an Individualized 3D Printed Visual & Tactile Tool: Enhancing Visual Perception for the Argus II Retinal Prosthesis.

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gonzalez, M.C. Aguilar, C. Rowaan, J.A. Parel, Ophthalmic Biophysics Center, University of Miami School of Medicine, Miami, Florida, UNITED STATES|B.L. Lam, N.Z. Gregori, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|N.Z. Gregori, K. Zann, Ophthalmology, Miami VA Healthcare System, Miami, Florida, UNITED STATES|J.A. Parel, Brien Holden Vision Institute, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The ability to interpret the artificial visual stimulus created by the Argus II retinal prosthesis can vary with the user's perceptual capabilities. Outcomes and proficient use may be improved through consistent training with self-administered rehabilitation tools in the home setting. An individualized 3D printed tool that allows the user to integrate both tactile and visual stimulus could help deliver personalized, in home ultra-low vision rehabilitation. This study investigates the feasibility of training with an individualized tool designed to improve shape and pattern recognition as well as spatial awareness.

Methods: Using CAD software, a board with an integrated grid for holding colored tokens was designed and printed using a 3D printer (Figure 1). Additionally, a holder was designed and printed to support the board at a comfortable angle, facilitating image capture by the Argus II camera. The initial board grid and tokens was mailed to the patient, and feedback describing visualization were shared. This iterative design cycle was repeated three times, until a token size, color and board grid spacing was achieved, such that the patient could easily visualize the tokens and create shapes and patterns. Using a mobile phone, the patient transmitted videos and photos of shapes and patterns, with audio descriptions of the visualization experience (Figure 2).

Results: A custom visual-tactile rehabilitation tool was created based on an interactive design process, with detailed feedback from a collaborating Argus II recipient. The patient was able to utilize the board for various visual exercises utilizing tactile feedback and provide constructive criticism for design improvement. The customized angle of the board minimized neck strain and reduced glare. This customizable tool introduced variability in daily exercises aimed to improve perception capabilities of patients implanted with the Argus II retinal prosthesis.

Conclusions: Incorporating a customized visual tactile tool for ultra-low vision rehabilitation at a patient's home can improve interpretation of the visual precepts delivered by the Argus II retinal prosthesis. In addition, the interactive, exploratory design process, increased patient engagement, with self-report indicating an increased Argus II retinal prosthesis utilization.

CONTROL ID: 3545611

SUBMITTER (NAME ONLY): Collynn Woeller

TITLE: Elucidating the role of the aryl hydrocarbon receptor and the insulin-like growth factor 1 receptor in Thyroid Eye Disease orbital fibroblasts.

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Woeller, E. Roztocil, C. Hammond, M. Gonzalez, S.E. Feldon, Department of Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: In Thyroid Eye Disease (TED), the connective tissue behind the eye becomes inflamed and enlarged. As orbital tissue expands, patients develop proptosis, diplopia, optic neuropathy and in severe cases, blindness. Cigarette smoking increases the chances of developing TED by more than 7-fold. Currently, there is no cure for TED and targeted treatments are limited. The insulin-like growth factor 1 receptor (IGF1R) and the aryl hydrocarbon receptor (AHR) pathways are implicated in inflammation and TED tissue remodeling. The goal of this work is to better define these pathways so that novel therapeutics can be identified.

Methods: Orbital fibroblasts (OFs) were treated with the IGF1 with or without cigarette smoke extract. The endogenous AHR ligand FICZ was used to activate AHR in OFs. IGF1R expression was depleted by IGF1R specific siRNA. AHR knockout OFs were generated using CRISPR/Cas9n. Cell proliferation was measured by BrdU incorporation and inflammatory cytokine production was analyzed by RT-qPCR and ELISA. Activation of downstream signaling cascades known to be upregulated in TED and involved in tissue remodeling (PI3K/Akt and MAPK/Erk) were detected by Western blot.

Results: IGF1R activation induced proliferation and PI3K/Akt signaling in OFs while smoke exposure increased inflammatory cytokine levels. Ligand activation of AHR reduced PI3K/Akt, MAPK/Erk signaling and cell proliferation. In contrast, knockout of AHR resulted in increased proliferation, increased inflammatory cytokine expression and elevated MAPK/Erk signaling.

Conclusions: These studies show that AHR can block IGF1R mediated proliferation and PI3K/Akt signaling in OFs. AHR also reduces MAPK/Erk signaling driven by cigarette smoke exposure. These data suggest that the AHR pathway is a promising target to attenuate detrimental signaling and tissue remodeling that occurs in TED.

CONTROL ID: 3545615

SUBMITTER (NAME ONLY): Brendan Tamm

TITLE: Estimating Patient Demand for Oculoplastic Surgeons in the United States Using Google Search Trends

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tamm, H. Pakhchanian, D. Belyea, C. Geist, Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University School of Medicine, Morgantown, West Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oculoplastic surgeons who undergo an accredited fellowship have the expertise necessary to manage myriad facial and orbital surgeries. With the aging Baby Boomer population, demand for cosmetic and non-cosmetic eyelid and facial procedures is likely to grow, and patients may use search engines to identify potential oculoplastic surgeons for their healthcare needs. Currently, the United States is facing a severe shortage of oculoplastic surgeons with an unequal distribution across the United States. The regional public demand for ASOPRS-trained oculoplastic surgeons remains unknown and is the topic of this investigation.

Methods: Google Trends was queried for data from 2004-2019 to find the average relative search volume (RSV) for the term “blepharoplasty” in each state. The number of oculoplastic surgeons from each state was acquired through the ASOPRS directory, and then divided by the 2019 Census Bureau population estimates to find the concentration of specialists per capita values. The RSV values were then divided by the per capita values to estimate the demand index of oculoplastic surgeons for each state.

Results: The relative demand index (RDI) was highest in Montana, New Mexico, North Dakota, South Dakota, and Wyoming as these states all have zero ASOPRS oculoplastic surgeons. RDI is lowest in the District of Columbia (5.0), Utah (12.0), and Wisconsin (12.0). The greatest specialist concentration per 10,000 people was in DC (0.0798), Rhode Island (0.0377), and Utah (0.0343), and lowest in Hawaii (0.00706), Louisiana (0.0107), and Idaho (0.0112). The highest search volumes (RSV) were in Hawaii (100) Florida (92), and California (89), and lowest in Vermont (45), Idaho, Iowa, Wisconsin, and Wyoming (all at 50).

Conclusions: The findings highlight which populations may be saturated and which may have a significant unmet need for ASOPRS-trained oculoplastic surgeons and the essential services that they provide. Strikingly, multiple states are without any ASOPRS oculoplastic surgeons and would greatly benefit from their addition to the healthcare community.

CONTROL ID: 3545624

SUBMITTER (NAME ONLY): wim Quint

TITLE: Loss of Gap Junction Delta-2 (GJD2) gene orthologs leads to refractive error in zebrafish

SESSION TITLE: Refractive control: Molecular and Anatomical

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: SNPs close to GJD2, a gene encoding a gap junction protein, have been consistently found to influence the risk of refractive error (RE) and myopia. To functionally investigate the pathophysiological link between GJD2/Cx36 and RE, we evaluated biometrical, optical, and electrophysiological changes in gjd2 deficient zebrafish eyes.

Methods: Here, we studied depletion of two zebrafish GJD2 orthologues, gjd2a (Cx35.5) and gjd2b (Cx35.1). The expression profiles of both genes were assessed by IHC and single-cell RNA-seq. Axial length (AL) was measured by SD-Optical Coherence Tomography (SD-OCT) (n=40) at 1.5-3 months post fertilization (mpf). RE was measured between 1.5-9mpf (n=20). Cataracts were visualized by SD-OCT and differential interference contrast microscopy. A linear mixed model was used to evaluate differences between mutant and WT control fish for AL, RE and lens opacity. Electroretinograms (ERGs) were recorded in 2.5 mpf fish (n=22) and differential B-wave amplitudes analyzed by one-way ANOVA.

Results: Our expression studies showed that both gjd2a (Cx35.5) and gjd2b (Cx35.1) are expressed in the fish retina; only Cx35.1 (gjd2b) is also expressed in the lens.

Depletion of gjd2a led to hyperopia, characterized by decreased AL (~50µm at 1.5-3mpf, P<0.001) and corresponding ascending RE relative to WT (~+2D at 1.5mpf to ~+8D at 9mpf, P<0.001). ERG showed a decreased B-wave amplitude in gjd2a mutants (p<0.001).

We found no alterations in axial length in the gjd2b mutants between 1.5-3mpf. However, we observed a progressive and severe nuclear cataract affecting 100% of the eyes at 6mpf (~28% increase in opacity, p<0.001). The cataract was accompanied by a myopic shift in refractive status (~-5D at 1.5mpf to ~-10D at 9mpf, p<0.001) and late-onset increase in AL (~77µm at 6mpf, P<0.001).

Conclusions: This work in zebrafish showed that both gjd2a (Cx35.5) and gjd2b (Cx35.1) cause changes in refractive status, thereby providing the first evidence for a functional role of GJD2 in refraction. Both mutants showed biometrical and optical alterations, interestingly, in opposite directions. The absence of Cx35.5 led to hyperopia and a significant electrophysiological defect, whereas the absence of Cx35.1 resulted in a severe opacification of the lens and, as a result, a myopic defocus and late-onset axial elongation. We conclude that aberrant electrical gap junction signaling

leads to defective emmetropization.

CONTROL ID: 3545628

SUBMITTER (NAME ONLY): Timothy Tang Lee Say

TITLE: Adalimumab therapy in patients with vision threatening uveitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The aim of this multicentre retrospective study was to review the outcomes of a large group of patients treated with systemic biologic therapy.

Methods: Retrospective chart review of patients with refractory non-infectious active uveitis treated with adalimumab was conducted. The main outcome measures were ability to reduce prednisolone dose, ability to taper immunosuppressives, final visual acuity and time to treatment failure or relapse.

Results: Forty-Six (46) uveitis patients on adalimumab were included in the study. There were 26 (56.5%) male patients and 20 (43.5%) female patients with 43 (93.5%) patients having bilateral active uveitis. The most common anatomical uveitis phenotype was panuveitis (n=17, 37.0%), followed by anterior uveitis (n=12, 26.1%), posterior uveitis (n=10, 21.7%) and intermediate uveitis (n=7, 15.3%). The most common diagnosis of patients on adalimumab was idiopathic uveitis (undifferentiated) (n=19, 41.3%). During follow-up, 35 (76.1%) patients were able to taper and discontinue corticosteroids, while 10 (21.7%) patients were able to taper corticosteroids <7.5mg per day. One (2.2%) patient required a prednisolone dose of 10 mg and one (2.2%) is on a weaning dose of steroids expected to be below 7.5mg/day. The mean visual acuity at the latest follow-up of the worse eye was logMAR 0.42 (SD 0.72), while the mean visual acuity of the better eye was logMAR 0.19 (SD 0.34). Of the 89 eyes, 21 (23.6%) eyes improved by at least 2 lines, 5 eyes (5.6%) deteriorated by 2 or more lines while vision was unchanged in the remaining 6 (70.8%) eyes. The person-years to recurrence was 1 in 12.47 person-years for adalimumab, with a 17.4% (8 patient) relapse rate. In this study, the length of time between diagnosis and commencement of adalimumab was shorter if diagnosed in 2016 or later, compared to diagnosis prior to 2016 (p<0.001). There were no serious adverse events.

Conclusions: This study highlights the importance of commencing adalimumab early in patients with sight threatening or poorly controlled uveitis to maximise visual outcomes, decrease ocular complications, and to reduce prednisolone dosage.

CONTROL ID: 3545630

SUBMITTER (NAME ONLY): Erin Flynn

TITLE: Readability Analysis of Laser Eye Surgery (LASIK) Online Patient Educational Material.

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Geist, Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|R. Raiker, Ophthalmology, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|E. Flynn, H. Pakhchanian, Ophthalmology, The George Washington University School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Laser-Assisted In Situ Keratomileusis (LASIK) is a popular ophthalmic procedure many patients with poor eyesight consider getting. With the easy accessibility of the internet, many patients will use it gain more knowledge about the procedure and determine whether they should get it or not. However, there is scant information on how easy it is for patients to easily understand online patient educational materials (PEM). The goal of this study was to analyze the readability of online PEM on LASIK.

Methods: Using the google search engine, the term "LASIK" was searched, and the top 10 results were picked for analysis. Results that meant for medical professionals and results containing extraneous text not pertinent to the procedure were excluded. The body of text from each website was then analyzed using ten validated tests for readability assessment: Flesch Reading Ease Test (FRE), Flesch-Kincaid Grade Level (FKGL), Simple Measure of Gobbledygook (SMOG), Coleman-Liau Index (CLI), Gunning Fog Index (GFI), New Dale-Chall Readability (NDC), FORCAST, Fry Graph Readability (FG), Raygor Readability Estimate (RRE), and New Fog Count (NFC).

Results: The mean (SD) readability scores were 46 (10.2), 11.2 (2.1), 13.3 (1.6), 11.7 (1.7), 13.5 (2.0), 11.6 (2.5), 11.4 (0.5), 13 (2.7), 12 (2.8), 9.9 (1.9) for FRE, FKGL, SMOG, CLI, GFI, NDC, FORCAST, FG, RRE, and NFC, respectively. All ten of the mean readability scores were well above the fourth to sixth grade reading level as recommended by the National Institute of Health and the American Medical Association for PEM.

Conclusions: These findings demonstrate that the average patient would have difficulty comprehending PEM based on LASIK, thus hindering their ability to make informed decisions on whether they should get the procedure. It's crucial that healthcare workers consider spending more time in designing PEM that's easily understandable as this will lead to better outcomes and improved patient satisfaction.

CONTROL ID: 3545631

SUBMITTER (NAME ONLY): Muhammad Numan Sarfraz

TITLE: Corneal and Pathology Services Interaction – to improve patient's care

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To analyse 10 years data of corneal and conjunctival pathology specimens, from a tertiary eye care corneal service in the UK.

Methods: This retrospective single-centre study was conducted from August 2010 to December 2019, to analyse demographics, characteristics and type of corneal samples sent to the ocular pathology department (Sheffield, UK) as part of the clinical practice at tertiary care hospital in the UK.

Results: 1376 corneal and conjunctival specimens were analysed from 534 patients which includes 324 (60.7%) males with mean age 58.3 (SD 20.3; range 05-103 years); 680 (49.2%) samples were taken from right eye, 1175 (85.3 %) were corneal and 201 (14.7 %) were conjunctival pathology specimens. Patient to sample ratio was 1:2.5 (534/1376) while 345 (64.6%) patients had more than one sample. 905 (65.7%; 99.5% corneal) were corneal/conjunctival impression cytology, followed by 274 (19.9%) corneal tissues and 195 (14.1 %) conjunctival tissue. Most common corneal clinical diagnosis was limbal stem cell deficiency (LSCD; n=569; 41.3%), followed by corneal regrafts (n=71; 5.2%) and Fuchs' endothelial dystrophy (n=64; 4.7%). Most common conjunctival diagnosis was pterygium (n=50; 3.6%), followed by ocular surface neoplasia (n=39; 2.8%) and conjunctival necrosis due to chemical burn (n=13; 0.9%). Maximum number of samples were sent in 2014 (n=224; 16.3%) related to a higher proportion of corneal impression cytology specimens as part of an autologous limbal stem cell transplantation study. Moreover, in most of the cases there was a strong agreement between clinical and pathology diagnosis (n=1214; 88.3%).

Conclusions: In our service there were more samples from males and most of the patients had more than 1 sample. More than two thirds of samples were corneal and mainly taken for impression cytology to assist in the diagnosis of limbal stem cell deficiency and assessment of response to limbal transplant treatment, after chemical burn. Most of the time clinical and pathological diagnosis was in agreement, however, there was disagreement in 162 (11.7%) samples, mainly related to a slight disparity in severity grading of LSCD.

Close collaboration with an ocular pathology service is an integral part of corneal service provision in the UK and must be encouraged. It provides essential diagnostic support to be able to deliver a safe and efficient corneal service to patients.

CONTROL ID: 3545635

SUBMITTER (NAME ONLY): Wun-Ting Li

TITLE: Asynchronous Electrical Stimulation Improves Spatial Resolution with Subretinal Electrodes

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Li, National Tsing Hua University, Hsinchu, TAIWAN|

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ABSTRACT BODY:

Purpose: Electrical stimulation using retinal prosthesis has been a promising strategy for helping patients with retinal degenerative diseases such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD). However, multiple electrodes applying stimulation simultaneously in retinal prosthesis decreases spatial resolution, which is one of the major challenges. In this study, we recorded the spiking response of retinal ganglion cells (RGCs) under two neighboring stimulating electrodes either applying electrical stimulations synchronously or asynchronously to assess the crosstalk effect.

Methods: The retinas dissected from adult C57BL/6J mice were placed onto a microelectrode array (MEA) with the photoreceptor (bottom) side down. Whole-cell current clamp recordings were used to record the spiking responses of RGCs. An anodic-biphasic voltage pulse from 0.1 V to 2.4 V was delivered from one electrode or two neighboring electrodes synchronously or asynchronously.

Results: When the dominated stimulating electrode (under the recorded cell) and the subordinated stimulating electrode (the neighbor electrode) stimulated the RGC synchronously, the threshold voltage required to activate the RGC was lowered comparing to the dominated stimulating electrode alone. In the dominated stimulating electrode leading experiment, the spikes resulting from the subordinated stimulating electrode were significantly less than the one from the subordinated electrode alone. In the subordinated stimulating electrode leading experiment, the spikes resulting from the dominated stimulating electrode decreased as the delay time of the dominated stimulating electrode increased. By separating these recorded RGCs into two groups based on their membrane potential (MP) changes, the cells with hyperpolarized MP had less spiking responses than the cells with depolarized MP after stimulation.

Conclusions: Although both neighboring electrodes stimulating the RGC synchronously can decrease the threshold voltage, nearby cells were also stimulated by the neighboring electrodes, which reducing the spatial resolution . In this study, we demonstrate that two neighboring electrodes stimulated the RGC asynchronously can effectively prevent cells from generating unwanted spikes. Among these RGCs, cells that exhibit long-term hyperpolarization after stimulation were more difficult to generate the second spike by the neighbor electrode.

CONTROL ID: 3545640

SUBMITTER (NAME ONLY): Jialing Fu

TITLE: HSP90 is a dominant heat shock protein and plays an important role in preventing stress-induced apoptosis during cataractogenesis.

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Fu, X. Gong, Z. Shuyu, Y. Wang, L. Wang, Q. Nie, M. hou, J. Xiang, Y. xiao, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: Heat shock proteins play important roles in mediating cellular stress responses and protect the internal milieu against damage. Changes in the expression levels of these proteins are often related to various human diseases. In the present study, we have analyzed different heat shock proteins including HSP90, HSP70, HSP60 and HSP40 in human normal and cataractous lenses of different age groups (from 50 years old to 89 years old).

Methods: Normal human lenses of 50 and 60 years old, and cataractous lenses of different age groups (from 50 years old to 89 years old) were used as material. Mouse lens epithelial cell line, aTN4-1 cells were used to knockdown HSP90 through CRISPR/Cas9 technology. Automated western immunoblotting was used to analyze the changes of different heat shock proteins in normal or cataractous lenses. CellTiter-Glo® luminescent cell viability assay and live/dead assay were used to detect apoptosis. ChIP and EMSA were used to analyze HSF1/HSF4/SP4 control of HSP90 gene expression.

Results: Among the 4 heat shock proteins, HSP90 is the most abundant and HSP40 is the least abundant (about 15-fold less than that of HSP90) in both normal and cataractous lenses. Compared with HSP90, HSP70 and HSP60 are about 8-fold less in both normal and cataract patients. Compared with normal lenses, HSP90 and HSP40 are downregulated in cataractous lenses. In contrast, HSP70 and HSP60 are upregulated from transparent lenses to cataractous lenses. In different age groups of cataractous patients, the levels of HSP90, HSP70 and HSP40 remain relatively stable from 50s to 70s. HSP60 displays significant downregulation from 60s to 70s. From 70s to 80s, HSP70 displays significant downregulation, and HSP60 resumes its level detected in 50s and 60s. In mouse lens epithelial cells, CRISPR/Cas9-mediated knockdown of HSP90 enhances oxidative stress-induced apoptosis.

Conclusions: our results demonstrated that HSP90 is a dominant heat shock protein in the ocular lenses and plays an important role in preventing stress-induced apoptosis and cataractogenesis. (Supported by the grants, #81770910, #81970787, from the NSFC, the grant, 2019B1515120014 from the NSFG and the Fundamental Funds, 3030901010110 of the State Key Laboratory of Ophthalmology of Zhongshan Ophthalmic Center, and the Graduate Scholarship from Sun Yat-sen University).

CONTROL ID: 3545646

SUBMITTER (NAME ONLY): Elisa Peixoto

TITLE: The role of the EPCR pathway in protecting endogenous repair cells in the choriocapillaris

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Peixoto, S. Chambers, S. McKeown, L. Allen, P. Bertelli, R.J. Medina, A. Stitt, School of Medicine, Dentistry and Biomedical Science, Queen's University of Belfast, Belfast, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: A key feature of age-related macular degeneration (AMD) is atrophic pathology in the choriocapillaris (CC). It could be considered that loss of the CC, at least in part, relates to the age-related decline in endogenous vascular repair mechanisms creating hypoxia in the outer retina. We hypothesised that the CC harbours vessel-resident endothelial progenitors which could become senescent and dysfunctional with age and impair normal homeostasis and repair. Recently, the endothelial protein C receptor (EPCR) has been identified as a marker of progenitors known as endothelial colony forming cells (ECFCs). This study aimed to investigate EPCR and its ligand, APC, in ECFCs in the context of the CC.

Methods: Mouse choroidal flatmounts were investigated for presence of EPCR. Western blot, RT-PCR, flow cytometry, 3D-tube formation in matrigel, choroidal explant, immunofluorescence for Lectin/CD31/CD201, b-galactosidase staining, xCelligence system. For multiple comparisons, we used one-way analysis of variance (ANOVA) and paired two tailed t-test analysis. $p \leq 0.05$ were considered significant.

Results: EPCR was present in sub-populations of cells in the murine CC and in choroidal explants. ECFCs senescence lead a significant decrease in the gene and protein expression of EPCR ($p=0.0002$). ECFCs exposed to hypoxia (1% and 5% O_2) showed a marked decrease in the EPCR gene and protein expression when compared to normoxic conditions ($p=0.002$). APC treatment prevented hypoxia-induced decrease in ECFC tubulogenesis and improved barrier function ($p \leq 0.05$). The knockdown of EPCR by siRNA lead a significant reduction in tubulogenesis ($p < 0.0001$), and this was also accompanied by decreased expression of eNOS and CCBN2 ($p < 0.0001$). We also observed an alteration of quiescent markers but not the senescence pathway. Choroidal explants exposed to EPCR siRNA showed a significant decrease of the sprouting in the matrigel and the treatment with APC re-established the vessel growth.

Conclusions: EPCR is present in the CC which may relates to ECFC-like cells resident in these vessels. Regulation of the EPCR-APC pathway impact on progenitor function and could be a potential therapeutic avenue to enhance endogenous repair of the CC, especially in the context of AMD.

CONTROL ID: 3545647

SUBMITTER (NAME ONLY): Hun Lee

TITLE: Efficacy and safety of induced pluripotent stem cell-derived corneal endothelial-like cell transplantation in rabbit animal model of corneal endothelial failure

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Lee, Y. Han, J. Park, S. Han, S. Moon, J. Kim, H. Tchah, Ophthalmology, Asan Medical Center, Songpa-gu, Seoul, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: To evaluate the efficacy and safety of transplantation of the Peripheral blood mononuclear cell (PBMC) induced pluripotent stem cell (iPSC)-derived corneal endothelial-like cells into corneal endothelial failure animal model

Methods: PBMC iPSCs were generated using the iPS Reprogramming Kit with StemPro-34 medium and cultured under standard iPSC culture condition. Differentiation of iPSCs into corneal endothelial-like cells via neural crest cells (NCC) was induced using a conditioned medium in vitro. After 10 days culture of NCC with human endothelium serum free media, the phenotype of iPSC-derived corneal endothelial-like cells was detected by immunofluorescence. Related cell markers of iPSC-derived corneal endothelial-like cells were analyzed by quantitative real-time PCR. The cultured iPSC-derived corneal endothelial-like cells were transplanted into the rabbit anterior chamber by direct cell injection.

Results: After 10 days culture of NCC with human endothelium serum free media, corneal endothelial cell-related markers, including zonula occludens-1 (ZO-1) and Na^+/K^+ ATPase, were expressed in the iPSC-derived corneal endothelial-like cells, showing well preserved hexagonality. The expression of ATP1A1, COL8A1, and AQP1 was higher in the iPSC-derived corneal endothelial-like cells, compared with the NCC and PBMC iPSCs. In animal experiment, increased corneal transparency was achieved after anterior chamber injection of the iPSC-derived corneal endothelial-like cells. PCR from the genomic DNA extract of central cornea which was enucleated 3 weeks after cell injection showed a positive result for human mitochondrial band, whereas negative band noted in the non-treated rabbit.

Conclusions: This preclinical study confirmed the therapeutic ability of the iPSC-derived corneal endothelial-like cells in vivo. Our findings demonstrated that iPSC-derived corneal endothelial-like cells could be a promising source for cell therapy in corneal endothelial dysfunction.

CONTROL ID: 3545648

SUBMITTER (NAME ONLY): Raquel Gil-Cazorla

TITLE: Feasibility of using Soft Contact Lenses as Sampling Vehicle for Dopamine in the Ocular Environment.

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Gil-Cazorla, N. Boychev, N.S. Logan, Optometry, Aston University, College of Health and Life Sciences, Birmingham, UNITED KINGDOM|V. Franklin, Aston University Chemical Engineering and Applied Chemistry, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To determine the feasibility of using soft hydrogel contact lenses as non-invasive sources for dopamine measurements

Methods: This pilot study included 20 patients, age 18-30 years old, with myopia -0.75D to -5.00D. Three different designs of soft hydrogel lenses (single vision spherical and dual focus in Omafilcon A and extended depth of focus in Etafilcon A) lenses were worn for an 8-hour period and then collected, initially in 1ml saline and then dry. The tear envelopes containing the dopamine were extracted and these extracts analysed using a direct competitive chemiluminescent enzyme linked immunosorbent assay (ELISA) dopamine kit (ENZO Life Sciences UK)

Results: Minimal variation was observed between the lens types in terms of the dopamine level recovered for analysis Omafilcon A 442.1 ± 82.7 pg/ml and Etafilcon A 455.1 ± 67.7 pg/ml ($p=0.038$)

Data, as would be expected due to the different sampling methods, is higher than a previously reported study using Schirmer strips and capillaries as shown in Table 1.

The assay method has sufficient sensitivity to detect dopamine in tear fluid (down to the pStep 1: Title/Bodyicogram/ml level as shown in Table 1).

Conclusions: The findings demonstrate that a soft hydrogel contact lens can be used as a non-invasive sampling vehicle to remove the tear envelope and allow dopamine detection from the anterior ocular environment. Different lens types did not adversely affect the recovery rate from the tear envelop.

By combining different sampling methodologies this will enable a greater understanding of the diurnal and longitudinal variation in dopamine levels using both snapshot assessment via Schirmer strip, ophthalmic sponge or capillary tube and non-invasive tear envelop sampling. This will provide insights into the role of dopamine and other neurotransmitters to better understand factors involved in myopia progression.

CONTROL ID: 3545653

SUBMITTER (NAME ONLY): Ricardo Soares

TITLE: Topical Insulin - Utility and results in refractory Neurotrophic Keratopathy in stages 2 and 3

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Soares, C. Arêde, J. Fernandes, C. Ferreira, J. Sequeira, Ophthalmology Department, Centro Hospitalar Vila Nova de Gaia e Espinho, PORTUGAL|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the clinical progression of patients with refractory Neurotrophic Keratopathy (NK) in stages 2 and 3 that were treated with topical insulin

Methods: Retrospective case-series analysis of 20 patients (21 eyes - 13 to 92 years of age) with NK in stages 2 and 3 that were treated with off-label topical insulin from October of 2018 to October 2020. Patients included were refractory to standard medical and/or surgical treatment. Primary outcome of the study was the complete resolution of the persistent epithelial defect or ulcer. The secondary outcomes were improvement of visual acuity and increase in corneal transparency. Patient data including best corrected visual acuity (BCVA), corneal transparency, corneal sensitivity and previous treatments were analysed. Every patient applied topical insulin drops (1 unit /1 mL) 4 times per day, a therapeutic contact lens and prophylactic fluoroquinolone drops. Treatment was continued until NK persistent epithelial defect (PED) or ulcer resolved and then tapered accordingly. Patients discontinued treatment if condition did not improve or worsened within 30 days. Anterior segment photos images were taken on each visit. Data was compared before and after treatment in both groups (NK stage 2 and stage 3) using paired t-test and p-value significance level was set at 0.05.

Results: Nineteen of twenty-one eyes (90%) had complete resolution of NK PED and/or ulcer within 7-45 days of follow-up. Both patients that did not fully respond to treatment had contact lens fitting problems and treatment was stopped although some improvement was noted. A temporary tarsorrhaphy was performed in one of these patients, to no avail. When insulin drops were re-introduced with a tarsorrhaphy in place, full reepithelialisation was achieved. Visual acuity significantly improved after treatment [$p < 0.05$]. However, as expected, higher improvements in BCVA were seen in patients with NK stage 2 when compared to NK stage 3. Corneal transparency also improved in both groups albeit it increased more in NK stage 2 eyes once again. No side-effects were reported during full extent of treatment.

Conclusions: Our results suggest that topical insulin drops could be an effective therapeutic in refractory NK due to its high efficacy, accessibility, low-cost and low morbidity. However, more investigation in this area is warranted.

CONTROL ID: 3545656

SUBMITTER (NAME ONLY): Anna Verschueren

TITLE: What happens during aging: a combined study of the retinal and choroidal anatomy using 3D immunohistochemistry.

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Verschueren, M. Darche, L. Boucherit, M. Paques, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts Centre d'investigation clinique, Paris, Île-de-France, FRANCE|A. Verschueren, M. Darche, L. Boucherit, M. Paques, Institut de la vision, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Aging is associated with various degenerative changes in the retina, including some of the most destructive and widespread ocular pathologies, such as glaucoma or age-related macular degeneration. As neurodegeneration is by nature evolving, distinguishing it from normal aging of the tissue is crucial. 2D histology (eg sectioning of tissues) may miss spatial information, since the manifestation of aging can be focal. Furthermore, the combined investigation of the aging retina and choroid is interesting since these structures are interdependent. Here we chose to use immunohistochemistry and confocal imaging to search for anatomical changes in retinal and choroidal cells across human donor's tissues.

Methods: Five human donors with no registered ocular diseases were analyzed. Peripheral retina and choroid underwent immunohistochemistry allowing investigation of different cell types and the protein expression patterns. As choroid and RPE are highly pigmented tissues, an original depigmentation protocol was developed and performed before immunohistochemistry. Retinal and choroidal samples were then whole-mounted and imaged using a confocal microscope, allowing 3D reconstruction of the cells population and structures of interest.

Results: Observing photoreceptors, we observed a clear degradation of the cellular anatomy and opsin localization with increasing age. Cones and rods presented nuclei displacement towards the RPE and opsin mislocalization toward the IPL, a pattern which was clearly age-dependant. The oldest subjects also presented a high density of Iba1 positive migratory cells (phagocytes).

Ghost capillaries segments (acellular and/or obstructed) were conspicuous in the extreme periphery of the retinal vascular network, shrinking its maximal extension.

RPE cells increased in size, and more RPE cells detached from the Bruchs membrane during tissue preparation. With age, the choriocapillaris density dramatically decreases, cell repartition changes (especially smooth muscle positive cells) and the whole tissue thins.

Conclusions: We are initiating here a systematic study of the manifestations of normal aging of retinal and choroidal tissues using immunohistochemistry. Microglial infiltration in the outer retina, ghosts capillaries, enlargement of RPE cells and modification of the photoreceptor intracellular arrangement were the most striking features.

CONTROL ID: 3545665

SUBMITTER (NAME ONLY): Derek Orshan

TITLE: Correlations Between Pattern Electrophysiology and Estimated Retinal Ganglion Cell Count in Glaucoma Suspects

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|A. Tirsi, S. Park, S.A. Obstbaum, C. Tello, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|A. Tirsi, V. Gliagias, B. Wong, J. Tsai, S. Park, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|P.H. Derr, Diopsys Inc., New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Combined structure-function index (CSFI) which derives retinal ganglion cells (RGC) estimates by combining standard automated perimetry (SAP) and optical coherence tomography (OCT) measurements into an age-adjusted algorithm, has been proven to significantly correlate with histologically derived count. In this prospective cross-sectional study, we investigated the relationship between estimated RGC count and steady state pattern electroretinogram (ssPERG) parameters in glaucoma suspects (GS).

Methods: Ten subjects (60% female, 20 eyes) were enrolled in this study conducted at the Manhattan Eyes, Ears, and Throat Hospital. Subjects were divided into two groups of GS with normal RGC function and GS with RGC dysfunction based upon ssPERG testing results. All study subjects underwent comprehensive ophthalmologic examinations including OCT, SAP and ssPERG. RGC counts were estimated using the CSFI, a statistical model that combines structural [OCT-derived average retinal nerve fiber layer thickness (aRNFLT)] and functional [SAP-derived mean deviation 24-2 (MD)] parameters. The following ssPERG parameters Magnitude (Mag), MagnitudeD (MagD) and MagnitudeD/Magnitude ratio (MagD/Mag ratio) were used in the analysis.

Results: Independent sample t-tests revealed that all ssPERG parameters, estimated RGC count, aRNFLT, and MD were significantly reduced in GS with RGC dysfunction relative to control subjects ($p < 0.015$ for all parameters). A significant reduction in estimated RGC count was found in the GS with RGC dysfunction (752103 ± 97827 vs 1023711 ± 99364) respectively ($p < 0.001$). Pearson and partial (age-adjusted) correlation analyses revealed that all ssPERG parameters significantly correlated with MD ($r > 0.46$, $p < 0.049$). MagD and MagD/Mag ratio significantly correlated with aRNFLT ($r > 0.47$, $p < 0.044$), with average ganglion cell layer and inner plexiform layer (GCL/IPL) thickness ($r > 0.47$, $p < 0.042$). Pearson and partial (age-adjusted) correlation analyses revealed stronger linear relationships between all ssPERG parameters and estimated RGC count ($r > 0.58$, $p \leq 0.009$) than between ssPERG and independent measures of CSFI.

Conclusions: Glaucoma suspects with RGC dysfunction present with decreased estimated RGC count when compared to controls, and ssPERG parameters correlate stronger with the estimated RGC count than with independent measures of CSFI.

CONTROL ID: 3545668

SUBMITTER (NAME ONLY): Ghasem Yazdanpanah

TITLE: Rheological and Proteomics Characterization of Thermoresponsive Hydrogel from Porcine Cornea Extracellular Matrix for Corneal Tissue Engineering Purposes

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Fabricating thermoresponsive hydrogels from decellularized tissues is a trending approach to develop novel therapeutic biomaterials for tissue engineering purposes. There are differences in the characteristics of the produced hydrogel related to the source of the tissue as well as the decellularization and solubilization protocols. Detailed characterization of the hydrogels will support the efforts to optimize their application as biomaterials for tissue engineering and therapeutics. Here, we fabricated an in-situ thermoresponsive hydrogel from decellularized porcine cornea extracellular matrix, COMatrix (COrneal Matrix), and characterized its structure and thermoresponsive rheological behavior (heat-induced Sol-Gel transition) as well as exploring its protein composition using proteomic approaches.

Methods: The COMatrix hydrogel was fabricated by decellularization and partial digestion of porcine cornea. The gelation was induced by mild-heat (37°C). The turbidimetric gelation kinetics was evaluated by pre-warmed spectrophotometer. The rheological gelation kinetics and properties of COMatrix was evaluated with a temperature controlled rheometer. The protein composition of COMatrix was mapped using mass spectrometric proteomics.

Results: COMatrix forms a transparent gel (10 minutes gelation time) after in-situ curing with heat, characterized by alteration in light absorbance and rheological indexes. . The highest elastic shear modulus (G') and highest viscous modulus (G'') for 25 mg/ml hydrogels were 83.3±4.2 Pa and 12.9±7.2 Pa for 25 mg/ml samples. The rheological characterization of heat-formed COMatrix gel shows similar behavior to common biomaterials utilized in tissue engineering. The fibrillar structure of COMatrix gel was observed by scanning electron microscopy as the density of fibers attenuates in lower concentrations. Mass spectrometric proteomic analysis revealed that COMatrix hydrogel is rich in extracellular matrix proteins with known regenerative properties such as lumican, keratocan and laminin in addition to structural collagen proteins.

Conclusions: COMatrix hydrogel is a naturally driven biomaterial with favorable biomechanical properties and protein content with potential application as a therapeutic biomaterial in ocular regeneration and tissue engineering.

CONTROL ID: 3545681

SUBMITTER (NAME ONLY): Ngozi Chidi-Egboka

TITLE: One hour of smartphone use induces ocular discomfort and reduces blinking in children.

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.C. Chidi-Egboka, I. Jalbert, B. Golebiowski, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA]

Commercial Relationships Disclosure (Abstract): Ngozi Chidi-Egboka: Commercial Relationship: Code N (No Commercial Relationship) | Isabelle Jalbert: Commercial Relationship: Code N (No Commercial Relationship) | Blanka Golebiowski: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Smartphone use by children is increasing rapidly, but the ocular impacts are unknown. This study examined the effect of 1 hour of smartphone use on symptoms, tear film and blinking in children.

Methods: Forty-five children aged 6–15 years (mean 10.1 ± 2.6 years; 20M:25F) with healthy eyes and no binocular vision problems completed this prospective study. Children played games on a smartphone continuously for 1 hour and were masked to the study purpose. Symptoms were measured before and after using Symptoms Assessment in Dry Eye (SANDE), Instant Ocular Symptoms Survey (IOSS), Numerical Rating Scale (NRS). Tear film lipid layer thickness (LLT) (LipiView® interferometer.), tear meniscus height (TMH) and non-invasive tear break-up time (NIBUT) (Oculus® Keratograph 5) were assessed at the same timepoints. Spontaneous blink rate (blinks per minute) and interblink interval (time of full eyelid opening, seconds) were assessed in situ, at baseline (during conversation) and throughout the 1 hour of smartphone gaming, using a novel wearable eye tracking headset (Pupil Labs GmbH). Blink rate and interblink interval were compared between baseline and at 10 minutes intervals during smartphone use with repeated measures ANOVA and post hoc comparisons with Dunnett's test and Bonferroni correction. Associations were examined using Pearson correlation.

Results: Ocular surface symptoms increased following 1 hour of smartphone use (SANDE +7.3 units, $p=0.01$; NRS overall +6.6, $p=0.01$; NRS comfort +8.5, $p=0.01$; NRS tiredness +11.2, $p=0.004$; IOSS +1.3, $p<0.001$), but tear film (LLT, TMH, and NIBUT) remained unchanged. Mean group blink rate reduced from 20.7 ± 9.9 blinks/min during conversation to 7.4 ± 5.2 blinks/min within 10 minutes of smartphone use ($p<0.001$), and interblink interval increased (3.1 s vs 8.4 s; $p<0.001$). Blink rate and interblink interval remained unchanged throughout 1 hour of smartphone use. There were no significant associations between changes in blink rate, interblink interval and symptoms.

Conclusions: Blinking in children can be successfully assessed in situ using a wearable eye tracking device. Smartphone use quickly resulted in dry eye symptoms, slowed the blink rate to one-third, with much longer open eye periods between blinks. In the short-term, this was not accompanied by disturbances to the tear film.

CONTROL ID: 3545684

SUBMITTER (NAME ONLY): Sudeep Mehrotra

TITLE:

Time Series Data Analysis of Gene Expression with Age in Mouse Retinal Pigment Epithelium

SESSION TITLE: Retinal diseases: molecular and biochemical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Mehrotra, A.V. Segre, Ocular Genomics Institute, Massachusetts Eye and Ear, Massachusetts, UNITED STATES|S. Mehrotra, G. Gnanaguru, P.A. D'Amore, A.V. Segre, Department of Ophthalmology, Harvard Medical School, Massachusetts, UNITED STATES|G. Gnanaguru, P.A. D'Amore, Schepens Eye Research Institute of Massachusetts Eye and Ear, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related dysfunction and/or death of retinal pigment epithelial (RPE) cells have been associated with various eye diseases, such as age-related macular disorders (AMD). Identifying age-related gene expression changes in the RPE may help shed light on pathogenic mechanisms that affect age-related vision loss or blindness.

Methods: RNA was collected from mouse RPE at 4 different time points of ages: 6 months (M), 12 M, 18 M, and 21 M. Mice, all male and the same genotype background, were kept on identical diet and light exposure regimes. PolyA RNA-Sequencing was performed on three-four mouse RPE replicates per age group. An un-stranded, paired end (PE) library preparation was performed. Samples were multiplexed on the Illumina's sequencer for 75 cycles. An average sequencing coverage of 22.3 million high-quality reads was achieved across all replicates and age groups. The STAR aligner was used to align PE reads and featureCount was used to quantify gene expression. SmartSVA was applied to account for hidden confounding factors on gene expression and normalize between samples. To perform differential gene expression, we used a combination of two programs: ImpulseDE2 and DESeq2. ImpulseDE2 implements an impulse-based model to capture "monotone" and "transient" changes across the time points. The likelihood-ratio test (LRT) implemented in DESeq2 was applied to compare among all four time point combinations. Genes with Benjamini-Hochberg adjusted P-value <0.05 in both methods were considered a set of high confidence genes whose expression changes with age. g:Profiler was used for enrichment of transcription factor (TF) regulation.

Results: There were 352 high confidence genes ($q < 0.05$), whose expression significantly increased (average 5-fold) or decreased (average 8.3-fold) between 6 M to 21 M in mouse RPE. These genes formed five clusters with different patterns of up or downregulation in early and late ages. The 352 genes were enriched for targets of 111 TFs ($q < 0.05$), including ZF5 found to be associated with Stargardt disease and E2F transcription factor 1 (E2F1) associated with AMD.

Conclusions: We present a new methodological process for identifying genes differentially expressed across different time points with RNA-Seq data. In addition, this study identified age-related genes in mouse RPE that can be used to further investigate the role of aging in eye disease.

CONTROL ID: 3545687

SUBMITTER (NAME ONLY): Youngsoo Baek

TITLE: Discriminating between healthy and glaucomatous eyes using a Bayesian macular deviation map

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Baek, S. Berchuck, A.A. Jammal, S. Mukherjee, F.A. Medeiros, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the ability of a novel Bayesian deviation map of macular ganglion cell complex (mGCC) thickness to discriminate between healthy and glaucomatous eyes. Our Bayesian modeling improves glaucoma diagnosis by accounting for the known structural relationship between the macula and the circumpapillary retinal nerve fiber layer (cpRNFL).

Methods: The study included data from 1279 eyes of 393 patients for which mGCC scans were available. The most recent pairs of images for the left and right eye was used per patient for cross-sectional analysis. Macular thickness measurements were analyzed on the 8-by-8 posterior pole grid, while cpRNFL measurements were derived from the 768-point circle scan. A Bayesian linear mixed model was constructed with a novel prior incorporating clinical knowledge of the structural relationship. We compared the Bayesian deviation map to a raw version to assess discrimination between healthy and glaucoma cases. Abnormality was defined as the proportion of negative deviations. Discrimination was measured using both area under the receiver operating characteristic curve (AUC) and partial AUC (pAUC) in the clinically relevant 85-100% specificity range.

Results: Of the 393 pairs of images, 333 were those of glaucoma patients and 60 of healthy ones. The Bayesian model was trained on a random 80% subset, with 20% held out for testing. Five-fold cross validation (CV) was used for more robust assessments. There was a notable improvement in the average pAUC of the Bayesian deviation map (0.49; 95% confidence interval [CI] 0.32-0.75) compared to the raw map (0.44; CI 0.25-0.79). For 95% specificity, average sensitivity of the Bayesian map was .42 (CI 0.30-0.75) versus .32 (CI 0.23-0.78) for the raw map.

Conclusions: A novel Bayesian deviation map incorporating structural relationships between macula and peripapillary RNFL performed significantly better to detect glaucomatous damage in the macula.

CONTROL ID: 3545689

SUBMITTER (NAME ONLY): Huan fen Zhou

TITLE: Serial Analyses of Clinical Spectrums and Outcomes in Chinese Women with Pregnancy-induced Optic Neuritis

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Zhou, S. Wei, Chinese PLA General Hospital, Beijing, Beijing, CHINA|

Commercial Relationships Disclosure (Abstract): Huan fen Zhou: Commercial Relationship: Code N (No Commercial Relationship) | Shihui Wei: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this study was to investigate the clinical spectrums and outcomes in pregnancy-related optic neuritis (ON).

Methods: We analysed the clinical subtype and prognosis of women with pregnancy-related ON during pregnancy or within 1 year postpartum or after abortion in the neuro-ophthalmology department of the First Medical Centre at the Chinese People's Liberation Army General Hospital (PLAGH) from January 2014 to December 2017.

Results: A total of 54 patients, including 21 (38.9%) idiopathic ON (ION), 27 (50.0%) aquaporin-4 (AQP4)-ON and 6 (11.6%) myelin oligodendrocyte glycoprotein (MOG)-ON patients, who experienced 58 informative pregnancies and 67 episodes of pregnancy-related ON were assessed. Among the ON attacks, there were 11 (16.4%) during pregnancy and 56 (83.6%) within 1 year postpartum or after abortion, including 33 (49.3%) in the first trimester. Fourteen (25.9%) patients with ON onset before pregnancy had a higher relapse rate during PP1 than within 1 year before pregnancy ($p=0.021$). Twenty-four (85.7%) eyes with ION and nine (100%) with MOG-ON had significantly better visual outcomes ($p\geq 0.5$) than those with AQP4-ON (14, 35%) ($p<0.001$ and $p<0.001$, respectively). Two AQP4-ON patients respectively had a premature birth and a low baby weight. There were no birth defects or stillbirths.

Conclusions: The study demonstrated that there is a significant increase in ON attacks after delivery especially during the first trimester. MOG-ON had extremely better visual recovery. AQP4-ON was the most common subtype of pregnancy-related ON, which should be given more additional attention about the complications.

CONTROL ID: 3545694

SUBMITTER (NAME ONLY): Kristin Hösel

TITLE: Ocular manifestations and SARS-CoV-2 analysis in tears in patients with COVID-19

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hösel, J. Roider, Ophthalmology, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|C. von der Burchard, Ophthalmology, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|D. Schunk, Internal Medicine, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|J. Franzenburg, Clinical Chemistry, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|D. Frank, Internal Medicine III, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|D. Frank, DZHK, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|R. Junker, Clinical Chemistry, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|T. Bahmer, Clinical Medicine I, Christian-Albrechts-Universität zu Kiel, Kiel, Schleswig-Holstein, GERMANY|

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ABSTRACT BODY:

Purpose: There are only few reports on ocular symptoms and manifestations in association of COVID-19 disease. The objective of this study is to describe ocular manifestation in the anterior and posterior segment of the eye and additionally analyze viral prevalence in tears of patients with COVID-19 disease.

Methods: Hospitalized patients with COVID-19 treated from April 16th to December 15th 2020 at the university hospital in Kiel, Germany, were prospectively screened for ocular manifestations or any abnormalities in anterior and posterior segment. Reverse transcriptase-polymerase chain reactions (RT-PCR) from conjunctival swabs (Schirmer strip method) were analyzed for SARS-CoV-2 in all patients.

Results: 37 (25 male, 12 female) patients were enrolled in this study. 1 out of 37 patients demonstrated conjunctivitis; 6 patients demonstrated chemosis of conjunctiva, all 7 of them were ventilated. One patient who was hospitalized with atypical branch retinal vein occlusion was tested positive for systemic COVID-19 in routine nasopharyngeal screening although completely asymptomatic. He was therefore recruited for the study. His conjunctival swabs were positive in both eyes. Interestingly, this patients showed general symptoms of COVID-19 pneumonia 5 days later and was hospitalized.

All other patients were negative for SARS-CoV-2 in the conjunctival swabs.

In 11 out of 37 patients vascular alterations and potentially disease specific manifestations of fundus were found: retinal hemorrhages in one or both eyes in 5 patients, cotton-wool spots in 5 patients, tortuosity in 5 patients. One patient demonstrated branch artery occlusion, one with branch retinal vein occlusion (the patient mentioned above). In this patient, it is noteworthy that atypically many cotton-wool spots were present, leading to a pizza-like fundus appearance (image 1).

Conclusions: This study suggests that the risk of viral transmission via tears is low. However, the findings might suggest that tears are infectious at an early, preclinical disease stage. Various vascular fundus abnormalities were found in the study including hemorrhages, cotton-wool spots, tortuous vessels and vascular occlusion. Due to the study design, it is unclear whether these were correlated to systemic comorbidities, or whether they were caused or exacerbated by COVID-19. However, given the numerous vascular side-effects of COVID-19 disease, some correlation is thinkable.

CONTROL ID: 3545695

SUBMITTER (NAME ONLY): Daniel Chung

TITLE: Correlations between progression markers in rod-cone dystrophy due to mutations in RHO, PDE6A, or PDE6B.

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.C. Chung, P. VINOT, M. Marussig, L. Thiébault, B. Pom, S. Boissel, SparingVision, FRANCE|C. Andrieu, S. Mohand-Said, I. Audo, J. Sahel, Clinical Investigation Center 1423, CHNO des Quinze-Vingts, INSERM-DGOS, Paris, FRANCE|C. Zeitz, T.D. Leveillard, S. Mohand-Said, I. Audo, J. Sahel, INSERM, CNRS, Institut de la Vision, Sorbonne Université, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: Using accurate and robust markers to evaluate the course of rod-cone dystrophy, also known as Retinitis Pigmentosa (RP), remains pivotal for a better understanding of the disease and for the evaluation of new treatments. Using the data collected in the PHENOROD 1 study (NCT03975543), we analyzed the correlation between structural and functional parameters.

Methods: Data was extracted from 110 medical records (between 2007 and 2019) of patients followed at the National reference center for rare diseases of Quinze-Vingts Hospital (Paris, France). The evidence of mutations in RHO, PDE6A, or PDE6B, at least 2 visits, and no other condition impacting vision than RP were the inclusion criteria for this study. Intra-ocular pressure, best-corrected visual acuity (BCVA), color vision alteration on the panel D-15, static and kinetic visual field, the preservation of the hyper reflective outer retinal bands on spectral-domain optical coherence tomography (SD-OCT), and the size of the ring of increased short-wavelength fundus autofluorescence (SWAF) were analyzed. Correlations between all parameters were evaluated using linear regressions and Pearson correlation coefficient.

Results: The strongest correlation was observed between the SD-OCT and the static Visual Field results. The length of preserved External Limiting Membrane (ELM) was positively correlated on both eyes to the foveal sensitivity at 30° ($r=0.93$). Positive but weaker correlations were also found between the preserved horizontal ellipsoid zone width and the foveal sensitivity at 10° ($r=0.71$). However, BCVA measures were poorly correlated with other functional markers such as static or kinetic visual field (respectively $r=0.37$ and $r=0.53$ for BCVA (LogMAR) vs the kinetic VF diameter using the II1e isopter or the static VF foveal sensitivity at 30°. This weak correlation was also observed when using structural markers from the SD-OCT and SWAF ($r=0.21$ and $r=0.37$ for respectively the correlation of BCVA (LogMAR) / EZ length and BCVA (LogMAR) / horizontal inner diameter of the hyper autofluorescent ring).

Conclusions: Strong correlations were observed between functional and structural parameters evaluated on patients with RP. These results could help defining new composite markers to evaluate the disease severity. They are also of interest when evaluating the efficacy of new therapies for treating patients with a slow disease progression.

CONTROL ID: 3545698

SUBMITTER (NAME ONLY): Aditya Uppuluri

TITLE: Epidemiologic Trends in Consumer Product-Associated Open Globe Injuries in Patients 21 and Over: An Analysis of the National Electronic Injury Surveillance System

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Uppuluri, S. Uppuluri, M.A. Zarbin, N. Bhagat, Department of Ophthalmology and Visual Science, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|P.S. Patel, Robert Wood Johnson University Hospital, New Brunswick, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: The objective of this study is to identify epidemiologic trends in consumer product-related open globe injuries (OGIs) in adult patients over 20 years of age.

Methods: This study utilizes data from the 2000-2019 National Electronic Injury Surveillance System (NEISS), a database created by the United States Consumer Product Safety Commission to collect data on consumer product-related injuries. Cases of open globe injury were identified based on the description of the injury provided in the "narrative" variable and the admission status of the patient. Patients were divided into two age groups: 21-64 years of age and 65+ years of age (elderly). IBM SPSS 23 was used to perform statistical analysis.

Results: Between the years 2000 and 2019, there were 14,880 weighted cases of consumer product-associated OGIs. The average age of patients with OGIs was 52.8 years, 47.7 years in men versus 66.0 in women ($p < 0.001$). Of the injuries, 72.2% occurred in men, and 70.4% occurred in patients between 21 and 64 years of age. Majority (82.9%) of the OGIs in the younger cohort, occurred in men; however, most (53.2%) of the OGIs in the 65+ cohort were noted in women ($p < 0.001$). With respect to day of the week, 30.5% of OGIs in adults over 20 years of age presented to the ED over the weekend. OGIs in the 21-64 cohort mainly involved home workshop equipment (20.2%), sports and recreation (16.2%), and non-nail construction materials (12.8%); in the elderly, OGIs most commonly involved furniture (30.6%), non-nail construction materials (22.4%), and sports and recreation (6.8%). In men, OGIs involved home workshop equipment (20.8%), sports and recreation (16.9%), and non-nail construction equipment (11.9%); by comparison, in women, furniture (26.2%), non-nail construction materials (25.5%), and bathroom fixtures (6.2%) were commonly associated products. In the elderly, 1.9% of OGIs were associated with wheelchairs, and they were all seen in women.

Conclusions: Majority of OGIs in the 21-64 years age cohort were seen in men; however, in the 65+ cohort, most OGIs occurred in women. Home workshop equipment, sports and recreation, and non-nail construction materials were the top 3 consumer product categories that caused OGIs in adults over 20 years of age. Almost 4% of OGIs in elderly women were a result of wheelchair traumatic injury.

CONTROL ID: 3545700

SUBMITTER (NAME ONLY): Qian Nie

TITLE: The E3 Ligase PIAS1 Regulates p53 Sumoylation to Control Stress-Induced Apoptosis of Lens Epithelial Cells through Proapoptotic Regulator Bax

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Nie, H. Chen, L. Wang, M. hou, D.W. Li, Sun Yat-Sen University Zhongshan Ophthalmic Center State Key Laboratory of Ophthalmology, Guangzhou, Guangdong, CHINA|

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ABSTRACT BODY:

Purpose: The protein inhibitor of activated STAT-1 (PIAS1) is one of the well-known SUMOylation E3 ligases and has been shown implicated in different biological processes including control of apoptosis. We previously demonstrated that apoptosis of lens epithelial cells (LECs) induced by stress factors acts as the common cellular basis for non-congenital cataractogenesis. Whether PIAS1 is implicated in the stress-induced lens pathogenesis remains elusive. Here we present evidence to show that PIAS1 is implicated in the stress-induced lens pathogenesis. Mechanistically, PIAS1 controls p53 sumoylation at K386 residue to control stress-induced apoptosis through the proapoptotic regulator Bax.

Methods: Mouse lenses were treated with glucose oxidase (GO) to induce cataract formation. QRT-PCR and western blot were used for analyzing gene expression. Both in vitro mutagenesis and sumoylation as well as Co-IP were used to confirm PIAS1 catalysis of p53 sumoylation. PIAS1 expression construct was generated to establish PIAS1 expression stable line. CRISPR/Cas9 technology was used to silence PIAS1, p53 or Bax expression. CellTiter-Glo® luminescent cell viability assay was used to detect apoptosis.

Results: In the GO-induced cataract model, expression of PIAS1 was significantly downregulated. While overexpression of PIAS1 in mouse LECs accelerates apoptosis, its knockout enhanced viability. Downstream PIAS1, we have identified that members of the Bcl2- family play an important role.

Conclusions: PIAS1 is implicated in stress-induced pathogenesis of the ocular lens. PIAS1 regulates stress-induced apoptosis of lens epithelial cells through control of p53 sumoylation and its downstream target, the proapoptotic target, Bax. (Supported by grants from National Natural Science Foundation of China, 82000876, 81770910, 81970787, 81700821, 81970784, 81900842) and the grant from Guangdong province (2019B1515120014) as well as the Fundamental Funds from the State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University (3030901010110).

CONTROL ID: 3545701

SUBMITTER (NAME ONLY): Sandrine Zweifel

TITLE: Detecting conversion to exudative neovascular age-related macular degeneration using machine learning

SESSION TITLE: AI in the retina: Clinical Applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Zweifel, M. Wiest, K. Fasler, T. Hamann, Department of Ophthalmology, UniversitätsSpital Zurich, Zurich, Zurich, SWITZERLAND|D. Peremot, A. Bondarenko, Rīgas Tehniskā universitāte Datorzinātnes un informācijas tehnoloģijas fakultāte, Rīga, Rīgas pilsēta, LATVIA|A. Mislevics, Department of Artificial Intelligence and Systems Engineering, Rīgas Tehniskā universitāte, Rīga, LATVIA|

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ABSTRACT BODY:

Purpose: Building an expert system for automatic detection of conversion from non-exudative age-related macular degeneration (AMD) to exudative neovascular AMD using optical coherence tomography (OCT) imaging data in a real-world setting.

Methods: 907 AMD patients (40 944 OCT stacks) were labelled as either “early/intermediate”, or “advanced non-neovascular”, or “advanced neovascular non-exudative” or “advanced neovascular exudative AMD” based on their first visit in our database. Eyes exhibiting diseases other than AMD were excluded. All images labelled as “advanced neovascular exudative AMD” were categorized as “post conversion”, the remaining labels were categorized as “pre conversion”. Different inputs (single B-scans, sets of B-scans as separate images, sets of B-scans as 3-dimensional volume) to ML models were evaluated focusing on reliable detection of “post conversion” stage. Special attention was devoted to model performance evaluation, where datasets were split into train and test sets ensuring that distribution of critical attributes is preserved between the sets.

Results: The primary validation dataset comprised of 347'573 B-scans (13 342 OCT stacks) of 304 patients (33.2% male, 66.8% female), with a mean age of 79 years (7.6 SD) at first visit. The mean follow-up time was 3.6 (3.141 SD) years, 12'382 out of 13'342 OCT stacks were labelled as “post conversion”. The model using sets of B-scans as separate images achieved an area-under-curve (AUC) of 0.9138 in differentiating post conversion from pre conversion OCT stacks. 10 465 of 12 382 OCT stacks labelled as post conversion were correctly classified, while 810 of 960 OCT stacks labelled as pre conversion were correctly classified as non-converted (Figure 1).

Conclusions: Our ML model using a clinically heterogeneous OCT data set can effectively detect conversion from non-exudative to exudative neovascular AMD. Considering the limited amount of data, the relatively simple ML model architecture and the time-efficient labelling process, the achieved ML model performance seems very promising. Further training is required to evaluate whether our proposed ML model can achieve even higher performance and will be able to predict the time to/from conversion.

CONTROL ID: 3545704

SUBMITTER (NAME ONLY): Sameh Soliman

TITLE: Ophthalmic involvement in PHACES syndrome: Prevalence, spectrum of anomalies and outcomes

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: PHACES Syndrome includes Posterior fossa malformations, infantile Hemangiomas (95% facial, IFH) with Arterial, Cardiac, Eye and Sternal anomalies. Data on ophthalmic involvement are limited with variable prevalence. We aim to present a large cohort of patients with PHACES highlighting prevalence, spectrum of anomalies and outcomes of ophthalmic involvement.

Methods: A retrospective, non-comparative, single-institutional observational case series was performed. All patients with documented PHACES syndrome diagnosed and managed between 2000-2019 at a single tertiary referral center were reviewed. Data collected included gender, age, diagnostic criteria (Major and minor), IFH distribution, ocular presentation, ophthalmic/visual interventions, follow-up and visual acuity. Primary outcome measures were the frequency and spectrum of ocular involvement. The secondary outcomes were final visual acuity (Poor visual outcome was defined as final visual acuity worse than 20/200), long-term ocular sequelae and need for surgical intervention. Simple descriptive statistics calculating frequencies and mean was utilized.

Results: Forty-three infants [33 females (77%), mean presenting age 8 weeks] were reviewed. Six infants (14%) had primary congenital ocular anomalies. These included diagnostic criteria [optic nerve anomalies (6), anterior segment dysgenesis (1) and retinal vascular anomalies (1)], and non-diagnostic abnormalities [persistent pupillary membrane (2)]. Twenty-nine infants (67%) had secondary ophthalmic involvement due to IFH [ptosis (20 mild, 9 severe), proptosis (9), strabismus (6)]. After mean follow-up 8.7 years post-IFH diagnosis, 8/29 children required surgical intervention [Strabismus (6), entropion (2), ptosis (2), optical iridectomy (1)], all with orbital/conjunctival hemangioma ($p=0.03$). Final visual acuity ranged between 20/20 to 20/80 in 26/29 and $<20/200$ in 3/29 children (all had optic nerve anomalies). One child died from associated cardiac compromise.

Conclusions: Identifying common ophthalmic associations in PHACES syndrome was impactful for both diagnostic and vision rehabilitation purposes. Monitoring for and management of periocular IFH complications showed promising visual acuity outcomes.

CONTROL ID: 3545705

SUBMITTER (NAME ONLY): Thomas Clahsen

TITLE: Genetic variability of lymphangiogenesis in Collaborative Cross mice: a powerful tool to identify novel endogenous regulators of lymphangiogenesis

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Lymphangiogenesis is involved in several diseases like corneal graft rejection, tumor metastasis, and dry eye disease. The healthy cornea is an avascular and alymphatic tissue with a distinct limbal lymphatic vascular arcade. The genetic background significantly influences the architecture of this limbal lymphatic arcade and of corneal lymphangiogenesis. The Collaborative Cross (CC) population is a large panel of recombinant inbred mouse strains derived from a genetically diverse set of eight founder strains.

Methods: Using the lymphatic vessel architecture at the limbal border of the normally avascular cornea, a quantitative trait under strong genetic influence, was used here as a model system to identify new candidate genes regulating lymphangiogenesis. Quantitative trait locus (QTL) analysis was used to combine phenotypic information (e.g. vessel area) and genotypic data (e.g. molecular markers) to reveal possible candidate genes contributing to the observed variation in the analyzed trait. Whole mounts of naïve corneas from 9 different CC mice were stained with the lymphatic vessel marker LYVE-1. The vessel area, number of branching points, endpoints, and sprouts were analyzed using cellF.

Results: The comparison of the different CC strains showed a significant difference in lymph vessel area between the CC mice and the high-lymphangiogenic C57BL/6 mice. We identified CC lines showing significantly lower lymphatic vascularized area, whereas other lines showed significantly higher lymphatic vascularized area compared with C57BL/6 mice. In the QTL analysis, we identified eight loci with a LOD score >5 associated with the morphometric parameters investigated which contain promising genes. For instance, we identified on chromosome 7 two loci, one of them harboring tyrosinase, thus confirming the results from earlier C57BL/6 x BALB/c intercross and validating the approach using CC mouse lines.

Conclusions: Using CC mice we identified several new loci associated with the morphometric parameter that contain promising genes that may play important roles in the regulation of lymphangiogenesis. Overall, our findings show that CC mice are a valid and powerful tool for the identification of new endogenous modulators of lymphangiogenesis. These modulators may serve as novel therapeutic targets for eye diseases associated with pathologic lymphangiogenesis.

CONTROL ID: 3545712

SUBMITTER (NAME ONLY): Ana Roldan

TITLE: Implementation of the Glaucoma Computerized Adaptive Testing System (GlauCAT) to measure the quality of life (QoL) among glaucoma patients in a tertiary eye care setting

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study aims to assess: (a) the feasibility of GlauCAT in a busy glaucoma clinic; and (b) the correlation of patients' responses on five QoL domains with the severity of glaucoma.

Methods: We conducted a cross-sectional study of 138 English-speaking adults aged ≥ 18 years attending a tertiary eye center glaucoma clinic. Patients with a history of intraocular surgery 90 days before enrollment and/or with cognitive impairment were excluded. GlauCAT, a tablet-based survey, uses item banks and CAT methods to measure the impact of glaucoma and its treatments on five QoL domains listed in Table 1. The domain scores ranged between 1-100, with higher scores representing better QoL outcomes. Feasibility was assessed using a 4-point satisfaction survey and the percentage of patients who completed GlauCAT without assistance. Differences in scores between glaucoma severity groups were assessed using the Kruskal-Wallis test.

Results: 69.6% of patients who completed GlauCAT did so without assistance. The satisfaction survey score had a mean of 3.49 ± 0.53 ; no statistically significant difference in mean scores was found between the severity groups ($p=0.8$). The mobility domain score was higher, with a mean of 93.3 ± 8.6 , in the glaucoma suspect group compared to 91.7 ± 11.9 in the early glaucoma group and 79.5 ± 27.1 in the moderate-severe group ($p=0.001$). The same trend was observed in the concerns domain; the moderate-severe glaucoma group had a significantly lower mean score of 69.8 ± 19.8 , followed by the early glaucoma group with 81.1 ± 14.5 and the glaucoma suspects group with a mean of 86.3 ± 8.9 ($p=0.001$). There was also a significant difference in activity limitation scores by severity group, with higher scores in the glaucoma suspect group (mean 87.0 ± 15.3) than in the moderate-severe glaucoma group (mean 72.8 ± 25.1 , $p=0.003$). The ocular comfort and emotional well-being domains were not statistically significantly different between the three groups of glaucoma severity ($p=0.776$ and $p=0.149$, respectively).

Conclusions: Patients with more severe disease reported greater limitations. GlauCAT is a promising tool for assessing and monitoring glaucoma patients' QoL, as it can be self-administered with high patient satisfaction.

CONTROL ID: 3545715

SUBMITTER (NAME ONLY): Catherine Agathos

TITLE: Visual search performance across adulthood and in individuals with AMD

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Visual cancellation tasks evaluate how individuals identify relevant information among clutter. This work examined how visual search is affected by healthy aging and AMD in the Bells test cancellation task.

Methods: 98 participants from the SilverSight French cohort were included in this study: 43 young adults (YA, 30 ± 4.8 years), 12 middle-aged adults (MA, 51.2 ± 5.9 y), 36 older adults (OA, 74.4 ± 4.4 y), and 7 individuals with AMD (78.6 ± 7.8 y). Participants had to find and cancel 35 bell symbols among 280 distractors while wearing a mobile eye-tracker. We examined the number of cancellations, test duration, the time and distance between cancellations, search efficiency (Q-score) and organization (Best-R). Fixation number, duration and dispersion, inter-fixation duration and distance as well as scan-path metrics were extracted from gaze data. All save the AMD group underwent a visuo-cognitive screening, including UFOV, TMT, figural and working memory tests.

Results: OA made fewer cancellations than YA and were less efficient than both YA and MA groups (lower Q-score). Successive cancellations of OA were further apart in both time and space, compared to YA. OA were also slower than YA to complete the test and more variable than YA in both inter-cancellation time and distance. OA made more fixations and showed longer scan-path lengths, compared to YA. All healthy participants showed similar search orders (Best-R values), fixation duration and dispersion, inter-fixation time and distance, and % of the scene covered during the search. Search efficiency and test duration correlated significantly with selective visual attention (UFOV 3), processing speed (TMT part A), figural memory, and working memory span.

AMD patients had lower performance, compared to age-matched visually healthy subjects, on the cancellation task on all metrics, and they showed larger inter-individual variability. They made longer fixations with greater dispersion amplitudes and fewer fixations in total. Fixations were further apart in both time and space, linked to jumping between PRLs depending on gaze direction.

Conclusions: Visual search degrades with age, in association with attention, processing speed, and memory decline. The deficits in search found in AMD patients are the result of visual system losses overlaid on the normal age-related loss caused by cognitive/attention decline.

CONTROL ID: 3545718

SUBMITTER (NAME ONLY): Ravin Sajnani

TITLE: Comparison of outcomes and complications between navigated laser (NAVILAS) and pattern scanning laser (PASCAL) systems used in the management of treatment-naïve proliferative diabetic retinopathy (PDR).

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sajnani, A. Oh, P. Prasad, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|K. Chen, Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pan-retinal photocoagulation (PRP) is an effective treatment to prevent severe vision loss in PDR. NAVILAS and PASCAL are newer laser delivery systems that can more efficiently deliver PRP, but little is known about how these two systems compare in post-treatment sequelae. The aim of this study was to evaluate the differences in visual outcomes and complications between the NAVILAS and PASCAL systems used in PDR treatment.

Methods: We completed a retrospective study comparing 30 laser-naïve eyes (24 patients) treated with NAVILAS compared to 14 eyes (13 patients) treated with PASCAL. Exclusion criteria included receiving an anti-VEGF (anti-vascular endothelial growth factor) injection in the 3 months preceding laser treatment, concomitant vitreous hemorrhage (VH) at the time of treatment, having already been planned for surgery by the laser treatment date, and any pre-existing retinal vascular pathology (i.e. central retinal artery/vein occlusion). Best-corrected visual acuity (BCVA) and intraocular pressure were measured on the date of initial PRP and at 6-9 months. The number of additional laser treatments (PRP fill), anti-VEGF injections, episodes of VH, and surgeries within a year of initial laser treatment were compared between the two groups.

Results: Age, pre-treatment visual acuity, and glycated hemoglobin (HbA1c) were similar between the groups. Both groups had a similar change in BCVA at 6-9 months (logMAR $+0.12 \pm 0.33$ standard deviation in the NAVILAS group vs $+0.27 \pm 0.64$ in the PASCAL group; $p=0.73$). There was a similar need for PRP fill (NAVILAS 43% vs PASCAL 50%; $p=0.68$) and anti-VEGF injections (47% vs 50%; $p=0.52$). Both groups had a similar incidence of VH (30% vs 21%; $p=0.72$) and development of neovascular glaucoma (3% vs 7%; $p=0.54$). Rates of subsequent surgery were also similar between groups (27% vs 29%; $p=1.00$).

Conclusions: Treatment of PDR with PRP by either NAVILAS or PASCAL delivery systems appears to yield similar visual and complication outcomes by one year.

CONTROL ID: 3545719

SUBMITTER (NAME ONLY): Katelyn Swindle-Reilly

TITLE: Injectable Alginate Hydrogels for Traumatic Optic Neuropathy

SESSION TITLE: Optic Neuropathies - Pathophysiology and Therapies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Traumatic optic neuropathy (TON) is a common, untreatable injury resulting in blindness. Prior candidate treatments for TON do not address secondary injury mechanisms, namely the generation of reactive oxygen species (ROS). We hypothesize that by addressing these secondary mechanisms via an injectable drug delivery vehicle loaded with a ROS scavenger, methylene blue (MB), greater neuronal cell survivability can be achieved.

Methods: Alginate hydrogels were synthesized at various polymer and crosslinker concentrations using design of experiments. Hydrogels were formed by internal crosslinking with insoluble calcium carbonate and proton donor, D-glucono-lactone. Viscoelastic properties of hydrogels were characterized using dynamic shear rheology. The cytotoxicity and ROS scavenging ability of the hydrogels loaded with MB concentrations of 0.0, 0.05, 0.25, 0.50, 1.0, and 2.0 g/L were analyzed through MTS and DCF assays, respectively, on ARPE-19 cells. A two tailed student t-test was used for statistical analysis.

Results: By varying components of the gels, a significant influence on complex shear modulus and gelation time were observed. Lower concentration (alginate and crosslinker) hydrogels corresponded to lower complex shear modulus whereas higher concentration hydrogels had higher complex shear modulus. Hydrogel swelling and MB release were analyzed. Hydrogels with low alginate concentrations had the most cumulative MB release (~90%); however, no hydrogel completely released all MB within the 12-day in vitro study, due to hydrogel degradation. Two formulations demonstrated excellent cell viability at >95% following 24 hr exposure compared to DPBS control. ROS studies showcased MB as an effective scavenger at concentrations 0.50 g/L and above in which cell viability was maintained ~50% following exposure to 600 μM H_2O_2 . The presence of MB was also found to significantly increase cell survival in the presence of oxidative stress when loaded into low and high concentration hydrogels ($p < 0.01$).

Conclusions: Our results are consistent with our hypothesis that by inhibiting ROS induced damage, higher cell survivability can be achieved. The proposed drug delivery system has the potential to improve upon the limited treatment options for TON. Given the in vitro drug release and biocompatibility results, these hydrogels have potential to deliver MB to protect against ROS. Future work will include long-term and in vivo validation studies.

CONTROL ID: 3545720

SUBMITTER (NAME ONLY): Christina Eckmann-Hansen

TITLE: Retinal microcystoid lacunae in autosomal dominant optic atrophy: relation to visual function

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the prevalence of microcystoid lacunae in patients with autosomal dominant optic atrophy (ADOA) and their relation to visual function and retinal thickness.

Methods: The study included 159 participants with verified ADOA, with a mean age of 44.35 (SD 19.9, range 7-86) years. Study participants with mutation in the OPA1 gene were assessed for best-corrected visual acuity (BCVA, in ETDRS letters), contrast sensitivity (in logCS), optical coherence tomography (Spectralis, Heidelberg) and adaptive optics fundus photography (RTX-1, Imagine Eyes). Data were analyzed with a mixed model adjusted for age and sex with family and eye as random effects using RStudio statistical software. Optically empty microcystoid spaces in the ganglion cell layer and inner plexiform layer, presumably lacunae left by degenerated ganglion cells, were mapped by inspection of the two sets of images.

Results: 34 patients (21 %) including 19 males and 15 females had microcystoid lacunae, and 125 including 64 males and 61 females did not have microcystoid lacunae. The genotype distribution of the patients with microcystoid lacunae was 16 with c.2826_2836delinsGGATGCTCCA, 4 with c.983A>G, 4 with 2496+4_2496+5delinsGTAAC, 4 with 2614-9A>, 2 with c.1516+5G>A, 2 with c.2708_2711delTTAG, 1 with c.(32+1_33-1)_(678+1_679-1)delG and 1 with c.2707+1G>C.

Patients with and without microcystoid lacunae had a BCVA of 66.2 and 70.0 ETDRS letters (difference -3.82, 95%CI -11.6;4.0, P=0.6), a contrast sensitivity of 1.555 and 1.561 logCS (difference -0.006 (95%CI -0.11;0.10, P=0.9), a nerve fiber layer volume of 0.53 and 0.58 mm³ (difference -0.05, 95%CI -0.10;-0.002, P=0.04) and a ganglion cell layer volume of 0.75 and 0.78 mm³ (difference -0.03 ,95%CI -0.09;0.02, P=0.3), respectively.

Statistical analysis showed moderately reduced visual acuity in patients with microcystoid lacunae. Normal and near-normal visual function was seen only in participants without microcystoid lacunae, who nevertheless were found at all levels of visual function, including severely decreased visual function.

Conclusions: In ADOA, microcystoid lacunae was found in 21% of the study participants, and tended to be found in patients with moderate visual acuity reduction, suggesting that cavities left by dead ganglion cells disappear with decreasing visual function.

CONTROL ID: 3545722

SUBMITTER (NAME ONLY): Jaehyun Jung

TITLE: Apparent viewpoint of shifted view through prisms

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Jung, E. Peli, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Jung, E. Peli, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Field of view (FoV) through prisms (shifted view) brings the view from the blind field into the residual seeing field. This “shift” has been illustrated in the literature as a lateral shift on a flat screen orthogonal to the primary position of gaze. It is not a linear shift in the distance domain but should be interpreted as an angular shift (a rotation of the viewpoint). The apparent viewpoint of the shifted view through the prisms may be located outside of the eye. To understand the viewpoint changes in the shifted view and further investigate the impact on detection, we analyzed and demonstrated the apparent viewpoint of the shifted view.

Methods: We modeled peripheral 57Δ Fresnel (30° power and FoV) and our 100Δ distortion-free multi-periscopic prisms (MPPs; 45° power and FoV) as prescribed for homonymous hemianopia (HH). Rays originating from the eye and deflected through the prisms were traced and extended back by optical ray-tracing simulation (LightTools), which formed an apparent viewpoint. To verify the viewpoint changes, the scene through the prism and the scene without the prism were photographically captured by the camera at the location of the eye and the apparent viewpoint, respectively.

Results: The apparent viewpoint of the shifted view was formed outside of the eye (not only rotated but also translated from the eye). While the apparent viewpoint of the shifted view through 57Δ Fresnel prisms was slightly diverged due to prism distortion, MPP provides a focused apparent shifted viewpoint. The rotation of the viewpoint (toward the prism base) was the same as the nominal prism power. The translation was close to the width of the prism when the prism power and the angular span of the prism are the same (the preferred fitting for HH). The photographic depictions of the shifted view through MPP and the scene without MPP at the translated and rotated camera confirmed the same scene and perspective. However, the scene through the Fresnel prism was further distorted and thus different from the scene captured at the apparent viewpoint.

Conclusions: We demonstrated that the shifted view through the prism is the same as the scene observed by the rotated eye with slight head translation. However, the prism distortion (stronger in higher power refractive prisms) further deteriorates the viewpoint changes.

CONTROL ID: 3545724

SUBMITTER (NAME ONLY): Jessica Yuen Wuen Ma

TITLE: Phagocytic function is reduced in the mouse retinal pigmented epithelium with age

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a leading cause of irreversible vision loss in the elderly. A reduction in RPE phagocytosis of the photoreceptor outer segments (POS) has been implicated in the formation of waste deposits observed in the fundus of patients with AMD and in aging. The aim of this study was to investigate how the phagocytic function of the RPE changes with age using the mouse as a model.

Methods: Using immunohistochemistry and super resolution microscopy, phagocytosis of POS was investigated in murine RPE whole mounts from young (3 months, n=3) and old mice (20-21 months, n=3), which were stained using ZO1 as an RPE marker, rhodopsin for engulfed POS, and cathepsin D for lysosomes. The area of RPE cells, number of nuclei and, number of phagosomes in the basal and apical RPE were quantified in central, mid-peripheral and peripheral eccentricities. Gene expression changes in the RPE phagocytosis pathways were investigated using isolated RPE/choroid from 3 (n=6) and 24 months old (n=6) mice using RNASeq.

Results: With age, the RPE cell size in the periphery increased significantly. The number of cell nuclei decreased with eccentricity, however, there was no effect of age. The amount of rhodopsin-positive phagosomes per RPE cell area increased at all eccentricities with age and it was associated with an increase in phagosome number in the basal RPE cells but not the apical RPE. However, the proportion of phagolysosomes did not change suggesting undigested POS accumulate in the RPE with age. The expression of genes important for phagocytosis during initiation and engulfment such as MERTK and TYRO3 were significantly downregulated (FDR<0.05). Meanwhile, mRNA expression of PLXNB1 and SEMA4D that are involved in the termination of phagocytosis were upregulated significantly (FDR<0.05).

Conclusions: Overall, the results of this study suggest a decline of phagocytotic function in the aging murine RPE. More work is required to determine whether the aging changes observed in this study exacerbate pathology in those predisposed to AMD.

CONTROL ID: 3545725

SUBMITTER (NAME ONLY): Nishant Sinha

TITLE: Collagen Expression in mini Ossabaw pigs Cornea with Type II Diabetes

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.R. Sinha, Biomedical Sciences, University of Missouri, Columbia, Missouri, UNITED STATES|A.C. Hofmann, P. Balne, R.R. Mohan, S.S. Chaurasia, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes mellitus (DM) is the leading cause of legal blindness in working age adults worldwide. Diabetic retinopathy has a major impact on vision; thus, it is extensively studied and the primary concern for physicians. However, diabetic patients appear to have more frequent corneal problems compared to non-diabetic patients. Currently, 18% of corneal transplants in the United States come from diabetic donors. We reported young Ossabaw pigs fed a western diet show signs of early diabetic retinopathy.

Methods: Ossabaw pigs have metabolic syndrome and type II diabetes mellitus making them the closest model to study human type II diabetes. In this study, we identify collagen changes in corneal stroma caused by type II DM. Corneal tissue collected from 6 month old Ossabaw mini pigs fed a western diet with high fat/high fructose corn syrup/high choleric content for 10 weeks were used to prepare mRNA for qPCR, and 8 um cryosections for IHC, H and E, and mason trichome stains. Collagen measuring parameters include collagen I (COL I), Collagen III (COL III), and total collagen.

Results: We found altered levels of Col I and II in pigs on western diet compared to regular diet. Masson's Trichome stain showed increased levels of collagen in diabetic corneas compared to healthy age-matched corneas.

Conclusions: Diabetic Ossabaw pig demonstrated notably altered expression of structural parameters suggesting the vulnerability of the corneal tissue to diabetic conditions.

CONTROL ID: 3545726

SUBMITTER (NAME ONLY): Aleksandra Sedova

TITLE: Reconstruction of apical processes (AP) originating from human retinal pigment epithelium (RPE) cell bodies by 3D connectomics technology

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To determine for the first time the number, dimensions, branching points, and signal generating organelle contents of apical processes (AP) of human RPE cells using 3D connectomics technology; these membrane specializations function in photoreceptor phagocytosis (PMID 16301) and retinoid processing (PMID 15336505).

Methods: A whole globe of a 21-year-old male Caucasian organ donor with an unremarkable macula was processed via rapid organ recovery. Perifoveal epoxy-embedded RPE was imaged by serial block-face scanning electron microscopy. In our ongoing study the image stack is annotated manually with computer assistance by expert readers using TrakEM (ImageJ).

Results: The 3D dataset displayed complete ultrastructural preservation with fully attached neurosensory retina and allowed the reconstruction of RPE cells. Our initial results from this tissue sample indicate 313 APs originating from the apical part of one RPE cell body and extending into the interphotoreceptor matrix. These interact with outer segments of 38 rod photoreceptors (cones were not accessible). 57% of APs show branching with 21% having one branch, 13% two branches, 8% three branches and 14% four branches or more resulting in a total of 814 endtips of APs. The mean length of a single AP branch was 1694 ± 1558 (standard deviation) nm. APs without branching showed a mean length of 1423 ± 1237 nm from start to endtips. The diameter of an apical process ranged from 135 to 615 nm. APs of one single RPE cell contained 67 melanosomes and 3 lipofuscin granules, which is in range of previously published data by our group.

Conclusions: Our 3D connectomics approach revealed that hundreds of APs derive from the apical part of a single RPE cell body, ensheath photoreceptors and contain the majority of RPE cell melanosomes; the latter are known contributors to OCT reflectivity via Mie scattering.

Results will impact interpretation of clinical OCT images. They will also help elucidate an ultrastructural basis of how rod-mediated dark adaptation is modulated. This functional biomarker for incident age-related macular degeneration localizes to the photoreceptor-RPE-choriocapillary interface (PMID 33344065).

CONTROL ID: 3545727

SUBMITTER (NAME ONLY): Jacque Duncan

TITLE: Adaptive optics scanning laser ophthalmoscopy (AOSLO) measures in USH2A-related retinal degeneration

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although USH2A-related retinal degeneration is among the most common forms of Usher syndrome type 2 (USH2) and autosomal recessive retinitis pigmentosa (ARRP), prior studies have not described cone structure with high-resolution images. Adaptive Optics Scanning Laser Ophthalmoscopy (AOSLO) is a non-invasive method of visualizing cone photoreceptors with high resolution. We describe baseline cone spacing and explore inter-grader and inter-test variability using data collected in a multicenter, international natural history study of USH2A-related retinal degeneration.

Methods: Two baseline AOSLO montages of the cone mosaic were obtained from each of 14 participants (6 USH2, 8 ARRP; 4 female; 11 white) with USH2A-related retinal degeneration. Two graders masked to disease category measured cone spacing, cone density and an image quality score; poor quality images were confirmed not gradable by a masked clinician. Cone spacing measures were converted to Z-scores based on 37 normal subjects. Inter-test and inter-grader variability were evaluated using intraclass coefficient (ICC) and Bland-Altman plots. Association between cone spacing and clinical characteristics were assessed by linear mixed effects regression.

Results: Median age of participants at enrollment was 38 years (range: 20-59). Median disease duration was 14 years (interquartile range, IQR: 11-19) in USH2 and 6 years (IQR: 4-14) in ARRP participants. Cone spacing ranged from 0.78-2.44 arc minutes. Cone spacing was associated with eccentricity ($P < 0.001$), but no significant difference was observed by clinical diagnosis or disease duration. Bland-Altman plots showed high concordance between

baseline 1 and baseline 2 (mean differences near 0, ICC = 0.71). Grader 2 reported slightly lower values than grader 1 (ICC=0.7). Quality score was higher in baseline 1 than baseline 2 ($P = 0.02$). Greater inter-grader variation was found in regions with poor image quality ($P < 0.001$).

Conclusions: The baseline AOSLO data revealed similar cone spacing between USH2 and ARRP participants. Image quality was significantly lower for the second baseline montage, suggesting one baseline image is sufficient. Adding a qualitative image quality score can be a useful approach to handle inter-grader inconsistencies while minimizing the loss of data.

CONTROL ID: 3545729

SUBMITTER (NAME ONLY): Guoge Han

TITLE: Medium Chain Acylcarnitine Abnormalities Implicate Mitochondrial Dysfunction in Laser-induced Choroidal Neovascularization (CNV) in Brown Norway Rats

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Han, P. Wei, Ophthalmology, Tianjin Eye Hospital, Tianjin, Tianjin, CHINA|

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ABSTRACT BODY:

Purpose: Acylcarnitine Abnormalities are implicated in the plasma of age-related macular degeneration (AMD) patients, but the mechanism by which peripheral blood lipid dysfunction affecting retinal metabolism remains unclear. We determined whether different forms of acylcarnitine (from C0-C18) concentrations in the retina, which reflecting lipid and mitochondrial metabolism, differed between control and Laser-induced CNV in BN rats.

Methods: Laser-induced choroidal NV (CNV) in rats was examined by fundus fluorescein angiography and permeability assay using Evans blue as tracer. Confirmation of key acylcarnitine identities was conducted using high mass accuracy liquid chromatography-tandem mass spectrometry. Medium chain acyl coenzyme A dehydrogenase (MCAD) was also measured using Western blotting and its enzyme activity was determined by MCAD Activity Assay Kit.

Results: Thirty-two metabolites related to acylcarnitine metabolism were identified in blood and retina from CNV and controls. After multivariable adjustment, C2-carnitine levels were significantly lower in blood of CNV rats compared to controls (0.51 ± 0.02 (standard error) compared to (1.10 ± 0.10) , $p = 0.01$). Decanoyl-carnitine levels were significantly higher in CNV compared to controls (2.84 ± 0.15 compared to 1.01 ± 0.05), $p = 0.01$). Other forms of acylcarnitines examined were not significantly different between cases and controls. Alteration of MCAD expression and activity were evident in the retina of laser induced CNV model.

Conclusions: Increased levels of C10 carnitine were observed in the retina of Laser-induced CNV rats model compared to controls. These changes may be attributed to dysregulated mitochondrial metabolism, reprogrammed lipid metabolism and impaired MCAD activity in the CNV eye. Our findings provide biochemical insights into the mechanisms of age-related ocular changes.

CONTROL ID: 3545736

SUBMITTER (NAME ONLY): Lauren Hennein

TITLE: Impact of a Vision Screening and Spectacle Correction Program on Educational Development in Preschoolers from Low-Income Communities

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Hennein, C. Lees, A. Nakayoshi, A.G. de Alba Campomanes, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate educational development in low-income preschoolers who failed vision screening and were prescribed glasses compared to those who passed vision screening.

Methods: This prospective cohort evaluated the difference in a variety of developmental domains through the Desired Results Developmental Profile (DRDP) between low-income preschoolers who failed vision screening and were prescribed spectacle (study group) compared to those who passed (control group) in San Francisco, Alameda and San Mateo County during the 2017 to 2018 academic year. The difference in the domains between the two groups were calculated with a t-test at Fall 2017 (baseline), Winter 2018 and Spring 2018. The difference in the mean change in domain scores between the two groups were calculated from Fall 2017 (baseline) to the end of the academic year (Spring 2018).

Results: Twelve thousand and seven preschoolers were included (n=107 in the study group and n=1100 in the control group). The mean age was 50.2 months (range 34.8 to 66.5 months). One-hundred and ninety children failed vision screening with a true-positive rate of 56.3% (107/190). The mean baseline scores in all eight domains was lower in the study group compared to the control group by a range of 0.9 to 24.9 points; this difference was statistically significantly lower in the "History – Social Sciences (HSS)" (24.9 points; p=0.038) and "Visual and Performing Arts (VPA)" (24.17 points; p=0.039) domains. The mean scores were not significantly different at the Winter 2018 and Spring 2018 timepoints between the two groups. The difference in the mean change in domain scores from Fall 2017 to Spring 2018 between the two groups was higher in the study group in five of the eight domains (range -4.66 to 10.1 points), however this was not statistically significant.

Conclusions: Low-income preschoolers who were prescribed glasses performed worse in all eight categories of development assessments at the start of the academic year, with a significant difference in HSS and VPA. There were no significant differences in scores between the two groups at the mid- and end of the academic year and the study group experienced a larger increase in scores for the majority of domains over the course of the academic year. This suggests that glasses may assist low-income preschoolers in catching up in their educational development assessments.

CONTROL ID: 3545742

SUBMITTER (NAME ONLY): Muhammad Shirazi

TITLE: Multi-modal and multi-scale retinal imaging with angiography

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.F. Shirazi, M. Pircher, Center for Medical Physics and Biomedical Engineering, Medizinische Universitat Wien, Vienna, Wien, AUSTRIA|J. Andilla, M. Cunqueiro, P. Loza-Alvarez, ICFO-The Institute of Photonic Sciences, SPAIN|D. Andrade De Jesus, L. Brea, S. Klein, T. Walsum, Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|K. Grieve, M. Paques, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, FRANCE|M.W. Torm, M. Larsen, Rigshospitalet, Kobenhavn, DENMARK|N. Lefaudeux, X. Levecq, N. Chateau, Imagine Eyes, FRANCE|

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ABSTRACT BODY:

Purpose: To demonstrate the results of a compact multi-modal and multi-scale retinal imaging instrument with angiographic functional extension and to explore its imaging performance.

Methods: The system has two imaging modes that are operated simultaneously: scanning laser ophthalmoscopy (SLO) and optical coherence tomography (OCT). The field of view of both imaging modes can be changed between a standard large field-of-view mode and a high-resolution small field-of-view mode for cellular resolution imaging using adaptive optics (AO) correction of ocular aberrations. The SLO is operated at a central wavelength of 790 nm and records images at 13 Hz. The swept-source OCT is operated at 1060 nm with an A-scan rate of 200 kHz, which translates to a B-scan rate of 200 Hz. The AO correction is operated in closed loop at 10 Hz. Further, OCT angiography in large and small field-of-view modes can be achieved by acquiring 4 B-scans per position. An intensity based angiographic evaluation is used for the visualization of vessel networks. The dimensions of the entire instrument are 490 mm x 500 mm x 500 mm, including motorized translation stages that enable 3D tracking of the pupil position.

Results: Images recorded in healthy volunteers with the large field-of-view mode (40 deg x 30 deg) show comparable quality as obtained with commercial systems. The attached figure shows representative images recorded with the instrument. The axial and lateral resolution is 7 μ m and 4.4 μ m respectively in AOOCT, while the lateral resolution is 3.3 μ m in AOSLO. Images recorded with the high resolution AO-SLO mode show individual cone photoreceptors at half-degree from fovea and beyond. The high resolution of the OCT allows tomographic and en-face views of individual photoreceptors, discrimination between cone and rod end tip layers, and visualization of the Henle fiber layer border. The angiographic evaluation shows the vessel network and choriocapillaris in both large and small fields of view.

Conclusions: The combination of OCT and AO improves the lateral resolution, thereby enhancing the visualization of individual photoreceptors. The application of OCT angiography further enhances the appearance of the capillaries, e.g. their thickness in the en-face AOOCTA images. This multi-modal and multi-scale approach allows for a rapid identification of regions of interest in the large field-of-view mode and for a more detailed analysis in the high-resolution mode.

CONTROL ID: 3545746

SUBMITTER (NAME ONLY): Natalie Hudson

TITLE: Regulation of inner blood retina barrier integrity induces a geographic atrophy-like phenotype in animal models

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Hudson, E. Ozaki, A. Reddy, K. Byrne, S. Doyle, M. Campbell, The University of Dublin Trinity College, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Recently, we have developed a novel approach to elucidate the early initiating factors that may underlie the pathology of dry age-related macular degeneration (AMD), and specifically its end-stage Geographic Atrophy (GA). Suppression of claudin-5 levels, the most highly enriched tight junction protein at the inner blood-retinal barrier (iBRB), leads to retinal pigment epithelium (RPE)-like atrophy. Here, we sought to characterise novel animal models that allow us to assess the effect of claudin-5 levels on RPE due to varying claudin-5 expression levels in greater detail to identify the kinetics of damage observed and the downstream effectors that lead to RPE atrophy.

Methods: We have compared three novel animal models 1) RNAi based inducible claudin-5 knockdown mice, 2) Cldn5+/- mice and 3) C57BL6/J mice sub-retinally injected with adeno-associated virus (AAV) vectors expressing shRNA targeting claudin-5, or non-targeting control to characterise the effect of constant claudin-5 suppression on retinal and RPE integrity. Each cohort of mice were either fed a normal or high cholesterol diet for varying lengths of time to assess RPE atrophy progression. All mice were imaged by optical coherence tomography (OCT) to examine RPE integrity and fundus fluorescein angiography (FFA) to assess retinal blood vessel integrity and compared to littermate controls. Immunohistochemical, protein and transcript analysis was undertaken following sacrifice.

Results: Assessment of these three mouse models shows that RPE atrophy progression varies depending on the level of claudin-5 expression at the iBRB and is exacerbated when addition of high cholesterol chow was provided as determined by OCT and FFA.

Conclusions: These novel animal models may be beneficial in understanding GA pathology and development in greater detail. Targeted stabilization and regulation of claudin-5 expression at the inner retinal vasculature may have therapeutic potential for preventing GA onset and development.

CONTROL ID: 3545749

SUBMITTER (NAME ONLY): Markus Ritter

TITLE: Ultra-high field functional MRI based population receptive field mapping of retinal dystrophies

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Population receptive field (pRF) mapping methods allows mapping visual field losses due to retinal pathology, as recently shown in a study on retinal scotoma sizes at 3T. MRI scanners operating at ultra-high magnetic field (7 Tesla and above) offer increased sensitivity and specificity of brain activation maps, but also pose additional challenges in image acquisition and subject handling, particularly in clinical populations.

Methods: Ten eyes from 10 patients clinically and genetically diagnosed with Stargardt disease (STGD) (age: 29 ± 9.7 ; 4 female) were included in the study. Data was acquired on a 7 Tesla MAGNETOM scanner using a 32-channel head coil with 1mm isotropic resolution using the CMRR multi-band EPI sequence. Visual stimulus consisted of a moving, flickering bar covering the central 14° visual angle. In addition, patients were examined using optical coherence tomography (OCT, Heidelberg Spectralis) and microperimetry (MP-3, Nidek). Data was analyzed using mrVista to obtain retinotopic maps. Visual field coverage based on above-threshold voxels from the pRF-analysis allows for a direct comparison with retinal sensitivity maps as measured by MP.

Results: Four patients were excluded due to attention deficits or excessive movement during the MRI measurements. All remaining patients had framewise displacement (FD) values of 0.025 ± 0.004 mm and 5068 ± 2162 V1 voxel activated (mean \pm stddev). Figures show MP and pRF results of two exemplary patients with macular scotoma confined to the central 2° visual angle. It can clearly be seen that uncovered areas on the coverage maps obtained by ultra-high-field fMRI resemble areas with functional loss in MP.

Conclusions: This is the first demonstration of ultra-high field pRF mapping in patients with STGD. Coverage maps obtained from pRF data provide information complementary to conventional ophthalmic examination and allow for objective assessment of retinal dysfunction.

CONTROL ID: 3545754

SUBMITTER (NAME ONLY): Jan-Erik Fleger

TITLE: Real-time temperature controlled cw-laser treatment in rabbits

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Laser photocoagulation is widely used in retinal treatment. However, the tissue effect is only partially correlated to laser energy due to inter- and intraindividual alterations in retinal pigment epithelium (RPE) pigmentation. This leads to wide variations in laser effect and decreases treatment reliability and reproducibility. Optoacoustic measurement and control of retina temperature can solve this problem by adjusting the laser power in real-time onto a target temperature. With this temperature-guided irradiation, reliable and reproducible laser-tissue effect can be achieved for non-damaging heating. The aim of the study is to validate a control module by measuring and controlling laser power and real-time temperatures.

Methods: 5 eyes of 3 rabbits received a retinal temperature regulated laser treatment with a conventional 532nm continuous wave (cw) laser (Zeiss VisuLas 532). A custom-build control module (Medical Laser Center Luebeck) was used, which is optically coupled between the treatment laser and the slit lamp. It adjusts the pre-set laser power, depending on the current tissue temperature. Per pre-marked areal (5-6 in each eye) nine 200µm lesions (100ms exposure time) with uprising temperatures (45°C to 69°C in steps of 3°C) were applied. The mean applied laser power and mean real-time temperature over the last 20ms were measured.

Results: For the same target temperature, the controlled laser power showed significant differences. The following shows the mean applied laser power (\pm standard deviation and max/min values) over the last 20ms of irradiation for the target temperatures 51°C (14.8mW \pm 7.2, 31.0mW/0.9mW), 60°C (24.6mW \pm 9.3, 42.4mW/2.2mW) and 69°C (35.00mW \pm 12.8, 56.8mW/4.6mW). The real-time temperature displayed an overall accuracy of 3.5 % to the pre-set target temperature over the last 20ms of irradiation.

Conclusions: The results demonstrate that the control module was able to achieve reproducible and reliable real-time temperature-controlled irradiation. This will allow for more consistent subvisible laser treatment.

CONTROL ID: 3545757

SUBMITTER (NAME ONLY): Ajoy Vincent

TITLE: Retinal Phenotyping of a murine model of Lafora Disease

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vincent, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|A. Vincent, K. Ahmed, X. Zhao, Genetics and Genome Biology, SickKids Research Institute, Toronto, Ontario, CANADA|B. Minassian, Pediatric Neurology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lafora disease (LD) is an autosomal recessive progressive neurologic disorder caused by mutations in EPM2A or EPM2B genes, both involved in glycogen structural integrity. Defective function of EPM2A or EPM2B results in accumulation of malformed insoluble glycogen termed Lafora bodies (LBs) in the central nervous system. This study aimed to characterise the retinal phenotype of Epm2a^{-/-} mice to characterize retinal neuronal changes in LD.

Methods: The study was approved by the animal care committee at the Toronto Center for Phenogenomics. Five to seven knockout (KO; Epm2a^{-/-}) and control (WT) littermates were examined at two time points (10 and 14 months, respectively). Mice were injected 0.01 ml/g body weight of anesthetic solution (combination of 100mg/ml Ketamine and 20mg/ml Xylazine). Electroretinogram (ERG) testing was performed following overnight dark adaptation (DA) using Lab Cradle (Diagnosys LLC). A scotopic intensity series ERG was performed (9 steps; 0.0025 cd.s.m⁻² – 10 cd.s.m⁻²) followed by a 10-minute light adaptation (LA; 30 cd.m⁻²). Subsequently, LA ERGs were performed using a 5 cd.s.m⁻² stimulus flash to four stimulus frequencies (5 - 20 Hz). Retinal optical coherence tomography (OCT) and fundus imaging was performed using Phoenix MICRONTM. Periodic acid Schiff-Diastase (PASD) staining of the retina was performed to ascertain LB deposition. After staining, slides were imaged at 40x using 3DHistech Panoramic Flash II Slide Scanner, analyzed using 3DHistech CaseViewer software and LBs were counted using 3DHistech QuantCenter. Regions of interest were selected on the retinal sections, and a scenario was built in QuantCentre that distinguishes LBs from background and other structures.

Results: Retinal photographs were normal in both KO and WT mice. There was no significant difference in DA and LA ERG b-wave amplitudes between KO and WT mice groups at 10 and 14 months. The total retinal thickness was similar in both KO and WT groups. On PASD staining, LBs were observed only in KO mice in inner plexiform layer (IPL) and inner nuclear layers. Upon quantification, average number of LB accumulation in IPL in KO mice were 1743±533 and 2615±915 per mm², at 10 and 14 months, respectively.

Conclusions: This Epm2a^{-/-} mice model demonstrates LB deposition in the bipolar cell nuclear layer and its synapse with retinal ganglion cells. Adaptive optics retinal imaging could visualize them in vivo and serve as a useful biomarker for LD.

CONTROL ID: 3545759

SUBMITTER (NAME ONLY): Andrew Tsin

TITLE: Reduced Expression of Interphotoreceptor-Retinoid Binding Protein (IRBP) in Diabetic Retinopathy – Cell and Postmortem Study

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.T. Tsin, R.R. Rodriguez, D. Gonzalez, Molecular Science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|T. Zou, Pathology, University of Massachusetts System, Boston, Massachusetts, UNITED STATES|F. Gonzalez-Fernandez, Ophthalmology, University of Mississippi, University Park, Mississippi, UNITED STATES|

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ABSTRACT BODY:

Purpose: Rods and cones secrete IRBP, the major soluble protein component of the interphotoreceptor matrix. In addition to protecting and trafficking visual cycle retinoids, IRBP may have a neuroprotective role as there is an inverse relationship between the level of vitreous IRBP and severity of diabetic retinopathy (DR). The mechanism and location of reduced IRBP expression is not understood. Here, we investigated IRBP expression in-vitro in response to glucose and VEGF. Globes from diabetic patients were used to characterize retinal location of IRBP.

Methods: 1.5×10^6 661W and Y79 cells, which express cone and rod-like phenotypes, respectively were treated with 5.5 or 30 mM glucose with or without VEGF (10ng/ml) for 24 hrs. In 661W cells, IRBP and GAPDH mRNAs were quantified by RTPCR, and IRBP in conditioned media by ELISA. Human globes studies were obtained through the NDRI. Death to placement in 10% formalin was <10.5 hrs except in one control. Cases: Diabetes (2 no DR, 4 non-proliferative, 2 proliferative); and normal controls (6 cases). Donors age range was 30-98 yrs. Clinical histories were correlated with gross and histopathology, and serial sagittal sections prepared through the fovea. IHC compared the distribution of IRBP and peanut agglutinin binding matrix domains, with that of the choroidal proteins albumin, and BIGH3.

Results: High glucose (30 mM) resulted in a 1.44 increased IRBP mRNA in 661W cells (vs 1.34 for cells treated with 5.5 mM glucose). IRBP in the conditioned media in high glucose was ~3 X times greater compared to low glucose (13.1 vs 4.5 pg/ml). VEGF reduced IRBP secretion in cells in high (to 5.0 pg/ml) vs low glucose (0 pg/ml). IRBP in the media of Y79 cells were similar (70 vs 74 pg/ml for high and low glucose, respectively). Only a small decrease of IRBP level was noted in Y79 cells with VEGF treatment (69 vs 68 pg/ml). Ocular Pathology showed: Except when the postmortem interval was > 12 hrs, IRBP was restricted to the IPM; albumin and BIGH3 to the choroid. In DR, IRBP was reduced in the IPM, and albumin was often present.

Conclusions: Taken together our studies show that hyperglycemia results a reduction of IRBP within the interphotoreceptor matrix. VEGF mediated reduced IRBP expression may contribute to the pathogenesis of DR.

CONTROL ID: 3545761

SUBMITTER (NAME ONLY): Mengyu Wang

TITLE: Artificial Intelligence Assessment of Optic Cup Shape Patterns in Glaucoma

SESSION TITLE: Structure/function relationships

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To assess optic cup shape patterns in glaucoma with unsupervised artificial intelligence (AI).

Methods: The first Cirrus OCT scans of the optic nerve head (ONH) from each eye with signal strength ≥ 6 were selected. The optic cup shape was represented as the vertical positions of the inner limiting membrane (ILM) with respect to the lowest ILM vertical position in each eye. Scans with ONH centers deviating more than 0.3 mm from the scan center were excluded. The OCT scans were registered with respect to ONH centers in the right eye format. The Humphrey SITA standard 24-2 visual fields (VFs) tested within three months of the OCT tests were selected. An unsupervised AI method termed non-negative matrix factorization was applied to assess the cup shape patterns. The cup shape patterns were correlated with VF and OCT diagnostic parameters. We compared if using the cup shape patterns improved the prediction of VF loss using linear regression with model selection to remove redundant features.

Results: We determined 14 cup shape patterns (Figure 1) from 9,854 OCT scans. The brighter regions in the cup shape patterns indicate the more informative zones with greater variations across patients. Mean deviation (MD), retinal nerve fiber layer thickness (RNFLT) and ONH related parameters including rim area, disc area, average cup-disc (CD) ratio, vertical CD ratio and cup volume (Table 1) were most negatively correlated with Patterns 5, 4, 4, 12, 14, 14 and 14 (r : -0.15, -0.21, -0.45, -0.42, -0.60, -0.57 and -0.49, $p < 0.001$), and were most positively correlated with Patterns 10, 10, 14, 5, 5, 7 and 5 (r : 0.30, 0.28, 0.39, 0.54, 0.59, 0.52 and 0.78, $p < 0.001$), respectively. The Worse MD and thinner RNFLT were most strongly correlated with higher coefficients of Patterns 10 and 12, which represent inferior and superior cupping. The adjusted multiple r (r_m) to predict MD separately using the cup shape patterns, ONH related parameters, and 12 clock hour RNFLT were 0.50, 0.51 and 0.56, respectively, which the model combining the cup shape patterns and ONH related parameters (adjusted r_m : 0.60, $p < 0.001$) outperformed. The model (adjusted r_m : 0.63) combining all three types of features outperformed ($p < 0.001$) the model combining existing RNFLT and ONH parameters (adjusted r_m : 0.59).

Conclusions: The cup shape patterns correlated with established diagnostic parameters and improved the structure-function relationship in glaucoma.

CONTROL ID: 3545763

SUBMITTER (NAME ONLY): John Vanston

TITLE: Influence of stimulus size, intensity, & natural eye motion on small-field color perception

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Vanston, A.E. Boehm, W.S. Tuten, A.J. Roorda, School of Optometry and Vision Science Graduate Group, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stimulating single cones with spots of 543nm light has been shown to elicit various color sensations. These percepts vary mainly along a red-green axis, yet large fields of this wavelength invariably appear green and highly saturated. It remains unknown what conditions, if any, reliably yield veridical color percepts at the photoreceptor scale. Notably, naturalistic viewing includes eye motion, which causes many cones to sample the stimulus across time. The current study varied stimulus size and intensity under two eye motion conditions in order to better understand how chromatic percepts are constructed from cone signals.

Methods: Stimuli comprised 543nm spots of light presented at ~1 deg temporal eccentricity using an adaptive optics scanning laser ophthalmoscope. This system corrects for the optical aberrations of the eye and provides high-precision eye tracking and stimulus delivery. On each trial small spots of light were delivered to the retina over 500 ms. Stimuli were presented at two sizes (~2 and 4 arcmin, respectively), two intensities (1x and 6x detection threshold), and two eye motion conditions. In the first condition, stimuli were presented to a fixed position on the retina; in the second condition, stimuli were initially presented to a predefined retinal location, but subsequently allowed to drift across the moving cone mosaic. On each trial subjects (n = 3) reported the perceived saturation (rating scale of 1-5) and hue (red, white, or green) of the stimulus.

Results: The mean likelihood that subjects reported green increased for larger and higher intensity stimuli, with size increasing this likelihood from 74% to 85% and intensity increasing it from 72% to 86%. Similar results were found for saturation, with larger size resulting in a 7% increase in mean saturation rating and higher intensity resulting in a 10% increase. Varying eye motion resulted in a difference of only 1% in both measures. The amount of eye motion was found to be uncorrelated to the saturation rating on a trial-to-trial basis.

Conclusions: When small groups of cones were stimulated with 543 nm light, increases in stimulus size and intensity resulted in percepts that appeared more saturated and more consistently greenish, rather than reddish or whitish, in hue. Whether these spots of light were stabilized on the retina or allowed to drift freely across it made little difference in hue or saturation reports.

CONTROL ID: 3545764

SUBMITTER (NAME ONLY): Dimitrios Christaras

TITLE: Peripheral refraction measured from through-focus double-pass imaging

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Christaras, H.S. Ginis, Department of Research, Athens Eye Hospital, GREECE|D. Christaras, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|P. Artal, Laboratorio de Optica, Universidad de Murcia, Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: Peripheral refraction is a relevant information in different areas of clinical optics, such as myopia or cataract. We have developed and validated an optical instrument and a corresponding method for the in-vivo assessment of peripheral defocus and astigmatism from the recording of through-focus double-pass images.

Methods: An optical setup was developed to acquire non-cycloplegic, double-pass through focus images of the eye at 0, 15 and 30 degrees of visual angle. A 2-mm diameter infrared laser diode (780nm) beam was projected on the ocular fundus with the appropriate relay optics via a tunable lens capable of inducing +5D to -18D of defocus. The ocular fundus was then imaged through the full natural pupil of the eye and the same relay optics and the tunable lens on a CMOS sensor. A series of through focus images was acquired at a step of 0.1D and best focus was established by finding the image where peak intensity value was maximum. The magnitude of astigmatism was determined by finding the two defocus images where the ratio of the ellipse's minor axis in their shape was minimized. Astigmatism was then defined as the dioptric difference between those two images and the axis of astigmatism was defined as the axis of the image with the highest defocus value.

Results: Using appropriate off-axis fixation of the subject, the refractive measurement was performed at 0, 15 and 30 degrees of visual angle at a temporal horizontal visual field. The procedure was validated in-vivo in 2 healthy subjects and each measurement was repeated twice to determine the repeatability of the measurement. Repeatability in central and peripheral refraction measurement was within 0.25D sphere and cylinder for both subjects. Both subjects exhibited a myopic periphery with respect to the foveal refraction (-0.7 and -1.4D at 30 degrees). The difference of astigmatism between the 30 degrees field angle and central vision was in the myopic direction for both subject (-3.3 D and -2.6D) respectively where the more refractive axis was horizontal. At each eccentricity the measurement lasted a few seconds.

Conclusions: An instrument and an associated method was developed for the fast, in-vivo assessment of central and peripheral refraction. The refraction obtained from this method pertains to the actual refraction optimizing the double-pass images of the eye and is free of errors associated to refractometry and wavefront sensing at elliptical pupils.

CONTROL ID: 3545772

SUBMITTER (NAME ONLY): Yusuf ARIK

TITLE: A human pluripotent stem cell-derived organ-on-a-chip model of the outer blood-retinal barrier for understanding age-related macular degeneration

SESSION TITLE: Ocular disease models: molecular mechanisms and therapeutic approaches

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is an eye disorder of malfunctioning tissues in the outer blood-retinal barrier (oBRB): the retinal pigment epithelium (RPE), the underlying "Bruch's membrane" and the adjacent choroidal capillary bed. To understand disease pathology and develop new therapeutic concepts, in vitro models are needed where physiological and morphological changes of tissues can easily be monitored, and conditions can be manipulated. To this end, we developed an organ-on-a-chip model (OOC) of the oBRB based on human induced pluripotent stem cell-derived cells (hiPSC) and evaluate its future use as an in vitro model of drug development for AMD.

Methods: Human iPSC-RPE and iPSC-endothelial cells (EC) were derived based on protocols from Regent et al. (2019) and Orlova et al. (2014) respectively. The PDMS-based OOC was composed of a top channel for RPE culture as a monolayer, and a bottom channel where ECs were cultured in a microvessel of a well-defined geometry patterned within collagen-I using a subtractive method of micropatterning. Expression of cell-cell adhesion markers was analyzed by immunocytochemistry, and barrier function of endothelial cells was assessed with a clinically relevant technique analogous to fluorescein angiography.

Results: OOC was fabricated using injection molding, which minimizes labor intensive fabrication and provides device consistency. Devices were placed on a rocking platform inside an incubator to facilitate gravity driven medium flow in channels. Healthy cell population growth was confirmed by cell-cell adhesion markers. EC barrier was assessed by perfusion of fluorescently labeled dextran where lower permeability compared to only RPE containing devices was observed.

Conclusions: The OOC developed in this study models the outer BRB by recapitulating the tissue microenvironment. integration of iPSC-derived cells from AMD patients could provide insights for individualized testing and the evaluation of new treatments.

CONTROL ID: 3545773

SUBMITTER (NAME ONLY): Peter Reinach

TITLE: PRMT1 Enhances Corneal Epithelial Wound Healing

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Reinach, Q. Cao, D. Yan, School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|

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ABSTRACT BODY:

Purpose: Post-translational protein arginine methylation is a fundamental modification of many different essential cellular processes. Protein arginine methyltransferase 1 (PRMT1) is a type I member of the PRMT family, and it is critical for catalyzing such modulation. However, its role in mediating corneal epithelial renewal remains unknown. In the present study, we characterize its involvement in corneal epithelial wound healing (CEWH) and thereby gain insight into how it affects this process.

Methods: An Alger brush was used to debride the corneal epithelium in mice. Western blot was performed to detect the PRMT1 protein expression level during CEWH in this tissue. Human corneal epithelial cells (HCECs) were transfected with siRNA targeted to knock down PRMT1 expression using Lipofectamine RNAiMAX. MTS and a scratch wound-healing assay evaluated the effects of PRMT1 on HCEC proliferation and migration, respectively. Flow cytometry determined cell cycle progression. Corneal epithelial-specific Prmt1 deletion mice were generated using the Cre-lox system.

Results: The PRMT1 protein expression level was significantly upregulated during CEWH. Prmt1 deletion significantly delayed in vivo CEWH. Furthermore, downregulation of PRMT1 only inhibited HCEC migration without altering either their cell cycle progression or proliferation.

Conclusions: PRMT1 upregulation promotes CEWH through stimulating cell migration. This association indicates that increasing the protein arginine methylation status warrants further evaluation as a potential option to promote this process in a clinical setting.

CONTROL ID: 3545781

SUBMITTER (NAME ONLY): Frank Brodie

TITLE: Ex vivo evaluation of the peripheral retina utilizing a mirrored contact with optical coherence tomography

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Brodie, R.P. McNabb, W. Raynor, J.D. Li, L. Vajzovic, J. Izatt, C.A. Toth, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many important retinal diseases that would benefit from evaluation with optical coherence tomography (OCT), such as retinal breaks and retinoschisis are frequently located in the peripheral retina. However, clinical OCT imaging is generally confined to capturing the posterior pole. We describe a new method for capturing OCT images of the peripheral retina using a mirrored contact lens.

Methods: An ex vivo porcine eye was set up for standard 25 gauge 3 port pars plana vitrectomy with the Alcon Accurus system (Fort Worth, TX). Using the Leica Proveo 8 with BIOM widefield viewing system (Wetzlar, Germany) we created a retinal break approximately 1 mm posterior to the ora serrata with the vitreous cutter.

Results: Transillumination of the break using the endoilluminator confirmed the peripheral location externally at 5 mm posterior to the limbus - Figure 1A. Using the microscope, we directly visualized the break with a Goldmann-type 3 mirror contact lens – Figure 1B. Our research surgical microscope-integrated OCT (MIOCT) system, consisting of a 400 kHz 1050 nm swept source engine, was directed through the Goldmann 66° mirror and captured B-scans of the retina. We were able to identify retinal vessels, normal peripheral retina and the iatrogenic break within the OCT images– Figure 1C.

Conclusions: Use of a mirrored contact lens to obtain OCT images of the peripheral retina is a promising new technique to evaluate peripheral retinal anatomy. It can be used to identify sites with and without retinal pathology in the periphery. Additionally, this technique has the potential to examine the vitreous base.

CONTROL ID: 3545782

SUBMITTER (NAME ONLY): Maëlle Vilbert

TITLE: Objective assessment of corneal transparency in the clinical setting: Identification and correction of acquisition artifacts in SD-OCT images

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To develop an automated algorithm for clinical spectral domain OCT (SD-OCT) images, capable of correcting hyperreflective artifacts associated with the instrumental configuration and the patient's eye position.

Methods: The automated pre-processing algorithm (Python Software Foundation, v2.7.4) developed standardizes raw images (flattening, segmentation, normalization) and computes a correction mask from each OCT image. Our approach is based on the Principal Component Analysis (PCA) of the in-depth stromal OCT signal, which enables the statistical computation of the device's point spread function and permits its compensation (Fig.1). The mean stromal intensity depth profile is then extracted and analyzed via our previously developed method designed to quantify the photon mean free path in the stroma (R Core Team, v3.6.3) as objective measure of corneal transparency. We tested our method and associated algorithm on clinical SD-OCT images acquired with an RTVue-100 OCT device (Optovue, Inc.). n=37 normal corneas (aged 33 ± 8 years) were studied (2 images per eye). Patients were chosen according to the inclusion criterion of pre-refractive surgery, implying clear and healthy corneas.

Results: Results are shown in Fig.2. Boxplots depict the photon mean free path values (I_s) obtained by our image-analysis method for each eye imaged. Typical I_s values are on the order of 500 – 1000 μm . We obtain a log-normal distribution of results for data up to the third quartile with a 6.9 % coefficient of variation: $\langle \log(I_s) \rangle = 6.1 \pm 0.4$ dB, Shapiro-Wilk test p-value = 0.5.

Conclusions: Our pre-processing algorithm is capable of robust detection and correction of clinical SD-OCT image artifacts. It enables to determine numerical values of scattering mean free path in vivo using unmodified clinical diagnostic devices. Future steps will include a correlation of our method with clinical data (e.g., corneal densitometry) obtained by other methods (Bland-Altman comparison), as well as with other clinical measures (e.g., visual acuity).

CONTROL ID: 3545784

SUBMITTER (NAME ONLY): Harilaos Ginis

TITLE: Peripheral refraction and image quality in a pseudophakic eye model

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.S. Ginis, S. Tsoukalas, A. Pennos, D. Christaras, A. Livir-Rallatos, Department of Research, Athens Eye Hospital, Glifada, Attica, GREECE|P. Artal, Laboratorio de Optica, Universidad de Murcia, Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate peripheral refraction and image quality in a physical model of the pseudophakic eye where the axial position of the intraocular lens (IOL) and the radius of curvature of the retina could be varied. This device is used to compare the performance of a standard Monofocal IOL to a new type of IOL with an inverted meniscus shape designed to improve peripheral image quality.

Methods: The model of the pseudophakic eye had realistic dimensions with a cornea made of PMMA (radius of curvature 7.73mm, conic constant -0.24) an iris at a depth of 3.55mm (3mm pupil) and an IOL holder with variable distance (0.5 to 1.5mm) from the pupil, simulating a postoperative anterior chamber depth ranging from 4.05 to 5.05 mm. The volume of the artificial eye was filled with distilled water. A board level camera (DFM 72BUC02-ML, Imaging Source, Germany) in a water-tight container with a 200µm glass window was introduced to allow direct recording of retinal images. The camera was mounted on a rotating base where the center of rotation was on the optical axis of the system and the radius ranged from 11 to 13 mm to model different retinal radii of curvature. For each field angle (0, 10, 20, 30 and 40 degrees) the retinal image was optimized for spherocylindrical error using trial lenses. Two types of IOLs were evaluated: a standard monofocal (CT Lucia601P, Zeiss, Germany) and a new meniscus shaped one (ArtIOL, Voptica SL, Spain).

Results: The retinal images recorded revealed a deterioration of retinal image quality with field angle. Peripheral defocus ranged from -1.0 D to +7.5 D depending on retinal curvature, IOL position and IOL type. Astigmatism was up to -7.5 D for the standard IOL and was reduced to -3.5D for the meniscus IOL. The condition with the increased IOL depth (5.05mm) required the insertion of a higher power IOL by 1D to maintain central focus without adjusting the overall eye's axial length. The condition of increased chamber depth and increased IOL power resulted to a small (0.5D) decrease in the relative defocus in the periphery. Astigmatism in this condition was higher in the standard IOL (-9.0 D) and remained unchanged for the meniscus type IOL.

Conclusions: The experimental setup allowed the direct recording of the retinal image at large field angles. The meniscus-type IOL exhibited less peripheral astigmatism in all conditions and it was more robust in terms of the axial depth of the IOL than the standard lens.

CONTROL ID: 3545785

SUBMITTER (NAME ONLY): Haiyan Li

TITLE: TGF β 2 modulates YAP/TAZ activity in human trabecular meshwork cells through ERK and ROCK signaling pathways

SESSION TITLE: Glaucoma: molecular, biochemical and biomechanical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Li, P.S. Ganapathy, S. Herberg, Ophthalmology & Visual Sciences, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|H. Roberts, D.W. Stamer, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary open angle glaucoma (POAG) is associated with increased trabecular meshwork (TM) stiffness and elevated levels of transforming growth factor beta2 (TGF β 2) in the aqueous humor. YAP/TAZ are important mechanotransducers and have been implicated in the pathogenesis of POAG. However, the molecular underpinnings of YAP/TAZ activity modulation in TM cells under glaucomatous conditions are not well understood. The purpose of this study is to elucidate how TGF β 2 and substratum stiffness regulate YAP/TAZ in human TM (HTM) cells using viscoelastic biomimetic hydrogels.

Methods: Primary HTM/glaucomatous HTM (GTM) cells were isolated from surgical discard corneal rims/donor POAG globe and validated using accepted protocols. HTM/GTM cells were plated on soft photocrosslinked hydrogels (collagen I, elastin-like polypeptide and hyaluronic acid) or stiff glass coverslips/tissue culture polystyrene and stimulated with 2.5 ng/ml TGF β 2 \pm ERK inhibitor (U0126; 10 μ M)/ROCK inhibitor (Y27632; 10 μ M). YAP/TAZ were knocked down in HTM cells using siRNA. Vinculin, YAP/TAZ, transglutaminase 2 (TGM2), TGF β 2, fibronectin (FN), α -smooth muscle actin (α -SMA) and phospho-myosin light chain (p-MLC) expression were determined by qRT-PCR, immunoblotting and immunocytochemistry analyses.

Results: HTM cells displayed increased vinculin puncta density, cell spreading and YAP/TAZ nuclear localization/activation when cultured on stiff substratum vs. soft hydrogels. On hydrogels, TGF β 2 exposure induced a more rounded HTM cell shape with decreased nuclear aspect ratio ($p < 0.001$). GTM cells and TGF β 2-induced HTM cells showed decreased p-YAP (cytoplasmic; inactive) and increased nuclear YAP/TAZ (active) together with increased downstream TGM2 vs. normal HTM cells. U0126 completely abolished TGF β 2-induced YAP/TAZ expression and nuclear translocation as well as TGM2 activation. Y27632 slightly rescued TGF β 2-induced YAP/TAZ activation. YAP/TAZ depletion using siRNA resulted in decreased expression of TGM2, TGF β 2, FN, α -SMA and p-MLC ($p < 0.001$), all associated with cell contractility and tissue stiffening.

Conclusions: Our data suggest that substratum stiffness and TGF β 2 modulate YAP/TAZ activity in HTM cells under simulated POAG conditions to varying degrees through ERK and ROCK signaling pathways. YAP/TAZ play critical roles in regulating HTM cell contractility associated with HTM stiffness and POAG pathogenesis.

CONTROL ID: 3545792

SUBMITTER (NAME ONLY): Haroun Al-Mohamed

TITLE: Digital Hess Screen test : a novel method for quantitative measurement of strabismus

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Al-Mohamed, I. Kelly-Pérez, A. Prinz, M. Bende, T. Oltrup, M. Leitritz, T. Bende, University-Eye-Hospital Tübingen, Eberhard-Karls-Universität Tübingen Medizinische Fakultät, Tübingen, Baden-Württemberg, GERMANY

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ABSTRACT BODY:

Purpose: To increase the accuracy of Strabismus Measurements using a new fast digital technique based on the Hess test.

Methods: The proposed system is based on the Hess screen test by using dual-coloured glasses to disrupt fusion and to enable a fovea-to-fovea test. It consists of glasses and a PC connected to a beamer. The glasses are coloured blue and red which guarantees monocular vision by disrupting fusion. To make sure the patient has no diplopic images, the room lights must be dimmed. At one side of the glasses is mounted a 9-axis sensor (Adafruit BNO055) which transfers the rotation data of the head via a Bluetooth connection (Adafruit Feather M0 BLE) to the PC. Additional to the 9-Axis sensor, a time-of-flight sensor (Pololu VL53L1X) is mounted to measure the distance of the head to the wall. Via the beamer, two objects on a black background are presented on the wall. Through the movements of the head a simulated red cross can be moved. The aim of the test is to move the cross in the centre of the projection where a blue square is presented.

To simulate the ocular deviations, glasses with different prism dioptres from 1-40 degrees are used during the test. The strabismus test via the designed system was compared with the conventional Hess screen test.

Results: Using a stepper motor the accuracy of the 9-Axis sensor was defined to one degree in pitch, yaw and roll. Using the designed glasses visual gazes up to 25° degrees are possible. Examination time is up to 60 seconds measuring both eyes at a particular gaze. Also it was possible to measure extreme and small-angle strabismus.

Conclusions: This designed system and technique allow to carry out fast and accurate strabismus measurements, the results are close to the given and measured by conventional Hess test. With this technique, the measuring system design can be simplified and the costs reduced.

CONTROL ID: 3545793

SUBMITTER (NAME ONLY): David Hughes

TITLE: Exposure to a diabetic-like milieu in vitro alters metabolism in human microvascular endothelial cells

SESSION TITLE: Mitochondria in ocular diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The retinal capillary endothelium experiences marked fluctuations in hyperglycaemia and ischemia as diabetic retinopathy (DR) progresses. This study has assessed the changes of metabolism and related function in human retinal microvascular endothelial cells (HRMEC) exposed to long term high glucose and hypoxia conditions in vitro

Methods: HRMEC obtained from human donors were grown in to 25 mM L-glucose or 25 mM D-glucose (HLG, HDG) for four weeks and then also exposed to hypoxia (1% O₂, 5% CO₂) for 24 hours. The metabolic flux of both the extracellular acidification rate (ECAR) and oxygen consumption rate (OCR) was assessed using the Seahorse XF analyser. To assess in vitro functionality assays such as tubulogenesis, proliferation, and migration, along with barrier analysis using the xCELLigence system were utilised. Pharmaceutical compounds were also utilised to modulate the responses of key metabolic genes

Results: Compared to controls HDG cells demonstrated reduced ECAR from 24.4 to 16.4 (mpH/min) in normoxia and 44.8 and 35 (mpH/min) in hypoxia ($P \leq 0.01$). Furthermore, OCR was reduced in normoxia from 61.4 to 52.9 (pmol/min) ($P \leq 0.05$), however in hypoxia HDG showed increased levels in relation to control 25.8 to 17.3 (pmol/min) ($P \leq 0.01$) assessed by the Seahorse XF analyser. HDG treated HRMECs also displayed decreased tubulogenic capacity in normoxia which further decreased in hypoxia ($P \leq 0.001$). HDG reduced proliferative potential ($P \leq 0.001$) and was shown to increase median cellular size ($P \leq 0.001$). Migration of cells was also reduced in scratch wound assays and migration and barrier formation were shown to be hindered ($P \leq 0.01$). HDG cells demonstrated reduced ECAR from 24.4 to 16.4 (mpH/min) in normoxia and 44.8 and 35 (mpH/min) in hypoxia ($P \leq 0.01$). Furthermore, OCR was reduced in normoxia from 61.4 to 52.9 (pmol/min) ($P \leq 0.05$), however in hypoxia HDG showed increased levels in relation to control 25.8 to 17.3 (pmol/min) ($P \leq 0.01$) assessed by the Seahorse XF analyser.

Conclusions: HRMEC exposed to long term exposure of HDG and then hypoxia appear to have severely affected functionality and altered metabolism. As endothelial cells normally have a remarkable dependency on glycolytic metabolism which allows for growth and repair, these alterations are relevant to vascular pathology occurring in DR.

CONTROL ID: 3545794

SUBMITTER (NAME ONLY): Suveera Dang

TITLE: Estimating Patient Demand for Ophthalmologists in the United States using Google Trends

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Currently, there are around 18,500 ophthalmologists practicing in the United States. However, the American Association of Medical Colleges (AAMC) estimates a shortage of ophthalmology providers in 2025. It is well known that the prevalence of cataracts, macular degeneration, glaucoma, and diabetic retinopathy is highest in the elderly. There is expected to be an increase in the percentage of population aged 65 and older from 2017 to 2032. Despite this increase in population and the expected shortage of ophthalmologists, little research has attempted to quantify current demand for ophthalmologists on a regional level. This study sought to estimate demand for ophthalmologists using internet search engine data. Furthermore, it compared the level of demand with the number of ophthalmology providers in that area to address whether there is a shortage.

Methods: Google Trends were analyzed from 2004-2019 to find the average relative search volume (RSV) for the term "Ophthalmologist" of each state to determine patient interest. Furthermore, supply of ophthalmologists was identified by utilizing the Medicare Physician Compare National Database. This is a publicly accessible database that quantifies board-certified ophthalmology providers per state who accept Medicare. For each region, the number of providers was then divided by the 2019 Census Bureau population estimates to find the concentration of specialists per capita values. The RSV values were then divided by the per capita values to estimate the demand index of ophthalmologists for each state.

Results: The relative demand index was highest in South Dakota (100), Michigan (83), Delaware (82), Texas (78), and Arizona (76) (Figure 1). The greatest specialist concentration per 10,000 people was in Montana (1.62), DC (0.85), Hawaii (0.40), and Maryland (0.41) and lowest in Oklahoma (0.19), New Mexico (0.19), Texas (0.19) and Wyoming (0.17). The highest search volumes (RSV) were in Delaware (100), Michigan (100), and South Dakota (93) and the lowest volumes were in Alaska (36), Wyoming (27), and North Dakota (36).

Conclusions: With an aging population and an estimated shortage of ophthalmologists, the findings from this study will better delineate areas with an unmet need for ophthalmologists. This can provide helpful information to ophthalmologists when deciding on job allocation or practice building.

CONTROL ID: 3545797

SUBMITTER (NAME ONLY): Sara Patterson

TITLE: Conserved neural mechanisms for direction selectivity in the primate retina

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Detection of motion direction is an essential visual function and a classic model for neural computation. This has been studied intensely in the non-primate retina where starburst amacrine cells (SACs) provide directionally-tuned inhibition to ON and ON-OFF direction-selective retinal ganglion cells (dsRGCs). While SACs are present in primates, their circuitry is largely unknown and the existence of dsRGCs remains an open question. Resolving the long-standing debate over primate retinal direction selectivity requires a detailed wiring diagram of SAC circuitry.

Methods: We reconstructed the structure, synapses and circuitry of ON SACs from a serial block-face scanning electron microscopy volume of macaque central retina. Postsynaptic RGC reconstructions were compared to RGCs labeled by injections of the retrograde tracer rhodamine dextran into the nucleus of the optic tract and dorsal terminal nucleus of the accessory optic system (NOT-DTN).

Results: First, we confirmed that the neural mechanisms supporting direction selectivity in mammalian SACs are conserved in primate. Mechanisms identified included a proximal-distal distribution of input-output synapses along each dendrite, reciprocal inhibition from other SACs and temporally-diverse bipolar cell input. Next, we reconstructed all postsynaptic RGCs. SACs targeted a single RGC type resembling some of the RGCs labeled from the NOT-DTN as well as the mammalian ON-sustained dsRGCs. These RGCs were rare (<1% of all RGCs) with large overlapping dendritic fields that cofasciculated with the SAC plexus. The overlapping RGCs may encode different directions as nearby dendrites rarely received input from the same SACs. The extensive SAC input to the RGCs was directionally tuned, as predicted from the angles of presynaptic SAC dendrites.

Conclusions: Here we show that the necessary machinery for direction selectivity exists within the primate retina, earlier in the primate visual system than classically thought, and implements many of the elementary motion detection strategies found across vertebrate species. Our results shed light on the nature of primate motion processing by identifying which aspects of the mammalian retinal direction selectivity circuit were conserved and which were not. For example, we did not find SAC input to an ON-OFF dsRGC homolog. The RGCs reported here are candidate homologs to the mammalian ON dsRGCs that contribute to optokinetic nystagmus.

CONTROL ID: 3545798

SUBMITTER (NAME ONLY): Byron Lam

TITLE: NIGHT study: natural progression of choroideremia

SESSION TITLE: Advances in Diagnosis and Management of Retinoblastoma and Congenital Eye Diseases

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: This ongoing, 2-year, prospective, multicenter, observational study (NIGHT: NSR-CHM-OS1, NCT03359551) investigates the natural progression of choroideremia.

Methods: Enrollment is completed and includes 322 adult males with genetically confirmed choroideremia and active disease visible within the macula. Eyes were classified at baseline into 3 cohorts by best-corrected visual acuity (BCVA): ≥ 74 Early Treatment of Diabetic Retinopathy Study (ETDRS) letters (201 eyes), 34-73 ETDRS letters (382 eyes), and < 34 ETDRS letters (61 eyes). The analyses were conducted on participants who completed the 20-month study (186 participants [368 eyes]). Visits occurred at 4-month intervals; BCVA, preserved area of ellipsoid zone (EZ), preserved area of autofluorescence (PAF), microperimetry, contrast sensitivity, color vision, and reading-speed tests were assessed periodically. Endpoints other than BCVA were assessed only through 12 months (237 participants [468 eyes]).

Results: Change from baseline in most assessments demonstrated a consistent but modest decline. The mean (95% CI) change in BCVA from baseline to Month 12 was 0.9 (0.3, 1.5) and from baseline to Month 20 was -0.5 (-1.2, 0.2). Linear regression suggests BCVA decreases slowly, at approximately 0.5 letters annually, although loss is higher and progresses slightly faster in older individuals. When assessing effects of age on BCVA change over a 20-month period (adjusting for baseline BCVA), participants in their seventies lost ~ 1.9 letters. All other assessments decreased consistently from 4 to 12 months in all 3 BCVA cohorts. Mean (95% CI) change from baseline was -14.65% (-15.58, -13.72) in PAF and -15.07% (-16.39, -13.75) in preserved EZ area; mean (95% CI) change from baseline in microperimetry was -0.56 dB

(-0.77, -0.35). Changes from baseline in contrast sensitivity and color vision were minimal. Reading speed was highly variable.

Conclusions: Participants with choroideremia slowly lose vision. Older patients with a more advanced disease may experience greater decline over a 20-month interval. PAF and preserved EZ area decreased at each visit. Contrast sensitivity, color vision, and reading speed were not reliable measures of disease progression. This study reinforces the importance of BCVA, preserved EZ area, and PAF as measures of natural choroideremia progression.

CONTROL ID: 3545800

SUBMITTER (NAME ONLY): Zhe Pan

TITLE: 10-Year Progression of Myelinated Retinal Nerve Fibers. The Beijing Eye Study 2001/2011

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Pan, C. Wei, Y. Wang, J. Jonas, Beijing Tongren Hospital, Beijing, Beijing, CHINA|J. Jonas, Ruprecht Karls Universität Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To assess the 10-year changes of myelinated retinal nerve fibers (MRNF) and the related systematic and ocular factors in a population-based cohort study.

Methods: Out of 4439 participants aged 40+ years and who participated in the Beijing Eye Study in 2001, 2695 (66.4% of the surviving) individuals were followed in 2011. All participants underwent a detailed physical and ocular examination. Eyes with detected MRNFs at baseline were included into the present study. Changes in the appearance of the MRNFs were examined using a flicker method of fundus photographs taken at baseline and at follow-up. The area covered by the MRNFs was delineated and measured with the Image J program. The progression rate was defined as the ratio of the MRNF area at study end divided by the MRNF area at baseline.

Results: Out of 35 eyes (29 participants) with detected MRNFs at baseline, 23 eyes from 20 individuals (11 women, 55%) were re-examined in 2011. Out of these 23 persons, 17 participants (85%) had unilateral MRNFs, while three participants had bilateral MRNFs. An increase in the size of MRNF area was detected in all 19 eyes with clear images from both visits, while the quality of the fundus photographs of 4 eyes did not allow a quantitative follow-up examination. The mean MRNF area was $4233 \pm 3670 \mu\text{m}^2$ (range: $178\text{--}11643 \mu\text{m}^2$) and $5243 \pm 4092 \mu\text{m}^2$ (range: $196\text{--}13297 \mu\text{m}^2$), at baseline and at follow-up, respectively ($P < 0.001$). The MRNF area increased by $1010 \pm 1026 \mu\text{m}^2$ ($18\text{--}3967 \mu\text{m}^2$) or by $47\% \pm 74\%$ ($9\text{--}315\%$). A more pronounced enlargement of MRNF area was associated with a higher serum concentration of low density lipoproteins ($P < 0.001$, $B = 0.53$, 95%CI: 0.30, 0.77), a MRNF location distant from the optic disc as compared to a peripapillary location ($P = 0.001$, $B = -0.89$, 95%CI: -1.34, -0.44), and a smaller MRNF area at baseline ($P = 0.02$, $B = -0.09$; 95% CI: -0.16, -0.02).

Conclusions: An enlargement of the MRNF area was commonly found in adults in a population-based 10-year follow-up study. The finding is of importance for the natural history and pathogenesis of myelination within the globe, and may perhaps give some clues for the intracranial myelination.

CONTROL ID: 3545807

SUBMITTER (NAME ONLY): Monica Sandoval

TITLE: Assessment of mental health needs in children and guardians in pediatric low vision rehabilitation clinics

SESSION TITLE: Visual Impairment and Quality of Life

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.A. Sandoval, S. Lopper, T. Schwartz, Division of Pediatric Ophthalmology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|L. Alfano, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|S. Lopper, T. Schwartz, Department of Ophthalmology, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Children with vision impairment and their families may find themselves isolated from their peers as they navigate typical developmental challenges in addition to a physical handicap. To assess the perceived need for a social work component in the multidisciplinary care model for pediatric low vision rehabilitation, children and their guardians evaluated in low vision clinics at Cincinnati Children's Hospital Medical Center (CCHMC) and West Virginia University Ruby Memorial Hospital (WVU) were surveyed.

Methods: Survey respondents included 107 guardians and 87 children seen previously for low vision rehabilitation at CCHMC or WVU. Surveys were completed after low vision diagnosis and during or after participation in multidisciplinary vision rehabilitation clinics. Respondents were asked about the desire for additional services or benefits at the time of diagnosis and after including: support and peer groups, summer camps, after school programs, specialized training, and other services. Participants were also asked about emotional response to the diagnosis. Survey data were examined to determine thematic trends in child and guardian responses.

Results: At the time of diagnosis, 93% (100/107) of guardians and 71% (62/87) of children would have preferred referral to at least one service or benefit. At the present time, 82% (88/107) of guardians and 70% (61/87) of children report a desire for additional services. Guardians report feeling "sad" and "overwhelmed" about their child's diagnosis [(41% (44/107) and 53% (57/107) respectively]. Comparatively, 34% (30/87) of children reported feeling "sad" and 31% (27/87) feel "overwhelmed". Only 54% (58/107) of guardians and 39% (34/87) of children report having the knowledge or support to navigate their feelings. Additionally, 54% (58/107) of guardians and 44% (38/87) of children report they would have seen a counselor at the diagnosis visit had one been provided as standard care.

Conclusions: Children with vision impairment and their guardians have mental health concerns and would likely benefit from having access to additional services and programs. We are recommending inclusion of a social worker or other service provider as a standard care component to multidisciplinary vision rehabilitation services after the diagnosis of a visually impairing condition for families to address the mental health needs identified by this survey.

CONTROL ID: 3545808

SUBMITTER (NAME ONLY): Michael Peng

TITLE: Characterizing CLAN formation and dynamics in a transformed HTM cell line

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Peng, C.K. Sugali, N.P. Rayana, J. Dai, W. Mao, Department of Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|W. Mao, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cross-linked actin networks (CLANs) in trabecular meshwork (TM) cells may contribute to increased IOP by altering TM cell function and stiffness. CLANs have been observed in TM cells and tissues, but little is known about their formation or dynamics. We developed a transformed TM cell line that forms spontaneous, fluorescently labeled CLANs. Using live cell imaging, we characterized the actin dynamics of transformed HTM cells treated with latrunculin B.

Methods: A stable cell line was constructed by transducing transformed glaucomatous TM (GTM3) cells with the pLenti-Lifeact-EGFP-BlastR lentiviral vector. CLANs in cells were further increased upon treatment with different concentrations of blasticidin. The transduced GTM3 cells were treated with 1uM latrunculin B for 2 hrs, and time lapse fluorescent images were recorded in 1 min intervals during treatment and 2 hrs after removal of the agent.

Results: The transformed human TM cell line with stably transduced Lifeact-GFP expression cassette demonstrated the morphology of actin stress fibers and the spontaneous formation of CLANs using fluorescent microscopy. The number of CLANs in cell cultures were increased when treated with high concentrations of blasticidin at 10ug/ml ($p<0.05$, $N=3$) and 20ug/ml ($p<0.05$, $N=3$). Using live cell imaging, we found that CLANs were more resistant to actin depolymerization agent latrunculin B, as compared to actin stress fibers.

Conclusions: Live cell imaging of a CLAN forming transformed human TM cell line suggests that CLANs are a stable structure and likely play an important role in elevated outflow resistance and glaucoma.

CONTROL ID: 3545811

SUBMITTER (NAME ONLY): Tomoaki Murakami

TITLE: Factors Predicting Treatment Frequency of Ranibizumab Injections during the Second Year in Diabetic Macular Edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Anti-VEGF therapy is the first-line for diabetic macular edema (DME), although its socioeconomic burden is a serious concern. We therefore investigate the predictors of the treatment frequency in the second year under as-needed intravitreal ranibizumab (IVR) injections for DME.

Methods: In this retrospective study, we reviewed 65 eyes of 60 patients with center-involved DME who received pro re nata (PRN) IVR injections following three monthly loading doses. The central subfield thickness (CST) and qualitative findings were assessed on spectral domain optical coherence tomography (SD-OCT) images. We then investigated whether parameters at baseline or 12-month visit were associated with the treatment frequency in the second year.

Results: The number of ranibizumab injections decreased from 6 (4-8) during the first year to 2 (0-3) during the second year ($P<0.001$), despite the maintenance of functional efficacy from 12- to 24-month visits. The injection numbers during the first year ($\rho=0.259$, $P=0.037$) but not during the second year ($\rho=0.152$, $P=0.226$) were modestly related to logarithm of the minimum angle of resolution (logMAR) improvement at 24 months. Multivariate analyses revealed that CST and hyperreflective walls in foveal cystoid spaces at baseline were associated with the number of IVR injections during the second year ($\beta=0.363$, $P=0.003$ and $\beta=0.234$, $P=0.048$, respectively). The treatment frequency during the second year was also related with CST ($\beta=0.266$, $P=0.012$), hyperreflective walls ($\beta=0.394$, $P=0.002$), and the cumulative doses of ranibizumab injections ($\beta=0.294$, $P=0.006$) at 12-month visit.

Conclusions: CST and hyperreflective walls in foveal cystoid spaces are designated as predictors of treatment frequency of ranibizumab injections during the second year in DME.

CONTROL ID: 3545815

SUBMITTER (NAME ONLY): Jarrod Harman

TITLE: Sex- and strain-dependent phenotypes in the resting mouse retina: ERG, metabolism, structure, and proteome.

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: For decades, male inbred mice have served as the foundation of preclinical studies, even with the availability of established outbred mouse strains, which better represent the genetic diversity observed in humans. Moreover, given differences in the prevalence of ocular diseases between men and women, more focus should be directed at the preclinical level to understand how biological sex affects disease pathogenesis and treatment. For these reasons, we measured critical molecular components of retinal health, including the functional response to light, metabolism, structure, and the proteome, to delineate baseline differences between male and female inbred and outbred mice.

Methods: Adult C57BL/6J (inbred) and Swiss Webster-ND4 (SWND4; outbred) mice were studied. Scotopic electroretinograms (ERGs) were performed to quantify the retinal response to light. We performed mitochondrial stress tests (Seahorse) using ex vivo retinal punches to determine O₂ consumption rates. Next, we performed spectral domain optical coherence tomography (OCT) to quantify retinal layer thicknesses. Quantitative mass spectrometry (MS) and bioinformatics were used to determine protein abundance and phenotypes. This work is compliant with ARVO's Statement for the Use of Animals in Ophthalmic and Vision Research.

Results: Male mice of both strains exhibit more robust a-wave and b-wave ERG amplitudes relative to females (P<0.002). Functional metabolic assays showed that, in both strains, female mice exhibit higher oxygen consumption rates than males (P<0.05). OCT revealed female C57BL/6J mice possess thicker photoreceptor layers than males (P<0.02). Proteomic MS analysis of the retina identified extensive sex- and strain-dependent differences. Of ~3400 and ~3600 retinal proteins identified in inbred and outbred mice, respectively, 107 were differentially expressed (FC >1.5) by strain, and 124 by sex.

Conclusions: Our data indicate that, in the resting state, many distinct sex- and strain-dependent, molecular and structural phenotypes exist in the adult mouse retina that contribute to statistically significant functional differences at both electrophysiologic and metabolic levels. These baseline differences raise serious concerns about assuming the anatomic, physiological, and pathophysiological translational relevance of preclinical results derived from retinal investigations based on a single sex or strain.

CONTROL ID: 3545816

SUBMITTER (NAME ONLY): Djida Ghoubay

TITLE: Three-dimensional analysis of neural crest cell migration during corneal development using tissue clearing and light-sheet microscopy

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Ghoubay, A. Tidu, Q. Rappeneau, V. Borderie, Institut de la vision, Paris, Île-de-France, FRANCE|D. Ghoubay, A. Tidu, V. Borderie, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: The cornea, the outermost layer of the eye, is formed by the migration of two waves of neural crest cells, the first wave gives rise to the endothelial layer and the second wave to the stromal one. The epithelial layer has an ectodermic origin. The study of the embryonic formation of the cornea is largely made in two dimensions, restricting the overall comprehension of his development. Recent advances in tissue-clearing techniques enable imaging of fluorescently labeled organs and entire organisms on a cellular level in three dimensions without the need for sectioning.

The objective of our study was to follow the migration of the neural crest cells in mice and zebrafish at different embryonic stages using advanced tissue clearing and three-dimensional imaging technologies. This allowed us to best characterize all steps leading to the formation of the cornea.

Methods: C56BL/6 mice and zebrafish embryos were fixed and analyzed by full-field optical coherence microscopy. After whole-mount immunostaining for Sox10 and β 3 Tubulin, We combined 3-dimensional imaging of solvent cleared organ (3DISCO) procedure (embryos were cleared in successive baths of tetrahydrofuran solution for de-hydration, dilapidation was performed in dichloromethane solution and finally, the embryos were cleared in dibenzyl ether solution), light-sheet microscopy, and Imaris software to 3D map neural crest cells migration within a whole eyeball.

Results: Migrating neural crest cells were observed before they arrived in the cornea; these cells follow the nerves and lose their neural crest marker before penetrating the cornea. Embryonic corneal morphology, organization, and layer formation were observed by FFOCM and 3D imaging. The population of the primary cornea with neural crest cells was associated with layer formation and shape acquisition.

Conclusions: We illustrate here that the combination of the 3DISCO clearing method with light-sheet microscopy, and immunostaining represents a rapid and reliable method to analyze embryonic cornea formation. This technology could also prove extremely useful to study the eye as a whole for a better understanding of eye disorders.

CONTROL ID: 3545817

SUBMITTER (NAME ONLY): Tara Tovar-Vidales

TITLE: miRNA Expression in Glaucomatous and TGF β 2 Treated Lamina Cribrosa Cells

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Tovar-Vidales, N. Lopez, R. Rangan, A.F. Clark, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: During glaucoma, there is a remodeling of the extracellular matrix (ECM) in the optic nerve head (ONH), the site of initial ON damage. ONH derived lamina cribrosa (LC) cells synthesize ECM proteins to support the ONH. However, LC cells are adversely affected in glaucoma and cause detrimental changes to the ONH. LC cells respond to mechanical strain by increasing expression of the profibrotic cytokine transforming growth factor-beta 2 (TGF β 2) and ECM proteins, including collagen. Moreover, microRNAs (miRNAs) regulate ECM gene and protein expression in different fibrotic diseases, including glaucoma. A delicate homeostatic balance between profibrotic and anti-fibrotic miRNAs may contribute to remodeling of the glaucomatous optic nerve head. We want to understand the epigenetic regulation of the ECM in the optic nerve head. The purpose of this study was to determine whether modulation of anti-fibrotic miRNAs alters the expression of ECM in human LC cells.

Methods: Primary human normal (n=3 strains) and glaucoma (n=3 strains) LC cells were derived from human donor eyes. Normal and glaucomatous LC cells were grown to confluency and treated with or without TGF β 2 (5ng/ml) for 24 hours. Differences in expression of miRNAs were analyzed using miRNA qPCR arrays. Primary LC cells were transfected with candidate miRNA mimics, inhibitors, or non-targeting siRNA (10nM) to determine ECM expression levels for collagens I and IV in human LC cells, using immunocytochemistry.

Results: miRNA PCR arrays showed that the miR-29 family was significantly decreased in glaucomatous LC cell strains compared to age-matched controls. TGF β 2 treatment significantly downregulated the expression of multiple miRNAs, including miR-29c-3p, compared to controls in LC cells. LC cells transfected with miR-29c-3p mimics or inhibitors modulated the expression of ECM proteins as seen by immunocytochemistry.

Conclusions: TGF β 2 modulates the expression of several miRNAs in cultured human LC cells that appear to stimulate a profibrotic environment and may be responsible for pathogenic remodeling of the optic nerve head in glaucoma. New therapeutic targets for miRNAs within the ONH could be identified that stop or slow the pathogenesis of glaucoma, preserving ONH structure and function.

CONTROL ID: 3545820

SUBMITTER (NAME ONLY): Chloe Stanton

TITLE: A cellular model for Brittle Cornea Syndrome

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Stanton, C. Drake, A. Findlay, Z. Mustafa, S. Campbell, V. Vitart, The University of Edinburgh MRC Human Genetics Unit, Edinburgh, Edinburgh, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The corneal stroma accounts for 90% of corneal thickness in humans, and is a major determinant of visual acuity. The rare recessive condition Brittle Cornea Syndrome (BCS), characterised by extreme thinning of the cornea and sclera and general connective tissue dysfunction, results from loss of function mutations in the poorly understood genes ZNF469 or PRDM5. PRDM5 (PR/SET Domain 5), a widely expressed transcription factor, plays an important role in extracellular matrix (ECM) production by skin fibroblasts and in bone. It is an excellent candidate to regulate ECM development and maintenance in keratocytes, the cells that synthesise the corneal stroma. Using an in vitro model of PRDM5 deficiency we aimed to elucidate the mechanisms by which PRDM5 maintains the transcriptional and proteomic profile of keratocytes to influence stromal thickness in health and disease.

Methods: CRISPR-Cas9 genome editing was used to recapitulate human BCS mutations in PRDM5 in a human keratocyte cell line, hTK. Cell lines were subject to transcriptomic profiling, and the impact of PRDM5 mutation upon the composition of cell-derived matrices assessed using western blotting, immunostaining and mass spectrometry.

Results: Homozygous frameshift mutations in PRDM5 created using CRISPR-Cas9 genome editing resulted in premature termination codons preceding all 16 C2H2 zinc finger domains, mimicking the consequences of pathogenic mutations identified in BCS patients. Expression of PRDM5 was reduced in the edited cell lines, and PRDM5 protein was not detected in cell lysates, consistent with nonsense mediated decay of mutant transcripts. The expression of genes with important roles in keratocytes was altered by loss of function of the transcription factor PRDM5, changing the composition of ECM in vitro.

Conclusions: The creation of a cellular model of PRDM5 dysfunction in a keratocyte cell line offers a unique entry point for investigating the poorly understood regulatory processes shaping the stroma in health and disease. Transcriptomic and proteomic analyses highlight pathways that contribute to the development and maintenance of a healthy corneal stroma. Work remains to determine whether these pathways may be modulated for diagnostic or therapeutic benefit in conditions such as BCS or keratoconus where the cornea thins progressively over time. Furthermore, the mechanisms uncovered by this study may have wider implications in connective tissue disorders.

CONTROL ID: 3545821

SUBMITTER (NAME ONLY): Jason Bacharach

TITLE: Clinical responsiveness to RVL-1201, a novel oxymetazoline 0.1% ophthalmic solution for the treatment of acquired blepharoptosis: results from two phase 3 clinical studies

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: RVL-1201 (oxymetazoline 0.1%) is a novel pharmacologic agent administered as a once-daily eye drop for the treatment of acquired blepharoptosis in adults. Phase 3 clinical data support the efficacy of RVL-1201, demonstrating significant mean improvement of superior visual field deficits and elevation of the upper eyelid. Clinically, it is important to define the overall responsiveness of the study population to treatment to fully ascertain the robustness of the treatment effect. The purpose of this analysis was to evaluate the proportion of subjects demonstrating a positive response to once-daily RVL-1201 administration.

Methods: In two randomized, double-masked, placebo-controlled phase 3 clinical studies, N=304 subjects received RVL-1201 or vehicle once daily in both eyes for 42 days. This analysis evaluated the proportion of subjects demonstrating a positive clinical response to RVL-1201 (relative to their pre-dose baseline measurement on treatment day 1), with respect to the primary study efficacy endpoint: number of points seen in the top 4 rows of the Leicester Peripheral Field Test (LPFT). For LPFT assessment, 'any improvement,' '≥50% improvement,' and '≥90% improvement' were defined as a >0% increase, ≥50% increase, and ≥90% increase, respectively, in the number of points seen versus baseline.

Results: Two hours following RVL-1201 instillation on treatment day 14 (n=203 RVL-1201; n=101 vehicle), 87.8% of subjects demonstrated some degree of improvement (>0%) on the LPFT, 40.8% of subjects demonstrated ≥50% improvement, and 16.8% of subjects demonstrated ≥90% improvement on this measure of superior visual field function. In contrast, 60.8%, 18.6%, and 5.2% of subjects in the vehicle group demonstrated any improvement, ≥50% improvement, and ≥90% improvement, respectively.

Conclusions: These data support previously reported efficacy findings from phase 3 clinical studies. A large proportion of subjects demonstrated a positive response to once-daily RVL-1201 administration (superior visual field improvement). These results substantiate RVL-1201 as a potentially promising non-surgical treatment option for patients with acquired blepharoptosis.

CONTROL ID: 3545822

SUBMITTER (NAME ONLY): Eric Romanowski

TITLE: Are COVID-19 Antivirals Active against Adenovirus?

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.G. Romanowski, K.A. Yates, J.E. Romanowski, R.P. Kowalski, The Charles T. Campbell Ophthalmic Microbiology Laboratory, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, PA, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Presently, there is no FDA approved antiviral therapy for the treatment of adenovirus (Ad) ocular infections, the most common ocular viral infection worldwide. During the COVID-19 pandemic, much attention has been placed on several potential antiviral treatments for SARS-CoV-2 infections. Remdesivir, hydroxychloroquine, ivermectin, and umifenovir (Arbidol) have been touted as potential COVID-19 treatments. The goal of the current study was to determine whether these potential COVID-19 antivirals produced in vitro antiviral activity against a panel of ocular adenovirus types.

Methods: The 50% inhibitory concentrations (IC_{50}) of remdesivir (REM), hydroxychloroquine (HCQ), ivermectin (IVM), and umifenovir (UMF) and cidofovir (CDV) (positive antiviral control) were determined for the human Ad types Ad3, Ad4, Ad5, Ad7a, Ad8, Ad19/64 and Ad37 using standard plaque-reduction assays on A549 cells. Briefly, cells infected with ~100 PFU of the Ad types were treated with final concentrations of the antivirals of 100, 10, 1.0, 0.1, 0.01 and 0.001 μ M. After incubation, the numbers of plaques from each virus/drug concentration were counted and the mean IC_{50} concentrations from 2-3 assays were determined by regression analysis.

Results: The range of mean in vitro IC_{50} concentrations for each antiviral across the range of Ad types are as follows: The positive antiviral control, CDV, ranged from 0.47 - 9.62 μ M; REM ranged from 0.21 - 11.27 μ M; UMF ranged from 3.72 - 64.8 μ M; IVR ranged from 2.60 - 201.3 μ M; and HCQ was > 10 μ M for all Ad types because of toxicity to the A549 cells demonstrated at the 100 μ M concentrations. REM produced lower IC_{50} concentrations than CDV for 5 of 7 Ad types.

Conclusions: REM demonstrated anti-adenovirus activity in vitro in a range similar to that demonstrated by cidofovir. UMF and IVR demonstrated less antiviral activity than CDV and REM. The anti-adenovirus activity of HCQ could not be accurately determined. Further investigation of REM as an antiviral for adenovirus is indicated.

CONTROL ID: 3545824

SUBMITTER (NAME ONLY): John Rodriguez

TITLE: Blue Color Contrast Test in non-advanced age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Rodriguez, M. Chapin, G. Wallstrom, M.B. Abelson, Ora, Massachusetts, UNITED STATES|G. Wallstrom, statistics and data corp, Arizona, UNITED STATES|M.B. Abelson, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cone dysfunction is a known pathological process in age-related macular degeneration (AMD). However, it is unclear if blue color sensitivity is affected in early stages of AMD. In this study, a new blue color sensitivity test was used to assess visual function in non-advanced AMD subjects.

Methods: Subjects with non-advanced AMD N=14 (grade 1 to 4 on AREDS simplified scale) and normal controls N=25 (AREDS grade 0) with best visual acuity (VA) 20/25 or better during their baseline visit were included. Color contrast sensitivity was tested using a computerized system. Testing was done for the study eye, with best correction in place and non-tested eye occluded. The stimulus was a blue Landolt C target presented on an equiluminant background. Two background levels of high mesopic and low mesopic levels were used. For each background, the stimulus was initially presented at high contrast level which then progressively reduced in contrast. Threshold was determined based on a stair-case method. For each background, the minimum contrast needed to correctly identify the stimulus orientation was recorded as the threshold. Subjects also underwent other common visual tests such as standard ETDRS VA, and low luminance 2.0 neutral density (ND) ETDRS VA.

Results: Blue color sensitivity showed worsening in the non-advanced AMD group compared to age-matched normal group, for both high mesopic and low mesopic levels, although the results did not reach statistical significance. Mean threshold in the high mesopic background was 0.14 ± 0.08 in AMD group and 0.11 ± 0.06 in normal group ($p=0.12$). Mean threshold in the low mesopic background was 0.29 ± 0.15 in the AMD group and 0.22 ± 0.08 in the normal group ($p=0.09$). Both normal subjects and non-advanced AMD subjects showed reduced sensitivity in low mesopic testing condition compared to high mesopic testing. No difference between the two groups were found using other common tests such as standard ETDRS VA and 2.0 ETDRS VA.

Conclusions: Blue color contrast testing could capture subtle color contrast deficits in early/intermediate stages of AMD and may be useful test for assessing color function in AMD studies.

CONTROL ID: 3545830

SUBMITTER (NAME ONLY): Raquel Goldhardt

TITLE: Peripapillary Halos in Inflammatory Optic Neuritis of Birdshot Chorioretinopathy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Goldhardt, M. Khodeiry, X. Liu, T.A. Albini, M. Sayed, G. Gregori, R.K. Lee, Bascom Palmer Eye Institute - Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|R. Goldhardt, Ophthalmology, Miami VA Healthcare System, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Peripapillary halos (PPHs) are peripapillary changes observed in normal eyes and eyes with different disorders. Recognizing the microstructure and mechanism of development of these halos will help clinicians understand the different associated retinal and optic nerve head (ONH) pathologies. We report the in-vivo histologic characterization of PPH in birdshot chorioretinopathy (BSCR) patients.

Methods: Prospective series of 6 eyes of 3 patients with convalescent BSCR. In addition, to complete ophthalmic examinations, patients underwent ONH imaging using swept-source optical coherence tomography (SS-OCT), color and red-free photography, and fundus autofluorescence (FAF).

Results: In SS-OCT scans across the area of PPH, we observed thinning and interruption of retinal pigment epithelium-Bruch's membrane (RPE-BM) complex. These halos are a circumferential form of α - zone RPE-associated crescentic PPH, unlike the PPHs observed with myopia and normal aging that are mainly associated with β -zone atrophy. We hypothesize that circumferential PPH (versus crescentic PPA) is the result of swelling of the ONH associated with BSCR papillitis, due to stretching, thinning, and tearing of the retinal layers attached to and surrounding the border tissue of Elschnig (considered to be the optic disc border). After resolution of ONH edema, the retinal layers no longer are fully attached to the disc border and have an atrophic circumferential ring around the ONH (a halo) that is PPH.

Conclusions: PPH in BSCR patients might be used as a clinical marker for prior inflammatory optic neuropathy.

CONTROL ID: 3545832

SUBMITTER (NAME ONLY): Koray Kavakli

TITLE: Vision simulator for cataract screening using holographic near-eye display with pupil tracker

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Cataracts is caused by progressive clouding of the crystalline lens, and the only treatment is surgical replacement of the cataractous lens with an artificial intraocular lens (IOL). There are many specialized equipment (e.g. retinoscopy, aberrometers, optical coherence tomography, biometers) for the diagnosis of cataract; however, the performance of preoperative vision simulators is not sufficient for predicting postoperative visual acuity and existing devices are incapable of correcting aberrations and they are limited to static pinhole exit pupils. Holography is viewed as the ultimate display technology that can offer natural 3D with all required focus and depth cues. In this study, we propose a holographic vision simulator that provides best-corrected visual acuity of the eye with cataracts before the patient goes through cataract surgery.

Methods:

The wave-front computation algorithms in computer generated holography (CGH) enables essential features such as the ability to control the phase, size and shape of the light beam entering through the eye-pupil for an effective cataract vision simulator. Our instrument detects the small, non-cataractous regions on the crystalline lens, and directs the light beam with exit pupil shaping and pupil tracking. Holographic display shows a virtual Snellen Chart at the desired depth through these regions onto the retina, while correcting the existing refractive errors including myopia, hyperopia, and astigmatism.

Results: Ten patients with various degrees of cataracts went through eye examinations before testing the simulator instrument. All the patients demonstrated better visual acuity when tested in our holographic simulator compared to the conventional eye examination. Patients without retina diseases performed 20/40 vision, whereas the patients with AMD or glaucoma performed 20/70 vision.

Conclusions: Our holographic vision simulator was able to predict the postoperative visual acuity level of the patients before going to cataract surgery. Our augmented reality display device overperforms the existing vision simulators. This device can also be used for matching the right patient to the right choice of intraocular lenses (trifocal, monofocal, EDoF). Further studies are needed to optimize the outcomes of this selection process.

CONTROL ID: 3545833

SUBMITTER (NAME ONLY): Zahra Bakhtiar

TITLE: Internet Search Engine Queries on Blue Light Glasses in the United States

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Bakhtiar, Y. Shah, S. Gad, N. Bhagat, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many retailers advertise eyeglasses that filter out blue light from digital devices to prevent eye problems, despite the lack of scientific evidence and contradictory claims that blue light from digital devices cause any eye disease. Patients use search engines to learn about topics such as blue light filtering eyeglasses that are advertised or offered to them. In this study, we characterize the Google search term frequency patterns for insight into the increasing popularity of blue light filtering eyeglasses.

Methods: We conducted a retrospective search query analysis using Google Trends (GT) for the search term “blue light glasses,” and “glasses” as a control. Queries were restricted to web search queries in all categories by Google users in the United States (US), from January 1, 2010 to December 31, 2020. GT search term interest over time is provided as relative query frequency (RQF), which is the interest relative to the peak popularity of the search term for the given region and time period.

Results: There is a pattern of exponentially increased searches for “blue light glasses” since December 2015, with peak popularity in September 2020. The increased RQF in January 2019 (26) and April 2020 (71) may correlate with the total lunar eclipse in the US on January 20-21, 2019, and the start of the Covid-19 pandemic that had many people transition to using digital devices for work and school from home, respectively. The September 2020 peak popularity may correlate with the beginning of the academic year.

The GT pattern for the search term “glasses” was analyzed to determine if the dates of the increased RQFs for “blue light glasses” corresponded to similar dates for “glasses.” GT showed a positive linear trend in searches for “glasses”, with peak popularity in August 2017, which may be associated with the total solar eclipse in the US on August 21, 2017.

Conclusions: Although there is a lack of evidence that blue light from digital devices cause eye disease and that blue light filtering eyeglasses can prevent these eye problems, there is a trend of increasing searches for blue light glasses over time. Retailers increasingly continue to advertise and sell blue light filtering eyeglasses; ophthalmologists should be aware of this trend and educate their patients and the public on the lack of evidence for such eyeglasses, and instead focus on healthy habits that can help prevent eye strain from using digital devices.

CONTROL ID: 3545834

SUBMITTER (NAME ONLY): Fangfang Qiu

TITLE:

Plasmacytoid Dendritic Cells Depletion Promotes Retinal Neovascularization in the Mouse Model of Oxygen-Induced Retinopathy

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Qiu, B. Kenyon, D.L. Harris, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|B. Kenyon, Program in Neuroscience, Tufts University School of Graduate Biomedical Sciences, Boston, Massachusetts, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center; Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously demonstrated that plasmacytoid dendritic cells (pDCs) reside in the retina and that their frequency is increased during retinal neovascularization (NV). This study aims to investigate the role of pDCs in retinal NV.

Methods: Oxygen-induced retinopathy (OIR) was induced, by exposing pups to 75% oxygen from postnatal day (P)7 to P12, and then returning them to room air until P17 in order to cause retinal NV. pDCs were depleted by administration of diphtheria toxin (DT) to pDC-DTR (pDC-DTR OIR + DT) mice at P11, with C57BL/6N wild-type mice receiving DT (WT OIR + DT) and pDC-DTR mice receiving PBS (pDC-DTR OIR + PBS) as controls. Retinal vasculature was visualized by immunostaining with isolectinB4, and leakage assessed using FITC-Dextran. pDC effects on human retinal endothelial cells (HRECs) proliferation and tube formation were assessed in vitro using transwell co-cultures. Data were analyzed by one-way ANOVA with Bonferroni's post-Hoc test.

Results: pDC-DTR pups had a similar retinal vascular density and morphology compared to WT at P7, P12, and P17. The area of retinal NV (n=5/group) was increased in pDC-DTR OIR + DT ($7.77 \pm 1.21\%$), compare to pDC-DTR OIR + PBS ($4.12 \pm 0.60\%$; $p < 0.05$) and WT OIR + DT ($4.46 \pm 0.73\%$; $p < 0.05$) mice, particularly in the peripheral retina, with $6.88 \pm 1.42\%$, $2.17 \pm 0.30\%$ ($p < 0.01$), and $2.83 \pm 0.94\%$ ($p < 0.05$), respectively. The area of leakage (n=3/group) was larger in pDC-DTR OIR + DT ($19.91 \pm 3.97\%$), compared to pDC-DTR OIR + PBS ($5.92 \pm 2.27\%$; $p < 0.05$), and WT OIR + DT ($7.41 \pm 1.84\%$; $p < 0.05$) mice. Following 48h of co-culture with 5×10^3 , 10×10^3 , or 20×10^3 pDCs, HRECs proliferation was decreased in a density-dependent fashion to $73.0 \pm 2.63\%$ ($p < 0.01$), $66.4 \pm 1.51\%$ ($p < 0.001$), and $52.7 \pm 1.51\%$ ($p < 0.001$) of control (HRECs alone). The proliferation was decreased to $74.1 \pm 1.57\%$, $52.7 \pm 2.40\%$, and $39.2 \pm 2.10\%$, respectively, at 24 h ($p < 0.001$), 48h ($p < 0.001$), and 72h ($p < 0.001$) after co-culture with 20×10^3 of pDCs in a time-dependent fashion. The tube length was decreased to $69.5 \pm 2.41\%$, and $62.3 \pm 2.98\%$, respectively, at 12h after co-cultured with pDCs at a density of 5×10^3 ($p < 0.01$), and 20×10^3 ($p < 0.05$).

Conclusions: pDCs play an inhibitory role in retinal NV in the mouse model of OIR, via direct inhibition of HRECs, providing new insights into retinal angiogenesis and pDCs function, suggesting therapeutic potential of pDCs for neovascular diseases.

CONTROL ID: 3545835

SUBMITTER (NAME ONLY): Divya Narayanan

TITLE: Longitudinal evaluation of variable contrast flicker test in non-advanced age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Narayanan, J.D. Rodriguez, M.B. Abelson, Ora, Inc, Massachusetts, UNITED STATES|G. Wallstrom, Statistics & Data Corporation, Arizona, UNITED STATES|M.B. Abelson, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is important to identify sensitive visual function endpoints that can capture visual deficits during early stages of dry age-related macular degeneration (AMD) for development of novel therapeutics for non-advanced AMD. In this study, we report longitudinal follow-up data on subjects whose baseline results on assessing various visual function tests were previously published.

Methods: Subjects with non-advanced AMD N=23 (grade 1 to 4 on AREDS simplified scale) and normal controls N=34 (AREDS grade 0) with best visual acuity (VA) 20/25 or better during their baseline visit were followed up longitudinally one year later. Several visual function tests were re-evaluated including common tests such as standard ETDRS VA, ETDRS VA (2.0 neutral density (ND)), Pelli-Robson contrast sensitivity (CS) and novel tests including the variable contrast flicker (VCF) test and low luminance tablet reading, both developed at Ora. For Ora-VCFTM test the minimum contrast needed to detect the stimulus was recorded as the threshold. For tablet reading, reading speed was recorded in words per minute (wpm). Differences between the groups were compared. Change from baseline visit was calculated.

Results: Longitudinal follow-up data was available for 53/57 subjects from baseline visit. Consistent with results from the baseline visit, at the follow-up visit the Ora-VCFTM test found significant differences between non-advanced AMD (mean 0.59 ± 0.25) and normal controls (0.37 ± 0.15) ($p=0.0002$). At the follow-up visit, the Ora-VCFTM threshold changed by 0.048 in AMD group and 0.068 in normal group ($p=0.79$). Reading speed using low luminance tablet was not significantly different during the follow-up visit (126.2 ± 33.5 wpm in AMD and 134.6 ± 42.6 in normals, $p=0.45$). No difference between the groups were found using the commonly used VA tests in the follow-up visit. The mean ETDRS LogMAR VA was 0.07 ± 0.12 in AMD group and 0.06 ± 0.09 in normal group ($p=0.80$). The mean 2.0ND VA was 0.28 ± 0.14 in AMD and 0.27 ± 0.13 in normal group ($p=0.81$). The mean Pelli-Robson CS was 1.58 ± 0.20 in AMD and 1.74 ± 0.23 in normal group ($p=0.009$).

Conclusions: The Ora-VCFTM contrast sensitivity test using a flickering target, was consistently able to identify visual dysfunction in non-advanced AMD. Ora-VCFTM test could serve as an endpoint for early and intermediate AMD therapeutic trials.

CONTROL ID: 3545837

SUBMITTER (NAME ONLY): Claudia Thieme

TITLE: Anterior Segment swept source OCT for filtering bleb evaluation after Gel Stent implantation

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Thieme, R. Burk, Ophthalmology, Klinikum Bielefeld Rosenhohe, Bielefeld, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: The outcome of filtration surgery depends on filtering bleb (FB) persistence. The aim of this study is to evaluate bleb morphology and persistence by anterior segment swept source OCT (ASOCT) after Gel-Stent-Implantation (XENTM).

Methods: ASOCT scans (Anterior ®, OCT II, Heidelberg Engineering) of the FB were recorded in 44 eyes of 44 glaucoma patients (30 primary open-angle-glaucoma (pOAG), 11 secondary open-angle glaucoma with pseudoexfoliation (sOAG with PEX) and 3 with pigmentdispersion; 17 female, 27 male; mean age 71 ±12 years; visual field Median MD 10.3; Median sLV 6.4) at 97 days (±52 days, T1) and 690 days (±242 days, T2) postoperatively. FB morphology was classified as microcystic (m), mixed (mx) or absent (a) according to the ASOCT scans. Correlations between FB classification, postoperative intraocular pressure (IOP) and medical therapy (TX) were analyzed with IBM SPSS Statistics Version 21.

Results: AT T1, FB classification was n=39 (m), n=1 (mx) and n=4 (a). FB classification at T2 resulted in n= 19 (m), n=14 (mx) and n=11 (a). IOD reduction was significant (T0 to T1: mean 6.8±1.3, p=0.000; T0 to T2: mean 7.6±1.9, p=0.000). MED reduction was significant (T0 to T1: mean 2.4±0.2, p=0.000; T0 to T2: mean 2.8±0.5, p=0.000). Bleb classification remained stable in n=18. A change of bleb classification between T1 und T2 occurred in 26 eyes : m to mx (n=13); m to a (n=9); mx to a (n=1); a to m (n=2) and a to mx (n=1).The revision rate at 180 days was 55.6% and at 365 days 72.2%.

Conclusions: By ASOCT scans, most filtering blebs after XEN Gel stent implantation have a microcystic appearance in the short postoperative period. However, bleb appearance may change in the follow up period. Further studies are needed to evaluate long term bleb persistence.

CONTROL ID: 3545839

SUBMITTER (NAME ONLY): Eric Bankaitis

TITLE: Therapeutic Efficacy of BIOP 653.1 in a Rabbit Model of Chronic Retinal Neovascularization

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Bankaitis, J. Prater, D. Culp, Powered Research, LLC, Morrisville, North Carolina, UNITED STATES|D. White, Biophtha, Inc., Suwanee, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We proposed to test retention of vascular leakage-inhibiting function in a novel anti VEGF/anti IL17a antibody, BIOP 653.1 (Biophtha, Suwanee, GA), versus Aflibercept (Regeneron Tarrytown, NY) in a chronic DL-a-Aminoadipic acid (AAA)-induced vascular leakage model.

Methods: Dutch Belted rabbits were injected intravitreally (IVT) with 1.0 mg of AAA (Sigma) in left (OS) eyes two weeks prior to 50 mL IVT administration of Aflibercept (2 mg; Group 1) or BIOP 653.1 (2.5 mg; Group 2). Right eyes (OD) remained non-AAA-treated in Group 1 and Group 2. Group 2 OD received BIOP 653.1 to assess test article safety. Evaluations at day -2 prior to dose at day 0 confirmed leakage induction and animals were stratified across groups according to leakage severity. Slit lamp biomicroscopy was used to evaluate ocular inflammatory scores (Hackett-McDonald [HM]) alongside monitoring of intraocular pressure (IOP) on days -2, 1, 3, 7, 14 and 28. Fluorescein angiography and fundoscopy were performed on days -2, 7, 14, 21 and 28. Background-normalized total leakage signal was determined by image analysis to quantify changes in leakage signal over time.

Results: AAA-induced vascular leakage occurred in 10/10 rabbits by day -2. Resolution of leakage was comparable between Aflibercept and BIOP 653.1, suggesting that BIOP 653.1 retained leakage-inhibiting anti VEGF function. By day 14 HM scores were elevated in OS eyes treated with BIOP 653.1 compared to Aflibercept-injected OS eyes, and HM scores remained elevated thereafter. Results from IOP measurements and ocular exams were documented.

Conclusions: BIOP 653.1 is a novel multifunctional antibody with anti VEGF and anti IL17a components. Biophtha partnered with Powered Research to determine if anti VEGF activity is retained through BIOP 653.1 engineering and manufacture using an established rabbit model. Here we demonstrate inhibition of vascular leakage by BIOP 653.1 with efficacy comparable to that of Aflibercept. BIOP 653.1 is early in development and a likely candidate for studies to determine half-life and durability of effect. We did not expect effects from the BIOP 653.1 IL17a component due to low sequence conservation between human and rabbit IL17a epitopes. Testing in primates will be needed to assess activity of the BIOP 653.1 anti IL17a component.

CONTROL ID: 3545841

SUBMITTER (NAME ONLY): Ana Villaplana Velasco

TITLE: Image quality adjustment can compensate for fractal dimension interocular/intraocular variability and improve disease associations

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Villaplana Velasco, E. Pairo-Castineira, T. MacGillivray, A. Tenesa, M.O. Bernabeu, The University of Edinburgh, Edinburgh, Edinburgh, UNITED KINGDOM|M. Rama Krishnan Mookiah, S. Hogg, E. Trucco, University of Dundee, Dundee, Dundee, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: There is increasing evidence that retinal vascular fractal dimension (D_f) is associated with multiple diseases, like diabetes or cardiovascular events. It is currently unknown whether inter/intraocular D_f variability may affect these associations and to which extent.

Methods: We segmented and classified ~195,000 fundus images available in UK Biobank (UKB) using VAMPIRE and by reproducing a SVM classifier based on the scans' white pixel ratio, largest connected component and number of connected components, respectively. This classifier was trained with 448 UKB images which previously were manually graded for quality. We computed an automated quality score from the SVM encapsulating the clarity, connectivity, and length of each scan. We then derived D_f from ~73,000 good quality scans with VAMPIRE. We estimated Pearson's correlation (r^2) and association estimates between D_f measures of participants with both eyes scanned and those with two scans of the same eye. We used quality-corrected D_f measures, stratified by left-right eye, to calculate r^2 and association estimates with health data from UKB

Results: Although the D_f population mean and S.D. was equal in both eyes (1.48 ± 0.03), we found a moderate interocular r^2 and effect on D_f ($r^2 = 0.61$, $P\text{-val} < 2e-16$ and $\beta = 0.59$). We found a moderate intraocular r^2 in scans of the same eye taken at different times ($r^2_{\text{left}} = 0.59$, $P\text{-val} < 2e-16$ and $r^2_{\text{right}} = 0.61$, $P\text{-val} < 2e-16$), implying that there are participants with irreproducible D_f . Differences in fundus images' quality explained those cases where the D_f disparity of the same eye was higher than a S.D. unit. Interestingly, we found that quality score has the greatest effect on D_f ($\beta_{\text{left}} = 3.4E-02$, $P\text{-val} < 2e-16$ and $\beta_{\text{right}} = 3.3E-02$, $P\text{-val} < 2e-16$). Association estimates with quality corrected D_f were 2 S.D units smaller than no-corrected D_f ones, suggesting that this adjustment improves the estimation and should be included. Lastly, our results show that decreasing D_f is associated and negatively correlated with cardiovascular diseases, i.e. coronary artery disease, as previously reported

Conclusions: This study supports that inter/intraocular variability in D_f is influenced by image quality, which can lead to spurious associations. Obtaining a quality score helps evaluating imaging datasets and controls for this effect in further associations analysis

CONTROL ID: 3545842

SUBMITTER (NAME ONLY): Susmita Bose

TITLE: Fabrication of a MMP-9 triggered biomaterial for corneal wound healing

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bose, C. Phan, L.W. Jones, School of Optometry and Vision Science, University of Waterloo, Waterloo, Ontario, CANADA|C. Phan, L.W. Jones, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|E. Yim, Chemical Engineering, University of Waterloo, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Corneal injury, arising from surgery or trauma, cause tremendous pain. A soft bandage contact lens provides mechanical protection from the blinking lids while allowing the patient to continue to use their normal vision. It would be immensely beneficial if these bandage lenses could also deliver ophthalmic drugs to aid wound closure. Multiple studies have shown elevated levels of matrix metalloproteinase (MMP) enzymes, particularly MMP-9 and MMP-2, in a corneal wound. The purpose of this study was to evaluate the release of a corneal wound healing agent, Bovine Lactoferrin (BLF), from a MMP-9 triggered drug delivery material at a normal corneal temperature that could aid corneal injury.

Methods: Gelatin methacrylate (GelMA) and photoinitiator (Irgacure 2959) were mixed together in PBS to obtain a solution with 30% (w/v) of GelMA. The mixture was incubated at 60°C for 48 hours. BLF was added to the mixture and centrifuged for 10 mins at 5000 rpm. The mixture was incubated for another 30 mins at 60°C before being pipetted into a mould, and then incubated at 4°C for 1 h, and then polymerized in a UV chamber for 5 mins (GelMA+) producing circular shaped discs (diameter = 6 mm, thickness = 650 µm). The samples (n=4) were washed in 1 mL of PBS for 24 hours to remove any loosely bound drug. After washing, the samples were placed in varying concentrations of MMP-9 at 37°C for 5 days. At t = 0, 1, 12, 24, 48, 72, 96, 120 hours, 200 µL of the release media was withdrawn and the amount of BLF determined by ELISA.

Results: The BLF released increased over time ($p < 0.0001$) and with increasing concentrations of MMP-9 ($p < 0.0001$). This indicates that MMP-9 degraded the 30% (w/v) GelMA+ material to facilitate the release of the bound wound healing agent from the polymer network. Overall, the drug release was sustained for the entire 5 day period for all MMP-9 concentrations ($p < 0.001$).

Conclusions: GelMA+ is a biocompatible material that is suitable for delivering therapeutics. The results suggest that increased concentrations of MMP-9 lead to an increase in BLF release. Results support that GelMA+ could be used as an enzyme-triggered ocular drug delivery.

CONTROL ID: 3545843

SUBMITTER (NAME ONLY): Yan Chen

TITLE: Roles of RPE mTOR signaling in choroid homeostasis

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Chen, C. Litwin, K. Youngsil, Department of Ophthalmology, OUHSC, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|J. Cai, Department of Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported that hyperactivation of the mechanistic target of rapamycin complex 1 (mTORC1) in the retinal pigment epithelium (RPE) leads to RPE dysfunction, followed by degeneration of the photoreceptor and choroid. The goal of the current project is to investigate the underlying mechanisms that link hyperactive mTORC1 signaling in the RPE and choroid atrophy.

Methods: RPE-specific, TSC1-deficient mice were established by crossing TSC1-floxed mice with transgenic mice with Bestrophin promoter-driven Cre expression. Choroid thinning was examined on both histological sections and cryosections. Flow cytometry analysis was used to characterize and compare cell populations of choroid between RPE-TSC1 deficient mice and littermates. The expression level of target genes were measured at both mRNA and protein levels using q-RT PCR and western blot, respectively. The subcellular and tissue distributions of the proteins were examined using immunostaining on both cryosections of the posterior eye and flat-mounted RPE/choroid or choroid tissue only. The level of secreted vascular growth factors was determined by ELISA. Visual functions were measured by electroretinogram (ERG).

Results: RPE-specific TSC1 deficient mice had choroid thinning. There was a progressive loss of choroicapillary markers. When analyzed for major regulators of choroidal vessel growth and homeostasis, we found increased production of Angiopoietin-2 from RPE with TSC1-deficiency.

Conclusions: Hyperactive mTORC1 in the RPE caused choroid atrophy via RPE-derived Angiopoietin-2. Expression of Angiopoietin-2 in the RPE indicates the paracrine effects in addition to the canonical autocrine regulation of choroidal endothelial function.

CONTROL ID: 3545844

SUBMITTER (NAME ONLY): Hamid Ahmadi

TITLE: sFLT01-anti-ANG2: a Novel Potent Inhibitor as a Next-generation Anti-angiogenic Molecule

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Ahmadi, Ophthalmic Research Center, Research Institute for Ophthalmology and Vision Science, Shahid Beheshti University of Medical Sciences, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|H. Latifi-navid, Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|Z. Soheili, Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|M. Sadeghi, Department of Medical Genetics, National Institute of Genetic Engineering and Biotechnology, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|S. Samiei, Blood Transfusion Research Center, High Institute for Research and Education in Transfusion Medicine, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|E. Ranaei Pirmardan, Molecular Biomarkers Nano-Imaging Laboratory, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|S. Taghizadeh, Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|F. Zakeri, Department of Molecular Medicine, National Institute of Genetic Engineering and Biotechnology, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|S. Arab, Department of Biophysics, School of Biological Sciences, Tarbiat Modares University, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|S. Tajbakhsh, Bahar Medical Laboratory, Tehran, IRAN (THE ISLAMIC REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Current treatment for neovascular age-related macular degeneration includes intravitreal injection of anti-vascular endothelial growth factors (anti-VEGFs). However, clinical experience demonstrates that the efficacy of such therapies is restricted due to the overlapping and compensatory alternative angiogenic pathways. Here, we introduce a new anti-angiogenic molecule (sFLT01-anti-ANG2) that neutralizes VEGF, Placental Growth Factor, and Angiopoietin2 simultaneously and reduces the initiation of associated signaling pathways.

Methods: We investigated sFLT01 molecule components via bioinformatics tools and got access to its sequences. We augmented the nucleotide sequence of sFLT01 by another genetic syntax, against Angiopoietin2. Therefore, we analyzed the tertiary structures of the molecule with MODELLER and Nanome. The best models were applied in docking analysis with ClusPro. The cloning process of the construct in the AAV2 vector was performed and the result was confirmed by PCR and restriction enzyme digestion. RNA extraction and condition media collection were performed following the transfection of HEK293T cell line by AAV2-sFLT01-anti-ANG2. Expression of the gene of interest and its protein output was evaluated by real-time PCR and western blotting respectively. To confirm the functional anti-angiogenic potency of the protein, tube formation assay, phospho-Tie2 assay, and ligand-receptor interaction ELISA were performed

Results: The sFLT01-anti-ANG2 molecule was designed by bioinformatics tools and cloned into the pAAV-MCS vector. HEK293T cells were successfully transduced. RT-qPCR represented that the gene was expressed 4000 fold in HEK293T cell culture. Western blot technique confirmed the presence of this protein in the condition media collected from transfected HEK293T cell culture. The decrease in vascular network observed in tube formation assay showed that the molecule was functional. Also, the reduced amount of absorption observed from phospho-Tie2 assay (0.172.5/1.034,1.0455) and Ang2-Tie2 interaction ELISA assay (0.558/0.995,0.868) demonstrated effective function of this molecule.

Conclusions: We propose that targeting various angiogenic pathways by sFLT01-anti-ANG2 may be a fundamental approach in development of the next generation antiangiogenic therapeutic drugs.

CONTROL ID: 3545845

SUBMITTER (NAME ONLY): Terrence Murphy

TITLE: Stage 1 Macular Holes Potentially Closed with Topical Therapy

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Murphy, C. Shah, M.W. MacCumber, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|A. Mackin, D. Skondra, Ophthalmology, University of Chicago Pritzker School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Several case series have demonstrated a potential role for the closure of small stage 4 macular holes with topical therapy. Drops have included a non-steroidal anti-inflammatory drug (NSAID), steroid, and/or carbonic anhydrase inhibitor (CAI). We now report the first such case series for the treatment of stage 1 (outer lamellar) macular holes in eyes with PVD.

Methods: A retrospective case series of patients with stage 1 macular holes at two Chicago-based institutions was conducted to evaluate the efficacy of drop therapy, dose response, and loss of effect with premature discontinuation with recommended therapy.

Results: Four eyes in 4 patients were included in this series and all cases had some amount of intraretinal or subretinal fluid contributing to the partial-thickness macular hole. All had posterior vitreous detachment (PVD) and epiretinal membrane. Eyes were started on topical NSAID and steroid, and 3 cases were treated with CAI as well. One patient was unable to tolerate topical difluprednate due to steroid response and progressed to a small stage 4 hole, but after adjunctive oral acetazolamide the hole regressed to a stage 1 hole and then closed completely. All 4 cases had complete resolution of fluid and closure of the macular holes which persisted after tapering of topical therapy. Similar therapy for 4 eyes with stage 1 macular holes that did not have PVD failed to close.

Conclusions: Topical therapy is a relatively benign treatment that can potentially cause resolution of not only small stage 4 macular holes but also stage 1 (outer lamellar) holes in eyes with PVD. This may be due to the reduction in hydrational forces in line with the tractional-hydrational theory of macular holes. Topical therapy may allow some patients avoid vitrectomy surgery. Since stage 1 macular holes can close spontaneously, a randomized clinical trial would be required to prove benefit. Stability of long-term closure also requires further research.

CONTROL ID: 3545847

SUBMITTER (NAME ONLY): Alfrun Schönberg

TITLE: Effect of sCD83 on macrophages in corneal high-risk transplantation

SESSION TITLE: Corneal immunology and neovascularization I

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Schönberg, G. Braun, C. Cursiefen, F. Bock, Experimental Ophthalmology, Uniklinik Köln, Köln, Nordrhein-Westfalen, GERMANY|K. Peckert-Maier, A. Wild, D. Royzman, L. Stich, A. Steinkasserer, E. Zinser, Department of Immune Modulation, University Hospital Erlangen, Erlangen, Bavaria, GERMANY|

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ABSTRACT BODY:

Purpose: Severe inflammation of the cornea abrogates its immunological and angiogenic privilege and eventually leads to corneal blindness. Under these high-risk conditions, vision-restoring corneal transplants have dramatically reduced chances for graft acceptance. Pro-inflammatory macrophages comprise 60 % of all infiltrating immune cells in a rejected graft. We hypothesize that administration of the immunomodulatory protein sCD83 leads to a shift from pro-inflammatory classically activated macrophages (CAM), characterized among others by TNF- α , IL-6 and CD86 expression, to anti-inflammatory alternatively activated macrophages (AAM), characterized among others by CCL22, CCL17, and MSR-1 expression, and thereby promotes corneal graft acceptance.

Methods: In a model of high-risk corneal transplantation (C57BL/6 donor and BALB/c recipient mice), 50 μ g/ml sCD83 was administered locally 2 days prior to keratoplasty (KPL). Macrophages in the draining lymph nodes (dLNs) of the recipient were analyzed by flow cytometry 2 weeks post KPL. The allograft survival was determined by grading the opacity of the grafts weekly for 8 weeks. sCD83 was also administered during cultivation of BMDMs and its effect analyzed in flow cytometry and MLR experiments.

Results: In the dLNs of sCD83-treated recipients, the frequency of MSR-1⁺ AAMs was significantly increased while significant less CD86⁺ CAMs were detected 2 weeks post KPL. 8 weeks post KPL, the number of Foxp3⁺ Tregs in the dLNs was increased and the graft survival was significantly higher in the sCD83 group. In vitro, sCD83 induced a tolerogenic phenotype in BMDMs as the expression of CCL17, CCL22 and MSR-1 was significantly upregulated while the expression of CD83 and CD86 was significantly downregulated. In co-culture experiments showed sCD83-treated BMDMs an impaired ability to induce allogeneic T cell proliferation while increased numbers of Foxp3⁺ Tregs were detected. TNF- α as well as IL-6 concentrations were decreased in co-culture supernatants when BMDMs were treated with sCD83.

Conclusions: Our results are consistent with our hypothesis that administration of sCD83 leads to a shift from CAM to AAM which prolongs allograft survival in a high-risk corneal transplantation model. Thereby, we not only confirmed the important role of macrophages in the transplant setting, but also demonstrated the beneficial potential of their modulation by sCD83 to prolong corneal graft survival.

CONTROL ID: 3545851

SUBMITTER (NAME ONLY): Lea Rodriguez

TITLE: Tau limits visual plasticity in adult mice

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Rodriguez, J.B. Mdzomba, S. Joly, F. Zine-Eddine, V. Pernet, Ophthalmology, Centre Hospitalier de l'Universite Laval, Sainte-Foy, Quebec, CANADA|L. Rodriguez, J.B. Mdzomba, F. Zine-Eddine, Ophthalmology, Universite Laval Faculte de medecine, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Tau is a microtubule-associated protein that has been involved in glaucoma. Its physiological function in the visual system is unknown. The aim of this study was to investigate the contribution of Tau to the maturation and the plasticity of the intact mouse visual system.

Methods: Western blotting and immunofluorescent analysis of Tau isoform (T3R and T4R) expression were performed on retinae and visual cortices from postnatal day 1 (P1) to P360. To induce visual plasticity, monocular deprivation (MD) was realized by suturing right eyelids. After 5 days of MD, the expression of Tau isoforms, Erk, a modulator of neuronal plasticity, and acetylated tubulin, a microtubule instability marker, was followed in the visual cortex (VC) by Western blotting. Visual function was assessed by electroretinogram (ERG) recordings, optokinetic reflex (OKR) and visual evoked potential (VEP) recordings in the left binocular VC in response to left and right eye stimulations, in young adult (3-5 months) and old (20-24 months) WT and Tau knockout (Tau KO) mice. VEPs were used to calculate an ocular dominance index (ODI). Retinal ganglion cell (RGC) survival was quantified on retinal flat-mounts.

Results: In the first postnatal month, T3R downregulation and T4R upregulation in retinal and VC lysates were associated with the decline in neuronal plasticity occurring during the critical period. ERG recordings and RGC survival showed no difference between WT and Tau KO during aging. The OKR of Tau KO vs WT did not differ. In contrast, the ODI was significantly weaker in Tau KO than in control WT. In MD mice, Western blot and immunofluorescent analyses revealed increased expression of Tau isoforms in the VC of the deprived eye, suggesting an implication of Tau in visual plasticity. The rise in OKR sensitivity induced by MD was statistically higher in Tau KO than in WT during aging, suggesting that Tau limits the activation of neuronal plasticity in the VC. After MD, the ODI of Tau KO was similar to that of WT and to nondeprived Tau KO. Western blot results showed increased levels of Erk in Tau KO relative to WT mice. Interestingly, the Tau KO cortex contained less acetylated tubulin, indicating possible increased microtubule instability in the absence of Tau.

Conclusions: Our results suggest a new function for Tau in the adaptive plastic mechanisms operating in the adult visual brain subjected to sensory experience changes. Tau may limit visual plasticity in adult mice.

CONTROL ID: 3545858

SUBMITTER (NAME ONLY): Wei Zhang

TITLE: Injury dependent angiogenic responses in the cornea

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Zhang, K. Hadrian, C. Cursiefen, F. Bock, Ophthalmology Department, Universitat zu Koln, Cologne, Nordrhein-Westfalen, GERMANY]

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ABSTRACT BODY:

Purpose: Pathologic insults like transplant rejection or trauma lead to blindness and to a so called “high-risk situation” with increased rejection rates after subsequent keratoplasty. These insults cause different immunological tissue responses. Aim of this study was to evaluate the impact of different types of corneal injury on hem- and lymphangiogenesis.

Methods: We used 5 types of corneal injury model and naïve corneas as control (n=5 each). The suture model is the intrastromal placement of three 11.0 nylon sutures. A 2 mm filter disc soaked in 1 M NaOH was placed on the central corneal surface for 30s and the eyes were washed with PBS as the alkali burn model. Incision injury was performed in the central cornea with a linear perforating incision with 1 mm length. Corneal grafts were placed into an avascular recipient bed as the normal-risk keratoplasty model (NR-KPL). Corneal grafts were placed into the suture-induced neovascularized recipient as the high-risk keratoplasty model (HR-KPL). C57BL/6 mice were used as donor tissue in KPL and all others were Balb/c mice. 1 week after incision and 2 weeks after all other different injuries, corneas were excised and stained with CD31 and LYVE-1 for the quantification of blood vessels and lymphatic vessels.

Results: HR-KPL and NR-KPL initiated the highest hemangiogenesis (HA), significantly higher than all other groups. Suture placement induced the second most powerful angiogenic response, significantly higher than alkali burn, incision and naïve eyes. Alkali burn evoked the third most powerful HA-response, significantly higher than naïve eyes. The incision model did not induce angiogenesis. Regarding lymphangiogenesis (LA), NR-KPL provoked the highest response, significantly higher than all other groups except HR-KPL. LA in HR-KPL was significantly higher than all other groups except NR-KPL and suture placement. Suture placement and alkali burn had a significantly higher LA compared to incision and naïve eyes. Incision provoked no significant LA compared to naïve corneas. Regarding LYVE-1+ macrophages, only NR-KPL and suture placement showed significantly more infiltration.

Conclusions: Different types of corneal injury cause different types and degrees of neovascularization. In conclusion, different high-risk situations might result in different corneal graft survival rates. Therefore, also the potential clinical treatment of different injuries in the future might need to be customized.

CONTROL ID: 3545860

SUBMITTER (NAME ONLY): Elisabeth Brunner

TITLE: AO-OCT imaging of the retina with a pyramid wavefront sensor

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Brunner, M.F. Shirazi, W. Drexler, R.A. Leitgeb, C.K. Hitzenberger, M. Pircher, Center for Medical Physics and Biomedical Engineering, Medizinische Universität Wien, Wien, Wien, AUSTRIA|J. Shatokhina, R. Ramlau, Johann Radon Institute for Computational and Applied Mathematics, Linz, Oberösterreich, AUSTRIA|

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ABSTRACT BODY:

Purpose: To investigate the performance of a pyramid wavefront sensor (P-WFS) for adaptive optics (AO) imaging in visual science. The P-WFS, first introduced in astronomy, promises greater sensitivity and more flexibility than the well-established Shack-Hartmann (SH-)WFS. However, ophthalmic applications of the P-WFS have not met the performance of the SH-WFS so far.

Methods: The P-WFS was implemented as an add-on (see Fig. a)) to a SH-WFS based spectral domain AO optical coherence tomography (OCT) setup. The instrument provides an axial resolution of 4.5 μm at 840 nm central wavelength and an A-scan rate of 250 kHz. For wavefront sensing, part of the imaging light returning from the retina is used. The scanning motion of the imaging beam over the retina creates an averaging effect in the WFS data which is essential for successful AO correction with the P-WFS (see Fig. b)). Retinal images were recorded in the fovea of several healthy volunteers with the P-WFS and the SH-WFS in a single session. En-face visualization of the photoreceptor layer via segmentation and cross-sectional image data allow for a comparison of the two sensor types.

Results: The representative image data displayed in Fig. c) show en-face images of the photoreceptor mosaic and B-scan images obtained with the P-WFS and the SH-WFS. The power spectra of the enface images show the ability of the instrument to resolve the photoreceptors using either sensor type. With the P-WFS, single cone photoreceptors close to the fovea centralis can be visualized in almost the entire fovea clearly matching the image quality achieved with the SH-WFS. It is subject of on-going investigation if the clearer appearance of the photoreceptor cells and the higher clarity of the Yellott's ring obtained for the P-WFS data is due to a general superiority of the sensor in ophthalmic applications.

Conclusions: The suitability of the P-WFS for AO imaging in visual science is demonstrated in vivo with AO-OCT. The parallel implementation of the P-WFS and a SH-WFS allows for a direct comparison of the two sensor types. Photoreceptor cells could be visualized in the fovea with both sensors demonstrating the high resolution capability of the system. The image quality obtained with the P-WFS equals or even outperforms that of the SH-WFS indicating that the P-WFS can be a promising alternative for the SH-WFS in ophthalmic imaging.

CONTROL ID: 3545861

SUBMITTER (NAME ONLY): Kelsey Bradshaw

TITLE: A computational model of neovascularization in wet age related macular degeneration

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bradshaw, A. Kjar, M. Cotner, J. Fielding, T. Teeples, Z. Zhang, E. Vargis, Utah State University, Logan, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: In age-related macular degeneration (AMD), retinal pigment epithelial (RPE) cells overexpress pro-angiogenic proteins, such as vascular endothelial growth factor (VEGF), causing the growth of new blood vessels. This neovascularization can be simulated by developing a computational behavioral model to predict the extent and probable location of blood vessel growth based on the production of VEGF by the RPE. Computational modeling allows for more high throughput, time efficient, and inexpensive experiments than in vitro or animal models.

Methods: The computational model mimics the space between a choroidal parent vessel and the RPE layer as a 2-dimensional matrix. The lower boundary of the matrix represents the RPE layer and serves as a point source of VEGF. The VEGF diffuses towards the upper boundary of the matrix which represents a parent vessel in the choroid from which new blood vessels will grow. Tip cells in the parent vessel react to increasing levels of VEGF by secreting protease. The protease degrades the fibronectin of the extracellular matrix allowing the tip cell to escape the parent vessel and form a new blood vessel. In the computational model, tip cells move in a biased random walk with the probability of moving to an adjacent location based on chemoattractance which is calculated using the concentration of free VEGF, the amount of protease secreted by the tip cell, and the extent of fibronectin degradation. This methodology provides an effective prediction of the extent and location of neovascularization given VEGF production values. These results will then be validated with live imaging HUVEC cell migration studies.

Results: Our model produces a graphical representation of blood vessel growth, as well as 3D graphs of VEGF, protease, and fibronectin concentrations. Consistent with data found in scientific literature, there is a larger extent of blood vessel growth with higher VEGF expression and new blood vessel growth is biased towards higher concentrations of VEGF. These results will be validated by our HUVEC cell migration studies.

Conclusions: With the parameter values found through experimentation, the model accurately predicts blood vessel growth over time when RPE cells are overexpressing VEGF in wet AMD. The computational model reduces test variables and provides parameters for lab experiments saving researcher time and money.

CONTROL ID: 3545862

SUBMITTER (NAME ONLY): Leyna Boucherit

TITLE: 3D visualization of human retina cells' anatomy using expansion microscopy

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ocular pathologies are the most common sensory impairments that greatly impact quality of life. While direct consequences of the pathologies can now be followed using cutting-edge in vivo imaging, the cellular causes and degeneration of these pathologies still call for histological studies. These studies are currently restricted when trying to reach nanoscale resolution by the availability of rare and expansive microscopes (such as electron or bi-photon microscope).

We recently implemented in the team an innovative histological technic called Expansion Microscopy (ExM). This technique, based on physical, isotropic expansion of tissues, allows nanoscale imaging of biological specimens with conventional microscopes.

Here, we describe the first use of this technique in the human retina, to visualize and render in 3D the anatomy of retinal cells in physiological and pathological conditions.

Methods: Retinas were isolated and fixated in paraformaldehyde, before performing immunohistochemistry. Samples were embedded in an acrylamide gel to which fluorophores were anchored. The tissue was then enzymatically digested, expanded in water and imaged using either confocal or light-sheet fluorescent microscopy.

Results: Thanks to the nanoscale resolution allowed by this technique, we were able to study in 3D for example the anatomy of physiological and pathological cones photoreceptors, from opsin migration to the structural deformation of photoreceptors retinal layer.

Conclusions: By implementing ExM in the eye, this project made subcellular study easily accessible, thus broadening the field of possible nanoscale studies in ocular pathologies.

CONTROL ID: 3545865

SUBMITTER (NAME ONLY): Yara Lechanteur

TITLE: Supplement intake and plasma nutritional biomarkers reduce risk for second eye progression in age-related macular degeneration.

SESSION TITLE: AMD: clinical research - diet/metabolism/big data

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y.T. Lechanteur, T.J. Heesterbeek, A.I. Den Hollander, L. Lores de Motta, I.E. Acar, E.K. de Jong, B.J. Klevering, C.C. Klaver, C. Hoyng, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|A.I. Den Hollander, L. Lores de Motta, I.E. Acar, E.K. de Jong, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|C.C. Klaver, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To determine the cumulative incidence rate of second eye progression in patients with unilateral neovascular age-related macular degeneration (nAMD) over 10 years follow-up; and to study the effect of supplement use, genetic variants, and plasma nutritional biomarkers on second eye progression.

Methods: This is a historical prospective cohort study.

We selected 240 patients nAMD in one eye and non-advanced AMD in the second eye. We performed multivariate Cox regression survival analysis for second eye progression. Variables included in the model were the intake of supplements, a genetic risk score (GRS) based on 52 AMD-associated variants, and 24 plasma nutritional biomarkers, including levels and ratios of fatty acids (FA), polyunsaturated fatty acids (PUFA), monounsaturated fatty acids (MUFA), saturated fatty acids (SFA), omega-3 fatty acids (FA ω 3), omega-6 fatty acids (FA ω 6), docosahexaenoic acids (DHA), linoleic acid (LA), and levels of carotenoids, α -carotene, β -carotene, α -lycopene, β -lycopene, β -cryptoxanthin, lutein, zeaxanthin, retinol and vitamin E. The main outcome measure was the development of nAMD in the second eye.

Results: The cumulative incidence rates for second-eye progression to nAMD were 8%, 15%, 25%, 45%, 58% and 68% after 1-, 2-, 3-, 5-, 7-, and 10-years follow-up respectively, showing a declining trend in the progression rate after five years. Supplement use was protective for second eye progression (HR 0.6, P=0.010). Patients with a GRS \geq 4 were at higher risk for progression compared to patients with a GRS \leq 0 (HR 6.7, P=0.021). The highest quartiles of DHA/FA ratio (>1.20) and zeaxanthin level (>0.75 μ mol/L) were found to be protective for second eye progression compared to the lowest quartiles (HR 0.5, P=0.025 and HR 0.5, P=0.019, respectively). Supplement use was no longer significantly associated with second eye progression after correction for plasma DHA/FA ratio and zeaxanthin levels.

Conclusions: The risk of second eye progression in patients with unilateral nAMD is 10% per year in the first 5 years, and declines to approximately 5% per year after 5 to 10 years. Patients should consider taking supplements and adhere a healthy lifestyle to pursue high plasma DHA/FA ratio and zeaxanthin levels in order to reduce the risk of second eye progression and remain eyesight for a longer period.

CONTROL ID: 3545867

SUBMITTER (NAME ONLY): Annette Stengele

TITLE: Repeatability and agreement of higher order aberrations for different devices

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.L. Stengele, M. Koeppe, T. Naujokaitis, G.U. Auffarth, Ophthalmology, Ruprecht Karls Universität Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: The aim of the study was to compare the most important higher order aberrations provided by the Pentacam AXL Wave and the iTrace.

Methods: Prospective, randomised study with three consecutive measurements per eye and each device, the Pentacam AXL Wave (Oculus) and the iTrace (Tracey Technologies). Each patient completed all measurements at the same day and all measurements had good quality scores.

Forty two patients (34 right and 38 left eyes) ranging in age from 20 to 63 year (mean age was 36 ± 14 years) took part in this study. None of the patients had any known ocular pathology, all eyes were phakic.

The most crucial higher order aberrations (trefoil 30° and 0° , coma 90° and 0° and spherical aberration) of the complete eye were analysed for a 3mm zone. Repeatability was assessed with standard deviation (SD). Bland-Altman analysis was used to assess agreement between the devices.

Results: Repeatability

The mean values of the analysed HOAs and their standard deviations are: trefoil 30° - Wave $-0,021\mu\text{m} \pm 0,011$, iTrace $-0,016\mu\text{m} \pm 0,013$; trefoil 0° - Wave $-0,003\mu\text{m} \pm 0,009$, iTrace $-0,001\mu\text{m} \pm 0,012$; coma 90° - Wave $0,005\mu\text{m} \pm 0,011$, iTrace $0,008\mu\text{m} \pm 0,012$; coma 0° - Wave $0,001\mu\text{m} \pm 0,009$, iTrace $0,008\mu\text{m} \pm 0,012$; sph aberr - Wave $0,011\mu\text{m} \pm 0,005$, iTrace $0,01\mu\text{m} \pm 0,007$. A paired-samples t-test was conducted to compare the means of the devices. Only the differences of the coma 0° were statistically different ($p < .05$).

Agreement

A Bland-Altman analysis revealed the following mean differences, standard deviations and limits of agreement for the two devices ($\text{mean}_{\text{DIFF}} = \text{mean}_{\text{WAVE}} - \text{mean}_{\text{ITRACE}}$): trefoil 30° - $\text{mean}_{\text{DIFF}} -0,005\mu\text{m} \pm 0,029$, $\text{LOA}_{\text{low}} -0,062$, $\text{LOA}_{\text{upp}} 0,052$; trefoil 0° - $\text{mean}_{\text{DIFF}} -0,002\mu\text{m} \pm 0,029$, $\text{LOA}_{\text{low}} -0,059$, $\text{LOA}_{\text{upp}} 0,055$; coma 90° - $\text{mean}_{\text{DIFF}} -0,015\mu\text{m} \pm 0,027$, $\text{LOA}_{\text{low}} -0,068$, $\text{LOA}_{\text{upp}} 0,038$; coma 0° - $\text{mean}_{\text{DIFF}} -0,006\mu\text{m} \pm 0,032$, $\text{LOA}_{\text{low}} -0,068$, $\text{LOA}_{\text{upp}} 0,056$; sph aberr - $\text{mean}_{\text{DIFF}} 0,002\mu\text{m} \pm 0,017$, $\text{LOA}_{\text{low}} -0,031$, $\text{LOA}_{\text{upp}} 0,035$.

Conclusions: In general, the higher order aberrations were rather low what can be explained by the relatively young and healthy study population. The small standard deviations indicate good repeatability for both devices, however, those of the Pentacam AXL Wave tended to be smaller than the ones of the iTrace. Agreement between the devices was high even so this result remains to be confirmed for larger zones and pathological eyes, e.g. keratoconus.

CONTROL ID: 3545868

SUBMITTER (NAME ONLY): Ashik Mohamed

TITLE: Peripheral defocus of polymethylmethacrylate spherical optic monofocal intraocular lenses

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To evaluate the peripheral defocus of monofocal intraocular lenses (IOLs), thereby quantifying the accuracy of laser ray tracing (LRT) measurements of peripheral defocus.

Methods: Data were acquired on 14 polymethylmethacrylate spherical optic monofocal IOLs (overall length 12.5 mm, optic diameter 6.0 mm). The power (D) of the IOLs used were 17.5, 18, 18.5, 19, 19.5, 20, 20.5, 21, 22, 22.5, 23, 23.5, 24 and 24.5. IOLs were placed in a custom-built combined LRT and optical coherence tomography (OCT) system (Ruggeri et al, BOE 2018). Ray trace experiments were performed for incidence angles ranging from -30° to +30° in 5° increments using a raster scan (6 mm x 6 mm) with 0.25 mm spacing. An image sensor mounted on a positioning stage below the IOL acquired ray-intercept spots at different axial positions and a custom program calculated the ray slopes from the spot positions. At each angle, lens power was calculated by finding the axial position that minimizes the root-mean-square diameter of the spot pattern formed by the central 169 rays corresponding to the central 3 mm zone. For each IOL, the measured relative peripheral defocus (Figure 1) was compared to the value obtained using optical theory. The theoretical peripheral defocus was the position of the circle of least confusion calculated assuming that the IOL is a thin lens with the aperture stop located at the plane of the lens.

Results: The measured peripheral defocus (D) increased significantly (all $p \leq 0.001$) with increasing incidence angle (IOL power adjusted mean of +0.27, +0.78, +1.85, +3.25, +5.54 and +8.60 at $\pm 5^\circ$, $\pm 10^\circ$, $\pm 15^\circ$, $\pm 20^\circ$, $\pm 25^\circ$ and $\pm 30^\circ$ respectively). The IOL power mean difference (D) between the measured and predicted peripheral defocus (Figure 2) was +0.03, -0.21, -0.24, -0.74, -0.76 and -0.59 at $\pm 5^\circ$, $\pm 10^\circ$, $\pm 15^\circ$, $\pm 20^\circ$, $\pm 25^\circ$ and $\pm 30^\circ$ respectively.

Conclusions: The IOL power increases with increasing field angle corresponding to a shift towards myopic peripheral defocus. The LRT-OCT system accurately measures the peripheral power.

CONTROL ID: 3545871

SUBMITTER (NAME ONLY): Navdeep Gogna

TITLE: Identifying gene interaction effects in Adipor1 and Mfrp double mutant mice

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Adipor1^{-/-} and Mfrp^{rd6} mutant mice share similar disease characteristics such as photoreceptor (PR) degeneration, hyperopia, and uniformly flecked retina. Further, Adipor1 expression in RPE is lost in Mfrp mutant mice. Currently, MFRP function and its association with the ADIPOR1 protein are not well understood. The aim of this study was to identify individual gene contributions and digenic epistatic interactions between Adipor1 and Mfrp genes, in order to have a better understanding about their functional relationship and shared or individual pathways that lead to the shared common phenotypes.

Methods: Adipor1 and Mfrp mutant mice were outcrossed and resulting F1 offspring were intercrossed to produce Adipor1/Mfrp double mutant mice with nine possible genotypic combinations. Mice (n = 10-16/genotype, both genders) were analyzed for PR degeneration by histology and axial length measured by calipers. Two-way ANOVA and post-hoc analysis was used to study gene interaction effects.

Results: For PR degeneration, both the single (Adipor1^{-/-}/Mfrp^{+/+}, Adipor1^{+/+}/Mfrp^{rd6/rd6}) and double (Adipor1^{-/-}/Mfrp^{rd6/rd6}) mutants showed significant (p< 0.0001) degeneration as compared to wild type (Adipor1^{+/+}/Mfrp^{+/+}) mice. Both genes showed significant main effects and significant gene interaction effects confirming that PR degeneration due to one gene is dependent on the PR degeneration caused by the other gene. For axial length, while both genes showed significant main effects, no gene interaction effects were seen (p = 0.267). This confirms that while both the genes individually contribute to decrease in axial length, they do not interact to decrease the axial length and the decrease due to one gene is independent of the decrease due to another gene.

Conclusions: The observation of an interaction between two mutations is the first step towards uncovering the mechanism through which the genes of interest affect the measured phenotype. Our study confirms that both Adipor1 and Mfrp genes interact and are possibly part of the same pathway that lead to PR degeneration. On the other hand, our study suggests that even though a decrease in axial length is observed in both mutant strains, the genes do not interact and don't contribute to axial length changes via the same pathway. This study therefore provides important insight into the complexity of interactions between ADIPOR1 and MRFP that govern different disease characteristics.

CONTROL ID: 3545873

SUBMITTER (NAME ONLY): TINGYU CHU

TITLE: Promoting axon growth in human iPSC derived retinal ganglion cells by membrane-bound magnetic nanoparticles

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. CHU, C. Chiao, Life science, National Tsing Hua University, Hsinchu, TAIWAN|

Commercial Relationships Disclosure (Abstract): TINGYU CHU: Commercial Relationship: Code N (No Commercial Relationship) | Chuan-Chin Chiao: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Axon growth of implanted retinal ganglion cells (RGCs) is an important step in restoring vision for glaucoma and retinal degenerated patients. Magnetic composite materials which can be manipulated non-invasively and functionalized easily have been reported to enhance filopodial elongation of RGCs by exerting mechanical tension.

Methods: Magnetic nanoparticles (MNPs) were added in isolated human iPSC derived RGCs, and magnetic field was applied continuously for 3 days to observe RGC axon growth length and direction in vitro. These isolated human iPSC derived RGCs with membrane-bound MNPs were injected into mouse retinas, and the elongation of transplanted RGC axons was assessed in vivo.

Results: The data shows that MNPs promoted RGC axon regeneration and guided RGC axon growth toward the direction of magnetic field significantly in vitro (Fig 1). When the magnetic field was applied in vivo, transplanted RGCs showed increased axon elongation and directed growth.

Conclusions: The present study demonstrates that MNPs are a potential therapeutic strategy in promoting axon regeneration and growth in RGCs. Future application of this approach may be using MNPs coated with growth factors to further facilitate RGC axon growth.

CONTROL ID: 3545878

SUBMITTER (NAME ONLY): Ankita Kotnala

TITLE: Identification of fluorophores from human retina by TLC coupled MALDI and LC-MS/MS analysis

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kotnala, D.M. Anderson, J.A. Fincher, K.L. Schey, Vanderbilt University, Nashville, Tennessee, UNITED STATES|A. Kotnala, J. Messinger, C.A. Curcio, Department of Ophthalmology and Visual Sciences, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ankita Kotnala: Commercial Relationship: Code N (No Commercial Relationship) | David Anderson: Commercial Relationship: Code N (No Commercial Relationship) | Jarod Fincher: Commercial Relationship: Code N (No Commercial Relationship) | Jeffrey Messinger: Commercial Relationship: Code N (No Commercial Relationship) | Christine Curcio: Commercial Relationship(s);Heidelberg Engineering:Code F (Financial Support);Hoffman La Roche:Code F (Financial Support) | Kevin Schey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: A prominent aging change in human retinal pigment epithelium (RPE) under investigation for its role in age-related macular degeneration (AMD) is the accumulation of lipofuscin. Prior compositional analyses of lipofuscin revealed the fluorescent bisretinoid A2E, yet imaging mass spectrometry results suggest the presence of additional fluorophores of unknown origin. The purpose of this study is to identify and characterize new retinal fluorophores.

Methods: Human eyes (n=3) (white donors > 80 years of age) were obtained from the Advancing Sight Network. The retina was carefully removed, extracted using Folch extraction solvent, and fluorophores were separated using high performance thin layer chromatography (HPTLC) RP-18 plates using chloroform: methanol 1:1(v/v) with TFA as mobile phase. After visualization with UV absorbance and autofluorescence microscopy, fluorescent bands were separated manually and subjected to MALDI analysis using a solariX 9.4T FT ICR mass spectrometer (Bruker Daltonics) and LC-MS/MS using a Q-Exactive HF instrument (Thermo Scientific).

Results: Seven well-separated bands having UV absorbance and fluorescence properties were detected by TLC. A2E was identified in band 5 based on accurate mass measurement but was not located in the most fluorescent band. Mass spectra obtained from MALDI revealed the presence of high molecular weight species ranging from m/z 700-1100 in the intensely fluorescent bands (bands 3, 6 and 7). The molecular identity of m/z 782.557, 828.531, 711.980, 758.490 and 797.888 obtained from the most intensely fluorescent bands is currently under investigation using tandem mass spectrometry.

Conclusions: A TLC method was developed to separate retina extracts with separated bands having differing absorbance and fluorescence properties compared to A2E. The strategy will help us in the identification of fluorophores of unknown origin which may have implications in the onset of AMD.

CONTROL ID: 3545884

SUBMITTER (NAME ONLY): Mukharram Bikbov

TITLE:

Intraocular Pressure and Its Determinants in a Very Old Population. The Ural Very Old Study

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Bikbov, G. Kazakbaeva, E. Rakhimova, Ufimskij naucno-issledovatel'skij institut glaznyh boleznej, Ufa, Bashkortostan, RUSSIAN FEDERATION|S. Panda-Jonas, Institute of Clinical and Scientific Ophthalmology and Acupuncture Jonas&Panda, Heidelberg, GERMANY|J. Jonas, Department of Ophthalmology, Ruprecht Karls Universitat Heidelberg, Mannheim, GERMANY|

Commercial Relationships Disclosure (Abstract): Mukharram Bikbov: Commercial Relationship: Code N (No Commercial Relationship) | Gyulli Kazakbaeva: Commercial Relationship: Code N (No Commercial Relationship) | Songhomitra Panda-Jonas: Commercial Relationship: Code N (No Commercial Relationship) | Ellina Rakhimova: Commercial Relationship: Code N (No Commercial Relationship) | Jost Jonas: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess the distribution of intraocular pressure (IOP) and its determinants in a very old population.

Methods: The population-based Ural Very Old Study (UVOS) was performed in a rural and urban region of Bashkortostan/Russia and consisted of 1526 (81.1%) out of 1882 eligible individuals aged 85+ years. As part of a series of medical and ophthalmological examinations, we measured IOP upon non-contact tonometry.

Results: The study included 1042 (68.3%) individuals with available IOP readings (mean age:88.1±2.7 years). Mean IOP was 14.6±5.3 mmHg (median:14 mmHg; range:6-60mmHg; 95%confidence interval (CI): 14.3,15.0) and 15.1±5.1mmHg (median:14mmHg; range:5-49mmHg; 95%CI: 14.8,15.4) in the right eyes and left eyes, respectively. In multivariable analysis, higher IOP was associated (regression coefficient r:0.35) with the systemic parameters of younger age (standardized regression coefficient beta:-0.08; non-standardized regression coefficient B:-0.13; 95%CI: -0.26, -0.01; P=0.04), female sex (beta:0.15; B:1.26; 95%CI:0.57,1.94; P=0.001) and higher systolic blood pressure (beta:0.18; B:0.03;95%CI:0.02,0.04; P<0.001), and the ocular parameters of thicker central corneal thickness (beta:0.18; B:0.02; 95%CI:0.01,0.03; P<0.001), longer axial length (beta:0.09; B:0.32;95%CI:0.05,0.60; P=0.02) and status after cataract surgery (beta:-0.13; B:-0.26; 95%CI:-1.59,-0.37;P=0.002). In that model, the IOP measurements increased by 0.19 mmHg (95%CI: 0.10,0.27) for each increase in central corneal thickness by 10 µm. In an univariate analysis, the IOP readings increased by 0.21 mmHg (95%CI: 0.13,0.29) for each increase in central corneal thickness by 10 µm.

Conclusions: In this population-based recruited study population aged 85+ years, IOP decreased with older age and increased with blood pressure and was higher in females. As in younger populations, the IOP readings were dependent on central corneal thickness, increased with longer axial length and were lower in eyes after cataract surgery.

CONTROL ID: 3545887

SUBMITTER (NAME ONLY): Rachel Vincent

TITLE: Gellan Hydrogel Eyedrop Promotes Wound Healing and Prevents Fibrosis of Cornea by Preferentially Absorbing Pro-Fibrotic Proteins

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.C. Vincent, R.J. Moakes, A.D. Metcalfe, R.L. Williams, L.M. Grover, Chemical Engineering, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|R.C. Vincent, G.R. Wallace, S. Rauz, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|G.F. Butt, S. Rauz, Birmingham and Midlands Eye Centre, Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, Birmingham, UNITED KINGDOM|G.F. Butt, Academic Unit of Ophthalmology, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|A. Logan, Biomedical Sciences, University of Warwick, Coventry, West Midlands, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Corneal opacity is a leading cause of sight impairment worldwide. Gellan gum is a water soluble, anionic polysaccharide that, may be used to form optically clear fluid gel eyedrops. Previously, it has been shown that gellan fluid gel (FG) significantly reduces markers of corneal scarring in a murine model of microbial keratitis. This study looks into why gellan FG is so effective at preventing fibrosis and scarring.

Methods: Cultured human primary corneal fibroblasts were treated with 5 ng/ml Transforming Growth Factor b1 (TGFb1) with or without 27.5% v/v gellan FG. Samples were analysed for changes in expression of mRNA after 24 and 80 hours by RT-PCR. Cultured human dermal primary fibroblasts were treated with 10 ng/ml TGFb1 with or without 20% v/v gellan FG. Samples were analysed for total collagen content using a hydroxyproline assay. Data analysed using unpaired t-test.

Affinity of different proteins for quiescent and fluid gels was compared by incubating equal volumes of hydrogel and phosphate buffered saline (PBS) contain protein. Rate of absorption for each protein was determined by measuring the amount of protein remaining in the PBS was measured using a total protein assay or ELISA at multiple time points.

Results: Gellan FG significantly inhibited TGFb1 mediated upregulation of smooth muscle actin a, fibronectin, collagen 1A1 and collagen 3A1 mRNA expression in human corneal fibroblasts ($p < 0.05$), indicating an anti-scarring effect. Gellan FG also prevented TGFb1 stimulated collagen production in human dermal fibroblasts ($p < 0.01$).

Proteins with a net positive charge under physiological conditions (isoelectric point (pI) > 7) have a significantly higher affinity for gellan than those with a neutral or net negative charge (pI = or < 7). Gellan eye drop absorbed 80% of fibrogenic TGFb1 (pI = 8.6), but only 22% of Epidermal Growth Factor (pI = 4.5). Hydrogel made from agarose, an uncharged polysaccharide, did not preferentially absorb proteins depending upon their net charge.

Conclusions: In addition to mechanically protecting the wound bed and providing lubrication, gellan FG absorbs and sequesters proteins from the wound bed by diffusion coupled with electrostatic association. The gellan dressing alters the trophic profile of the wound and reprograms the extracellular signalling microenvironment by selectively absorbing proteins.

CONTROL ID: 3545888

SUBMITTER (NAME ONLY): Cátia Gomes

TITLE: GLAUCOMA PATIENT PLURIPOTENT STEM CELL-DERIVED ASTROCYTES CONTRIBUTE TO RETINAL GANGLION CELL NEURODEGENERATION

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Gomes, J.S. Meyer, Department of Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|C. Gomes, T. Cummins, J.S. Meyer, Stark Neurosciences Research Institute, Indianapolis, Indiana, UNITED STATES|K. VanderWall, K. Huang, A. Allsop, S.S. Lavekar, C. Fligor, T. Cummins, Department of Biology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|Y. Pan, Indiana BioMedical Gateway Program, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Cátia Gomes: Commercial Relationship: Code N (No Commercial Relationship) | Kirstin VanderWall: Commercial Relationship: Code N (No Commercial Relationship) | Kang-Chieh Huang: Commercial Relationship: Code N (No Commercial Relationship) | Yanling Pan: Commercial Relationship: Code N (No Commercial Relationship) | Anna Allsop: Commercial Relationship: Code N (No Commercial Relationship) | Sailee Lavekar: Commercial Relationship: Code N (No Commercial Relationship) | Clarisse Fligor: Commercial Relationship: Code N (No Commercial Relationship) | Theodore Cummins: Commercial Relationship: Code N (No Commercial Relationship) | Jason Meyer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal ganglion cell (RGC) degeneration is a primary characteristic of glaucoma, although non-cell autonomous mechanisms have been implicated in RGC dysfunction. Astrocytes associate with RGCs in the nerve fiber layer of the retina and optic nerve, where they can contribute to RGC neurodegeneration. However, the mechanisms by which astrocytes promote neurotoxicity and contribute to glaucoma remain unknown.

Methods: Human pluripotent stem cells (hPSCs) can serve as powerful tools for the in vitro study of neurodegenerative diseases, including neuron-glia interactions. Using hPSC-derived cells from a glaucoma patient with an Optineurin (OPTN) E50K mutation (linked to inherited forms of glaucoma) as well as isogenic control cells obtained by CRISPR/Cas9 gene editing, we explored how the OPTN(E50K) mutation affects RGC-astrocyte interactions leading to neurodegeneration.

Results: hPSC-derived OPTN(E50K) astrocytes exhibited a hypertrophic shape and increased branching, as well as autophagy dysfunction and altered mitochondrial dynamics. Transcriptional analysis showed upregulation of the inflammatory pathway and downregulated axonal guidance in OPTN(E50K) astrocytes, suggesting they confer neurotoxicity and/or a lack of neurosupportive roles. Therefore, the contribution of astrocytes to RGC neurodegeneration was determined through co-cultures. Importantly, compared to the effect promoted by isogenic control astrocytes, OPTN(E50K)-astrocytes induced degenerative phenotypes in RGCs, including decreased neurite length and complexity, together with increased excitability, in both OPTN(E50K) and isogenic control RGCs. Conversely, isogenic control astrocytes were capable of rescuing degenerative phenotypes observed in OPTN(E50K) RGCs. Glaucomatous astrocytes secrete reduced levels of certain growth factors, suggesting a deficit in their neurosupportive role. In accordance, the incubation of OPTN(E50K) RGCs with these factors increased neurite branching and synaptic protein expression, highlighting the role of astrocyte-derived factors in RGC support.

Conclusions: These results are the first of its kind to identify a neurotoxic phenotype in hPSC-derived astrocytes from a glaucomatous source, as well as to identify a role for astrocytes in the neurodegenerative process through non-cell autonomous mechanisms, highlighting these glial cells as novel potential therapeutic targets in glaucoma.

CONTROL ID: 3545891

SUBMITTER (NAME ONLY): Jeremy Lavine

TITLE: Interleukin-6 is necessary and sufficient for choroidal angiogenesis

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lavine, S. Droho, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jeremy Lavine: Commercial Relationship: Code N (No Commercial Relationship) | Steven Droho: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Despite monthly intravitreal injection therapy, 15% of neovascular age-related macular degeneration (nAMD) patients lose vision. Interleukin-6 (IL6) is a pro-inflammatory and pro-angiogenic cytokine that is correlated with AMD progression and nAMD activity. We hypothesize that anti-IL6 therapy is a potential therapeutic for nAMD.

Methods: All experiments were performed on 10-12 week-old C57BL6/J mice. Wildtype (WT) and Il6^{-/-} mice underwent laser injury. Choroidal neovascularization (CNV) area was measured on choroidal flatmounts by ICAM-2 immunofluorescence on Day 14. Choroidal explants were cultured from WT mice for 7 days in Matrigel with and without exogenous IL6 (10 ng/ml) addition on Day 2, 4, and 6. IL6 levels were measured from posterior eye cups via ELISA on Day 3 after laser in WT and Ccr2^{-/-} mice. IL6 receptor expression was detected by immunofluorescence staining of whole eye frozen sections with IBA1 and lectin. Wildtype and Il6^{-/-} mice underwent laser injury followed by multiparameter flow cytometry on Day 3 to investigate macrophage infiltration.

Results: Male and female Il6^{-/-} mice demonstrated a 42% reduction (p<0.01, N=24-25 mice per group) in CNV area without sex-specific effects. Exogenous IL6 stimulated ex vivo choroidal angiogenesis by 131% (p<0.001, N=5 per group). Since IL6 is a pro-inflammatory cytokine produced by macrophages, which are essential for laser-induced CNV, we measured IL6 levels in WT and Ccr2^{-/-} mice. IL6 levels increased 1.15-fold (p<0.001, N=4-5 per group) in both genotypes, suggesting that classical monocyte-derived macrophages are dispensable for the increased IL6 production after laser. Next, we found that the IL6 receptor is expressed in choroidal endothelial cells and macrophages after laser injury. Due to IL6 receptor expression in macrophages, we investigated the effects of IL6-deficiency on macrophage recruitment using multiparameter flow cytometry. We found that laser injury increased the number of MHCII⁻ (13.0 to 15.0-fold, p<0.05), MHCII⁺CD11c⁻ (4.9 to 8.4-fold, p<0.05), and MHCII⁺CD11c⁺ (5.9 to 6.5-fold, p<0.01) macrophages (N=5-10 per group), with no differences between wildtype and Il6^{-/-} mice.

Conclusions: IL6 is both necessary and sufficient for choroidal angiogenesis. IL6 is not produced by classical monocyte-derived macrophages and signals to endothelial cells and/or macrophages to stimulate choroidal angiogenesis without affecting macrophage numbers.

CONTROL ID: 3545894

SUBMITTER (NAME ONLY): Mary Ann Stepp

TITLE: Epithelial IL-2 receptor expression and its effects on corneal nerves

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Stepp, S.P. Ghosh, G. Tadvalkar, Anatomy and Cell Biology, George Washington School of Medicine and Health Sciences, Washington, District of Columbia, UNITED STATES|J. Alam, C.S. De Paiva, Ocular Surface Center, Department of Ophthalmology, Cullen Eye Institute,, Baylor College of Medicine, Houston, Texas, UNITED STATES|W.W. Kao, V.J. Coulson-Thomas, Department of Ophthalmology, University of Cincinnati, Cincinnati, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mary Ann Stepp: Commercial Relationship: Code N (No Commercial Relationship) | Sonali Ghosh: Commercial Relationship: Code N (No Commercial Relationship) | Gauri Tadvalkar: Commercial Relationship: Code N (No Commercial Relationship) | Jehan Alam: Commercial Relationship: Code N (No Commercial Relationship) | Winston Kao: Commercial Relationship: Code N (No Commercial Relationship) | Vivien Coulson-Thomas: Commercial Relationship: Code N (No Commercial Relationship) | Cintia De Paiva: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The IL-2 receptor (IL-2R) is composed of three different chains, α (CD25), β , and γ . CD25 is the binding arm of the receptor and critical for IL-2 signaling. CD25 is expressed primarily on immune cells, but an epithelial expression of CD25 has been reported in epithelia, including the cornea. We showed that CD25 null mice develop a Sjögren-like Syndrome, with ocular alterations, including loss of intraepithelial corneal nerves and decreased corneal mechanosensitivity. However, the role of epithelial CD25/IL-2 signaling has not been thoroughly investigated.

Methods: Corneal epithelium from 14-week old female C57BL/6 mice were collected and subjected to real-time PCR. Tear washings were collected and assayed for IL-2 and IL-1 β . Laser scanning confocal microscopy evaluated the expression of CD25 within the corneal epithelium in wild-type C57BL/6 mice. Tet-On Krt12^{rtTA} (Keratin 12-reverse tetracycline-trans-activator knock-in), tet-O-Cre, and CD25^{flox} lines were mated to create a conditional, doxycycline-inducible Krt12^{rtTA/rtTA}/tet-O-Cre/CD25^{flox/flox} ternary mouse line (hereafter named CD25 ^{Δ/Δ CEpi}) where CD25 is ablated only in the corneal epithelium after administration of doxycycline in chow. Offspring of both sexes were subjected to a doxycycline diet for four weeks, and corneal sensitivity was measured with a Cochet-Bonnet esthesiometer at eight weeks of age.

Results: In wild-type mice, mRNA expression of CD25, IL-2R β , and IL-2R γ was present in the corneal epithelium. IL-2 was detected in tears of naïve mice, while IL-1 β was below the level of detection. Confocal microscopy showed that CD25 immunoreactivity is present in the cell membrane of apical and subapical epithelial cells but not in basal cells or intraepithelial nerves. A significant decrease in corneal sensitivity was observed in the induced-CD25 ^{Δ/Δ CEpi} mice compared to doxycycline-fed binary littermates Cre⁽⁻⁾, non-induced CD25 ^{Δ/Δ CEpi} mice, and binary littermates Cre⁽⁻⁾ mice on a regular diet.

Conclusions: All three chains of the IL-2R are expressed in the corneal epithelium. IL-2 is present in tears, bathing the ocular surface. Our results indicate that CD25/IL-2 epithelial signaling is important for corneal nerve homeostasis. Future studies are needed to delineate the mechanisms of how IL-2 preserves corneal nerves.

CONTROL ID: 3545896

SUBMITTER (NAME ONLY): Philip Mzyk

TITLE: A20 may alter the fibrotic response within the trabecular meshwork by attenuating TGF β 2-TLR4 signaling crosstalk

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Mzyk, C.M. McDowell, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Philip Mzyk: Commercial Relationship: Code N (No Commercial Relationship) | Colleen McDowell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Although the ECM in TM cells is known to be important in IOP regulation, the molecular mechanisms involved in generating a glaucomatous environment in the TM are not completely understood. Recently we identified a molecular pathway, TGF β 2-TLR4 signaling crosstalk, as an important regulator of glaucomatous damage in the TM which contributes to fibrosis. Here we continued our studies on a novel molecular target, A20 (also known as TNFAIP3), within this pathway which may help to block pathological TGF β 2-TLR4 signaling, ultimately leading to new treatments to prevent the development and progression of glaucoma.

Methods: Primary human trabecular meshwork (TM) cells were grown to confluence, switched to serum free media, and then treated for 48hrs with TGF β 2 (5ng/mL), TLR4 inhibitor (TAK-242, 15 μ M), A20 inducer (Vitamin E, 100 μ M), TGF β 2 and TLR4 inhibitor, TGF β 2 and Vitamin E, or PBS as a control. Lysates were either collected and immunoblotted for A20 and fibronectin expression, or for A20 analysis by RT-PCR.

Results: RT-PCR and immunoblotting showed that A20 is expressed in primary human TM cells. A20 message increased ($p=0.0052$) when the TLR4 pathway was inhibited. Immunoblotting of cell lysates from primary TM cell strains showed that TGF β 2, a known inducer of fibrosis, increases fibronectin expression ($p=0.0035$), while at the same time decreasing the expression of A20 ($p=0.0019$). Both direct inhibition of TLR4 (with TAK-242) and direct induction of A20 (with Vitamin E) showed a trending increase in A20 expression on immunoblots. Concurrent treatment with both TGF β 2 and Vitamin E also showed an increase in A20 levels.

Conclusions: This ongoing study reports the expression of A20 in primary cells as it relates to the TGF β 2-TLR4 crosstalk pathway. A20 was easily detectable by PCR analysis and increased with TLR4 inhibition. Low basal expression of A20 was detected at the protein level, which has also been reported in other cell types. However, treatment with TGF β 2, TLR4 inhibitor, or Vitamin E did modulate A20 protein expression. Therefore, TGF β 2-TLR4 crosstalk may be an important mechanistic pathway in the development of fibrotic TM damage and A20 may be able to alleviate some fibrotic responses by attenuating the TLR4 pathways ability to induce fibrosis.

CONTROL ID: 3545897

SUBMITTER (NAME ONLY): Hirut Kollech

TITLE: Conforming versus nonconforming meshes in the finite element modeling of the human lamina cribrosa

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.G. Kollech, Computational Modeling and Simulation, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.P. Vande Geest, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Hirut Kollech: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Vande Geest: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The biomechanics of the optic nerve head region including the lamina cribrosa (LC) and sclera is fundamental for the development of glaucoma. Several finite element (FE) approaches have been utilized to investigate the material properties of this region. Although both subdomain and full geometries are used to model the LC, the difference between conforming mesh (based on the geometry & structure) and nonconforming mesh has not been quantified. The purpose of this study is to investigate the differences between a conforming and nonconforming mesh on a small region of a human LC.

Methods: A nonglaucomatous human eye was imaged using a multiphoton microscope during a pressure inflation experiment. Second-harmonic generation images were collected and utilized to generate a 3D segmentation geometry. A small subdomain region was created from the segmented LC and meshed using a conforming tetrahedral mesh, a nonconforming hexahedral mesh, and a nonconforming tetrahedral mesh (shown in each panel where red indicates collagen in the LC). Element sizes were varied in each of the groups and FE simulations were run using identical boundary conditions, load, and material parameters. A few locations were selected to output displacement.

Results: The mesh convergence study within each of the three groups is shown in the Figure where Panels A, B and C display the conforming tetrahedral, nonconforming hexahedral, and nonconforming tetrahedral meshes. The percent error was calculated using the conforming finest mesh as a reference. The conforming mesh showed a maximum of 6.2 ± 0.3 % error variation and the error was smaller than 1% for element sizes greater than 1 million. The hexahedral mesh had a maximum error of $69.8 \pm 8.2\%$ at the coarse mesh and that of the nonconforming tetrahedral mesh was $57.8 \pm 4.2\%$.

Conclusions: The non-conforming mesh simulations result in $< 5\%$ error at finer mesh sizes. While the geometry in this study was small and the conforming mesh simulations were not computationally demanding, generating conforming FE simulations for complex structures such as the LC require large computational resources. Therefore, mesh-converged nonconforming models that result in small errors can be a great alternative. We are currently using these results to estimate the size of FE problems in our full LC.

CONTROL ID: 3545898

SUBMITTER (NAME ONLY): Seongjin Seo

TITLE: Differential requirement of NPHP1 for compartmentalized protein localization during photoreceptor outer segment development and maintenance

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Seo, P. Datta, J.T. Cribbs, Ophthalmology and Visual Sciences, University of Iowa College of Medicine, Iowa City, Iowa, UNITED STATES|S. Seo, P. Datta, J.T. Cribbs, Institute for Vision Research, University of Iowa College of Medicine, Iowa City, Iowa, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Seongjin Seo: Commercial Relationship: Code N (No Commercial Relationship) | Poppy Datta: Commercial Relationship: Code N (No Commercial Relationship) | J Cribbs: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Nephrocystin (NPHP1) is a ciliary transition zone protein and its ablation causes nephronophthisis (NPHP) with partially penetrant retinal dystrophy. This study is to determine the roles of NPHP1 in photoreceptors and uncover the molecular/genetic basis of the incomplete penetrance of retinal dystrophy in NPHP1-associated nephronophthisis.

Methods: Nphp1 gene-trap (Nphp1^{gt}) and Cep290^{fl} mice were obtained from the Jax lab (Nphp1^{tm1Jgg}/J; #013169 and Cep290^{tm1Jgg}/J; #013701). Nphp1 expression from normal and Nphp1^{gt/gt} mice was examined by immunoblotting, immunohistochemistry, and RT-PCR. Localization of various inner segment and outer segment proteins was examined by immunohistochemistry. Retinal functions were examined by electroretinography (ERG). Physical interactions of NPHP1 mutant variants with other NPHP proteins were tested by immunoprecipitation.

Results: In Nphp1^{gt/gt} retinas, inner segment plasma membrane proteins including STX3, SNAP25, and IMPG2 accumulate in the outer segment when outer segments are actively elongating. This phenotype, however, is spontaneously ameliorated after the outer segment elongation is completed. Retinal degeneration also occurs temporarily during the photoreceptor maturation but stops afterward. We found that the Nphp1^{gt} allele, which was previously described as null, was hypomorphic due to the production of a small quantity of functional mRNAs derived from nonsense-associated altered splicing and the consequent production of near-full-length, internal deletion mutant proteins. The mutant protein appears to retain most, if not all, functions of full-length NPHP1 as determined by in vitro studies. We further show that Nphp1 genetically interacts with Cep290, another NPHP gene, and that a reduction of Cep290 gene dose results in retinal degeneration that continues until adulthood in Nphp1^{gt/gt} mice.

Conclusions: Our data show that NPHP1 is essential to prevent infiltration of inner segment plasma membrane proteins into the outer segment during the outer segment development, but its requirement diminishes as photoreceptors mature. Our study also suggests that additional mutations in other NPHP genes may influence the penetrance of retinal dystrophy in human NPHP1 patients.

CONTROL ID: 3545904

SUBMITTER (NAME ONLY): Ward Fickweiler

TITLE: Association of Vitreous Retinol Binding Protein 3 with Diabetic Retinopathy in Type 1 and Type 2 Diabetes

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Fickweiler, H. Park, K. Park, T. Boumenna, J. Gauthier, I. Wu, G.L. King, Research Division, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|W. Fickweiler, J. Cavallerano, L.P. Aiello, J.K. Sun, Beetham Eye Institute, Joslin Diabetes Center, Boston, Massachusetts, UNITED STATES|J. Cavallerano, L.P. Aiello, J.K. Sun, G.L. King, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Joslin 50-Year Medalist Study identified elevated concentrations of retinal specific protein, Retinol Binding Protein 3 (RBP3) in people with 50 years or longer duration of type 1 diabetes and no to mild non-proliferative diabetic retinopathy (NPDR), suggesting potential to neutralize toxic effects of hyperglycemia on the vascular and neuronal retina. This study correlated RBP3 levels in the vitreous with diabetic retinopathy (DR) severity and progression in a large group of people with type 1 and type 2 diabetes.

Methods: Vitreous samples (n=213) were obtained during vitreoretinal surgery at the Joslin Beetham Eye Institute (n=58) and from post-mortem eyes (n=155) of Medalists. RBP3 concentration was measured by two self-developed ELISAs using either colorimetric or luminescent assays with a linear detection range of 10 pM to 15 nM and inter-experimental variation of <5%.

Results: Elevated vitreous RBP3 concentration was associated with less severe DR in all eyes ($p<0.0001$), post-mortem Medalist specimens ($p<0.0001$) and surgical samples from type 1 and type 2 diabetic patients with shorter diabetes duration (mean \pm SD 26.5 \pm 12.7 yrs, $p=0.03$). RBP3 concentration in subjects with no diabetes (NDM, median: 22.4 nM) and no to mild NPDR (15.7 nM) were increased compared to moderate-severe NPDR (8.2 nM, $p<0.01$ and $p=0.01$, respectively), active proliferative DR (PDR, 8.4 nM, $p<0.0001$ and $p=0.0003$, respectively) and quiescent PDR (3.5 nM, $p<0.0001$, both). Vitreous RBP3 concentration was associated with age (point estimate 0.06, $p=0.008$), diabetes duration (0.04, $p=0.05$), triglycerides (-0.01, $p<0.05$), neuropathy (-0.07, $p=0.02$), albumin/creatinine ratio (-0.01, $p<0.0001$), and panretinal laser (-1.06, $p=0.01$), but not with A1c ($p=0.68$). There was no difference in RBP3 concentration between people with type 1 and type 2 diabetes ($p=0.44$). Vitreous RBP3 concentrations were highly correlated between fellow eyes ($r=0.86$, $p<0.0001$). Further, in participants with longitudinal follow up, higher RBP3 concentrations were associated with reduced risk of PDR development over time ($n=34$, $p<0.001$).

Conclusions: These data suggest that higher RBP3 concentration in the vitreous is associated with less severe DR and slower rates of progression to PDR, supporting its therapeutic potential for prevention of DR worsening in people with diabetes.

CONTROL ID: 3545907

SUBMITTER (NAME ONLY): LORRAINE NORTH

TITLE: A Prospective study of type 1 and type 2 Diabetics examining the correlation between antioxidant levels and neuronal layer loss. (DECAN study)- An exploratory Study

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. NORTH, G.V. Menon, M. Chandran, Frimley Health NHS Foundation Trust, Frimley, Surrey, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: The aim of this study was to examine the relationship between retinal neuronal layer changes assessed using spectral domain optical coherence tomography (SD-OCT) with dietary intake of foods in patients with type 1 and type 2 diabetes with or without diabetic retinopathy.

Methods: Patients with type 1 and type 2 diabetes patients were recruited from the diabetic eye clinics at Frimley Park Hospital. A cross sectional study with a longitudinal element was carried out, 204 participants were recruited to the DECAN study. Outcome measures were dietary intake assessed using a food frequency questionnaire (FFQ), and optical coherence tomography (OCT).

Results: The results of the study showed that both outer nuclear layer (ONL) and the inner nuclear layer (INL) showed statistically significant associations with Vitamin B12, Pantothenic acid, copper and selenium. Selenium was seen to be associated with a thinner INL. The ONL showed a statistically significant association with vitamin B12, indicating that an increase in Vitamin B12 results in a thicker ONL whereas an increase in pantothenic acid is also associated with a thinner ONL.

Conclusions: This study has added to the growing evidence that oxidative stress, antioxidants and neurodegeneration are critical factors in the pathogenesis of diabetic retinopathy early on.

The study showed promising results for further research that could lead to an interventional trial using a supplementation of selenium which has not been previously reported.

CONTROL ID: 3545909

SUBMITTER (NAME ONLY): Kendal Lee

TITLE: Limited Hyperoxia Induced Retinopathy Alters Retinal Vasculature, Pericyte Count, and Gene Expression

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Lee, T. Tedeschi, A. Fawzi, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kendal Lee: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Tedeschi: Commercial Relationship: Code N (No Commercial Relationship) | Amani A Fawzi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While the Oxygen Induced Retinopathy (OIR) model is the most widely studied animal model used to mimic Retinopathy of Prematurity (ROP), the more recent Limited Hyperoxia Induced Retinopathy (LHIPR) model reflects more advanced pathological phenotypes seen in ROP. In this study, we expand upon the findings of the LHIPR model to show vascular changes that mimic other retinopathies.

Methods: Wild type C57Bl/6J mouse pups were exposed to 65% oxygen from P0 until P7 to model LHIPR. After P7, pups were returned to room air oxygen levels and allowed to recover until endpoints of P21 or P30. LHIPR pups were euthanized along with their age-matched control room air (RA) pups and eyes were harvested. For each mouse, one eye was fixed and prepared for flatmount immunolabeling of retinas and RNA was collected from the other for qPCR analysis. For the flatmounts, endothelial cells were labeled with CD31 antibody and pericytes were labeled with NG2 antibody. NG2 positive pericyte counts were scored by two masked readers. For qPCR experiments, a CD31 antibody/magnetic bead complex was used to isolate endothelial cells from dissociated retinas to purify RNA and perform first strand cDNA synthesis. Relative fold gene expression of endothelial PDGFB, an endothelial-derived pericyte growth factor, was quantified in the endothelial fraction.

Results: We found that LHIPR retina displayed a decrease of vessel density in P21 and P30 flatmounts (P21 $p < 0.05$, P30 $p < 0.001$). The P21 LHIPR flatmounts showed no relative difference in the number of pericytes. In contrast, P30 LHIPR flatmounts had a 34% pericyte loss relative to RA (P30 RA: 1.00 ± 0.05 , P30 LHIPR: 0.66 ± 0.07 , $p < 0.001$). The qPCR data showed a decrease (P21 $p > 0.05$, P30 $p < 0.001$) in PDGFB in P30 LHIPR endothelial samples, and not in P21.

Conclusions: Our study expands on the LHIPR model where we observe decreased vessel density, pericyte loss, and changes in gene expression involving endothelial-derived pericyte growth factors. These retinal vascular alterations mimic a spectrum of clinical retinopathies, including diabetic retinopathy.

CONTROL ID: 3545914

SUBMITTER (NAME ONLY): Brenda Brankin

TITLE: Blood retinal barrier tight junction expression modulation by NRF2 agonists

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Brankin, C. McCormack, S. Meaney, Biological and Health Sciences, Technological University Dublin, Dublin, Dublin, IRELAND|

Commercial Relationships Disclosure (Abstract): Brenda Brankin: Commercial Relationship: Code N (No Commercial Relationship) | Conor McCormack: Commercial Relationship: Code N (No Commercial Relationship) | Steve Meaney: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Oxidative stress may contribute to RPE cell damage in progressive degenerative diseases such as age-related macular degeneration (AMD). Nuclear factor erythroid 2-related factor 2 (NRF2) is a key modulator of the antioxidant response and represents a potential modifying factor to limit the extent of oxidative stress in the eye. We examined how modulation of NRF2 activation influenced the expression of tight junctional genes, trans-epithelial electrical resistance (TEER) and barrier permeability in an ARPE-19 cell model.

Methods: ARPE-19 cells were treated with varying concentrations sulforaphane (SFN) or brusatol (BRL), or a combination, for 24 hours. Cell viability was assessed via resazurin reduction. Gene expression was determined by quantitative RT-PCR, using the comparative threshold cycle method and PPIA as the endogenous control. TEER and barrier permeability experiments were carried out on confluent monolayers cultured for up to four weeks in TransWell plates. Comparative studies with histone deacetylase inhibitors (HDACi) were used to assess the contribution of the known HDACi effect of SFN on the experimental readouts. The student's t-test was used for statistical comparisons, with $P < 0.05$ considered significant.

Results: SFN and BRL appear well tolerated by ARPE-19 cells and modify the expression of classic antioxidant response genes (superoxide dismutase (SOD), thioredoxin-1 (TRX1)). The effects of BRL were only apparent at 100-200 nM, concentrations while those of SFN were concentration dependent (peak induction at 10 mM). SFN modulated the expression of several tight junction genes including Claudin-1 (CLDN1), occludin (OCCLDN) and zona occludens-1 (ZO1), again in a dose dependent manner. TEER was modestly, but significantly, reduced under these conditions. Analogous experiments with BRL resulted in a suppression of gene expression and an increase in TEER. Computational analysis identified potential antioxidant response elements (ARE) in the CLDN1 gene that may explain the observed effects on mRNA expression.

Conclusions: We show that the natural compounds SFN and BRL can modulate tight junction proteins in ARPE-19 cells at low doses. The functional effects of SFN on TEER appear to be driven by the HDACi activity of SFN rather than the NRF2 effect, as the effects of other HDACi and SFN on TEER are consistent despite variable changes in gene expression.

CONTROL ID: 3545915

SUBMITTER (NAME ONLY): Holly Rosenzweig

TITLE: Disruption of Nod2 within T cells causes uveitis: Implications for Blau Syndrome

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H.L. Rosenzweig, E.J. Lee, E. Vance, R. Napier, Molecular Microbiology & Immunology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|H.L. Rosenzweig, E.J. Lee, E. Vance, S. Lashley, R. Napier, VA Portland Health Care System, Portland, Oregon, UNITED STATES|B. Binstadt, Pediatric Rheumatology, Allergy and Immunology, University of Minnesota, Minneapolis, Minnesota, UNITED STATES|R.R. Caspi, Immunoregulation, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nod2 (nucleotide-binding oligomerization domain-containing 2) is an important anti-microbial receptor. However, mutations in NOD2 result in Blau Syndrome, typified by uveitis. We recently uncovered a T cell-intrinsic mechanism for Nod2 in suppression of Th17-immunity and experimental autoimmune uveitis (EAU). Nod2 is induced upon antigen-recognition in CD4⁺ T cells; hence we examined how Nod2 disruption controls T cell receptor (TCR)-triggered responses under homeostatic conditions in Nod2^{-/-} mice as well as in patients with Blau Syndrome.

Methods: Naive (CD62L^{hi}CD44^{lo}) CD4⁺ T cells purified from WT vs. Nod2^{-/-} mice were differentiated under Th17 polarizing conditions (CellXVivo) and Th17 cells quantified by flow cytometry. For TCR-ligation, purified memory (CD62L^{lo}CD44^{hi}) CD4⁺ T cells from naive mice were stimulated with anti-CD3/CD28 antibodies, and activation state (CD69) and cytokine production were measured by flow cytometry (n=4 mice/genotype x 3 experiments). Data were analyzed by two-tailed Mann-Whitney U test, and p<0.05 was considered significant. Peripheral blood mononuclear cells from Blau Syndrome patients (heterozygote NOD2 1147G->A mutation, n=2) or healthy controls (n=3) were stimulated with PMA/ionomycin.

Results: Nod2 was dispensable for conventional Th17 differentiation of naïve, mouse T cells. Rather, Nod2 functioned within memory (antigen-experienced) CD4⁺ T cells, with Nod2^{-/-} memory cells producing significantly greater amounts of IL-17, RORγt and CD69 after continued TCR-stimulation. Transcriptional analysis of early TCR-signaling events revealed a unique profile involving IL23r, Ccl25, Ccr7, and Cxcl2 regulation by Nod2 in memory cells. Importantly, continued TCR-stimulation of CD4⁺ T cells from Blau Syndrome patients recapitulated the exacerbated IL-17 phenotype. Further immunoprofiling indicated enhanced cell surface expression of CCR7 in Blau patients vs. controls, which was further increased upon TCR-ligation; whereas production of cytokines IL-2, IFNγ and TNF was impaired based on kinetics of TCR-activation.

Conclusions: Our data support Nod2 as a homeostatic factor in T cells, which suppresses responses of antigen-experienced Th17 cells and uveitis. Thus, loss of proper Nod2 function within T cells could be involved in the pathology of Blau Syndrome; thereby presenting new therapeutic options for patients.

CONTROL ID: 3545919

SUBMITTER (NAME ONLY): Parisah Moghaddampour

TITLE: Acuity of Emergency Room and Inpatient Ophthalmology Consultations at a Level 1 Trauma Center

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Moghaddampour, J.A. Dunbar, L. Khazaeni, Ophthalmology, Loma Linda University Medical Center, Loma Linda, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to investigate the acuity of all ophthalmology consults from the emergency department and inpatient ophthalmology consultations at a level 1 trauma center in Southern California.

Methods: This was a retrospective chart review of patients evaluated by the ophthalmology consultation service at Loma Linda University Medical Center from June 2016 to May 2017. Age, gender, consulting service, reason for consult, diagnosis, and recommended follow up were recorded. The level of acuity of pre-consult was defined based on the reason for the consult and was stratified to three levels: acute, chronic, and screening exams. The post-consult acuity level was updated based on the result of the consult: emergent, acute, chronic, and other. Eleven diagnosis were labeled as emergent. Ophthalmology procedures and surgeries performed within 48 hours were recorded.

Results: A total of 2043 charts were reviewed with an average of 170 new consults per month. Pre consult acuity included 69% acute consults, 4.3% chronic, and 25% screening exams. Post consult acuity included 24% emergent, 51% acute, 15% chronic, not urgent, or negative, and 10% were considered other. Of those with pre-consult acuity considered acute, 25% were updated to emergent after ophthalmologic exam with 30% requiring emergent surgery. Roughly 25% of all consults were screening exams, and of those two-thirds were negative screens or chronic diagnoses.

Conclusions: Acuity stratification of reasons for ophthalmology consultation may be useful in designing guidelines for emergency department and inpatient ophthalmologic exams. Further studies at other medical centers are needed to customize such guidelines.

CONTROL ID: 3545921

SUBMITTER (NAME ONLY): Juan F. ZAPATA-DIAZ

TITLE: Clinical outcomes of a new set of complementary premium multifocal intraocular lenses

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.F. ZAPATA-DIAZ, M. Ortega-García, J. Lajara-Blesa, R&D, Vista Ircovisión Oftalmólogos, Murcia, Murcia, SPAIN|J.F. ZAPATA-DIAZ, Cristalens Industrie, Lannion, FRANCE|J. Lajara-Blesa, Universidad Catolica San Antonio de Murcia Facultad de Ciencias de la Salud, Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: To evaluate the clinical outcomes and the complementarity of the new set of multifocal intraocular lenses (IOLs) Artis Symbiose (Cristalens Industrie, France).

Methods: Twenty patients were implanted with the Artis Symbiose Mid IOL in the dominant eye, and the Artis Symbiose Plus IOL in the contralateral eye after phacoemulsification. Inclusion criteria were: age over 50 years, cataract or refractive lens exchange patients, pupil diameter between 2 and 4 mm in photopic conditions, DEWS ≤ 2 in the scale of dry eye severity. Exclusion criteria were any pathology or condition that could affect the outcomes and the performance of the measurements and expected postoperative residual astigmatism ≤ 0.75 D. Monocular and binocular defocus curves were assessed at 1-2 months with ETDRS charts at 4 m. Distance, intermediate (90 and 70 cm), and near (40 cm) visual acuity, contrast sensitivity (CSV-1000, VectorVision, USA), light disturbances (LDA, Binary Target, Portugal), and patient satisfaction (VF-14 questionnaire) were assessed at least 6 months after surgery.

Results: Mean monocular defocus curves of both eyes met at 2.00 D of defocus. The binocular defocus curve showed a visual acuity of 0.10 logMAR or better from 0 to 3.00 D of defocus (Figure 1). Uncorrected distance, intermediate (90 cm and 70 cm), and near visual acuity were -0.03 ± 0.08 , 0.03 ± 0.13 , 0.03 ± 0.11 , and 0.06 ± 0.10 (mean \pm SD) logMAR respectively. Contrast sensitivity was within normal values for patients age. Binocular light distortion index was 9.93 ± 5.30 % and patient satisfaction 93.37 ± 7.31 %.

Conclusions: Monocular defocus curves demonstrated the complementarity of the Artis Symbiose Mid & Plus IOLs. The mean binocular defocus curve showed a depth-of-field of 3.00 D with visual acuity 0.1 logMAR or better. Uncorrected visual acuity was good at all evaluated distances. Contrast sensitivity was normal and patient satisfaction was very high.

CONTROL ID: 3545925

SUBMITTER (NAME ONLY): Heike Kroeger

TITLE: Proteostasis Modulation through ATF6 Signaling Supports Cone Photoreceptor Differentiation in Retinal Organoids

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Kroeger, Cellular Biology, The University of Georgia, Athens, Georgia, UNITED STATES|J.M. Grandjean, R.L. Wiseman, Molecular Medicine, Scripps Research Institute, La Jolla, California, UNITED STATES|W. Chiang, Developmental Neurobiology, Okinawa Institute of Science and Technology Graduate University, Okinawa, Okinawa, JAPAN|D. Bindels, Cellular and Molecular Biology, University of California San Diego, La Jolla, California, UNITED STATES|R. Mastey, J. Carroll, Ophthalmology & Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|J. Okalova, N.J. Grimsey, College of Pharmacy, UGA, The University of Georgia, Athens, GA, US, academic, Athens, Georgia, UNITED STATES|A. Nguyen, Pathology, University of California San Diego, La Jolla, California, UNITED STATES|E. Powers, J.W. Kelly, Chemistry, Scripps Research Institute, La Jolla, California, UNITED STATES|J.W. Kelly, Scripps Research Institute Skaggs Institute for Chemical Biology, La Jolla, California, UNITED STATES|M. Michaelides, Retina and Genetics, University College London, London, London, UNITED KINGDOM|M. Michaelides, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|J.H. Lin, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Unfolded Protein Response (UPR) is a conserved regulatory mechanism of the Endoplasmic Reticulum (ER) initiated to maintain protein homeostasis. Dysregulation of the UPR is implicated in the pathology of many human diseases associated with ER stress. Inactivating genetic variants in the UPR regulator Activating Transcription Factor 6 (ATF6) cause severe congenital heritable vision loss, presented as impaired visual acuity and loss of color vision. Cone photoreceptors are dysfunctional in this disease, but the pathomechanisms involving the lack of functional ATF6 is unknown. Furthermore, there are no treatments for people carrying these mutations.

Methods: To investigate the functional role of ATF6 during photoreceptor development, we generated retinal organoids from patient iPSCs carrying ATF6 disease-causing variants and ATF6 null hESCs generated by CRISPR. Retinal organoids underwent surface-scanning live imaging to examine morphology of WT and ATF6 mutant rods and cones, and confocal immunofluorescent microscopy of sectioned retinal organoids. In parallel, adaptive optics laser-scanning confocal ophthalmoscopy (AOSLO) was performed to visualize photoreceptor morphology from the ATF6 mutant patient stem cell donors used in this study. RNAseq analysis was performed to establish rod and cone gene expression profiles of WT and ATF6 mutant retinal organoids. Rescue of cone photoreceptor cells in ATF6 mutant retinal organoids was investigated using a small molecule ATF6 agonist.

Results: Cone photoreceptor cells in ATF6 mutant retinal organoids lacked inner and outer segments concomitant with absence of cone phototransduction gene expression; while rod photoreceptors developed normally. Adaptive optics retinal imaging of patients with disease-causing variants in ATF6 also showed absence of cone inner/outer segment structures but preserved rod structures, mirroring the phenotypes observed in our retinal organoids. We

further show that the ATF6 agonist activates ATF6 to restores the transcriptional activity of ATF6 disease-causing variants and stimulates the growth of cone photoreceptors in patient retinal organoids.

Conclusions: These results reveal that ATF6 is essential for the formation of functional human cone photoreceptors, demonstrating that pharmacologic targeting of ATF6 signaling is a therapeutic strategy that needs to be further explored for blinding retinal diseases.

CONTROL ID: 3545927

SUBMITTER (NAME ONLY): Katie Bales

TITLE: Exercise promotes retinal astrocyte plasticity and protects against retinal degeneration

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Bales, M.T. Pardue, J.H. Boatright, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|K. Bales, J.H. Boatright, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|A. Chacko, M.T. Pardue, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The neuroprotective effects of exercise in regions of the central nervous system have been well documented, although the underlying molecular mechanisms remain elusive. We previously demonstrated that exercise is also protective to the degenerating retina. Here we explore the potential role of retinal astrocytes as mediators of exercise-induced retinal neuroprotection using a light-induced retinal degeneration model (LIRD) that exhibits phenotypes found in patients with retinal degenerations.

Methods: Male adult BALB/c mice (n=48) were assigned to active(A)-dim, inactive(I)-dim, inactive (I)-LIRD and active (A)-LIRD groups. Active mice were exercised on a treadmill (1 hr/d at 10 m/min) for two weeks, then LIRD was induced with bright light exposure (4000 lux for 4 hrs). Active groups were exercised an additional week. Inactive controls were placed on static treadmills for the same duration and schedule. At week three, retinal function was assessed using electroretinography (ERG). One week after LIRD, retinal flat mounts were stained for astrocytes using GFAP and quantitatively assessed using Skeletonize analyses (ImageJ) for population density, and GFAP expression and Sholl analyses for astrocytic branching and dendritic arborization. A proximity ligase assay (PLA) was used to detect astrocyte and brain-derived neurotrophic factor (BDNF) interaction in active groups compared to inactive groups. Data were analyzed by 2-way ANOVA (mean±SEM).

Results: LIRD diminished retinal function as measured by ERG. Importantly, retinal function in A-LIRD groups were significantly preserved compared to I-LIRD groups based on a-wave (p=0.041) and b-wave (p=0.003) amplitudes. Retinal flat mounts from A-LIRD mice had more astrocytes (A-LIRD: 9.00±0.35; I-LIRD: 4.00±0.29 # of cells per image) and cellular branching (A-LIRD: 93.4±3.47; I-LIRD: 40.95±4.40[PM1] # branches per cell; p<0.0001). PLA showed increased cellular interaction between GFAP and BDNF in retinas from active groups compared to inactive groups.

Conclusions: Our results suggest that the protective effects of exercise on retinal degeneration may be due to BDNF signaling mediated by astrocytes. These studies provide important insights into the molecular mechanisms that govern exercise-induced retinal neuroprotection. This information may be useful in optimizing exercise interventions for patients with progressive retinal degenerations.

CONTROL ID: 3545928

SUBMITTER (NAME ONLY): Raquel Deering

TITLE: A novel method to rapidly expand and perform single cell sequencing on T cells from vitreous biopsies

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Pathogenic T cells in the vitreous of patients are a hallmark of autoimmune uveitis. Characterizing intravitreal phenotypes and T cell receptor (TCR) sequences at the single cell level would enable downstream tests to identify the cognate antigens recognized by intravitreal T cells. Typically, too few viable T cells from vitreous biopsies are available to allow direct single cell sequencing (scSEQ) technologies to be applied. Thus, we developed a novel ex vivo rapid T cell expansion culture method on vitreous biopsies to enable scSEQ for TCR identification.

Methods: Vitreous biopsies were collected at the time of steroid-eluting implant replacement. Samples were centrifuged at 4° C to concentrate cells and reduce the volume of vitreous fluid, which inhibits T cell proliferation in culture. The pellets were transferred to tissue culture wells containing irradiated PBMC feeder cells separated from vitreous cells by a well insert that is permeable to growth factors produced by feeder cells while maintaining a physical barrier between feeder and vitreous cells. The media contained supportive T cell cytokines (IL-7, IL-15, IL-2) and the T cell stimulus anti-CD3 antibody (OKT3 clone). Although T cell stimulants were provided, the culture also supported B and NK cells during the 7-day culture period. After 7 days, total cultured vitreous cells were collected and applied to the 10X Genomics Chromium single cell capture and parallel whole genome transcriptome and TCR sequencing.

Results: We first expanded vitreous T cells from a patient with sarcoidosis-related intraocular immune infiltration. Following 7-day expansion and scSEQ analysis, we observed that 675 out of 681 cells expressed CD3. A unique TCR alpha and beta chain was detected in 547 CD3+ cells with a total of 34 clonotypes. Among the top 12 most frequent clonotypes, the number of cells sharing the same clonotype ranged from 5 to 172. These expanded cells were comprised of both CD4 and CD8+ T cells. TCR clonality analysis revealed that T cells from both subsets were clonally expanded.

Conclusions: Using a novel ex vivo rapid expansion protocol for fresh vitreous biopsies, we found that T cells can be analyzed by single cell methods. This approach allows sensitive and in-depth profiling of T cells and provides T cell subtype and clonotype information from auto-immune uveal diseases.

CONTROL ID: 3545929

SUBMITTER (NAME ONLY): Anne Zebitz Eriksen

TITLE: Generation of Three-dimensional Stem Cell Derived Eye Organoids with Corneal Features

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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Commercial Relationships Disclosure (Abstract): Anne Zebitz Eriksen: Commercial Relationship: Code N (No Commercial Relationship) | Timothy Blenkinsop: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Human stem cell derived in vitro models of cornea tissue can aid our understanding of the process of wound healing and may be useful for pharmacological screening, in a cost effective manner, while reducing the reliance on animal experiments. Previous reports of 3D corneal colonies demonstrate corneal features, but require a dissection step that may reduce scalability. Here, we report the generation of 3D eye organoids from human embryonic stem cells (hESCs), with cornea characteristics independent of dissection

Methods: H9 ESCs were seeded at 3000 cells/well in a 96 ultra-low bind well plate in mTeSR media with 2.5% matrigel and 2µM Thiazovivin (THIA). Differentiation into eye organoids were stimulated at day 2 by changing to differentiation media (DM): GMEM with 10% knockOut Serum Replacement, 1mM Sodium pyruvate, 1mM non-essential amino acids, 2mM L-glutamate, 1% penicillin-streptomycin solution and 55µM β-mercaptoethanol. Corneal specification was enhanced at day 32-46 by changing to DM:CnT-PR (1:1) with 10ng/mL keratinocyte growth factor (KGF) and 2µM THIA, before changing to maintenance media; DMEM:F12, 2% B-27 supplement, 10ng/ml KGF and 2µM THIA at day 48. Corneal features were characterized by immunohistochemistry (IHC).

Results: By day 20, ≈20% (N=3x96) of the organoids formed transparent blebs interpreted as pre-cornea formation. At day 28, organoids show pigmented regions (RPE or iris pigment cells). By day 48, organoids show transparent, opaque and pigmented regions, Figure 1. IHC revealed an organized outer layer consisting of tightly packed cells (epithelium) on top of a thin acellular structure reminiscent of Bowman's membrane (BM). The epithelial layer was positive for corneal markers: TP63α, PAX6, ZO-1, Keratin 15 and Keratin 12 (Figure 2). Cells found beneath the putative BM were vimentin positive and resemble keratocytes of the corneal stroma (Figure 2).

Conclusions: We report a method for culturing 3D eye organoids from hESCs exhibiting features resembling the three outer layers of the cornea; Epithelium, BM and stroma. These organoids may be useful to study wound healing and identification of therapeutic compounds.

CONTROL ID: 3545931

SUBMITTER (NAME ONLY): Liujiang Song

TITLE: Injection volume alters recombinant Adeno-associated Virus 8 transduction efficiency and biodistribution

SESSION TITLE: Corneal disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Subconjunctival (SC) administration of AAV vectors exhibit capsid serotype-dependent transduction in the cornea and broad transduction of ocular/peri-ocular tissues, demonstrating its suitability to treat ocular diseases. In addition to viral capsid serotype and physiological factors, administration volume affect AAV vector transduction efficiency. Herein, we explored the role of administration volume in AAV gene delivery, biodistribution, and transduction efficiency following SC injection.

Methods: The relationship between injection volume, vector transduction, and vector biodistribution was evaluated in wild type mice using multiple doses of self-complementary AAV8-CMV-GFP vectors. Sixty female C57BL/6J mice aged 6-8 weeks were randomly divided into no injection, low-volume (7 μ l containing either 5e8 vg or 5e9 vg or vehicle), and high-volume (70 μ l containing either 5e8 vg or 5e9 vg or vehicle) injection groups. Ocular clinical parameters were collected prior to and after the injections. Animals were sacrificed at 3 months following the injection and tissues were harvested for immunofluorescence staining, vector genome biodistribution and transgene expression analysis.

Results: A single SC injection of AAV8 (7 μ L), resulted in efficient transduction of the ocular muscles (Fig. 1); in contrast, a ten-fold higher injection volume of the same dose exhibited little to no detectable transduction in the ocular muscles, and trended towards higher transduction efficiency in the peripheral cornea (Fig. 2). The transduction pattern was a dose-independent phenomenon that correlated well with vector genome biodistribution.

Conclusions: Taken together, the collective data indicate that injection volume dramatically alters AAV8 tissue transduction and biodistribution in the ocular and peri-ocular compartments following SC injection. Specifically, low-volume SC injection of AAV8 vectors could be ideal for therapy of ocular muscular diseases such as oculopharyngeal muscular dystrophy; Alternatively, AAV8 vectors administered in a high volume have apparent relevance for the treatment of ocular surface diseases including limbal stem cell deficiency and/or dry eye disease. Therefore, optimization of multiple experimental factors is necessary to achieve maximal transduction efficiency and desired tissue targeting, while concurrently decreasing vector production burden and immunological concerns.

CONTROL ID: 3545935

SUBMITTER (NAME ONLY): Ronald Zambrano

TITLE: Optimal Retinal Nerve Fiber Layer Sampling Location with OCT in Rhesus Monkeys.

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zambrano, A. Vellappally, P. Alexopoulos, M. Wu, J.S. Schuman, H. Ishikawa, G. Wollstein, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|M. Wu, M. Liu, Departments of Population Health and Environmental Medicine, NYU Langone Health, New York, New York, UNITED STATES|J.S. Schuman, H. Ishikawa, G. Wollstein, Department of Biomedical Engineering, NYU Tandon School of Medicine, Brooklyn, New York, UNITED STATES|A.D. Melin, Departments of Anthropology and Archaeology and Medical Genetics, University of Calgary, Calgary, Alberta, CANADA|J.P. Higham, Department of Anthropology, NYU College of Arts and Sciences, New York, New York, UNITED STATES|A.O. Barron Arrambide, J. Danias, Departments of Ophthalmology and Cell Biology, SUNY Downstate Health Sciences University, Brooklyn, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the least variable sampling location for OCT retinal nerve fiber layer (RNFL) thickness measurements on rhesus macaque monkeys, for determining the preferred sampling location.

Methods: In vivo three-dimensional spectral-domain OCT scans (Leica, Chicago, IL) were obtained as raster scan data (400x400x1024) in a 5x5x1.6 mm region (human equivalent, not the actual size in the monkey eye) centered on the optic nerve head (ONH) of 33 healthy adult rhesus macaques (19 males, 14 females; ages 3.0-10.7 years). The ONH scans of 48 eyes were analyzed using OCT segmentation software of our own design to calculate point-by-point RNFL thickness measurements. Mean RNFL thickness was computed on consecutive concentric circles within the scan window, centered on the geometric ONH center and starting at the optic disc margin (between 64-119 circles). The least variable RNFL measurement area was identified in the vicinity of the RNFL peak within the 2 μ m deviation.

Results: The least variable RNFL was observed in between 98.88 ± 11.82 and 114.4 ± 11.32 pixels from the ONH center with the peak RNFL at 106.42 ± 11.55 pixels (Figure 1). Note that the number of available eyes in each sampling location varied as detailed in Figure 2. For comparison, the radius of the OCT scan circle conventionally used in humans is 1.7 mm, or 136 pixels, from the center of the ONH.

Conclusions: In order to obtain less variable circumpapillary RNFL thickness measurements on rhesus macaque monkey eyes, it is recommended to use a sampling circle with a radius of approximately 106 pixels from the ONH center, which is smaller than the human equivalent.

CONTROL ID: 3545937

SUBMITTER (NAME ONLY): Kavitha Anbarasu

TITLE: Glaucomatous Optineurin-E50K mutation causes human retinal ganglion cell death by causing mitophagy defects

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Anbarasu, J.S. Meyer, A. Das, Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|M. Surma, J.S. Meyer, A. Das, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|K. Huang, Biology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|D.J. Zack, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reducing intraocular pressure (IOP) remains the only treatment for Primary Open-Angle Glaucoma but damage can continue despite IOP reduction. Understanding the molecular mechanism underlying retinal ganglion cell (RGC) death remains elusive as a major challenge is the limited availability of human RGCs. Aim of this study is to use human stem cell differentiated RGCs (hRGCs) with a glaucoma causing mutation to investigate cellular mechanisms and identify potential therapeutic targets.

Methods: We used CRISPR engineered human pluripotent stem cell reporter lines to differentiate and immunopurify hRGCs. For glaucoma modeling, we used patient derived induced pluripotent stem cells (iPSCs) and CRISPR mutated human embryonic stem cells (hESCs) with the Optineurin-E50K (OPTN-E50K) mutation, a widely accepted cause for a subpopulation of normal tension glaucoma. We used western blot for measuring mitophagy by LC3B lipidation and qPCR for mitophagy gene expression. Mitochondrial metabolic defects were analyzed using the Seahorse analyzer and RGC viability/apoptosis was assessed by fluorescence/luminescence-based assay. Statistical comparison between two independent groups was done by student's t-test and among multiple groups by One-way Anova with Dunnett's correction.

Results: Our study shows the glaucomatous OPTN-E50K mutation causes mitophagy defects in hRGCs. OPTN belongs to the mitophagy adaptor protein group which shares LC3 interacting (LIR) domain and ubiquitin binding domain (UBD) through which the mitophagy process is initiated. E50K hRGCs showed activation of other adaptor genes such as P62 and NDP52, possibly as a response to overcome the mitophagy defects. Mitophagy defects lead to the accumulation of damaged mitochondria, causing mitochondrial metabolism defects and cellular toxicity. Indeed, we observed reduced mitochondrial activity in the E50K hRGCs when compared to wild-type (Wt) cells. Mitophagy defects should lead to cellular toxicity in E50K hRGCs in presence of mitochondrial stress. Indeed, we observed increased cell death for the E50K hRGCs in presence of the mitochondrial toxic drug CCCP.

Conclusions: Our study showed that the glaucomatous E50K mutation causes mitophagy defects leading to hRGC death and implicates mitophagy pathway proteins as possible therapeutic target for OPTN associated glaucoma.

CONTROL ID: 3545942

SUBMITTER (NAME ONLY): Megan McDonald

TITLE: Comparative Assessment of OCT Segmentation Metrics between Manual Corrected Image Processing and Machine Learning in Severe Inflammatory Disease and Retinal Dystrophy

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. McDonald, C. Chen, M. Ramos, J. Whitney, K. Baynes, P.M. Kaiser, D. Burton, S. Sharma, J.P. Ehlers, S. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the differences in optical coherence tomography (OCT) segmentation metrics between machine learning based assessment and an expert-reader corrected logic based algorithm in eyes with severe outer retinal diseases. A machine learning based segmentation model created from normal, diabetic retinopathy and age related macular degeneration eyes was assessed in this experiment. OCT images from severe outer retinal diseased eyes (uveitis patients with syphilitic retinitis and retinitis pigmentosa) were analyzed and compared to a manually corrected expert readers.

Methods: 21 eyes were included in this experiment (9 RP and 12 syphilitic). For this analysis, the inner limiting membrane (ILM), outer nuclear layer (ONL), ellipsoid zone (EZ), and retinal pigment epithelium (RPE) were segmented using both deep learning and a logic based algorithm (LBA) with expert reader (ER)-corrected segmentation. The intraclass correlation coefficients (ICC) for ER-corrected LBA and machine learning were calculated and compared using segmentation metrics for central subfield thickness and central subfield volume. Intraclass correlation coefficients were created (MS-Excel, RealStatistics 2020) with 95% confidence intervals.

Results: ICC scores were highest for total retinal thickness measurements including central subfield thickness (.619) and central foveal mean thickness (.826). Machine learning displayed poor correlation when compared to ER-corrected LBA for all EZ based measures including EZ/RPE central subfield thickness (ICC 0.062) and central subfield volume (ICC 0.059). Enface based measures including maps detailing zero micron thickness and less than 20 micron thickness also had poor correlations. When separating out by disease subtype, there were no differences between correlations in syphilis retinopathy nor in RP.

Conclusions: In this machine learning model created from normal, AMD and DR pathologies, there was poor correlation to expert readers when assessing EZ based metrics in eyes with severe outer retinal pathology. Though our numbers are small, specific models created from manually graded severe retinal pathology may be needed to improve performance when assessing these complicated eyes. When assessing severe EZ pathology, our results suggest that manual grading is still needed.

CONTROL ID: 3545943

SUBMITTER (NAME ONLY): Dongsheng Yan

TITLE: A Genome-wide Map of RNA m⁶A Modification in mouse retina

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Yan, G. Luo, X. Chen, W. Xu, School of Ophthalmology and Optometry, Wenzhou Medical University, Wenzhou, Zhejiang, CHINA|

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ABSTRACT BODY:

Purpose: RNA m⁶A methylation has been implicated in controlling the development and maintenance of neurons. However, an extensive in-depth analysis of its involvement and profile in the retina is still lacking. Here we systematically characterized m⁶A modification pattern on a genome-wide scale in mouse retina.

Methods: Global m⁶A assays determined RNA m⁶A modification levels in the retinas of newborn and 8-week-old mice. Quantitative RT-PCR analyses detected the expression levels of RNA Methyltransferase Complex genes- METTL3, METTL14, and WTAP. We performed genome-wide RNA m⁶A modification analyses of mouse retina using m⁶A RNA immunoprecipitation followed by high-throughput sequencing (MeRIP-Seq). Using bioinformatics, we analyzed genes affected by the m⁶A marks in mouse retina.

Results: Global m⁶A RNA modification levels were significantly decreased in adult mouse retina as compared to newborn mouse retina. METTL3, METTL14, and WTAP expression levels were significantly downregulated in adult mouse retina. MeRIP-Seq identified typical patterns of global m⁶A methylation exhibited at exons, introns, stop codons, 5'UTR, and 3'UTR regions. Bioinformatic analyses revealed a complex m⁶A-mRNA regulatory network in mouse retina.

Conclusions: Our genome-wide RNA m⁶A modification profile provides a comprehensive picture of epitranscriptomic regulatory mechanism in mouse retina.

CONTROL ID: 3545945

SUBMITTER (NAME ONLY): chia chun liu

TITLE: The neurite outgrowth response of cultured retina ganglion cells upon extrinsic stimulations

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. liu, National Tsing Hua University, Hsinchu, TAIWAN|

Commercial Relationships Disclosure (Abstract): chia chun liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal ganglion cells (RGCs) of postnatal mouse retinal explants can regenerate neurites by either light or electrical stimulation. However, previous studies focused on neurite outgrowth in the whole mount retina and less attention has been paid in discussing the effect on individual RGCs. In the present study, we aimed to examine the neurite outgrowth response of isolated RGCs upon different external stimulations.

Methods: The retinas from 18 to 24 mice of 2 days old were used to purify primary RGCs by immunopanning. For the electrical stimulation group, cultured RGCs were given 200 mV, 100 Hz, monophasic electrical stimulation for 100 ms and rest for 2 seconds, repeated for 30 mins, using the multielectrode array (MEA) at DIV2 (Days in vitro). The neurite outgrowth was stained with calcium AM (1:1000) for 10 minutes at 37 degrees at DIV3. For the blue light stimulation group, cultured RGCs were transfected with ChR2 proteins via AAV2, then applying 20 Hz (25-ms pulse width) blue light ($\sim 680 \text{ cd}/\text{m}^2$, 470 nm) to stimulate RGCs for 1 hour at DIV1, and observed the neurite outgrowth at DIV2 and DIV3.

Results: Despite the MEA substrate used in the present study was glass, which is not the optimal surface for neurite outgrowth of RGCs, and yet the extent of neurite outgrowth with electrical stimulation was significantly larger than the ones without electrical stimulation. Similarly, neurite outgrowth of RGCs with the presence of ChR2 upon blue light stimulation was significantly longer than the ones without the presence of ChR2 upon blue light stimulation.

Conclusions: The present study suggests that increased neural activity of RGCs upon light or electrical stimulation can significantly promote neurite outgrowth of cultured neurons at DIV2. In the future, it will be informative to analyze the RNA expression profile of RGCs after external stimulation in order to identify genes or a network of gene expression that are responsible for promoting RGC axon growth.

CONTROL ID: 3545946

SUBMITTER (NAME ONLY): Jinhong Pan

TITLE: Dynamin Family Members and Protection of Ocular Surface Epithelia

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Pan, R. Martínez-Carrasco, M. Fini, Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|J. Pan, R. Martínez-Carrasco, M. Fini, New England Eye Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jinhong Pan: Commercial Relationship: Code N (No Commercial Relationship) | Rafael Martínez-Carrasco: Commercial Relationship: Code N (No Commercial Relationship) | M Elizabeth Fini: Commercial Relationship(s);University of Southern California:Code P (Patent)

ABSTRACT BODY:

Purpose: We recently showed that dynasore protect ocular surface epithelial cells and their mucosal glycocalyx against oxidative stress by shifting the unfolded protein response (UPR) in the endoplasmic reticulum (ER) towards homeostasis via calcium dynamics (PMID 32791188). Dynasore is a cell-permeable small molecule inhibitor of dynamin family GTPases responsible for membrane fusion/fission events, discovered after screening a small molecule library for inhibition of DNM2 GTPase activity and endocytosis (PMID:16740485). Our goal is to identify molecular target(s) of dynasore that determine cytoprotective effect.

Methods: A cell culture model of human immortalized corneal limbal epithelial (HCLE) cells was used (PMID: 12766048). Cultures were stressed by application of t-butyl hydroperoxide (3mM) for 2 hrs while treating or not treating (control) with dynasore (Sigma). Cytoprotective effect was quantified using the WST-1 metabolic assay (Sigma). RNA was extracted with RNeasy kit (Qiagen). First strand cDNA was synthesized by reverse transcription. qPCR was performed with cDNA and specific primers using SYBR®Green. Western blot was performed with the total protein extracted using RIPA buffer.

Results: We determined in dose-response experiments (0.5-80 μ M) that dynasore protects cells with an EC50 of $6.0 \pm 0.8 \mu$ M (n=16). qPCR was performed to determine which members of the dynamin family are expressed by HCLE cells (Fig. 1). Of the 3 classic dynamins, DNM2 is dominant while DNM1 has low expression. Of the 3 ER-localized atlastins, ATL3 is dominant while ATL1 has low expression. Of the 2 mitochondria-localized mitofusins, MNF2 is dominant. By western blot, we observed ATL3 dimerization increased in stressed cells, however, this was not inhibited by dynasore.

Conclusions: We have identified, for the first time, dynamin family members expressed by ocular surface epithelia. Dimerization of ATL3, which brings two ER membranes into contact, increases in cells subjected to oxidative stress. This is consistent with UPR-mediate ER-phagy to eliminate misfolded proteins and restore metabolic homeostasis. ATL3 dimerization does not appear to be targeted by dynasore at the current condition.

CONTROL ID: 3545949

SUBMITTER (NAME ONLY): Jessica Henry

TITLE: Gold nanorod in vivo molecular imaging of choroidal neovascularization using OCT and photoacoustic microscopy in rabbits

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Henry, V. Nguyen, Y. Li, Y.M. Paulus, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|V. Nguyen, NTT-Hi Tech Institute, Nguyen Tat Thanh University, Ho Chi Minh City, Ho Chi Minh, VIET NAM|W. Zhang, X. Wang, Y.M. Paulus, Biomedical Engineering, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Enhanced detection of choroidal neovascularization (CNV) can lead to improved visual acuity in patients by providing targeted treatment and monitoring of disease progression. This study uses functionalized gold nanorods conjugated with targeting RGD peptides (GNR-RGD) as contrast agents in the presence of a custom-built photoacoustic microscopy (PAM) and OCT imaging system. This combination is used to optimally distinguish the margins of CNV in rabbits.

Methods: CNV models were generated in two groups of New Zealand rabbits. 3 rabbits received laser-induced RVO with 50 mg/kg Rose Bengal and laser illumination. A pulse duration of 0.5 s and a laser spot size of 75 μ m were used with a power of 150 mW for the first 20 spots and 300 mW for an additional 20 spots. 3 other rabbits received subretinal injection of 750 ng human vascular endothelial growth factor (VEGF-165) at a concentration of 100 μ L/mL in 1% bovine serum albumin mixed with 20 μ L Matrigel. The models were monitored for 28 days until CNV had developed. All then received IV injection of 0.4 mL of targeting GNR-RGD (2.5 mg/mL). The injection was synchronously monitored with PAM and OCT and further imaged using fundus photography, OCT, PAM, FA, and ICGA at 2, 8, 24, and 72h and 5-14 days post-injection to provide visualization of GNR.

Results: IV administration of GNR-RGD into rabbit CNV models yielded a signal enhancement of 27.2-fold for PAM and 171.4% for OCT. The OCT and PAM signal peaked at 48 h post-injection. The PAM images were obtained at 578 and 700 nm, which permitted improved discernment of normal vasculature from CNV. Histological analysis and TUNEL assay showed no evidence of cell damage or death.

Conclusions: These images demonstrate that GNR-RGD can effectively localize to CNV regions to provide improved contrast and molecular imaging. For this reason, contrast-enhanced PAM and OCT provide a possible method of precise detection of CNV without harming ocular structures.

CONTROL ID: 3545950

SUBMITTER (NAME ONLY): Matjaz Mihelcic

TITLE: A novel rebound technology-based method for measuring corneal sensitivity

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mihelcic, Optometry, Optika Mesec, Bled, Slovenia, SLOVENIA|J. Päällysaho, M. Raudasoja, V. Honkanen, V. Seppä, M. Salkola, Icare Finland Ltd., FINLAND|P. Schollmayer, Eye hospital, University Medical Centre Ljubljana, Ljubljana, SLOVENIA|

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ABSTRACT BODY:

Purpose: Corneal sensitivity is an important factor in several ocular and systemic conditions, however, current measurement methods for corneal touch sensitivity are rather complicated and impractical to use. In a prospective clinical study, we evaluated a novel type of rebound technology based esthesiometry (RTE).

Methods: One hundred and eight subjects with mean age of 51,5 years (SD 18,2) were included in the study. The method used was a rebound technology-based prototype instrument employing a lightweight probe driven by a magnetic field. The corneal sensitivity of the subject was assessed by establishing the minimal perceivable kinetic energy probe velocity touching the center of the cornea for about 2 milliseconds. Test subjects used trigger button to report sensation. The stimuli were implemented in linear increments, starting with 0.67 μ J and ending with 26.01 μ J of energy (on average), in 10 steps, where velocity of the probe, the impact level, was linearly scaled. Thresholding algorithm was set to increase the stimulus intensity gradually, then to assess the final threshold by bracketing up and down. The final result was defined as the lowest intensity of the probe to which participants responded successfully twice. Classic Cochet – Bonnet (C–B) esthesiometer was used for comparison.

Results: All 216 eyes were successfully measured from which 26 exceeded the measuring range of the RTE and were excluded from the results. Average measured corneal sensitivity with the RTE was at the level of 3.4 μ J (SD 5.4 μ J) and with the C–B esthesiometer, 54.7 mm (SD 8.8 mm). The correlation of both types of measurements was $r = -0.70$ at significance level $p < 0.001$. The average within-subject deviation of the positive responses around the threshold obtained with RTE was 0.98 μ J. Dividing measurements to normal versus decreased corneal sensitivity using cut-off values of 56 mm (C-B) and 1.0 μ J (RTE) resulted in agreement between the two methods in 83 % of tested eyes.

Conclusions: We propose a novel method for corneal esthesiometry using rebound technology which could represent a practical and reliable way of measuring the corneal touch sensitivity in a clinical practice.

CONTROL ID: 3545951

SUBMITTER (NAME ONLY): ZIHE XU

TITLE: Associations between myopia risk variants and retinal electrophysiological parameters: a role of KCNQ5 in myopia development

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. XU, X. Jiang, C.J. Hammond, O.A. Mahroo, P.G. Hysi, King's College London Section of Ophthalmology, London, London, UNITED KINGDOM|X. Jiang, O.A. Mahroo, University College London Institute of Ophthalmology, London, London, UNITED KINGDOM|Z. XU, C.J. Hammond, P.G. Hysi, King's College London Department of Twin Research and Genetic Epidemiology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Numerous myopia risk loci have been identified, but underlying mechanisms remain unclear. Retinal signalling pathways are thought to be involved in controlling refractive development. The electrical responses of retinal neuronal populations can be recorded non-invasively in vivo from human subjects as the electroretinogram (ERG). We investigated associations between myopia risk loci and ERG parameters.

Methods: Adult twins from the TwinsUK cohort underwent ERG recordings incorporating the International Society for Clinical Electrophysiology of Vision (ISCEV) protocol. Recordings were made with conductive fibre electrodes in the lower conjunctival fornix. In participants with genotypic information, we explored associations between ISCEV ERG parameters and allelic dosages of 1361 exonic variants that were previously associated with refractive error. Genetic associations were quantified using univariate linear mixed models, adjusted for age and sex and genetic relatedness between family members. Secondary analyses, adjusting for the strongest known genetic effects in adjacent genomic regions associated with myopia, were used to explore the origin of the association signals in the respective loci.

Results: Genotypic information was available for 187 participants. One candidate risk locus (rs2840795) near the gene KCNQ5, showed the most significant association ($p = 7.84 \times 10^{-5}$) with an ISCEV parameter, namely the b-wave peak time elicited in the dark-adapted response to white flashes ($3 \text{ cd m}^{-2} \text{ s}$). The association remained significant even after adjustment for two additional common known polymorphisms (SNPs) at the KCNQ5 locus. The ERG b-wave response to this stimulus arises in bipolar cells driven by both rod and cone photoreceptors.

Conclusions: The association between the locus at KCNQ5 and ERG b-wave peak time suggest the possibility that changes in patterns of KCNQ5 expression or function might affect the timing of retinal bipolar cell signals generated in response to photoreceptor light-evoked responses. Immunohistochemistry studies in primate retina have shown KCNQ5 in the retinal pigment epithelium and neural retina, including in photoreceptor inner segments, which would be consistent with this effect. It is possible that alterations in bipolar cell responses are involved in conferring susceptibility to myopia.

CONTROL ID: 3545954

SUBMITTER (NAME ONLY): Andrew Vanslette

TITLE: Pharmacokinetics of OTX-CSI, a Cyclosporine Intracanalicular Insert, in Surgically Induced Dry Eye Beagle Dogs

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vanslette, C.D. Blizzard, A. Driscoll, M. Cheung, M.H. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Andrew Vanslette: Commercial Relationship(s);Ocular Therapeutix:Code E (Employment) | Charles Blizzard: Commercial Relationship(s);Ocular Therapeutix:Code E (Employment) | Art Driscoll: Commercial Relationship(s);Ocular Therapeutix:Code E (Employment) | Matthew Cheung: Commercial Relationship(s);Ocular Therapeutix:Code E (Employment) | Michael Goldstein: Commercial Relationship(s);Ocular Therapeutix:Code E (Employment)

ABSTRACT BODY:

Purpose: Cyclosporine and punctal plugs are used for the treatment of dry eye disease (DED) to increase tear production and tear conservation, respectively. OTX-CSI, a cyclosporine intracanalicular insert, combines the two modalities into a single treatment, and is designed to provide sustained release cyclosporine along with punctal occlusion. The objective of this study was to investigate the pharmacokinetics of cyclosporine drug released from OTX-CSI in a dry eye model following administration in beagle dogs.

Methods: Dry eye was surgically induced in the right eye of 12 beagle dogs by removal of lacrimal glands while the left eye was untreated (healthy). Ten days after surgery, OTX-CSI was administered in the canaliculus of both eyes on Day 0. Schirmer tears test were performed in both eyes pre-surgery (baseline prior to surgery on Day -10), post-surgery (Day -3, -2 and -1) and post-insertion of OTX-CSI (Days 11, 20 and 29) to monitor tear production. Tear fluid samples were collected using 10 mm Schirmer test strips at 3 hours, 1, 7, 14 and 28 days post-insertion and analyzed for cyclosporine concentrations by liquid chromatography tandem mass spectrometry.

Results: Mean Schirmer Tear Test Score was higher in healthy eyes at all timepoints post-baseline compared to dry eyes and was sustained through Day 29 showing successful induction of dry eye model (Figure 1). Mean tear fluid cyclosporine concentrations in the dry eye group were generally higher compared to concentrations in healthy eyes at most time points (Table 1) likely due to less dilution of the cyclosporine on the ocular surface with the reduced tear fluid production of surgically induced dry eyes. OTX-CSI was well tolerated and not associated with any substantial ocular findings and had no adverse effects on general, non-ocular health.

Conclusions: OTX-CSI successfully released cyclosporine into the tear fluid of surgically induced dry eyes of beagle dogs as demonstrated by cyclosporine concentrations greater than or equal to concentrations in healthy eyes. The reduction in tear fluid production (typically seen in dry eye subjects) does not appear to inhibit transport of cyclosporine to the tear fluid in beagle dry eyes. The insert is currently being evaluated for efficacy and safety in a Phase 2, randomized, masked, vehicle-controlled, multicenter clinical trial in subjects with dry eye (NCT04362670).

CONTROL ID: 3545958

SUBMITTER (NAME ONLY): Sam LaMagna

TITLE: Psychophysical Absolute Threshold in Mice is Inversely Related to Stimulus Duration

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. LaMagna, Y. Umino, Y. Guo, E.C. Solessio, Ophthalmology and Visual Sciences, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|E.C. Solessio, Neuroscience and Physiology, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stimulus duration and psychophysical threshold have an inverse linear relationship up to a critical duration, beyond which thresholds approach a constant value. While the mechanism governing this phenomenon in the amphibian visual system is understood, the mechanism setting the critical duration in mammals is unknown. An obstacle to defining this process is that the threshold-duration relationship has yet to be characterized in a genetically modifiable mammalian model organism. This study seeks to characterize the psychophysical threshold-duration relation in wild type mouse. We expected mice to exhibit a similar inverse-linear relationship as observed in humans and amphibian (Barlow 1958; Haldin et al 2009).

Methods: Absolute visual threshold was measured in 3 male C57 BL6/J mice using a modified 1-alternative forced choice task (Umino et al 2018). Dark adapted mice were trained, via operant conditioning, to visit one of two ports depending on whether a brief, dim stimulus was presented. Hit and False Alarm rates were calculated to determine a sensitivity index (d') value for each stimulus intensity to construct psychometric functions. Mice first learned the task with a bright, 2s stimulus under light adapted conditions. Mice were then slowly introduced to briefer stimuli and dimmer conditions. After achieving a stable d' value for a dim 60msec stimulus, multi-intensity trials for data collection began. Radiometric measures of stimulus intensity were converted to $R^*/\text{rod/s}$ (Lyubarsky et al 2004).

Results: Average d' values were well fit to stimulus intensity with log-linear models ($R^2 \geq 0.75$; $\alpha = 0.05$ ANOVA) at each duration (30ms-2s). At 30ms the absolute threshold, the intensity at the predicted $d' = 1$, was $0.27 R^*/\text{rod/s}$ ($SE = +/ - 0.11$). Assuming total temporal summation, this is $\sim 0.008 R^*/\text{rod}$. Each mouse exhibited an inverse linear relation between log-threshold and log-duration up to 250-500ms, below which, data is well fit with a linear equation on log-log axes, with slopes of -1.7, -2.0, and -2.9.

Conclusions: In wild type mice, absolute visual thresholds have an inverse relationship with stimulus duration. Unexpectedly, mice exhibit a supra-linear relation between stimulus duration and threshold. This study establishes a foundation to further study threshold-duration relationships in transgenic mouse lines, allowing us to dissect the neural circuits underlying temporal summation in the visual system.

CONTROL ID: 3545960

SUBMITTER (NAME ONLY): Donna Welch

TITLE: Vanishing optotype reading test in non-advanced age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Welch, J.D. Rodriguez, D. Narayanan, M.B. Abelson, Ora, Inc, Andover, Massachusetts, UNITED STATES|M.B. Abelson, Ophthalmology, Harvard University, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose:

During early stages of age-related macular degeneration (AMD), patients experience difficulty in everyday tasks including reading under low luminance (mesopic) and low contrast conditions. In this study, vanishing optotypes reading test using nine levels of contrast was used to assess visual function in AMD.

Methods:

Subjects with non-advanced AMD N=11 (grade 1 to 4 on AREDS simplified scale) and normal controls N=24 (AREDS grade 0) with best visual acuity (VA) 20/25 or better during their baseline visit were included. Vanishing optotype reading test was done using a computerized system. Testing was done for the study eye, with best correction in place and non-tested eye occluded. Passages comprising of a series of pepper words was presented on the screen. Each passage was of the same length and same font size but reduced in contrast as the test progressed. Nine different contrast levels ranging from high to low (0.29 to 0.02) were tested. A practice session was given prior to the actual test to get the subject acclimated with the test process. For each passage, reading speed and accuracy was documented. The time taken to read each passage accurately was recorded in words per minute (wpm).

Results: Both non-advanced AMD and normal subjects showed a clear trend of reduced reading performance with reduced contrast levels, although statistical significance was not reached. For example, mean (\pm SD) reading speed in normals and AMD subjects was 93.1 ± 21.3 and 89.5 ± 22.4 wpm at high contrast level (0.23), 84.4 ± 23.4 and 76.8 ± 24.0 wpm in mid contrast level (0.13) and was 10.4 ± 16.6 and 12.2 ± 12.3 wpm in low contrast level (0.02), respectively. The difference between normal and AMD groups showed a clear separation at mid and low contrast levels with AMD subjects showing reduced reading performance than normal group. Reading speed (wpm) at 0.09 contrast was 68.4 ± 26.4 in AMD and 77.8 ± 20.9 in normal group ($p=0.23$) and at 0.04 level was 18.7 ± 23.7 in AMD group and 28.4 ± 21.2 in normal group ($p=0.20$). Reading performance was similar in normals and AMD subjects for high contrast levels (0.29) (95.0 ± 19.3 wpm in normals and 95.2 ± 16.8 in AMD, $p=0.98$).

Conclusions: Reading test using vanishing optotype with varying contrast as a target shows promise to assess visual performance in AMD subjects and could be useful in clinical trials.

CONTROL ID: 3545963

SUBMITTER (NAME ONLY): Ellen Ingolfssland

TITLE: Erythropoietin (rHuEPO) administration to neonatal rats with oxygen-induced retinopathy (OIR) inhibits transcriptomic pathways central to retinal vascular development

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Ingolfssland, M. Molomjams, M. Georgieff, Pediatrics, University of Minnesota Academic Health Center, Minneapolis, Minnesota, UNITED STATES|L.K. McLoon, Ophthalmology and Visual Neurosciences, University of Minnesota Academic Health Center, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recombinant human erythropoietin is increasingly being used to treat or prevent anemia in preterm infants, but its association with retinopathy of prematurity (ROP) is complex. rHuEPO may reduce the risk of retinal hypoxia and neovascularization that anemia poses, but rHuEPO itself is known to trigger angiogenic pathways. We tested the hypothesis that rHuEPO administration would rescue retinal inflammatory and angiogenic transcriptomic pathways in a preclinical model of OIR and anemia.

Methods: Retinopathy was induced with the 50/10 oxygen-induced-retinopathy (OIR) model in Sprague Dawley rat pups. Anemia was induced by phlebotomy to a hematocrit of 18-20%, a 50% reduction from baseline hematocrit. rHuEPO was administered to 50% of the pups in the anemic and non-anemic groups from P10 to P20. Rats were euthanized at P20, RNA was isolated from whole retinal lysates, next generation sequencing was performed, and differentially expressed genes were mapped onto disease or function pathways by Ingenuity Pathway Analysis. Differentially expressed genes (DEG) were identified using absolute \log_2 fold change $\geq 1.5x$ with corrected-p value <0.05 and false discovery rate <0.05 .

Results: Anemia activated the transcriptomic pathway infection of mammalia (Z-score 1.5) and weakly activated pathways of vasculogenesis and angiogenesis (Z-score 0.6, 0.3 respectively) ($p<0.01$ for all). rHuEPO in the anemic, OIR pups resulted in no differentially expressed pathways related to vasculogenesis, angiogenesis, or inflammation. rHuEPO in the OIR pup without anemia inhibited multiple pathways involved in vascular development, e.g. cell movement, endothelial cell migration, vasculogenesis, angiogenesis, development of vasculature and inflammatory response, and activated pathways of apoptosis and infarction (Table 1).

Conclusions: At the time point of peak neovascularization, late rHuEPO administration inhibits multiple pathways important in vascular development in the non-anemic retinal transcriptome. Administering rHuEPO to the anemic rat pup rescued pathways of infection, suggesting an anti-inflammatory effect, and angiogenesis and vasculogenesis. rHuEPO may provide a protective effect against abnormal retinal vascularization in the at-risk retina.

CONTROL ID: 3545967

SUBMITTER (NAME ONLY): Whitney Stuard

TITLE: IGFBP-3 mediates mitochondrial homeostasis during hyperosmolar stress

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Stuard, D.M. Robertson, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Whitney Stuard: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Robertson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Purpose: The insulin like growth factor binding protein 3 (IGFBP-3) is a pleiotropic protein with known roles in cell growth and survival. Our prior findings suggest that IGFBP-3 may play a novel role in mitochondrial homeostasis in corneal epithelial cells (CECs). The purpose of this study was to determine expression levels of IGFBP-3 in CECs exposed to hyperosmolar stress and in a mouse dry eye model.

Methods: Methods: Telomerase-immortalized human corneal epithelial (hTCEpi) cells were cultured in serum-free keratinocyte basal media (330 mOsm, isotonic control). To induce hyperosmolar stress, cells were cultured in 450 mOsm media with or without recombinant human (rh)IGFBP-3 for 2, 6 or 24 hours. Mitochondrial respiration, morphology and polarization were assessed using Seahorse, transmission electron microscopy, MitoTracker and TMRE staining, respectively. Mitophagy was examined by live cell fluorescent imaging, immunofluorescence and western blotting. ROS levels were quantified using Amplex red. Dry eye was induced in C57BL6/N mice by injecting the extraorbital lacrimal gland with 20 milliunits of botulinum toxin. Mice were assessed for dry eye using phenol red thread and corneal staining using fluorescein at baseline, 7, 14 and 28 days. IGFBP-3 expression was quantified in both models at all time points using an IGFBP-3 sandwich ELISA.

Results: Results: Intra- and extracellular levels of IGFBP-3 were decreased in hTCEpi cells exposed to hyperosmolar stress. Intracellular levels of IGFBP-3 were also decreased in the corneal epithelium of mice with clinical signs of dry eye. hTCEpi cells in hyperosmolar culture further showed a loss in mitochondrial membrane polarization. This was associated with a shift towards a glycolytic phenotype and an increase in mitophagy. Mitochondria in cells exposed to hyperosmolar stress were small and irregular with a balloon-like morphology and loss of cristae. Cells co-treated with rhIGFBP-3 had a metabolic profile similar to control cells. There was a corresponding reduction in mitophagy. Mitochondrial morphology were elongated with intact cristae.

Conclusions: Conclusions: Taken together, these data confirm an important role for IGFBP-3 in the regulation of mitochondrial homeostasis in CECs exposed to hyperosmolar stress. Further studies are needed to determine the mechanism by which IGFBP-3 regulates these mitochondrial changes and metabolism.

CONTROL ID: 3545969

SUBMITTER (NAME ONLY): Puttur Santhoshkumar

TITLE: Cell-penetrable, protease-resistant α A-crystallin-derived peptide chaperone triggers cell stress response pathways and alleviates β -amyloid engendered toxicity in *Caenorhabditis elegans*

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Santhoshkumar, S. Srivastava, S. MAHALINGAM, M. Saddala, K. Sharma, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|G. Broitman-Maduro, A. Verma, M.F. Maduro, Cellular , Molecular and System Biology, University of Riverside, Riverside, California, UNITED STATES|A. Bhatia, J.S. Kirkwood, Institute for Integrative Genome Biology, University of Riverside, Riverside, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mini-chaperones derived from α A-crystallin, with their inherent anti-aggregation and anti-apoptotic properties, have therapeutic properties. A second generation mini-chaperone peptide, having cell-penetrating and protease-resistant properties (CPPRMC), was synthesized using L- and D- amino acids. This study aimed to evaluate the therapeutic efficacy of CPPRMC and unravel the mechanism of peptide action using cell culture and *C. elegans* model systems.

Methods: The anti-oxidant and anti-apoptotic properties of the CPPRMC was evaluated in sodium iodate-treated ARPE-19 cells. The effect of peptide treatment (50 μ g every two days along with *E. coli* OP50 food source) on the wild-type (N2) worm lifespan was tested at 20°C. Tolerance to chemical-stimulated oxidative stress (50 mM Paraquat, 50 μ M Juglone, and 40 mM glucose) was evaluated using peptide-fed N2 worms (Day-5). The CPPRMC's ability to attenuate beta-amyloid aggregation-induced paralysis and survival was tested in the CL4176 strain expressing β -amyloid peptide. RNA sequencing and high-throughput untargeted metabolic profiling (polar and non-polar) were also performed to compare differentially expressed genes and metabolites across experimental conditions.

Results: The Sodium iodate-induced (1 mM) oxidative stress and cytotoxicity were suppressed entirely in CPPRMC treated (5 μ M) ARPE-19 cells. Peptide treatment increased the lifespan of N2 worms by 18%. N2 worms pretreated with 50 μ g CPPRMC for 24h at 20°C and then subjected to thermal stress at 35°C showed a 43% increase in survival as equated to vehicle control. Peptide treatment delayed AD-related paralysis and extended worm's survival (17%) after temperature up-shift in CL4176. RNA-seq analysis showed the upregulation of genes responsible for lifespan increase, and the polar and non-polar metabolic profiling revealed altered metabolites involved in the lifespan.

Conclusions: The increased worm lifespan and alleviation of A β -induced toxicity up on CPPRMC treatment are likely mediated by the activation of molecules involved in stress response pathways. Our findings signify the therapeutic prospective of CPPRMC against aging and age-concerned AD.

CONTROL ID: 3545971

SUBMITTER (NAME ONLY): Baojian Fan

TITLE: Whole Genome Sequencing of Large Consanguineous Pedigrees from South India Identifies New Candidate Genes for Lens Thickness

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Fan, D.S. Friedman, J.L. Wiggs, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|P. Ferdina Marie Sharmila, N. Soumittra, S. Sarangapani, SNONGC Department of Genetics and Molecular Biology, Vision Research Foundation, Chennai, INDIA|L. Vijaya, R. George, Medical Research Foundation, Sankara Nethralaya, Chennai, INDIA|J.L. Haines, Department of Population and Quantitative Health Sciences, Cleveland Institute for Computational Biology, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lens thickness is an important risk factor for cataract, myopia and glaucoma. Identifying genes contributing to this quantitative trait may effectively identify genetic risk factors predisposing to related complex diseases. Previously we performed genome-wide linkage analyses in 16 consanguineous pedigrees from South India and identified 3 novel genetic loci (3p22.3, 5q31.1 and 6q27) for lens thickness. The purpose of this study is to refine the candidate genes in these loci using whole genome sequencing.

Methods: 279 individuals of 23 consanguineous pedigrees from South India were measured for lens thickness using Pentacam (Oculus, Inc., Lynnwood, WA). Whole genome sequencing was performed using the Standard Coverage PCR-Free WGS platform (read length: 2 x 150bp; coverage: 30x) at the Broad Institute. Homozygosity mapping was conducted using PLINK (v1.9) and detectRUNS (v0.9.6). Gene-based association test was performed for both rare and common variants using famSKAT-RC (v1.1.0). Age and sex were included as covariates. Multiple testings were corrected using the Bonferroni method.

Results: Homozygosity mapping revealed 4, 22 and 3 candidate genes in the 3p22.3, 5q31.1 and 6q27 loci, respectively. Gene-based association test further refined the candidate genes to CLASP2 ($P = 1.43 \times 10^{-6}$) and FBXL2 ($P = 1.41 \times 10^{-6}$) in the 3p22.3 locus, CXXC5 ($P = 1.04 \times 10^{-8}$), CYSTM1 ($P = 2.93 \times 10^{-6}$), ECSCR ($P = 7.76 \times 10^{-8}$), MATR3 ($P = 4.28 \times 10^{-8}$), PAIP2 ($P = 1.15 \times 10^{-7}$), PSD2 ($P = 1.69 \times 10^{-8}$), SIL1 ($P = 8.93 \times 10^{-8}$) and UBE2D2 ($P = 4.34 \times 10^{-8}$) in the 5q31.1 locus, and PACRG ($P = 1.07 \times 10^{-6}$) in the 6q27 locus.

Conclusions: We identified 11 candidate genes for lens thickness. Among these genes, MATR3 and PAIP2 are highly expressed in the mouse lens. Mutations in SIL1 are known to cause Marinesco-Sjögren syndrome, an autosomal recessive cerebellar ataxia complicated by cataracts, developmental delay and myopathy. These findings provide new insights into the genetic etiologies of lens thickness and related diseases.

CONTROL ID: 3545972

SUBMITTER (NAME ONLY): Raji Shyam

TITLE: Mitochondrial ROS leads to lysosomal dysfunction and autophagy impairment in an animal model of Congenital Hereditary Endothelial Dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Shyam, D.G. Ogando, M. Choi, J.A. Bonanno, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|P.B. Liton, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our goal is to understand how loss of the membrane protein Slc4a11 produces Congenital Hereditary Endothelial Dystrophy. In the current study, we ask if autophagy flux and lysosomal function are affected in Slc4a11 KO cells and determine whether mitochondrial ROS is responsible for any dysfunctions.

Methods: All experiments were conducted in 8 week old Slc4a11 WT and KO mice or in immortalized mouse WT and KO cell lines. Western Blot analyses were conducted using traditional (SDS-PAGE) or Simple Protein Wes® system. In order to quench mitochondrial ROS, cells were treated with 2mM MitoQ for 16 hours and animals were subject to i.p injections of 0.068mg on alternate days for four weeks.

Results: In Slc4a11 KO tissue, we observed an increase in autophagy substrate P62 (2.5 ± 0.5) and reduced lysosomal proteins; vATPase (0.2 ± 0.08), Cathepsin B (0.1 ± 0.02), Cathepsin D (0.1 ± 0.01), TFEB (0.1 ± 0.01) relative to WT. With MitoQ treatment, we observed a significant improvement in lysosomal protein expression and decrease in P62 levels. MitoQ treatment in Slc4a11 KO animals also showed improvement in two main disease characteristics, corneal endothelial cell density ($20 \pm 2.2\%$ improvement) and decreased corneal edema ($35 \pm 1.9\%$ reduction).

Conclusions: We show that mitochondrial ROS induced lysosomal dysfunction in Slc4a11 KO corneal endothelia. MitoQ treatment improved lysosomal function, autophagy, decreased corneal edema and improved corneal endothelial cell density.

CONTROL ID: 3545977

SUBMITTER (NAME ONLY): Hasan UI Banna

TITLE: Measurement of posterior ciliary artery perfusion velocity with super-resolution ultrasound localization microscopy

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. UI Banna, J. Palko, Ophthalmology, West Virginia University Eye Institute, Morgantown, West Virginia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Hasan UI Banna: Commercial Relationship: Code N (No Commercial Relationship) | Joel Palko: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: We evaluated the potential of super-resolution ultrasound localization microscopy (ULM) as a method to measure perfusion velocity in absolute metrics within the posterior ciliary arteries and their anastomoses.

Methods: Porcine ocular tissue from a local abattoir was dissected immediately following the sacrifice of the animal. The ophthalmic artery was further dissected and cannulated with micro-tubing attached to a microvolume syringe pump and in-line pressure transducer. A dilute microbubble (MB) ultrasound contrast agent (Vevo Micromarker) in 10% dextran and heparin was used to perfuse the whole globe. The anterior chamber was cannulated to manometrically maintain IOP at 25 mm Hg. Using a 50-MHz ultrasound transducer (Vevo2100, FUJIFILM VisualSonics) at a frame rate of 100 Hz, 3 sec of continuous image data was recorded with a mean arterial pressure of 60 mm Hg. Singular value decomposition was applied to separate tissue signal from the microbubble flow signals. A sparse recovery process was used to estimate the center position of the MB onto a high-resolution grid using knowledge of the MB point spread function and signal intensity. Multi-Hypothesis tracking in combination with Kalman filtering were used to incorporate the position and velocity information from prior frames to predict the position of each microbubble in each frame. The accuracy of the algorithm was validated using controlled velocity experiments in a 230 μ m inner diameter tubing system and by manually tracking MBs in the long posterior ciliary arteries (figure 1).

Results: Validation studies in controlled velocity tube experiments resulted in a root-mean-square error of 0.28 mm/s (controlled velocity range of 1.0 to 10.0 mm/s). The mean velocity within the long posterior ciliary artery was 4.18 mm/s using the tracking algorithm and 4.06 mm/s with manual MB tracking.

Conclusions: Super-resolution ULM provides spatial resolution beyond the acoustic diffraction limit. This technique has the potential to measure vascular perfusion in absolute metrics within regions of the globe that cannot currently be measured using conventional optical techniques.

CONTROL ID: 3545979

SUBMITTER (NAME ONLY): Helena Feenstra

TITLE: Long-term follow-up of chronic central serous chorioretinopathy patients after primary treatment of oral eplerenone or half-dose photodynamic therapy and crossover treatment: SPECTRA trial report No. 3

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Feenstra, T.J. van Rijssen, E. van Dijk, C.J. Boon, Ophthalmology, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|R. Diederens, R. Schlingemann, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|C. Hoyng, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: We performed an open-label, multicenter, randomized controlled trial to compare the anatomic and functional efficacy and safety of primary treatment with either half-dose photodynamic therapy (PDT) or oral eplerenone treatment, with or without crossover treatment in patients with chronic central serous chorioretinopathy (cCSC).

Methods: After the baseline visit of the SPECTRA trial, eligible patients were randomized in a 1:1 allocation ratio. Treatments involved indocyanine green angiography (ICGA)-guided half-dose PDT versus oral eplerenone for 12 weeks. Crossover treatment was performed in patients with persistent subretinal fluid (SRF) on optical coherence tomography (OCT) scanning at the first follow-up visit. The 2 crossover groups included 38/46 patients (82.6%) of the patients who received primary oral eplerenone, and 11/50 patients (22.0%) of the patients who received primary half-dose PDT. The presence of SRF on OCT, best-corrected visual acuity (BCVA), and both retinal and foveal sensitivity on microperimetry were evaluated during a final follow-up visit at 12 months after baseline.

Results: Out of the 96 patients who were evaluated at first follow-up visit, 49 patients had persistent SRF on OCT (38 in the eplerenone group and 11 in the half-dose PDT group). Out of 90 the patients who had a final follow-up visit, 38/39 (97.4%) in the group with primary resolution after half-dose PDT, 7/7 (100%) in the group with primary resolution after eplerenone, 30/35 (85.7%) in the group who received crossover from eplerenone to half-dose PDT, and 5/9 (55.5%) in the group who received crossover from half-dose PDT to eplerenone group, had a complete resolution of SRF on OCT. There were no differences in BCVA and retinal or foveal sensitivity between the groups at final visit.

Conclusions: Half-dose PDT is the treatment of choice for achieving complete resolution of SRF in cCSC, even after previous eplerenone treatment. Twelve months after baseline visit, most patients treated with half-dose PDT (either primary or crossover treatment) still had a complete resolution of SRF. Crossover after half-dose PDT to eplerenone is less likely to result in complete SRF resolution at long-term follow-up.

CONTROL ID: 3545981

SUBMITTER (NAME ONLY): Leo Hahn

TITLE: Clinical and genetic spectrum of patients with GUCY2D-associated retinal dystrophies

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To describe the spectrum of retinal dystrophies associated with GUCY2D, and to identify potential clinical endpoints and optimal patient selection for future (gene) therapy.

Methods: This multicenter retrospective study reviewed medical records of 52 affected patients from 30 unrelated families for medical history, symptoms, best-corrected visual acuity (BCVA), ophthalmoscopy, visual field, full-field electroretinography and retinal imaging (fundus photography, spectral-domain optical coherence tomography (SD-OCT), fundus autofluorescence).

Results: Patients had autosomal dominant cone-rod dystrophy (CORD; n=39; 75%) and autosomal recessive Leber congenital amaurosis (LCA; n=13; 25%). The mean follow-up time was 11.4±11.8 years for CORD and 5.7±4.4 years for LCA. The mean age at onset was 21.5±18.7 years and 0.4±1.0 years, respectively. For CORD, the mean Snellen BCVA at first visit was 0.25±0.22 (0.60±0.65 logMAR), and on average decreased with 0.07 (1.15 logMAR) per 10 years (p<0.003). In LCA patients, Snellen BCVA ranged from no light perception to 0.10 (1.00 logMAR). In CORD patients, the integrity of the ellipsoid zone (EZ) and external limiting membrane (ELM) on SD-OCT were significantly correlated with BCVA (Spearman's r=-0.685 p=0.001 and r=-0.61 p=0.004, respectively).

Conclusions: LCA associated with GUCY2D mutations resulted in severe congenital visual impairment. GUCY2D-associated CORD showed a later onset and a relatively slow decrease of visual acuity, possibly suggesting a relatively large window of opportunity for future (gene) therapy. Severe visual impairment in the CORD group was generally reached in the 5th decade of life. The integrity of ELM and EZ may be suitable structural endpoints for future gene therapeutic studies in CORD.

CONTROL ID: 3545984

SUBMITTER (NAME ONLY): Laura Valdez

TITLE: Stem Cell Protection for AMD Intervention

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.L. Valdez, Molecular Science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pigmented epithelium (RPE) cells are located between the choroid and photoreceptors within the eye and are essential to provide nutrients from blood to rods and cones, as well retinoids of the visual cycle. Vision loss and ocular diseases are attributable to the degeneration or dysfunction of the RPE cells, leading to blindness. One of the major ocular problem from RPE dysfunction is macular degeneration. Age-related macular degeneration (AMD) can be frequently diagnosed in elderly patients. The purpose of this study is to provide important information on the molecular pathway on RPE survival to minimize rejection of RPE cell in transplantation to restore vision in AMD patients. This study poses as a cell model for iPSC-RPE in either 5.5 or 30mM glucose conditions in proinflammatory or hypoxic environments to determine if IL8 can act as possible cell protectants against different glucose concentrations in proinflammatory and hypoxic conditions.

Methods: iPSC-RPE were seeded in fetal RPE media of MEM, N1 supplement, glutamine, nonessential amino acids, taurine .25mg/mL, hydrocortisone 10ng/mL, triiodothyronine 13ng/mL, 15%FBS, 1%pen/strep, in a humidified 5%CO₂ incubator with a temperature of 37°C. In order to determine the iPSC-RPE cell proliferation/viability, cell viability prior to treatment, 12hrs after treatment and 72hrs after treatment was determined using the Trypan Blue Method. Cells were treated with LPS 10µg/mL, Cobalt Chloride 1mM/mL, IL8 12.5ng/mL or 25ng/mL, 0mM/mL, 5.5mM/mL, or 30mM/mL of glucose. Cell culture media supernatants was collected and stored in -80°C. MCP-1 and RANTES were identified using a multiplex ELISA.

Results: Wells treated with 12.5ng/mL of IL8 in 30mM of glucose went from 11,700 cells at 12hrs to 2,060,000 cells at 72hrs. In comparison, wells treated with 25ng/mL of IL8 and increased from 11,700 cells at 12hrs to 258,000 at the end of treatment at 72hrs. RANTES showed a significant increase at 72hrs whereas MCP-1 expressed significant increase at 12hrs. The results from a Two Way ANOVA calculated the interaction effect and identified RANTES expression was significant at 72hrs comparable to MCP-1 expression at 12hrs.

Conclusions: Increased viable cell number in response to IL8 treatment suggest IL8 may provide protection for iPSC-RPE and MCP-1/RANTES expression. This study was essential in understanding possible therapeutic treatment models for AMD.

CONTROL ID: 3545985

SUBMITTER (NAME ONLY): Anthony Therattil

TITLE: Preoperative Imaging and Surgical Outcomes After Epiretinal Membrane Peeling in Pediatric Combined Hamartoma of the Retina and Retinal Pigment Epithelium

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Therattil, S. Cai, A. Ponugoti, C.A. Toth, L. Vajzovic, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore preoperative features of multimodal retinal imaging that may correlate with postoperative visual outcomes following pars plana vitrectomy with epiretinal membrane peeling (PPV/MP) in pediatric patients with combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) associated with epiretinal membrane (ERM) and decreased visual acuity.

Methods: A retrospective chart review was performed of pre- and post-operative visual acuity, fundus photographs, fluorescein angiograms, and spectral-domain optical coherence tomography (OCT) images among children with CHRRPE (diagnosed by a pediatric retinal surgeon at the Duke Eye Center between 2010 and 2020) with associated ERM who underwent a single PPV/MP, with at least 3 months of postoperative follow-up.

Results: Among 8 included patients, mean age at time of surgery was 7.69 years (range, 3 months to 13 years). 5 children were male. 5 lesions were peripapillary with or without macular involvement, 2 were localized to the macula, and one was peripheral with associated macular dragging. After a mean 26.38 months of postoperative follow-up, 3 patients had improved vision, 3 lost up to 2 lines of vision, 1 had stable fix and follow vision, and 1 had no wince to light (and questionable wince to light preoperatively). Among 6 patients with Heidelberg Spectralis OCT scans, mean preoperative central foveal thickness (CFT) was $725 \pm 279 \mu\text{m}$, with a mean decrease in CFT of $161 \pm 151 \mu\text{m}$ at last follow-up. For 2 patients, OCT scans were available but not retinal thickness measurements. Patients with the greatest improvement in vision postoperatively had preoperative CFT $< 700 \mu\text{m}$, absence of fovea-involving leakage on fluorescein angiography, and intact outer retinal layers on OCT. Patients with decreased or minimally improved vision postoperatively had fovea-involving leakage on fluorescein angiography and irregular or disrupted subfoveal outer retinal layers.

Conclusions: A combination of fluorescein angiography and OCT structural features may identify children who will have the greatest visual acuity gains after PPV/MP for CHRRPE associated with ERM.

CONTROL ID: 3545988

SUBMITTER (NAME ONLY): Jon Whitney

TITLE: Multi-resolution Deep Learning Convolutional Networks for Improvements in OCT Retinal Layer Segmentation

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Whitney, D. Sevgi, S. Srivastava, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Accurately segmenting OCT images requires both a high-resolution understanding of the specific boundary between medically significant regions, as well as an understanding of the broader context of the imaging boundary. Our group has developed an approach which uses a combination of low-magnification (low-mag) convolutional models to detect regions of interest where the specific retinal boundary is likely to be located, as well as high-magnification (high-mag) models which create high-resolution annotations within those regions of interest. The goal of this project was to measure segmentation performance improvements resulting from multi-scale approaches in images that require both large-scale contextual information and precision.

Methods: A total of 111,000 annotated OCT images were used in training and testing. For this analysis, a single retinal layer, the internal limiting membrane (ILM), was utilized for evaluation purposes. Three training methodologies were tested. One method processed OCT images using a high-resolution patch system and divided images into 128x128 patches. A second method utilized a low-mag model where training images were compressed into 128x128 patches. A third high-mag model was trained leveraging the low-mag model to center a 128x128 patch around where the low-mag model indicated the location of the retinal boundary of interest. The performance of these models was compared by measuring the average pixel distance away from manual ground truth.

Results: The patch-diced model had an average offset of 12 pixels (stdev 15 pixels) which demonstrated high resolution but poor regional context. The low-mag model had an average offset of 4.9 pixels (stdev 0.92 pixels), and the highmag-lowmag combination had an average offset of 2.6 pixels (stdev 0.93 pixels). The differences between each of the populations average distance from ground truth were statistically significant (p values less than 0.025).

Conclusions: These results demonstrate the potential for enhanced retinal layer segmentation performance through a multi-model approach using both low and high-mag system. The combined model approach provides assessment of both regional contextual information and subsequent high-resolution modeling for improved segmentation precision.

CONTROL ID: 3545998

SUBMITTER (NAME ONLY): John Miller

TITLE: Prevalence and Distribution of Venous Loops and Association with Retinal Ischemia in Diabetic Retinopathy Using Widefield Swept-Source Optical Coherence Tomography Angiography (WF SS-OCTA)

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.B. Miller, R. Le, Y. Cui, E.S. Lu, Y. Zhu, R. Katz, I. Garg, J. Wang, Y. Lu, R. Zeng, I. Lains, D. Elliott, D. Husain, J.W. Miller, L.A. Kim, D.M. Wu, Retina Service, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal venous loops (RVLs) are rare findings in diabetic retinopathy (DR). Bek reported 7.7% prevalence of RVLs in patients with proliferative DR (PDR) using color fundus photography (CFP). However, previously reported prevalence of RVLs may be underestimated due to limited detection of vascular abnormalities on CFP. This study aimed to determine RVL prevalence, distribution and associated microvascular changes using WF SS-OCTA.

Methods: Retrospective, observational study including diabetic patients with proliferative DR (PDR), non-proliferative DR (NPDR) and no DR. All patients were imaged with WF SS-OCTA using Angio 6×6mm and Montage 15×15mm scan protocols centered on the fovea. Images were independently evaluated by two graders for the presence of RVLs and other DR lesions including nonperfusion areas (NPAs) and neovascularization (NV). RVLs were classified as type I or type II according to the branching level of the feeder vessel. Type I RVLs emerge from larger veins encompassing the first and second branching level from the central retinal vein; type II RVLs emerge from the third or higher branching level. A binary logistic regression model (outcome: presence of RVLs) was used for statistical analyses.

Results: One hundred and ninety-five eyes of 132 diabetic patients (n = 31 without DR; 57 NPDR and 107 PDR) were included. Among them, 22 eyes (11%) had RVLs on WF SS-OCTA. The prevalence of RVLs was higher in PDR eyes compared to NPDR eyes (18% vs. 5%, p<0.05, Chi-square test). Type II RVLs were more prevalent than type I RVLs (p<0.001, Chi-square test). In terms of distribution, RVLs were more likely to originate from superior (vs. inferior) and temporal (vs. nasal) veins (p<0.05, Chi-square test). More advanced severity of DR (OR = 4.495, 95% CI: 1.177-17.161, p = 0.028) and younger age (OR = 0.961, 95% CI: 0.926-0.998, p = 0.037) were associated with the presence of RVLs. NPAs and NV area/number were not significantly correlated with the presence of RVLs.

Conclusions: WF SS-OCTA is useful for the identification of RVLs in patients with DR. Severity of DR, but not ischemia-related imaging biomarkers, was associated with the presence of RVLs in our cohort. Further longitudinal studies may be needed to identify the role of RVLs in DR progression and retinal ischemia.

CONTROL ID: 3546003

SUBMITTER (NAME ONLY): Luke Wiley

TITLE: Evaluating the tropism of chimeric helper-dependent adenoviral vectors for delivery of large genes.

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Wiley, E.R. Burnight, D. Ochoa, M.M. Collins, K. Varzavand, E.M. Stone, R.F. Mullins, B.A. Tucker, I. Han, Ophthalmology & Visual Sciences, The University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite success with retinal gene therapy using adeno-associated viruses (AAVs), many disease-causing genes, like ABCA4 or USH2A, are too large for packaging into a single AAV. One option for delivery of large retinal genes is helper-dependent adenoviruses (HDAd5). However, we recently showed that HDAd5 primarily targets Müller cells, not photoreceptors and elicits an inflammatory response. The purpose of this project is to evaluate the tropism and photoreceptor transduction efficiency of two chimeric HDAd5s.

Methods: Chimeric HDAd5s carrying eGFP under the control of the cytomegalovirus promoter (CMVp) were purchased from Creative Biolabs: HDAd5 constructed with the adenovirus 5 (Ad5) backbone and either an Ad3 or Ad35 fiber [HDAd5/3-CMVp-eGFP (HDAd5/3) and HDAd5/35-CMVp-eGFP (HDAd5/35)]. For testing in vitro, hTERT-immortalized human induced pluripotent stem cell (iPSC)-derived retinal progenitor cells were transduced with 10 μ L of HDAd5, HDAd5/3 or HDAd5/35 (1×10^6 vg/ μ L per well) and assessed via fluorescent microscopy at 72-hours post-transduction. For in vivo analysis, we utilized Sprague Dawley and RNU^{+/-} rat lines and subretinally injected 10 μ L of HDAd5/3 or HDAd5/35 viral particles (1×10^6 vg/ μ L per eye) or sterile buffer and assessed injected eyes at 3- and 7-days post-injection via immunohistochemistry and confocal microscopy.

Results: EGFP-positive retinal progenitor cells were observed at 72-hours post-transduction in wells treated with HDAd5, HDAd5/3 or HDAd5/35. There were noticeably more eGFP-positive cells in HDAd5/3- and HDAd5/35-treated cultures compared to HDAd5-treated wells. Fundus photography demonstrated that both HDAd5/3 and HDAd5/35 produced a speckled eGFP expression pattern, suggestive of photoreceptor cell transduction at 3- and 7-days post-injection in each Sprague Dawley and RNU^{+/-} rats. Confocal microscopy showed prominent eGFP expression within the retinal pigmented epithelium and neural retina.

Conclusions: Compared to HDAd5, chimeric HDAd5/3 and HDAd5/35 produced more eGFP-positive cells when delivered to human iPSC-derived retinal progenitor cells. Subretinal injection of HDAd5/3 and HDAd5/35 also produced eGFP expression in the retinal pigmented epithelium and neural retina of Sprague Dawley and RNU^{+/-} rats. Future studies will further characterize the tropism and transduction efficiency of chimeric HDAd-mediated gene transfer in the neural retina.

CONTROL ID: 3546005

SUBMITTER (NAME ONLY): Alexandra Sipatchin

TITLE: Impact of unconstrained head movements to scotoma and enhanced scotoma simulation in virtual-reality (VR) smooth pursuit gaming

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Sipatchin, M. García García, S. Wahl, Universitätsklinikum Tübingen
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ABSTRACT BODY:

Purpose: The impact over visual tasks of a simulated central scotoma in healthy subjects overcomes interfering complications associated with retinal diseases or aging. Patients with age-related macular degeneration (AMD), do not benefit from a head-unrestrained viewing in a smooth pursuit task. The current study investigates the role of a head-unrestrained setting over a simulated and enhanced scotoma applied to healthy participants in a smooth-pursuit task to look for similar head-movement strategies.

Methods: Participants were asked to pursue a moving target with unrestricted head movement while playing a 2D Pong game in VR. The moving target consisted of a 3° ball moving with an average velocity of 21.74°/s (SD: ±0.63) from one side to the other of the screen following a randomised triangular trajectory. The subjects controlled both paddles to keep the moving ball inside the playing area. Five participants were tested in 3 conditions: normal, scotoma, and augmented scotoma simulation. In the 2nd condition, eye-tracking was used to simulate a 12° circular scotoma occluding the central visual field (VF). In the 3rd condition, a 2° circular augmentation, with a diameter of 27° was implemented around the simulated scotoma. Figure 1 shows an example of a target trajectory in the 3rd condition. Each condition was tested for 15 minutes within 5 min blocks. Head velocity was calculated as the head position vector's velocity changes across subsequent frames. Velocity was averaged across each condition for each subject. A Kruskal–Wallis test investigated the effect of condition type over median head velocity.

Results: Individuals with no simulation, simulated and augmented simulated scotoma have similar head velocities with no effect across the three conditions over the head movement strategy, $\chi^2(2) = 0.38$, $p = .83$.

Conclusions: As previous studies using patients showed, head velocity was not affected in head-unrestrained VR gaming smooth pursuit task in normal, scotoma simulated, and augmented simulated scotoma conditions. The congruence of the results with the literature indicates that these new VR simulations can be further utilised to investigate oculomotor control under common eye disorders for future patient use.

CONTROL ID: 3546006

SUBMITTER (NAME ONLY): Jason Keil

TITLE: Endophthalmitis, visual outcomes, and management strategies in eyes with intraocular foreign bodies

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.M. Keil, P.Y. Zhao, A.F. Durrani, L. Azzouz, D.N. Zacks, Kellogg Eye Center, Department of Ophthalmology and Visual Sciences, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|M.J. Huvard, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|V.S. Dedania, Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify risk factors for endophthalmitis and poor visual outcomes in cases of retained intraocular foreign body (IOFB) and management strategies for these cases.

Methods: A retrospective chart review was conducted in 88 eyes of 88 patients suffering traumatic injury with retained IOFB at the University of Michigan between January 2000 and December 2019. Medical records were reviewed to identify the nature of the injury, IOFB composition, and presenting characteristics of each eye as well as the surgical and antimicrobial strategies employed. Details of the injury, IOFBs, and clinical presentation were utilized to identify factors associated with clinical outcomes. Visual outcomes and development of endophthalmitis were additionally evaluated for association with treatment modalities.

Results: This cohort developed endophthalmitis at a rate of 11.4% (4.5% presented with endophthalmitis, 7.1% of the remaining eyes developed endophthalmitis after initial intervention). Delayed presentation and organic IOFB were significantly associated with development of endophthalmitis. Retinal detachment, wound length greater than 5 mm, and poor presenting visual acuity were associated with poor final visual outcome. Antibiotic prophylaxis was given to all patients, though agents and routes of delivery varied. Primary and deferred removal of posterior segment IOFBs were associated with similar rates of endophthalmitis.

Conclusions: Poor presenting visual acuity and severity of injury as measured by large wound and retinal detachment correlate with poor visual outcome. Prompt globe closure and antimicrobial prophylaxis is critical for infection prevention. Deferred IOFB removal may carry similar risk of endophthalmitis as primary removal.

CONTROL ID: 3546008

SUBMITTER (NAME ONLY): Yao Tong

TITLE: Inhibition of RPE ferroptosis by necroptosis inhibitor Necrostatin-1

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Tong, Y. Wu, J. Ma, S. Wang, Tulane University, New Orleans, Louisiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a degenerative disorder of the macula, the region of central retina responsible for the greatest visual acuity. Oxidative stress and aging of retinal pigment epithelial (RPE) cells are the major reason of AMD. 4-Hydroxynonenal (4-HNE) is a major product of lipid peroxidation which takes part in ferroptosis of cells. Also, 4-HNE is accumulated in aging cells and could be related to several age-related diseases. The mechanism of RPE cell death under oxidative stress is still controversial. The goal of the current study is to determine RPE cell death mechanisms using 4-HNE and RSL3 treatment models.

Methods: ARPE-19 or human primary RPE cells were treated with 4-HNE or RSL3, and cell viability was tested 24 hours later. The effect of apoptosis, necroptosis, pyroptosis and ferroptosis pathways on cell survival was tested using specific inhibitors. Cellular ATP and ROS levels were measured. Cell morphology was observed under a light microscopy, PYCARD and RIPK3 expression was used to visualize inflammasomes and necrosomes that are involved in pyroptosis and necroptosis, respectively. Lipid ROS, a ferroptosis marker, was tested using BODIPY reagent.

Results: 1. 4-HNE induces RPE cell death in a concentration-dependent manner which can be rescued by ferroptosis inhibitors (Lip-1 and Fer-1) and both upstream and downstream necroptosis inhibitors (RIPK1 inhibitor Nec-1 and MLKL inhibitor NSA respectively), but not apoptosis or pyroptosis inhibitors; 2. Ferroptosis inducer RSL3 induces RPE cell death in a concentration-dependent manner which can be rescued by Lip-1, Fer-1, and Nec-1, but not NSA; 3. Both 4-HNE and RSL3 induce RIPK3 activation in RPE cells which can be inhibited by Lip-1, Fer-1, and Nec-1; 4. Both 4-HNE and RSL3 induce lipid ROS accumulation in RPE cells which can be inhibited by Lip-1, Fer-1, and Nec-1 but not NSA.

Conclusions: Both RSL3 and 4-HNE can induce RPE ferroptosis. Ferroptosis is associated with RIPK3 activation, therefore representing one type of necroptosis. However, 4-HNE but not RSL3-induced RPE death can be inhibited by MLKL inhibitor NSA. RIPK1 inhibitor Nec-1 is likely a better inhibitor for RPE ferroptosis compared to MLKL inhibitor NSA, possibly because RIPK1/3 activation can induce other types of cell death when MLKL is inhibited.

CONTROL ID: 3546009

SUBMITTER (NAME ONLY): Palaiologos Alexopoulos

TITLE: Under pressure: Response of the lamina cribrosa pore tortuosity to acute pressure changes

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Lamina cribrosa (LC) deformation is hypothesized to be a major cause of glaucoma. The LC undergoes different forms of stress both anteriorly from intraocular pressure (IOP), as well as posteriorly and circumferentially from subarachnoid cerebrospinal fluid pressure (CSFP) and the sclera. The purpose of this study was to determine possible in vivo changes in the path of the lamina pores under different IOP settings while maintaining fixed CSFP.

Methods: Spectral-domain OCT scans (Leica, Chicago, IL) of the optic nerve head (ONH) were acquired in vivo under different pressure settings from healthy rhesus monkeys. IOP was controlled using a gravity-based perfusion system through a needle inserted into the anterior chamber. CSFP was maintained at the baseline opening pressure via gravity-based perfusion system through cannulation of the brain's lateral ventricle (range 8-12mmHg). Scans were acquired at baseline IOP (15mmHg), high (30 mmHg) and very high IOP (40-50 mmHg) and registered in 3D. Pores from shared regions were automatically segmented using a previously described segmentation algorithm. The path of each pore was tracked based on the calculated geometric centroid of each pore. The tortuosity of each pore path was defined as the total actual distance of the centroid path divided by the minimal distance between the first (most anterior) and last (most posterior) pore centroids.

Results: 7 eyes from 6 healthy adult Rhesus macaque were analyzed. The mean value of the pore path tortuosity varies between eyes at baseline IOP levels (range: 1.16-1.68; Table). Two main overall patterns of pore path tortuosity were detected in response to increased IOP at fixed CSFP: 4 eyes became more tortuous (M2, M5, M8, M11); in the rest of the eyes (M6 OD, M6 OS, M10) the pore paths remained either unchanged or showed a variable response. No statistically significant change ($p > 0.05$) was observed in this small sample in either the subject-specific analysis or the analysis of the pooled combined values of the pore path tortuosity.

Conclusions: Baseline pore tortuosity as well as the response of the pores to acute IOP increase varies between eyes. Further investigation is warranted to determine if these differences are associated with glaucoma susceptibility.

CONTROL ID: 3546012

SUBMITTER (NAME ONLY): Nathaniel Jackson

TITLE: Characteristics Associated with Proliferative Sickle Cell Retinopathy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Jackson, R. Muhtadi, A. Radparvar, J. Lin, U. Mian, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|J. Lin, U. Mian, Ophthalmology & Visual Sciences, Montefiore Medical Center, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blinding retinopathy in sickle cell disease is usually associated with vitreous hemorrhage or tractional retinal detachment, which are preceded by neovascularization (NVE) of the retina. There is currently no widely accepted framework for predicting progression to proliferative sickle retinopathy (PSR). We evaluated serial fluorescein angiograms (FA) to identify variables associated with PSR in this descriptive retrospective qualitative study.

Methods: Serial FA's of 7 patients with sickle cell disease (4/7 SC, 1/7 SS, 1/7 SB, 1/7 S-O Arab) with progression of retinopathy to PSR were reviewed. All patients were seen at Montefiore Medical Center in Bronx, New York. Progression was defined as new NVE or increase in size or fluorescence of persistent NVE. FA were reviewed by 3 medical students trained by 2 retina specialists. Agreement on variables was obtained at time of grading. Variables included distance of retina visualized, capillary dropout (CD), arteriovenous loops at vascular border (AV Loop), arborization with and without staining, and CD posterior to vascular border (CDPB). Variables were evaluated by clock hour ± 0.5 centered on the temporal ON. Clock hours without visible border due to hemorrhage, blurred image, or lack of image were excluded from analysis. Distance of variables from temporal ON was calculated with unit of distance, X, equal to the distance between temporal optic disc and fovea. Student's T-test and chi-square test of independence were used to analyze the data.

Results: 288 total clock hours were analyzed, 163 contained visualizable border, and 18 contained NVE. CDPB and arborization with and without staining were significantly more common in clock hours with NVE. There was also significantly less distance captured in the images of clock hours with NVE. CD and AV loops trended towards being more common in clock hours with NVE.

Conclusions: It is important to perform routine serial FA's in patients with sickle cell disease to better evaluate the risk of developing NVE. Patients who have FA's with CDPB and/or arborization should be followed more closely as these characteristics may indicate a higher chance of developing proliferative disease.

CONTROL ID: 3546013

SUBMITTER (NAME ONLY): Yonghong Jiao

TITLE: Genotype-phenotype correlations in a Chinese cohort of CFEOM patients with KIF21A and TUBB3 mutations

SESSION TITLE: Ocular dysmotility and misalignment: Basic and Clinical studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Jiao, D. Wang, H. Jia, Q. Chang, Y. Liang, Q. Ma, Beijing Tongren Hospital, CHINA|

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ABSTRACT BODY:

Purpose: KIF21A and TUBB3 are two common pathogenic genes identified by congenital fibrosis of extraocular muscles (CFEOM) which is an inherited nonprogressive neuromyopathy. This study aims to explore the phenotype-genotype correlations in Chinese CFEOM patients with KIF21A and TUBB3 mutations, and to discover further understanding of gene functional.

Methods: Thirty-nine subjects from familial or sporadic CFEOM cases with clinical examinations, MRI findings and positive genetic test results were enrolled for retrospective case series study. MRI was used to evaluate orbital, encephalic, and intracranial nerve integrity. Ocular motor nerves diameters and extraocular muscle (EOM) volumes were measured.

Results: Genetic testing indicated that 53.8% patients harbored KIF21A mutations (p.R954W, p.R954Q, p.F355S), 30.8% with TUBB3 mutations (p.R262C, p.R262H, p.R380C, p.E410K, p.S78T), and 15.4% with others. All familial patients were detected with pathogenic mutations in KIF21A (68.4%) or TUBB3 (31.6%). Among subjects with KIF21A and TUBB3 mutations, all subjects showed typical ocular manifestation; two subjects (9.5%) with KIF21A mutations and 4 subjects (33.3%) with TUBB3 mutations showed other systemic malformations (e.g., congenital finger contractures, funnel chest etc.). MRI revealed hypoplasia of oculomotor nerve (CN3) and the atrophy of corresponding extraocular muscles. Mean±SD CN3 diameter in TUBB3 group was 1.03±0.45 mm, slightly but not significantly smaller than the diameter in KIF21A group, which measured 1.11±0.39 mm. Fifteen subjects (71.4%) with KIF21A mutations had unilateral or bilateral abducens nerve (CN6) absence and one subject (6.3%) with TUBB3 mutations had bilateral absence. Meanwhile, SR, IR and LR volumes in subjects with KIF21A were significantly smaller than those in TUBB3 group ($p < 0.001$). Besides, the phenotypes of TUBB3 mutations were notably differ from each other. Five patients (66.7%) in TUBB3 had intellectual disabilities with dysplasia of the midline commissural structures (anterior commissure, corpus callosum etc.).

Conclusions: KIF21A and TUBB3 are hotspot mutation genes and KIF21A is the main pathogenic gene in Chinese CFEOM. CN3 and its innervated extraocular muscles are most often affected. TUBB3 group had more systemic malformations and brain developmental defects. Moreover, TUBB3 group had a better correspondence between genotype and phenotype.

CONTROL ID: 3546014

SUBMITTER (NAME ONLY): Kazuya Oikawa

TITLE: Optic nerve head (ONH) glial activation molecular signature across disease stages in a feline glaucoma model

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mechanisms of axonal insult within the ONH in glaucoma are not fully understood. This study aimed to delineate ONH molecular alterations in chronic stages of glaucoma, in an inherited feline model with ONH structure comparable to humans.

Methods: ONH tissues from 10 LTBP2^{mut/mut} cats with glaucoma and 5 wt control cats (age 1-3 yrs) were used to generate cDNA libraries for RNAseq. Weekly intraocular pressure (IOP) data and optic nerve axon counts were available for all subjects. Differentially expressed genes (DEGs) were identified using DESeq2 (false discovery rate < 0.05), and g:Profiler was used for functional enrichment analysis. DEGs in chronic glaucoma were compared to DEGs in an RNA-seq dataset generated by our lab from ONH tissues of LTBP2^{mut/mut} cats prior to axon degeneration. Transcriptomic findings were validated by RNAscope in situ hybridization (ISH) and by immunolabeling (IF) of archived ONH tissue sections. For confirmatory studies, data were compared between groups by two-tailed unpaired t-test or ANOVA (p < 0.05 considered significant).

Results: Mean and cumulative IOP over 10mths prior to tissue collection were consistently higher in LTBP2^{mut/mut} than in wt cats. Stratifying subjects by optic nerve damage based on histological evaluation (mild [MLD], moderate [MOD] and severe [SEV] damage), 77, 882 and 1878 DEGs were identified, respectively, in glaucoma relative to age-matched controls. Functional analysis of DEGs in chronic, established glaucoma (MOD and SEV groups) identified upregulated DEGs ascribed to cell adhesion, immune/inflammatory responses, and MAPK cascade, and downregulated DEGs associated with metabolism, fatty acid synthesis, actin cytoskeleton and myelination. Comparing these DEGs in established chronic glaucoma to those in pre-degenerative, early-stage disease, 111 DEGs were shared between stages, including significant upregulation of HP and TNC. ISH confirmed expression of HP and TNC in the ONH, but with sub-regional differences in expression. TNC was highly expressed in the prelaminar - laminar regions and HP in the laminar and retrolaminar regions. ISH and IF identified astrocytes as the predominant ONH cell-type expressing these gene products.

Conclusions: Early and chronic stages of glaucoma share a reactive astrocyte molecular signature. Gene expression changes are more complex and enhanced in chronic glaucoma.

CONTROL ID: 3546015

SUBMITTER (NAME ONLY): Marianne Price

TITLE: Descemet stripping endothelial keratoplasty: 15-year outcomes

SESSION TITLE: Corneal transplantation and surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Price, Cornea Research Foundation, Indianapolis, Indiana, UNITED STATES|F. Price, Price Vision Group, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endothelial keratoplasty has become the gold standard for treating corneal endothelial dysfunction, but little is known yet about the long-term outcomes. Therefore, this study was designed to evaluate 15-year outcomes of Descemet stripping endothelial keratoplasty (DSEK).

Methods: This retrospective, observational study assessed postoperative outcomes through 15 years in an initial consecutive series of 360 DSEK cases performed between December 2003 and December 2005 at a single center. The main outcomes were graft survival and immunologic rejection rates determined by Kaplan-Meier and proportional hazards analysis, central corneal thickness (CCT) measured with ultrasonic pachymetry, and best spectacle-corrected visual acuity (BSCVA) assessed with a Snellen chart.

Results: The transplant indications were Fuchs dystrophy (n=301, 84%), bullous keratopathy (n=34, 9%), and previous keratoplasty failure (n=25, 7%), and the mean age at the time of DSEK was 69 ± 12 years. At 15 years, 50 grafts were replaced or failed (14%), 136 (38%) were in patients known to have died, and 55 of the remaining 174 grafts (32%) were examined. The 15-year graft failure/replacement rate was 22%, taking loss to follow up into consideration. Fifteen grafts were replaced within the first year because of early failure to clear (n=9) or unsatisfactory vision associated with excessive graft thickness or wrinkles (n=6), and 35 experienced late endothelial failure (11 after clinically evident immunologic rejection and 24 without evidence of rejection). Glaucoma filtration surgery (present in 34 eyes, 9%) was associated with a 4-fold increased risk of graft failure (p<0.0001). The median CCT remained stable at 650 to 660 microns from 6 months to 15 years. The median BCVA among all examined eyes was 20/40 from 3 to 12 months and 20/30 from 2 to 15 years.

Conclusions: DSEK provided superior long-term visual rehabilitation and had a 15-year survival rate comparable to that of the previous standard, penetrating keratoplasty, when performed for similar indications. The DSEK failures that occurred within the first year were mostly associated with the learning curve at a time when techniques and instrumentation were still being developed and refined.

CONTROL ID: 3546021

SUBMITTER (NAME ONLY): Bhavya Harjai

TITLE: Ensemble classifiers for an objective prediction of severity of uveitis based on measurement of aqueous flare and first-order patient characteristics

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: SUN (Standard Uveitis Nomenclature) scoring is subjective, hence its use to characterize the severity of inflammation in mild-to-moderate uveitis is clinically challenging. By leveraging objective measurements of the intensity of light scatter (ILS; as a measure of aqueous flare), we intend to achieve a robust prediction of the severity of inflammation by machine learning (ML) for enhanced clinical management of uveitis through consistent grading and granular indexing of the inflammation.

Methods: Patients diagnosed with uveitis were graded by SUN scores, and their ILS were recorded using a laser flaremeter (Kowa FM700). Normal subjects with no pathology served as controls. Ensemble method classifiers were used to predict the severity of inflammation based on ILS and first-order patient characteristics, which included the type of uveitis, status of iris/lens/pupil/cornea, and comorbidities such as diabetes.

Results: Fig. 1 is the summary of ILS in uveitis patients and normals. Regression showed a weak correlation between ILS and the SUN grade ($p < 0.0001$, $r^2 = 0.41$ on \log_2 of ILS). To train supervised ML classifiers, SUN scoring by one expert clinician was treated as the ground truth. Since our challenge is to distinguish mild-to-moderate uveitis, we focused only on data of patients with SUN scores of 0 and 1+. The dataset was imbalanced as the # of eyes w/SUN grade of 1+ was smaller compared to the # of eyes w/grade 0. Therefore, we explored data balancing approaches. The approach of the balanced bagging classifier, which incorporates under-sampling of the data, produced an F1 score of 0.92 with an accuracy of 90%. Another approach relied on SMOTE for data oversampling. The resulting balanced dataset was used to train the Random Forrest classifier, resulting in an F1 score of 0.88, with an accuracy of 83%. The classifier also identified the mean and SD of ILS as the top features of importance, thereby validating the significance of ILS measurements for grading the severity.

Conclusions: The aqueous flare is reliable for objective quantification of the intraocular inflammation. Our analysis has shown that ILS and its SD can reliably train ML models to grade uveitis on par with expert clinicians. Further optimization of the ML models and additional data on patients with Grade 1+ can be expected to enhance the performance of the ensemble methods.

CONTROL ID: 3546022

SUBMITTER (NAME ONLY): jiannong dai

TITLE: Overexpression of actin associate proteins promotes cross-linked actin networks (CLANs) formation in trabecular meshwork cells

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. dai, M. Peng, N.P. Rayana, C.K. Sugali, W. Mao, Ophthalmology, Indiana University Department of Ophthalmology, Indianapolis, Indiana, UNITED STATES|W. Mao, Biochemisctry, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elevated TGF β 2 in the aqueous humor is one of the most studied biomarkers of glaucoma. TGF β 2 induces excessive extracellular matrix proteins as well as the formation of cross-linked actin networks (CLANs) in trabecular meshwork (TM) cells. CLANs are complex web-like structures. Our previous studies identified four actin-associated proteins including caldesmon, calponin, tropomyosin and myosin light chain which are enriched in CLANs. In this study, we determined if these proteins promote CLAN formation in the TM.

Methods: Lentiviral vectors were constructed to express fusion proteins of caldesmon/calponin/ myosin light chain/tropomyosin+GFP. Primary human TM (HTM) cells were cultured close to confluency and transduced with different lentiviral vectors or a control vector (GFP only) at an MOI of 1:125 in triplicates (N=3) in 24-well plates. The cells were cultured up to 2 months. Some HTM cells were treated with 5ng/ml TGF β 2 as a positive control. At the end of the study, the cells were fixed and stained with phalloidin-Alexa-568 and DAPI for actin filaments and nuclei, respectively. To quantitate the number of CLAN-positive cells, ten fluorescent images per well were captured. The total number of fluorescent positive cells per image was counted and the percentage of CLAN-positive cells over total cell numbers per image (PCPC) per well was determined. PCPCs were compared using one-way ANOVA and post-hoc tests.

Results: The baseline level of PCPC in the GFP overexpression group was 4.3% \pm 0.2%. In comparison, there was a 7-fold increase in PCPC (38.0% \pm 2.0%; P<0.001) in TGF β 2 treated cells. There was about 2-fold increase of PCPC in the myosin light chain group (7.3% \pm 1.5%; P>0.05) and tropomyosin group (8.5% \pm 3.8%, P>>0.05), about 4-fold increase in the caldesmon group (19.3% \pm 2.5%; P<0.05), and about 6-fold increase in calponin (26.0% \pm 4.0%; P<0.01). The greatest increase was observed in the cells overexpressing all four proteins with about 11-fold increase in PCPC (51.0% \pm 14.2%; P<0.001), and this increase was higher than that in TGF β 2-treated cells (P<0.01).

Conclusions: Caldesmon, calponin, tropomyosin and myosin light chain work individually or synergistically to promote CLAN formation in primary HTM cells.

CONTROL ID: 3546023

SUBMITTER (NAME ONLY): Kaitlyn Sapoznik

TITLE: Small retinal arteriole remodeling in diabetes and hypertension measured by AOSLO

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Sapoznik, T. Gast, R. Warner, B. Walker, S.A. Burns, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retinal microvasculature is remodeled in hypertension and in diabetes but little is known about the actual remodeling that occurs in human in vivo small arterioles ($<50\text{ }\mu\text{m}$) due to limitations in imaging techniques. High-resolution retinal imaging allows us to visualize and measure the fine structure of small retinal arterioles non-invasively. We used adaptive optics scanning laser ophthalmoscopy (AOSLO) to investigate the differences in arteriolar remodeling in retinal arterioles with diameters under $50\text{ }\mu\text{m}$ in diabetes and hypertension.

Methods: The posterior pole of 52 participants was imaged with the Indiana AOSLO sampled at $1\text{ }\mu\text{m/pixel}$ or less with a video rate of 28 frames/s. After the imaging session, MATLAB (Mathworks Inc., Natick, Ma) was used to correct for eye movements to create averaged images. Custom MATLAB software was used to measure the vessel wall structure of arteriole segments less than $50\text{ }\mu\text{m}$ in diameter from the imaging sessions. 72 arteriole segments from control participants, 156 arteriole segments from participants with diabetes, and 41 arteriole segments from participants with hypertension were measured. The differences the wall thicknesses, wall-to-lumen ratios (WLR), wall-cross sectional area (WCSA), and the retinal arteriole index (a ratio of the actual to predicted lumen diameter based on the outer diameter to actual inner diameter from control data) were analyzed in SPSS (IBM SPSS Statistics for Windows, Chicago, IL) using Welch's ANOVA and the Games-Howell post hoc test.

Results: A statistically significant difference was present for the arteriole index, wall-to-lumen ratio, and wall thickness between the control group and the group with diabetes ($p<.001$) and between the control group and hypertension group ($p<.001$). There was no difference between any groups for the wall cross-sectional area. For all parameters there was no difference between the groups with hypertension and diabetes

Conclusions: Our results suggest that despite the loss of myogenic control in diabetes, there is similar vascular remodeling occurring in the two diseases in small retinal arterioles. Most of our sample of participants with diabetes were also hypertensive suggesting that hypertension is driving the remodeling observed. In addition, the similarity of WCSA between all three groups suggest that the remodeling occurring in the vessels maintains wall volume, which is consistent with eutrophic remodeling.

CONTROL ID: 3546030

SUBMITTER (NAME ONLY): Vahitha Shameem Nizamudheen

TITLE: Nonsense suppression therapy in an animal model of Usher 1D syndrome

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Nizamudheen, K. Gregory-Evans, C.Y. Gregory-Evans, Ophthalmology, The University of British Columbia, Vancouver, British Columbia, CANADA|A. Yanai, The University of British Columbia, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Usher syndrome 1D (USH1D) is an autosomal recessive condition characterized by severe deafness, vestibular dysfunction and progressive vision loss. Cadherin 23(CDH23) is a structural protein present in stereo cilia of mechanosensory hair cells of the cochlea. In photoreceptors CDH23 is thought to mediate membrane–membrane adhesion between the inner segment membranes of neighboring photoreceptor cells and at synapses, to keep the synaptic cleft in close proximity. We have obtained a mouse model Y2209X line (Cdh23) which has a nonsense mutation in Cdh23. Homozygous Cdh23 mice exhibited head shaking, circling behavior and a reduction in the ERG response. In this study, we hypothesized that manipulation of Cdh23 dosage by a nonsense suppression strategy could rescue the disease phenotype in this animal model.

Methods: Two drug treatment protocols was performed (i) Prenatal: time-mated pregnant mice received daily subcutaneous injections of 30 µg/g Ataluren® and then the offspring received the same daily injections from P4 to P90. (ii) Postnatal: mice from P4-P90 received daily injections of 30 µg/g Ataluren®. ERGs were measured at P45 and P90 and P120. After treatment, IHC was performed to confirm Cdh23 protein expression and the trafficking of photoreceptors proteins. Structural benefits in photoreceptors were studied by immunohistochemistry and by transmission electronmicroscopy.

Results: We characterised this mouse model of USH1D (Cdh23) that had a nonsense mutation in Cdh23. The Cdh23 mouse was significantly smaller than wildtype mice and did not survive past 60 days of age. As with other models of USH1D, we did not find any structural abnormalities in the Cdh23 retinal structure. However, we found abnormalities in light-induced trafficking of proteins including rhodopsin, arrestin, α -transducin and recoverin. When Cdh23 mice were treated with Ataluren®, Cdh23 protein was expressed in the connecting cilium, the trafficking defects were rescued and electrical response to light were improved. The mice survival rate was increased to P120 and the circling behaviour was reduced.

Conclusions: These data show for the first time that nonsense suppression in a mouse model of USH1D was able to rescue the major phenotypic features observed in the homozygous mutant mice. We conclude that translational readthrough by the small molecule Ataluren® improved the disease phenotype in this mouse model.

CONTROL ID: 3546033

SUBMITTER (NAME ONLY): Saoud Al-khuzaei

TITLE: Genotype-phenotype correlation of novel variants in ABCA4

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Al-khuzaei, C. Foster, M. shah, R.E. MacLaren, P. Charbel Issa, S.M. Downes, Oxford Eye Hospital, Oxford, Oxfordshire, UNITED KINGDOM|S. Al-khuzaei, S. Broadgate, M. shah, R.E. MacLaren, P. Charbel Issa, Nuffield Laboratory of Ophthalmology, University of Oxford, UNITED KINGDOM|S. Halford, S.M. Downes, Nuffield Laboratory of Ophthalmology, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|M. Shanks, P. Clouston, Oxford Medical Genetics Laboratory, University of Oxford, Oxford, Oxfordshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Stargardt disease (STGD1) associated with mutations in ABCA4 is genetically and phenotypically heterogeneous. Phenotypes range from yellow-white flecks in the macula with varying degrees of atrophy, some with more extensive distribution; bull's eye maculopathy, to a more severe chorioretinal atrophy. In this study, we report novel variants in the ABCA4 gene and describe their genotype-phenotype correlation.

Methods: Patients with novel sequence variants were identified from a large cohort of clinically diagnosed STGD1 patients with at least two variants in ABCA4, by the Oxford Medical Genetics Laboratories. Phenotyping included: visual acuity, Goldmann visual field and electrophysiology testing, optical coherence tomography (OCT), false-color ultra-widefield and fundus autofluorescence (AF) imaging. This study was carried out in accordance with the tenets of the declaration of Helsinki, with ethics approval.

Results: In this cohort of 20 patients, we identified 19 novel variants in ABCA4 of which 7 were missense mutations, 7 frameshift mutations, 1 whole exon deletion, 1 nonsense mutation, and 3 splice site mutations. The phenotypes in this cohort included the typical flecks seen in STGD1, macular atrophy and peripapillary sparing disease. Other features identified in these patients included; foveal sparing disease, a region of reduced foveal AF surrounded by a ring of raised AF, and widespread chorioretinal atrophy.

Conclusions: We describe 19 novel variants in ABCA4 and their associated phenotypes in a cohort of STGD1 patients. The identification of novel variants is important, as defining ABCA4 variants as pathogenic underpins genetic counselling, helps to confirm the diagnosis and in the future identify potential candidates for recruitment to therapeutic trials.

CONTROL ID: 3546034

SUBMITTER (NAME ONLY): Pavlina Tsoka

TITLE: An experimental model of Escherichia coli-induced endophthalmitis in rodents

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Tsoka, M.K. Tsilimbaris, Laboratory of Optics and Vision, University of Crete Medical School, Heraklion, GREECE|E. Scoulica, E. Magkafouraki, Laboratory of Clinical Microbiology and Molecular Microbiology, University of Crete Medical School, GREECE|

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ABSTRACT BODY:

Purpose: Bacterial endophthalmitis can lead to significant vision loss even after prompt and proper treatment. So far, there are only a handful of studies on experimental models of bacterial endophthalmitis due to gram-negative organisms in small rodents. The purpose of this study was to establish an Escherichia coli-induced experimental model of endophthalmitis in rats suitable for potential pharmaceutical intervention.

Methods: Bacterial endophthalmitis was induced in both male and female Sprague-Dawley rats. Animals received an intravitreal injection of viable Escherichia coli (E. coli) of two different strains; U13 which is susceptible to moxifloxacin and U27 which has an inducible resistance to moxifloxacin. Several inocula were tested in a range from 10.000 colony – forming units (CFUs)/eye to 840.000 CFUs/eye. Clinical scores were evaluated in vivo with slit lamp biomicroscopy and direct ophthalmoscopy and animals were euthanized at 0, 24, 48 and 72 hours post intravitreal injection, eyes were enucleated, and bacterial growth rate was assessed.

Results: An inoculum of 10.000 CFUs/eye of E. coli U13 resulted in conjunctival hyperemia, purulent exudations, iritis and miosed pupils (posterior synechiae) at 24 hours with mild to moderate average inflammatory scores in the two-thirds of the animals. The signs of clinical inflammation were not progressed at 48 or 72 hours, while the bacterial load remained stable with an average of 10^5 CFUs/eye. However, in all experiments, one-third of the animals demonstrated significantly lower clinical scores. On the contrary, higher inocula (> 70.000 CFUs/eye) of E. coli U13 resulted in moderate to severe inflammatory signs even at 24 hours. In addition to E. coli U13, an inoculum of even 100 CFUs/eye of E. coli U27, resulted in severe inflammation and particularly high clinical scores within the 72-hours timeframe.

Conclusions: Escherichia coli-induced experimental endophthalmitis can be achieved in rats and is a highly reproducible model of gram-negative bacterial endophthalmitis. Low inocula of E. coli strain U13 result in mild to moderate progress of the inflammatory signs, thus allowing pharmaceutical intervention. Further experimentation is currently ongoing in order to evaluate novel liposomal formulations that are specifically designed for sustained intraocular release of moxifloxacin.

CONTROL ID: 3546035

SUBMITTER (NAME ONLY): Catalina Garzon

TITLE: The impact of neighborhood factors on physical activity in older adults with glaucoma

SESSION TITLE: Visual Impairment - Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Garzon, A. Mihailovic, J. E. S.K. West, P.Y. Ramulu, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|D.S. Friedman, Massachusetts Eye and Ear, Harvard Medical School, Boston, Massachusetts, UNITED STATES|L.N. Gitlin, College of Nursing and Health Professions, Drexel University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate if neighborhood factors are associated with physical activity in older adults with visual impairment.

Methods: Persons with glaucoma or suspected glaucoma had accelerometer-defined physical activity collected over 7-days and summarized as average daily steps and non-sedentary minutes. Census block and tract numbers were utilized to collect the following neighborhood characteristics: Area Deprivation Index, fraction of residents living below the federal poverty line, and average crime rate per 100k people, categorized as low (<2,500), medium (2,500-5,000) and high (>5,000). Based on the integrated visual field (VF) sensitivity, participants were categorized to mild, moderate or severe VF loss from glaucoma. Multivariable negative binomial regression models evaluated the effect of neighborhood factors on physical activity for all participants, and participants stratified by severity of the VF loss.

Results: The 230 study participants were on average 70 years old; about half were female, and about third Black. Average daily steps and non-sedentary minutes were lower with higher area deprivation index (rate ratio [RR]=0.96 per 1 decile, 95%CI=0.93 to 0.99, p=0.007 and RR=0.96 per 1 decile, 95% CI=0.94 to 0.98, p=0.001, respectively). Average non-sedentary minutes were also lower for those living in areas with higher fraction of residents below the federal poverty line (RR=0.92 per 10% increase, 95% CI=0.85 to 0.98, p=0.02). Both, average daily steps and non-sedentary minutes, also decreased significantly in those with severe VF loss who lived in the areas with higher fraction of residents below the federal poverty line (RR=0.78 per 10% increase, 95% CI=0.63 to 0.96, p=0.02, and RR=0.76 per 10% increase, 95% CI=0.66 to 0.88, p<0.001, respectively). Neither average daily steps nor non-sedentary minutes were associated with crime rates (p>0.11 for all) for the whole group, though much less activity was noted in those living in higher vs. lower crime rate areas amongst participants with severe VF loss (RR=0.32, 95% CI=0.17 to 0.58, p<0.001, and RR=0.36, 95% CI=0.23 to 0.57, p<0.001, respectively).

Conclusions: Neighborhood characteristics might be important drivers of mobility in glaucoma patients, especially in those with the severe VF loss. Interventions to overcome activity limitations may be particularly important in this group.

CONTROL ID: 3546036

SUBMITTER (NAME ONLY): Belinda Jiao

TITLE: Ocular Inflammatory and Retinal Vascular Occlusive Adverse Events of Intravitreal anti-VEGF Injections: A Systematic Review and Network Meta-analysis

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Jiao, E. You, M. Hébert, A. Dirani, Université Laval Faculté de médecine, Québec, Québec, CANADA|K. Chemali, Faculty of Medicine, Université de Montréal, Montréal, Québec, CANADA|S. Jin, McGill University, Montréal, Québec, CANADA|

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ABSTRACT BODY:

Purpose: To perform a systematic review and network meta-analysis (NMA) of ocular adverse events (OAE) including endophthalmitis, inflammatory events and retinal vascular occlusive events secondary to anti-VEGFs for the treatment of neovascular age-related macular degeneration (nAMD).

Methods: A comprehensive search of Pubmed was conducted of all studies from inception until June 2020. Eligible publications included ≥ 50 patients and reported OAE of interest including endophthalmitis, uveitis, iritis, vitritis, vasculitis and ocular vascular occlusions.

Results: The search identified 7303 articles. 95 studies involving 302978 eyes were included in the systematic review and 23 comparator studies involving 261995 eyes in the NMA.

Incidence rates (IR) (total number of events n/total number of study eyes N) for endophthalmitis, inflammatory OAE and vascular occlusions were reported for each agent. Denominators for IR were based on total number of eyes across all studies that examined each complication. IR of endophthalmitis ranged from 0.27% (336/124,299) for ranibizumab to 1.2% (15/1251) for abicipar. IR of inflammatory OAE ranged from 0.9% (164/18153) for ranibizumab to 16.2% (203/1251) for abicipar. IR of vascular occlusions ranged from 0.085% (8/9460) for ranibizumab to 0.95% (8/841) for bevacizumab. Only abicipar reported retinal vasculitis at an IR of 1.8% (22/1251).

A NMA comparing the agents showed that the odds ratios (OR) (95% confidence intervals) for endophthalmitis from least to most likely with abicipar as reference were bevacizumab OR 0.097 (0.0075, 1.25), ranibizumab OR 0.13 (0.012-1.51), aflibercept OR 0.24 (0.018, 3.07), abicipar 1.00 (1.00, 1.00) and brolucizumab OR 1.12 (0.031, 40.1). For inflammatory OAE, the OR were: ranibizumab OR 0.008 (0.0011-0.59), bevacizumab 0.013 (0.0015, 1.09), aflibercept 0.096 (0.0069, 1.32), brolucizumab 0.44 (0.026, 7.24) and abicipar 1.00 (1.00, 1.00). Finally, the OR for vascular occlusive events were aflibercept OR 0.008 (0.00014, 0.55), brolucizumab OR 0.035 (0.00034-3.69), ranibizumab OR 0.044 (0.0026, 0.72), bevacizumab OR 0.15 (0.0065, 3.49) and abicipar 1.00 (1.00, 1.00).

Conclusions: The reported rates of OAE are generally low across the different anti-VEGFs but appear higher for newer agents brolucizumab and especially, abicipar. Further trials are needed to adequately assess their safety profile.

CONTROL ID: 3546041

SUBMITTER (NAME ONLY): Leslie Ramos

TITLE: Effect of Rho-kinase Inhibition on a Patient-Derived Model of Proliferative Vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Ramos, D. Amarnani, L.A. Kim, Retina, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|N. Singh, L.A. Kim, Retina, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is a common complication of open globe trauma and recurrent retinal detachment currently lacking medical treatment. Migration and proliferation of retinal cells, the formation of contractile membranes, and subsequent retinal detachment are hallmarks of PVR. This study aims to investigate the effect of Rho-kinase inhibition using an in vitro patient-derived cell and ex vivo explant model of PVR.

Methods: PVR membranes from human donors were cultured into a single cell suspension after digestion with enzymes creating primary PVR cell cultures. Explants were made from fragments of PVR membranes embedded into Matrigel. The effect of Rho-kinase inhibition using ROCK1 and ROCK2 inhibitors: ripasudil, netarsudil, fasudil and Y-2762 were tested. We examined the response of these inhibitors on cell proliferation of PVR cell cultures at two concentrations, selected from the IC50. The effects of ripasudil (150 nM and 300 nM), netarsudil (30 nM and 60 nM), fasudil (500 nM and 1 µM), and Y-2762 (500 nM and 1 µM) were evaluated at 24 hours. The effect of Rho-kinase inhibitors at 1 µM was tested on our PVR explant. Phase contrast images were taken at 7 and 14 days, and outgrowths were measured.

Results: At 24 hours, ripasudil (300 nM) and netarsudil (60 nM) revealed a 11% and 13% reduction in proliferation in PVR cells, whereas fasudil showed a 39% reduction in proliferation at 500 nM and a 87% reduction at 1 µM concentration. Similarly, Y-2762 showed a significant 80% reduction at 500 nM and an almost complete (94%) reduction in the proliferation of PVR cells. Robust outgrowths were observed growing from the freshly isolated PVR explant samples at 7 and 14 days (28.58 mm and 207 mm respectively) post embedding in Matrigel in culture. Ripasudil (0.8 mm and 15 mm), and netarsudil (4.2 mm and 37 mm) successfully inhibited and reduced explant growth at 7 and 14 days. The explants treated with fasudil (1 µM) and Y-2762 (1 µM) showed no outgrowths and almost complete inhibition of migration at all time points.

Conclusions: Currently, there are no specific therapeutic agents to prevent PVR. Common in vitro models of PVR rely primarily on RPE cell cultures to mimic early PVR, whereas our model relies on patient-derived PVR membranes. Our assays, when used in drug screens, may be beneficial at identifying potential therapies likely to work in preclinical and clinical trials for PVR.

CONTROL ID: 3546042

SUBMITTER (NAME ONLY): Frank Proudlock

TITLE: Feasibility of Handheld Optical Coherence Tomography in Children with Craniosynostosis

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Proudlock, S.R. Rufai, R.J. McLean, S. Teli, I. Gottlob, M.G. Thomas, Ulverscroft Eye Unit, University of Leicester, Leicester, Leicestershire, UNITED KINGDOM|C. Bunce, Clinical Trials Unit, Royal Marsden NHS Foundation Trust, London, London, UNITED KINGDOM|N. Jeelani, Craniofacial Unit, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|N. Jeelani, University College London Great Ormond Street Institute of Child Health Library, London, London, UNITED KINGDOM|S.R. Rufai, R. Bowman, V. Panteli, Clinical and Academic Department of Ophthalmology, Great Ormond Street Hospital for Children NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To determine whether handheld optical coherence tomography (OCT) is feasible in children with craniosynostosis.

Methods: This was a single-centre, prospective observational study. Fifty patients with syndromic and non-syndromic craniosynostosis were approached between February 13th 2020 and October 1st 2020. Patients were excluded if they could not cooperate with handheld OCT imaging or were aged over 18 years old. Main outcome measures included feasibility, including patient recruitment and handheld OCT image acquisition success rates. Main secondary outcome measures included visual acuity (VA), fundoscopic examinations and 48-hour intracranial pressure (ICP) assessments.

Results: All 50 children were successfully recruited (100%). At least one ONH image was obtained in 43 children (86%), while bilateral ONH imaging was successful in 37 children (74%). Of the 43 included children, median age was 66.3 months (range: 1.9-156.9 months; IQR: 37.8-44.9). LogMAR chart VA was available in 31 of 43 patients. Median VA was 0.1 logMAR (range: -0.06 – 1.30; IQR 0.02 – 0.2). Fundoscopy was successful in 40 of 43 patients. ICP assessments were available in five patients, demonstrating normal ICP in two, reduced intracranial compliance in one and raised ICP in two – these were not identified on fundoscopy but correctly identified on handheld OCT.

Conclusions: Handheld OCT is feasible in children with craniosynostosis. This represents the first study of its kind. Further work is required to determine whether handheld OCT represents an effective screening tool for intracranial hypertension in this patient population.

CONTROL ID: 3546043

SUBMITTER (NAME ONLY): Nakul Singh

TITLE: Racial Disparities in Cataract Surgery Outcomes

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Singh, S. Bal, A.C. Lorch, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nakul Singh: Commercial Relationship: Code N (No Commercial Relationship) | Sila Bal: Commercial Relationship: Code N (No Commercial Relationship) | Alice Lorch: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess differences in cataract surgery outcomes by race in order to better understand delivery of surgical care to diverse patient populations.

Methods: Massachusetts Eye and Ear surgical outcomes were assessed between January 1, 2019 and December 31, 2019. Patient's self-identified race/ethnicity were extracted from the medical record and collapsed into broader categories of White, Black, Hispanic, Asian, declined/unavailable, and other for race. Cataract surgery outcomes were intraoperative complications(Descemet's tear, posterior capsule tear, vitreous loss, anterior vitrectomy, dropped lens, and zonular dialysis), final refractive error within 1 diopter of target refraction, and loss to follow up. Logistic regression was performed to estimate the odds ratios between categories.

Results: A total of 2,874 patients underwent cataract surgery and were included in the analysis (White=2,121, Asian=212, Black=202). Patients reporting their race as Asian had increased odds of an intra-operative complication (OR 3.29, CI 1.46-7.38, p-value <0.001) compared to self-reported White patients. Patients reporting their race as Black (OR 0.65, CI 0.46- 0.93) or other (OR 0.66, CI 0.46-0.94) were less likely than self-reported White patients to be within 1 diopter of target refraction. Patients reporting their race as Black (OR 1.91, CI 1.33-2.76) or other (OR 1.79, CI 1.22-2.60) had increased odds of loss to follow up.

Conclusions: There were racial disparities in cataract surgery outcomes in intraoperative complications, target refraction, and loss to follow up. These findings warrant further investigation into these disparities and development of programs that improve equity of cataract care.

CONTROL ID: 3546044

SUBMITTER (NAME ONLY): Michael Reid

TITLE: Ocular Distribution of Pegcetacoplan in Rabbits Following a Single Intravitreal Injection.

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Reid, Research and Translational Medicine, Apellis Pharmaceuticals Inc, Watertown, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Michael Reid: Commercial Relationship(s);Apellis Pharma:Code E (Employment)

ABSTRACT BODY:

Purpose: Geographic Atrophy (GA) is an advanced stage of age-related macular degeneration (AMD); a major cause of blindness affecting almost 1 million people in the US alone. GA is characterized by a loss of RPE, photoreceptors, and atrophy of the choriocapillaris. Dysregulation of the complement system is a contributor to the pathogenesis of AMD. Polymorphisms in C3, factor H and factor B are associated with risk of AMD and upregulation of the complement pathway leads to C3 opsonization of photoreceptors and RPE. Since C3 is the central component of all three complement pathways, inhibition of C3 represents a promising approach to treat GA. Pegcetacoplan (APL-2), a PEGylated cyclic peptide inhibitor of C3, slowed GA lesion growth in a Phase II (FILLY) study and is being investigated in ongoing Phase III trials (DERBY and OAKS). Intravitreal (IVT) injection remains the most efficient route to reach the diseased tissues in the posterior section of the eye. However, therapeutics delivered from the vitreous to the retina must traverse multiple biological barriers; including the inner limiting membrane (ILM) which is considered the main filtration barrier between the retina and vitreous.

Methods: An ocular distribution study of pegcetacoplan in New Zealand white rabbits was conducted to measure concentrations in aqueous humor (AH), iris-ciliary body, vitreous humor (VH) and the retina/RPE/choroid. Pegcetacoplan was administered as a single IVT dose of 12 mg and animals were euthanized for tissue/fluid compartment collection on Days 1, 3, 7, 14 and 28. Isolated tissues were analyzed by LC-MS/MS methods specific for each matrix.

Results: Peak concentrations in each ocular compartment were reached 24 hours with the exception of VH which plateaued between 24 and 96 hours. Exposure in the retina/RPE/choroid and AH was generally 3- and 6-fold lower than VH, respectively. Elimination half-life was ~5 days in each ocular compartment in rabbits compared to 3 days in cynomolgus monkeys.

Conclusions: Pegcetacoplan has rabbit vitreal kinetics in the range of marketed anti-VEGF biologics and does traverse the ILM in adequate concentrations supporting the posology in the clinical studies.

CONTROL ID: 3546049

SUBMITTER (NAME ONLY): Carla O'Neale

TITLE: Studies of Native AQP0 Structure and Protein Interactions

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. O'Neale, K.L. Schey, Department of Biochemistry, Vanderbilt University, Nashville, Tennessee, UNITED STATES|H. McDonald, I. Zagol-Ikapitte, K.L. Schey, Vanderbilt University Mass Spectrometry Research Center, Nashville, Tennessee, UNITED STATES|S.R. Harvey, V.H. Wysocki, Department of Chemistry and Biochemistry, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The lens microcirculation system is required to maintain transparency; however, how this system is established and maintained as a function of age is not well understood. Aquaporin-0 (AQP0) plays important roles in lens fiber cell adhesion and water permeability. The purpose of this study is to structurally characterize AQP0 through Native mass spectrometry (Native MS) and to develop a method to analyze AQP0-protein interactions via hydrogen deuterium exchange-mass spectrometry (HDX-MS) using AQP0-calmodulin interactions as a model.

Methods: Bovine lens membranes were solubilized in 1% octylglucoside and AQP0 was purified via anion exchange chromatography. HDX-MS: After incubation in D₂O, the HDX process was quenched, proteins were digested using pepsin, and resulting peptides separated and analyzed via liquid-chromatography mass spectrometry on a Waters Xevo G2-XS QToF. Data were analyzed using Waters PLGS and DynamX software. Native MS: Purified AQP0 was buffer exchanged into C₈E₄ detergent in 200 mM ammonium acetate, introduced into a Thermo Exactive Plus EMR Orbitrap or a Thermo Q Exactive Plus UHMR mass spectrometer using nanoelectrospray ionization and dissociated by collision induced dissociation (CID) or by surface induced dissociation (SID).

Results: HDX-MS: After optimization, significant sequence coverage was obtained for both AQP0 (75%) and calmodulin (90%) that includes coverage of the C-terminal tail of AQP0. As expected, AQP0 loop and C-terminal tail peptides displayed greater deuterium incorporation relative to transmembrane regions. Native MS: Multiple AQP0 proteoforms of intact tetrameric AQP0 were identified in isolated AQP0 fractions including phosphorylated and lipidated AQP0. Chromatographic separation allowed enrichment of un-, mono-, and di-phosphorylated forms.

Conclusions: HDX-MS methodology was optimized to yield good sequence coverage for lens membrane protein AQP0 which sets the stage for examining AQP0-protein interactions. Deuterium uptake data suggest AQP0 loop and C-terminal tail regions to be dynamic and solvent exposed whereas transmembrane regions remain largely solvent protected. Multiple proteoforms of tetrameric AQP0 were identified via Native MS which will allow us to compare unphosphorylated and phosphorylated AQP0 to understand the effects of phosphorylation on AQP0 function. Native MS data show di-phosphorylation to be the highest degree of phosphorylation of intact tetrameric AQP0.

CONTROL ID: 3546050

SUBMITTER (NAME ONLY): Amanda Petrelli Cicerone

TITLE: Numerous Protein Mutations Detected in FEVR Patients Using a New Custom Ampliseq Targeted-Sequencing Panel

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Petrelli Cicerone, W.A. Dailey, M. Sun, N. Haque, A. Guzman, K. Mellert, K.A. Drenser, K.P. Mitton, Eye Research Institute, Oakland University, Rochester, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Analyze the first subset of 69 patients with Familial Exudative Vitreo Retinopathy (FEVR) who were sequenced using a custom Ampliseq targeted gene panel that includes 7 genes (NDP, CTNNB1, TSPAN12, KIF11, FZD4, LRP5, ZNF408) that are potentially involved in FEVR.

Methods: A custom Ampliseq targeted-panel (180 amplicons) for 8 genes was designed with illumina's DesignStudio Sequencing Assay Design for complete coverage of 83 exons with 25 bp adjacent intron sequence. Seven of the genes are applicable to FEVR: NDP (ChrX), CTNNB1 (Chr3); TSPAN12 (Chr7); KIF11 (Chr10), FZD4 (Chr11), LRP5 (Chr11), ZNF408 (Chr11). Ampliseq libraries were pooled and sequenced using the Illumina iSeq-100 platform. Variant impacts and allele frequency data were determined from ClinVar and The Genome Aggregation Databases (gnomAD).

Results: For the seven genes that are applicable to FEVR, a total of 35 variants were found that alter protein sequence, with the following relative distribution: NDP 1/35 (2.9%), CTNNB1 1/35 (2.9%), TSPAN12 1/35 (2.9%), KIF11 3/35 (8.6%), FZD4 10/35 (28.6%), LRP5 13/35 (37.1%), ZNF408 6/35 (17.1%). Types of protein changes were: single amino acid change (77.1%), amino acid deletion (8.6 %), and amino acid insertion (2.9%).

Conclusions: A custom Ampliseq targeted-sequencing Orphan Pediatric Retinal Disease panel (version 2, 8 genes) developed by our lab provided extensive sequencing coverage of all exons and detected 35 protein-altering variants in a set of 69 FEVR patients. 76% of the variants were found in three genes: FZD4, LRP5, and ZNF408. The testing format greatly reduces associated costs and now facilitates greater access to genetic testing for Families with this very rare inherited retinal disease.

CONTROL ID: 3546052

SUBMITTER (NAME ONLY): Nai-Wen Fan

TITLE: IFN γ ⁺IL17⁺ effector T cells are the principal source of memory Th17 cells in dry eye disease

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Fan, Y. Chen, S. Chauhan, R. Dana, ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|N. Fan, Ophthalmology, Taipei Veterans General Hospital, Taipei, TAIWAN|

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ABSTRACT BODY:

Purpose: Our previous work has identified two CD44^{low} effector Th17 subsets that contribute to acute inflammation in dry eye disease (DED): CD4⁺IFN γ ⁻IL-17⁺ ("single-positive" eTh17) and CD4⁺IFN γ ⁺IL-17⁺ ("double-positive" eTh17/1). Subsequently, memory Th17 cells (mTh17; CD4⁺CD44^{hi}IL17⁺IFN γ ⁻) become the principle mediators sustaining the chronic inflammation in DED. We have further demonstrated linear generation of mTh17 from effector T precursors driven by IL-23. This study aims to determine the differential contribution of eTh17 vs. eTh17/1 subsets to mTh17 in DED.

Methods: Six- to eight-week old female C57BL/6 mice were exposed to desiccating stress in a controlled environment chamber for 14 days to induce acute DED. Draining lymph nodes (DLNs) were collected, and eTh17 and eTh17/1 were isolated using IL-17 and IFN- γ cytokine secretion assay kits combined with FACS sorting, and then were individually adoptively transferred to Rag1 knockout (KO) mice that had been exposed to desiccating stress for 14 days. Immediately after transfer, Rag1 KO recipients were removed from desiccating stress and received intraperitoneal injection of anti-IL23 receptor antibody or control IgG. Disease severity was evaluated by corneal fluorescein staining, and T cell response was assessed at day 12 after cell transfer.

Results: Rag1 KO mice subjected to desiccating stress did not develop DED. Upon receiving acute DED-derived eTh17 or eTh17/1, both groups of Rag1 KO recipients developed disease at day 3 post-cell transfer, however, only eTh17/1 group, but not eTh17 group, showed persisting disease by day 12 along with the development of mTh17 cells in DLN (P<0.05). Blockade of IL-23 signaling significantly reduced disease severity in eTh17/1 recipients at day 12, as well as prevented the generation of mTh17 cells (P<0.05).

Conclusions: eTh17/1 cells generated in acute inflammation are the principle precursors of mTh17 cells that persist for long term and sustain the chronicity of inflammation in DED.

CONTROL ID: 3546057

SUBMITTER (NAME ONLY): Hiroaki Ito

TITLE: Histopathological and immunohistochemical study of metastatic orbital tumors

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Ito, G. Nassrallah, S. Bergeron, J. Coblentz, A.A. Goyeneche, M.N. Burnier, The MUHC-McGill University Ocular Pathology & Translational Research Laboratory, McGill University, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Metastatic orbital tumors are rare and account for 3% of orbital lesions. It can be the initial manifestation of a systemic metastatic disease, and accurate pathological diagnosis is crucial. The objective of this study is to report 10 orbital metastases and to further understand these histopathological and immunohistochemical (IHC) characteristics.

Methods: From 8018 cases reviewed, 203 orbital lesions including 28 malignant tumors were collected at the MUHC-McGill University Ocular Pathology & Translational Research Laboratory from 2006 to 2020. Among the malignant tumors, 11 cases were metastatic. Ten of the metastatic cases were selected based on complete clinical history and available slides.

Results: Of the 10 patients with metastatic orbital tumors, 6 were women and 4 were men. The mean age was 68 years (range 52-83). Pathological examination revealed 70% (7/10) of carcinomas: metastatic breast carcinoma (3/10); adenocarcinoma consistent with metastasis of a prior cutaneous carcinoma (2/10) prostatic carcinoma (1/10); poorly differentiated carcinoma with a past history of skin squamous cell carcinoma (SCC) (1/10). The other three cases were plasmacytoma (2/10) and mucosal melanoma (1/10). All cases of breast carcinoma were positive for Estrogen Receptors (ER). Prostatic carcinoma was confirmed by PSA and NKX3.1. The two adenocarcinomas of the skin showed IHC findings which cannot exclude the possibility of breast origin: one case was 70-year-old female mucinous carcinoma, positive for ER, CK7, GATA3; the other was 53-year-old male signet-ring adenocarcinoma, positive for CK7, CK20, GATA3, BRST2. In both cases, no breast primary lesion was found, and the prior skin lesions showed similar morphology and IHC profile. Poorly differentiated carcinoma with a past skin SCC was positive for CK7 and negative for CK20, p40. The findings are consistent with metastasis from skin. In plasmacytoma, monoclonality was confirmed by light chain restriction with kappa and lambda. Melanoma was positive for HMB45 and Melan A.

Conclusions: The use of a panel of immunohistochemical markers is crucial for the final diagnosis of orbital metastasis. The histopathological and immunohistochemical findings may be inconclusive particularly in cases of cutaneous carcinoma. Careful interpretation and clinicopathological correlation are essential for final diagnosis.

CONTROL ID: 3546059

SUBMITTER (NAME ONLY): Megan Ruben

TITLE: Iodine-125 Plaque Radiotherapy for Retinoblastoma Recurrence following Intra-arterial Chemotherapy

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ruben, M. Eiger-Moscovich, A. Yaghy, S. Tadepalli, C. Shields, Wills Eye Hospital Ocular Oncology Service, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the efficacy and toxicity of Iodine-125 (I-125) plaque radiotherapy for residual or recurrent retinoblastoma following intra-arterial chemotherapy (IAC).

Methods: In a retrospective review, clinical records of all children with retinoblastoma that received I-125 plaque radiotherapy after IAC on the Ocular Oncology Service at Wills Eye Hospital between December 1, 2009 and April 30, 2020 were reviewed.

Results: There were 41 retinoblastomas in 41 eyes of 41 patients treated with I-125 plaque radiotherapy after IAC, including 21 females (51%) and 20 males (49%) with a median age at plaque treatment of 32 months (range 9-71 months). The most common indication for I-125 plaque radiotherapy was recurrence of solid tumor with or without overlying subretinal/vitreous seeds (n=33, 80%), subretinal seeds alone (n=6, 15%), and vitreous seeds alone (n=2, 5%). The median irradiated basal diameter was 9 millimeters (mm) (range 2-16 mm) and median thickness was 4 mm (range 1-7 mm). Mean radiation dose to tumor apex was 3483 centigray. There was complete tumor control at the target site in 39 eyes (95%) at median follow-up of 20 months (range 1-109 months) after plaque radiotherapy. This included control within the target site for solid tumor (31/33, 94%), subretinal seeds (6/6, 100%), and vitreous seeds (2/2, 100%). A subgroup of solid tumor and/or subretinal seeds was identified, which occurred within an ischemic retinal/choroidal field, confirmed on fluorescein angiography and associated with highly calcified mass (n=24 cases). This select group demonstrated tumor control in 22/24 (92%). Visual acuity at last follow-up was 'fix and follow' in 13/14 (93%) of pre-verbal patients and 20/400 or better in 10/22 (45%) of verbal patients. Using Kaplan-Meier analysis, radiation complications at 2 years included vitreous hemorrhage (37%), retinopathy (28%), papillopathy (18%), and cataract (18%). Enucleation was necessary in 5 eyes (12%) for recurrence outside of the irradiated area, chronic vitreous hemorrhage, and/or total retinal detachment.

Conclusions: In this analysis, Iodine-125 plaque radiotherapy provided 95% tumor control for selected retinoblastomas that failed IAC, including those in an ischemic field, untreatable with further chemotherapy. Radiation-related side effects should be anticipated in these eyes already exposed to substantial chemotherapy.

CONTROL ID: 3546064

SUBMITTER (NAME ONLY): Emilia Zin

TITLE: AAV delivery of progranulin to retinas of progranulin-null mice is time-sensitive

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.A. Zin, Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|J. Tran, J.G. Flannery, University of California Berkeley School of Optometry, Berkeley, California, UNITED STATES|D. Han, J.G. Flannery, Helen Wills Neuroscience Institute, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neuronal ceroid lipofuscinosis (NCL) is a family of neurodegenerative lysosomal storage diseases. NCL type 11 (CLN11) is caused by biallelic mutations to the progranulin gene, leading to seizures, ataxia and vision loss. Patients and a murine model (PGRN^{-/-}) show retinal thinning, accumulation of autofluorescent lipofuscin, and increase in microglial activation. As a recessive neurodegenerative disease, CLN11 is an ideal candidate for gene replacement therapy; however, both brain and retina require AAV gene delivery. This study aimed to deliver two different AAV constructs, 7m8-scCAG-PGRN and AAV92YF-scCAG-PGRN, to the retinas of PGRN^{-/-} mice at four different timepoints, with the objective of stalling retinal degeneration.

Methods: Plasmids were packaged into two different capsids (7m8 and AAV92YF) using the triple transfection method and titered via qPCR. PGRN^{-/-} cohorts received intravitreal injections of 7m8-scCAG-PGRN in one eye and PBS in the contralateral eye at different timepoints: 1, 6, and 12 months old. Mice that received AAV92YF-scCAG-PGRN were intravenously injected at post-natal day 3 or 4 (P3-4). At 12 months old, cohorts injected at P3-4, 1 and 6 months old had their retinas imaged by optical coherence tomography (OCT) and were enucleated. The cohort injected at 12 months old were imaged and enucleated at 18 months old. Retinal thickness was measured using OCT cross-sections. Retinas were cryosectioned and immunohistochemistry was performed. Lipofuscin was quantified through fluorescent imaging.

Results: Animals that received AAV92YF-scCAG-PGRN showed a statistically significant improvement in overall retinal thickness and in photoreceptor layer thickness. However, animals injected with 7m8-scCAG-PGRN at month 1 and 6 showed no improvement in retinal thickness, while animals injected at 12 months old showed retinal thinning in comparison to contralateral controls. All cohorts show improvements in lipofuscin deposits when expressing PGRN.

Conclusions: Animals receiving PGRN at the earliest timepoint (P3-4) show improvement in retinal thickness, while the oldest cohort (12 months old) show retinal thinning when expressing PGRN. This points to a potentially toxic effect of PGRN delivery in elderly animals, which are reportedly more immune-reactive than age-matched wild-type mice. However, reduction in lipofuscin deposits indicate an improvement in lysosomal function, regardless of cell loss.

CONTROL ID: 3546068

SUBMITTER (NAME ONLY): Wennan Lu

TITLE: Photoreceptor death and RPE oxidative stress model of chloroquine retinopathy

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Lu, A.H. Jassim, N. Mas Gomez, C.H. Mitchell, Basic and Translational Science, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|C.H. Mitchell, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chloroquine has been linked to retinopathy for decades in humans, characterized by central visual loss and bull's eye maculopathy. We have developed a mouse model of chloroquine retinopathy to identify key steps in disease progression. The association of chloroquine induced retinal toxicity with oxidative stress and lipid peroxidation of RPE cells was examined.

Methods: Chloroquine retinopathy was induced by injecting chloroquine (50mg/kg) intraperitoneally into adult C57BL/6J mice 3x/week for 6-8 weeks. Retinal and/or RPE material was analyzed by histology, TUNEL staining, protein immunoblot, ELISA, and qPCR. Electroretinography (ERG) was used to monitor retinal function. ARPE-19 cells were used for in vitro experiments.

Results: ERG analysis detected a moderate reduction in both the a-wave and b-wave, with increases in implicit time. Spider graphs indicated a corresponding loss of outer nuclear layer cells in chloroquine treated retinae. TUNEL analysis detected increased apoptotic DNA fragmentation in photoreceptor nuclei; no corresponding signal was detected in RPE cells. RPE/choroid material from chloroquine-treated mice displayed an increase in HNE-adducted proteins detected with both Elisa and immunoblots. Chloroquine treatment increased the number and size of lysosomes, the amount of mitochondrial staining and expression of mitochondrial biogenesis genes in vitro.

Conclusions: This study suggests that the loss of photoreceptors accompanying moderate chloroquine treatment is associated with lysosomal stress, mitochondrial biogenesis and oxidative stress in RPE cells. How these stresses in the RPE lead to photoreceptor death requires further investigation.

CONTROL ID: 3546072

SUBMITTER (NAME ONLY): James Randleman

TITLE: Determining the Utility of Epithelial Thickness Mapping in Refractive Surgery Evaluations

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Randleman, L. Asroui, W.J. Dupps, Ophthalmology, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine how the addition of corneal epithelial thickness maps impacts patient screening for refractive surgery candidacy.

Methods: A retrospective evaluation of 100 consecutive patients who were screened for refractive surgery candidacy was conducted. For each patient, screening based on Scheimpflug tomography, clinical data, and patient history was done and a decision on eligibility for corneal refractive surgery, and choice of surgery, was made by two masked reviewers. The reviewers were then shown the patient's epithelial thickness maps derived from OCT. The percentage of screenings that changed after evaluating the epithelial thickness maps, with regards to candidacy for surgery, surgery of choice, and ranking of surgical procedures from most favorable to least favorable, was determined.

Results: Candidacy for corneal refractive surgery changed in 17% of patients after evaluation of the epithelial thickness maps, with 41.18% of the changes resulting in screening out patients, and 58.82% screening in patients. In the subset of patients that remained eligible candidates for surgery, the surgery of choice changed in 20.83% of cases after evaluating the epithelial thickness maps. In that same subset, the ranking of surgical procedures, from most favorable to least favorable, changed in 36.11% of cases, with 13.89% of patients losing eligibility, and 11.11% gaining eligibility, for one or more surgical procedure. In the subset of patients in which eligibility for surgery, surgery of choice, and ranking of surgical procedures from most to least favorable did not change, the epithelial thickness maps increased the reviewers' confidence in their decision in 49.12% of cases, decreased their confidence in 17.54% of cases, and had no impact on their level of confidence in 33.33% of cases.

Conclusions: Epithelial thickness mapping derived from OCT imaging of the cornea alters candidacy for corneal refractive surgery, as well as choice of surgery, in a substantial percentage of patients, and is thus a valuable tool for screening evaluations. Overall, the use of epithelial thickness maps results in screening in a slightly larger percentage of patients for corneal refractive surgery.

CONTROL ID: 3546074

SUBMITTER (NAME ONLY): Alex Holland

TITLE: Efficacy of Forced-Choice versus ETDRS visual acuity testing

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Holland, A. Wei, A.N. Vu, U. Mehta, J.K. To, A.W. Browne, Gavin Herbert Eye Institute, Department of Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|A.W. Browne, Department of Biomedical Engineering, Institute of Clinical and Translational Science, University of California Irvine, Irvine, California, UNITED STATES|U. Mehta, Western University of Health Sciences, Pomona, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Electronic displays of randomized Snellen acuity charts are common; however, the accuracy of a forced-choice visual acuity (FCVA) test has not been explored. The purpose of this study is to assess the test-retest reliability (TRR), criterion validity (CV), and discriminant validity (DV) of the Early Treatment Diabetic Retinopathy (ETDRS) and FCVA test in a prospective comparative clinical study. We predict that there will be no difference between the logarithm of the minimal angle of resolution (logMAR) results of both exams.

Methods: Data of the right eye (69 healthy, 59 disease) from subjects 18-85 years, VA better than counting fingers, and no central vision loss were included. VA testing was done at 4 meters and repeated at least 1 hour later. Subjects were separated by primary ophthalmic diagnosis. Results were recorded in logMAR. All subjects ETDRS and FCVA results and TRR were analyzed with paired t-test, DV by independent t-test, and CV by Pearson correlation. All subject ETDRS and FCVA results were further analyzed by Bland-Altman (B-A) analysis.

Results: A paired sample t-test of all subjects between ETDRS and FCVA showed significant differences at the first visit (95% CI -.07 to -.02, $p < .01$), B-A analysis showed that 43% of subjects had at least 0.1 difference in logMAR between testing modalities. CV analysis demonstrated $r=0.836$ with p value less than .01. TRR analysis showed insignificant differences at two different time points. DV analysis showed significant differences amongst disease and healthy subjects within each test.

Conclusions: ETDRS and FCVA exams showed high TRR, but a significant difference was detected between ETDRS and FCVA. Though FCVA may solve issues such as crowding and memorization, the significant difference between logMAR results suggests that FCVA cannot replace ETDRS at this time.

CONTROL ID: 3546077

SUBMITTER (NAME ONLY): Moloy Goswami

TITLE: Glutaminase deficiency disrupts the bioenergetic and antioxidant fidelity of photoreceptors to induce rapid degeneration

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Goswami, E. Weh, H. Durmutla, H. Hager, S. Chaudhury, C.G. Besirli, T.J. Wubben, Visual Sciences and Ophthalmology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|C. lyssiotis, Internal Medicine, Division of Gastroenterology, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glucose metabolism has been central in the study of photoreceptor cell physiology. However, recent evidence shows that fuel sources besides glucose can be utilized to meet the metabolic needs of photoreceptors. Therefore, we sought fundamental insight into the contribution of glutamine (Gln) as a potential alternative fuel source to photoreceptor metabolism, function, and survival.

Methods: Targeted metabolomic analyses was performed in 661W cells grown in uniformly labeled ¹³C-Gln in the presence or absence of the glutaminase (GLS) inhibitor, CB-839. 661W cell viability and redox status were measured with luminescent-based assays (Promega). To study the role of Gln catabolism in vivo in photoreceptors, GLS was deleted from rod photoreceptors (Gls cKO) in animals expressing cre-recombinase under the control of the rhodopsin promoter and a floxed Glis gene. The effect of GLS deletion on the survival of the photoreceptors was examined using in vivo and ex vivo analyses.

Results: Glis expression was over 20 times greater than its paralog, Glis2, in 661W cells and predominantly segregated to mitochondria. Treatment with CB-839 in 661W cells increased cellular Gln and decreased Gln-derived Glu. Furthermore, α-ketoglutarate, succinate, aspartate and malate were severely depleted underscoring that Gln contributes to TCA cycle. Additionally, inhibiting GLS reduced the biosynthesis of glutathione (GSH), altered redox homeostasis (GSH/GSSG ratio) and increased reactive oxygen species. Concomitantly, GLS inhibition reduced cell survival. In the mouse retina IHC, RT-PCR, and western blot analyses demonstrated that GLS is the predominant isoenzyme, enriched in photoreceptor inner segments, and segregated more to the mitochondrial than cytosolic fraction. IHC and western blot validated the rod-specific knockdown of GLS protein levels of the Glis cKO mouse. Glis cKO mice demonstrated comparable outer retinal thickness to wild-type animals at P14 with rapid photoreceptor degeneration evident by P21.

Conclusions: This study demonstrates that Gln catabolism via GLS is critical for redox balance, mitochondrial metabolism, and photoreceptor survival. Insight into the contribution of Gln to photoreceptor metabolism, function and survival may provide a framework for developing novel therapeutic approaches to prevent blindness in retinal degenerations.

CONTROL ID: 3546079

SUBMITTER (NAME ONLY): Mohamed Elsharkawy

TITLE: Automated diagnosis and grading of dry age-related macular degeneration using optical coherence tomography imaging

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To classify the different grades of age-related macular degeneration (AMD) using optical coherence tomography (OCT) images, we propose an automated computer-aided diagnostic (CAD) system capable of identifying clinically meaningful OCT features. The proposed CAD system differentiates between normal eyes and two different grades of AMD: 1) early AMD, and 2) intermediate AMD.

Methods: The proposed CAD system started with segmenting OCT layers. Then, the system performed an estimation calculation for global biomarkers from the segmented OCT images. These biomarkers are first- and second-order reflectivity, thickness, and curvature. Those features were fed into an artificial neural network (ANN) to classify these images. The extracted image-derived markers are represented using cumulative distribution function (CDF) descriptors. The constructed CDFs are then described using their statistical measures, i.e., the 10th through 90th percentiles with a 10% increment.

Results: The performance of the proposed CAD system was evaluated on 300 OCT images. Clinical grades were determined based on multi-modal imaging including OCT. The differentiation between normal eyes, and those with early or intermediate AMD using the fusion of the extracted features achieved an accuracy of 96% using the leave-one-subject-out cross-validation technique. The ANN feature fusion showed better performance compared with individual markers.

Conclusions: The proposed CAD system demonstrated a high capability to distinguish between normal eyes and two other grades of dry AMD using multiple biomarkers derived from OCT images.

CONTROL ID: 3546083

SUBMITTER (NAME ONLY): Luciano Quaranta

TITLE: A comparison of ultrasound pachymetry vs. rotating Scheimpflug camera, swept-source OCT, spectral-Domain OCT and non-contact specular microscopy.

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Quaranta, C. Bruttini, G. De Angelis, R. Ceccuzzi, E. Micheletti, R. Fausto, F. Bertuzzi, F. Ruoli, I. Riva, University of Pavia - IRCCS Fondazione Policlinico San Matteo, Pavia, Italy, ITALY|

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ABSTRACT BODY:

Purpose: To evaluate the agreement between different commercially available instruments and UltraSound Pachymetry(USP) on measurements of Central Corneal Thickness (CCT).

Methods: An observational, cross-sectional study. Two-hundred and eighteen eyes of 109 healthy patients were enrolled, and sequentially examined by means of USP, Swept-Source Optical Coherence Tomography (SS-OCT Casia), Spectral-Domain Optical Coherence Tomography (SD-OCT Optovue), Non-Contact Specular Microscopy (NCSM) and Rotating Scheimpflug Camera (RSC). The sequence of examination was randomized, except for USP, the last to be performed. With each instrument, the same examiner acquired 3 consecutive CCT measurements per eye, and the average value was used for the analysis. Linear correlations between CCT values acquired with different instruments and USP were computed, to test the strength of measurement associations. Bland-Altman plots were drawn to describe measurement agreement between optical instruments and USP.

Results: Mean CCT values (\pm SD) were 549.82 ± 29.95 , 552.34 ± 27.74 , 538.28 ± 26.88 , 525.18 ± 29.02 , and 563.58 ± 52.73 μ m, respectively for USP, RSC, SS-OCT Casia, SD-OCT Optovue and NCSM. Figure 1 shows the correlation coefficients (r) of SS-OCT Casia, SD-OCT Optovue, RSC, NCSM vs. UPS were 0.914, 0.882, 0.902 and 0.398, respectively ($p < 0.001$ for all the correlations). When evaluating the Bland-Altman plots, as illustrated in Figure 2, SD-OCT Optovue showed the highest mean difference of CCT measurements against USP ($+24.63$ μ m), while the lowest mean difference was achieved by RSC (-2.53 μ m). Intermediate values were obtained by NCSM and SS-OCT Casia (-13.77 , $+11.54$ μ m respectively).

Conclusions: The results support the use of optical methods as a viable alternative to USP pachymetry. Of the tested instruments, RSC proved as the best alternative to USP, with a strong correlation of measurements ($r=0.902$) and a good agreement (mean difference with USP: -2.53 μ m). Furthermore, SS-OCT Casia showed a good correlation with the USP gold standard.

CONTROL ID: 3546088

SUBMITTER (NAME ONLY): Xin Wei

TITLE: Theoretical Comparison of Peripheral Defocus between Object Space and Image Space by Optical Modeling

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Wei, Medennium Inc., California, UNITED STATES|P.S. Kollbaum, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|J. Dong, Aier Eye Hospital Group, Changsha, Hubei, CHINA|

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ABSTRACT BODY:

Purpose: As the retina is a tilted image plane in the peripheral visual field to the incident beam, the perceived defocus on the peripheral retina in image space is different from the measured peripheral defocus in object space, where the incident beam is normal to the instrument's detection plane. This study investigates the theoretical difference between the object-space defocus and image-space defocus in the peripheral visual field.

Methods: A wide-angle model eye was constructed to match published measures of peripheral defocus in object space (Atchison et al. 2006). The measured object-space defocus was modeled by minimizing the blur size on the autorefractor's detection plane through tracing rays from the retina to the object space along the peripheral line of sight. The image-space defocus was estimated by minimizing the blur size on the tilted retina through tracing parallel rays reversely along the same lines of sight. The differences between and object-space defocus and image-space defocus were compared at 0°, 10°, 20°, and 30° for 3.75, 5.0, and 6.5 mm-diameter pupils.

Results: Along the foveal line of sight, the object-space defocus is the same as the image-space defocus. In the periphery, a significant amount of the dioptric difference is observed. In particular, for myopic eyes, the measured object-space defocus underestimates the image-space defocus. For 3.75-mm pupil, the differences are 0.3 D and 0.4 D along 20° and 30° lines of sight. The gap becomes larger as the pupil size increases. Specifically, along the 30° line of sight, the defocus difference increases to 0.6 D for a 6.5-mm pupil.

Conclusions: In the peripheral visual field, the object-space defocus and image-space defocus are different. Unlike foveal vision, to interpret image-space defocus on the peripheral retina from defocus measurements in object space, optical analysis using a wide-angle eye model is required. This step is crucial for designing wide-angle-viewing optics for the eye.

CONTROL ID: 3546089

SUBMITTER (NAME ONLY): Rooban Nahomi

TITLE: Inhibition of ischemia/reperfusion-induced retinal capillary degeneration in mice by peptain-1

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.B. Nahomi, M. Nam, C. Hougen, N. Carrillo, R.H. Nagaraj, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal capillary endothelial cells undergo apoptosis in diabetic retinopathy (DR). Peptain-1 is a cell-permeable α B-crystallin-derived peptide and it exhibits strong antiapoptotic properties. Here, we investigated the ability of peptain-1 to inhibit apoptosis in cultured retinal endothelial cells and in retinal capillaries of mice subjected to retinal ischemia/reperfusion (I/R) injury.

Methods: Human retinal endothelial cells (HRECs) were treated with peptain-1 or scrambled peptides (200 μ g/ml) for 3 h, and a combination of pro-inflammatory cytokines [IFN- γ (50 U/ml) + TNF- α (20 ng/ml) + IL-1 β (20 ng/ml)] for 48 h. Twelve-week-old C57BL/6J mice were subjected to I/R injury by elevating the intraocular pressure to 120 mmHg for 60 min followed by reperfusion. Peptain-1 or scrambled peptide (500ng/ μ l of PBS) was injected intravitreally immediately after and one week after I/R injury. The PBS injected eyes were used as vehicle controls and the animals were euthanized on day 14 post-I/R injury. Abnormalities in the retinal capillaries were evaluated by staining the elastase-digested retinal blood vessels using Periodic acid–Schiff stain.

Results: Our results suggest that peptain-1 entered HRECs and blocked the pro-inflammatory cytokine-mediated apoptosis. Intravitreally injected peptain-1 was distributed throughout the retina after 4 h. The I/R injury caused a significant increase in acellular capillaries in the retina (3.5-fold when compared to controls), while intravitreally injected peptain-1, but not scrambled peptide, protected those cells from I/R injury (1.5-fold increase when compared to the control group).

Conclusions: Our study demonstrated that peptain-1 protects retinal capillary cells from I/R injury and suggests that it could be used as a therapeutic agent to prevent capillary cell death in DR.

CONTROL ID: 3546093

SUBMITTER (NAME ONLY): Matthew Fung

TITLE: Development of a Novel Bioartificial Surgical Outflow Tract Model for Rapid Screening of Anti-Fibrotics Adjuvants

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Fung, J.J. Armstrong, Western University Schulich School of Medicine & Dentistry, London, Ontario, CANADA|H. Liu, C.M. Hutnik, Ivey Eye Institute, London, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Although surgical glaucoma intervention has made significant progress over the past few decades, advances in stemming postoperative fibrosis have lagged. To assess the utility of novel anti-fibrotic drugs for glaucoma filtration surgery (GFS), cell culture-based models are initially employed. Currently, these models do not recapitulate the perfusion of aqueous humor (AH) through subconjunctival tissues. We engineered a perfused three-dimensional collagen-based cell culture system containing human Tenon's capsule fibroblasts (HTCFs) that continuously record afferent perfusion line pressure as an analog for intraocular pressure. Elevated transforming growth factor-beta 1 (TGFβ1) in the AH is associated with GFS failure. We evaluated the effects of perfusing exogenous TGFβ1 with or without verteporfin – a TGFβ1 pathway inhibitor – on afferent perfusion line pressure within this novel culture system.

Methods: HTCFs were cultured within 3D collagen matrices that were covalently bonded to the edges of a flow chamber slide. Cell culture media was perfused through the HTCF-containing collagen matrix at the rate of physiological AH production. Continuous afferent perfusion line pressure was recorded over a 72-hour period, and light and fluorescent microscopy were used to assess 3D cell morphology and tissue architecture within the collagen matrix and cell lysate was probed for alpha-smooth muscle actin (α-SMA) via western blot.

Results: HTCF collagen cultures perfused with TGFβ1 showed significantly elevated afferent line pressure compared to vehicle control over 72hrs, with an average pressure of 35mmHg and 17mmHg respectively (p<0.05). Confocal microscopy confirmed the presence of a 3D matrix containing HTCFs within the chamber slides. HTCFs treated with TGFβ1 demonstrated increased proliferation and organization within the chamber. Western blot revealed elevated α-SMA in TGFβ1 compared to vehicle-treated replicates. Verteporfin co-perfusion ameliorated elevated afferent line pressures and decreased α-SMA.

Conclusions: Perfused 3D collagen matrices containing HTCFs can generate outflow resistance in vitro. Addition of exogenous TGFβ1 to the perfusate causes increased outflow resistance, and inhibition of TGFβ1 through verteporfin mitigated this effect. These findings support this culture system as a platform for the discovery of anti-fibrotic drugs for glaucoma surgery.

CONTROL ID: 3546094

SUBMITTER (NAME ONLY): Charles Blizzard

TITLE: Ocular Pharmacokinetics of OTX-DED, a Sustained-release Intracanalicular Insert Delivering Dexamethasone, in a Canine Model

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.D. Blizzard, A. Desai, A. Driscoll, M. Cheung, M.H. Goldstein, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular surface inflammation plays a key role in all types of dry eye disease (DED) and corticosteroids are well-established as a fast-acting and effective treatment for signs and symptoms of DED. OTX-DED is an intracanalicular insert containing 0.2 mg of dexamethasone entrapped in a hydrogel matrix designed to provide sustained-release dexamethasone to the ocular surface. OTX-DED is similar to DEXTENZA (dexamethasone ophthalmic insert) 0.4 mg (indicated to treat post-ophthalmic surgery inflammation and pain) but contains lower doses of dexamethasone and a shorter intended duration of therapy. The objective of the study was to characterize the pharmacokinetics of the 0.2 mg dose of OTX-DED in a beagle model.

Methods: OTX-DED inserts containing 0.2 mg dexamethasone were placed into the canaliculus of beagle dogs. Beagle dogs were selected as the animal model since the morphometry of the nasolacrimal system provides an appropriate sized puncta and canaliculus. Tear fluid samples were collected using 10 mm Schirmer test strips from beagle dog eyes throughout the study duration after insertion of OTX-DED into the canaliculus and concentrations of dexamethasone in tear fluid were measured using liquid chromatography with tandem mass spectrometry.

Results: The average dexamethasone concentration in the beagle tear fluid of the 0.2 mg dexamethasone insert is presented in Figure 1. Results demonstrated sustained drug release into the tear fluid with concentrations declining over the study duration as the dexamethasone became depleted from the insert. This decrease in tear fluid concentration is evidenced in the 0.2 mg dose after 14 days. The profile demonstrates sustained levels of dexamethasone in the tear fluid through 7 days followed by a tapering from day 7 to 14 days with a complete release of dexamethasone from the insert by 17 days.

Conclusions: OTX-DED at a dose of 0.2 mg delivered dexamethasone to the ocular surface for approximately 14 days. Comparatively, DEXTENZA (0.4 mg) delivered dexamethasone to the ocular surface up to 28 days. In vivo dexamethasone release data indicates a shorter duration of drug release for the 0.2 mg dose compared to the 0.4 mg from the hydrogel insert in the beagle model.

CONTROL ID: 3546097

SUBMITTER (NAME ONLY): Odalys Torne

TITLE: Trabecular meshwork pathology in a feline model of glaucoma due to LTBP2 mutation

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Torne, K. Oikawa, G.J. McLellan, Surgical Sciences - School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|K. Oikawa, J.A. Kiland, G.J. McLellan, Ophthalmology and Visual Sciences, University of Wisconsin-Madison School of Medicine and Public Health, Madison, Wisconsin, UNITED STATES|L. Teixeira, Pathobiological Sciences - School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary congenital glaucoma (PCG) is an important cause of irreversible childhood blindness. LTBP2 mutations have been identified as causative for both human and feline PCG, but mechanisms of intraocular pressure (IOP) elevation remain unknown. We hypothesized that LTBP2 mutation causes pathology in the conventional aqueous outflow pathway. Ultrastructure of the trabecular meshwork (TM) was studied by transmission electron microscopy (TEM) and aqueous angiography (AA) evaluated more distal components of the outflow pathway in feline eyes, prior to and at the onset of significant IOP elevation.

Methods: Eyes from 11 LTBP2^{-/-} cats (2 neonates and 9 at 10- 12wks) and 6 age-matched control eyes (1 neonate and 5 at 10-12wks) were paraformaldehyde fixed, anterior segments dissected, and sectors post-fixed in glutaraldehyde, osmicated and processed and sectioned for TEM. To evaluate distal aqueous outflow pathways, indocyanine green AA was performed in 1 PCG (10- 12 wks) and 5 aged-matched control eyes <2hrs post-mortem, imaged by Spectralis HRA+OCT (Heidelberg Engineering).

Results: The angle appeared open and TM and angular aqueous plexus (AAP; analogous to Schlemm's canal) were visualized by TEM in both normal and mutant cats. In neonates, the still immature TM and AAP were morphologically comparable between PCG and control eyes. However, at 10-12wks, differences were evident between the two groups. In eyes of PCG cats, TM cells had an elongated, attenuated appearance and the inter-trabecular spaces of the corneoscleral TM appeared collapsed, with lower percentage of open space (P= 0.0006) relative to controls. Subjectively, TM beams appeared similar between groups, with regular collagen bundles and elastin cores, but less fibrillar material surrounding the core structure of the more proximal TM beams in PCG. The AAP and distal outflow channels still appeared patent in the juvenile PCG cats as supported by AA and OCT. All 10-12 wk-old cats regardless of disease status had nearly 360° circum-limbal AA signal, visible within <5 mins of commencing tracer perfusion.

Conclusions: In this model of PCG related to LTBP2 mutation, TM, inter-trabecular spaces, AAP and more distal outflow pathways appear normal at birth. Subsequent development of TM cellular pathology and TM and JCT ECM pathology coincides with onset of IOP elevation.

CONTROL ID: 3546100

SUBMITTER (NAME ONLY): Aaron Michalko

TITLE: Phase resolved OCT to measure laser induced refractive index change (LIRIC) in hydrogel

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Michalko, L. Zheleznyak, Clerio Vision, Inc., Rochester, New York, UNITED STATES|V. Pandiyan, R. Sabesan, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: LIRIC is a non-invasive method for correcting aberrations in hydrogels, IOLs and the cornea. As such, the need exists for non-destructive metrology of LIRIC-induced optical phase change. Here we demonstrate the feasibility and validation of parallel phase resolved OCT for measurements of optical phase change induced by LIRIC in hydrogel.

Methods: To produce the LIRIC sample, a femtosecond laser was focused inside a 0.5 mm thick hydrogel button (Contamac, Acofilcon A) and scanned throughout a single layer. Seven rectangular regions (0.1 x 0.4 mm each) of LIRIC piston wavefronts were induced. Each region was written at a distinct laser power (0.7 to 1.0 W, in 0.05 W steps). The LIRIC-induced phase shift was subsequently measured in two methods: (a) phase-resolved line-scan OCT and (b) phase-shifting interferometry (PSI). The line-scan, spectral domain OCT ($\lambda=820$ nm, $\Delta\lambda=80$ nm) was used to image a 3.5x2.5 mm field-of-view on the hydrogel. The 3D phase distribution was obtained in the reconstructed complex volume after segmenting the LIRIC layer in depth. The PSI consisted of a Mach-Zehnder interferometer ($\lambda=632$ nm) with a piezo-driven phase-shifting mirror in the reference arm. LIRIC was quantified from both OCT and PSI by computing the difference in optical phase between written and unwritten regions of the hydrogel.

Results: The intended spatial profile of the LIRIC-induced wavefront was readily reproduced in both measurements. Both measurement techniques (OCT and PSI) showed a predictable increase in the magnitude of phase change with increasing laser power. With OCT, it ranged from 76 ± 58 to 376 ± 91 nm at 0.7 and 1.0 W, respectively. With PSI, it ranged from 61 ± 29 to 334 ± 40 nm. The OCT and PSI measurements were highly correlated (R-squared = 0.99).

Conclusions: Phase resolved OCT was shown to accurately measure optical phase change in hydrogels induced via femtosecond laser processing (LIRIC).

CONTROL ID: 3546101

SUBMITTER (NAME ONLY): Heather Chandler

TITLE: Platelet-Derived Growth Factor Receptor β Promotes Cataract Formation

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.L. Chandler, J.A. Geisler, G.M. Sizemore, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Heather Chandler: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Geisler: Commercial Relationship: Code N (No Commercial Relationship) | Gina Sizemore: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate how in vivo hyperactivation of platelet-derived growth factor receptor (PDGFR) β alters lens homeostasis and induces epithelial-mesenchymal transition (EMT) in lens epithelial cells (LEC).

Methods: In a mouse model of mesenchymal-specific PDGFR β activation using the Fsp-cre transgene (herein referred to as β KI mice), lens phenotype was monitored over time. Standard histologic processing and immunohistochemistry (IHC) were used to evaluate morphologic changes and expression of PDGFR β and α -smooth muscle actin (SMA) in the lens.

Results: β KI mice began to develop spontaneous cataracts at 16 weeks of age while control mice did not (n=6). Histologic evaluation of lenses from β KI mice at approximately 26 weeks of age (n=6) demonstrated LEC proliferation and EMT with extracellular matrix deposition and fibrosis. By comparison, lenses from control mice were histologically normal. Expression of Fsp1-cre in LEC was confirmed using a Rosa reporter and expression of PDGFR β in LEC was confirmed with IHC. As mice continued to age (up to 67-72 weeks; n=8), cataracts advanced and became hypermature in the β KI mice, while control lenses remained transparent. Cataractous lenses were positive for α SMA expression, as observed with IHC, while control lenses were negative. No differences in outcome measures were observed when comparing males and females.

Conclusions: Overall, the pronounced spontaneous cataract formation in β KI mice compared to age-matched control mice, and resultant histologic changes, indicate that PDGFR β activation is important for induction of EMT in LEC. Further, hyperactivation of PDGFR β is a primary contributor of cataract formation.

CONTROL ID: 3546102

SUBMITTER (NAME ONLY): Jeremy Reitingner

TITLE: Comparison of IOP Response to Timolol Versus Latanoprost

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Reitingner, Creighton University School of Medicine, Omaha, Nebraska, UNITED STATES|D. Reed, J. Gilbert, S.E. Moroi, Kellogg Eye Center, University of Michigan, Ann Arbor, Michigan, UNITED STATES|D. Reed, J. Gilbert, C.B. Toris, S.E. Moroi, Department of Ophthalmology and Visual Sciences, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|T. Kristoff, Department of Ophthalmology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|V. Gulati, S. Fan, C.B. Toris, Stanley M Truhlsen Eye Institute, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|A. Kazemi, J. McLaren, A.J. Sit, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prostaglandin analogues and beta-blockers are effective intraocular pressure (IOP) lowering drugs commonly used for glaucoma. However, there remain a sizeable number of nonresponders to these treatments. This study used both iCare and pneumatonometry to identify the IOP response to latanoprost and timolol under monotherapy.

Methods: We examined 212 eyes from 106 ocular normotensive, non-glaucomatous volunteers (76% female, 55.5 ± 8.9 years of age) from the EDEN consortium. At baseline, IOP was measured by iCare at 9AM and 11AM, and pneumatonometry at 11AM. Subjects were randomized and treated in both eyes (OU) with either 0.005% latanoprost once daily or 0.5% timolol twice daily for 7 days, with measurements repeated on day 8 of each treatment. After a 6-week washout, subjects switched drug arms. IOP-responders were those having an IOP reduction of $>15\%$ OU, while mixed responders had an IOP reduction of $>15\%$ in one eye (OD or OS). Treatment effects and intereye correlations on IOP were analyzed using Spearman's rho, two-tailed paired t-tests and Fisher's Exact Test.

Results: As compared to baseline, timolol and latanoprost effectively lowered IOP by 13% OD (14% OS) and 17% OD (18% OS), respectively ($p < 0.0001$, pneumatonometry). Twenty-two subjects (21%) failed to respond to either latanoprost or timolol OU. IOP response to timolol did not predict IOP response to latanoprost, however, latanoprost responders tended to also respond to timolol. More subjects were IOP-responders OU when taking latanoprost compared to timolol ($p < 0.007$), with 54% responding to latanoprost and 28% responding to timolol (pneumatometry) (Figure 1). In patients given timolol, a higher non-response rate was found when measuring with pneumatonometry as opposed to iCare ($p = 0.037$) (Figure 1).

Conclusions: In this group of healthy subjects, a significant amount did not respond to either timolol or latanoprost. Even though the drugs represent two different mechanisms of action (timolol decreasing aqueous flow and latanoprost increasing uveoscleral outflow), non-response to one drug did not predict response to another. A new study is underway to determine if this pattern persists in patients with ocular hypertension.

CONTROL ID: 3546103

SUBMITTER (NAME ONLY): Ken Kitayama

TITLE: Decreased odds of glaucoma surgery in racial/ethnic minorities in the IRIS Registry

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Kitayama, V. Tseng, F. Yu, A.L. Coleman, Center for Community Outreach & Policy, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|F. Yu, Biostatistics, UCLA Fielding School of Public Health, Los Angeles, California, UNITED STATES|K. Kitayama, A.L. Coleman, Epidemiology, UCLA Fielding School of Public Health, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare the odds of glaucoma surgery in minority racial/ethnic groups against that of white patients in the American Academy of Ophthalmology (AAO) Intelligent Research in Sight (IRIS) Registry database.

Methods: This was a cross-sectional study using 2015-2017 IRIS Registry public use data of glaucoma patients from over 3,000 practices across the United States. The outcome of interest was three-year prevalence of glaucoma surgery by type, including incisional surgery (IS) (trabeculectomy, tube shunts), minimally invasive glaucoma surgery (MIGS) (canaloplasty, trabecular/suprachoroidal bypass, transscleral cyclophotocoagulation), and laser surgery (LS) (laser trabeculoplasty). The primary exposure was race/ethnicity, including American Indian/Alaska Native (AI/AN), Asian, Black, Latino, Multi, Native Hawaiian/Pacific Islander (NH/PI), white, and unknown. Logistic regression modeling was performed to estimate odds of IS, MIGS, and LS by racial/ethnic group, controlling for age, sex, insurance type, geographic region, and glaucoma severity.

Results: The study sample included a total of 7,566,572 unique patients, of whom 74,028 (0.98%) received IS, 119,410 (1.58%) MIGS, 236,902 (3.13%) LS, and 7,172,833 (94.80%) received no surgery. Racial/ethnic groups with decreased odds of all glaucoma surgery types compared to white patients included Asians (IS odds ratio [OR]: 0.80, 95% confidence interval [95% CI]: 0.76-0.84; MIGS OR: 0.79, 95% CI: 0.76-0.82, LS OR: 0.88, 95% CI: 0.81-0.95), Latinos (IS OR: 0.97, 95% CI: 0.94-0.99; MIGS OR: 0.92, 95% CI: 0.90-0.94; LS OR: 0.95, 95% CI: 0.94-0.97), NH/PI (IS OR: 0.52, 95% CI: 0.40-0.69; MIGS OR: 0.66, 95% CI: 0.55-0.80; LS OR: 0.75, 95% CI: 0.66-0.86), and unknown race (IS OR: 0.65, 95% CI: 0.64-0.67; MIGS OR: 0.81, 95% CI: 0.79-0.82; LS OR: 0.73, 95% CI: 0.72-0.75). Compared to white patients, Black patients had increased odds of IS (OR: 1.26, 95% CI: 1.23-1.28), decreased odds of LS (OR: 0.96, 95% CI: 0.95-0.98), and no difference in odds of MIGS (OR: 1.01, 95% CI: 0.99-1.03).

Conclusions: In the 2015-2017 AAO IRIS Registry sample, most minority racial/ethnic groups (Asians, Latinos, NH/PI, unknown race) were found to have decreased odds of all glaucoma surgery types when compared to white patients, after adjusting for covariates. Additional population-based studies are necessary to further examine differences in rates of glaucoma surgery across racial/ethnic groups.

CONTROL ID: 3546107

SUBMITTER (NAME ONLY): Rene Ruckert

TITLE: Long-term safety and efficacy of ISTH0036 – a selective TGF- β 2 blocking antisense oligonucleotide in preclinical and Phase 1 clinical studies.

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ruckert, M.R. Munk, K. Wosikowski, M. Janicot, Isarna Therapeutics GmbH, Munchen, Bayern, GERMANY|R. Ruckert, M.R. Munk, eyegnos consulting, Bern, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Transforming Growth Factor beta 2 (TGF- β 2) has been widely described as a key cytokine involved in the pathophysiology of ocular disease. ISTH0036 is a 14-mer modified antisense oligodeoxynucleotide selectively targeting TGF- β 2 mRNA. It exhibits potent activity in murine models of choroidal neovascularization (CNV). ISTH0036 induced a decrease in neovascularization, vascular leakage, fibrotic development, as well as blockage of epithelial-to-mesenchymal transition. The presented studies explored pharmacokinetics (PK), pharmacodynamics (PD), and toxicity in rabbits and non-human primates (NHP) and long-term safety in a first-in human Phase1 trial to support further developments.

Methods: Long-term safety in Phase 1 was assessed after single ITV injection up to 12mo. PK, ocular tissue distribution, PD (target engagement), and long-term toxicity were studied upon single and repeated IVT administration(s) in rabbits and Cynomolgus monkeys. Results were compared with observations in the CNV model to support development in retinal diseases.

Results: In the Phase 1 study, single ITV injection of ISTH0036 in patients after Trabeculectomy was well tolerated and safe out to 12-months. One subject with several (preexisting) risk factors developed cataract. Rabbits and NHPs were treated with single or repeated IVT administration(s) for up to 9mo. Toxicology profile was established and pointed at lens opacification as dose-limiting toxicity in both species. Long-lasting target engagement was observed in relevant eye tissues in animals; with TGF- β 2 mRNA downregulation in retina and lens, and TGF- β 2 protein reduction in vitreous humor (VH). Interestingly, evidence of much longer target engagement (up to 4 months, after single drug administration) was observed in NHPs.

Conclusions: Compared tests of ISTH0036 in rabbits and NHPs resulted in similar toxicity profile, although with higher dose-dependent sensitivity observed in Rabbits. Pronounced and long-lasting time- and dose-dependent ocular tissue distribution and target engagement in retina and VH was observed, with longer effects observed in NHPs. Aligned with biological efficacy demonstrated in preclinical models, and preliminary evidence of safety in a first-in-human study, these results strongly support the planned Phase 2 development of ISTH0036 in wAMD and DME.

CONTROL ID: 3546109

SUBMITTER (NAME ONLY): Margaret Chang

TITLE: Immunogenicity profile of the Port Delivery System with ranibizumab in patients with nAMD

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Chang, Retinal Consultants, Sacramento, California, UNITED STATES|K. Maass, G.J. Spicer, N. Singh, S. Blotner, M. Maia, Genentech Inc, South San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Port Delivery System with ranibizumab (PDS) is an investigational drug delivery system for the continuous intravitreal release of ranibizumab (RBZ) via a permanent indwelling intraocular implant. The phase 2 Ladder and phase 3 Archway trials demonstrated that treatment with PDS with a customized formulation of RBZ 100 mg/mL (PDS 100 mg/mL) was generally well tolerated and had comparable efficacy to monthly intravitreal RBZ. Immunogenicity is important in assessing safety and efficacy of recombinant therapeutics and was monitored in both trials.

Methods: Ladder (NCT02510794) patients (pts) were randomized to PDS with RBZ 10, 40, or 100 mg/mL, or monthly intravitreal RBZ 0.5 mg (monthly RBZ). Archway (NCT03677934) pts were randomized to treatment with PDS 100 mg/mL with fixed 24-week refill exchanges (Q24W) or monthly RBZ (Q4W). As both trials enrolled pts with nAMD responsive to anti-VEGF treatment, immunogenicity analyses focused on incidence of treatment-emergent (TE) anti-drug antibodies (ADAs) and neutralizing antibodies (NAbs). We report ADA status in Ladder (end of study) and Archway (primary analysis) and the impact of ADA status on serum PK at week 24, and on visual and safety outcomes at week 40 in Archway.

Results: In Ladder, there was no apparent dose response on incidence of TE-ADAs across PDS arms (6.9%-15.3%). Incidences of TE-ADAs with PDS 100 mg/mL were relatively low in Ladder (15.3% [9/59]) and Archway (11.7% [29/247]), and comparable or slightly higher than monthly RBZ (Ladder: 14.6% [6/41]; Archway: 5.5% [9/164]). Overall incidences of TE-NAbs were low with both monthly RBZ and PDS 100 mg/mL (Ladder: 0%-3.4%; Archway: 2.4%-5.3%). In Archway, over 40 weeks, presence of ADAs in PDS 100 mg/mL pts did not appear to impact mean (95% CI) change from baseline in BCVA versus ADA negative pts (0.0 [-2.8, 2.8] vs 0.2 [-1.0, 1.5] ETDRS letters, respectively) or postoperative (>37 days) incidence of ocular AEs (41.2% [14/34] vs 38.0% [81/213]), intraocular inflammation (including endophthalmitis; 2.9% [1/34] vs 5.6% [12/213]), or iritis (0% [0/34] vs 1.4% [3/213]); there was no apparent trend for an effect of ADA status on serum PK or incidence of non-ocular AEs.

Conclusions: The immunogenicity profile of PDS 100 mg/mL was comparable to that of monthly RBZ, with no apparent impact of ADAs on outcomes. These data further support the efficacy and tolerability of PDS 100 mg/mL Q24W in nAMD.

CONTROL ID: 3546110

SUBMITTER (NAME ONLY): Claus von der Burchard

TITLE: Self-Examination Low-Cost Full-Field OCT (SELFF-OCT) for Age-Related Macular Degeneration

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. von der Burchard, J. Tode, C. Ehlken, K. Purtskhvanidze, J. Roider, Department of Ophthalmology, Christian-Albrechts-Universität zu Kiel Medizinische Fakultät, Kiel, Schleswig-Holstein, GERMANY|H. Sudkamp, M. Moltmann, P. Koch, M. Müntz, M. vom Endt, T. Kepp, D. Theisen-Kunde, G. Huttmann, Medizinisches Laserzentrum Lubeck GmbH, Lubeck, Schleswig-Holstein, GERMANY|J. Tode, Department of Ophthalmology, Medizinische Hochschule Hannover, Hannover, Niedersachsen, GERMANY|B. Heimes-Bussmann, M3 Macula Monitor Münster, Augenzentrum am St. Franziskus-Hospital Münster, Münster, GERMANY|I. König, Institute of Medical Biometry and Statistics, University of Lübeck, Lübeck, GERMANY|

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ABSTRACT BODY:

Purpose: Self-Examination Low-Cost Full-Field Optical Coherence Tomography (SELFF-OCT) is a novel OCT technology that was specifically designed for home monitoring of age-related macular degeneration (AMD). First clinical findings have been reported before [1]. This trial investigates an improved prototype for AMD patients and focusses on device operability and diagnostic accuracy compared with established spectral-domain OCT (SD-OCT). [1] von der Burchard C et al. Self-examination low-cost full-field OCT (SELFF-OCT) for patients with various macular diseases. Graefes Arch Clin Exp Ophthalmol, 2020, DOI: 10.1007/s00417-020-05035-6.

Methods: We performed a cross-sectional study in patients with age-related macular degeneration. Patients received short training in device handling and then performed multiple self-scans with the SELFF-OCT according to a predefined protocol. Additionally, all eyes were examined with standard SD-OCT, performed by medical personnel. All images were graded in a reading center by at least 2 blinded investigators for different biomarkers and the necessity of anti-VEGF treatment.

Results: In total, 85 eyes of 45 patients with AMD were measured with SELFF-OCT. Compared to prior prototypes, advancements in technology and an improved patient interface enhanced image quality and reduced motion artifacts. In 86% of all examined eyes, OCT self-acquisition resulted in interpretable retinal OCT volume scans. In these patients, the sensitivity for detection of anti-VEGF treatment indication was 0.94 [confidence interval 0.79-0.99] and specificity 0.95 [0.82-0.99]. Sensitivity and specificity for the detection of single biomarkers were 0.9/0.98 for subretinal fluid, 0.57/0.95 for intraretinal fluid and 0.76/0.95 for pigment epithelium detachment.

Conclusions: SELFF-OCT was used successfully for retinal self-examination in most patients, and it could become a valuable tool for retinal home-monitoring in the future. Improvements are in progress to reduce device size and to improve handling, image quality and success rates.

CONTROL ID: 3546111

SUBMITTER (NAME ONLY): Morgan Ringel

TITLE: Ex vivo ophthalmic surgical guidance using intraoperative spectrally encoded coherence tomography and reflectometry (iSECTR)

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ringel, E. Tang, Y. Tao, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intraoperative optical coherence tomography (iOCT) during ophthalmic surgeries provides high-resolution, volumetric imaging, which benefits surgical decision-making. However, live 4D visualization of surgical maneuvers remains challenging due to the OCT field-of-view (FOV) requiring manual adjustment and tracking. Here, we demonstrate a multimodal, intraoperative spectrally encoded coherence tomography and reflectometry (iSECTR) imaging system that combines OCT and en face reflectance imaging. We believe that this system addresses current limitations in iOCT imaging by enabling registration and tracking of serial OCT volumes with surgical regions-of-interest using high-speed en face images of the surgical field.

Methods: The spectrally encoded reflectometry (SER) and OCT imaging relays were designed to share the objective lens of a Zeiss VISU 200 surgical microscope and a binocular indirect ophthalmomicroscope (Oculus BIOM 3). A custom scan-head was designed to contain the iSECTR optics, scanning galvanometers, fold mirrors, and optomechanics (Fig. 1(A)). iSECTR was folded into the surgical microscope imaging path using a dichroic mirror and a custom 400 kHz 1060 nm swept-source (Axsun) engine with a 2 GS/s per channel digitizer was used to simultaneously acquire en face SER and cross-sectional OCT images.

Results: Retinal surgery was simulated in ex vivo porcine eyes using 25G forceps. SER and OCT projection images show FOV co-registration with the surgical microscope FOV captured with a documentation camera. iSECTR volumes were acquired with 2560x500x2500 pix. (spectral x lateral x lateral). All three images show the surgical forceps and a prominent retinal vessel. The cross-sectional OCT view shows the forceps and surrounding retinal layers (Fig. 1(B)-(E)).

Conclusions: An iSECTR system featuring a custom scan-head enclosure was integrated with a Zeiss VISU 200 surgical microscope, and the system was used to image simulated retinal surgery in ex vivo porcine eyes. Clinical translation of iSECTR will benefit ophthalmic surgical guidance by enabling region-of-interest tracking iOCT imaging of surgical maneuvers and tissue dynamics.

CONTROL ID: 3546113

SUBMITTER (NAME ONLY): Vivian Paraskevi Douglas

TITLE: Impact of COVID-19-related lockdown on intravitreal injection clinic in an academic institution

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Douglas, K.A. Douglas, D.G. Vavvas, J.W. Miller, J. Miller, Retina, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|V. Douglas, K.A. Douglas, J. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We sought to analyze the changes in clinical care following the restrictions that were implemented in Massachusetts in response to COVID-19 pandemic as well as to depict the visual outcomes in patients receiving intravitreal injections as part of a treatment regimen for either exudative age-related macular degeneration (AMD), diabetic retinopathy (DR), central or branch retinal vein occlusion (CRVO, BRVO).

Methods: A retrospective analysis of the intravitreal injection clinics of three retina specialists at Massachusetts Eye and Ear from December 2019 to June 2020 was performed. Demographic data of patients with either wet AMD, DR, CRVO or BRVO were collected. Descriptive statistics were used to quantitatively summarize the features of our cohort and box plots to illustrate the spread and differences of visual acuity among groups over time.

Results: A total of 1,086 visits were scheduled within this period and more than a quarter of these visits were not completed [801 (74%) completed vs 285 (26%) cancel or no show; $p=0.000$]. The mean age of our cohort was 72.5 ± 13.2 years (males: 72.48 ± 13.2 ; females: 74 ± 12.4 ; $p=0.0524$). Out of 259 cancel visits, 240 visits (93%) were canceled by the patients and 19 visits (7%) by the provider/institution ($p=0.000$). There was no significant difference in the appointment status (completed, cancel, no show) among males and females, among different providers, or diagnoses ($p=0.225$, $p=0.131$ and $p=0.234$ respectively). Asians and Caucasians were more likely to complete their visits (80% and 74% respectively) compared to patients of Hispanic, African American and American Indian ethnicities where more cancel/no show visits were observed (40%, 29% and 29% respectively; $p=0.002$). The highest numbers of cancel/no show appointments were reported in March (48.8%) and April (45.6%) and were significantly different when compared to the other months ($p=0.000$).

Conclusions: Intravitreal therapy is the standard care for a variety of retinal disorders and adherence to the proposed treatment regimen is important to maximize the visual acuity benefits and maintain the gains in the long term. In this cohort it was noted that vast majority of visits were canceled by the patients whereas underrepresented minorities were more likely not to complete their scheduled visits which could be partially explained by the fact that these groups are also disproportionately affected by COVID-19.

CONTROL ID: 3546114

SUBMITTER (NAME ONLY): Nestor Mas Gomez

TITLE: TRPML1 channels activation facilitates lysosomal exocytosis and reduces autofluorescent lysosomal accumulations, opsin retention and lipid peroxidation in RPE cells compromised by chloroquine

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Mas Gomez, W. Lu, C.H. Mitchell, Department of Basic & Translational Sciences, University of Pennsylvania School of Dental Medicine, Philadelphia, Pennsylvania, UNITED STATES|C.H. Mitchell, Department of Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nestor Mas Gomez: Commercial Relationship: Code N (No Commercial Relationship) | Wennan Lu: Commercial Relationship: Code N (No Commercial Relationship) | Claire Mitchell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Excessive lysosomal accumulations are associated with multiple neurodegenerations including age-related macular degeneration. Treatment to reduce these accumulations is of broad interest. Lysosomes store calcium, and the regulated efflux through TRPML1 channels contributes to the fusion of lysosomal membranes with the plasma membrane during lysosomal exocytosis. We previously identified functional TRPML1 channels on RPE lysosomes. Here we ask whether TRPML1 activation can facilitate lysosomal exocytosis and clearance of accumulations in RPE cells

Methods: Experiments were performed on confluent aged ARPE-19 cells. Autofluorescence (AF) at 488 ex/560 em was determined in a Fluoroskan plate reader and microscopically. Extracellular acid phosphatase (AP) was measured with a standard colorimetric kit. Cells were fed with bovine photoreceptor outer segments (POS) using a pulse chase protocol to minimize interference in phagocytosis; cells were fed 1×10^6 POS/ml for 2 h (pulse), medium alone for 2 h (chase), then 20 h in control or chloroquine (CHQ) medium. Opsin levels were determined with immunoblots. Lipid peroxidation were determined from measurements of Bodipy-C11

Results: Cellular accumulations were induced by exposing ARPE-19 cells to CHQ for 7 days followed by 24 hr exposure to U18666A (U18). CHQ/U18 treatment increased AF accumulations. Exposure of these cells to TRPML1 agonist ML-SA1 reduced AF levels. To determine whether ML-SA1 increased lysosomal exocytosis, extracellular levels of lysosomal AP were determined. ML-SA1 increased extracellular levels of AP in both control and CHQ-treated cells, suggesting ML-SA1 triggered lysosomal exocytosis. Furthermore, the effect of TRPML1 on opsin turnover was investigated. RPE treated with CHQ and loaded with POS showed a significant rise in opsin on immunoblots. Critically, ML-SA1 decreased retention of opsin in CHQ-treated cells.

Conclusions: Activation of TRPML1 in compromised RPE cells increased lysosomal exocytosis and decreased lysosomal autofluorescence. In cells loaded with POS, CHQ treatment increased opsin retention and lipid peroxidation, while TRPML1 activation decreased both. Further investigation is needed to identify how TRPML1 activation enhances lysosomal clearance in compromised RPE cells

CONTROL ID: 3546115

SUBMITTER (NAME ONLY): Gibran Butt

TITLE: Public perceptions of eye symptoms and hospital services during the first COVID-19 lockdown in the UK.

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.F. Butt, G.R. Wallace, S. Rauz, P.I. Murray, Academic Unit of Ophthalmology, University of Birmingham, University of Birmingham, Birmingham, Birmingham, GB, academic, UNITED KINGDOM|J. Hodson, Medical Statistics, Queen Elizabeth Hospital Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Health seeking behaviour is influenced by driving factors and barriers to action. It has been suggested that such behaviour may have been linked to the negative impact of the COVID-19 pandemic on health care service provision and delivery. This study aimed to explore the health seeking beliefs held by the British public in relation to eye symptoms, and assess how these were influenced by the first COVID-19 lockdown.

Methods: Methods: An anonymous web-based survey was made publicly available and disseminated through mailing lists and social media between June and August 2020. In addition to baseline demographics (including postcode-derived indices of deprivation), the survey sought respondents views on the severity and urgency of the need for medical review for four ophthalmic (dry eye disease, conjunctivitis, microbial keratitis and painless vision loss) scenarios on a five-point scale. Regarding urgency of medical review, respondents were asked to answer questions twice: once ignoring the COVID-19 pandemic, and once taking this into account.

Results: A total of 402 respondents completed the survey, with a mean age of 61.6 years, and of whom 253 (63.1%) were female and 348 (87.7%) of white ethnicity. Scores for symptom severity and urgency of medical review increased significantly with the severity of the clinical scenario (both $p < 0.001$). However, respondents gave significantly lower scores for urgency of medical attention when accounting for the COVID-19 pandemic (compared to no pandemic) for all scenarios (all $p < 0.001$). Younger age, greater deprivation and non-white ethnicity were correlated with a lower perception of seriousness and urgency of medical attention.

Conclusions: During the first UK lockdown of the COVID-19 pandemic, reduced urgency of medical review for ocular and systemic pathologies was reported in response to the pandemic, and represents a barrier to health seeking behaviour. This has the potential to critically delay medical review and timely management, negatively impacting patient outcomes. Younger individuals with higher deprivation and non-white ethnic backgrounds may be at greater risk of this.

CONTROL ID: 3546124

SUBMITTER (NAME ONLY): Mirna Mina

TITLE: Investigating the Role of Porcn in Optic Vesicle Morphogenesis

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mina, S. Ramirez, S. Fuhrmann, Vanderbilt Eye Institute, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|S. Ramirez, S. Fuhrmann, Cell and Developmental Biology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mirna Mina: Commercial Relationship: Code N (No Commercial Relationship) | Sara Ramirez: Commercial Relationship: Code N (No Commercial Relationship) | Sabine Fuhrmann: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Congenital ocular malformations, such as microphthalmia, anophthalmia, and coloboma (MAC), are responsible for 25% of childhood blindness. Focal Dermal Hypoplasia is an x-linked dominant disorder that is often associated with MAC and caused by mutations in Porcn, a membrane bound O-acyl transferase that is required for the palmitoylation of Wnt ligands. Previous studies in frogs and zebrafish have demonstrated that the non-canonical Wnt pathway is essential for early eye formation. However, little about the role of non-canonical Wnt signaling in eye development is known in mammals. Here, we inactivate Porcn in mouse to interfere with non-canonical Wnt signaling and examine its effect on early eye formation and tissue patterning.

Methods: PORCN is inactivated in mouse embryos at embryonic day (E)6.5-E7.5 by tamoxifen-inducible, ubiquitous ROSA26^{CreER}. Affected male embryos with conditional deletion of Porcn are analyzed by immunohistochemistry (minimum n=3) using antibodies for eye field developmental markers PAX6, SIX3, LHX2, RX, OTX2 and the optic vesicle markers MITF and VSX2.

Results: Porcn mutants show a range of defects, depending on the time of inactivation. Tamoxifen treatment at E7.5 results in arrested eye morphogenesis in less severely affected Porcn mutants; the optic vesicle is reduced and does not invaginate to form an optic cup. At E10.5, MITF and VSX2 labeling reveals lack of expression in the RPE and neural retina, respectively. Similarly, OTX2 is not detectable in the optic vesicle. The pan-ocular marker PAX6 is expressed at slightly lower level in the mutant optic vesicle and lens ectoderm. Surprisingly, Six3 expression is detectable in the retina and lens ectoderm of Porcn mutants, indicative of eye field formation. Currently, we are investigating expression of additional ocular genes critical for ocular morphogenesis and patterning (e.g. LHX2, RX, COUPTF2, PAX2), including at earlier stages. In addition, our goal is to rescue ocular defects in Porcn mutants in vitro by non-canonical Wnt activation.

Conclusions: Porcn is required for proper formation of the optic vesicle and differentiation into retina and RPE, possibly to regulate transition from the eye field to optic vesicle stage. We predict that this occurs via non-canonical Wnt signaling.

CONTROL ID: 3546127

SUBMITTER (NAME ONLY): Christian Viehland

TITLE: 400 kHz handheld OCTA system designed for rapid imaging of supine and non-compliant subjects

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Viehland, C.A. Toth, J. Izatt, Biomedical Engineering, Duke University Pratt School of Engineering, Durham, North Carolina, UNITED STATES|X. Chen, D. Tran-Viet, S. Mangalesh, R. Imperio, C.A. Toth, J. Izatt, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity and many other pediatric retinal diseases have a vascular etiology. However, most commercial OCT angiography (OCTA) systems are large table systems that cannot be used to image pediatric or other non-cooperative subjects. Even if they could be brought to the bed side, OCTA image acquisition with these systems takes tens of seconds as they use relatively slow 100 kHz engines. To address this need we have previously reported a 200 kHz handheld OCTA (HH-OCTA) system, allowing for capture of OCTA images from infants at the bedside in 3 to 6 seconds. This work describes the continued development of the HH-OCTA system via the integration of 400 kHz OCT engine

Methods: We developed a 400 kHz OCT engine based on a 400 kHz VCSEL laser (Thorlabs inc.) and used our previously reported HH-OCTA scanner that has an ergonomic grip optimized for supine imaging, $\pm 10D$ refractive error correction, and a $30 \times 30^\circ$ degree field of view. OCT and OCTA images were taken from consented, healthy volunteers lying in a supine position. OCT images were taken over an $\sim 10 \times 10$ mm field of view using a 950 A-scan/B-scan, 128 B-scan/volume scan protocol (0.374s), and a 950 A-scan/B-scan and 4x averaged 128 B-scan protocol (1.495s). OCTA images were acquired over an $\sim 6 \times 3$ mm field of view with 500 A-scans/ B-scan, 250 lateral locations sampled with 4 repeated B-scans (1.8s). OCTA images were generated in post processing using speckle variance and graph cut based segmentation was used to create projections of the vasculature. Optical power was set in accordance with the ANSI Z80.36 standard Light Hazard Protection for Ophthalmic Instruments and all human subjects research was performed under protocols approved by the Duke University institutional review board in accordance with the Declaration of Helsinki.

Results: Representative HH-OCT and OCTA images from normal subjects are shown in fig. 1.

Conclusions: We demonstrated a 400 kHz HH-OCT probe capable of acquisition of OCTA images from supine subjects in 1.8s. We believe that the increase in speed for both structural OCT and OCTA images will facilitate bedside imaging in infants.

CONTROL ID: 3546135

SUBMITTER (NAME ONLY): Martin Michl

TITLE: Quantifying the clinical evaluation of retinal fluid change in real-world OCT images using deep learning

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Michl, F. Goldbach, G. Mylonas, G. Deak, T. Alten, S. Sacu, H. Bogunovic, B. Gerendas, U. Schmidt-Erfurth, Ophthalmology and Optometry, Medizinische Universität Wien, Wien, Wien, AUSTRIA

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ABSTRACT BODY:

Purpose: To quantify and compare the clinical evaluation of intra- and subretinal fluid (IRF, SRF) change between eye care professionals with different degrees of experience in retinal diseases in spectral-domain optical coherence tomography (SD-OCT) images of neovascular age-related macular degeneration (nAMD) patients.

Methods: We included SD-OCT data of patients who were diagnosed with nAMD and treated at our retina department and are part of the Vienna Imaging Biomarker Eye Study (VIBES) registry. There were 28 to 120 days between two visits and anti-VEGF injections were either given between the two visits or on the day of the second visit. A fully automated algorithm based on deep learning was used to quantify the change in IRF/SRF between visits. Firstly, the segmentation performance and clinical utility of each scan was determined by manual inspection. Secondly, retina specialists, ophthalmology residents, ophthalmologists working in private practice and orthoptists were asked to grade the IRF/SRF change between visits, following a standardized questionnaire.

Results: SD-OCT volumes of 230 visit pairs were included in our analysis. Manual inspection of all scans revealed a detectable fluid change of approximately 5nl. We therefore excluded scans with a fluid volume of <5nl at the first visit and fluid change of <5nl to the follow-up visit.

Conclusions: Artificial intelligence allows a precise assessment of fluid change over time, and thus an optimized management of macular edema. Our study determines the variability in the clinical assessment of retinal fluid change and the significance of retina- and OCT related experience for an accurate clinical evaluation of macular edema.

CONTROL ID: 3546136

SUBMITTER (NAME ONLY): Ratnakar Tripathi

TITLE: Effects of mustard gas exposure to the corneal basement membrane and epithelial-stromal attachment to human cornea ex vivo

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Tripathi, N.R. Sinha, P. Balne, S. Gupta, J.T. Rodier, P.R. Sinha, S.S. Chaurasia, R.R. Mohan, University of Missouri Department of Veterinary Medicine and Surgery, Columbia, Missouri, UNITED STATES|R. Tripathi, N.R. Sinha, P. Balne, S. Gupta, J.T. Rodier, P.R. Sinha, S.S. Chaurasia, R.R. Mohan, Harry S Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|N. Hesemann, Ophthalmology, MU Health Care Mason Eye Clinic-University Hospital, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sulfur mustard (SM) exposure to the eye causes many keratopathies and vision loss. The damage to various corneal components and underlying mechanisms are still largely unknown. This study investigated the effects of SM on the corneal epithelial basement membrane and epithelial-stromal attachment using a human corneal ex vivo organ culture model.

Methods: An ex vivo human cornea organ culture model available in the lab was used. Thirty donor healthy human corneas suitable for research were purchased from various Eye Banks. Corneas were placed into a well of a standard 6-well tissue culture dishes on a sterile customized corneal conformer to maintain in culture for long durations. Each well was fed with MEM medium having 10% FBS (4.5-5.5ml), allowing corneal endothelium to continually bathed in medium with an air-lift environment. The axial cornea air-exposed received one drop of medium every 8h to prevent corneal desiccation. Cultures were maintained in a humidified 5% CO₂ incubator at 37°C for 2-4 weeks in +/- SM analog (200µM of Nitrogen Mustard). An eight mm circular filter disc was used for SM exposure to the cornea. Standard H&E staining, real-time quantitative RT-PCR (qRT-PCR), western blotting, and Immunofluorescence (IFC) techniques were used to study cellular and molecular parameters.

Results: The vehicle-treated human cornea revealed normal corneal epithelium, epithelial basement membrane, epithelial-stromal association, stromal arrangement, and endothelium in H&E staining. Conversely, SM exposure to cornea demonstrated varying levels of damage to the corneal epithelium, epithelial basement membrane, epithelial-stromal association, stromal arrangement, and endothelium under similar culture conditions in H&E staining. The IFC and qRT-PCR data showed a significant change in the level of integrin β 4 ($p<0.001$), Collagen XVII ($p<0.01$), and Col IV ($p<0.001$) compared to vehicle-treated control. Tested proteins play a crucial role in the maintenance of normal corneal architecture and function. The Western blot analyses validated findings of the IHC and qRT-PCR.

Conclusions: Mustard gas exposure to the human eye compromises corneal basement membrane and epithelial-stromal attachment crucial for maintaining refraction.

CONTROL ID: 3546138

SUBMITTER (NAME ONLY): Ryan Chinn

TITLE: Diagnosis of vergence and accommodation deficits in children and adolescent with concussion using established clinical criteria versus normative data.

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.N. Chinn, C. Marshall, E.K. Wiecek, A.S. Shah, A. Raghuram, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|E.K. Wiecek, A.S. Shah, A. Raghuram, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|T.L. Roberts, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|K.K. Hawash, Neurology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|K.K. Hawash, Neurology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|M. O'Brien, Sports Medicine, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|M. O'Brien, Orthopedic Surgery, Harvard Medical School, Boston, Massachusetts, UNITED STATES|R. Stevens, Neurology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have established that convergence insufficiency and accommodative dysfunction are diagnosed more frequently following concussion as compared to the general population. However, conclusions are limited due to inconsistent diagnostic criteria and a lack of non-concussed control data. We compare the frequency of vergence deficits (VD, i.e., convergence insufficiency, convergence excess, and fusional vergence deficit) and accommodation deficits (AD) in concussed individuals to control participants using both established clinical criteria (ECC) and the distribution of normal clinical data.

Methods: Retrospective cohort study at Boston Children's Hospital. Non-concussed control group: n = 30 (median age: 9.2 years, IQR: 8.1 -10.6.), evaluated in 2016, Concussed group: n = 256 (median age: 15.2 years, IQR: 13.6 - 16.8) evaluated from 2012 to 2020. Both groups had visual acuity 20/30 or better in each eye; complete clinical assessment of vergence and accommodation; no strabismus, amblyopia, or other ocular pathology. Normal accommodation was determined by Hofstetter's formula ($15 - 0.25 \times \text{age}$). VD and AD were identified using both of the following methods: 1) ECC and 2) clinical findings falling outside the 95th percentile of control group criteria (CGC). Fischer's exact test and Chi-square Test assessed group differences.

Results: In the ECC in control data, 67% failed near point of convergence (NPC) (≥ 6 cms) and 33% failed monocular accommodative facility (MAF) (≥ 6 cycles per minute (cpm)). There was a difference in frequency of AD (33 vs 13%, $p=0.02$), but no change in VD (7 vs 7%, $p>0.05$) between ECC vs CGC respectively in controls. In the concussed group, the failure rate was higher for NPC (79 vs 52%, $p=0.001$), convergence amplitude (48 vs 59%, $p<0.01$) and MAF (64 vs 35%, $p<0.001$) using ECC vs CGC respectively. There was a difference in frequency of AD (81 vs 72%, $p=0.015$), but no change in VD (51 vs 50%) between ECC and CGC respectively in the concussed group.

Conclusions: We found using ECC for NPC ≥ 6 cm and accommodative facility ≥ 6 cpm resulted in higher failure rates in the control and concussed groups than would be expected. The differences between ECC and CGC emphasize the need for a larger sample of normative data and careful consideration of criteria used for diagnosis of visual deficits in concussion.

CONTROL ID: 3546146

SUBMITTER (NAME ONLY): Pratap Challa

TITLE: Elevated levels of GDF-15 in both the Aqueous Humor and Serum of Primary Open-Angle Glaucoma Patients

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Challa, R. Maddala, L. Ho, S. Karnam, S.S. Stinnett, R. Vann, V. Rao, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|A. Osterwald, C. ullmer, F. Hoffmann-La Roche Ltd, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Growth/differentiation factor 15 (GDF-15), which belongs to the TGF-beta superfamily of growth factors, is recognized as an all-cause mortality/stress marker and prognostic protein of various diseases. GDF-15 also serves as a key regulator of various cellular pathways. Having detected the presence of GDF-15 in human and mouse aqueous humor (AH) samples and secretion of GDF-15 by trabecular meshwork (TM) cells, in this study we evaluated the levels of GDF-15 in both AH and serum samples obtained from primary open-angle glaucoma patients.

Methods: AH and blood samples were collected following informed consent from glaucoma and cataract patients who underwent surgery at the Duke Eye Center. Serum samples and cell/tissue debris free AH samples were analyzed for GDF-15 content by ELISA. Data were compared between age and gender matched glaucoma and cataract patients.

Results: GDF-15 levels in AH (n=50) and serum (n=54) samples derived from the same patients were significantly elevated in POAG patients ($P<0.001$; Wilcoxon rank sum test of difference between medians equal to zero) by ~10-fold and 79%, respectively, compared to samples from cataract patients (n=33-39). Moreover, analysis of a larger set (n=117) of AH samples from POAG patients also showed a significant ($P<0.001$; by ~9 fold) elevation in the levels of GDF-15 relative to AH from cataract patients (n=113). GDF-15 levels were elevated in both male and female glaucoma patients, with no apparent gender differences. Similarly, both African American and Caucasian glaucoma patients exhibited elevated levels of GDF-15 with no significant racial differences.

Conclusions: In support of a previous report, this large sample size study not only reveals significantly elevated levels of GDF-15 in the AH but also in the serum of POAG patients compared to non-glaucoma patients. These findings indicate that serum GDF-15 levels might serve as a biomarker for the diagnosis of POAG. Additionally, the robustly elevated levels of GDF-15 detected in the AH of glaucoma patients warrants studies to investigate the role of GDF-15 in the pathobiology of ocular hypertension and glaucoma.

CONTROL ID: 3546150

SUBMITTER (NAME ONLY): Grant Slagle

TITLE: Miotic-assisted Rotational Extraction of Incarcerated Iris at the Slit Lamp

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.E. Sponsel, Vision Sciences, University of the Incarnate Word, San Antonio, Texas, UNITED STATES|W.E. Sponsel, Ophthalmology, WESMDPA, San Antonio, Texas, UNITED STATES|G. Slagle, Clinical Research, Sponsel Foundation, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Iris incarceration as a complication of glaucoma filtering surgery generally requires surgical intervention. We describe a novel technique for removal of incarcerated iris and restoration of bleb filtering capacity that can be safely performed at the slit lamp, dubbed rotational extraction of incarcerated iris (REII). A retrospective analysis of visual function and intraocular pressure (IOP) control was done in eyes treated with REII.

Methods: The patient is positioned at a securely locked slit lamp with two assistants. One drop of 0.5% proparacaine hydrochloride ophthalmic solution is administered to the affected eye. The eye is cleansed with betadine 5% sterile ophthalmic prep solution. Using sterile technique, 0.7mL of carbachol 0.01% intraocular solution is drawn into a 30G needle. With the bevel facing up, the needle is bent to 45° before inserting it using the dominant hand (at 11:00 or 2:00) tangentially into the anterior chamber (AC) via a peripheral corneal approach. 0.2mL carbachol is injected into the AC before the needle engages the iris over the zonule near the incarceration site. The needle is rotated downward using the cornea as a fulcrum, freeing the iris. Then the remaining 0.5mL carbachol is injected into the AC.

We retrospectively evaluated all patients who received REII between 1/1/2015 and 1/1/2021. IOP (Goldman applanation tonometry) and LogMAR visual acuity (VA) were measured at the time of REII, and at 1 month and 3 months post-procedure. Paired, two tailed t-tests with Bonferroni correction were used for all comparisons using Microsoft Excel (Redmond, Washington, USA).

Results: Forty-one eyes (46% left) of 41 patients (44% female, mean age \pm SD 64.7 \pm 10.7) were treated with REII. Median time to iris incarceration from surgery date was 50 days (range 1- 1906). Mean pre-REII IOP \pm SD was 33.1 \pm 14.4 mmHg, which reduced to 11.4 \pm 6.0 mmHg (66% reduction) day-of procedure ($P<0.01$) and remained reduced to 14.6 \pm 7.2 mmHg (56%, $P<0.01$) and 18.6 \pm 9.0 mmHg (44%, $P<0.01$) at 1 and 3 months, respectively. LogMAR VA was 0.78 \pm 0.8 log units at baseline, was unchanged at 1 month (0.70 \pm 0.8 log units, $P=0.14$), and improved at 3 months (0.50 \pm 0.6 log units, $P<0.01$).

Conclusions: Iris incarceration can be effectively managed at the slit lamp by REII, which can restore bleb filtering capacity and provide sustained reduction in IOP.

CONTROL ID: 3546151

SUBMITTER (NAME ONLY): Jean Bennett

TITLE: Five-Year Post-Injection Results of the Phase 3 Trial of Voretigene Neparvovec-rzyl in Biallelic RPE65 Mutation-Associated Inherited Retinal Disease

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To present 5-year post-injection results for the multi-luminance mobility test (MLMT) and full field light sensitivity threshold test (FST) endpoints in the original intervention and delayed intervention groups of the phase 3 voretigene neparvovec-rzyl (VN) study in biallelic RPE65 mutation-associated inherited retinal disease.

Methods: Patients were randomized to either original intervention (OI:bilateral subretinal VN at baseline; n=20) or delayed intervention (DI:VN after 1 year; n=9). The primary endpoint was Multi-Luminance Mobility Test (MLMT) at 7 standard light levels as measured by a change score. The first secondary endpoint was full-field light sensitivity threshold (FST). The five-year timepoint was analyzed for OI and DI groups individually and combined OI group plus DI group.

Results: For OI patients at Year 5 (n=18) and DI patients at Year 5 (n=7), the MLMT mean (SD) bilateral light level change score was 1.6 levels (1.2) and 2.4 levels (1.6), respectively compared to baseline. The combined (OI plus the DI groups) mean bilateral light level change score was 1.8 (1.3) (N=25). Mean change in white light FST in \log_{10} (cd.s/m²) was -2.02 (1.45) \log_{10} at Year 5 for OI patients (n=17) and -2.57 (1.21) \log_{10} at Year 5 for DI patients (n=7). The mean change in white light FST in \log_{10} (cd.s/m²) was -2.18 (1.38) for the combined OI and DI group (N=24).

Conclusions: Visual improvements are maintained for at least 5 years after VN administration for both the OI and DI patients.

CONTROL ID: 3546155

SUBMITTER (NAME ONLY): Heather Schmitt

TITLE: Genetic susceptibility to Loxl1 knockout-induced elastosis in a mouse model

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Schmitt, T. Watkins, K. Hake, M. Kuhn, G. Li, D.W. Stamer, M.A. Hauser, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pseudoexfoliation glaucoma (PEXG) is an ocular manifestation of the systemic elastotic disease pseudoexfoliation syndrome (PEX), and can be diagnosed by fibrillary deposits in the anterior chamber and significantly increased intraocular pressure (IOP). PEX-related extracellular matrix dysregulation can manifest as pelvic organ prolapse, inguinal hernia, aortic aneurism, or COPD. Consistent with these pathologies, polymorphisms in the lysyl oxidase-like 1 (LOXL1) gene, which codes for an elastin crosslinking and assembly enzyme, impart significant risk for PEX. Thus, changes in LOXL1 expression may lead to elevated IOP in PEXG, as the outflow tissues that regulate IOP are highly elastic. Here, we use a Loxl1 knockout mouse model to investigate genetic susceptibility to the elastotic phenotypes associated with Loxl1 depletion.

Methods: 129S.C57Bl/6.Loxl1^{+/-} mice were backcrossed onto the C57Bl/6 background for 6 generations (N6). Two month old N6 and mixed background 129S/N6 (N1) Loxl1^{+/+}, ^{+/-} and ^{-/-} mice were analyzed for systemic phenotypes including anal prolapse, skin elasticity, total weight, and morphological changes in major organs. Ocular phenotypes monitored include IOPs and histology of anterior and posterior segments.

Results: Prolapse prevalence was significantly higher in N6 C57Bl/6 mice in comparison to mixed background mice ($p < 0.0001$). In mixed 129S/N6 (N1) Loxl1^{-/-} mice, significant increases in skin tiring ($p = 0.0235$) and reduction in elastic recovery ($p = 0.0294$) were observed. The tiring effects of skin after repeated stretch were significantly higher in Loxl1^{-/-} animals versus Loxl1^{+/+} and ^{+/-} littermates ($p = 0.0010$). Knockout of Loxl1 in the N6 C57Bl/6 mice led to significant weight loss ($p < 0.05$), and systemic and ocular tissues exhibited enlarged luminal spaces histologically. Knockout of Loxl1 in mixed background mice lead to significantly increased IOP ($p < 0.0001$), but no significant IOP increase was observed in the N6 C57Bl/6 mice.

Conclusions: Genetic background significantly affects the systemic and ocular phenotypes of elastosis associated with Loxl1 knockout. This data shows for the first time that susceptibility to Loxl1 knockout-induced elastosis depends upon genetic modifiers that may contribute to phenotypic severity of PEX, providing a foundation for studying gene targets associated with this susceptibility that are relevant in human patients.

CONTROL ID: 3546158

SUBMITTER (NAME ONLY): Seth Hubbard

TITLE: Uncovering the molecular mechanism of cytoskeletal regulation in rod photoreceptors

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.T. Hubbard, A.K. Gross, Honors College, Science and Technology Honors Program, The University of Alabama at Birmingham College of Arts and Sciences, Birmingham, Alabama, UNITED STATES|M.G. Hubbard, H.J. Levi, A.K. Gross, Neurobiology, University of Alabama at Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been shown that nuclear distribution protein C (NUDC) modulates F-actin dynamics through F-actin severing protein cofilin1 (CFL1). We have shown NUDC is critical in the morphogenesis of rod photoreceptor disks in *X. laevis* tadpoles as well as in mice. We hypothesize that NUDC regulates F-actin through CFL1 in rods as it does in other cell types. Since CFL1 is regulated in other cell types upon phosphorylation at the serine at position 3 in the protein, we hypothesize that expression of phospho-mimics or phosphonull mutants of CFL1 will affect F-actin levels and outer segment (OS) disk formation. Here we seek to uncover the regulatory action of CFL1 and the molecular mechanisms governing F-actin architecture in rod OS by generating transgenic *X.laevis* expressing mutants of CFL1 and shRNAs against CFL1.

Methods: We are preparing transgenic *X. laevis* tadpoles expressing wild type CFL1 (CFL1), constitutively active phospho-null CFL1 (CFL1^{S3A}), dominant negative phospho-mimic CFL1 (CFL1^{S3D}) as well as shRNA directed against CFL1, under the rod opsin promoter. Immunohistochemistry (IHC), proximity ligation assays and dot blot analysis using solubilized retinas of key proteins are being performed WT *X. laevis* tadpoles, as well as those expressing CFL1, CFL1^{S3A}, CFL1^{S3D} and shRNA against CFL1. We will use fluorescent microscopy to visualize key proteins such as NUDC, CFL1, rhodopsin, actin, transducin, arrestin and others to uncover their localization within the rod cell. We will utilize transmission electron microscopy (TEM) images of photoreceptor ultrastructure using ultrathin sections of 2wk old *X. laevis* tadpoles.

Results: We have found CFL1 is expressed in the inner segment (IS) of *X. laevis* and mouse photoreceptors. Through the proximity ligation assay we found CFL1 is < 40nm to NUDC in the IS and at the base of the OS in rods of mouse and *X. laevis*. We have prepared transgenic *X. laevis* tadpoles and are currently analyzing the localization of key proteins and ultrastructure of photoreceptors in these animals.

Conclusions: We have demonstrated that CFL1 is expressed in rod photoreceptors and is near NUDC in at the base of the OS, supporting our hypothesis that NUDC is working through CFL1 to regulate F-actin levels. Further analysis is ongoing. This work critical to further our understanding of the molecular mechanism of disk regulation and morphogenesis.

CONTROL ID: 3546160

SUBMITTER (NAME ONLY): Norianne Ingram

TITLE: The strength of center-surround antagonism in retinal ganglion cell receptive fields is light-dependent and affects stimulus-response filtering in the spatial and temporal domains

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Ingram, F. Rieke, Physiology and Biophysics, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Contemporary studies in visual neuroscience look to understand how adaptive modulations and circuit routing affect stimulus encoding across layers of the retina. At the output of the retina, retinal ganglion cells (RGCs) are able to encode rapid stimulus fluctuations despite the relatively slow input they receive from upstream photoreceptors. They also have receptive fields that display center-surround antagonism, in which lateral inhibition driven by the surround inhibits responses generated from stimulating the center (Barlow, 1957). Previous studies in mouse show that the spatial dimensions of center versus surround change with background light conditions (Hoggarth et al., 2015; Farrow et al., 2013). It is not known if all RGC subtypes undergo similar shifts, to what degree circuit mechanisms like changes in rod-cone signal routing are responsible, and if other receptive field features such as surround-dependent temporal filtering are similarly dependent on light level.

Methods: To answer these questions in the primate retina, we make electrophysiological recordings from primate RGCs with stimuli that span 8 orders in magnitude in light intensity. We measure light-dependent shifts in spatial and temporal receptive fields through this entire range of stimuli and in multiple RGC subtypes.

Results: Both parasol and midget RGC receptive field spatial dimensions show similar trends in light dependence. In addition, we show for the first time, that the strength of surround-mediated temporal filtering also depends on the background light intensity. Interestingly in ON-parasol RGS, the effects of surround-mediated temporal filtering are greater in dim light, a condition in which the surround contributes little to the spatial receptive field.

Conclusions: The light-dependent changes in these receptive field features demonstrated in this study are likely to have large effects stimulus tuning and encoding in both the spatial and temporal domains. Adaptation of receptive field characteristics should play an important role in an organism's ability to perform complex visual tasks which depend on correlations between space and time (e.g. motion detection) as well as modulate circuit-defined limitations in perception.

CONTROL ID: 3546161

SUBMITTER (NAME ONLY): Suzanne Daly

TITLE: Evaluation of zonular anatomy using ultrasound biomicroscopy in patients with pseudoexfoliation

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Daly, D. Coleman, G. Moazami, D. Trief, R.H. Silverman, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pseudoexfoliation syndrome is a connective tissue disorder first described in the eye in 1917. It has a genetic component associated with mutations in the lysyl oxidase-like 1 gene (LOXL1) at the locus 15q22. More commonly seen in Scandinavian and Northern European populations, its prevalence in all populations increases with age. Characterized by deposition of fluffy “dandruff-like” material composed of amyloid, laminin, elastic fibers, collagen and basement membrane on ocular structures, diagnosis is made on slit-lamp examination where gray-white flakes are evident at the pupillary margin and on the anterior lens capsule. The purpose of this study is to evaluate the utility of ultrasound biomicroscopy (UBM) in delineating capsular and zonular enhancement.

Methods: Retrospective review of 98 UBM consecutive patients over the past year was conducted. Examinations were performed using Quantel Aviso UBM system with 50 MHz probe with ClearScan standoff to place anterior segment in focal zone. Cineloop data were obtained in all four quadrants as well as centrally in horizontal and vertical orientations. Pseudoexfoliation (PEX) was evident as enhancement of the zonular fibers, presence of echogenic debris on the anterior lens capsule and/or secondary atrophic changes in the iris (“moth-eaten” appearance of iris stroma). Data was analyzed for relationship to sex and age.

Results: UBM consistent with PEX was observed in 10 of 98 patients. Results showed no significant relationship with sex (Chi-square =.527, p=.468). PEX patients were, on average, approximately 10 years older than non-PEX subjects (65.4±14.0 versus 54.8±21.6 years), but this did not reach statistical significance (t=-1.52, p=.132).

Conclusions: Pseudoexfoliation syndrome is a major risk factor for complications during cataract surgery related to weakened capsule and zonular apparatus. It is also the most common form of secondary glaucoma as pigment and exfoliative material in the trabecular meshwork and Schlemm’s canal results in increased outflow resistance and elevation of intraocular pressure. Ultrasound biomicroscopy can be a useful adjunct in delineation of the disease, especially because retroiridal structures are unable to be visualized with anterior segment OCT.

CONTROL ID: 3546164

SUBMITTER (NAME ONLY): Monica Jablonski

TITLE: Mining the BXD Family of Mice to Better Model the Natural Progression of Glaucoma

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Jablonski, R. Simpson, X. Wang, W. White, T. Hollingsworth, The University of Tennessee Health Science Center Department of Ophthalmology Hamilton Eye Institute, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is the leading cause of irreversible blindness worldwide. Despite this, a complete understanding of the disease and its pathogenesis remains a struggle due to the lack of high fidelity spontaneous polygenetic models that recapitulate the human phenotype. In recent years, the BXD mouse family has emerged as a source of spontaneous models of ocular disease. It is the purpose of this study to identify natural polygenetic mouse models of primary open angle (POAG), primary angle closure (PACG), and normotensive (NTG) glaucoma by mining the BXD family and provide them as a valuable resource for the vision research community.

Methods: BXD strains were selected by evaluating data from previous studies that include the density of dead axons, ON damage scorings, and IOP. Eight strains were selected for further study. Functional/anatomical analyses including optical coherence tomography (OCT), optokinetic nystagmus (OKN), full field and pattern electroretinograms (ERG/PERG), and IOP measurements were performed every 3 months from the age of 1 month to 12 months. Gonioscopy was performed at 12 months to determine if the angle was open or closed. Histological and ultrastructural analyses of the eye/optic nerve will be performed after euthanasia at 12 months.

Results: Although this study is still in progress, preliminary data highlight BXD50 and BXD51 as possible models of POAG. Both strains exhibit open angles, decreased ERG and PERG amplitudes, and loss of contrast sensitivity by 12 months. Interestingly, the two strains vary greatly in IOP over their lifetimes with BXD50 reaching a maximum IOP of 28 mmHg, while the maximum IOP of BXD51 was 41 mmHg.

Histological analysis of the eye/optic nerve is in progress to evaluate optic nerve damage and RGC health.

Conclusions: The BXD family of mice offers valuable insights into ocular disease pathogenesis. Of the strains we selected, BXD50 and BXD51 present POAG-like phenotypes. Ongoing studies are being performed to better characterize plausible spontaneous models of PACG and NTG, thereby providing additional valuable tools for the future study of glaucoma.

CONTROL ID: 3546171

SUBMITTER (NAME ONLY): Salma Ferdous

TITLE: Pan-retina deletion of Lsd1 during retinal development causes visual function and morphological defects

SESSION TITLE: Ocular disease models: molecular mechanisms and therapeutic approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Ferdous, I. Gefke, V. Summers, J.H. Boatright, J.M. Nickerson, Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study was to investigate the role of Lsd1 in retinal development by deleting Lsd1 in all retinal progenitor cells. Lysine specific demethylase 1 (Lsd1) is the only histone demethylase that is able to demethylate mono- and di-methyl groups on H3K4 and H3K9. Previously, we have shown that Lsd1 is ubiquitously expressed throughout the developing retinoblast and in the majority of mature retinal neurons (Ferdous et. al IOVS 2019 PMID: PMC6827424) . Using a Chx10-Cre driver line, we generated a transgenic mouse line to delete Lsd1 through the entire retinoblast lineage. Chx10 is a transcription factor that is expressed in all retinal progenitor cells (RPCs) starting about embryonic day 14.5 (E14.5) and is critical to progenitor cell proliferation and specifically bipolar cell determination. We hypothesize that deletion of Lsd1 early in retinal development will result in either 1) a failure of RPCs to proliferate or 2) the death of RPCs due to transcriptional abnormalities which could result in a reduction in retinal thickness and subsequently visual function defects.

Methods: After generating Chx10-Cre Lsd1 lox/lox mice, we tested mice at P30 and P45 for visual function, using electroretinograms (ERGs), and in vivo imaging to obtain SD-OCT and cSLO images. Afterwards, eyes were enucleated and fixed for H&E staining and immunocytochemistry staining.

Results: We have observed a marked reduction in ERGs a- and b- waves in both scotopic and photopic conditions as well as cone flicker responses at P30 and P45 compared to littermate Cre negative controls. This decrease in visual function is corroborated with reductions in total retinal thickness and ONL thickness as measured from SD-OCT images at both ages. H&E stained sagittal sections indicate the same retinal thinning. Additionally, there is an increase in TUNEL positive cells in the Chx10-Cre Lsd1 loxlox compared to controls.

Conclusions: Our data supports the notion that Lsd1 is necessary for neuronal development specifically in the retina. Adult Chx10-Cre Lsd1 lox/lox mice show impaired visual function and retinal morphology and future experiments will continue to characterize the timeline of morphological defects during embryonic development as well as investigate epigenome and transcriptome abnormalities leading to these defects.

CONTROL ID: 3546173

SUBMITTER (NAME ONLY): TJ Hollingsworth

TITLE: Elucidating Mouse Models of Retinal Disease Using Systems Genetics and the BXD Family of Mice

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Hollingsworth, W. White, M.M. Jablonski, Ophthalmology, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|A. Swaroop, Neurobiology Neurodegeneration & Repair Laboratory, National Eye Institute, Bethesda, Maryland, UNITED STATES|E.Y. Chew, DECA - Clinical Trials Branch, National Eye Institute, Bethesda, Maryland, UNITED STATES|D. Ashbrook, R. Williams, Genetics, Genomics, and Informatics, The University of Tennessee Health Science Center College of Medicine, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Animal models of human retinal degenerations (RDs) have been of interest to the vision community for decades. Generating high fidelity models has been hit-or-miss and is often dependent upon the disease itself. Of the RDs, age-related macular degeneration (AMD) is one the most elusive phenotypes to mirror due to numerous genetic polymorphisms and environmental factors associated with it. Recently, the BXD family of mice has become a valuable tool for modeling various ocular diseases. This study's purpose is to apply a systems genetics approach to the BXD mouse family to better model human AMD, providing the vision community with polygenetic pre-clinical models of AMD.

Methods: We identified 27 genes associated with human AMD and, of these, 11 have polymorphisms in the BXD family of mice that are predicted to change gene function in a similar manner to that seen in humans. We chose 6 strains of mice with various combinations of the 11 genes with the goal of selecting mice with various presentations of AMD. The 6 BXD strains and C57B/6J controls are aging from 6 to 18 months. Optical coherence tomography (OCT), full field electroretinogram (ERG), funduscopy/fluorescein angiography (FA) and optokinetic nystagmus (OKN) measurements are performed every 3 months. Histological and ultrastructural analyses will be performed upon euthanasia at 18 months.

Results: Preliminary data indicates BXD34 as a possible AMD model due to drusen-like deposits observed by funduscopy along with degeneration near the central retina by OCT. It also exhibits vascular leakage and a loss of both contrast sensitivity and a- and b-wave amplitudes of the ERG. We have excluded the BXD32 and BXD79 strains as plausible AMD models. BXD32 exhibits markedly rapid degeneration similar to recessive retinitis pigmentosa (RP). BXD79 has phenotypes of high blood glucose, obesity, vascular leakage, and early onset retinal degeneration occurring between 6 months and 9 months of age making it a possible model of diabetic retinopathy (DR).

Conclusions: Currently, BXD34 exhibits the most AMD-like phenotype among the 6 strains chosen for characterization by exhibiting drusen-like deposits and both anatomical and physiological declines in retinal health. BXD32 and BXD79 may better serve as spontaneous models of RP and DR, respectively. Further investigation into these strains is necessary to confirm them as true models of the respective diseases.

CONTROL ID: 3546175

SUBMITTER (NAME ONLY): Rachel LoPilato

TITLE: Studying the regulatory contributions by Fringe glycosyltransferases to the NOTCH1 pathway during angiogenic development of the mouse retina

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.K. LoPilato, R.S. Haltiwanger, Biochemistry and Molecular Biology, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|H. Kroeger, J.D. Lauderdale, Cellular Biology, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|N.J. Grimsey, Pharmaceutical and Biomedical Sciences, University of Georgia College of Pharmacy, Athens, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Angiogenesis of the retina is mediated in part by cell-cell signaling through the NOTCH1 receptor and its ligands Jagged1 (JAG1) and Delta-Like ligand 4 (DLL4). O-Fucosylation of Ser/Thr residues in the Epidermal Growth Factor-like (EGF) repeats by Protein O-fucosyltransferase 1 (POFUT1) is necessary for receptor activation by both ligands, and addition of b1,3-GlcNAc to O-fucose by Fringe glycosyltransferases reduces NOTCH1 activation during interaction with JAG1 while enhancing NOTCH1 activation during interaction with DLL4. We generated a mouse model to study the regulatory contributions by Fringe glycosyltransferases during angiogenic development of the mouse retina.

Methods: Using CRISPR/Cas9 to knock in a three base pair change from ACC to GTG, we made a T/V substitution at Thr₂₃₂ of the NOTCH1 protein in a C57BL/6J mouse. This mutation excludes the O-fucose site at EGF6 as a substrate for POFUT1 and Fringe, and previous in vitro studies show that this mutation rescues the inhibitory effect of JAG1 signaling through Fringe-modified NOTCH1 with no changes to the enhancing effect of DLL4 signaling through Fringe-modified NOTCH1. Retinas from P5-P6 and adult mice were stained with Isolectin B4 to visualize the endothelial vasculature, and a Mask Sholl Analysis was performed to quantify the vascular density of the retina.

Results: Preliminary data from P5-P6 mutant retinas show decreased vascular density compared to wildtype as well as a growth delay from the inner retina to the outer retina. This phenotype extends into the adult stage with reduced endothelial staining and a less severe growth delay.

Conclusions: A loss of vascular density is consistent with published mouse models showing hyperactivation of NOTCH1 through knockdown of Jag1 or with the opposite gain of vascular density from treatment with the λ -secretase inhibitor DAPT, which is an established inhibitor of Notch signaling. These data suggest that we uncoupled Fringe-mediated regulation of NOTCH1-JAG1 signaling from Fringe-mediated enhancement of NOTCH1-DLL4 during angiogenic development of the mouse retina. We are currently immunostaining and measuring transcript levels of components in the NOTCH1 pathway to confirm the genetic mechanism by which we observe this phenotype.

This work was supported by NIH grants GM061126 and T32GM107004.

CONTROL ID: 3546177

SUBMITTER (NAME ONLY): Allison Ludwig

TITLE: Synapse formation and in vitro synaptic tracing in hPSC-derived retinal neurons

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Synapses—the basic unit of neuron function—are a central challenge of retinal cell replacement therapies for blinding eye disorders. Synapse formation within human pluripotent stem cell (hPSC)-derived retinal organoids (ROs) has been observed by electron microscopy, but the capacity for de novo synaptogenesis among hPSC-derived retinal neurons (RNs) following isolation from ROs has not been definitively established. In this study, we validated a synaptic tracing assay to screen for functional synapses in vitro among dissociated hPSC-RN cultures.

Methods: A monosynaptic retrograde tracing assay using a GFP-encoding lentivirus (lenti-GFP) and mCherry-encoding pseudotyped rabies virus (RaV) was modified to assess hPSC-RN synapse formation. Stage 2 (D80) ROs were dissociated and plated onto 96 well plates. 10 days post-plating, cultures were treated with lentiviral constructs to label a subset of RNs. After 5 days, cultures were infected with RaV, which enters only lenti-GFP-transduced cells. Synaptic tracing cultures were fixed 5 days post RaV transduction (D100) to screen for the presence of potentially postsynaptic (GFP+ and mCherry+) and presynaptic RNs (GFP-, mCherry+). To control for material transfer, a glycoprotein-null, RaV transmission-incompetent lentivirus was used. Confocal and high-content images were taken for qualitative and quantitative analysis.

Results: RaV-mCherry and lenti-GFP vectors labeled pre- and potentially postsynaptic RNs in dissociated hPSC-RN cultures. RaV transmission to presynaptic RNs was significantly greater ($p < 0.0001$) in experimental cultures (~6.3% of all cells) relative to control cultures (<1.5%), validating the assay for presynaptic RN identification. Functional synapses, as demonstrated by RaV transmission, were identified in post-dissociation cultures. Major classes of hPSC-RNs, including photoreceptors (PRs), ganglion cells (GCs), and interneurons were detected among traced presynaptic cells. PRs and GCs—neurons of particular importance for cell replacement—represented ~40% and ~28% of traced presynaptic cells, respectively.

Conclusions: This study successfully demonstrates the use of a synaptic tracing assay to identify de novo synapse formation among hPSC-RNs isolated from ROs in vitro. While overall synaptic formation rates were expectedly low, this system represents a platform for high-throughput testing of methods to improve hPSC-RN synapse formation in vitro.

CONTROL ID: 3546180

SUBMITTER (NAME ONLY): Cristy Ku

TITLE: Treatment outcomes in 11 patients with RPE65-retinopathy receiving voretigene neparvovec-rzyl

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.A. Ku, M.M. da Palma, A. Igelman, A. Lauer, S. Bailey, P. Yang, M.E. Pennesi, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|J.L. Duncan, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report on the outcomes of patients with RPE65-associated retinopathy treated with FDA-approved voretigene gene replacement therapy at a single treatment site.

Methods: This is a retrospective study on patients with RPE65-associated retinopathy treated with voretigene neparvovec-rzyl. Records, imaging, and diagnostics were reviewed including fundus autofluorescence (FAF), optical coherence tomography (OCT), full-field stimulus threshold (FST), kinetic visual fields, dark-adapted two color visual fields (2cDAP), full-field ERG (ffERG). FST was performed and analyzed on Espion ColorDome LED full-field stimulator system and Diagnosys software, and dark-adapted two color perimetry on the Octopus 900 Haag-Streit perimeter.

Results: A subretinal injection of voretigene was administered into 19 eyes from 11 patients (pt) with an average age of 20.82 YO (range 4-38 YO). FST was performed for 11 eyes (from 6 pts) with improvements seen in 10 eyes. There was an average gain in FST of 13.3 dB (range 4.9-17.6, SD 8.92 dB) with the short-wavelength stimulus (blue), and 8.1 dB (range 2.5-15.0, SD 5.43 dB) with the long-wavelength stimulus (red). When 1 year or longer follow-up data was available (10 eyes from 5 pts), gains in sensitivity were maintained in all treated eyes. 2cDAP field was performed for 10 eyes (from 6 pts) with all eyes showing an improvement in mean sensitivity to the blue stimulus, with an average improvement of 10.91 dB (range 2.0-22.2, SD 4.98 dB). 9 out of 10 eyes (from 6 pts) showed an improvement to the red stimulus, with average improvement of 4.73 dB (range 0.8-10.0, SD 2.37 dB). Gains in 2cDAP was sustained in all patients with follow-up at 1 year. ffERG was performed in 14 eyes (from 8 pts) with a greater than 50% improvement in 5 eyes (from 3 pts). Improved OCT findings were observed in 7 eyes (from 4 pts). Patients also reported moderate to significant subjective improvement in nyctalopia (9 pts), overall vision (6 pts), color vision (3 pts), and nystagmus (2 pts).

Conclusions: A majority of patients with RPE65-associated retinopathy treated with voretigene showed improvements in FST and dark-adapted perimetry. Dark-adapted perimetry may be a sensitive outcome that provides topographical information in relation to the treatment area. Several patients reported significant subjective improvement in color vision, a potential outcome measure to systematically evaluate in the future.

CONTROL ID: 3546183

SUBMITTER (NAME ONLY): Jingyi Tang

TITLE: Mismatched higher-order wavefront aberrations between eyes affect disparity signal quality and reduce stereoacuity following laser refractive surgery for myopia

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tang, S. Metlapally, New England College of Optometry, Boston, Massachusetts, UNITED STATES|C.M. Schor, University of California Berkeley School of Optometry, Berkeley, California, UNITED STATES|P.K. Vaddavalli, J.C. Reddy, The Cornea Institute, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S.R. Bharadwaj, Prof Brien Holden Eye Research Centre, Hyderabad, Telangana, INDIA|S.R. Bharadwaj, Brien Holden Institute of Optometry and Vision Sciences, Hyderabad, Telangana, INDIA|S. Sarkar, India Vision Institute, Chennai, Tamil Nadu, INDIA|

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ABSTRACT BODY:

Purpose: Stereoacuity deterioration following keratorefractive surgeries is attributed to an increase in the magnitude and interocular differences in post-operative higher-order aberrations (HOAs) (Sarkar et al, 2020). This study modeled the contributions of interocular HOA differences induced by refractive surgery to disparity visibility and binocular matching using cross-correlation analyses.

Methods: We recruited subjects (n=99) with myopia and astigmatism ≤ 1.5 D who underwent Femtosecond Laser-Assisted In situ Keratomileusis (FS-LASIK, n=38), PhotoRefractive Keratectomy (PRK, n=26) or SMAll-Incision Lenticule Extraction (SMILE, n=35). Post-cycloplegic HOAs and stereoacuities were measured for 6mm diameter pupils pre-operatively, and 1, 4, 12 and 24 weeks post-operatively. Left and right eye retinal image pairs were convolved with respective HOA-derived point spread functions. Optical effects on disparity signal quality were modeled computationally using four metrics derived from binocular cross-correlation functions, namely, signal width, signal height, signal-to-noise ratio, and height-to-width ratio (Metlapally et al, 2019). We assessed covariation of cross-correlation metrics with corresponding psychophysical measures of stereoacuity. We also compared the three refractive surgeries for their binocular outcomes using analyses of variance.

Results: Increased interocular average and difference in the magnitude of HOAs caused sustained worsening of stereoacuity (Sarkar et al, 2020). Stereoacuity strongly covaried with the four cross-correlation metrics ($p < 0.001$, $r = 0.725$, -0.630 , -0.732 and -0.786 , respectively, for the four metrics above). The changes from the pre-operative to the 24-week time point for each of the cross-correlation metrics differ significantly among the three refractive surgeries. Altogether, SMILE showed better binocular outcomes than LASIK or PRK ($p < 0.001$).

Conclusions: Mismatched HOAs add disparity noise by differentially altering the properties of the retinal images of the two eyes, and negatively affect binocular matching and disparity visibility. Computational analyses point to disparity noise as a possible mechanism through which HOAs induced following refractive surgery make extracting stereoacuity difficult. They also suggest better binocular outcomes for SMILE than LASIK or PRK.

CONTROL ID: 3546185

SUBMITTER (NAME ONLY): Melina Cavichini Cordeiro

TITLE: Evaluation of real world efficacy of Artificial Intelligence assisted image co-localization

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We wished to compare the ability to human observers (retinal doctors) to co-localize pathological structures from different platforms. We compared traditional co-localization techniques (side-by-side with human observers) to an AI technique which overlaid the images with AI algorithms and then alternated the images using the previously described automated alternation flicker method. We determined time to localize the lesions and accuracy of both methods.

Methods: Images taken with a Topcon color fundus camera showing diabetic retinopathy (4 eyes), AMD (5 eyes) and central vein occlusion (2 eyes) were analyzed for a masked clinician, lesions of interest were identified and marked with a circle. Infrared SLO images of the same fundus showing the corresponding area were then also selected. For the side-by-side (SBS) method, two retina specialists identified the corresponding lesion on the unmarked IR image and drew it digitally with the color image in the side. For the AI overlaid images, the same specialists identified the lesion on the unmarked IR and drew it digitally as it was being presented by automated alternating flicker along with the color image. A total of 53 lesions from 11 fundus image pairs were analyzed 2 times, one time for each method, in different days, for each specialist. Image analysis was done in random order. Time to find each lesion in each method was measured and recorded for the same person in all attempts.

Results: The time to find the lesions was faster in the overlay method ($p < 0.01$). Out of 106 (combined total between both observers) gradings 19 lesions were missed in the SBS method and zero missed lesion in the overlay method. The average decentration (difference in lesion center normalized to lesion radius) was 22% and 27% for observers 1 and 2 in the overlay study. No significant difference between the graders ($p = 0.127$). The average decentration was 59% and 56% for observers in the SBS method. No significant difference between the graders ($p = 0.265$). However, there is a statistic difference when we compare SBS and overlay methods pooled for both graders ($p = 0.0000607$).

Conclusions: The overlay method permits more rapid and accurate co-localization of lesions from different imaging platforms. It is easier and more accurate than the side-by-side method, which is closer to the "normal" approach to analyze different images in clinical and image reading settings.

CONTROL ID: 3546188

SUBMITTER (NAME ONLY): Michael Allingham

TITLE: Mitochondrial dysfunction causes retraction of Müller cell lateral processes.

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.J. Allingham, S. Cousins, P.S. Mettu, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Michael Allingham: Commercial Relationship: Code N (No Commercial Relationship) | Scott Cousins: Commercial Relationship: Code N (No Commercial Relationship) | Priyatham Mettu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Müller cell perisynaptic lateral processes provide support to retinal synapses and are critical for vision. Currently, the mechanisms regulating Müller cell lateral process maintenance and retraction are poorly understood, particularly in vivo. We tested the hypothesis that Müller cell mitochondrial dysfunction causes retraction of lateral processes using a model of retinal vein occlusion (RVO).

Methods: RVO was induced after intravenous injection of rose bengal (66mg/kg) using a 532nm laser to place 3-7 applications at 80 mW and 50 micron spot size directed at two retinal veins 1 disc diameter from the nerve. Negative control consisted of placing an equal number of laser spots without targeting the retinal vein. Male and female C57BL/6J mice aged 7-9 months with confirmed absence of *Crb1*^{rd8}, GLAST-CreER and Rosa26 mTmG mice were obtained from Jackson Labs. Elamipretide, a mitochondrial protective drug, was administered intraperitoneally (2mg/kg/day) using prevention and intervention strategies. Retinal histology and Müller cell lateral process morphology was evaluated on day 7 following induction of RVO. Mitochondria dysfunction was evaluated by quantifying superoxide and flavoprotein autofluorescence. Significance was determined using nonparametric statistical testing with $p < 0.05$ considered significant.

Results: After RVO, mitochondria dysfunction was induced within the retinal plexiform layers where lateral processes are located, seen as increased superoxide and flavoprotein autofluorescence. This was prevented by treatment with mitochondria protective compound, elamipretide. RVO resulted in retraction of Müller cell perisynaptic lateral processes in the inner and outer plexiform layers. Lateral process length and the diameter of the lateral process arbor were quantified and reductions found to be statistically significant ($p < 0.05$). Markers of lateral processes including GLAST, GluR3, AQP6 and T567 phospho-ezrin were quantified by confocal microscopy and found to be greatly reduced following RVO ($p < 0.05$). Elamipretide treatment using either intervention or prevention approaches significantly preserved Müller cell lateral processes and markers ($p < 0.05$).

Conclusions: RVO causes retraction of Müller lateral processes. Treatment with elamipretide, a mitochondria protective drug, prevents and reverses these changes. This suggests that mitochondrial function is required for maintenance of lateral processes.

CONTROL ID: 3546197

SUBMITTER (NAME ONLY): Neil Vallabh

TITLE: Baseball- and softball-related ocular trauma emergencies in the US

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Vallabh, W.W. Motley, Pediatric Ophthalmology, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Neil Vallabh: Commercial Relationship: Code N (No Commercial Relationship) | W. Motley: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Baseball has long been called America's pastime. As the first professional sport in the US, baseball has been a source of great pleasure and leisure; however, the sport is also associated with occurrence of ocular trauma. We performed a retrospective analysis assessing baseball-related ocular injury incidence and trends across the US.

Methods: We analyzed ten years of emergency department (ED) data from the US Consumer Product Safety Commission's National Electronic Injury Surveillance System (2009-2018). We identified baseball- and softball-related ocular trauma (BOT, collectively) presenting to EDs. We grouped patients by age in years (y): Pediatric, ≤ 17 y; Adult, ≥ 18 y. We analyzed normality with both Shapiro-Wilk tests and Q-Q plots and variances with Levene's tests. We performed Student's t-, Welch's t-, and Mann-Whitney U tests and calculated 95% confidence intervals (CI).

Results: From 2009-2018, an estimated 25816 (CI [21780-29852]) patients presented to US EDs with BOTs. Pediatric patients experienced 67.6% (n=17442) of BOTs; Adults, 32.4% (n=8375). Median patient age was 14y (interquartile range, 10-23y). Patients age 0-4y experienced 1.3% (n=342) of BOTs; 5-9y, 18.6% (n=4799); 10-14y, 35.4% (n=9149); 15-19y, 15.5% (n=3989); 20-24y, 7.0% (n=1797); 25-34y, 8.6% (n=2209); 35-44y, 6.6% (n=1706); 45-54y, 4.5% (n=1173); ≥ 55 y, 2.5% (n=656).

Primary diagnoses were contusion/abrasion (51.2%, n=13230), other (34.8%, n=8994), laceration (3.3%, n=844), conjunctivitis (3.0%, n=782), foreign body (2.9%, n=750), hematoma (2.4%, n=621), or hemorrhage (2.3%, n=595). Mean annual BOT incidence decreased by 630 ± 336 (CI [5.91- ∞]; p=.0487) in 2014-2018 compared to 2009-2013. Annual BOT incidence decreased by 32.0% from 2009 (n=2909; CI [1918-3901]) to 2018 (n=1998; CI [941-3056]) and peaked in 2012 (n=4040; CI [2919-5160]), yielding a decrease of mean annual incidence from 2897 ± 717 in 2009-2013 to 2267 ± 222 in 2014-2018.

Conclusions: Nearly 2600 patients presented to US EDs with BOTs annually. Pediatric patients presented with BOTs more frequently than adults. Incidence of BOTs has decreased in recent years, which may suggest an increase in the use or efficacy of protective sporting equipment. We encourage the use of protective eyewear when playing baseball and softball.

CONTROL ID: 3546198

SUBMITTER (NAME ONLY): Safal Khanal

TITLE: Human Meibum and Tear Film Derived (O-acyl)-Omega-Hydroxy Fatty Acids as Biomarkers of Tear Film Dynamics

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Meibomian gland dysfunction (MGD) produces alterations in the tear film (TF) lipid layer that causes excessive evaporation of tears from the ocular surface and subsequent increased osmolarity leading to dry eye disease. However, the molecular mechanism underlying TF evaporation has yet to be understood. This study aimed to investigate the association between (o-acyl)-omega-hydroxy fatty acids (OAHFAs) derived from TF and meibum and TF evaporation in a cohort of healthy and MGD subjects.

Methods: Of 195 eligible subjects (18–84 years, 62.6% female), 178 and 170 subjects provided both TF optical coherence tomography (OCT) imaging and mass spectrometry data for tears (n = 178) and meibum (n = 170). The rate of TF thinning (μm/min) was measured in the right eye of each subject using an ultra-high-resolution, custom-built OCT. Tear and meibum samples from the right eye of each subject were infused into the SCIEX 5600 TripleTOF mass spectrometer in the negative ion mode. Intensities (m/z) of pre-identified OAHFAs were measured with Analyst 1.7TF and LipidView 1.3 (SCIEX) and normalized by internal standards, and then correlated with TF thinning rate using Spearman's correlations.

Results: Out of 76 OAHFAs detected in meibum samples, intensities of 28 OAHFAs had statistically significant negative correlations with TF thinning rate (all p < 0.05). These OAHFAs were: 18:2/16:2, 18:0/22:1, 18:0/23:0, 18:2/24:1, 18:1/24:1, 18:0/24:1, 18:0/24:0, 18:1/25:0, 18:1/26:1, 18:0/26:1, 18:1/28:1, 18:0/28:0, 18:0/28:1, 18:2/30:1, 18:1/30:1, 18:0/30:1, 18:0/31:2, 18:1/31:0, 18:2/32:2, 18:2/32:1, 18:1/32:1, 18:0/32:1, 18:1/33:0, 18:2/34:2, 18:2/34:1, 18:1/34:1, 18:2/36:1, 18:1/36:1. In contrast, there were statistically significant positive correlations between intensities of two meibum-derived OAHFAs (18:2/18:1, 16:1/28:3) and TF thinning rate (both p < 0.05). Of 78 OAHFAs detected in tear samples, intensities of six OAHFAs (18:0/24:0, 18:0/26:0, 18:2/27:2, 18:2/27:0, 18:2/28:2, and 18:2/29:2) were positively correlated with TF thinning rate, while one OAHFA (18:0/22:1) was negatively correlated (all p < 0.05).

Conclusions: Several OAHFAs derived from the human tear film and meibum showed significant associations with alterations in TF thinning. These findings suggest that OAHFAs could be implicated in the mechanism underlying the stabilization and evaporation (or thinning) of TF in health and MGD.

CONTROL ID: 3546201

SUBMITTER (NAME ONLY): Ann Yung

TITLE: Characterization and Development of a Novel Loteprednol Etabonate Eluting Adhesive Ocular Patch

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Yung, R. Dana, Schepens Eye Research Institute, Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|S. Gholizadeh, X. Chen, N. Annabi, Department of Chemical and Biomolecular Engineering, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Appropriate care of ocular injuries is vital to the preservation of vision. Full-thickness injuries are especially challenging in low-resource or emergency settings as current standards of care involve high surgical skill, equipment, and complex drug regimens. Nanoparticle (NP) based drug delivery systems (DDS) allow for localized tissue targeting with controlled drug release and dosages. Many anti-inflammatory ophthalmic drugs are class II compounds with low bioavailability due to their hydrophobic nature. Herein, we demonstrate a novel DDS by loading drug-laden micelles into a visible light photopolymerizable hydrogel patch with the potential to seal ocular injuries and elute a hydrophobic anti-inflammatory drug.

Methods: Micelle building blocks were synthesized via radical polymerization to create poly(ethylene glycol)-b-(N-(2-hydroxypropyl) methacrylamide-co-oligolactate (PEG-b-(pHPMAm-co-Lac_n)). Micelle characterization utilized gel permeation chromatography (GPC) to obtain the polydispersity index (PDI), and proton nuclear magnetic resonance (¹H NMR) to measure molecular weight (Mw). Micelle physicochemical properties were obtained with dynamic light scattering (DLS) and zetasizer analysis. Loteprednol Etabonate (LE) was encapsulated into micelles and loading efficiency and in vitro drug release were measured using high performance liquid chromatography (HPLC). Lastly, LE loaded micelles were incorporated into the patch composed of methacrylated biopolymers with varying concentrations.

Results: Synthesized micelle characterization showed a block co-polymer with Mw of ~20 kDa and a PDI of 1.46. LE was successfully loaded into micelles with a size of 100-120 nm and loading efficiency of ~ 30%. Micelles were stable for up to five days of incubation in buffer solution at 37°C. A first order (sustained) release of LE was demonstrated for 10 days, with 98% drug released on day 10. Micelles loaded into the patch showed complete and sustained release of LE within 10 days. DLS analysis of release media showed retention of micelles within the hydrogel network.

Conclusions: The adhesive patch successfully loads a hydrophobic drug and allows for sustained release for up to 10 days. Our NP DDS can address critical factors in ocular injury care by its potential use in ocular injury sealing and drug delivery which can increase drug bioavailability without need for complicated and high frequency drug regimen.

CONTROL ID: 3546202

SUBMITTER (NAME ONLY): Niloofar Hatami

TITLE: Cystathionine β -synthase as novel regulator of lymphangiogenesis

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Lymphangiogenesis is critically involved in tissue fluid balance, immune responses, corneal graft rejection, and dry eye disease. The healthy cornea is an avascular and alymphatic tissue with a distinct limbal lymphatic vascular arcade. The genetic background significantly influences the architecture of this limbal lymphatic arcade and corneal lymphangiogenesis. By using the BALB/c x C57BL/6 intercross for QTL analysis we identified and functionally characterized a novel potential candidate gene responsible for the differences in the limbal lymphatic vessel architecture on chromosome 17, the cystathionine β -synthase (CBS) gene.

Methods: To analyze the effect of CBS on human dermal lymphatic endothelial cells (HDLECs) aminooxyacetic acid (AOAA), a pharmacological inhibitor for CBS, was used in vitro. Proliferation and migration of HDLEC after treatment with AOAA was measured by using IncuCyte Zoom and the expression of lymphangiogenic factors was quantified by using qRT-PCR.

In vivo, three 11-0 nylon sutures were placed into the cornea stroma of C57BL/6 mice for 14 days. The treatment group received AOAA as eye drops three times per day for 14 days. Control mice received an equal amount of PBS. Vessel area was analyzed by using cellF software.

Results: In vitro experiments showed that the inhibition of CBS with the inhibitor AOAA in HDLECs resulted in a significant dose-dependent decrease in proliferation compared with control HDLECs. HDLECs treated with the inhibitor show also significantly delayed wound closure compared to the control. In addition, qRT-PCR revealed that the treatment with AOAA influences the expression of lymphangiogenic factors and their receptors. Fourteen days after the inflammatory insult in vivo, the total surface area of the vessel ingrowth into the cornea of AOAA treated and control treated C57BL/6 mice was assessed and the AOAA treated C57BL/6 mice showed a significantly lower lymphatic surface area compared to control treated C57BL/6 mice, indicating that CBS is also involved in inflammation-induced lymphangiogenesis in vivo.

Conclusions: In this study we identified cystathionine β -synthase as a novel endogenous regulator of lymphangiogenesis. CBS reduces not only proliferation and migration, but it also influences the expression of lymphangiogenic factors and their receptors. This opens new treatment avenues in diseases associated with pathologic lymphangiogenesis, such as corneal graft rejection.

CONTROL ID: 3546203

SUBMITTER (NAME ONLY): Jillian Foltz

TITLE: Morphometric analysis of rat optic nerve head (ONH) astrocytes grown in a 3D cell culture system

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: ONH astrocyte reactivity is an early response to elevated IOP, a key risk factor in glaucomatous optic neuropathy. To better understand astrocyte mechanobiology, we have developed a 3D hydrogel cell culture system to mimic the in situ ONH environment. Here our goals were: (i) to quantify morphology of astrocytes cultured in this system, as assessed by semi-automated image analysis, and (ii) compare to in situ morphology.

Methods: Primary astrocytes isolated from rat ONH were cultured in a synthetic hydrogel based on 4-arm polyethylene glycol norbornene (PEG-4NB) macromer functionalized with 1.0 mM RGD for 2 to 14 days. Astrocytes within hydrogels were stained with DAPI and phalloidin and imaged using a Leica DM6 fluorescent microscope at post-seeding day 5. Images were skeletonized (AnalyzeSkeleton plugin in ImageJ/FIJI), and individual astrocytes were isolated (n=11). The number and length of astrocytic processes were then quantified from each astrocyte and used to calculate branching frequency (number of processes emanating directly from the cell body divided by total number of processes), a measure of branching complexity. This morphometric quantity was then compared to data in the literature (Butt et al., J Neurocytology, 1994).

Results: We successfully identified, segmented, and analyzed astrocytes from hydrogel cultures. Branching patterns were qualitatively similar to astrocytes in situ; however, quantitative analysis showed that cultured astrocytes had higher branch frequency than cells in situ (Fig. 2, chi-squared test, χ^2 (df=8) = 116.68, p < 0.001).

Conclusions: Qualitative morphological similarities of astrocytes in situ vs. those cultured in 3D hydrogels suggest that the PEG-4NB hydrogel system is a viable model for studying ONH astrocyte mechanobiology. However, astrocytes grown in 3D hydrogels are less elongated and branch more frequently than in situ, possibly explained by the additional constraints imposed in situ on the astrocytes by the cylindrical optic nerve shape. Ongoing efforts seek to develop this 3D hydrogel cell culture system, along with image analysis tools, as a novel platform for studying the mechanobiology of astrocytes in glaucoma.

CONTROL ID: 3546207

SUBMITTER (NAME ONLY): Shan Suthaharan

TITLE: An automated choroid segmentation approach using transfer learning and encoder-decoder networks

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Suthaharan, Computer Science, University of North Carolina at Greensboro, Greensboro, North Carolina, UNITED STATES|G. Chhablani, Computer Science, Birla Institute of Technology and Science Pilani - K K Birla Goa Campus, Zuarinagar, Goa, INDIA|K.K. Vupparaboina, J. Sahel, K.K. Dansingani, J. Chhablani, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Deep neural networks have been used for choroidal segmentation using OCT images. However, the complexities of choroidal structure require the use of a large amount of data and computational time for training a model. We hypothesize that integration of transfer learning to an encoder-decoder network can enable latent features to be detected under the constraint of limited data. We tested this hypothesis with a computational framework that adapts geometrical transformations, spatially adaptive augmentation, and variance scaling weight initialization.

Methods: We used 120 OCT image-mask pairs of the choroid and randomly assigned 96 of them for training and 24 for validation. We augmented the training set to 1248 images using rotation and flipping. All images were resized to 128×128 pixels using bilinear interpolation and then masks were binarized. We built U-Net and UNet++ (encoder-decoder network) models on a VGG-19 backbone for allowing pretrained (PT) ImageNet weights in the encoder. We adapted a Glorot uniform initialization otherwise. We experimented with freezing (FR) the first 30% of the backbone layers when using transfer learning while using the final layer outputs for U-Net and UNet++. The models were trained for 10 epochs using Dice-score loss as a quantitative measure, and a model performance was evaluated using an average precision as a qualitative measure.

Results: We obtained average precision scores of 0.92 for U-Net and UNet++. The integration of transfer learning yielded an average increase of 2% in U-Net and 4% in UNet++. A subjective (visual) evaluation confirmed that the segmented choroidal regions are meaningful (Fig. 1) with respect to the increase in precision values. Freezing of the initial layers slightly reduced the precision value.

Conclusions: The transfer learning approach can significantly help to improve encoder-decoder networks for choroidal segmentation in OCT scans. Our computational framework comprises U-Net and UNet++ on a VGG-19 backbone and uses the PT encoder to perform choroidal segmentation. Our future research will include more rigorous subjective evaluation with choroidal OCT images of unhealthy eyes to develop a fully automated choroidal segmentation system.

CONTROL ID: 3546211

SUBMITTER (NAME ONLY): Mariana DuPont

TITLE: Retinal vessel density and tortuosity is associated with severity of pulmonary artery hypertension

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.D. DuPont, M.B. Grant, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|S. Lambert, The University of Alabama at Birmingham School of Public Health, Birmingham, Alabama, UNITED STATES|A. Rodriguez-Martin, The University of Alabama at Birmingham School of Health Professions, Birmingham, Alabama, UNITED STATES|T. Yilmaz, A. Foderaro, C. Ventetuolo, Brown University Warren Alpert Medical School, Providence, Rhode Island, UNITED STATES|C. Ventetuolo, Brown University School of Public Health, Providence, Rhode Island, UNITED STATES|T. Lahm, Indiana University Department of Medicine, Indianapolis, Indiana, UNITED STATES|O. Hernandez, The University of Alabama at Birmingham College of Arts and Sciences, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pulmonary arterial hypertension (PAH) is characterized by systemic inflammation, endothelial dysfunction, and smooth muscle cell hypertrophy. PAH is classically considered an isolated small vessel vasculopathy of the lungs with peripheral pulmonary vascular obliteration. Diagnosis and monitoring of PAH patients require frequent procedures, including invasive hemodynamics with an average time to diagnosis of over two years after symptom onset. Systemic manifestations of PAH are increasingly acknowledged, but data remains limited. We hypothesized that retinal vascular changes could be associated with markers of PAH severity.

Methods: Using VESSEL GENERational Analysis (VESGEN), a non-invasive, user-interactive computer software that assigns branching generation of large (1) to small (9) vessel.

Results: We examined fluorescein angiograms from controls (n=6) and group 1 PAH subjects (n=9) and correlated retinal vessel parameters with pulmonary hemodynamic endpoints from right heart catheterization. The tortuosity of PAH retinal vessels increased compared to controls ($P<0.001$). Retinal vessel area density, a vascularity indicator, correlated negatively with right heart catheterization hemodynamics (right atrial pressure, ($p=0.04$, $r=-0.50$; mean pulmonary arterial pressure, $p=0.02$, $r=-0.55$; pulmonary capillary wedge pressure, PCWP, $p=0.0017$, $r=-0.72$. PCWP also negatively correlated with arterial density ($p=0.04$, $r=-0.51$). Smaller, more fragile vessels (generations 6-9) correlated positively with vessel area density, superior vena cava oxygen saturation (SVCO₂) ($p=0.04$, $r=0.53$), and pulmonary arterial oxygen saturation (PAO₂) ($p=0.01$; $r=0.70$). Normal vessel tortuosity that typically ranges from 1 to 1.15 pixel/pixel was greater in PAH arteries (1.17 ± 0.041) and veins (1.17 ± 0.040).

Conclusions: In conclusion, we show that 1) reduced retinal vascularity (density) was associated with worsening pulmonary hemodynamics and 2) higher than normal tortuosity in PAH subjects. This investigation suggests that retinal changes may be associated with PAH severity. Use of FA and VESGEN in PAH is feasible and may facilitate early, non-invasive detection of PAH by careful determination of changes in retinal vessel tortuosity.

CONTROL ID: 3546216

SUBMITTER (NAME ONLY): Yuval Cohen

TITLE: The Ambient Light in Nursery School and Children's Refraction

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: .To measure the effect of nursery school light intensity on refraction and pupil size

Methods: A total of 1260 children age 4-5 years from 27 nursery school were examined. Light intensity was tested by Luxmeter device (Lux) inside and outside the nursery school. Pupil size, corneal reflex and non cycloplegic refraction were measured by the Plusoptix vision screening device. Data analysis was performed using Pearson coefficient and Chi-square tests

Results: The mean age of included children was 4.8 ± 0.22 years ($N=1184$). Light intensities of the low, medium and high intensity nursery schools were 343, 461, 602 lux, respectively (ANOVA, $P<0.01$) with mean refraction of $+0.54 \pm 0.9$, $+0.74 \pm 0.6$, and $+0.84 \pm 0.6$ diopters, respectively. (ANOVA, $P<0.0001$) Pupil size was larger as light intensity increased.

Conclusions: In the nursery school, the higher the indoor light intensity the greater the refraction. Light dependent pupil diameter is less likely to be involves in refractive development. Monitoring the nursery school light intensity should be part of the child safety.

CONTROL ID: 3546218

SUBMITTER (NAME ONLY): Anam Akhlaq

TITLE: Prediction of Best-Corrected Visual Acuity from Optical Coherence Tomography in Patients with Neovascular Age-Related Macular Degeneration Using Deep Learning

SESSION TITLE: AI in the retina: Prediction models

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Akhlaq, S.A. Kherani, P.A. Campochiaro, T. Liu, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|C. Jones, T. Liu, Malone Center for Engineering in Healthcare, Johns Hopkins University, Maryland, UNITED STATES|C. Jones, Radiology AI Lab, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Using deep learning (DL), this pilot study aimed to demonstrate that function in the form of visual acuity can be predicted from pathologic structural alterations due to neovascular age-related macular degeneration (nAMD) in optical coherence tomography (OCT) images.

Methods: This retrospective analysis included 2443 OCT volumes from 341 eyes of 294 patients with nAMD. Only the foveal line scan from each OCT volume was used. We train a deep convolutional neural network using transfer learning for the binary task of predicting better or worse than 20/40 BCVA. A cut off VA of $\geq 20/40$ was chosen, as it is the accepted cut-off value for driving in most states in the US and $\geq 20/40$ has been used in several large clinical trials to characterize good visual outcomes in nAMD patients. The BCVA recorded at each corresponding clinic visit was used as ground truth. The entire dataset (BCVA $\geq 20/40$ 1097 images; BCVA $< 20/40$ 1346 images) was split randomly at the patient level into training (82.8%), validation (12.3%) and testing (4.9%).

Results: For the binary classification task of distinguishing between better and worse than BCVA 20/40, our DL algorithm achieved an accuracy of 80.0%, precision of 80.0%, recall of 79.0%, with the area under the ROC of 86.2%.

Conclusions: We have developed a DL algorithm that is capable of predicting function (BCVA) from structure (OCT images) in nAMD. As the next step, we plan to collect more training data and refine our algorithm for more fine-grained BCVA predictions, which if successful, could lead to the development of a novel DL-based OCT metric that can be used to monitor treatment efficacy in nAMD.

CONTROL ID: 3546219

SUBMITTER (NAME ONLY): Yang Liu

TITLE: Optic nerve head astrocyte mechanotransduction in congenital glaucoma

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Liu, North Texas Eye Research Institute, Pharmacology & Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yang Liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In congenital glaucoma, the ocular developmental abnormalities cause high intraocular pressure which places mechanical stress on the optic nerve head (ONH) and leads to optic nerve degeneration. Untreated or treated late children develop irreversible blindness. Astrocytes are the major glial cells in the ONH. Astrocytic mechanotransduction transduces mechanical stress to biological signals and regulates cell activity. In this study, we investigated the mechanosensing channels involved in ONH astrocyte mechanotransduction in an early-onset glaucoma mouse model.

Methods: Homozygous *egl1* mutant mice were obtained from the Jackson Laboratory. Intraocular pressure (IOP) was measured in conscious mice using the TonoLab tonometer. Mice were sacrificed and the ONH were collected before, 1 and 4 weeks after IOP elevation. Primary mouse ONH astrocytes were also cultured from the *egl1* mice and subjected to mechanical stretch of 10% strain for 2 hours using a FlexCell Tension System. Real time quantitative PCR was performed to assess the expression levels of mechanosensing channels in the ONH tissue. The astrocytic location of significantly regulated genes in the ONH was further validated by immunohistochemistry staining co-labeling with astrocyte marker glial fibrillary acidic protein (GFAP).

Results: The *egl1* mutant mice developed elevated IOP starting from 4 weeks of age (22.1 ± 3.7 mmHg vs. 16.5 ± 1.7 mmHg in age-matched wild type animals, Mean \pm S.D., $n=10-14$, $p<0.01$). Gene expression levels of mechanically activated ion channels of Piezo, transient receptor potential and potassium mechanosensing channel families were assessed. Expression levels of Piezo1 and Pkd2 in the ONH were upregulated in response to IOP elevation. Immunohistochemistry staining showed astrocytic location of elevated Piezo1 and Pkd2 in the ONH. After 2 hours of stretch, the morphology of astrocytes did not show significant changes; however, there was a significantly increased expression of Piezo1 and Pkd2 in stretch stimulated cells.

Conclusions: Mechanosensing channels Piezo1 and Pkd2 respond to mechanical stretch and IOP elevation. Piezo1's activity is regulated by Pkd2. The Piezo1 and Pkd2 interaction may play a role in ONH astrocyte reactivity in response to IOP elevation and contribute to pathogenesis of congenital glaucoma.

CONTROL ID: 3546221

SUBMITTER (NAME ONLY): Dhanesh Amarnani

TITLE: Identification of Drug Candidates using a Patient-Derived Model of Proliferative Vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Amarnani, S. Delgado-Tirado, L. Gonzalez-Buendia, M. O'Hare, J. Arboleda-Velasquez, L.A. Kim, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|W.A. Greene, H.H. Wang, Sensory Trauma Task Area, United States Army Institute of Surgical Research, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is a sight-threatening complication of retinal detachment and its surgical repair with no effective treatment. The aim of this study is to identify promising drug combinations with a potential synergistic effect by carrying out a screen in our primary culture model and an explant model of PVR.

Methods: Twelve candidate drugs were tested at 2 concentrations at 72 hours for their effects on proliferation and cytotoxicity in C-PVR cells. The most significant hits were tested in combination with other compounds to study combinatorial effects on proliferation. This effect was further evaluated in an ex vivo explant model, and total branch lengths were measured.

Results: At 5 μ M concentration 6 out of 12 drugs, bendamustine, semagacestat, daclatsvir, marbofloxacin, stavudine, and resveratrol significantly inhibited cell proliferation (20%, 30%, 16%, 30%, 19%, and 28% inhibition respectively). At 1 μ M concentration, 2 out of 12 drugs, bendamustine (25%) and semagacestat (28%) significantly inhibited proliferation. 30 μ M melphalan induced 74% inhibition, and a 60 μ M concentration reduced cell proliferation by 83%. Topotecan at 40 nM induced a 54% decrease in proliferation, and a 53% decrease was noted with 80 nM. Daunorubicin, 15 nM treatment resulted in a 50% reduction, while the 30 nM treatment resulted in a 53% reduction in proliferation. Likewise, with lenalidomide, 24% inhibition of proliferation was observed. The combination of melphalan or topotecan with other drugs showed a dramatic effect on the proliferation of C-PVR cells. Melphalan showed synergistic effect with all 10 drugs. In comparison, with topotecan, 6 out of 10 showed a synergistic effect in combination. No significant cell death was observed. Melphalan at 30 μ M (27.5 mm total branch length) and topotecan at 40 nM (34 mm total branch length) alone reduced the distance covered by outgrowths compared to vehicle (167 mm total branch length) in the explants. Explants treated with combination therapy showed an almost complete inhibition of any growth suggesting synergistic effect.

Conclusions: The majority of our candidate drugs showed dose dependent effects on C-PVR cell proliferation. Melphalan and topotecan in combination with other drugs successfully inhibited proliferation in vitro, and in an explant model of PVR suggesting synergistic effects of these agents when used as combination therapy.

CONTROL ID: 3546224

SUBMITTER (NAME ONLY): Gustavo Ortiz

TITLE: Role of Plasmacytoid Dendritic Cells in the Homeostasis of Retinal Blood Flow

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Ortiz, A. Jamali, D.L. Harris, P. Hamrah, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have recently demonstrated the presence of plasmacytoid dendritic cells (pDCs) in murine retina. In particular we have shown that pDCs are in close proximity to retinal vessels. Thus, we aimed to evaluate whether resident pDCs may mediate the homeostasis of retinal vasculature in the laser-induced choroidal neovascularization (CNV) mice model of age-related macular degeneration.

Methods: Six- to 8-week-old, BDCA2-DTR mice were intraperitoneally injected with 200 mg/ml of diphtheria toxin or PBS as pDC-depleted and sham-depleted animals respectively. pDC-depletion was corroborated by flow cytometry. Both naïve and laser-induced CNV depleted animals were evaluated in this study. CNV was performed on the same day of depletion. Three and 7 days after CNV induction, fluorescein angiography was conducted in sham and pDC-depleted animals. Fundus images were obtained; abnormal vascular leakage and scar size were quantified as fluorescence intensity and scar area (as normalized to optic disc) respectively. Further, we used our transgenic DPE-GFP^x RAG-1^{-/-} mice in which only pDCs express GFP, to quantify retinal GFP cells in naïve and after laser-induced CNV.

Results: Fluorescein angiography in naïve animals showed that vascular leakage was 1.5-fold ($p < 0.001$) and 1.4-fold ($p = 0.042$) increased after 3 and 7 days of pDC-depletion, respectively, compared with sham depleted. At 7 days after CNV induction, vascular leakage and scar area increased 4-fold ($p = 0.040$) and 2-fold ($p = 0.046$), respectively, in pDC-depleted animals. Additionally, retinal eGFP cells were CD11c^{low}, PDCA-1⁺, Ly6C⁺, Ly49Q⁺ and CD19⁻, CD3⁻, F4/80⁻, CD11b⁻. This population was increased 4-fold after laser-induced CNV as measured by flow cytometry and epi-fluorescent microscopy ($p < 0.001$).

Conclusions: pDCs are required to preserve vasculature homeostasis in naïve retinas. Moreover, pDC depletion in a clinically relevant model of AMD exhibits worse outcomes, including increased vascular leakage and scar size, indicating that pDCs may be necessary to limit disease.

CONTROL ID: 3546228

SUBMITTER (NAME ONLY): Zhongdi Chu

TITLE: A novel deep learning algorithm for the segmentation of pigment deposits using SS-OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Chu, X. Zhou, Y. Cheng, R.K. Wang, Department of Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|Y. shi, R. Laiginhas, G. Gregori, P.J. Rosenfeld, Department of Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop an algorithm to segment pigment deposits and to identify their axial positions relative to the retinal pigment epithelium (RPE) using swept source OCT (SS-OCT) data based on the appearance of hypo-transmission defects (hypoTDs).

Methods: A three-step algorithm was developed. Firstly, optical attenuation coefficient (OAC) was evaluated on a linear scale 3D SS-OCT. Bruch's membrane (BM), RPE, and inner limiting membrane (ILM) were segmented on the 3D SS-OCT cube. En face images from the slab of ILM to BM from the 3D OAC data were generated using sum projection as well as maximum projection. Axial positions of the pixels with the highest OAC along each A-scan were also calculated and their distances to BM were recorded as an elevation map. A composite RGB image (Figure 1) was generated using the OAC sum, max en face images, and the elevation map. Secondly, a deep learning model with the Unet configuration was trained to segment retinal pigment deposits from the RGB images generated in step one. Target labels were manually outlined by professional graders. Thirdly, the axial positions of pigment deposits segmented by the model were identified using the elevation map and compared to the RPE segmentation. Pigment deposits with a distance larger than 30 μm from the RPE were classified as intraretinal pigment deposits and otherwise RPE pigment deposits.

Results: A total of 152 scans from 52 eyes were collected for this study. 41 eyes were diagnosed with age-related macular degeneration (AMD) and 11 eyes showed no ocular pathology upon recruitment with long term plaquenil use in 1 eye, but no obvious retinopathy present. 132 scans were used for training (with an 80/20 split between training and validation) and 20 scans were used for testing. In the testing dataset, the model achieved an intersection over union (IoU) score of 0.75. Figure 2 shows an example of the final output of intraretinal pigment deposits and pigment deposits associated with the RPE as segmented by the proposed algorithm.

Conclusions: The proposed algorithm demonstrated a satisfactory performance for automatically segmenting pigment deposits and identifying their axial positions using SS-OCT data. This strategy could be potentially useful for tracking the appearance, size, and position of retinal pigment deposits in AMD patients as indicators of disease progression and for assessing the effect of therapies in clinical trials.

CONTROL ID: 3546230

SUBMITTER (NAME ONLY): Cindy Chen

TITLE: Automated Detection of Inflammatory Activity in Sarcoid Uveitis and Birdshot Chorioretinopathy Patients Using Optical Coherence Tomography and Fluorescein Angiography

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Chen, S. Sharma, A. Venkat, K. Baynes, E. Fisher, D. Burton, J. Deaner, M. Ramos, N. Karthik, K. Barekatin, P. Le, J. Bhangu, M.A. McDonald, P.M. Kaiser, J.P. Ehlers, S. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Automated quantification of ocular inflammation provides continuous measurements of inflammation and improves the ability to differentiate activity in uveitis management. This subgroup analysis evaluates the utility of automated imaging-based measures of ocular inflammation in sarcoid uveitis (SU) and birdshot chorioretinopathy (BC).

Methods: This is a subgroup analysis of the prospective imaging of inflammation study (IQI). Recently active uveitis patients were prospectively imaged using ultra-wide field fluorescein angiography (UWFA), spectral domain optical coherence tomography (SD-OCT), and anterior segment optical coherence tomography (AS-OCT) at baseline and follow-up visits. Patients were identified as active based on clinical exam with physician interpretation of imaging. A masked grader performed automated software analysis to measure total retinal leakage (TRL) measured on UWFA, OCT central subfield thickness (CST) and AS-OCT identification of cells. Activity was met based on one or more of the following criteria: TRL > 4%, CST > 350 microns, and AS-OCT > 8 cells/mm³. In this analysis, patients with SU and BC are analyzed. Central 3-disc diameter (3DD) leakage on UWFA and intraretinal fluid percentage on OCT were also analyzed.

Results: A total of 40 eyes from 20 patients (13 SU, 7 BC) with a total of 164 visits were evaluated. BC patients met activity threshold based on AS-OCT, SD-OCT, AND UWFA in, 19.5%, 10.7%, and 2%, respectively. In SU patients, activity was noted in 20% of UWFA, 16.2% of AS-OCT, and 5.8% of SD-OCT images. In SU patients, when determined active by any imaging modality, TRL, 3DD, CST, AS-OCT were increased compared to inactive visits. In BC, when FA and AS-OCT identified activity, there was an increase in TRL and AS-OCT compared to inactive visits. When SD-OCT determined activity, CST and 3DD were higher compared to inactive visits.

Conclusions: Patients with BC and SU are identified active more often based on AS-OCT and TRL on FA, respectively. An increase in all TRL, 3DD, CST, and AS-OCT in patients with active SU validates our automated

imaging software in detecting disease activity objectively. Based on our limited number of patients with BC, further investigation will be conducted to improve our ability to differentiate imaging activity in BC patients.

CONTROL ID: 3546234

SUBMITTER (NAME ONLY): Ireneusz Grulkowski

TITLE: Volumetric Optical Imaging and Quantitative Analysis of Age-Related Changes in Anterior Human Vitreous

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To characterize age-related changes in anterior vitreous with 3-D high-resolution Swept Source Optical Coherence Tomography (SS-OCT) and evaluate associations with vision.

Methods: This cross-sectional observational study included 49 phakic eyes of 49 patients (25 men and 24 women, mean age: 40.0 ± 19.3 yrs, range: 9-78 yrs). The anterior vitreous and the crystalline lens were imaged with a prototype SS-OCT operating at 1 μm in an enhanced vitreous imaging mode. OCT-derived parameters were: Vitreous Optical Density (VOD), Vitreous Opacification Ratio (VOR), and Lens Optical Density (LOD). Axial eye length (AL) was measured with optical biometry. Retinal point spread function was measured with a double-pass system to obtain objective scatter index (OSI). Contrast sensitivity was measured using a visual simulator, and area under log-log contrast sensitivity function (AULCSF) was calculated.

Results: The high sensitivity SS-OCT instrument allowed for visualization of the anatomy of the anterior vitreous body including gel vitreous, lacunae of liquefied vitreous, Berger's space, retrolental laminar structures, and fibrous opacified structures. VOD, VOR, and LOD showed high reproducibility (intraclass correlation coefficients 0.968, 0.975, and 0.998, respectively). VOD was highly correlated with VOR (Pearson's $R=0.96$, $p<0.000001$). VOD, VOR and LOD correlated with age ($R=0.48$, 0.58 , and 0.85 ; $p<0.001$ for each). VOR and LOD correlated with OSI ($R=0.36$; $p=0.0094$, and $R=0.3630$, $p=0.0096$, respectively). Furthermore, VOR negatively correlated with AULCSF ($R=-0.53$, $p<0.00009$). Multivariable regression confirmed a strong independent association between age and LOD, which seemed to mediate the relationships between age and VOD or VOR. AULCSF was linked to OSI.

Conclusions: SS-OCT enables visualization of age-related microstructural changes of the anterior human vitreous. Opacification of the anterior vitreous is associated with increased heterogeneity, and more scattering with degradation in contrast sensitivity function. While anterior vitreous opacities might induce CSF degradation, this more likely reflects central and posterior vitreous opacification, and can thus serve as a useful index for management of vision degrading myodesopsia.

CONTROL ID: 3546236

SUBMITTER (NAME ONLY): Anne Vielle

TITLE: Development of optimized protocols for the generation of Retinal Organoids from hiPSC

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vielle, Y.K. Park, M. Vergara, CellSight Ocular Stem Cell and Regeneration Program, Sue Anschutz-Rodgers Eye Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|A. Vielle, M. Vergara, Linda Crnic Institute for Down Syndrome, University of Colorado Anschutz Medical Campus, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stem cell-derived retinal organoids (RO) constitute powerful in-vitro tools to study human development, model disease, or test potential therapeutic drugs for retinal degenerative conditions. However, current protocols for retinal organoid generation present limitations such as variability in quantity, quality and reproducibility within and between batches, as well as extensive culture times. Such shortcomings limit the usefulness of these models and can confound outcome interpretation. Thus, establishing robust protocols to overcome the challenges of retinal organoid generation is essential for their application to drug screening and validation, as well as to the study of retinal development and disease.

Methods: We tested 5 different RO culture supplementation protocols, including different concentrations of retinoic acid (RA) or 9 cis retinal (9CisRal) as well as no supplement. Several parameters (yield, quality, development of photoreceptor outer segments) were longitudinally quantified over a 6-month time period to assess the outcomes of each condition. Additionally, we optimized the timing of implementation of a 96-well plate culture format more amenable to quantitative applications. Retinal integrity and structure were evaluated using immunostaining and TEM.

Results: Retinal organoid cultures supplemented with 9CisRal were remarkably superior in yield and photoreceptor outer segment elongation compared to all other conditions. Interestingly, this supplementation protocol also accelerated the timing of outer segment development by at least one month. Finally, we determined the optimal conditions to increase reproducibility in 96-well plate RO cultures.

Conclusions: This study compares the performance of different protocols for RO generation and highlights the conditions that lead to the most reproducible, high-quality retinal organoids. Although culture supplementation with RA or 9CisRal was confirmed to be far superior to lack of supplement, all conditions generated organoids with photoreceptor outer segments, albeit at different efficiency levels and times. Depending on the focus of interest, the addition of one supplement over the other may be more suitable. By optimizing the concentration and type of supplement, we have designed a robust protocol that will reliably produce retinal organoids for quantitative applications.

CONTROL ID: 3546239

SUBMITTER (NAME ONLY): Mihaela Gadjeva

TITLE: Nociceptors control innate responses to *Pseudomonas aeruginosa*

SESSION TITLE: Corneal immunology and neovascularization II

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.G. Gadjeva, D. Quellier, J. Lamb, ID, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is not known whether different pathogens induce distinct neuronal responses and how nociceptors affect infection outcomes.

Methods: To monitor nociceptor responses during bacterial infection, C57BL6/N mice were either infected or sham treated, corneal whole mounts harvested at 24h and 48h post-infection, and stained for bIII tubulin and CGRP. To chemically ablate TRPV1⁺ nociceptors, C57BL6/N mice were treated with three consecutive doses of RTX: 30 ug/kg, 70 ug/kg, and 100 ug/kg subcutaneously. The capsaicin eye wipe test was performed to evaluate functional deficiency of nociceptors. To quantify blink reflexes, mice were monitored using Cochet-Bonnet aesthesiometer. To determine the impact of TRPV1- positive neurons on keratitis susceptibility, RTX-treated mice and vehicle-treated control mice were infected with *P. aeruginosa* strain 6294 at 5×10^5 CFU/ml and bacterial burdens were quantified. Myeloid cellular infiltrates were evaluated using CD45, CD11b, Ly6G, ICAM-1 markers using flow cytometry and ImageStream analysis.

Results: Infection induced rapid loss of blink reflexes and collapse of subbasal plexus neuronal fibers. Resiniferatoxin (RTX)-treated mice showed significantly ablated corneal sensory neurons and a temporary mild decrease in blink reflexes, which was recovered. Infected RTX-treated mice exhibited decreased bacterial corneal burdens in the first 24h of infection, elevated myeloid trafficking of CD45⁺CD11b⁺Ly6G⁺ICAM-1⁻ neutrophils and reduced CD45⁺CD11b⁺Ly6G⁺ICAM-1⁺ neutrophils. Mechanistically, increased frequencies of CGRP-induced ICAM-1⁺ neutrophils in the infected vehicle-treated mice showed reduced neutrophil bactericidal activities.

Infected NaV1.8Cre DTA⁺ mice, lacking the NaV1.8 channel, showed decreased bacterial burdens at 24h and 48h post-infection, a phenotype which was stronger and more sustained when compared to the RTX-treated mice.

Conclusions: These data showed that sensory neurons can regulate corneal neutrophil responses in a tissue-specific manner affecting disease progression during *P. aeruginosa* keratitis. Hence, therapeutic modalities that control nociceptor activation could impact anti-infective therapies.

CONTROL ID: 3546240

SUBMITTER (NAME ONLY): Kevin Schey

TITLE: High Resolution Imaging Mass Spectrometry of Human Donor Eyes with Drusen and Subretinal Drusenoid Deposits

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.L. Schey, D.M. Anderson, A. Kotnala, J.A. Fincher, N.H. Patterson, J. Spraggins, Biochemistry, Vanderbilt University, Nashville, Tennessee, UNITED STATES|J. Messinger, C.A. Curcio, Ophthalmology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: The molecular basis of AMD is only partly understood. Photoreceptor death and vision loss has been linked to extracellular deposits on apical and basal aspects of the retinal pigment epithelium (RPE). The purpose of this study is to use high spatial and mass resolution imaging mass spectrometry (IMS) to molecularly characterize regions of pathology observed in the neural retina, drusen, subretinal drusenoid deposit (SDD), and between photoreceptors and RPE).

Methods: Human donor eyes were either frozen or fixed following ex vivo imaging to assess AMD pathology. Tissue sections of macular and peripheral regions were analyzed using a multimodal imaging strategy which includes MALDI IMS as well as DIC, autofluorescence, and stained tissue microscopy. Adjacent sections were stained with Periodic acid-Schiff-hematoxylin and hematoxylin-eosin for morphological analysis. IMS was performed at 10-15 μ m spatial resolution in both positive and negative ion modes on a Bruker Solarix 9.4T FTICR instrument with a modified MALDI source designed for high spatial resolution and a Bruker timsTOF flex instrument at 10 μ m spatial resolution. To enable high-precision registration of IMS and optical signals, tissue autofluorescence and reflectance images were acquired from sections before and after IMS experiments. Lipid identifications were performed via LC-MS/MS in negative and positive ion modes using a Q Executive HF instrument.

Results: High spatial resolution IMS combined with registration to tissue images enabled detection of distinct lipid signals in drusen and SDD. Lipid signals observed in IMS images display heterogeneity in deposits and differences between drusen and large numbers of signals in SDD. Both unesterified cholesterol and esterified cholesterol, previously seen by histochemistry, were observed surrounding and within drusen while sphingomyelin species were abundant within drusen and basal laminar deposits. Autofluorescence and DIC imaging allowed for visualization of SDD while MALDI IMS displayed a high number of signals relating to lipid and high mass signals possibly indicating glycolipids accumulating in these regions. Inner retina internal to SDD and pathology in the RPE layer were also found to have abnormal lipid signatures.

Conclusions: IMS technology provides spatially-resolved molecular analysis of retinal pathology and extracellular deposits in human donor eyes with AMD.

CONTROL ID: 3546247

SUBMITTER (NAME ONLY): Hajar Hassaniardekani

TITLE: Computational modeling of the impact of corneal surgical procedures on regional stress distribution within the stroma

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Hassaniardekani, M. Petroll, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|V. Varner, Bioengineering, The University of Texas at Dallas, Richardson, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have demonstrated that corneal keratocyte differentiation, motility and mechanical behavior are influenced by extracellular matrix (ECM) stiffness and mechanical stress. Most biomechanical models of the surgical techniques used to treat keratoconus or to correct for refractive errors focus on predicting corneal shape. Here, we have created finite element (FE) models to predict how these procedures impact the spatial distributions of mechanical stress to which keratocytes are exposed.

Methods: A 2D axisymmetric FE model was developed in ANSYS to simulate the re-distribution of mechanical stress within the cornea following corneal cross-linking (CXL), photorefractive keratectomy (PRK) or phototherapeutic keratectomy (PTK). The cornea was modeled as a Mooney-Rivlin hyperelastic material, as described previously. To simulate CXL, the stiffness of the anterior 50% of the cornea was doubled in a central, circular region (8 mm diameter). For PTK and PRK, standard clinical ablation profiles were incorporated. We also evaluated how altering the surgical parameters (e.g. size and stiffness of CXL area, PRK ablation depth), IOP or stromal material properties impacted the stress distribution in the cornea.

Results: We found that each surgical procedure substantially re-distributes mechanical stresses within the cornea (Figure 1). In the central cornea, following CXL, the stress in the anterior cornea increases, whereas the stress in the posterior cornea decreases. In contrast, stress in both the anterior and posterior cornea increase following PTK or PRK. In the corneal periphery, the stress distribution generally remained similar to the control (unoperated) cornea. Altering the simulated surgical parameters, IOP or material properties changed the magnitude of the responses, but the overall patterns of stress were similar. Because of the nonlinear stress-strain relationship, increases in stress also increase the effective tissue stiffness.

Conclusions: In addition to altering corneal shape, corneal surgical procedures can have a profound impact on the regional stress distribution within the stroma and its response to fluctuations in IOP. These factors may influence keratocyte wound healing responses and long term stromal physiology.

CONTROL ID: 3546248

SUBMITTER (NAME ONLY): Winston Lee

TITLE: Clinical and Genetics Characterization of Hypomorphic Variants in Stargardt disease

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Lee, Genetics & Development, Columbia University Irving Medical Center, New York, New York, UNITED STATES|W. Lee, J. Zernant, T. Nagasaki, R. Allikmets, Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|G.A. Fishman, Pangere Center for Inherited Retinal Diseases, Chicago Lighthouse, Chicago, Illinois, UNITED STATES|S.H. Tsang, R. Allikmets, Pathology & Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the ABCA4 gene are the most frequent cause of inherited macular disease, with phenotypes ranging from early onset fast progressing retinal degeneration to late onset mild cases of central atrophy. Phenotypic variability is caused by extensive genetic variation in the ABCA4 gene, and correlated with the combined effect of the two disease alleles on the ABCA4 function. In genetic screening, 5-10% of the Stargardt patients remain with only one ABCA4 disease allele identified after sequencing the ABCA4 gene. The aim of this study was to identify missing causal variants in ABCA4 monoallelic STGD1 patients from a large, well-characterized ABCA4 disease cohort.

Methods: Sequencing was performed on Illumina TruSeq platform. Pathogenicity of variants was assessed according to ACMG guidelines, combining information from allele frequency data in patients vs the general population, predictive algorithms (e.g., CADD), previous publications, and segregation analysis in families. Patient phenotypes were assessed from clinical and retinal imaging data.

Results: In 61/706 (8.6%) patients only one definitely pathogenic ABCA4 variant was identified in screening of the ABCA4 coding sequences. Subsequent sequencing of the non-coding intronic sequences has revealed several rare deep-intronic candidate variants in about half of the monoallelic STGD1 patients, while many cases remain genetically 'unsolved' without plausible candidate variants. Several rare ABCA4 missense variants (p.I1562T, p.V643G, p.V643M, p.G1591R, p.T897I) have been classified as benign or of uncertain significance despite moderate pathogenicity predictions, because they are not enriched in STGD1 patients. In our cohort, four 'unsolved' monoallelic STGD1 patients harbored the c.4685T>C (p.I1562T) variant opposite from a functionally deleterious ABCA4 mutation. They were diagnosed in 5th-7th decade and showed mild macular lesions with foveal sparing. We suggest that the rare p.I1562T variant shared between these 4 patients exhibiting similar mild late onset STGD1 phenotype, might be causal when in combination with a null allele. We do not exclude the role of other possible yet to be identified cis or trans modifying variants.

Conclusions: Rare missense variants previously considered benign or of uncertain significance may contribute to late-onset ABCA4 disease with mild macular symptoms and foveal sparing.

CONTROL ID: 3546251

SUBMITTER (NAME ONLY): Anil Tiwari

TITLE: Expression of Apical-Basal Polarity Determinants during Corneal Epithelial Stratification and Maturation.

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Apical-basal polarity (ABP) is essential to establish the apical barrier function in many epithelial tissues in the body including the cornea. Previously, we demonstrated that the corneal epithelial (CE) maturation and homeostasis depend on Krüppel-like transcription factor 4 (Klf4) that promotes epithelial identity and suppresses mesenchymal gene expression. We also demonstrated that the mature CE ABP is disrupted in the absence of Klf4. Here we evaluate the expression of ABP-determinants during CE stratification and maturation.

Methods: We employed 8 mm thick cryosections from postnatal day-8 (PN-8), PN-12, PN-14, and PN-90 wild type mouse eyes to evaluate the expression of ABP determinants Pals1, Par3, Scribble and Cdc42 during CE stratification and maturation by immunofluorescent staining.

Results: Immunofluorescent staining of sections from mature (PN90) mouse eyes revealed that Klf4 is most intensely expressed in the central CE, and gradually tapered off towards the periphery. ABP markers Pals1, Par3 and Cdc42 were prominently membrane-associated in the central and peripheral mature CE, while faint or no immunostaining was observed in the limbal region or the adjoining conjunctiva. Coincident with the mouse CE stratification, ABP markers Par3, Scribble and Cdc42 were more cortically organized in the PN-12 and PN-14 corneas compared with their diffuse expression in the unstratified PN-8 CE. As the CE matured (PN-90), immunostaining for these markers became more prominently organized in the cortical regions of the CE cells. We also observed that the basal CE has more Yap1 (a nuclear effector of Hippo signaling pathway involved in development, growth, repair, and homeostasis) expression during stratification (PN-12 to PN-14), compared with either the unstratified (PN-8) or fully mature CE (PN-90).

Conclusions: These results demonstrate dynamic changes in expression of ABP-determinants during CE stratification and their sub-cellular re-organization from being diffusely expressed at PN-8 to being cortically organized at PN-14 and PN-90. Based on these results, we suggest that Klf4 plays a key role in CE stratification by promoting relative enrichment of ABP-determinants in the central CE compared with the limbus or the conjunctiva.

CONTROL ID: 3546255

SUBMITTER (NAME ONLY): Mayur Choudhary

TITLE: Aryl hydrocarbon receptor (AHR): potential link between autophagy and inflammation in retinal pigment epithelial (RPE) cells.

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Choudhary, G. Malek, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|G. Malek, Pathology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mayur Choudhary: Commercial Relationship: Code N (No Commercial Relationship) | Goldis Malek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Increasing evidence suggests an association between autophagy, and age-related degenerative disorders. AHR is a transcription factor mainly known for its role in toxin metabolism. Recently however, it has also been shown to regulate inflammation and autophagy. Aged $Ahr^{-/-}$ mice exhibit several phenotypic features of dry AMD including increased expression of inflammatory markers in the RPE/choroid, as shown by RNAseq and morphological flatmount analyses. Herein, we further investigated the role of AHR expression and function in regulating inflammation and autophagy in RPE cells.

Methods: In vivo, aged $Ahr^{-/-}$ and $Ahr^{+/+}$ mice were used to (1) study inflammation in the sub-retinal space by staining RPE-choroid flatmounts for F4/80 (macrophages) and phalloidin (RPE cell borders); (2) generate a cytokine profile of the posterior retina; and (3) measure levels of autophagy proteins (LC3B, SQSTM1/p62, Beclin1, Atg5, Atg7) in the posterior retina. In vitro, human and mouse primary RPE cultures were used to study the effect of AHR knockdown and modulation of AHR activity (Agonists: n=4, Antagonists: n=2) on autophagy. Finally, we tested the therapeutic potential of modulating AHR activity (chronic/acute), on autophagy and inflammation in RPE cells exposed to oxidative insults.

Results: $Ahr^{-/-}$ mice displayed a significant upregulation of F4/80⁺ sub-retinal cells in aged mice as compared to $Ahr^{+/+}$ mice (3.5-fold in 12-14 month old, 3-fold in 18-22 month old, n=4, p<0.04). RPE-choroid protein lysates exhibited significant upregulation of LC3B in 12-14 month old (2.5-fold) as well as 18-22 month old (2-fold) in $Ahr^{-/-}$ mice as compared to $Ahr^{+/+}$ mice (n=4, p<0.05). Interestingly, RPE/choroid samples from a 12-14 month old cohort, showed significant downregulation of p62/SQSTM1 protein levels (2-fold, n=4, p<0.05). In vitro results, consistent with the in vivo findings, showed an induction of autophagosome formation in RPE cells as measured by LC3B II/ LC3B I ratio, with AHR knockdown (4.5-fold, n=3, p<0.05).

Conclusions: The absence of Ahr is associated with an increase in inflammation and autophagosome formation in the RPE-choroid milieu. These finding along with our previous reports of RPE cell dystrophy and accumulation of extracellular sub-RPE deposits in aged $Ahr^{-/-}$ mice, support the premise that targeting the AHR signaling pathway may improve RPE cellular turnover and health.

CONTROL ID: 3546257

SUBMITTER (NAME ONLY): Ashley Farre

TITLE: Transcriptional distinctions between LWS cone subtypes are regulated by thyroid hormone in zebrafish

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Farre, C. SUN, S. Hunter, D.L. Stenkamp, University of Idaho, Moscow, Idaho, UNITED STATES|M. Starostik, L. Gieser, M. English, A. Swaroop, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. Santhanam, E. Shihabeddin, J. O'Brien, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In humans, the long and middle wavelength-sensing cone opsins (LWS/MWS) are encoded in a tandemly replicated array. Zebrafish possess an orthologous tandemly replicated long wavelength-sensitive (lws) array. The differential regulation of human LWS vs. MWS is viewed as a stochastic mechanism, while there is evidence for trans-regulatory mechanisms in zebrafish. Our lab demonstrated thyroid hormone (TH) promotes *lws1* at the expense of *lws2* (Mackin et al., 2019, PNAS). The present work aims to identify additional transcriptional differences in the LWS1 vs. LWS2 cone populations, toward elucidating the genetic mechanisms underlying the differential regulation of LWS cone opsin expression.

Methods: We isolated GFP+ (LWS1) cones and RFP+ (LWS2) cones from dissociated retinas of adult male *lws:PAC(H)* zebrafish, using established FACS methods (Sun et al., 2018, Exp Eye Res). Bulk RNA-Seq was performed to identify differentially expressed (DE) transcripts of interest in these two cone populations. A separate, single cell RNA-Seq dataset obtained from adult retinas was used to complement this DE list with transcripts enriched in identified *lws1*- or *lws2*-expressing cones. Larval zebrafish were treated with TH, and qPCR and multiplex in situ hybridization of DE transcripts were performed.

Results: Based on a false discovery rate (FDR)<0.05, ~130 transcripts were enriched in LWS1 cones (~1.6 [AF1] % of LWS1 transcriptome), and ~93 transcripts were enriched in LWS2 cones (1.2% of LWS2 transcriptome), suggesting that these cone types are highly similar yet with a subset of distinct transcripts. Among the DE transcripts [SD(2) [AF3] were phototransduction components [*gngt2b*], transcriptional regulators [*hmgb1b*, *sox4a*, *meis2a*], and synaptic/cell adhesion molecules [*syt2*, *syph*, *adrm1*], and regulators of circadian rhythm [*cry1ba*, *aanat2*]. Preliminary qPCR and in situ data show some transcripts may also be DE in control vs TH-treated larvae, including *gngt2b* (qPCR: p<0.05, n=6).

Conclusions: This study identified several transcripts that were DE in LWS1 vs. LWS2 cones, which have been presumed identical aside from opsin expression. The DE transcripts include some involved in cone function. Some of those DE transcripts appear to be regulated by TH. This dataset provides foundations to investigate the mechanism by which *lws1* and *lws2* are differentially regulated, including candidates for functional testing.

CONTROL ID: 3546258

SUBMITTER (NAME ONLY): Paul Kenna

TITLE: Genotype / Phenotype correlation of autosomal dominant Retinitis Pigmentosa (adRP) due to deletion of the PRPF31 gene

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.F. Kenna, E. Duignan, H. Dempsey, Research Foundation, Royal Victoria Eye and Ear Hospital, Dublin, IRELAND|P.F. Kenna, A. Dockery, L. Whelan, G. Farrar, Ocular Genetics Unit, The University of Dublin Trinity College, Dublin, IRELAND|S. Roosing, Department of Human Genetics and Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, NETHERLANDS|

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ABSTRACT BODY:

Purpose: To describe the clinical features of adRP due to a novel heterozygous deletion of PRPF31 identified in an Irish family following whole genome sequencing (WGS).

Methods: Clinical tests performed included: ETDRS visual acuity, Goldmann perimetry, Full-field electroretinography (ERG), colour and autofluorescent fundus photography and optical coherence tomography. DNA samples underwent target capture next generation sequencing (NGS) of the exons of a panel of 260 inherited retinal disease-associated genes and WGS.

Results: The proband is one of 4 siblings. Her mother, deceased at age 80, had no vision problems. Her maternal grandmother was known to have had low luminance and independent mobility issues by her 5th decade. The proband had poor night vision at age 17 years and problems with steps, pavement edges etc, suggestive of visual field loss at age 25. Best-corrected visual acuities were 6/15 (0.4) right eye and 6/12 (0.5) left eye at age 52 and 1/25 (0.04) right eye and 1/30 (0.03) by age 66, despite bilateral, technically successful, cataract surgery. Peripheral visual fields were concentrically constricted to within 10° of fixation, with preservation of small temporal islands bilaterally, at age 54 years. She retained the same central field in each eye over subsequent assessments, despite loss of the peripheral islands. At age 54 no convincing rod or cone full-field ERG responses were recordable. Target panel NGS failed to detect any convincing pathogenic sequence variants. However, subsequent WGS identified a large (c. 28kb) heterozygous deletion on chromosome 19, encompassing the whole of PRPF31. Cross deletion polymerase chain reaction and Sanger sequencing confirmed presence of this deletion in her unaffected mother and absence in her 3 unaffected siblings.

Conclusions: Mutations in PRPF31 account for approximately 5% of adRP. Most are single base changes or deletions. Total deletion of the gene has been uncommonly reported. PRPF31 is an important component of the spliceosome, involved in pre-RNA splicing in RPE and photoreceptors. PRPF31 adRP is marked by reduced penetrance, as exemplified in this family. Total deletion of PRPF31 suggests haploinsufficiency as the causative mechanism and raises the possibility that gene replacement alone may be a therapeutic option, in contrast to a dominant-negative scenario where replacement alone is unlikely to result in benefit.

CONTROL ID: 3546259

SUBMITTER (NAME ONLY): Siva Pramodh Kambhampati

TITLE: A novel, easy-to-use hydrogel sealant (OcuPairTM) for temporary corneal repair

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kambhampati, H. Lin, S.C. Yiu, K. Rangaramanujam, Ophthalmology, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|S. Kambhampati, R. Sharma, S. Appiani, D. Saragnese, J. Cleland, K. Rangaramanujam, Ashvattha Therapeutics. Inc, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Traumatic eye injuries often pose a significant risk for blindness in military personnel. The injured eye needs immediate attention and should be temporary stabilized until soldiers are evacuated to operating facilities. For this purpose, we have developed OcuPairTM hydrogel sealant, a novel dendrimer-hyaluronic acid adhesive for temporary corneal repair and wound stabilization.

Methods: Photo-crosslinkable components of OcuPair, methacrylated dendrimer (D-MA) and methacrylated hyaluronic acid (HA-MA) were synthesized using scale-up amenable protocols and their stability was assessed at different storage temperatures. The gelation kinetics of OcuPair were evaluated using rheology. The performance of OcuPair in sealing different full thickness corneal wounds was evaluated ex vivo in porcine and rabbit eyes. In vivo (non-GLP) performance of OcuPair was evaluated in a rabbit model of corneal injury. GLP toxicity of OcuPair was evaluated in healthy rabbits by using scaled-up engineering batches.

Results: he OcuPair was designed and optimized to form a transparent and flexible hydrogel sealant within 90 seconds of exposure to blue light (365nm, 4W). OcuPair seals full thickness corneal and corneo-scleral wounds (collectively mimicking battlefield injuries) and withstood burst pressures up to 70mmHg in porcine eyes. OcuPair secured different corneal wounds (n=12 each) in rabbits. OCT and seidel test analysis of rabbit eyes demonstrate that OcuPair maintained good anterior chamber structure and normotensive IOP up to 5 days. Clinical assessment indicated the OcuPair is biocompatible with no signs of significant inflammation to corneal tissue. In contrast, cyanoacrylate group demonstrated significant leakage, inflammation, and corneal toxicity. A 28-day GLP ocular toxicity study demonstrated that OcuPair and its components are well tolerated by ocular tissues and do not induce toxicity to the cornea or other ocular tissues. No signs of genotoxicity, pyrogenicity or bacterial reverse mutations were observed with OcuPair.

Conclusions: During medical evacuation of critically injured soldiers, lifesaving efforts are focused on treating other injuries. Unfortunately, this increases the likelihood of enucleation or permanent vision loss. OcuPair is designed to be applied easily and stabilizes the eye during the evacuation. OcuPair may provide the eye a better chance of rehabilitation and preservation of vision.

CONTROL ID: 3546260

SUBMITTER (NAME ONLY): Tae-Hoon Kim

TITLE: In vivo OCT and OCTA monitoring of all retinal quadrants in the neurodegenerative mouse model

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kim, D. Klatt, X. Yao, Richard and Loan Hill Department of Bioengineering, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|X. Yao, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: As one part of the central nervous system, the retina manifests neuronal dysfunction and vascular abnormality in neurodegenerative diseases, such as Alzheimer's disease (AD). Early studies demonstrated that the pathological hallmarks appear selective to the retinal quadrant. This study aims to demonstrate in vivo optical coherence tomography (OCT) and OCT angiography (OCTA) monitoring of all quadrants of the neurodegenerative mouse retina.

Methods: Six-month-old 5xFAD (TG, N = 5) and wild-type mice (WT, N = 6) were used in this study. A custom-built OCT system ($\lambda = 810$ nm) was used for retinal imaging. Volumetric raster scans were acquired in 4 retinal quadrants (nasal, dorsal, temporal, ventral) per mouse. Each volume consisted of $4 \times 500 \times 500$ A-scans. Four repeated B-scans at each slow scan position were collected for OCTA construction. For quantitative analysis, we measured retinal thickness, vascular width, and vascular density. The artery and vein around the ONH were classified for width measurement. Retinal vascular layers were segmented into superficial vascular plexus (SVP), intermediate capillary plexus (ICP), and deep capillary plexus (DCP) for density measurement.

Results: Wide-field OCT and OCTA images were constructed by stitching 4 retinal volumes obtained from 4 different quadrants (Fig. 1), and each OCT/OCTA volume was individually analyzed for quantitative assessment. Inner retinal and outer retinal thickness were notably reduced in the dorsal and temporal quadrants of TG mice. Accordingly, whole retinal thickness was significantly lower in TG mice compared to WT mice (TG: 223.8 ± 5.3 μm ; WT: 229.5 ± 4.7 μm ; $P < 0.001$). A significant arterial narrowing in TG mice was also found (TG: 28.3 ± 4.8 μm ; WT: 33.6 ± 4.7 μm ; $P < 0.0001$). In addition, vessel densities in three plexuses were consistently low in TG mice. Especially, the ICP density reduction in TG mice was close to being statistically significant (TG: $13.7 \pm 2.6\%$; WT: $14.8 \pm 2.3\%$; $P = 0.056$), which suggests a tight correlation between neuronal and vascular degeneration.

Conclusions: In this study, we demonstrated wide-field OCT/OCTA monitoring of all retinal quadrants, which allowed to examine regional changes in the retina due to neurodegeneration. The wide field OCT/OCTA provides an imaging platform for longitudinal monitoring of AD-associated retinal degeneration and noninvasive assessment of therapy protocols.

CONTROL ID: 3546261

SUBMITTER (NAME ONLY): Chase Paterson

TITLE: Engineering models to replicate RPE cell detachment in vitro

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Paterson, J. Cannon, E. Vargis, Utah State University, Logan, Utah, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Chase Paterson: Commercial Relationship: Code N (No Commercial Relationship) | Jamen Cannon: Commercial Relationship: Code N (No Commercial Relationship) | Elizabeth Vargis: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) affected approximately 2 million Americans in 2010, and this number is expected to more than double by 2050 (National Eye Institute). In diseases like AMD, abnormal angiogenesis can lead to vision loss or blindness. While the cause of angiogenesis is unknown, previous work suggests that retinal pigment epithelial (RPE) cell detachment contributes through the imbalanced secretion of angiogenic proteins. Increased expression of pro-angiogenic proteins, like vascular endothelial growth factor (VEGF), and decreased expression of anti-angiogenic proteins, such as pigment epithelium-derived factor (PEDF), both contribute to angiogenesis. To see how RPE cell detachment affects angiogenic protein expression, we used micropatterning methods to control cell growth patterns. This method created affordable stencils that can be tuned to various stages of RPE degeneration and control cell detachment in vitro.

Methods: Real fundus images were analyzed with ImageJ software to isolate areas of retinal degeneration. These areas were combined using AutoCAD into a single shape for easier manipulation in culture while maintaining the total area of detachment. Soft lithography, a technique to fabricate shapes using a flexible mold, was used to create polydimethylsiloxane (PDMS) stencils. These stencils were placed in culture plates and seeded with primary porcine RPE cells that grew until confluency. The stencils were then removed, which introduced an area void of cell growth. Enzyme-linked immunosorbent assays and immunocytochemical staining will be used to determine how angiogenic protein expression changes with RPE cell detachment.

Results: Patterns with an area of approximately 47.6 mm^2 were created in AutoCAD. These patterns were formed into stencils that represented areas of RPE cell detachment and effectively controlled the growth of primary porcine RPE cells. One day after stencil removal, RPE cells began growing in the open spaces and angiogenic protein secretion of the RPE cells changed.

Conclusions: Engineered models of RPE cell detachment can be created from analyzed fundus images. The results of this research will elucidate relationships between varying stages of detachment and angiogenic protein expression. This understanding may increase the efficacy of current treatments and lead to additional therapeutics for retinal pathologies.

CONTROL ID: 3546266

SUBMITTER (NAME ONLY): Arina Korneva

TITLE: Dissociation enzyme treatment alters strain response of astrocytic lamina in explanted mouse optic nerve head

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Korneva, E. Cone-Kimball, H.A. Quigley, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|T.D. Nguyen, Mechanical Engineering, Johns Hopkins University Whiting School of Engineering, Baltimore, Maryland, UNITED STATES|T.D. Nguyen, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure the effect of short-term exposure to dissociation enzyme on the mechanical response of the optic nerve head (ONH) in explanted mouse eyes.

Methods: The ONH was imaged with two-photon laser scanning microscopy (Zeiss LSM 710) in explanted mouse eyes using previously-published inflation testing methods (FVB/N-Tg(GFAP-GFP)14Mes mice, both sexes, 3-8 months of age). Inflation tests were performed before and again after 60 minutes exposure to TrypLE Express (Gibco 12604013), a non-animal-derived recombinant enzyme and a purified trypsin alternative. These (n=8) were compared to sequential inflation of explants exposed only to buffer (n=8). Deformation of the astrocytic lamina (AL) and of connective tissues of the peripapillary sclera (PPS) was analyzed by digital volume correlation (Korneva et al., 2020). After inflation-testing, treated specimens were prepared either for transmission electron microscopy or for fluorescent immunolabeling with phalloidin to quantify changes in the actin network (Ling et al., 2020).

Results: AL nasal-temporal strain (Exx) increased significantly post TrypLE treatment (post: $3.59 \pm 1.10\%$, pre: $2.52 \pm 0.73\%$, $p=0.01$). AL superior-inferior strain (Eyy) also significantly increased post TrypLE treatment (post: $2.50 \pm 0.64\%$, pre: $0.86 \pm 0.75\%$, $p=0.002$). The change in AL strain after treatment with buffer was insignificant (Exx post: $2.77 \pm 1.17\%$, pre: $2.92 \pm 1.41\%$, $p=0.64$). The effect of TrypLE on PPS strain response was insignificant (Exx post: $0.00 \pm 0.34\%$, pre: $0.06 \pm 0.41\%$, $p=0.93$). The differences in PPS strain after TrypLE and buffer were similar (Δ Exx $p=0.99$, Δ Eyy $p=0.81$). The PPS maximum principal strain after TrypLE significantly increased from before treatment ($p=0.01$) but not compared to after buffer ($p=0.67$). Quantitative morphological analysis of astrocyte processes in these eyes will be presented.

Conclusions: TrypLe treatment led to greater strain of the AL but similar strain of the PPS in inflation testing of explanted mouse eyes. Morphological studies suggest that astrocyte junctional complexes to the PPS are disrupted in experimental mouse glaucoma eyes (Quillen et al., 2020). Comparisons of experimental alterations of mouse model tissue may elucidate the underlying mechanisms of optic nerve head remodeling.

CONTROL ID: 3546269

SUBMITTER (NAME ONLY): Gary Peh

TITLE: A robust approach to assess cellular yield from simple non-cultured endothelial cells (SNEC) harvesting technique for corneal endothelial cell-injection therapy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.S. Peh, K. Adnan, D. Neo, H. Ong, J.S. Mehta, Singapore Eye Research Institute, Singapore, SINGAPORE]

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ABSTRACT BODY:

Purpose: The aim of the study is to establish a robust approach in determining the corneal endothelial cell yield following a recently described simple non-cultured endothelial cells (SNEC) harvesting approach for cell-injection therapy.

Methods: Pairs of donor corneas deemed unsuitable for transplantation were procured for this study. Optimization studies were initially performed using primary human corneal endothelial cells (CECs) isolated and cultured to the second or third passage using a dual media approach. Propagated CECs (n=3) were dissociated where 2×10^6 cells were obtained, before being serially diluted into 4 concentrations, where a manual cell count together with two automated cell counts using 2 different cell counters (BioRad TC-20 & NucleoCounter NC-250) were compared. Remaining cells from each dilution were seeded, stabilized (48hrs) and assessed morphologically. Subsequent validation was performed on CECs isolated from independent donor pairs (n=3) via the SNEC harvesting approach as previously described. The isolated CECs were strain-filtered, spun down and resuspended in 1mL where 50uL were used for cell counting and the rest seeded onto FNC-coated WillCo-Dish, and stabilized for 48hrs before morphometric analysis were performed.

Results: Initial optimization experiments using cultivated primary CECs showed that the consistency of the cell counts by the two cell counters were comparable to that of manual cell counting across the various dilutions. These results could be corroborated by the respective morphological assessments. More importantly, these automated cell counts were accurate down to the range of approximately 1×10^5 cells, which was the estimated cell yield from the SNEC harvesting technique from a single donor cornea. Subsequent validation studies using 3 sets of paired donor corneas, and 1 single donor corneas showed consistency in overall cell yield for the paired corneas of $2.7 \pm 0.4 \times 10^5$, $3.1 \pm 0.1 \times 10^5$, $3.2 \pm 0.3 \times 10^5$; and for the single donor: $1.7 \pm 0.1 \times 10^5$.

Conclusions: With regulatory consideration in mind, the capacity to robustly and accurately determine the cellular yield of isolated single-celled CECs from SNEC harvesting technique for cell-injection therapy - as shown in this study, is essential for its translation towards clinical practice.

CONTROL ID: 3546270

SUBMITTER (NAME ONLY): Elise Orhan

TITLE: EYS809 Non-Viral Gene Therapy to Improve Convenience and Outcomes in Wet AMD

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Orhan, K. Bigot, P. Gondouin, R. Bénard, M. Piazza, R. BUGGAGE, F.F. Behar-Cohen, T. Bordet, Eyevensys, FRANCE|F.F. Behar-Cohen, Ophtalmopole, Hopital Cochin, Paris, Île-de-France, FRANCE|

Commercial Relationships Disclosure (Abstract): Elise Orhan: Commercial Relationship(s);Eyvensys:Code E (Employment) | Karine Bigot: Commercial Relationship(s);Eyvensys:Code E (Employment) | Pauline Gondouin: Commercial Relationship(s);Eyvensys:Code E (Employment) | Romain Bénard: Commercial Relationship(s);Eyvensys:Code E (Employment) | Marie Piazza: Commercial Relationship(s);Eyvensys:Code E (Employment) | Ronald BUGGAGE: Commercial Relationship(s);Eyvensys:Code E (Employment) | Francine Behar-Cohen: Commercial Relationship(s);Eyvensys:Code E (Employment) | Thierry Bordet: Commercial Relationship(s);Eyvensys:Code E (Employment)

ABSTRACT BODY:

Purpose: Even though VEGF inhibition is effective, there is a crucial need for longer-acting anti-VEGF agents to reduce the burden of repeated IVT injections and alternative therapeutic approaches to improve outcomes in wet AMD patients. Here, we evaluate a non-viral gene therapy approach to deliver aflibercept, a potent anti-VEGF inhibitor, or Decorin (DCN), an endogenous TGF-beta inhibitor with known anti-angiogenic and anti-fibrotic properties, to reduce choroidal neovascularization (CNV) in rats. Finally, we designed EYS809, a dual-gene plasmid, to deliver sustained concentrations of both proteins.

Methods: Aflibercept- or DCN-coding plasmids (30 µg/eye) were electrotransferred in the rat ciliary muscle 3 days prior laser-induced CNV. IVT injection of a human equivalent dose of aflibercept (15 mg/eye) or recombinant DCN (1 mg/eye) at disease induction served as positive controls, respectively. CNV leakage was assessed by fluorescein angiography (FA). Different dual gene expression cassettes delivering intraocular concentrations of aflibercept and DCN in rats were compared.

Results: Electrotransfection of plasmids resulted in sustained intravitreal production of aflibercept or DCN in the vitreous during the 2 week-study while aflibercept or DCN were quickly eliminated following IVT. Following both plasmid or IVT administration aflibercept reduced incidence of Grade 3 CNV lesions to 11% and 29%, respectively, vs. 59% in untreated rats. The percentage of eyes with at least one clinically relevant lesion was also reduced in both treatment groups (39% and 63%, respectively vs. 97% in untreated). Similarly, plasmid- or IVT-administered DCN reduced the incidence of Grade 3 CNV lesions to 36% and 24%, respectively vs. 59% in untreated rats with 60% and 66% of eyes having at least one clinically relevant lesion compared to 75% in untreated rats. The dual gene expression cassette expressing the highest concentrations of both proteins in rat pharmacokinetic assessments was designated as EYS809.

Conclusions: Our non-viral gene therapy sustained drug delivery approach to deliver anti-VEGF proteins to the eye could be a viable alternative to repeated IVT injections that have been associated with poor visual outcomes in wet AMD patients. The combined effect of aflibercept and DCN, expressed from the EYS809 dual-gene plasmid, is expected to provide benefits over aflibercept alone by also reducing CNV and subretinal fibrosis.

CONTROL ID: 3546271

SUBMITTER (NAME ONLY): Bradley Dougherty

TITLE: Pediatric Refractive Error Profile 2 (PREP2) Validation Study

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.E. Dougherty, L. Jordan, D.O. Mutti, E. Galko, J.J. Walline, The Ohio State University, Columbus, Ohio, UNITED STATES|D.A. Berntsen, L. Cardenas, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Pediatric Refractive Error Profile 2 (PREP2) is a survey to measure aspects of the vision-related quality of life of children with refractive error. The purpose of this study was to assess the validity of the survey and examine relationships between PREP2 scores and baseline characteristics of children enrolled in the BLINK Study, a randomized clinical trial to examine the effects of multifocal versus single vision soft contact lenses on myopia progression.

Methods: Subjects completed the survey after wearing their randomly assigned contact lenses for two weeks, and data were analyzed using Rasch analysis to assess measurement precision (person separation statistic), response category functioning, and unidimensionality. Additionally, Rasch analysis was used to estimate interval-level person scores for each scale. The relationships between the scale scores and age, gender, cycloplegic spherical equivalent, and treatment group were analyzed using ANOVA and Spearman correlation.

Results: 289 subjects were enrolled with mean \pm SD age of 10 \pm 1 years (range = 7 to 11). Mean cycloplegic spherical equivalent refractive error OD was -2.38 \pm 1.01 D (range = -0.82 to -5.49 D). Response category function and item fit to the Rasch model were good for all scales. There was no evidence of multidimensionality in the measures by principal component analysis of model residuals. Measurement precision, assessed by the Rasch person separation statistic, was less than ideal for most scales. The Symptoms scale performed best, with good person separation and no evidence of multidimensionality. There were gender differences in scores on the Symptoms ($P=.006$), Appearance ($P=.014$), and Handling ($P=.003$) scales. Scores on the Vision subscale differed by treatment assignment ($P=.03$), with lowest scores for the +2.50D add group. There were low but significant correlations between age and the Appearance ($p=.16$, $P=.007$), Handling ($p=.14$, $P=.02$), Peer ($p=.17$, $P=.003$), and Overall ($p=.13$, $P=.032$) scales. OD spherical equivalent refractive error was correlated with Peer scale score ($p=.17$, $P=.004$).

Conclusions: The PREP2 survey scales showed generally good fit to the Rasch model but could be improved with better measurement precision. Scores on several scales showed relationships with characteristics of myopic children including age, gender, and refractive error. Future studies could examine survey performance in a more heterogeneous sample.

CONTROL ID: 3546272

SUBMITTER (NAME ONLY): Brandon Kao

TITLE: Biocompatibility and Feasibility of VisiPlate, a Novel Ultrathin, Multichannel Glaucoma Drainage Device

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.W. Kao, T.A. Barbolt, S.M. Nicaise, G. Griggs, Avisi Technologies, California, UNITED STATES|B.W. Kao, University of California San Francisco, San Francisco, California, UNITED STATES|E. Meer, V. Lee, E.G. Miller-Ellis, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|R.A. Lewis, Sacramento Eye Consultants, California, UNITED STATES|I.K. Ahmed, Ophthalmology & Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Glaucoma drainage devices and minimally invasive glaucoma surgeries (MIGS) often present with tradeoffs in safety and durability of efficacy. Using a rabbit model, we examined the biocompatibility and feasibility of VisiPlate, a novel, ultrathin, tubeless subconjunctival shunt comprised of a network of microchannels.

Methods: Six naïve female New Zealand White rabbits received a total of nine implants, each composed of a 400 nm thick aluminum oxide core and coated with 2 µm of parylene-C. Three rabbits were implanted in the right eye with the contralateral eye untreated and monitored for 93 days. Another three rabbits received devices in both eyes and were monitored for 180 days, with 100 µL of 0.2 mg/mL mitomycin-C (MMC) application in the right eye. The surgical procedure involved a 60-90° peritomy and a stab incision through the sclera into the anterior chamber, 2 mm from the limbus. Tonometry, slit-lamp exam, clinical exam, fluorescein patency testing, and histopathology were performed.

Results: VisiPlate demonstrated statistically significant ($p<0.05$) intraocular pressure (IOP) lowering of 20-40% compared to baseline at each timepoint over the course of three months in the nine implanted eyes. All eyes developed blebs over the implant, and fluorescein testing demonstrated fluid patency at 22 days post-implantation. Slit lamp and clinical observations showed that VisiPlate was well tolerated, with low levels of conjunctival congestion, conjunctival swelling, aqueous flare, hyphema, and iris involvement from surgery that resolved over time. At sacrifice time points of 93 days and 180 days, the only notable observations were mild levels of conjunctival congestion in implanted eyes. Histopathology showed minimal tissue response and no obvious inflammation, fibrosis, or necrosis around the implant.

Conclusions: The results of this in vivo study demonstrate the biocompatibility and IOP-lowering effect of a multichannel, ultrathin subconjunctival shunt in a rabbit model. The data suggest that VisiPlate may safely enhance aqueous outflow and significantly reduce intraocular pressure.

CONTROL ID: 3546273

SUBMITTER (NAME ONLY): Anna Potenski

TITLE: Elucidating endothelial caspase-9 signaling pathways in retinal vein occlusion.

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.M. Potenski, Pharmacology, Columbia University, New York, New York, UNITED STATES|C. Troy, Neurology, Columbia University, New York, New York, UNITED STATES|C. Troy, Pathology, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-apoptotic induction of endothelial caspase-9 by retinal vein occlusion (RVO) sets off a signaling pathway causing edema, BRB breakdown, and eventual neuronal loss, however the exact mechanism of this pathway is still unknown. Previous studies by our lab have shown that knocking out endothelial caspase-9 diminishes the amount of edema and neuronal damage after RVO, suggesting that the endothelial caspase-9 is motivating the signaling pathway. Since this large induction of caspase-9 seems to be non-apoptotic which is atypical of the normal function, we are determining if the upstream activation of caspase-9 by Apaf-1 is the driving force behind the non-apoptotic signaling. These experiments will be carried out using inducible endothelial cell Apaf-1 knock out mice (Apaf-1 iECKO) and WT littermates who are injured with retinal vein occlusions.

Methods: 2-month-old Apaf-1 iECKO and WT littermate mice will undergo the RVO procedure previously described in Avrutsky, et al. Live imaging readouts will be used to track the pathology of the animals and compare to previous data from the caspase-9 iECKO mice. Immunohistochemistry and western blotting will be used to determine the presence of a known downstream target caspase-7 and to track the alteration in other proteins relevant to edema, BRB breakdown, and neuronal loss between injured vs. non-injured mice as well as the Apaf-1 iECKO vs. WT.

Results: This model has previously shown that the deletion of caspase-9 protects from edema and neuronal injury after RVO. Co-staining with TUNEL (marker for cell death) shows that endothelial cells aren't dying but neurons are. We know that this activation of caspase-9 within endothelial cells is non-apoptotic and will explore the activation of endothelial caspase-9 to determine why it is not carrying out its normal death signaling in the endothelial cells themselves but instead setting off a signaling cascade leading to neuronal death.

Conclusions: Endothelial caspase-9 sets off a signaling cascade leading to neuronal death and by eliminating the induction of endothelial caspase-9, we are able to prevent edema and BRB breakdown while preserving the neurons. The activation of caspase-9 specifically in endothelial cells seems to be different than its canonical function. Apaf-1 activation may be altered in this system and can be driving how caspase-9 is behaving in different cell types.

CONTROL ID: 3546274

SUBMITTER (NAME ONLY): Alexandra Lind

TITLE: Ophthalmological findings in adolescents born moderate-to-late preterm

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lind, E. Aring, T. Ovik, A. Karatepe, L. Raffa, Z. Popovic, M.A. Gronlund, Department of Clinical Neuroscience, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, SWEDEN|A. Lind, E. Aring, A. Karatepe, Z. Popovic, M.A. Gronlund, Department of Ophthalmology, Sahlgrenska University Hospital, Gothenburg, SWEDEN|L. Raffa, Department of Ophthalmology, King Abdulaziz University Hospital, Jeddah, SAUDI ARABIA|J. Dahlgren, Department of Pediatrics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, SWEDEN|

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ABSTRACT BODY:

Purpose: Individuals born moderate-to-late preterm (MLP), defined as 32–36 weeks of gestation, have an elevated morbidity risk compared with full-term individuals, including neurodevelopmental disorders and cognitive impairment. However, little is known of their ophthalmological development. Our previous studies have shown impaired ocular motility, heterophoria, abnormal retinal vascularization, and lower visual evoked potential amplitudes in MLP children. In the present ongoing study, MLP adolescents at 15–18 years of age were compared with full-term adolescents regarding visual and orthoptic status.

Methods: The MLP group consisted of 50 adolescents (26 girls; mean gestational age (GA) 35.0 weeks; mean age 16.5 years). Exclusion criteria were chromosomal abnormalities, severe malformations, syndromes, or being born to mothers with severe chronic diseases. Presently, the age-matched controls consisted of 35 adolescents (mean GA 40.4 weeks; mean age 16.6 years). Visual acuity (VA), refraction, motility, strabismus, convergence, accommodation, stereoacuity, and total axial length (TAL) were examined. Statistical analyses were performed using Fisher's exact test and Mann Whitney U-test.

Results: Mild ($\geq +0.5$ diopter (D) spherical equivalent (SE)) and moderate ($\geq +2.0$ D SE) hyperopia were more commonly found in the MLP group compared with controls (mild: 39/47 vs 19/34, $p=0.012$; moderate: 9/47 vs 1/34, $p=0.039$). Mild (≤ -0.5 D SE) and moderate (≤ -1.0 D SE) myopia were more frequently seen in the control group (mild: 2/47 vs 8/34, $p=0.015$; moderate: 1/47 vs 6/34, $p=0.038$). The TAL was shorter in the MLP group (right eye: mean \pm standard deviation (SD) 23.0 ± 1.2 mm vs 23.6 ± 0.8 mm, $p=0.024$; left eye: 22.9 ± 1.3 mm vs 23.6 ± 0.8 mm, $p=0.027$). Stereoacuity >60 seconds of arc was more commonly shown in the MLP group (17/50 vs 4/34, $p=0.023$). There was no significant difference between the groups regarding VA, strabismus, motility, convergence, or accommodation.

Conclusions: In the present study, both mild and moderate hyperopia were more commonly found in the MLP group at 15–18 years of age. Accordingly, myopia was more frequently shown in full-term adolescents. This was also reflected by the shorter TAL in the MLP group. Furthermore, subnormal stereoacuity was more commonly found in MLP adolescents. There was no significant difference concerning VA, strabismus, motility, convergence, or accommodation.

CONTROL ID: 3546275

SUBMITTER (NAME ONLY): Samuel Taylor

TITLE: Association of Age-related Macular Degeneration with Exfoliation Syndrome: The Utah Project on Exfoliation Syndrome

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Taylor, C. Paulson, C.J. Pompoco, K. Curtin, B.C. Stagg, B.M. Wirostko, Moran Eye Center, University of Utah Health, Salt Lake City, Utah, UNITED STATES|R. Ritch, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Exfoliation syndrome (XFS) is associated with COPD, obstructive sleep apnea, hernias, and atrial fibrillation. Studies suggest XFS may share pathogenetic relationships with age-related macular degeneration (AMD) due to underlying elastin and basement membrane dysfunction and repair. A retrospective analysis was conducted to assess the association between XFS and AMD.

Methods: Subjects were identified in the University of Utah Healthcare System (UUHCS) with an XFS diagnosis (ICD-9 codes 365.52 and 366.11) from 1996-2015. A conditional logistic regression accounting for individual matching on age and sex and adjusted for race, ethnicity, obesity, smoking history, and hypertension history was performed. The risk of AMD was estimated in patients age ≥ 60 y on 1/1/1996 (when electronic records became available) with an ICD-9 AMD diagnosis: 362.50 (unspecified/presumed nonexudative ('dry') if no history of exudative ('wet') AMD, 362.51 (dry AMD), 362.52 (wet AMD), 362.57 (drusen). Random non-XFS UUHCS controls matched 5:1 on age and sex comprised the comparison group for assessing AMD risk in this cross-sectional analysis.

Results: Of 3,082 UUHCS patients with an XFS diagnosis, 562 (18.2%) were positive for a diagnosis of any type of AMD. Of 15,418 controls, 1,160 had a history of any type of AMD (7.5%) (OR= 2.79; 95% CI= 2.47-3.10; $P<0.0001$). 245 (8.0%) of XFS patients and 347 (2.3%) of controls had a diagnosis history of wet AMD (OR=3.76; 95% CI= 3.16-4.47; $P<0.0001$). 300 (9.7%) XFS patients and 765 (5.0%) controls had a diagnosis of dry AMD (OR= 2.03; 95% CI= 1.76-2.34; $P<0.0001$). In XFS patients, increased risk of a wet AMD diagnosis was significantly higher than that of dry AMD (non-overlapping confidence intervals). Drusen, a very small group, was not analyzed separately.

Conclusions: XFS patients may have an increased risk of both wet and dry AMD compared to those without XFS. The increased risk of AMD associated with XFS was greater for wet AMD than dry AMD. XFS patients need to be followed closely for both AMD and glaucoma. Continued data analysis will explore associations at an individual eye level.

CONTROL ID: 3546276

SUBMITTER (NAME ONLY): Viral Kansara

TITLE: Suprachoroidally delivered DNA nanoparticles produce human Myosin7A protein in RPE-choroid in rabbits

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Kansara, L. Muya, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES|M.J. Cooper, R. Moen, Copernicus Therapeutics Inc., Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adeno-associated viral vectors (AAV) cannot accommodate large genes such as Myosin7A, limiting investigational gene therapy for Usher syndrome. A prior preclinical study demonstrated that non-viral DNA nanoparticles (DNPs), which can accommodate large genes, yield similar marker gene activity when administered suprachoroidally or subretinally, suggesting the potential for office-based gene therapy. This study evaluated ocular tolerability and transfectability of DNPs encoding human Myosin7A (hMyo7A) after either suprachoroidal (SC) or intravitreal (IVT) injection in rabbits.

Methods: The DNPs consisted of a single copy of plasmid DNA encoding hMyo7A. Dutch-Belted pigmented rabbits (N=4 per group) received a single SC (0.1 mL) or IVT injection (0.05 mL) of DNPs (either 4 or 8 mg/mL of DNA). Ocular tolerability, with or without prophylactic steroids, was assessed via slit lamp, indirect ophthalmoscopy, intraocular pressure (IOP), optical coherent tomography (OCT), electroretinography (ERG) and fundus photography (FP) for up to 3 months. Protein and RNA levels were measured in ocular tissues via ELISA and qRT-PCR, respectively at 3 months.

Results: OCT imaging confirmed reversible opening of the suprachoroidal space after SC injection of DNPs. The SC injection of DNPs was much better tolerated than IVT injection of DNPs. During the 3- month study, IVT injected DNPs resulted in signs of severe ocular inflammation as assessed by slit lamp, indirect ophthalmoscopy, OCT, FP, and ERG testing. Prophylactic steroid treatment showed no clinically meaningful improvement in ocular inflammation after IVT injections. The hMyo7A protein was detected in the RPE-choroid (68-105 ng/gm) at 3 months after SC or IVT injection with no statistically significant difference between the routes of administration. The hMyo7A protein levels were detected in sporadic retina samples. The RT-PCR data indicate that DNPs produce mRNA levels in the RPE-choroid that is in the range of 45%-160% of the endogenous rabbit Myo7A.

Conclusions: Suprachoroidally administered DNPs produced hMyo7 protein in RPE-choroid in rabbits. Given the potential for repeatable office-based large gene therapy, further studies are warranted to improve transfection of photoreceptor cells, and to evaluate efficacy and safety in higher species

CONTROL ID: 3546278

SUBMITTER (NAME ONLY): Margaret Maes

TITLE: A modified AAV2/6 enhances retinal microglial transduction in a layer-specific manner

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Maes, G. Wögenstein, G. Colombo, S. Siegert, Institute of Science and Technology Austria, Klosterneuburg, Niederösterreich, AUSTRIA|

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ABSTRACT BODY:

Purpose: Microglia are a critical component to retinal homeostasis and disease progression, yet we still lack an effective strategy to manipulate them in vivo. Adeno-associated viruses (AAVs) are a widely used tool for transducing cells in the retina, and can also be translated to the clinic for targeted gene therapy approaches. So far, targeting microglia with AAV in the retina has not been explicitly addressed, since microglia transduction in other CNS regions has proven to be challenging.

Methods: We performed intravitreal and subretinal injections in adult C57Bl6/J mice using a self-complementary capsid-modified AAV2/6^{TYF} harboring the GFP transgene under the microglia-specific CD68 promoter (scAAV2/6^{TYF}-CD68-GFP). Then, we modified the viral capsid to reduce interaction with heparin-binding sites, and finally, we inserted a double-floxed inverted open reading frame (DIO) into the AAV2 transfer vector (scAAV2/6^{d4}-CD68-DIO-GFP) to increase specificity. Two weeks post-injection, we performed immunostaining for GFP and the ionized calcium binding adaptor molecule 1 (Iba1), which labels the entire microglial population. We quantified the ratio of GFP/Iba1 double-positive cells to total Iba1-positive cells within each plexiform layer to determine microglial transduction efficiency.

Results: Subretinal or intravitreal injection of scAAV2/6^{TYF}-CD68-GFP showed greater microglial transduction efficiency in the plexiform layer closest to AAV delivery location. However, the overall transduction efficiency was low regardless of injection method, and non-specific transgene expression was prominent, especially in photoreceptors and Müller glial cells. Subretinal injection of our modified scAAV2/6^{d4}-CD68-DIO-GFP resulted in microglia-specific transgene expression and moderately increased transduction efficiency in the outer plexiform layer (OPL). Strikingly, we observed up to a three-fold increase in microglial transduction efficiencies under conditions that stimulate microglia.

Conclusions: We show that AAV-mediated microglial transduction in the retina is feasible, yet remains a challenge. Our modified AAV2/6^{d4} was microglia-specific and increased microglial transduction in the OPL, however our results suggest that additional factors contribute to substantial increases in transduction efficiency. Future work will need to identify how the retinal environment impacts AAV-mediated microglial transduction.

CONTROL ID: 3546279

SUBMITTER (NAME ONLY): Lake Larson

TITLE: Energy-dependent increases in femtosecond laser-induced ablations delivered to retinal surface

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Larson, J. Wang, D. Umstadter, Physics and Astronomy, University of Nebraska-Lincoln, Lincoln, Nebraska, UNITED STATES|Y. Zhou, Vet and Biomedical Sciences, University of Nebraska-Lincoln, Lincoln, Nebraska, UNITED STATES|D.E. Anderson, R. Xu, R.R. Krueger, Ophthalmology and Visual Science, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|G. Yoon, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our overall objective is to develop a femtosecond laser system designed to deliver pulses aimed at preventing and treating vitreoretinal disease. Here, we sought to determine the feasibility of delivering our laser to in vitro retinal surfaces, detect pulse energy-dependent changes in laser-induced burn patterns, and measure how vitreous degenerates pulse morphology.

Methods: In Experiment 1, equatorially bisected pig eyes (n=2) were mounted in our laser system. Single-shot ultra-short laser pulses (800nm; 10mm diameter spot size; 28fs pulse duration) were delivered from a Ti:Sapphire chirped-pulse-amplification laser system. Pulse duration was measured by a Frequency-Resolved Optical Gating (FROG) system and compressed by optimizing diffraction-grating optical compressor spatial parameters. Laser-induced retinal burns were imaged using scanning-electron microscopy. Total burn area was measured using ImageJ. One-way analysis of variance (ANOVA) was used to assess effects of pulse energy on burn area. In Experiment 2, laser pulses were passed through: (1) empty glass container; (2) glass container filled with pig vitreous to 20mm depth; and (3) same condition as (2) with compensated pulse parameters. Full-width half maximum (FWHM) of the pulse temporal and spectral profiles were extracted from FROG measurements.

Results: In Experiment 1, femtosecond laser-induced burns were observed in retinae. Total burn area ($\text{mm}^2 \pm \text{SD}$) was measured across four energy levels: 12nJ ($2,346.7 \pm 378.8$; n=4), 115nJ ($4,968.1 \pm 347.1$; n=2), 12mJ ($15,220.4 \pm 6974.3$; n=5), 21mJ ($7,174.1 \pm 2388.9$; n=5). One-way ANOVA revealed an effect of laser energy on total burn area ($F(3,12)=7.52$, $p=.0043$). In Experiment 2, vitreous degenerated pulse morphology. Relative to the empty glass container, 20mm of vitreous introduced a 78% increase in temporal FWHM and a 4% increase in spectral FWHM. Compensating for pulse morphology degeneration, by contrast, produced a 4% decrease in temporal FWHM and a 16% decrease in spectral FWHM relative to empty glass container.

Conclusions: Our femtosecond laser delivers ablative pulses that scale with pulse energy. Vitreous imposes non-zero degenerative effects on laser pulse morphology that can be corrected. These results will be informative for further developing this system to deliver therapeutic laser pulses aimed at preventing and treating vitreoretinal disease.

CONTROL ID: 3546280

SUBMITTER (NAME ONLY): Uwe Wolfrum

TITLE: Expression and subcellular localization of USH1C/harmonin in the human retina

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The human Usher syndrome (USH) is the most frequent cause of inherited combined deaf-blindness. USH1C encodes for the scaffold protein harmonin organizing the USH protein interactome. We aimed to decipher the expression profiles of harmonin isoforms and analyzed harmonin's subcellular localization in the cells of the human retina.

Methods: We analyzed and quantified the expression of harmonin isoforms in human retina by RT-PCR, RNAseq and Western blotting. Harmonin localization was studied in human and non-human primate retinas by immunofluorescence (LM) and immunoelectron (EM) microscopy. Protein-protein interactions were analyzed by co-immunoprecipitations and in situ proximity ligation assays.

Results: Although at least 20 harmonin isoforms were identified in the human retina, harmonin-a1 is the most frequently expressed variant. Bulk RNAseq of retinal cell populations revealed not only abundant expression in Müller glia cells, but also in retinal neurons including photoreceptor cells. LM and EM revealed harmonin localization in endfeet and apical microvilli of Müller glia cells. In photoreceptor cells, we found harmonin at adhesion complexes in the outer limiting membrane and calyceal processes of the inner segment. In addition, harmonin was detected in the synaptic pedicles of cones. In contrast, in rods, it was most abundant in the outer segments (ROS).

Conclusions: Our data are valuable for both gene therapy development and retinal cell biology. We identified harmonin-a1 as the most abundant harmonin isoform in human Müller glial and photoreceptor cells. Therefore, for gene therapy, we propose retinal delivery of harmonin-a1 using a vector that transduces both cell types. We hypothesize that harmonin organizes protein networks associated with the actin cytoskeleton in those cells. Of note, harmonin in ROS may participate in disk staking by interacting with actin and rhodopsin. Defects in harmonin might cause disruption of these protein networks and thus of retinal cell maintenance, leading to the retinal pathophysiology phenotype of USH1C.

CONTROL ID: 3546283

SUBMITTER (NAME ONLY): Erin Burnight

TITLE: Developing a CRISPR-mediated safe harbor strategy to correct patient-derived induced pluripotent stem cells

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.R. Burnight, L.R. Bohrer, J.A. Cooke, D. Ochoa, C.L. Ralston, E.L. Geary, M.A. Luse, R.F. Mullins, E.M. Stone, B.A. Tucker, Ophthalmology and Visual Sciences, University of Iowa, Iowa City, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: CRISPR-Cas9 genome editing has revolutionized basic and translational vision research. The ability to select for corrected disease-causing variants provides an effective strategy in disease modelling and development of cell therapy for inherited retinal diseases. However, in some cases the placement of the selection cassette interferes with expression from the target locus. We hypothesized that delivering CRISPR-Cas9 reagents, a donor template targeting the locus of interest, and a donor template carrying the selection cassette targeting a separate locus would address selection-based transcriptional interference at the intended locus. The purpose of this study was to develop a co-targeting strategy employing the AAVS1 safe harbor site as a selection locus.

Methods: We created a plasmid carrying a *S. pyogenes* Cas9 expression cassette and single guide RNA expression cassettes targeting both the locus of interest and the AAVS1 site. The CRISPR-Cas9 expression plasmid, a donor template carrying homologous sequence to the locus of interest, and a donor template carrying a puromycin selection cassette flanked by AAVS1 homology sequence were delivered to human cells via cationic lipid transfection and cultured under puromycin selection for 10-14 days. Genomic DNA was isolated from puromycin resistant clones and screened for modification at the locus of interest via PCR.

Results: We cloned and screened single guide RNAs targeting five loci: CRX, GRK1, VSX2, USH2A, and CEP290. We achieved successful co-targeting at all five loci as revealed by amplification of donor-target junctions and RFLP analysis. Clonal analysis at three loci – CRX, GRK1, and VSX2 – indicated co-targeting in 5%, 20%, and 35% of puromycin-resistant clones, respectively.

Conclusions: This work may accelerate the development of CRISPR-Cas9 therapies for inherited retinal dystrophies.

CONTROL ID: 3546284

SUBMITTER (NAME ONLY): Muhammad Abdulrazik

TITLE: Analyzing lubricant eyedrop touchdown and motion on dry ocular surface

SESSION TITLE: Corneal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Abdulrazik, Innovative Therapeutic Algorithms, East Jerusalem Biomedical Institute, East Jerusalem, PALESTINE, STATE OF

Commercial Relationships Disclosure (Abstract): Muhammad Abdulrazik: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Effective biotribological lubrication of dry ocular surface was reported as correlating with ocular comfort score and needs a minimum lubricant film thickness to be sustained significantly above thickness of natural tear film. This study aimed to analyze the dynamic interactions between lubricant droplet and ocular surface and to introduce the rate of droplet thinning, while droplet is spreading, as a benchmark for predicting lubricant biotribological merits.

Methods: Droplet touchdown on ocular surface triggered the recording of droplet motion. Ten frames per second were captured from AVI movie, framing a 40 microliter lubricant droplet above a face-up placed ocular surface of freshly excised rabbit eyeglobe at induced dry eye condition. Droplet boundaries, its contact angle and droplet cross-section width were auto-determined from captured frames by FTA-188 algorithm (First Ten Angstroms Inc.) allowing the extraction of droplet central-height (h) and base-area radius (r). Studied lubricants were cationic (CEM) and anionic (AEM) nanoemulsions (core oil, emulsifier, surfactant, and cationic or anionic entity) and polyanionic hyaluronate 0.1% (SH).

Results: Spreading of CEM droplet was swift and its height (h[CEM]) fell sharply. Between 0.1 and 0.3 seconds after touchdown, h[CEM] went from 0.5 ± 0.1 mm to 0.3 ± 0.1 mm ($p = .0291$) and then down to an approaching-zero plateau after 2 seconds. In contrast, the droplet height of AEM and SH went down moderately. In the 1-10 seconds interval, h[AEM] went down from 1.7 ± 0.3 to 1.2 ± 0.2 mm ($p = .0715$), and h[SH] went down from 2 ± 0.8 to 1.2 ± 0.6 mm ($p = .2321$). Regression analysis of h and r relationship returned $h = 0.4658e[-0.063r]$ ($R^2 = 0.9655$) for CEM, $h = 5.9312e[-0.354r]$ ($R^2 = 0.9993$) for AEM and $h = 3.9905e[-0.217r]$ ($R^2 = 0.9692$) for SH.

Conclusions: CEM droplet swift spreading reflects, in part, the electrostatic attraction of the cationic CEM to the anionic entities that dwell at ocular surface. Yet, the associated swift thinning of CEM droplet is not corresponding with favorable biotribological merits. In contrast, biotribological features can still be realized for the anionic AEM and SH, as both sustained a minimum film thickness significantly above thickness of natural tear film. The results showcase the merits of lubricant droplet motion imaging after topically applying a droplet on ocular surface and introduce the thinning rate of lubricant droplet as a biotribological benchmark.

CONTROL ID: 3546287

SUBMITTER (NAME ONLY): Christy Sheehy

TITLE: Inter & intra-day variability of microsaccades as recorded by the tracking scanning laser ophthalmoscope (TSLO)

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Sheehy, S. Condor-Montes, D. Bennett, L. Rani, A.J. Green, Neurology, University of California San Francisco, San Francisco, California, UNITED STATES|E. Bensinger, School of Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|E. Bensinger, Vision science graduate group, University of California Berkeley, Berkeley, California, UNITED STATES|A.J. Green, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantify inter & intra-day variability of microsaccades in a cohort of young, healthy controls.

Methods: We used a custom-built retinal tracker, the TSLO, to record microsaccades in a cohort of 14 healthy controls, ages < 40 years, at 9 different time points (3x a day (morning, afternoon & evening), for 3 days). Each session had 3 videos recorded per eye (6 traces per subject per session). Individuals were instructed to fixate for 10s on the upper right-hand corner of a 5°x5° imaging raster. Microsaccade characteristics of frequency, amplitude, peak velocity, & peak acceleration were calculated & compared for all time points to determine inter & intra-day variability & overall variation between subjects. Descriptive statistics were used to characterize measures of central tendency & variation for each of the microsaccade metrics.

Results: Our sample consisted of 14 participants, 121 sessions, & 608 traces. Participants had an average (std) microsaccade frequency of 0.84 Hz (0.52), average amplitude of 0.32° (0.11), average peak velocity of 43.68 °/s (14.02), & average peak acceleration of 13,920.04 °/s² (4,186.84). In general, we found only modest evidence of variability between traces, with consistently higher peak velocity &/or acceleration values for the 1st trace of each session. Trace 2 had a significantly lower average peak velocity of 3.93 °/s (p=0.02) & lower peak acceleration of 1,312.30 °/s² (p=0.023) than trace 1. Additionally, trace 3 had a significantly lower average peak acceleration than trace 1 by 1,657.14 °/s² (p=0.009). We detected a negligibly higher vertical velocity of 1.75 °/s (p=0.017) in trace 3 when compared to trace 2. Microsaccade frequency was the only metric to have a significant time of day difference, with evening values being slightly higher than morning recordings (0.098 Hz, p=0.007). We found no statistically significant differences in day-to-day measurements & no significant learning effect from session to session was observed in the metrics.

Conclusions: Utilizing our fixation stimuli & a 10 second recording paradigm, trace 1 showed statistical differences when compared to subsequent traces within a session. We saw a modest increase in the number of microsaccades between morning & evening sessions. No statistically significant differences in day-to-day measurements of microsaccades were observed, revealing no significant learning effect.

CONTROL ID: 3546289

SUBMITTER (NAME ONLY): Raymond Fang

TITLE: Measuring the Volume of the Limbal Crypts with visible-light Optical Coherence Tomography

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Fang, L. Beckmann, H. Zhang, Northwestern University, Evanston, Illinois, UNITED STATES|A.R. Djalilian, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Raymond Fang: Commercial Relationship: Code N (No Commercial Relationship) | Lisa Beckmann: Commercial Relationship: Code N (No Commercial Relationship) | Ali Djalilian: Commercial Relationship: Code N (No Commercial Relationship) | Hao Zhang: Commercial Relationship(s);Opticent Health:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Structural changes of the limbal stem cell niche are unknown in many ocular pathologies. Although studies have characterized the shape of the focal stromal projections of the palisades of Vogt, there is a dearth of studies examining the macroscopic structure of the limbal crypts. Consequently, a method for measuring the volume of the limbal crypts using visible-light optical coherence tomography (vis-OCT) imaging was developed.

Methods: One ex vivo human eye, positioned in a region where the palisades were most visible, was imaged with vis-OCT. A raster scan pattern with a field of view of 1 mm by 1 mm was used to acquire two images of the eye at different times and slightly different locations. For volume calculation, the first step was to identify the surface of the limbus. A combination of thresholding, outlier removal, and 3D parabola fitting was used to determine this surface. Next, the boundary of the stromal projections was identified. The inverse gradient was calculated and a fast marching scheme using the inverse gradient found the boundary of the stromal projections. An initial mask found from a threshold that under segmented the limbal crypts was used as a seed for the marching algorithm. An alternate method based on manual thresholding to find the stromal projection surface was implemented for comparison. The volume of the limbal crypts is the volume between the limbal surface and stromal projections.

Results: Repeated measurements of limbal crypt volume at slightly different locations yielded volume measurements of 3.5×10^7 cubic microns and 2.7×10^7 cubic microns. Volume changed by less than 2% as parameters differed when the fast marching scheme was used to determine the stromal projection boundary. However, volume changed by up to 27% when different manual thresholds were used.

Conclusions: We developed a method that is robust to changes in parameters for measuring the volume of limbal crypts. Such measurement has the potential to serve as a parameter for monitoring the health of the stem cell niche. However, additional investigation is needed to examine the consistency and capability in identifying pathological alterations.

CONTROL ID: 3546292

SUBMITTER (NAME ONLY): Jesus Jose Ferre Fernandez

TITLE: Deletion of conserved non-coding elements downstream of foxc1a in zebrafish affects its expression and produces ocular phenotype

SESSION TITLE: (Gen)omics and molecular mechanisms of ocular disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Ferre Fernandez, S. Muheisen, S. Thompson, E.V. Semina, Medical College of Wisconsin Department of Pediatrics, Milwaukee, Wisconsin, UNITED STATES|R.F. Collery, E.V. Semina, Department of Ophthalmology and Visual Sciences, Medical College of Wisconsin, Milwaukee, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: FOXC1 is a transcription factor involved in heart, craniofacial and ocular development in vertebrates. Mutations in FOXC1, along with mutations in PITX2, cause Axenfeld-Rieger syndrome (ARS) and explain approximately half of the ARS cases. However, there is still a significant number of patients with an unknown genetic cause. Expression and activity of transcription factors involved in development are finely controlled by their regulatory elements that are often evolutionarily conserved. It has been shown that mutations in those regulatory elements could be also pathogenic. The goal of this project is to discover regulatory elements for FOXC1 using zebrafish as a vertebrate model and relate this information to human eye development and disease.

Methods: BLAST alignments involving regions surrounding human FOXC1 and two orthologous zebrafish genes foxc1a and foxc1b were carried out to identify conserved sequences. CRISPR-Cas9 was used to generate zebrafish lines carrying deletions for the identified conserved elements. The obtained lines were characterized by gross morphology examination, OCT and histology analysis. Expression of foxc1a and foxc1b genes and encoded proteins was assessed by RT-qPCR, in situ hybridization with RNAscope probes and immunohistochemistry.

Results: We identified 3 elements downstream of human FOXC1 and 1 element upstream of FOXC1 that were conserved in zebrafish foxc1a or in both foxc1a and foxc1b. The deletion of a 152kb intergenic region comprising all 3 downstream elements (Δ CED1-3) resulted in a downregulation of both the foxc1a transcript and protein in developing zebrafish embryos. Homozygous Δ CED1-3 larvae die at 1 month post fertilization and present with enlarged anterior chambers of the eye and a significant pericardial and other organs' edema. Deletion of an 82.7Kb region containing only 2 out of the 3 downstream conserved elements (Δ CED2-3) produced a similar but milder phenotype. Deletion of elements upstream either foxc1a (Δ CEU1a) and foxc1b (Δ CEU1b) did not produce a visible phenotype.

Conclusions: The identified downstream conserved elements are essential for normal foxc1a expression and their deletion results in a phenotype consistent with foxc1/FOXC1 deficiency in zebrafish and humans. Further studies of these regions in human patients is likely to explain additional ARS cases.

CONTROL ID: 3546293

SUBMITTER (NAME ONLY): Mahavir Singh

TITLE: c-TBI Induced Ocular Dysfunction and its Mitigation by RIC

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Singh, A.K. George, R.P. Homme, D. Stanisic, J. Behera, N. Tyagi, S.C. Tyagi, Physiology, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: While cortical traumatic brain injury (c-TBI) is a leading cause of mortality, and morbidity worldwide, there are no effective pharmaceutical interventions for this condition. It is induced by a combination of complex primary, and secondary mechanisms that give rise to cellular death, inflammation, and neurological dysfunction in c-TBI patients. Furthermore, hyperhomocysteinemia (HHcy) led metabolic malfunctioning is a significant biological variable that could further contribute, and add to c-TBI heterogeneity, and related pathophysiology. Since remote ischemic conditioning (RIC) exerts endogenous protective effects that has the potential to become a therapeutic treatment in such complex medical conditions. Therefore, to understand the mechanisms of c-TBI derived neurological damage during HHcy, as well as the approaches that might promote its mitigation could help guide the development of therapeutic modalities for c-TBI patients that suffer from ocular dysfunction.

Methods: To study neurological injury to the eye in c-TBI patients, we used experimental groups of mice as follows: (i) Wild type C57BL/6J (WT), (ii) WT+ c-TBI, (iii) WT+RIC, (iv) WT + c-TBI + RIC, (v) CBS⁺/-, (vi) CBS⁺/- +c-TBI, (vii) CBS⁺/- + RIC, and (viii) CBS⁺/- + c-TBI + RIC. Retinal layers architecture, and intraocular pressure (IOP) were measured by optical coherence tomography (OCT), and tonometry. Vision guided behavior was tested in a light-dark chamber along with measurement of retinal functions via electroretinography (ERG). In addition, immunohistochemistry fluorescent antibody analysis was performed by confocal microscopy, and the retinal fluorescent angiography analysis was also carried out employing funduscopy. Our further investigations employing chromatin immunoprecipitation (ChIP) assay, creatine kinase (CK) analysis, zymography, western blotting, and Immunohistochemistry analyses aided in understanding the mechanistic of neurological injury to the eye.

Results: Interestingly, RIC was found to alleviate some of the detrimental effects to the eye in the HHcy mice that underwent experimental c-TBI manipulations.

Conclusions: This work highlights therapeutic potential of RIC towards reversing the harmful effects of c-TBI on vision especially during HHcy metabolic malfunctioning.

CONTROL ID: 3546295

SUBMITTER (NAME ONLY): Jose Javier Garcia-Medina

TITLE: The macula in dyslexia: a comparative OCT study.

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Garcia-Medina, E. Rubio-Velazquez, J. Zafra-Perez, Ophthalmology, Hospital General Universitario Jose M Morales Meseguer, Murcia, Murcia, SPAIN|N. Bascuñana-Mas, A. Palazon-Cabanes, Hospital General Universitario Reina Sofia, Murcia, Murcia, SPAIN|J. Garcia-Medina, Universidad de Murcia, Murcia, Murcia, SPAIN|M. Del-Rio-Vellosillo, Hospital Clinico Universitario Virgen de la Arrixaca, El Palmar, Murcia, SPAIN|M.D. Pinazo-Duran, Universitat de Valencia, Valencia, Comunitat Valenciana, SPAIN|

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ABSTRACT BODY:

Purpose: To compare thickness of different retinal segmentations between dyslexic individuals and controls at the macula, including the fovea, the parafovea and the perifovea.

Methods: Twenty dyslexic volunteers and twenty age- and sex-matched non-dyslexic controls underwent macular optical coherence tomography (OCT) scans in both eyes using the Early Treatment Diabetic Retinopathy Study protocol. The thickness of the fovea, 4 sectors of the parafovea and 4 sectors of the perifovea (temporal, nasal, superior and inferior sectors) were considered in the following segmentations: complete retina, outer retina, inner retina, outer nuclear layer + outer plexiform layer + inner nuclear layer (ONL+OPL+INL) and ganglion cell complex (GCC). The results of the right and left eyes were independently compared between groups.

Results: Significantly higher thickness in all the sectors of the parafovea and some sectors of the perifovea, but not the fovea, was found in right and left eyes in complete retina and inner retina in the dyslexic group. Plus, all sectors of the macula of ONL+OPL+INL in both eyes (including the fovea) were significantly thicker in the dyslexic group. In contrast, no thickness differences between both groups were found in any of the sectors of GCC or outer retina in any eye.

Conclusions: Middle retinal segmentation (ONL+OPL+INL) at the macula is thickened in dyslexia in both eyes as measured by OCT. This fact seems to induce thickening in inner retina and complete retina results at the macula in the context of this disorder. Considering that a certain degree of integration of visual stimuli takes place at middle retinal layers our results suggest that the retina could play a role in the development of the dyslexia.

CONTROL ID: 3546296

SUBMITTER (NAME ONLY): Reena Bapputty

TITLE: Diabetes modulates iodothyronine deiodinase 2 expression in the retina

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Bapputty, R. Gubitosi-Klug, Pediatric Endocrinology, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Reena Bapputty: Commercial Relationship: Code N (No Commercial Relationship) | Rose Gubitosi-Klug: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Clinical investigations associate hypothyroidism with an increased risk for microvascular complications, yet the role of thyroid hormone in the development of diabetic retinopathy is not clearly understood. The purpose of the current study is to investigate 1) thyroid hormone activating enzyme iodothyronine deiodinase 2 (Dio2) levels ex vivo in the retinas of diabetic and non-diabetic mice, 2) Dio2 expression in vitro in retinal cells grown in high glucose conditions, 3) effect of thyroid hormone supplementation on high glucose-mediated cell death in primary mouse retinal microvascular endothelial cells (mREC).

Methods: Dio2 gene expression was measured in control and 12-week streptozotocin-induced diabetic mouse retina by RNA sequencing and Real-time PCR. Mouse retinal microvascular astrocytes and mREC were cultured in normal (5 mM) or high glucose (25 mM) and Dio2 protein level was quantified in cell lysates by western blotting. Cell death was measured by trypan blue exclusion assay.

Results: Diabetes caused a significant decrease in Dio2 transcripts in the retina ($P=0.004$) and an overall 50% decrease ($p=0.0001$) in Dio2 gene expression in the retinas of diabetic mouse compared to non-diabetic mice. Retinal cells grown in high glucose demonstrated a significant reduction of Dio2 protein level in both mouse retinal astrocytes ($p=0.002$) and endothelial cells ($p=0.02$). Moreover, a significant protective effect of thyroid hormone supplementation on high glucose-induced endothelial cell death was observed with active hormone (T3) ($P=0.0079$) but not with prohormone (T4), supporting a loss of Dio2 activity in the presence of high glucose conditions.

Conclusions: Decreased intraretinal, active thyroid hormone level due to diabetes-induced loss of Dio2 may lead to apoptosis of both vascular and neuronal cells in the retina, a contributing factor to the pathogenesis of early diabetic retinopathy.

CONTROL ID: 3546298

SUBMITTER (NAME ONLY): Seth Fortmann

TITLE: TREM2+ choroidal macrophages regulate vascular and lipid homeostasis in the choroid and are lost in age-related macular degeneration (AMD)

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Fortmann, R. Rosencrans, Y. Adu-Agyeiwaah, M.B. Grant, Ophthalmology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|H. Patton, Biomedical Engineering, The University of Alabama at Birmingham School of Engineering, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Choroidal macrophages (cMΦ) are the predominant resident immune population in the choroid, and our goal is to characterize cMΦ heterogeneity and transcriptomic states in health and disease.

Methods: We reanalyzed publicly available bulk and single-cell RNA-sequencing (scRNA-seq) data from the choroids of 150 non-diseased and AMD donors (scRNA-seq: 7 controls, 2 AMD; bulk RNA-seq: 115 controls, 26 AMD).

Results: We identified 5 predominant myeloid populations including classical monocytes, nonclassical monocytes, conventional dendritic cells, monocyte-like macrophages, and cMΦ. cMΦ displayed a unique transcriptomic profile that was enriched for genes/pathways involved in phagocytosis, lipid metabolism, and immunosuppression. Of note, cMΦ contained uniquely high levels of TREM2 expression, a lipoprotein receptor that regulates the phagocytosis and removal of excess lipid. In macular AMD samples, cMΦ displayed a reduction in relative abundance and a transcriptomic shift that included upregulation of MHCII and NF-κB target genes and downregulation of TREM2 signaling modules. To expand our findings, we used bulk RNA-seq deconvolution and found a significant decrease in cMΦ in macular AMD samples (macular control=4.4%, macular AMD=1.6%, $p=0.006$). We confirmed that mouse cMΦ express TREM2 at baseline using publicly available scRNA-seq, immunofluorescence, western blot, and RT-qPCR. To test the hypothesis that TREM2 expression in cMΦ regulates vascular maintenance and lipid removal, we challenged TREM2 knock-out mice (TREM2KO) with 15wk of high-fat diet (HFD). Compared to WT mice on HFD, TREM2KO HFD mice showed an accelerated loss of visual function, assessed using optokinetic nystagmus (percent change from baseline at 10wk HFD: WT=-2.9% [$p=0.24$], TREM2KO=-20.9% [$p=0.0004$]). At 15wk of HFD, TREM2KO mice showed significantly decreased choroidal thickness on OCT (WT=49.5μm, TREM2KO=45.9 μm, $p=0.009$), significantly decreased choroidal vascular density in whole mount stains (vascular to avascular ratio: WT=1.6, TREM2KO=1.3 [$p=0.04$]) and significantly increased neutral lipid droplets (mean pixel intensity: WT=21.0, TREM2KO=25.9 [$p=0.04$]).

Conclusions: Together, these findings expand our understanding of cMΦ heterogeneity, abundance, and expression profiles in health and AMD, and identify TREM2 as a novel regulator of choroidal homeostasis that is lost in disease.

CONTROL ID: 3546301

SUBMITTER (NAME ONLY): Prisca Bustamante

TITLE: Potential mechanism of action of Mifepristone as antitumor treatment in Uveal melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Goyeneche, C. Telleria, J.V. Burnier, Department of Pathology, McGill University, Montreal, Quebec, CANADA|P.R. Bustamante, A. Laskaris, A.A. Goyeneche, M.N. Burnier, J.V. Burnier, Research Institute of the McGill University Health Centre, McGill University, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Mifepristone is an antiglucocorticoid and antiprogesterone drug that has emerged as a promising anti-cancer therapeutic agent. Our laboratory has previously shown mifepristone as a potent growth inhibitor of uveal melanoma (UM) cell lines. However, the mechanism of how mifepristone works on UM cells is still unclear. This work aimed to investigate the receptors possibly responsible for the observed actions of MF on UM.

Methods: Human MP41, MEL270 and OMM2.5 UM cell lines were used to analyze the mRNA expression of progesterone receptor (PR), progesterin and adipoQ receptor family member 8 (PAQR8), membrane-associated progesterone receptor component 1 (PGRMC1) and component 2 (PGRMC2), as well as the glucocorticoid receptor, receptor subfamily 3 group C member 1 (NR3C1). β -Actin was used as a reference gene. Gene expression was quantified using SybrGreen-based Real Time PCR. UM cells were exposed to vehicle (DMSO) and IC_{50} of mifepristone for 72 H. IC_{50} was detected by the CCK8 assay. RNA was extracted using the RNeasy Plus Micro kit. cDNA was synthesized using iScript. A breast cancer cell line (MCF7) was used as a positive control.

Results: According to gene expression analysis by qPCR, primary MP41 and MEL270 as well as metastatic OMM2.5 cells express the glucocorticoid receptor (NR3C1). UM cells also express the non-classical progesterone receptors: PAQR8, PGRMC1, PGRMC2, while classical nuclear PR appears to be absent. To evaluate the expression of the receptors in the absence and presence of mifepristone, the expression of receptors was quantified after cells were exposed to either vehicle or IC_{50} concentration of mifepristone (20 μ M). We found the expression of NR3C1, PAQR8, PGRMC1, PGRMC2 receptors to be downregulated compared to control conditions. The mRNA levels were normalized using β -Actin.

Conclusions: While non-classical progesterone receptors (PAQR8, PGRMC1 and PGRMC2) and a glucocorticoid receptor (NR3C1) were detected, classical nuclear PR was not found by qPCR in UM cells. Given the lack of PR in UM, the antiproliferative action of mifepristone on UM appears to be independent of classical nuclear PR expression. The cytostatic effect of mifepristone may be through an agonist action of NR3C1 and/or membrane PR such as PGRMC1 and C2. A better understanding of the mechanism of action of mifepristone in UM will help determine its therapeutic potential.

CONTROL ID: 3546304

SUBMITTER (NAME ONLY): Brian Gilger

TITLE: Intracorneal sequential dosing of AAV-ArsB clears corneal opacity associated with mucopolysaccharidosis VI in a feline model

SESSION TITLE: Corneal disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.C. Gilger, J.H. Salmon, D. Roberts, Clinical Sciences, North Carolina State University, Raleigh, North Carolina, UNITED STATES|B.C. Gilger, L. Song, J. Bower, M. Hirsch, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|L. Song, M. Hirsch, University of North Carolina at Chapel Hill Gene Therapy Center, Chapel Hill, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Brian Gilger: Commercial Relationship(s);University of North Carolina:Code P (Patent);NC Biotechnology Center:Code F (Financial Support);RainBio, Inc. :Code I (Personal Financial Interest);Bedrock Therapeutics, Inc:Code I (Personal Financial Interest) | Jacklyn Salmon: Commercial Relationship: Code N (No Commercial Relationship) | Darby Roberts: Commercial Relationship: Code N (No Commercial Relationship) | Liujiang Song: Commercial Relationship(s);University of North Carolina:Code P (Patent) | Jacquelyn Bower: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Hirsch: Commercial Relationship(s);University of North Carolina:Code P (Patent);NC Biotechnology Center:Code F (Financial Support);Rainbio, Inc.:Code I (Personal Financial Interest);Bedrock Therapeutics, Inc.:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Mucopolysaccharidosis VI (MPS VI) is a rare, autosomal recessive lysosomal storage disease caused by mutations in the ArsB gene encoding arylsulfatase B. Corneal blindness in MPS VI remains an important factor compromising quality of life and there is no effective treatment. The purpose of this study is to examine the efficacy, toxicity, and immune response to a single and sequential (opposite eye) intracorneal injection of AAV8-ArsB.

Methods: A MPS VI feline, homozygous for a null ArsB mutation and a second, asymptomatic heterozygote, were acquired at 75 days of age. AAV8 vectors packaged with optimized human ArsB cDNA were validated and characterized in vitro (UNC Gene Therapy Center) and injected unilaterally intracorneally (1e9 viral genomes (vg) / 50 uL volume) at 152 days, while the other eye was injected with PBS. Eight weeks following the initial injection, the opposite cornea was injected with AAV8-ArsB (1e9 vg/50 uL). Ophthalmic examinations (slit lamp biomicroscopy, tonometry, pachymetry, ophthalmoscopy, OCT) were performed prior to and following each injection. Corneal confocal microscopy was performed (endothelial cell counts) at 242 days, followed by euthanasia and histological and molecular tissue analyses.

Results: The homozygote MPS VI feline had diffuse mild corneal opacity and peripheral corneal vascularization that progressed until dosing, while the heterozygote had clear corneas. Following both initial and sequential dosing with AAV8-ARSB, the majority of corneal opacity in the homozygote cleared in AAV8-ArsB corneas within 3 weeks of dosing either cornea and remained clear and without signs of inflammation or immune response through the end of the study (90 days after initial injection). No signs of inflammation or toxicity was noted in either eye in the heterozygote following AAV-ArsB dosing.

Conclusions: Results after intracorneal AAV8-ArsB injections in MPS VI felines demonstrate that corneal intrastromal AAV gene therapy is safe and effective to reverse corneal opacity. Importantly, sequential dosing of the opposite eye with intrastromal AAV8-ArsB was clinically effective to clear corneal opacity with no clinical evidence of an inhibitory capsid antibody response or other adverse effects. These results generate optimism for the efficacy and safety for single dose treatments of corneal abnormalities associated with lysosomal storage disorders.

CONTROL ID: 3546305

SUBMITTER (NAME ONLY): Melisa Zisan Karslioglu

TITLE: The cellular degradative process in epithelial cells of lens capsule with exfoliation syndrome: A preliminary report

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Exfoliation syndrome (XFS) is an age-related systemic disorder involving the accumulation of amorphous protein aggregates within the extracellular matrix of many tissues, especially on the surface of the ciliary body, iris and lens. The autophagy dysfunction that causes a decrease in degradation of both denatured proteins and aging cellular organelles, may be thought to give rise to those aggregates in XFS. The aim of our study is to investigate different autophagy pathways and mitochondrial dysfunction in XFS.

Methods: Anterior lens capsules derived from microincision cataract surgery with XFS (n=13) were collected and compared to anterior lens capsules of age-matched healthy controls (n=17). The samples were placed in RNAlater and stored at -80 °C until they were used. RNA isolation was done and measured with the NanoDrop. The reverse transcription- polymerase chain reaction (RT- PCR) was performed for PTEN- putative kinase 1 (PINK1), PARKIN, BNIP3, NIX and LC3A, LC3B, p62 gene expressions.

Results: The mRNA expressions of PINK1, PARKIN and BNIP3 increased significantly in the lens epithelial cells with XFS compared to healthy controls ($p<0.05$), while the expression of NIX decreased significantly ($p<0.05$). The mRNA expressions of LC3A, LC3B and p62 were not significantly different in the samples with XFS compared to controls ($p>0.05$).

Conclusions: In this study, we found that mitophagy pathways are impaired in the lens epithelial cells with XFS compared to controls. This deterioration may shed light on the pathogenesis of the disease in the light of the impairment of degradative process in specific autophagy pathways and mitochondrial dysfunction. Further studies are needed to evaluate the protein expressions of the above-mentioned genes.

CONTROL ID: 3546307

SUBMITTER (NAME ONLY): Ekaterina Semenova

TITLE: Clinical characteristics and gene expression profile status in young patients with uveal melanoma:
Collaborative Ocular Oncology Group study #2 (COOG2) study

SESSION TITLE: Advances in Diagnosis and Treatment of Uveal Melanoma

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Uveal melanomas (UM) can be divided into prognostic groups based on gene expression profile (GEP) class 1 versus class 2, class 1A versus 1B, and preferentially expressed antigen in melanoma (PRAME) - versus PRAME+. The purpose of this study was to evaluate gthese factors in young patients.

Methods: 1756 patients from 26 centers were enrolled into COOG2 prospective study, all patients had tumor biopsy for genetic analysis. We analyzed clinical and genetic data from 76 patients 18-35 years of age and excluded 7 primary iris lesions resulting in 69 analyzed patients.

Results: A total of 69 patients between 18-35 years were analyzed. Average age was 30 years, with 35 female and 34 male.

3 patients had ocular melanocytosis. 9 tumors involved ciliary body. Largest basal diameter varied from 3 to19.3mm (mean11.5 mm) and tumor thickness 1.2-15.3 mm (mean 5.1 mm).

Primary treatment was brachytherapy with radioactive iodine (I-125) in 56 patients, enucleation 8 in eyes, proton beam therapy in 4 patients and observation in 1 patient. All patients underwent tumor biopsy (transscleral 18 patients, transvitreal 43 and enucleation 8 patients). GEP analysis revealed Class 1A (31 tumors, of them 10 PRAME +), followed by Class1B (27, of them 7 PRAME +) and Class 2 (10 tumors, of them 3 PRAME +).

Follow-up period is 1-56 months (average 19 months). No tumor recurrence was documented. Metastatic disease developed in 1 patient with Class 1A PRAME + large tumor (16 months after treatment, patient died at 37 months follow up).

Conclusions: Most young patients with UM have genomic profile consistent with very favorable prognosis (Class 1A PRAME -), even when they have clinical features that are considered to be high risk. This suggests that endogenous factors, such as immune regulation, may favor the evolution of less aggressive molecular subtypes of UM in younger patients. Further investigation and longer follow up is warranted to elucidate the biological factors in young patients that predispose them to better survival prognosis.

CONTROL ID: 3546308

SUBMITTER (NAME ONLY): JIE WANG

TITLE: Diagnosing and segmenting choroidal neovascularization in optical coherence tomographic angiography using deep learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To diagnose and segment choroidal neovascularization (CNV) in a real-world multi-center clinical optical coherence tomographic angiography (OCTA) dataset.

Methods: In this study, a total of 10125 OCTA scans from 2497 eyes, including 4260 CNV scans and 5865 non-CNV scans, were collected from 5 eye clinics. Selected scans included 3×3-mm and 6×6-mm macular scans. All scans were included regardless of image quality. CNV scans were collected from multiple diseases, including neovascular age-related macular degeneration (AMD), pathological myopia, polypoidal choroidal vasculopathy (PCV), and other rare retinal diseases. The non-CNV dataset consisted of a heterogenous group including healthy controls, non-neovascular AMD, diabetic retinopathy, branch retinal vein/artery occlusion, and central serous chorioretinopathy. Two experts (JW and KT) graded projection resolved OCTA images and manually delineated CNV membrane area using both en face of outer retina and cross-sectional OCTA images. Multiple representations of both en face and volumetric OCT&OCTA were fed into a custom designed hybrid multi-task convolutional neural network (CNN) that produces a CNV diagnosis and membrane segmentation. 5-fold cross-validation was applied to evaluate the performance of the proposed method.

Results: For CNV diagnosis, the sensitivities were 96% and 91% on 3×3-mm and 6×6-mm scans with 95% specificity, respectively. Of all scans with CNV, 2% of CNV scans were incorrect due to segmentation error preventing CNV detection. Of low quality scans (n=993) with a signal strength less than 50, CNV was correctly detected 97.3% of the time. The method was able to accurately diagnose CNV and segment CNV membranes on both 3×3-mm and 6×6-mm in neovascular AMD (Fig.1) and also showed reliable performance on challenging scans in other retinal disease, e.g. PCV, and myopia (Fig.2).

Conclusions: The proposed method can accurately diagnose and segment CNV in a real-world clinical dataset. These results could enable automated CNV screening and quantification in clinic and lead to improved artificial intelligence-aided CNV diagnosis.

CONTROL ID: 3546311

SUBMITTER (NAME ONLY): Sven Schnichels

TITLE: The expression of SARS-CoV 2-receptors in ocular tissue of normal and COVID-19 diseased patients

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Schnichels, D. Süsskind, J.M. Rohrbach, T. Bayyoud, F. Ziemssen, S. Thaler, J. Hurst, University Eye Hospital, Universitätsklinikum Tübingen, Tübingen, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To infect the eye, SARS-CoV 2 needs virus-specific receptors and coreceptors or proteases in the specific ocular tissue. The human angiotensin-converting enzyme-2 (ACE2) receptor represents the major gateway for SARS-CoV 2 to enter cells. Furthermore, the mammalian serine protease TMPRSS2 and the protease furin have been identified as relevant proteases for the interaction of the virus with ACE2. The expression status of these key receptors in ocular tissues is still not fully elucidated.

Methods: The expression profile ACE2, TMPRSS2, and furin were analyzed in fresh and fixed eyes from healthy donors, sections from eyes with other ocular diseases, and eyes from patients, who died from COVID-19. Protein expression was examined via immunohistochemical staining, mRNA expression was analyzed via quantitative real-time PCR.

Results: A relevant difference in the amount of expression of the receptors was observed between fixed and unfixed samples. Interestingly, the eyes from COVID-19 patients expressed a stronger signal than the tissues from non-infected patients. Noteworthy, the results were not consistent with all antibodies used. A pronounced mRNA expression of ACE2 was detected in fresh human cornea, 20 times stronger than in fresh human retina. In contrast, relevant protein expression of ACE2 was not found in fixed corneal samples, while the expression of ACE2 was detected in the retina in the same sections. TMPRSS2 was detected in fresh as well as fixed corneal and retinal samples.

Conclusions: ACE2 and TMPRSS2 were found in ocular tissue, although to a limited amount. The age of the sample, the method of preservation, the freshness of the tissue, and the selection of antibody/primer have an influence on the detection of the relevant receptor expression. In addition, COVID-19 patients might have a stronger expression of ACE2 in ocular tissue in comparison to non-infected patients. This effect will be investigated in further studies. In conclusion, the infestation of ocular tissue does likely not represent the main route of infection, due to the weak receptor expression.

CONTROL ID: 3546312

SUBMITTER (NAME ONLY): Nihar Bhattacharyya

TITLE: CTG18.1-mediated Fuchs Endothelial Corneal Dystrophy: defining unique signatures of transcriptomic dysregulation

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Bhattacharyya, N. Hafford-Tear, A.N. Sadan, C. Zarouchlioti, K. Muthusamy, S.J. Tuft, A.J. Hardcastle, A.E. Davidson, Institute of Ophthalmology, University of London, London, London, UNITED KINGDOM|K. Muthusamy, S.J. Tuft, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|P. Liskova, Univerzita Karlova, Praha, CZECHIA|

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ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is a common degenerative disease predominantly caused by an expanded (≥ 50 copies) CTG repeat (termed CTG18.1) in an intron of the transcription factor encoding gene TCF4. CTG18.1-mediated FECD is unique among repeat expansion diseases in its high frequency among the general population and a pathophysiology limited to corneal endothelial cells (CECs). Here we generated transcriptome data from primary CEC cultures to identify the differentially expressed transcripts that may represent key biomarkers to enhance understanding of the pathophysiology of FECD.

Methods: We extracted total RNA from primary CEC cultures from 10 unrelated individuals including: 4 unaffected controls, 3 CTG18.1-expansion negative FECD (NE-FECD) and 3 CTG18.1 expansion-positive (E-FECD) patients. RNA-seq libraries were prepared using oligo(dT) beads to enrich for poly-A mRNA and sequenced in accordance with standard Illumina paired-end protocols. Differential gene expression was assessed via DeSeq2 and adjusted with independent hypothesis weighting, while differences in pre-mRNA splicing were analyzed via IsoformSwitchAnalyzerR to identify canonical isoform variants.

Results: Of the 4,497 genes significantly (adj. p-value ≤ 0.05) differentially expressed in E-FECD, 1,248 were unique to E-FECD when compared with NE-FECD with 486 having a log2-fold difference of at least 1. Among these 486 genes, ontology analysis revealed enrichment of genes involved in signaling pathways, cell structure, extracellular matrices, and protein synthesis. Isoform analysis revealed 303 genes with significant differences in isoform expression between E-FECD and controls, 205 of which are predicted to produce a functional difference due to the inclusion or exclusion of a functional exon. Included within this dataset are genes with known MBNL1 splicing regulation, suggesting that splicing dysregulation could be due to sequestration of splicing factors by the CTG18.1-expanded transcript.

Conclusions: A comparison of transcriptomic profiles of control, E-FECD and NE-FECD provides a dataset of differentially expressed transcripts and aberrantly regulated pre-mRNA splicing events that uniquely occur in E-FECD. These data provide insight into disease mechanisms and highlight targets for CTG18.1 expansion-specific translational interventions.

CONTROL ID: 3546317

SUBMITTER (NAME ONLY): Paul Gomes

TITLE: Effectiveness of Bilastine ophthalmic formulation for the treatment of allergic conjunctivitis

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Allergic conjunctivitis (AC) is a common ocular disease with a growing incidence rate. Novel topical therapies add to a physician's armamentarium. The aim of this work was to evaluate the efficacy of three concentrations of Bilastine Eye Drops, as a multi-dose, preservative-free formulation, for the treatment of the signs and symptoms of AC.

Methods: This was a single-center, double-masked, randomized, vehicle-controlled, phase 2, dose ranging study conducted to assess the efficacy of bilastine ophthalmic formulation for treatment of the signs and symptoms of AC. The Ora-CAC[®] Allergen Challenge Model was used to assess acute allergic responses. Subjects must have had a history of ocular allergies and a positive skin test reaction to a seasonal or perennial allergen. On Day 1, 121 subjects with AC were randomized to receive Bilastine 0.2% N=30, 0.4% N=30, 0.6% N=31 or vehicle N=30. Two duration-of-action (16 hours post drop on Day 1 and 8 hours post drop on Day 15) and one onset-of-action (15 minutes post drop on Day 22) visits were conducted. The primary efficacy analyses (ocular itching) were conducted using analysis of covariance (ANCOVA) models. Least square (LS) means were estimated for each treatment and for the difference between each active treatment and vehicle at each visit and time point.

Results: All three concentrations of bilastine showed efficacy controlling ocular itching at 15 minutes and 8 hours post treatment. Bilastine 0.6% was also effective at 16 hours post treatment, compared to vehicle. Mean treatment differences at all time points were ≥ 1 unit for bilastine 0.6% ($P < 0.0001$). Statistically significant ($P < 0.05$) treatment effects were observed for bilastine 0.6% compared to vehicle in the secondary endpoint of conjunctival redness at all 3 visits. For the exploratory endpoints of tearing, eyelid swelling and nasal symptoms, treatment differences were statistically significant ($P < 0.05$) for bilastine 0.6% compared to vehicle at all 3 treatment visits. All concentrations showed a good overall safety profile with comfort scores comparable to vehicle.

Conclusions: Bilastine ophthalmic formulation is an effective and safe treatment for AC, with the 0.6% concentration exhibiting the most efficacy in reducing signs and symptoms lasting at least 16 hours post treatment, making it suitable for once-daily administration. Bilastine was well tolerated.

CONTROL ID: 3546321

SUBMITTER (NAME ONLY): Jacklyn Salmon

TITLE: Titration of x-ray whole body radiation dose to optimize the murine model of ocular graft vs host disease

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.H. Salmon, J. Nilles, D. Roberts, B.C. Gilger, Clinical Sciences, North Carolina State University, Raleigh, North Carolina, UNITED STATES|B.C. Gilger, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The murine ocular graft versus host disease (OGvHD) model is a well-established model of human OGvHD that develops following allogeneic hematopoietic stem cell transplantation (HSCT). The objective of this study was to optimize the total body irradiation (TBI) protocol in the murine OGvHD model when using X-RAD 320 irradiator to allow sufficient ablation of the recipient bone marrow (BM) while minimizing the ocular and systemic effects of acute radiation toxicity.

Methods: The major histocompatibility mismatch chronic OGvHD murine model was created, as described by Perez (2016; doi: 10.1016/j.bbmt.2016.07.012). Animal use was approved by the NC State University IACUC. BM from male C57BL/6 mice, 6-8 weeks of age, was collected from the femurs, tibias, and humeri then depleted of red blood cells and T cells. Splenocytes were collected, red blood cells were lysed, and remaining cells analyzed by flow cytometry. Female BALB/c mice, aged 6-8 weeks, were placed into an X-RAD irradiator (Accela, Inc.) programed at 320 Kv and 12.5 mA and administered 650 cGy (n=10), 700 cGy (n=4), or 750 cGy (n=10) x-ray TBI. Two hours after irradiation, mice were injected intravenously with 1×10^7 BM cells and 1×10^6 splenocytes. Following injection, body weights and tear production (phenol red test) were recorded, and scores (0-4) of the eyelid margins and corneal opacity were collected through day 42 after transplantation.

Results: By day 40 after TBI, mean body weight of the 650, 700, and 750 cGy groups decreased 19.27%, 8.66%, and 16.69% respectively. Mortality rates of these groups were 20%, 0%, and 50% respectively. Eyelid margins had immediate elevation in scores by day 1-3 in the 700 and 750 cGy groups, while corneal scores were elevated in the 700 and 750 cGy groups by day 8-9. Eyelid and corneal scores did not increase with 650 cGy until day 21. There was no significant difference in tear production between these groups.

Conclusions: OGvHD clinical findings appear to develop at approximately 21 days after TBI and HSCT, regardless of dose of TBI. However, TBI dose >650 cGy resulted in acute radiation induced ocular changes noted within the first week after TBI in addition to a higher body weight loss and mortality rate. To minimize TBI acute radiation ocular signs, which may confound interpretation of treatment effects, TBI x-ray radiation dose of less than 700 cGY is recommended.

CONTROL ID: 3546324

SUBMITTER (NAME ONLY): Jeong Pak

TITLE: Prevalence and Characteristics of Reticular Pseudodrusen in the Carotenoids in Age-Related Eye Disease Study 2 (CAREDS2)

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.W. Pak, S. Cleland, A. Domalpally, Z. Liu, B. Blodi, J.A. Mares, Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|S.T. Bailey, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K.M. Gehrs, Ophthalmology and Visual Sciences, University of Iowa Hospital & Clinics, Iowa City, Iowa, UNITED STATES|R.B. Wallace, Epidemiology, University of Iowa College of Public Health, Iowa City, Iowa, UNITED STATES|L. Tinker, Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reticular pseudodrusen (RPD) have been identified as an independent risk factor in the progression of age-related macular degeneration (AMD), particularly predictive of geographic atrophy. However, RPD characteristics are poorly defined in natural history studies. We determined the prevalence and morphological features of RPD using multimodal imaging and assessed associations with demographics, AMD status, and visual acuity in participants of CAREDS2, an ancillary study of the Women's Health Initiative.

Methods: Multimodal imaging included spectral domain optical coherence tomography (SD OCT) and infrared reflectance (IR) to identify RPD characteristics, such as presence, location (within or outside the ETDRS grid), peripapillary involvement, pattern, and RPD area. AMD features from SD OCT, IR, and color photographs were also assessed and AMD severity was categorized.

Results: In 927 eyes from 466 female participants (age 69 to 101), RPD were present in 130 eyes (14% of eyes, 16% of participants) and 76% participants with RPD had bilateral involvement. There was increasing prevalence with age; 7% in < 78 years, 14% in 78-83 years, and 30% in > 83 years. The AMD severity classification from the color photographs showed RPD in 2.4% of eyes with no AMD, 11.5% in early AMD, 25.1% in intermediate AMD and 51.1% in late AMD. Ribbon morphology (53%) was more common than dot morphology RPD (36%). RPD were mostly located both within and outside the ETDRS grid with primarily superior retinal distribution. Among eyes with RPD, 35% had peripapillary involvement which showed an increase with age. Mean RPD area was 17.4 (14.7) mm² and was not significantly associated with age (P = 0.10) or with AMD status (P=0.60). RPD were visualized with corresponding color fundus photography in only 38 eyes (4% of total eyes). Participants with and without RPD had a visual acuity ± standard error of 77.9 (1.4) and 81.3 (0.4) letters, respectively (P = 0.02).

Conclusions: The prevalence of RPD in the aging female population of CAREDS2 was associated with advancing age and AMD severity. RPD were also detected in eyes without other features of AMD which could represent an earlier disease state. Sensitivity for visualizing RPD was greatly enhanced using multimodal imaging with SD OCT and IR over color fundus photography.

CONTROL ID: 3546327

SUBMITTER (NAME ONLY): Tala Al-Khaled

TITLE: Evaluation of an Artificial Intelligence System (i-ROP DL) for Retinopathy of Prematurity Screening in Nepal using the Forus 3nethra neo and in Mongolia using the Retcam Portable[®]

SESSION TITLE: Retinopathy of prematurity/vein occlusion

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Our group has demonstrated the performance of the i-ROP Deep Learning (DL) system for retinopathy of prematurity (ROP) telemedicine screening programs in Nepal and Mongolia. The purpose of this study is to evaluate the performance of i-ROP DL in Nepal and Mongolia when increasing the number of infants included and conducting further analysis by country and fundus camera.

Methods: This retrospective study evaluated prospectively collected data from ROP screening programs in Nepal and Mongolia. Birth weight, gestational age, and ROP severity based on the International Classification of ROP (ICROP) guidelines were recorded. Fundus images were obtained with the Forus 3nethra neo in Nepal and the RetCam[®] Portable in Mongolia. The i-ROP DL system, previously trained on RetCam[®] images, was used to identify posterior pole images in the dataset and subsequently generated a mean vascular severity score (1-9). Analysis of variance was used to compare vascular severity scores to ROP categories by country. A p value ≤ 0.05 was considered statistically significant. Stata MP 13, SAS, and R statistical software programs were used.

Results: There were a total of 377 patients and 860 exams in Nepal and 321 patients and 917 exams in Mongolia. Average birth weight and gestational age were lower in Mongolia compared to Nepal (both $p < 0.001$). Overall disease prevalence of treatment-requiring ROP was 14% in Mongolia vs 2% in Nepal ($p < 0.001$). See Table 1. The ROP vascular severity score was higher in Mongolia compared to Nepal at the population level (3.5 vs. 2.5, $p < 0.002$).

Figure 1 displays the vascular severity scores overall and by category for Nepal and Mongolia.

Conclusions: In Mongolia and Nepal, the AI-generated vascular severity scores correspond to ICROP disease severity using two different camera systems, despite the i-ROP DL system not being previously trained on Forus 3nethra neo images. Vascular severity at the population level may be a useful tool for epidemiologic assessment of geographic and temporal variations in ROP severity.

CONTROL ID: 3546328

SUBMITTER (NAME ONLY): Leonid Zukin

TITLE: Ocular Sequelae of Uveitis and Their Associated Risk Factors: A National Medical Claims Database Study

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Uveitis and scleritis can cause a number of vision threatening complications if left untreated. Because the precise complications of each sub-type of uveitis can be relatively uncommon, it can be difficult to uncover clinically significant associations and risk factors for developing these complications. Here we employ a large national insurance claims database to conduct a retrospective case-control study of the long-term ocular sequelae of uveitis and scleritis.

Methods: The Optum Clinformatics Data Mart, a large national database, was used to obtain medical claims and demographic data. Patients with a diagnosis of uveitis/scleritis based on ophthalmologist or optometrist examination were included in the study. Medical claims data after 2007 was used and diagnosis codes were based on the International Classification of Diseases (ICD) 9th and 10th Revisions. Data was categorized on the basis of anatomic location/classification of uveitis – scleritis, anterior, intermediate, posterior, panuveitis. Multivariable logistic regression analysis was implemented to calculate odds ratios within each sequelae type on the basis of age, gender, ethnicity, socioeconomic status, education, smoking status, as well as numerous systemic medical comorbidities.

Results: Of the 115,876 patients with uveitis and scleritis identified in this study, 29.4% had scleritis, 51.7% had anterior uveitis, 0.6% had intermediate uveitis, 16.1% had posterior uveitis, and 2.3% had panuveitis. The most common sequelae were cataracts (18.8%), cystoid macular edema (2.9%), blindness (1.5%), chorioretinal scarring (1.5%), and choroidal neovascularization (1.0%). Multivariate analysis revealed that cataracts were more likely in panuveitis, cystoid macular edema was more likely in intermediate uveitis, blindness was more likely in panuveitis, and chorioretinal neovascularization and scarring were most likely in posterior uveitis. Multivariate analysis further demonstrated associations of each sequelae with various demographic parameters and medical co-morbidities.

Conclusions: This study demonstrates the utility of employing a large database and clinical informatics to study relatively uncommon ocular diseases and to elucidate key associations and risk factors for their vision threatening complications.

CONTROL ID: 3546329

SUBMITTER (NAME ONLY): Zhong-Lin Lu

TITLE: Hierarchical Bayesian modeling of E-ETDRS and FrACT test data

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: E-ETDRS and FrACT are the two most popular electronic visual acuity (VA) tests. To improve the precision of VA threshold estimates from the tests, we re-analyzed the E-ETDRS and FrACT data from 14 eyes in four Bangerter foil conditions in Zhao et al. (2021) with the qVA method and a hierarchical Bayesian model (HBM) based on the qVA method (Lesmes & Dorr, 2019).

Methods: The HBM consisted of hyperparameters and parameters at the population and individual test levels, each of which is a 2-dimensional Gaussian distribution of VA threshold and range. The covariances were set up to capture the cross- and within-test regularities. We compared the average half width of the 68.2% credible interval (HWCI) of the VA threshold and range estimates from the qVA and HBM analyses.

Results: The HBM analysis recovered the correlations between VA threshold and range from the E-ETDRS (0.527 and 0.058) and FrACT (0.755 and 0.218) datasets at the population and individual test levels (Fig. 1). Table 1 shows the average HWCI of the VA threshold and range estimates. The average HWCI of the VA threshold estimates from the E-ETDRS dataset were 0.050 and 0.039 logMAR from the qVA and HBM analyses, respectively, with a 22% reduction by the HBM. The average HWCI of the VA threshold estimates from the FrACT dataset were 0.049 and 0.043 logMAR, with an 11% reduction by the HBM. Compared with the qVA analysis, the HBM also significantly reduced the average HWCI of the range estimates from the E-ETDRS (from 0.148 to 0.072 logMAR, a 51% reduction) and FrACT (from 0.214 to 0.096 logMAR, a 55% reduction) datasets. In comparison, HBM analysis of the qVA data from the same subjects in the same testing conditions resulted in average HWCIs of 0.019 and 0.048 logMAR for VA threshold and range (Table 1).

Conclusions: Incorporating both cross- and within-test regularities, the HBM analysis greatly improved the precision of VA threshold and range estimates in the E-ETDRS (30 optotypes) and FrACT (45 optotypes) datasets, although the combination of the HBM and qVA test is the best option.

CONTROL ID: 3546330

SUBMITTER (NAME ONLY): Emily Cole

TITLE: Variability in plus disease diagnosis using single and serial retinal images

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: There has been demonstrated variability in plus disease diagnosis amongst ROP experts. There are subjective differences in the diagnostic cutoffs for pre-plus and plus disease. Features such as training, field of view, magnification, and tempo have been proposed as explanations. The purpose of this study is to assess changes in ROP diagnosis in single and serial retinal images.

Methods: 7 graders with expertise in ROP grading independently reviewed both single and 3 consecutive serial retinal images from 15 ROP cases on a secure web-based platform. Severity was assigned as plus, pre-plus, or none. A secondary analysis was performed using the previously validated i-ROP deep learning system to assign a vascular severity score (VSS) to each image, ranging from 1-9, with 9 being most severe disease. This score has been previously demonstrated to correlate with expert diagnosis and the ICROP. Mean plus disease severity was calculated by averaging 14 labels per image in both serial and single images.

Results: Assessment of serial retinal images changed the grading severity for >50% of the graders, though there was wide variability. Cohen's kappa ranged from 0.29 to 1.0. Changes in grading of serial retinal images was noted more commonly in cases of pre-plus disease, where the mean severity showed a borderline significant increase ($p=.08$). (Figure 1) The ROP VSS demonstrated good correlation with the range of expert classifications of plus disease, and overall agreement with the mode class ($p=0.001$) (Figure 2A). The VSS correlated with mean plus disease severity by expert diagnosis (correlation coefficient 0.89). (Figure 2B). The VSS also demonstrated agreement with disease progression across serial images which progressed to pre-plus and plus disease. (Figure 2C).

Conclusions: Clinicians demonstrated diagnostic variability with both single and serial images. However, the use of serial retinal images caused a change from pre-plus to plus disease, which represents a change in management. More aggressive graders tended to be influenced by serial images to increase the severity of their grading. The use of

deep learning as a quantitative assessment of plus disease can standardize diagnosis and treatment.

CONTROL ID: 3546331

SUBMITTER (NAME ONLY): Haoshen Shi

TITLE: Immunoregulatory and amyloid-clearing phenotypes of conditional miR-155-depleted microglia in the retina of AD-model mice

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A recent study in transgenic murine models of Alzheimer's disease (AD) described a unique microglial neurodegenerative phenotype (MGnD) that is triggered by amyloid- β plaque-mediated neuronal stress. The microRNA miR-155 was primarily characterized in relation to pro-inflammatory M1 microglia. However, recent research demonstrated regulatory role of miR-155 on neurodegenerative response in AD brain and its contribution to MGnD microglial phenotype differentiation. Our team identified the pathological hallmarks of AD in the neurosensory retina. We further found a tight correlation between the impacts of AD on brain and retinal pathology. Here, we sought to evaluate the roles of miR-155 depletion on microglial phenotypes associated with amyloidosis in the retina of transgenic murine models of AD.

Methods: The Cx3cr1-Cre^{ERT2} mice were used to specifically and transiently target miR-155 depletion in microglia (miR-155^{fl/fl}) and were further introduced into APP^{SWE}/PS1 ^{Δ E9} (ADtg) mice to generate Cx3cr1-Cre^{ERT2}:miR155^{fl/fl}:APP^{SWE}/PS1 ^{Δ E9} mice. Oral treatment of tamoxifen was applied to induce miR-155 deletion at 2 months of age. At 4 and 8 months, mice were sacrificed to extract retinas for different experimental measurements. These, included inflammatory marker assessment by meso scale discovery (MSD) analysis, global proteomic profiles by mass spectrometry (MS), and microglial phenotypes associated with retinal abluminal and vascular amyloidosis by histological examination.

Results: Our initial results demonstrate that miR-155 deletion decreased expression of multiple cytokines including IFN- γ , TNF α , IL-2, IL-6 and IL-12 in the retinas of ADtg mice, as well as reduced TNF- α in wild type mice. Retinal cross section showed deposition of A β ⁴² and A β ⁴⁰ in retinal parenchyma and blood vessels in ADtg mice at 8 months. The miR-155 deletion in microglia seems to enhance clearance of retinal A β deposition in 8-month-old ADtg mice. Intriguingly, distinct retinal proteome profiles were identified in the Cx3cr1-Cre^{ERT2}:miR155^{fl/fl}:APP^{SWE}/PS1 ^{Δ E9} mice.

Conclusions: Our data indicate that inhibiting miR-155 expression in CNS microglia may provide beneficial therapeutic effect in retinas of ADtg mice, including downregulating proinflammatory cytokines and enhanced A β clearance. These findings propose a potential new target for AD diagnosis and treatment.

CONTROL ID: 3546333

SUBMITTER (NAME ONLY): Aarthi Krishnan

TITLE: Bioinformatic Analysis reveals possible mechanisms of Aniridic Keratopathy

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Krishnan, A. Faranda, S.G. Novo, Y. Wang, M.K. Duncan, University of Delaware, Newark, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aniridic Keratopathy is a sight threatening manifestation of Aniridia, a genetic disease caused by Pax6 haploinsufficiency. However, the mechanisms underlying this keratopathy remain unclear. We performed unbiased transcriptome profiling of PAX6 mutant mouse corneas to understand the mechanisms involved in Aniridic Keratopathy.

Methods: RNA was isolated from PAX6 mutant (+/-) and wildtype corneas obtained from 20 week old mice (3 biological replicates of each) and transcriptome profiling performed by RNAseq. Differentially expressed genes (DEGs) were identified using bioinformatic pipelines and altered pathways identified via iPathway Guide (<https://advaitabio.com/>). DEGs in the Pax6 mutant cornea were compared to those obtained from prior corneal gene expression profiles including those differentially expressed between human cornea and conjunctiva (GEO Accession GSE38190). L1000CDS² analysis was performed on the LINCS server (<https://lincsproject.org/>)

Results: A total of 823 genes (514 upregulated and 309 downregulated) were differentially expressed in the 20-week-old PAX6 mutant mouse cornea. Inflammation, cytokine-cytokine receptors and angiogenesis were the most upregulated pathways in PAX6 mutant corneas. Conjunctival cytokeratins upregulate in the Pax6 mutant cornea, and while bioinformatics comparisons revealed that 95 genes that were upregulated in PAX6 mutant corneas normally are overexpressed in the conjunctiva compared to the cornea. Similarly, corneal cytokeratins are expressed at lower levels than normal in corneas from mice heterozygous for Pax6 mutations and a total of 33 genes that normally exhibit corneal preferred expression were downregulated in the Pax6 mutant cornea compared to wildtype. L1000CDS² analysis revealed histone deacetylase inhibitors as potential drugs capable of normalizing the mRNA transcriptome of Pax6 mutant corneas.

Conclusions: This analysis reveals the PAX6 mutant cornea expresses transcriptional signatures consistent with inflammation and angiogenesis. Further, transcriptome profiles are consistent with the Pax6 mutant corneal epithelium either being invaded by or transdifferentiating into, conjunctiva. Histone deacetylase inhibitors are potential drugs to reverse the corneal consequences of aniridia.

CONTROL ID: 3546334

SUBMITTER (NAME ONLY): Anastasia Gkiala

TITLE: Factors affecting macular pigment optical density in a healthy cohort using a new optical instrument

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gkiala, D. Christaras, A. Livir-Rallatos, H.S. Ginis, Department of Research, Athens Eye Hospital, GREECE|J. Mompean, P. Artal, Laboratorio de Optica, Universidad de Murcia, Murcia, Murcia, SPAIN|

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ABSTRACT BODY:

Purpose: The macular pigment is a yellowish pigment of nutritional origin, lying primarily at the macula. It is believed to play a protective role, shielding foveal photoreceptors from blue-light associated photochemical damage and oxidation from free-radicals. The purpose of this study was to collect macular pigment optical density (MPOD) values, measured with a new optical instrument in a healthy population.

Methods: The instrument uses two sources, a green and a blue, flickering at different frequencies and focusing a central disk of 3.5 degrees diameter and a concentric peripheral annulus of 1 degree on the ocular fundus. The reflected light from the fundus is collected by a high-speed, high sensitivity photodetector and the signal is then processed in the frequency domain. The value for the macular pigment optical density is subsequently computed from the processed signal and the appropriate mathematical equation based on a fundus light extinction model. The duration of the measurement is kept below 0.2 sec and it is done at a natural pupil. Our cohort consisted of 51 healthy volunteers with no known ocular pathology. Their age ranged between 19 and 61 years old with an average age 33.9 years. The demographic, lifestyle and dietary habits were recorded for all subjects, focusing mostly on the consumption of leafy green vegetables. The answers ranged from no consumption to everyday consumption. We grouped subjects based on their answers in frequent consumers (FC), those eating leafy vegetables every day or weekly, and in infrequent consumers (IC), those with monthly or no consumption.

Results: The measured MPOD values showed an age dependence ($p < 0.0005$) in both eyes, and therefore, the age-corrected sample was defined, where all MPOD values were normalised around a specific age value (35yo). The age corrected MPOD values for the FC group ranged from 0.29 to 0.54 D.U. with a mean of 0.39 D.U. while for the IC group ranged from 0.2 to 0.49 D.U. and a mean value of 0.35 D.U. The difference in MPOD between the two groups was small.

Conclusions: MPOD data were collected in a healthy population. The values were normalized according to age and were found to be slightly higher in the group that consumed vegetables frequently, that is on a daily or weekly basis. This finding is consistent with current bibliography stressing the positive effect of leafy green vegetables on macular pigment density values.

CONTROL ID: 3546336

SUBMITTER (NAME ONLY): Sushma Vishwakarma

TITLE: Potential of nanofibrous scaffolds in treating retinal inflammatory conditions via modulating microglial responses

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vishwakarma, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|S. Vishwakarma, CHEMICAL ENGINEERING, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|

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ABSTRACT BODY:

Purpose: Microglia, the resident immune cells that reside within the retina are involved in the maintenance of retinal homeostasis via surveying their microenvironment and communicating with other neurons. Microglia get activated under stress and depending on their phenotype, exert either neurotoxic or neuroprotective effects to other cells by secreting several cytokines and signaling molecules. Polymeric scaffolds have the ability to regulate cellular responses through precisely designed cues. The purpose of present study is to assess the effect of polymeric nanofibers on microglial polarization and immunomodulatory responses under hypoxia, and their potential for the treatment of retinal inflammatory conditions.

Methods: Human microglial CHME3 cells were grown on plain coverslips, as well as poly α -ester-based fibers possessing distinctly different topographies. Hypoxia was induced by the addition of CoCl_2 for 24 h. Cell viability was measured using Alamar blue assay, cell shape using immunofluorescence, gene expression using qPCR and protein expression using western blotting. Statistical significance was calculated using ANOVA with a p value < 0.05 considered significant.

Results: Microglial cells proliferated well on polymeric scaffolds, and followed the topographical cues. Under normoxia, microglia cultured on fibers with specific topographies displayed a predominantly pro-inflammatory phenotype. Specifically, IL-6, GM-CSF, TNF- α , and CXCL10 mRNA expression was significantly higher compared to the control group without nanofibers, and these trends largely reflected at the protein level too. Under hypoxia however, cells grown on fibers with different architectures showed a significantly higher viability, lower cell death and suppressed expression of the autophagy marker LC3 compared to the control group also cultured under hypoxia. Lysosomal proteins that protect the cells from apoptosis also showed higher expression when cultured on the scaffolds. Finally, expression of anti-inflammatory markers IL-4 and IL-10 was significantly higher on the scaffolds regardless of topography.

Conclusions: The regulation of microglial phenotype by using engineered nanofibers with tightly controlled properties provides new insights and a potential therapeutic approach for the development of immunomodulatory therapy for retinal inflammatory diseases.

CONTROL ID: 3546339

SUBMITTER (NAME ONLY): SANJEEB BHANDARI

TITLE: Cataract Surgery and the Risk of Progression to Late Age-Related Macular Degeneration: The Age-Related Eye Disease Study 2

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. BHANDARI, E. Agron, S. Vitale, D. Peprah, M. Farrell, T.D. Keenan, E.Y. Chew, Division of Epidemiology and Clinical Applications, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. Domalpally, Fundus Photograph Reading Center, University of Wisconsin, Madison, Wisconsin, UNITED STATES|T.E. Clemons, Emmes Corporation, LLC, Rockville, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cataract surgery in patients with age-related macular degeneration (AMD) alleviates vision loss from cataracts, but controversy exists whether it contributes to AMD progression. This study evaluated the risk of late AMD progression following incident cataract surgery in a prospective cohort within a controlled clinical trial of oral supplementation for the treatment of AMD – the Age-Related Eye Disease Study 2 (AREDS2).

Methods: Participants 50 to 85 years with bilateral large drusen or unilateral AMD were enrolled in the AREDS2 study from 82 retinal specialty clinics in the US between 2006 – 2008 and followed until the conclusion of the clinical trial in 2012. After the end of the trial, an additional 5-year of follow-up was conducted via telephone every 6 months until 2018. Clinical information obtained by telephone was verified by collecting medical records of treating physicians. A subset of the AREDS2 participants was also evaluated in a final in-clinic study visit. The incidence of late AMD in eyes that received cataract surgery after the baseline visit and before any evidence of late AMD was compared with those that remained phakic until the study completion. Eyes that had at least 2 years of follow-up after cataract surgery were included in the analysis. We used Generalized Estimating Equations (GEE) and Cox regression models that were adjusted for age, sex, smoking, education, and AMD severity. Late AMD was defined as the presence of geographic atrophy (macular atrophy ≥ 430 mm) or neovascularization on annual stereoscopic fundus photographs or medical record documentation.

Results: A total of 1229 eyes (30%), of the 4064 participants in the AREDS2 study, had cataract surgery at a mean (SD) of 5.7 (3) years from study enrollment. The risk of late AMD after a mean (SD) of 4.6 (2.8) years from cataract surgery was not significant, Risk Ratio from GEE: 0.92 (95% Confidence Interval [CI]: 0.56-1.49, $p=0.73$). The Cox regression model showed that there was no increased risk for progression to late AMD after cataract surgery: hazard ratios 0.96 (95% CI, 0.8 – 1.13, $p=0.60$) for the right eye and 1.05 (0.89–1.25, $p=0.56$) for the left eye.

Conclusions: Cataract surgery did not accelerate the rate of progression to late AMD among the AREDS2 participants with up to 10-year follow-up. This study provides data in counselling AMD patients who would benefit from cataract surgery.

CONTROL ID: 3546342

SUBMITTER (NAME ONLY): Shun-Yun cheng

TITLE: Low-dose rAAV-mediated inhibition of VEGF can treat neovascular pathologies without inducing retinal vasculitis

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The wet form of age-related macular degeneration (AMD) is characterized by neovascular pathologies that can result in edemas, which can lead to rapid vision loss if untreated. Inhibition of vascular endothelial growth factor (VEGF) has been used to successfully treat neovascular pathologies of the eye. Nonetheless, some patients require frequent intraocular anti-VEGF injections, raising the risk of complications from the procedure and the burden to both, doctors and patients. rAAV-mediated expression of anti-VEGF proteins is an attractive alternative to reduce the risk to affected patients. However, controversy remains as to the safety of sustained VEGF inhibition in the eye. Here, we test the safety and efficacy of delivering the anti-VEGF drug Conbercept (KH902) with adeno-associated virus (AAV) vectors in two mouse models of vascular pathology.

Methods: To test the efficacy of rAAV-KH902, we used the oxygen-induced retinopathy of prematurity model, as well as the laser damage-induced choroidal neovascularization model. The same cassette expressing KH902 from a ubiquitous promoter was packaged into four different rAAV serotypes. To assess the efficacy of rAAV-KH902, we quantified the number of aneurysms in the oxygen-induced retinopathy model and the number of edemas, as well as the size of the neovascular lesions in the laser damage model.

Results: We found that intravitreal delivery of rAAVs expressing KH902 can successfully reduce the number of aneurysms, edemas, as well as the growth of the choroidal neovascular lesions. Serotypes with high transduction efficiencies were found to induce, in a dose dependent manner, a vascular sheathing pathology that is characterized by immune cell infiltrates, reminiscent of vasculitis. We found that this pathology is accompanied by increased expression in vascular cells adhesion molecule 1 (VCAM1), which promotes extravasation of immune cells from the vasculature. Importantly, low viral doses were still able to reduce edemas and lesion size without causing any vascular sheathing pathology.

Conclusions: The data suggest that rAAV-mediated expression of anti-VEGF drugs can be employed safely for the treatment of neovascular eye pathologies. However, vector design needs to be taken into consideration when determining the appropriate therapeutic dose.

CONTROL ID: 3546343

SUBMITTER (NAME ONLY): Nan Hultgren

TITLE: SARS-CoV2 Infection damages RPE Function and Survival

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Hultgren, B. Burgess, D.S. Williams, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: SARS-CoV2 infection affect a wide range of tissues in the human body. Viral presence has been reported in the ocular environment and alterations in the retina by Optical Coherence Tomography have been reported in COVID patients. However, it is unclear if and how retinal cells are directly affected by the virus. Using cell culture models along with pseudotyped virus, we tested the hypothesis that the presence of SARS-CoV2 negatively affects several critical functions of the retinal pigmented epithelial (RPE) cells, and could have long-term effects on retinal health.

Methods: Polarized human ARPE-19 cells and wild type iPS-RPE cells were cultured using recently published protocols from our lab. Two main steps of the viral life cycle were modeled: 1) viral entry, using lentivirus pseudotyped with SARS-CoV2 Spike protein; 2) viral replication, by testing expression of SARS-CoV2 protein E and 3a, following lentiviral transduction. Cells were maintained on Trans-well filters for up to 6-weeks. Barrier function was evaluated by measuring trans-epithelial resistance (TER) and immunofluorescence labeling of tight-junction proteins. Phagocytic capacity was evaluated by testing ingestion and degradation of photoreceptor outer segments (POSs). General RPE morphology was evaluated using transmission electron microscopy. Changes in gene expression was examined by qPCR and Western Blot analysis.

Results: We confirmed a previous finding that RPE cells express the receptor ACE2 and protease TMPRSS2 necessary for viral entry. Using Spike-protein pseudotyped lentivirus, we found that human RPE, but not fibroblasts, can be infected via a Spike-ACE2 mediated mechanism. This specific mechanism of viral-entry alone (as opposed to VSV-mediated entry) caused significant changes in cell physiology, including alterations in cell junction and protein trafficking. Using expression of lentiviral SARS-CoV2 components, we found that the presence of protein E induced expression of several pro-inflammatory cytokines in the RPE cell, while protein 3a activated apoptosis in the RPE cells. These data suggest that SARS-CoV2 can infect and cause serious damage to RPE function and survival.

Conclusions: Damage to the RPE cells often precedes photoreceptor degeneration. Given our findings that SARS-CoV2 can cause severe damage to the function and survival of RPE cells, COVID19 patients may be at increased risk of long-term RPE pathogenesis and associated visual impairment.

CONTROL ID: 3546345

SUBMITTER (NAME ONLY): Avril Daly

TITLE: Cost of Illness Study of Inherited Retinal Diseases in the USA and Canada

SESSION TITLE: AMD and Retinal Disease Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Daly, O. Galvin, Retina International, IRELAND|S. Cheung, Deloitte, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Accurate data regarding prevalence of Inherited Retinal Diseases (IRDs), impact on individuals and families affected, and cost burden to the USA and Canadian economies was lacking. This hinders research, development and commissioning of clinical services, treatments, care pathways and clinical trials. Thus there is a need for a stronger evidence base to support value-for-money to regulatory bodies for treatments approved, and treatments progressing through clinical trials. To safeguard future research and service provision it was necessary to learn more about the IRD community.

Methods: The socioeconomic burden of IRDs in the USA and Canada was estimated using a cost of illness methodology applying a prevalence approach. Patient involvement was incorporated throughout project design and review. Analysis was based on targeted literature review and primary data collection (survey) of adults aged 18+, and parents of children (under 18) living with one of the following IRDs: Achromatopsia, Bardet-Biedl Syndrome, Best Disease, Blue Cone Monochromacy, Choroideremia, Cone Dystrophy, Cone-Rod Dystrophy, Leber Congenital Amaurosis (LCA), Leber Hereditary Optic Neuropathy (LHON), Retinitis Pigmentosa, Rod-Cone Dystrophy, Stargardt Disease, Usher Syndrome, and X-Linked Retinoschisis (n=687 USA; n=151 Canada).

Results: The greatest cost type in both countries was attributed to wellbeing and accounted for 63% (up to US\$20.043 billion), and 66% (CAN\$1.071 billion) of total IRD costs in the USA and Canada respectively. Productivity losses were the second highest burden in both the USA and Canada, amounting to US\$4.056 billion, and CAN\$205.1 million. Persons with an IRD in the USA and Canada were 28.8% and 24.4% less likely to be in paid employment than the general population. In the USA and Canada IRDs resulted in a 0.3% and 1.4% reduction in productivity while at work respectively. The health systems cost in both regions was low at US\$2.216 billion and CAN\$37.8 million respectively.

Conclusions: The highest costs incurred due to IRDs were attributed to well-being and loss of productivity, yet those affected by IRD do not regularly engage with health care systems. The data demonstrates clearly that the measurements used to assess the burden of vision loss need urgent review. The wellbeing of those living with an IRD is currently underserved and under resourced, and there is an urgent need for equality in accessing the workforce.

CONTROL ID: 3546347

SUBMITTER (NAME ONLY): Kevin Zhang

TITLE: Neuroprotection of transplanted human stem cell derived retinal ganglion cells: advancing cell replacement strategies for optic nerve regeneration

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.Y. Zhang, A. Nagalingam, P. Zhang, X. Chang, H.A. Quigley, D.J. Zack, T.V. Johnson, Wilmer Eye Institute, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|D.S. Welsbie, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neuronal transplantation has emerged as a potential therapy to restore vision in advanced optic neuropathies by repopulating RGCs. However, successful engraftment is limited by poor donor survival. Dual leucine zipper kinase (DLK) and leucine zipper kinase (LZK) signaling pathways regulate endogenous RGC apoptosis. Here, we examined the neuroprotective effects of DLK and LZK inhibition on human embryonic stem cell (hES) derived RGC transplantation by using transgenic and pharmacologic approaches.

Methods: Organotypic retinal explants from 8-week-old C57BL/6J mice were co-cultured with hES-RGCs on the vitreous surface for 1 week. We compared transplanted RGC survival in wildtype (WT) hES-RGCs versus CRISPR-Cas9 engineered DLK^{-/-} and LZK^{-/-} hES-RGCs. In addition, we assessed survival and neurite integration of WT hES-RGCs on pronase-treated explants co-cultured in regular media or media containing 1μM VX-680 (a kinase inhibitor with strong activity against DLK). Cell survival was quantified using tiled retinal wholemount confocal images. Donor neurite integration, normalized to the number of RGCs in area measured, was assessed in high resolution 3D confocal reconstructions using Imaris software.

Results: DLK^{-/-} hES-RGC survival was significantly greater than WT hES-RGCs (16.1±2.8% vs 9.2±3.3%, p<0.001); LZK^{-/-} hES-RGCs did not show neuroprotection over WT cells (10.0±1.6%, p>0.05). On pronase-treated retinas, VX-680 enrichment conferred significantly increased survival of donor RGCs compared to control (20.20±4.66% vs 16.04±2.14%, p<0.05). The percentage of donor RGCs with neurite integration was similar between groups (1.69±0.38% in VX-680 vs 1.76±0.89% in control, p>0.05). However, the total length and dendritic complexity of integrated neurites localized to the recipient inner plexiform layer were significantly higher in the VX-680 treated group (98.9±37.7 μm/mm²/RGC vs 41.83±27.8 μm/mm²/RGC, p<0.005; 2.81±0.34 branches/mm²/RGC vs 1.25±0.86 branches/mm²/RGC, p<0.001).

Conclusions: Transgenic DLK deletion and pharmacologic kinase inhibition with VX-680 promoted survival of transplanted hES-RGCs on organotypic retinal explants. DLK inhibition also demonstrated significantly higher donor neurite integration and dendritic complexity. Ongoing studies aim to examine the neuroprotective effects of DLK inhibition on transplanted hES-RGC survival in vivo.

CONTROL ID: 3546357

SUBMITTER (NAME ONLY): Angus Grey

TITLE: Spatial mapping of glucose uptake and metabolism in the bovine lens

SESSION TITLE: Lens Cell Biology and Regulation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Grey, A. Zahraei, K. Varnava, G. Guo, P.J. Donaldson, The University of Auckland Faculty of Medical and Health Sciences, Auckland, Auckland, NEW ZEALAND|N. Demarais, The University of Auckland Faculty of Science, Auckland, Auckland, NEW ZEALAND|

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ABSTRACT BODY:

Purpose: Glucose is the major nutrient in the lens, which is taken up by the lens from the aqueous humor. This study aims to map glucose uptake and metabolism in cultured lenses, and correlate the pattern of glucose uptake to glucose transporter distributions and abundance.

Methods: Ex vivo bovine lenses were incubated in AAH containing normoglycaemic stable isotopically-labelled (SIL) glucose (5mM) for 5min-20h. Lenses were then fixed in 2%PFA for 72h for immunofluorescence microscopy analysis, frozen for MALDI imaging mass spectrometry (IMS) analysis, or manually dissected into epithelium flat mount and cortical fibre cells for either MALDI IMS or proteomic analysis. For MALDI-IMS studies, 20um thick axial lens tissue sections were analysed by a MALDI-MS. For proteomics studies, membrane protein preparations generated by centrifugation were separated by SDS-PAGE, gel bands digested by trypsin, and peptides analysed by LC-MS/MS. For immunohistochemistry studies, 16um thick axial lens sections were labelled with primary antibodies specific for GLUT 1 or GLUT 3. Fluorescent secondary antibodies, and cell membrane marker were added, and images collected by confocal microscopy.

Results: MALDI-IMS maps of SIL glucose showed uptake at 5min was concentrated in the peripheral epithelium. At later timepoints, glucose distributed throughout the epithelium and the cortical lens fibres. Proteomic analysis of central and peripheral regions of the lens epithelium detected GLUT1 and 3, with GLUT 3 in higher abundance than GLUT1 throughout the epithelium, but with GLUT1:GLUT3 ratio increased in the peripheral epithelium relative to central. Microscopy localized GLUT1 and GLUT3 to epithelial cell membranes and young fibre cells. SIL glucose metabolites found in glycolysis, the sorbitol pathway, and UDP-glucose formation were mapped to cortical lens fibres, with distinct signal changes relative to endogenous glucose metabolite signal up to 20h incubation.

Conclusions: Mass spectrometry and immunohistochemistry have spatially mapped the major uptake site of glucose in bovine lens to the peripheral epithelium and cortical fibres. SIL glucose is rapidly metabolized in epithelial and fibre cells to many metabolites, which are most abundant in the metabolically more active cortical fibre cells in comparison to central fibres.

CONTROL ID: 3546361

SUBMITTER (NAME ONLY): benjamin MEMMI

TITLE: Freeze-dried versus cryopreserved amniotic membranes in corneal ulcers treated by overlay transplantation: a case-control study.

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. MEMMI, L. LEVEZIEL, J. KNOERI, A. LECLERE, M. DESPIAUX, N. Bouheraoua, J. NORDMANN, C. Baudouin, V. Borderie, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To assess cryopreserved (C-AM) versus sterilized chorion-free freeze-dried (FD-AM) amniotic membranes overlay transplantation for corneal epithelial defects in a French tertiary ophthalmology hospital

Methods: Between March and July 2020, when C-AM were not available due to the COVID-19 pandemic and to the national lockdown, 28 corneal ulcers underwent FD-AM overlay transplantation and were retrospectively compared to 22 corneal ulcers treated with C-AM during the same period in 2018. All patients had at least 3 months of follow-up and those who underwent combined surgeries were excluded. Ulcers were assessed at baseline and then at 1 and 3 months. Population demographics, follow-up time, ulcer etiologies, ulcer size, and complications were also recorded.

Results: Baseline characteristics and clinical features of both groups were comparable. There was no statistically significant difference in the number of overlay amniotic membrane transplantations ($p=0.52$) or early fall ($p=0.57$). At 3 months, the corneal healing rate was almost the same in both groups (89% and 91% for FD-AM and C-AM, respectively; $p=0.85$). Complications were evenly unusual (11% and 9% respectively; $p=0.92$). In logistic regression, the nature of the membrane did not influence corneal healing at 1 month ($p=0.42$) and 3 months ($p=0.99$) regardless of the depth of the ulcer. However, whatever the type of AM used, the deeper the ulcer was, the less likely it was to heal at 3 months ($p=0.02$).

Conclusions: This first study provides positive insight into the effectiveness of FD-AM as compared to C-AM when used as overlay transplantation for treating corneal ulcers.

CONTROL ID: 3546362

SUBMITTER (NAME ONLY): Marc Stadelmann

TITLE: Automated fovea and optic disc detection in the presence of occlusions in Fundus SLO Images

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Stadelmann, A. Mosinska, S. Apostolopoulos, C. Ciller, S. De Zanet, RetinAI Medical AG, SWITZERLAND|M. Gallardo, R. Sznitman, ARTORG Center for Biomedical Engineering, Universitat Bern, Bern, SWITZERLAND|M. Munk, Universitätsklinik für Augenheilkunde, Inselspital Universitätsspital Bern, SWITZERLAND|

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ABSTRACT BODY:

Purpose: To develop and validate a machine learning algorithm for accurate estimation of the optic disc and fovea center position in infra-red SLO fundus images including cases outside of the field of view or apparent occlusions of the landmarks.

Methods: To detect the coordinates of obstructed or out-of-view optic disc or fovea, we reformulated the task as a regression problem where a machine learning algorithm learns to predict an anatomically plausible coordinate system centered on the fovea. The prediction was obtained by training a neural network with EfficientNet backbone. To this end, a dataset of 1226 grayscale OCT localizer images (Heidelberg Spectralis, average field of view: 8.75x8.75mm) affected with either Retinal Vein Occlusion related Macular Edema, Diabetic Macular Edema or Age-Related Macular Degeneration with choroidal neovascularization, was annotated and randomly split into a train (1106) and a test set (120). The test set included 46 images for which at least 50% of the optic disc was outside field-of-view. An outlier-robust estimation (RANSAC) was used to determine the final fovea and optic disc location in an anatomical coordinate system. The detection was evaluated by computing the average distance between manual annotation and predicted location.

Results: The presented methodology was able to estimate the location of the optic disc with an average error of 0.07 mm and the fovea with an average error of 0.2 mm, independent of the diseases (Fig. 1).

The method showed good performance also in cases where optic disc or fovea were only partially visible or fully-occluded due to existing lesion or artificial image cropping (Fig. 2 bottom). The goodness of fit was a good surrogate of the detection error (Fig. 2 top).

Conclusions: The automated detection algorithm could identify fovea and optic disc locations with a high level of accuracy. The addition of RANSAC increased the robustness of the model also in the presence of occlusions and enabled quantification of the localization accuracy. This method allows the registration of longitudinal scans, even if the optic disc is not or only partially visible, as it is often the case on fovea-centered OCT scans.

CONTROL ID: 3546363

SUBMITTER (NAME ONLY): Flavia Messina

TITLE: Evaluation of the neuroprotective mechanisms of 7,8-Dihydroxyflavone and generation of corresponding sustained release nano/microparticles for improved ocular drug delivery

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Messina, H. Sundaramurthi, A. Moran, B.N. Kennedy, School of biomolecular and biomedical science, University College Dublin, Dublin, IRELAND|A. Cerquone Perpetuini, Novartis Ireland Ltd, Dublin, IRELAND|M. English, National Institutes of Health, Bethesda, Maryland, UNITED STATES|M. Brooks, A. Swaroop, National Eye Institute, Bethesda, Maryland, UNITED STATES|M. Dandamudi, N. O'Reilly, Waterford Institute of Technology, Waterford, IRELAND|A.L. Reynolds, School of veterinary medicine, University College Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: 7,8-Dihydroxyflavone (7,8-DHF), a reported TrkB agonist, improves vision in the atp6v^{ucd6} zebrafish model of inherited blindness. Here, the mechanism by which 7,8-DHF restores vision is investigated and biodegradable nano/microparticles for 7,8-DHF ocular drug delivery are characterized.

Methods: 3 days post fertilized (dpf) sibling or atp6v^{ucd6} larvae (n=5, N=3) were treated with 20-40 µM 7,8-DHF or 0.1% DMSO. Visual behaviour was assessed at 5 dpf by the optokinetic response assay (OKR). For mechanistic analysis, 60 eyes of 5 dpf atp6v^{ucd6} treated with 0.1% DMSO or 20 µM 7,8-DHF were analysed by RNAseq and differentially expressed genes/pathways identified using Cytoscape and gProfiler. PLGA nano/micro-particles incorporating 7,8-DHF were produced by single emulsion solvent evaporation, encapsulation efficiency analyzed by HPLC, and particle size or shape analysed by dynamic light scattering or scanning electron microscope.

Results: 20 µM 7,8-DHF rescues atp6v^{ucd6} visual function (p= 0.04). RNAseq identified 15,662 genes of which 58 were down regulated and 213 up regulated by 7,8-DHF. Following gProfiler analyses, among the down-regulated processes are genes related to inflammation, among the up regulated processes are genes related to translation. 7,8-DHF PLGA nanoparticles show ~59% drug encapsulation, mean size of 314 nm; the spherical microparticles of 3-30 µm display drug encapsulation of ~72%.

Conclusions: 7,8-DHF may rescue vision by decreasing inflammation in the eye. The biodegradable PLGA nano/microparticles display appropriate drug encapsulation and physiochemical properties. Future directions include characterization of efficacy and safety in biological systems.

CONTROL ID: 3546367

SUBMITTER (NAME ONLY): Michael Zilliox

TITLE: Longitudinal analysis of the microbiome in ocular surface diseases

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Zilliox, C. Mores, P. de Bustros, C.S. Bouchard, Ophthalmology, Loyola University Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously found that the ocular surface microbiome (OSM) can differ between each eye in approximately half of patients and healthy controls. In addition, we observed that the OSM was less diverse in patients with several ocular surface diseases (OSDs) compared to controls. However, longitudinal data has been lacking in these OSDs to understand the stability of the microbiome. We performed prospective, longitudinal observational studies to characterize the ocular surface microbiome OSM in OSDs.

Methods: Sterile swabs were used to collect samples from each eye of patients. Sterile technique and multiple controls were used to assess contamination during DNA extraction, amplification and sequencing using V4 primers of the 16S rRNA gene. Concurrent use of topical antibiotics, steroids, and bandage contact lenses (BCLs) was documented.

Results: Despite the low biomass of the ocular surface, we can detect a microbiome in ~50% of eyes sampled using sequencing. We observed that approximately half of patients had distinct microbiomes in each eye despite the eyes having similar diversity measures. In Steven's Johnson Syndrome (SJS), there were 5 ocutypes (defined as distinct microbiome communities) with the ocutypes being dominated by *Corynebacterium*, *Achromobacter*, *Stenotrophomonas*, *Staphylococcus* or a diverse population with no dominant genera. The *Corynebacterium* and *Staphylococcus* ocutypes were observed in other OSDs as well. Human pathogens not previously associated with SJS that were found included *Achromobacter*, *Stenotrophomonas* and *Sphingobacterium*. Alpha diversity was lower in SJS and DED patients compared to healthy controls and GVHD patients. Next, we performed longitudinal analysis of SJS patients and observed several interesting patterns, however, only 14% of eyes showed a stable microbiome over several weeks.

Conclusions: About half of patients had similar microbiomes in each eye. Microbiomes from OSDs had lower alpha diversity compared to controls. Longitudinal analysis has found that only 14% of eyes had a stable microbiome over time, suggesting global measurements for the microbiome, such as alpha diversity, may be more useful to define the OSM.

CONTROL ID: 3546372

SUBMITTER (NAME ONLY): Philip Dockery

TITLE: Likelihood of Germline Mutation with Solitary Retinoblastoma Based on Tumor Location at Presentation

SESSION TITLE: Advances in Diagnosis and Management of Retinoblastoma and Congenital Eye Diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. Dockery, M. Ruben, A. Yaghy, C. Shields, Wills Eye Hospital Ocular Oncology Service, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Philip Dockery: Commercial Relationship: Code N (No Commercial Relationship) | Megan Ruben: Commercial Relationship: Code N (No Commercial Relationship) | Antonio Yaghy: Commercial Relationship: Code N (No Commercial Relationship) | Carol Shields: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the likelihood of germline mutation in patients presenting with solitary retinoblastoma, based on tumor location at presentation.

Methods: Retrospective analysis of 482 consecutive patients with solitary, unilateral, unifocal retinoblastoma for likelihood of germline mutation (family history of retinoblastoma and/or genetic testing germline Rb1 mutation present and/or development of additional new tumors) based on overall tumor location at presentation (macular vs. extramacular).

Results: Of the overall group (n=482 consecutive patients) with solitary retinoblastoma, macular tumors at presentation were more likely to have a smaller basal diameter (12.5 mm vs. 18.9 mm, $p<0.001$) and thinner (6.1 mm vs. 10.7 mm, $p<0.001$) than extramacular tumors. Patients with tumors located in the macula were more likely to have a family history of retinoblastoma (13% vs. 2%, $OR=4.89$ [1.85–12.97], $p<0.001$) and to develop new tumors (10% vs. 4%, $OR=3.17$ [1.27–7.93], $p=0.014$) compared to patients with tumor located outside the macula at presentation. There was no statistically significant difference in genetic testing for Rb1 mutation (25% vs. 16%, $p=0.078$) or likelihood of germline mutation (23% vs. 14%, $p=0.066$).

Conclusions: Patients with solitary unilateral macular retinoblastoma are more likely to express phenotypic outcomes of germline retinoblastoma, such as development of new tumors and family history of retinoblastoma, while trending toward increased risk of possessing germline Rb1 mutation.

CONTROL ID: 3546375

SUBMITTER (NAME ONLY): Rikard Frederiksen

TITLE: Transducin translocation enables the recovery of responsiveness in bright persistent light in mouse rod photoreceptors

SESSION TITLE: Photoreceptors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Frederiksen, A. Morshedien, S.A. Tripathy, T. Xu, G.H. Travis, G.L. Fain, A.P. Sampath, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The high sensitivity of rod photoreceptors has led to the notion that they saturate when exposed to moderate light intensities, thus contributing little to vision in bright light. Recent studies have challenged this view and suggest that rods are able to avoid saturation under some conditions of bright persistent illumination. We tested the hypothesis that the light-dependent translocation of the G protein, transducin, causes a reduction in gain, allowing rods to escape saturation during prolonged illumination.

Methods: We recorded mouse rod photoresponses en masse using ex vivo electroretinogram (ERG) as well as single-cell suction electrode recording in the presence of steady, bright background light. Cone contributions were eliminated from ERGs by the use of $Gnat2^{-/-}$ mice. In addition, we recorded from $Gnat2^{-/-}$ $Gnat1^{-/-}$ $A3C^{+}$ mice in which the alpha subunit of transducin has an additional S-palmitoylation site that anchors it more tightly to cell membranes and thus impedes its translocation. The amount of pigment bleaching under experimental conditions was quantified using microspectrophotometry to measure spectral absorbance.

Results: During prolonged exposure to bright light ($10^4 - 10^6$ effective photons $\mu m^{-2} s^{-1}$) rods recovered responsiveness from initial saturation, increasing their response amplitude and sensitivity over a period of 30 - 90 minutes. In the $A3C^{+}$ mouse, responses in the presence of the background light were almost undetectable immediately after turning on background light and continued to be smaller, growing much more slowly in amplitude than in control retinas. In addition, control rods remained responsive even after light exposures that were calculated to bleach nearly all the rhodopsin. This finding was confirmed in both whole retina recording as well as single-cell recording, indicating that a mechanism of pigment regeneration within the rods themselves is required to sustain responsiveness during prolonged bright light exposure.

Conclusions: The reduction in outer-segment transducin and a novel mechanism of visual-pigment regeneration within the rod itself together enable rods to remain responsive over the whole of the physiological range of vision. In this way, rods are able to avoid an extended period of channel closure, which is known to cause photoreceptor death.

CONTROL ID: 3546379

SUBMITTER (NAME ONLY): Aruna Gorusupudi

TITLE: A synthetic very-long-chain polyunsaturated fatty acid (VLC-PUFA) enhances photoreceptor development in ELOVL4 knockout retinal organoids

SESSION TITLE: Ocular disease models: molecular mechanisms and therapeutic approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Gorusupudi, P.S. Bernstein, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|K. Eade, Scripps Health, San Diego, California, UNITED STATES|K. Eade, S. Harkins-Perry, S. Giles, Lowy Medical Research Institute, La Jolla, California, UNITED STATES|J.D. Rainier, Department of Chemistry, university of Utah, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent studies on VLC-PUFAs (C24-36) have revealed their specific presence and importance in retina. They are rarely consumed in diets and are specifically synthesized in vivo from long-chain PUFAs through the action of an enzyme known as ELOVL4. Genetic defects in ELOVL4 underlie the retinal pathology in Stargardt Type 3 (STGD3), a dominant, early-onset blinding disease with many symptoms that mirror dry age-related macular degeneration (dAMD). In a previous study, we chemically synthesized a VLC-PUFA (32:6 n-3) and measured its uptake in mouse retina and its beneficial effects on vision. In order to further study the role of VLC-PUFAs on photoreceptor development and maintenance, we supplemented 32:6 n-3 to ELOVL4 knockout retinal organoids.

Methods: We knocked out ELOVL4 in normal human iPSCs using CRIPR/Cas9 technology and generated retinal organoids using standard techniques. When the organoids had completed the phase of photoreceptor birth (17 weeks), the ELOVL4^{-/-} organoids were divided into two groups. One group was supplemented with 8 µM 32:6 n-3, while the control group received vehicle alone. Photoreceptor outer segment morphology and length were measured at 33 weeks of age.

Results: By 33 weeks of age, the vehicle-treated ELOVL4^{-/-} organoids had outer segments, but they appeared shorter and more disorganized than expected for normal human retinal organoids. The ELOVL4^{-/-} organoids supplemented with 32:6 n-3 had significantly longer outer segments (P<0.001) with normal morphology.

Conclusions: These results establish that ELOVL4^{-/-} organoids can be used as a model to study the pathophysiology and treatment of diseases associated with ELOVL4 dysfunction and that a synthetic VLC-PUFA can rescue abnormalities associated with absence of ELOVL4 activity. We are currently studying the ultrastructure of the outer segments of our treated and control organoids and the efficacies of n-3 versus n-6 VLC-PUFAs.

CONTROL ID: 3546380

SUBMITTER (NAME ONLY): Muriel Schornack

TITLE: Long-Term Management of Patients with Keratoconus

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Schornack, C.B. Nau, Mayo Foundation for Medical Education and Research, Rochester, Minnesota, UNITED STATES|J.S. Harthan, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|J.S. Fogt, The Ohio State University College of Optometry, Columbus, Ohio, UNITED STATES|E. Shorter, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|A.C. Nau, Korb and Associates, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study will examine the practice patterns of long term management of keratoconus patients including follow up visit, frequency of topography and surgery.

Methods: An internet-based, 22 question, IRB approved RED-Cap survey of providers who managed at least one KC patient per week. Descriptive analyses are presented. Some responses allowed more than one answer.

Results: Of the 296 respondents, 245 providers with an average of 23.1 +12 years in practice met entry criteria. Respondents (n=220) averaged caring for 27.2 +35 KC patients each month. Respondents follow stable KC patients as follows: 6 month intervals (n=76) or 12 months (n=142). Stable patients were administered topography as follows (n=299): Initial visit (n=91), every follow up visit (n=43), only if progression suspected (n=31), every 6 months (n=26), every year (n=126),more than a year (n=25). Most practitioners (n=222) follow unstable KC patients at 3 month (n=78) or 6 month (n=134) intervals, while few follow them annually (n=10). Unstable KC is followed with topography as follows (n=299): at every follow up (n=101), only if indicated (n=27) every 6 months (n=99) every 12 months (n=29). Respondents recommend crosslinking in the following situations (n=221): All patients (n=16), documented diseases progression regardless of age (n= 118), documented progression under 40 (n=75), Other (n=12). Respondents were asked to estimate the percentage of patients who had undergone crosslinking. Results were as follows (n=212): 0-10% (n=86), 11-25% (n=82), 26-50% (n=38), 51-75% (n=13), 76-100% (n=3). Respondents (n=222) were asked to estimate the percentage of patients with KC who had undergone corneal transplantation. Results were as follows: 0-10% (n=104), 11-25% (n=90), 26-50% (n=26), 51-75% (n=2), greater than 75% (n=0).

Conclusions: Practice patterns for long term management of keratoconus show wide variability in terms of follow up care and assessment of progression with point of care testing. While respondents stated that they often recommend crosslinking, there are still few patients who have undergone the procedure. Results from this survey support the recent trend for fewer patients with corneal transplants. Better patient outcomes might be achieved with more defined algorithms for follow up care and point of care testing.

CONTROL ID: 3546382

SUBMITTER (NAME ONLY): Victor Guaiquil

TITLE: Expression of axon guidance proteins in the cornea and trigeminal ganglia and their role in cornea neuro-epithelium regeneration.

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V.H. Guaiquil, G. Dimailig, C. Xiao, D. Lara, Q. Zhou, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Determine the expression and neurogenic potential of axon guidance proteins in the cornea.

Methods: The expression of axon guidance proteins belonging to the Semaphorins, Ephrins and Netrins families of proteins, and their associated receptors were evaluated by RT-qPCR and immunofluorescence staining (IF) in mouse trigeminal ganglia and cornea tissues. Corneas (n=3 per condition) were subjected to epithelium debridement and the recovery of gene and protein expression was analyzed at 0, 1, 3, 5, 7 and 14 days post injury. Gene expression was evaluated using predesigned mouse TaqMan gene expression assays using validated internal controls. Protein expression was analyzed by immunofluorescence staining, tissue cryosections were incubated with antibodies against different members of axon guidance proteins and imaged under a fluorescent microscope. The epithelium and subbasal nerves regeneration of injured corneas were evaluated in mice treated with axon guidance recombinant proteins and compared to vehicle controls. Slit lamp, Von Frey filaments and B3 tubulin staining were used to determine the epithelium recovery, nerve sensation and nerve regeneration respectively.

Results: We found that all axon guidance proteins evaluated are expressed in the trigeminal ganglia and cornea epithelium. In the trigeminal ganglia all proteins were found in the neuronal cell body and few of them were expressed in the axons projecting to the cornea. The receptors that are usually associated with these proteins such as Neuropilins, Plexins and VEGFRs were also present in both tissues with certain degree of variation. After corneal epithelium injury there was a fast recovery of axon guidance proteins gene expression. They initially colocalized within the basal cells in the epithelium and remained in the first two epithelial cell layers after two weeks post injury. Two of the axon guidance proteins studied in vivo, significantly enhanced nerve regeneration and may have pleiotropic effects since they induce neuronal growth on isolated neurons and accelerate epithelium recovery in scratch assays.

Conclusions: Axon guidance proteins are crucial for axonal targeting in the eye. In the adult cornea they are highly expressed in the steady state and quickly upregulated after injury. Their trophic and neuro-regenerative effects indicate that they may be essential for cornea repair.

CONTROL ID: 3546383

SUBMITTER (NAME ONLY): Lucy Mudie

TITLE: Performance of the Spot Vision Screener in Children with Down Syndrome and Other Special Needs

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Mudie, E. McCourt, R. Enzenauer, Ophthalmology, University of Colorado Health, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Amblyopia is the most common cause of monocular blindness in adults and children, and disproportionately affects developmentally delayed children; being up to 3 times more common in one study. After the age of 9, amblyopia becomes irreversible, highlighting the importance of early detection. The Welch-Allyn Spot Vision Screener (Spot) is a commonly used device for detecting amblyogenic risk factors. The Spot takes a photograph of the child's eyes and determines approximately their refractive power, eye alignment and if there are any visual obstructions (such as ptosis or cataract). The test typically lasts 6 seconds and is without any known risks. Prior studies have reported good accuracy of Spot in the general population, however its performance in patients with Down Syndrome and special needs is not substantiated. Our study assessed the efficacy of Spot at detecting various amblyogenic risk factors in developmentally delayed children.

Methods: Children with various disabilities or delays were recruited from the Children's Hospital of Colorado Eye Clinic, Special Care Clinic and the Sie Center for Down Syndrome. Participants had their photograph taken with Spot pre and post pupillary dilation, and this was then compared to a comprehensive eye exam in the Ophthalmology clinic.

Results: One hundred children participated in the study. Twelve children were unable to get images with Spot and 5 did not attend for their exam in the eye clinic. The mean age was 5.9 years (standard deviation, SD, 3.4). 64% were male and 58% were non-Hispanic white. The overall sensitivity of Spot was 90% and the positive predictive value was 80% in undilated subjects. The area under the receiver operator curve (AUROC) was 0.68 (95% confidence interval, CI: 0.57-0.79), and this was not significantly different from the AUROC of Spot accuracy after dilation (0.68, 95% CI: 0.54-0.81).

Conclusions: The Spot Vision Screener performed well in this cohort of special needs children, the children did not need to be dilated in order for the Spot to have good accuracy. Spot could be used by primary care clinics and vision screening programs to better triage which patients need to be referred to Ophthalmology.

CONTROL ID: 3546384

SUBMITTER (NAME ONLY): Marc-Antoine Millette

TITLE: Modulation of the acylation of the C-terminal segment of GRK1 drastically influences its solubility and membrane-binding properties

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Millette, C. Gagnon, C. Salesse, Universite Laval, Quebec, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: G-protein coupled receptors (GPCR) are key receptors in signal transduction. They are inactivated by G-protein coupled receptor kinases (GRK). GRK1 is the first member of the GRK family, which includes seven members. All GRK bind membranes via their C-terminal segment. Four GRKs are acylated at their C-terminus: GRK1 is farnesylated, GRK7 is geranylgeranylated, GRK4 and 6 are palmitoylated. The objective of this research work was to compare the extent of membrane binding of the 30 most C-terminus amino acid residues of GRK1 bearing three different acyl groups (palmitoyl, farnesyl and geranylgeranyl).

Methods: Infrared spectroscopy and circular dichroism measurements were performed to determine the secondary structure of the C-terminal segments. Fluorescence spectroscopy measurements were performed to gather information on the environment of tryptophan 531.

Results: Infrared and circular dichroism measurements showed these the acylated C-terminal segments adopt a random coil structure. Intrinsic fluorescence measurements suggest that the farnesylated segment of GRK1 is soluble in aqueous solution, whereas the palmitoylated segment is only partially soluble and the geranylgeranylated segment is aggregated. In addition, no significant increase in the fluorescence of the farnesylated segment was observed in the presence of sodium dodecyl sulfate (SDS). Moreover, measurements at increasing concentration of small unilamellar vesicles (SUVs) made of palmitoyl-oleoyl-phosphocholine (POPC) showed little modification in the position of the emission maximum, suggesting that this residue is not membrane embedded. In contrast, a drastic increase in fluorescence of the palmitoylated segment was observed in presence of SDS and SUVs, whereas an increase was only observed with SDS for the geranylgeranylated segment. Membrane binding to phospholipid monolayers shows a preferential binding of the farnesylated segment to unsaturated phospholipids, whereas a higher affinity to saturated phospholipids was observed for the palmitoylated segment.

Conclusions: The modification of the acylation of the C-terminal segment of GRK1 using either a farnesyl, a palmitoyl or a geranylgeranyl group drastically lowered its solubility. The preferential binding of the farnesylated segment for unsaturated phospholipids was modified in favor of saturated phospholipids with the palmitoylated segment.

CONTROL ID: 3546386

SUBMITTER (NAME ONLY): Jasmin J Weindler

TITLE: Aflibercept influences the immunocompetence of Dendritic Cells.

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Weindler, F. Bock, M. Hamdorf, C. Cursiefen, Ophthalmology, Uniklinik Köln, Köln, Nordrhein-Westfalen, GERMANY|

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ABSTRACT BODY:

Purpose: In the course of keratoplasty, inflammatory processes may lead to a higher risk of graft rejection by changing the immunocompetence of dendritic cells (DCs). Therefore, in this experimental in-vitro study the effect of Aflibercept on the differentiation of DCs was investigated.

We hypothesize that administration of Aflibercept during maturation of DCs can influence the immunocompetence of mature DCs by neutralizing autocrine/paracrine VEGF-A.

Methods: Peripheral Blood Mononuclear Cells of human blood donors (N= 5-6) were differentiated in DC-Medium containing IL-4 and GM-CSF. At the beginning of maturation of immature DCs into mature DCs either 40µg/ml Aflibercept or 40µg/ml Fc-IgG-control was given to the cells. Maturation of DCs was performed with cytokines (CS; containing IL-1b, IL-6, TNFa and PGE) or Lipopolysaccharide (LPS).

After entering the stadium of mature DCs flow cytometry was performed with the focus on DC-specific surface markers (CD11c, CD40, MHC II), co-stimulatory receptors for T-cell stimulation (CD80, CD83, CD86) and the VEGF receptors VEGFR1 and VEGFR2.

Also, RNA was harvested of treated mature DCs and mRNA-levels of VEGF-A and VEGFR1 were investigated by using Realtime-PCR (RT-PCR).

Statistical analysis was performed with GraphPad Prism using a t-test or Man-Whitney-U-test.

Results: Aflibercept administrated during maturation of dendritic cells induced significant upregulation of the receptor CD11c (CS: p: 0.0145; 111.7%±44.1) and a significant downregulation of the co-stimulatory receptors CD83 (LPS: p: 0.032; 97.4%±16.8) and CD86 (LPS: p: 0.047; 94.01%±6.7) as well as VEGFR1 (CS: p: 0.0095; 47.1%±19.1). Furthermore, the frequency of VEGFR1-positive cells decreased significantly under Aflibercept treatment (CS: p: <0.0001; 21.4%±14.7; LPS: p: 0.0001; 36.1%±8.5).

No differences of the VEGF-A-mRNA-level or the VEGFR1-mRNA level was seen in the RT-PCR.

Conclusions: Aflibercept has a direct effect on dendritic cell maturation. Aflibercept modulates DC immunocompetence by downregulation of the receptors CD83 and CD86. The downregulation of the receptor VEGFR1 as well as the reduced expression of VEGFR1 on DCs treated with Aflibercept suggest that Aflibercept interacts with this receptor or could have an effect on the binding of VEGF-A on this receptor.

CONTROL ID: 3546387

SUBMITTER (NAME ONLY): Jeffrey Wu

TITLE: High risk of mortality in sickle cell patients requiring pars plana vitrectomy

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wu, R. Muhtadi, A. Radpavar, N. Jackson, Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|P.D. Suman, A. Crouch, S. Curtis, C. Minniti, U. Mian, Montefiore Medical Center, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sickle cell disease (SCD) causes vascular occlusion associated with ischemia and increased mortality. SS genotype has been shown to have worse mortality than SC. Major complications of SCD that contribute to premature death include organ failure, acute sickle crisis, and stroke. Since these major complications of SCD are associated with increased vascular occlusion, we wanted to investigate if increased vascular occlusion in the retina could be a sign of worsening disease and therefore, a risk factor for increased mortality. There have not been studies looking at ophthalmic characteristics with SCD mortality. The goal of this study was to evaluate high risk ophthalmic characteristics that could be correlated more with deceased SCD patients.

Methods: This retrospective study included adult SCD patients seen routinely at Montefiore Medical Center (Bronx, NY) from January 2014 to June 2020. Patients were categorized as Deceased Patients (DP, n=57) and Living Patients (LP, n=985). Data on demographics, lab values, comorbidities, and ophthalmic care were obtained from Montefiore EMR (Epic, Verona, WI). Deceased patients were identified either from notification of the primary care provider or hospital records. Statistics were analyzed using R. Wilcoxon ranked sum test was used for continuous variables and Chi Square test was used for categorical variables unless the frequency counts were small (<10) in which case, a Fisher's exact test was used.

Results: The study included 1036 patients. 26 DP and 484 LP had at least one documented eye exam. Of these, DP were significantly older than LP ($p=0.003$). This difference was significant for SS patients ($p=0.004$) but not for SC ($p=0.81$). There were no significant differences between DP and LP in race or sex. DP were significantly more likely than LP to have had pars plana vitrectomy (PPV) ($p=0.007$). This significant difference was seen even when stratified for SS ($p=0.003$). There were no significant differences for diagnosis of proliferative sickle retinopathy (PSR) or laser retinopathy between DP and LP.

Conclusions: Higher rates of PPV in DP suggests that SCD patients requiring PPV may be at a higher risk of death. We recommend that SCD patients requiring PPV should be more carefully monitored regarding their general health.

CONTROL ID: 3546388

SUBMITTER (NAME ONLY): Brian Fitzpatrick

TITLE: Accurate machine-learning estimation of axial length distribution in human populations from refraction, corneal curvature, age and gender

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Fitzpatrick, I. Flitcroft, J. Loughman, Centre for Eye Research Ireland, Technological University Dublin, Dublin, Dublin, IRELAND|

Commercial Relationships Disclosure (Abstract): Brian Fitzpatrick: Commercial Relationship: Code N (No Commercial Relationship) | Ian Flitcroft: Commercial Relationship(s);Ocumetra Ltd:Code I (Personal Financial Interest) | James Loughman: Commercial Relationship(s);Ocumetra Ltd:Code I (Personal Financial Interest)

ABSTRACT BODY:

Purpose: Human axial length (AL) is one of the most important ocular biometric parameters when it comes to understanding, tracking, and treating many ocular diseases. Ophthalmic datasets featuring AL are relatively small since AL measurements require specialized costly equipment. Datasets featuring simpler biometric parameters such as refraction but without AL can be very large in comparison since these variables are more straightforward to measure. We introduce a new machine learning technique that leverages refraction, corneal curvature, age and gender data to obtain estimates of the AL distribution in a population that can be at least as accurate as those given by direct measurement and kernel density estimation.

Methods: A regression-based machine-learning model was generated to predict AL from refraction, corneal curvature, age and gender (auxiliary data) based on a training dataset (n=383 records). Kernel density estimation (KDE) which incorporated this imputed AL information was then performed on a testing dataset (n=3809 records). On big datasets this approach is computationally intensive, so methods to accelerate the computations were explored.

Results: Comparison of the imputed AL distribution with conventional kernel density estimation of measured AL in the testing dataset showed no significant difference on the KS test at the 0.05 level. A Fast Gauss Transform (FGT) based algorithm significantly shortened computational time. The FGT algorithm accelerated the process 321-fold for a dataset of 800 eyes and 2087-fold for 4000 eyes (figure 1). Mathematical modelling demonstrated that the bias and variance of the estimator depend primarily on the number of input AL observations, the number of auxiliary data observations, and the properties of the auxiliary data. As a sample of AL measurements only estimates the true population AL distribution, a large sample of auxiliary data using this algorithm can match or exceed the accuracy of a smaller sample of AL measurements (figure 2).

Conclusions: The machine learning technique introduced in this work can accurately estimate the population distribution of AL by using refraction, corneal curvature, age and gender auxiliary data. This allows for the development of improved population centile data for AL from a wide range of epidemiological sources, which may be applied clinically in areas such as myopia control.

CONTROL ID: 3546391

SUBMITTER (NAME ONLY): Aiswaryah Radhakrishnan

TITLE: Fixational Performance and Visual Function changes underwater in normal eyes

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Radhakrishnan, V.S. Ramasubramanian, Department of Optometry, SRM Institute of Science and Technology, Kattankulathur, Tamil Nadu, INDIA|

Commercial Relationships Disclosure (Abstract): Aiswaryah Radhakrishnan: Commercial Relationship: Code N (No Commercial Relationship) | Vivek Ramasubramanian: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Vision underwater is suboptimal and the human eye is poorly adapted to the aquatic environment. Differences in refractive index, illumination levels and image blur by the dynamic water environment contributes to altered vision underwater. In this study, we investigated changes in fixational eye movements, refractive error and vernier acuity with and without underwater blur in young normal eyes.

Methods: Fifteen young subjects (Age: 20 years to 35 years) with refractive error and otherwise normal ocular health participated in the measurements. None of the subjects had astigmatism $> 1D$ or any other ocular pathology. Fixational eye movements (FEM) were recorded while the subjects viewed a dynamic video target displayed on Display++ monitor using LiveTrack FM. Using an NVision-K 5001 openfield autorefractor, changes in spherical equivalent of refractive error (SEQ) during a reading task was measured every 30 seconds for 5 minutes. Vernier Acuity (VER) was measured using FrACT®. The reading task and the stimulus for VER were also presented on Display++ with the subject seated about 2m from the monitor. Underwater blur was simulated by generating turbulence and waves in water using mechanical motors, in a transparent tank placed between the subject and the monitor. All measurements were performed in a dim room illumination without and with underwater blur under binocular viewing conditions for each eye and for both eyes together. Overall the measurement lasted about 1.5 hours.

Results: FEM with and without underwater blur was significantly different ($p < 0.0001$, Fig.1). The mean increase in pupil size underwater was $0.2\text{mm} \pm 0.04$ ($p < 0.05$). The change in refraction was mostly hyperopic (64%) with maximum shift of $-0.10D \pm 0.25$ ($p = 0.6$, $U = 420.5$). On an average across subjects and eye, the difference in refractive error with and without underwater blur was $-0.02D \pm 0.34$ and was not statistically significantly different ($p = 0.26$, $U = 431$). The average VER with underwater blur ($18 \text{ arcsec} \pm 11$) was significantly lesser ($p = 0.0001$) than without underwater blur ($31 \text{ arcsec} \pm 20$).

Conclusions: No significant changes were observed in fixational eye movements and refractive status with underwater blur. A significant decrease in Vernier Acuity was observed with underwater blur. Our results imply that the subjects could probably experience difficulties in depth judgement in an aquatic environment.

CONTROL ID: 3546392

SUBMITTER (NAME ONLY): Matthew Mason

TITLE: Profile of vascular permeability factors in aqueous humor of diabetic macular edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mason, S. Ugarte, L. Christie, G. Rodrigues, F.J. Lopez, Allergan, an AbbVie company, California, UNITED STATES|K. Lashkari, Advanced Eye Centers Inc, North Dartmouth, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many growth factors and cytokines are involved in the onset of diabetic retinopathy (DR), some promoting increased vascular permeability and neovascularization and contributing to disease progression. Previous investigations into the proteomic signature of Diabetic Macular Edema (DME) have characterized a number of factors; however, many consist of circulating cytokines and chemokines. We hypothesized a model of DME progression, vascular breakdown and edema could be strengthened by comparing known and putative permeability associated markers in the aqueous of diabetic subjects with or without a diagnosis of DME.

Methods: Aqueous humor samples (AH) were collected from 3 sources: Healthy non-diabetic control subjects at cataract surgery (CTL), non-proliferative diabetic retinopathy with absence of DME (NPDR), and NPDR with DME (DME). Samples were collected at Advanced Eye Centers, Dartmouth, MA, and delivered to Allergan/AbbVie, Irvine, CA for analysis. Three multiplex panels (Luminex) spanning 47 soluble protein markers were used to detect protein levels in 108 subject samples (CTL: 42, NPDR: 35, DME: 31).

Results: Of the 47 markers surveyed in DME subject samples, 13 were significantly upregulated when compared to control or NPDR following age-corrected univariate ANCOVA with Dunnett's correction for multiple comparisons. Upregulated factors included angiopoietin 2, angiostatin, endothelin 1, hepatocyte growth factor, placental growth factor 1, stem cell factor, soluble epidermal growth factor receptor, soluble hepatocyte growth factor receptor, soluble urokinase plasminogen activator surface receptor, and thrombospondin 2 (p values < 0.001). Platelet-derived growth factor B dimer (PDGF AB/BB) was downregulated compared to CTL (p< 0.01).

Conclusions: The strength and potential predictive value of the prospective markers modeled here are demonstrated by principal components analysis (PCA), showing that >70% of variance could be preserved by only two components. These markers were strongly associated with DME when grouped by PCA and >87% of DME subjects could be sorted by a single component (+PC1). Further, >90% of CTL subjects were sorted by PC2 and showed strong positive correlation with expression of a single marker (PDGF AA/BB; 0.624). In summary, these data provide a focused examination of permeability factors in addition to VEGF and present a robust model of AH disease markers highly associated with DME.

CONTROL ID: 3546393

SUBMITTER (NAME ONLY): Jacques Charlier

TITLE: Evaluation of a new technique for the comparison of wide field eye fundus images and perimetry

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.R. Charlier, Research and development, Metrovision, Perenchies, Hauts de France , FRANCE|X. Zanlonghi, Clinique Jules Vernes, Nantes, FRANCE|

Commercial Relationships Disclosure (Abstract): Jacques Charlier: Commercial Relationship(s);metrovision:Code I (Personal Financial Interest) | Xavier Zanlonghi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The comparison of wide field eye fundus images (WFI) and functional tests is of great interest in a number of diseases of the retina. The purpose of this study was to evaluate a new technique for the comparison of WFI and wide field perimetry results (WFP).

Methods: WFI and WFP are both projections on a plane surface of the retina which can be approximated to a spherical shape. However, the projection of a retinal scotoma is different in the stereographic projection used in WFI and in the azimuthal equidistant projection used for perimetry. This results in differences in the localization and quantification of scotoma.

In a first study, a simulation software was used to evaluate the errors produced by these two projection modes for the position, shape and surface area of a scotoma of circular shape and constant surface area on the retina.

In a second study, we evaluated on 7 clinical cases with peripheral alterations the benefit of converting the representation of the WFP to WFI coordinates to allow the comparison of Goldmann perimetry results obtained with the MonCvONE perimeter (Metrovision) with wide field eye fundus images imported from OPTOS. Superposition was obtained by matching the positions of the fovea and optic disk.

Results: The following table summarizes the errors obtained with the two projection solutions.

When eccentricity to the fovea increases:

- measures of distances along meridians increase with WFI (+33% at 60d) and are constant with WFP,
- shapes of scotoma are preserved with WFI and become deformed with WFP (+21% at 60d)
- surface area is altered more significantly with WFI (+78%) than with WFP (+21%).

The following images show the results from a retinitis pigmentosa case with superposition of the eye fundus and Goldmann perimetry.

It shows that the discrepancy found with the WFP projection is corrected when using the WFI projection. The same is found for other cases when peripheral alterations are involved.

WFP projection WFI projection

Conclusions: The new method allows the comparison of eye fundus images and perimetry results at large eccentricities (over 20 degrees) and this is important to avoid significant errors in the position and quantification of scotoma.

CONTROL ID: 3546394

SUBMITTER (NAME ONLY): Runze Li

TITLE: Research the Anisotropy Property in Equator Sclera Using High Frequency Ultrasonic Elastography

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is one of the leading causes of blindness across the world, and elevated intraocular pressure is the most risky factor of the glaucoma. The equator sclera plays a pivotal role in vision as it provides stable mechanical support to the fragile optic nerve and retina under dynamic force loading condition. Previous research mainly focused on the mathematical modeling to predict its anisotropy property to the response of elevated IOP. In this study, we aim to use the high frequency ultrasonic array based elastography to investigate the anisotropy property of equator sclera experimentally in the superior, temporal, nasal and inferior locations under different IOP conditions.

Methods: A piezoelectric shaker was used to induce tissue motion instead of acoustic radiation force. The unscaled pig eye was connected with infusion line and IOP sensor. A mechanical shaker (mini-shaker type 4810; Bruel & Kjaer) was positioned at the anterior sclera to initiate elastic wave. An ultrasonic array (L22-14v; Verasonics Inc.) was positioned above the equator sclera and its beam was aligned to be parallel with the shaker.

Results: Fig. 1 shows one example in the superior location of the B-mode images and the corresponding spatial-temporal maps in different IOP in two different directions. The elastic wave speed can be acquired using liner regression algorithm of each wavefront with its corresponding lateral position (indicated by red lines). In the equator direction, from 10 mmHg to 30 mmHg, the elastic wave speed is 6.1 m/s, 11.83 m/s, 13.70 m/s, 14.35 m/s and 15.16 m/s respectively. The reconstructed Young's modulus is 111.63 KPa, 419.85 KPa, 563.07 KPa, 617.77 KPa and 689.48 KPa respectively. In the anterior to posterior direction, elastic wave velocities are 3.7 m/s, 4.26 m/s, 4.75 m/s, 5.46 m/s and 6.18 m/s, and the Young's modulus are 32.08 KPa, 54.44 KPa, 67.69 KPa, 89.43 KPa, 114.58 KPa correspondingly.

Conclusions: The equator sclera has the anisotropy property, it is stiffer along with the equator direction. These results demonstrate the feasibility of our system to investigate the anisotropy property in equator sclera with elevated IOP.

CONTROL ID: 3546396

SUBMITTER (NAME ONLY): Raymond Douglas

TITLE: Teprotumumab use in a real-world setting: expanded access program findings

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Teprotumumab was recently approved in January of 2020 to treat thyroid eye disease (TED). The purpose of this study was to evaluate the safety profile and Graves' ophthalmopathy quality of life questionnaire (GO-QOL) for a group of patients in which compassionate use of teprotumumab was deemed appropriate, prior to U.S. Food and Drug Administration (FDA) approval.

Methods: Adults with active, moderate-to-severe TED were scheduled to receive 8 infusions (10 mg/kg first infusion, 20 mg/kg thereafter) of teprotumumab over 21 weeks. Adverse events (AEs), lab assessments, vitals and GO-QOL (max QOL=100) were assessed.

Results: 22 patients (52.4±16.2 years, 64% female, 91% non-smokers, 7.2±3.0 months TED duration) from 8 sites were treated. 19/22 (86%) received 8 infusions (3 discontinued treatment due to COVID-19, personal choice, and hyperglycemia). Baseline Total GO-QOL was 47.8±21.4 (appearance [AP]: 42.9±26.7, visual function [VF]: 52.9±24.6). At Week 21, Total GO-QOL improved from baseline by 24.9±21.0 points (AP improved by 23.8±26.2, VF improved by 25.7±25.8), all large changes. All patients reported an AE. One patient suffered from appendicitis, which was deemed unrelated. Other AEs (>2 patients) included muscle spasms (n=11), fatigue (n=10), hypoacusis (n=5), headache (n=5), nausea (n=5), extremity pain (n=4), alopecia (n=4), hypertension (n=4), dry skin (n=3), diarrhea (n=3), tinnitus (n=3), myalgia (n=3), increased lacrimation (n=3), and hypogeusia (n=3). No new safety concerns were identified.

Conclusions: Teprotumumab resulted in large QOL improvements as demonstrated previously in controlled clinical trials. Safety findings were consistent with the previously established teprotumumab profile.

CONTROL ID: 3546398

SUBMITTER (NAME ONLY): Konstantinos A.A. Douglas

TITLE: Retinal microvasculature evaluation in patients with cystoid macular edema secondary to diverse ocular pathologies.

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Douglas, V. Douglas, I. Garg, R. Katz, J. Miller, Retina, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|K. Douglas, V. Douglas, I. Garg, R. Katz, J. Miller, Harvard Retinal Imaging Lab, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantitatively evaluate and compare the retinal microvasculature in patients with cystoid macular edema (CME) secondary to diabetes (DME), central retinal vein occlusion (CRVO), branch retinal vein occlusion (BRVO) and post-cataract surgery (pseudophakic CME; PCME) using optical coherence tomography angiography (OCTA).

Methods: In this observational study, 91 eyes (51 patients) with CME and their fellow eyes serving as controls underwent ophthalmologic examination and imaging using OCTA (Optovue XR Avanti, USA). The 3x3 en face angiograms (automatically segmented) of superficial capillary plexus (SCP) and deep capillary plexus (DCP) were analyzed using ImageJ program. Parameters analyzed were the foveal avascular zone (FAZ) size in the SCP, and vessel density (VD), vessel skeleton density (VSD) in the SCP and DCP. Descriptive statistics and mixed-effects multiple regression model accounting for inclusion of two eyes of same patient were used to quantitatively summarize the features of our cohort. The statistical analysis was performed using the statistics software SPSS (v 19; IBM Corp., Chicago, IL, USA). Results with a p value < 0.05 were considered significant.

Results: Ninety-one eyes (37 DME, 10 CRVO, 10 PCME, 9 BRVO and 25 control) were included in the analysis. Total mean age was 63.5±10.5 years (p=0.136) and no significant differences in other demographic characteristics were noted. Best corrected visual acuity (BCVA, measured in logMAR) was significantly different among groups (0.25±0.19, DME; 0.5±0.4, CRVO; 0.53±0.5, PCME; 0.67±0.53, BRVO; 0.05±0.09, controls; p<0.001). No significant differences were observed in FAZ size (p=0.17), VD (p=0.15) and VSD (p=0.18) in SCP using mixed-effects multiple linear regression analysis. Furthermore, VD (2.8±0.25, DME; 2.7±0.22, CRVO; 2.8±0.4, PCME; 2.8±0.21, 3.2±0.36, controls) and VSD (7.7±0.12, DME; 7.75±0.13, CRVO; 7.67±0.22, PCME; 7.73±0.15, BRVO; 7.52±0.14, controls) in DCP were significantly different among groups (p<0.001 and p<0.001 respectively).

Conclusions: To our knowledge this is the first study comparing the retinal microvasculature in patients with CME secondary to diabetes, CRVO, BRVO, post-cataract surgery and their fellow eyes. Our results revealed that fellow eyes of those patients had statistically significant higher VD and lower VSD measurements in DCP when compared to any CME group but not between groups.

CONTROL ID: 3546399

SUBMITTER (NAME ONLY): Nicolás Pérez-Llombet Quintana

TITLE: Identification of maternal and pregnancy risk factors in the development of retinopathy of prematurity in our area

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pérez-Llombet Quintana, O. Durán Carrasco, A. Afonso Rodríguez, M. Alberto Pestano, R. Abreu González, C. Fernández Núñez, M. Gil Hernández, Ophthalmology, University Hospital of La Candelaria, Santa Cruz de Tenerife, SPAIN|

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ABSTRACT BODY:

Purpose: Retinopathy of prematurity (ROP) is a vasoproliferative retinal disease that has a multifactorial origin and can cause serious vision disturbances. Our goal is to identify possible maternal risk factors (RF) and those associated with pregnancy for the development of ROP in newborns at risk examined in our center, between January 2015 and December 2019.

Methods: A descriptive and retrospective study was carried out analyzing maternal and pregnancy-related risk factors in newborns with a birth weight less than 1500 grams and a gestational age less than 32 weeks in a 4-year period (2015 - 2019). Subsequently, a comparative study was carried out between a group of patients who developed ROP and a control group without signs of ROP who presented similar characteristics in terms of weight and gestational age. Finally, the statistical analysis of the data was carried out using SPSS Statistics 22.0.

Results: 88 newborns were evaluated (15 of them affected by ROP and 73 healthy children) as well as maternal and pregnancy-related risk factors of their mothers. The mean age among the mothers of children with ROP was 32.8 +/- 5.49 years, while the mean age of the control group was 31.93 +/- 6.64 years.

Different maternal RF that may influence the development of ROP were studied. Among these, those that occurred most frequently in the group of mothers of children with ROP were cesarean delivery (73.3%), multiple pregnancy (53.3%), infections during pregnancy (40%), and premature rupture of membranes (33.3%). However, we only found statistically significant differences in the presence of multiple pregnancy for the development of the disease, with a confidence interval of 95% ($p = 0.037$).

Conclusions: The mothers of the newborns with ROP evaluated in our center presented various risk factors with relative frequency, such as cesarean delivery or infections during pregnancy. However, multiple pregnancy was the only factor that showed statistically significant differences compared to the control group ($p = 0.037$). Finally, it is necessary to emphasize the importance of maternal and pregnancy-related risk factors in the evolution of the newborns and in the development of ROP.

CONTROL ID: 3546400

SUBMITTER (NAME ONLY): Moawiya Alshunnar

TITLE: Outcomes and risk of reactivation of myopic CNV: Multi-Centre Study with long term follow up

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Long term outcomes and risk of reactivation of myopic choroidal neovascularisation (mCNV) are poorly understood. This study describes the treatment patterns, risk of reactivation and visual outcomes over ten years in a large cohort of patients.

Methods: Treatment-naïve eyes receiving at least one intravitreal anti-vascular endothelial growth factor (VEGF) injections for mCNV were included in the study. Data were generated during routine clinical care) between 09/2008 and 12/2018 utilising Medisoft Electronic Patient Record (EPR) data from 27 NHS sites in the UK. Main outcome measures included visual acuity (VA), number of injections, number of reactivations and number of visits.

Reactivations were defined as between 95 to 97.5 centile of distribution of injection interval in this study cohort.

Results: A total of 385 eyes of 380 patients receiving 1,822 injections were included. The mean age was 61.7 years old and the Female:Male was 2.25:1. Loess regression of Visual Acuity (VA) vs times 0, 6, 12, 24, 36, 48, and 60 months was 61, 64, 66, 66, 64, 61, and 59 (letters) . The end of an mCNV activity "reactivation" was determined to be 12 weeks (just below 97.5 centile of distribution of injection interval in this study cohort).

The mean number of injections was 3.12 injections during their first reactivation episode, which reduces to 2.04, 2.27, 2.36, 1.95, and 1.6 at their 2nd, 3rd, 4th, 5th, and 6th reactivation episode, respectively.

Conclusions: Our findings show that in the first four years of treatment, the VA is shown to have improved. However, past the fourth year, the VA steadily reduces. The data guides the temporal definition of the end of an mCNV reactivation and the number of treatments and the likelihood of further reactivations of disease activity occurring. These data will guide the counselling of patients and follow up intervals scheduling.

CONTROL ID: 3546401

SUBMITTER (NAME ONLY): Shreya Banerjee

TITLE: Vision and motor deficits due to loss of Vps11 function in a zebrafish model of genetic leukoencephalopathy

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Banerjee, L. Ranspach, X. Luo, R. Thummel, Ophthalmology, Visual and Anatomical Sciences, Wayne State University School of Medicine, Detroit, Michigan, UNITED STATES|L. Cianciolo, J. Fogerty, B.D. Perkins, Ophthalmic Research, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic Leukoencephalopathies (gLEs) are white matter disorders affecting the central nervous system, causing progressive abnormalities in the visual and motor systems. A mutation in Vacuolar Protein Sorting 11 (VPS11) has been identified as a causative allele of gLE in Ashkenazi Jewish individuals, with a carrier rate of 1:250. VPS11 forms membrane-tethering complexes with three additional VPS proteins to control crucial cellular processes in the endolysosomal and autophagy pathways. Here, we are characterizing two zebrafish vps11 mutant lines, vps11(plt) and vps11(KO), as potential models for gLE.

Methods: The DanioVision tracking system was used to monitor the movement of wild-type and mutant larvae at 5 and 7 days post-fertilization (dpf) (N>50 larva per time point per genotype). Two startle responses were utilized: a visual stimulus of alternating light and dark periods and an acoustic/mechanical stimulus of a loud tap. Output measurements included the distance travelled and velocity of movement. In addition, optokinetic response (OKR) analysis was performed using VisioTracker at 5dpf to test visual acuity (N>5 larva per genotype). One-way ANOVA with post-hoc Tukey's test was used to determine statistical differences between the groups.

Results: Behavioral analysis showed that vps11(plt) and vps11(KO) mutant fish could visualize changes in light and dark backgrounds, but OKR analysis indicated the animals were functionally blind and unable to make out an image at 5dpf. With regard to motor movement, no difference in response to alternating light-dark backgrounds was observed between the mutant and wild-type larvae at 5 dpf, but a significant reduction in movement and velocity of the mutants at 7 dpf ($p<0.01$; $p<0.01$) was observed. vps11(plt) and vps11(KO) mutants also showed significant reduction in movement to acoustic/mechanical stimuli at low ($p<0.01$; $p<0.01$) and high intensity ($p<0.01$; $p<0.05$). Together, these results suggest that loss of Vps11 function has a progressive defect on visual sensory and motor systems in zebrafish larvae.

Conclusions: Our findings support the use of zebrafish to further characterize the vision and motor defects associated with loss of Vps11 function.

CONTROL ID: 3546404

SUBMITTER (NAME ONLY): Anil Asrani

TITLE: Topical lacritin C-terminal peptide 'LacripepTM', significantly reduces both inferior corneal staining and burning/stinging in primary Sjögren's Syndrome dry eye

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.C. Asrani, M.G. Odrich, M.A. Carpenter, M.B. Logan, G.W. Laurie, TearSolutions, Inc., Charlottesville, Virginia, UNITED STATES|M.G. Odrich, Ophthalmology, University of Virginia, Charlottesville, Virginia, UNITED STATES|G.W. Laurie, Cell Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lacritin is a human tear protein with preclinical basal tear and corneal epithelial restorative properties encapsulated in the potent C-terminal synthetic peptide 'LacripepTM', (also known as 'N-94/C-6'). LacripepTM and natural C-terminal LacripepTM-like tear fragments also stabilize the tear film by interacting with the meibum fatty acid 'OAHFA'. Lacritin and fragments are selectively deficient or absent in almost all dry eye tears, particularly those from primary Sjögren's Syndrome. Here we test topical LacripepTM at two concentrations versus placebo as a natural replacement therapy in primary Sjögren's Syndrome - the first in human trial.

Methods: A double-masked, randomized, thirty-five center, first-in-human phase 2 study to evaluate the efficacy and safety of 0.005% and 0.01% LacripepTM in 204 subjects with dry eye associated with primary Sjögren's Syndrome was performed (ClinicalTrials.gov Identifier: NCT03226444) with both signs and symptoms assessed using NEI Workshop fluorescein corneal staining scoring and specific standardized patient symptomatology. Visit one initiated a two-week washout, followed by randomization at visit two, topical treatment TID for four weeks and a two-week washout. Endpoints were monitored after two and four weeks of treatment, and after treatment washout.

Results: After two weeks, 0.005% LacripepTM demonstrated a -0.4 reduction in inferior corneal staining (p value vs placebo 0.0055) - that segment of the cornea recognized as the most relevant in dry eye disease, as well as a -14.5 point reduction in complaints of burning and stinging (p value vs placebo 0.0024). LacripepTM was well tolerated and there were no serious treatment related adverse events. The results are consistent with a bell-shaped dose response (as seen in both preclinical and cell culture studies) and suggest the need for lower dose optimization.

Conclusions: LacripepTM appears to be rapidly efficacious for both sign and symptom in primary Sjögren's syndrome, the most severe form of dry eye. This is the largest ophthalmic trial to date in primary Sjögren's Syndrome dry eye and was the first-in-human clinical study conducted with LacripepTM as the active ingredient.

CONTROL ID: 3546406

SUBMITTER (NAME ONLY): Elvira Agron

TITLE: Geographic Atrophy and Reticular Pseudodrusen and Low-Luminance in the Age-Related Eye Disease Study 2

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Agron, C.A. Cukras, C.E. Malley, T.D. Keenan, E.Y. Chew, DECA, National Eye Institute, Bethesda, Maryland, UNITED STATES|T. Peto, Queens' University, Belfast, IRELAND|A. Domalpally, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|T.E. Clemons, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To correlate the presence of age-related macular degeneration (AMD) associated geographic atrophy (GA) and reticular pseudodrusen (RPD) with results of the night/dim light vision function captured on a night vision questionnaire (NVQ-10).

Methods: In a cross-sectional study of participants of the Age-Related Eye Diseases Study 2, AMD status was documented at the 5-year close-out study on ultrawide-field images divided into 3 zones: posterior pole (zone 1), peripheral (zone 2), and far periphery (zone 3). Zones 1 and 2 were divided into 4 quadrants: superonasal (SN), superotemporal (ST), inferonasal (IN), and inferotemporal (IT). Zone 3 was divided into superior and inferior. The reading center (Queens' University, Belfast) graded for presence of GA and RPD. The NVQ was administered. Specifically, the questions regarding driving at night and visual function in dim light/night were analyzed. Association between the presence of GA and RPD (analyzed separately) and two composite variables for driving and night/dim light vision were assessed using frequency tables and chi-square/Fisher's exact P-values.

Results: 889 eyes (450 participants) (mean age 72.5±8.1, female 58%) were analyzed. Comparing eyes with/without GA or RPD, statistically significant differences ($P < .001$ to $.01$) for % with difficulty in night/dim light vision were found for zone 1. In zones 2 and 3, higher differences were seen in the temporal regions with GA but not RPD. Comparing eyes with or without GA, significant differences were found for the % with moderate/extreme difficulty driving for zone 1 and the inferior regions of zone 2 ($P < .001$ to $.01$). No significant association was found between the presence of RPD in any zone and driving difficulty. Visual acuity was significantly lower for persons with low luminance difficulty and for eyes with GA in zone 1 ($P < .0001$).

Conclusions: Interestingly, the association was strongest with the GA or RPD located in the posterior pole or zone 1. This may be explained by rod distribution in the retina tend to be the highest around the paracentral area, located in zone 1. Despite having lesions in the more peripheral fields (zones 2 and 3), there is less of an impact on the function in dim light or at night. This provides further data to suggest the importance of patient reported outcome in our studies of disease progression/intervention.

CONTROL ID: 3546408

SUBMITTER (NAME ONLY): Manoj Prabhakar Nallabothula

TITLE: AutoPtosis: A dual model system for rapid and automatic detection of ptosis

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nallabothula, A. Aleem, P. Setabutr, J. Hallak, D. Yi, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ptosis is an eye condition where the upper eyelid droops. The current diagnosis for ptosis involves cumbersome manual measurements that are time-consuming and prone to human error. This work presents a fully automated and interpretable dual model system for rapid detection of ptosis that can help save the clinics and patients valuable resources.

Methods: The data for this study were queried from the Illinois Ophthalmic Database Atlas (I-ODA) that was developed by the Department of Ophthalmology at the University of Illinois Chicago. The dataset consisted of 820 facial images collected in a clinical setting and was augmented by 43 Flickr-Faces-HQ images. A subset of 100 images was hand-selected by an expert oculoplastic surgeon to create a held-out test set. All values reported in the results were derived from this test set.

The eye regions were extracted from the facial images and were fed into two pipelines, Deep Learning (DL) and Feature & Rule (FR). The DL used a 5-layer uni-eye convolutional neural network to learn data characteristics to predict ptosis likelihood and the FR extracted features to determine the marginal reflex distance (MRD1) and the iris visibility ratio (IR). AutoPtosis was a combination of both these pipelines, where a predictive model was trained using MRD1, IR, and DL's likelihood to predict ptosis.

Results: The DL performed well giving a 0.91 accuracy, 0.89 precision, 0.93 recall, and 0.95 AUC while FR gave 0.63 accuracy, 0.60 precision, 0.80 recall, and 0.77 AUC. When both pipelines were combined there was an improvement in accuracy to 0.95, precision to 0.96, recall to 0.96, and AUC to 0.98. We noticed an improvement especially in FR results when only clinical data was used. We also created class activation maps and direct feature visualization to interpret the most contributing eye regions for DL and iris, eye contours used for calculating MRD1 and IR respectively, that helps with error assessment.

Conclusions: AutoPtosis combined the preferable aspects of both DL and FR to create a rapid and automatic system for detection of ptosis all while achieving results almost as good as an expert physician. The models performed optimally under clinical settings and can be deployed there as a helping tool to generate results which can then be verified by physicians, saving the healthcare system and patients valuable resources.

CONTROL ID: 3546409

SUBMITTER (NAME ONLY): Cristhian Ildefonso

TITLE: MODELING ACCELERATED RETINAL AGING USING A DOMINANT MUTANT OF THE DNA POLYMERASE GAMMA SUB-UNIT 1

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.J. Ildefonso, E. Walsh, R.B. Ridley, A. Jafri, A.S. Lewin, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|R.B. Ridley, A.S. Lewin, Molecular Genetics & Microbiology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging is associated with a general decline in mitochondrial function and an increased accumulation of mitochondrial mutations. Retinas from age-related macular degeneration (AMD) patients have a higher incidence of mitochondrial mutations in their retina pigmented epithelium (RPE) layer than non-AMD controls. Polymerase subunit gamma 1 (POLG1) gene encodes the catalytic subunit of mitochondrial DNA (mtDNA). Expression of a dominant point mutant of this gene (POLG1(D1134A)) increases mitochondrial mutations and mitochondrial DNA depletion. This work aims to characterize the effects of POLG1(D1134A) expression in vitro using the RPE-like cell line ARPE-19.

Methods: We replaced the wild-type sequence of POLG1 for POLG1D1134A in a plasmid containing the AAV2 terminal repeats (pTR-POLG1(D1134A)). We transfected HEK293T cells with either pTR-POLG1, pTR-POLG1(D1134A), or pTR-GFP and quantified the differences in total mitochondrial DNA in these cells. The level of oxidative stress in these cells was also measured by MitoSox staining and flow cytometry. These plasmids were also electroporated in the RPE-like human cell line ARPE-19, followed by their growth in a glucose-free medium for four days. We used the Random Mutation Capture (RMC) assay to quantify the number of mutant mitochondrial genomes in each group by PCR.

Results: Transient transfection of HEK293T cells with pTR-POLG1(D1134A) plasmid led to a significant decrease in viability at 72 hours post-transfection compared to the wild type pTR-POLG1 transfected cells. We did not detect a significant difference in oxidative stress by flow cytometry between these groups. Electroporation of pTR-POLG1(D1134A) in ARPE-19 cells caused a significant accumulation of mutated mtDNA compared to either GFP or wild type POLG1 control groups.

Conclusions: The overexpression of POLG1(D1134A) decreases cell viability independent of oxidative damage. Furthermore, overexpression of this mutant gene also increases the accumulation of mtDNA mutations in a human RPE-like cell line. Thus, pTR-POLG1(D1134A) is a tool to study accelerated aging features due to mitochondria crisis.

CONTROL ID: 3546411

SUBMITTER (NAME ONLY): Pranita Hanpude

TITLE: BAP1 status and response to radiation in melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Hanpude, J.B. Massengill, C.M. Cebulla, F. Davidorf, M.H. Abdel-Rahman, Ophthalmology, The Ohio State University Wexner Medical Center, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The majority of uveal melanomas (UM) is managed using radiation based procedures. However, radiation retinopathy lead to irreversible vision loss within few years after treatment. BAP1 tumor suppressor gene is inactivated in up to 45% of UM patients. BAP1 is important in DNA repair and it could modify the tumor response to radiation. Here, we investigated the effect of BAP1 inactivation on response to radiation in a melanoma in-vitro model.

Methods: To assess the BAP1 role in response to treatment of melanoma cells we used CRISPR-Cas9 to knock out (KO) BAP1 in mouse melanoma cell line B16F10 and two UM cell lines 92.1 and Mel202. B16F10 cell line was selected as it has low mutation burden similar to UM cells and it could be used in-vivo tumor models in syngeneic C57BL6 mice without immunosuppression. We used RS-2000 irradiator to deliver various doses of ionizing radiation (IR) ranging from 10-80 Gy. For PARP inhibitor we used rucaparib at the average IC50 dose within 1h of IR. After 5 days, surviving cells were washed with PBS and fixed with 3% PFA and stained with 0.2% crystal violet then stain was extracted with 10% acetic acid and the optical density (OD) was determined by spectrophotometer at 600nm. The population survival rate was determined by the average ratio between the OD of the treated and untreated cells.

Results: The two UM cell lines Mel202 and 92.1 did not survive BAP1 knock down. B16F10 cells survived and multiple different clones of homozygous and heterozygous BAP1 KO cells were generated. BAP1 deletion and loss of expression were confirmed by sequencing and Western blot, respectively. Two B16F10 BAP1 KO clones in addition to the wild type were used for assessment. We observed increased cell death at different doses of radiation in BAP1 KO cell lines compared to BAP1 WT cells. Moreover, loss of BAP1 minimally increased the sensitivity of B16F10 cell line towards rucaparib.

Conclusions: Our results suggest that combination therapy of PARP inhibitor with IR could help to reduce the IR dosage in BAP1 mutant melanoma cells. Further studies on naturally occurring BAP1 mutant and wild type UM cell lines are ongoing.

CONTROL ID: 3546412

SUBMITTER (NAME ONLY): Christine Harman

TITLE: Biometric parameters and myopia in a canine model of open-angle glaucoma (OAG)

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess biometric parameters and refractive errors in beagle-derived dogs with Weill-Marchesani syndrome (WMS)-related OAG due to a G661R missense mutation in ADAMTS10.

Methods: A-scan parameters were measured in pre- and post-glaucomatous ADAMTS10-mutant (n=78) and normal control dogs (n=24) between 0.4 and 10.8 years of age (median ages: 25.6 and 31.1 respectively): anterior chamber depth (ACD), lens thickness (LT), vitreal chamber depth (VCD), and axial length (AXL). Refractive errors were measured in a subset of dogs (27 mutants, 11 normals) by streak retinoscopy. A total of 589 A-scans and 78 refractions were performed. Parameters were compared between groups by Student t-test with significance set at $p \leq 0.05$. Spearman's correlation coefficients were calculated between A-scan parameters and refractive errors and age, respectively.

Results: Regardless of age, A-scan parameters differed significantly between ADAMTS10-mutant and normal control dogs: AXL ($21.22 \pm 0.88\text{mm}$ vs. $20.62 \pm 0.52\text{mm}$; $p \leq 0.001$), LT ($7.21 \pm 0.31\text{mm}$ vs. $6.93 \pm 0.27\text{mm}$; $p \leq 0.001$), and VCD ($9.56 \pm 0.56\text{mm}$ vs. $9.34 \pm 0.31\text{mm}$; $p \leq 0.001$). AXL, LT, and VCD are significantly larger in ADAMTS10-mutant vs. normal dogs already at 1-2 years of age, before the increase in intraocular pressure (IOP) and development of OAG in mutants: AXL ($21.13 \pm 0.52\text{mm}$ vs. $20.79 \pm 0.58\text{mm}$; $p = 0.003$), LT ($7.14 \pm 0.30\text{mm}$ vs. $7.06 \pm 0.20\text{mm}$; $p = 0.013$), and VCD ($9.59 \pm 0.57\text{mm}$ vs. $9.34 \pm 0.24\text{mm}$; $p \leq 0.001$). ACD does not become significantly larger in mutant dogs until >4 years of age ($4.91 \pm 0.77\text{mm}$ vs. $4.37 \pm 0.35\text{mm}$; $p = 0.009$), when clinical detectable OAG is present. There was a significant difference in refractive errors between mutant and normal dogs ($-5.4 \pm 1.48\text{D}$ vs. $-0.2 \pm 0.63\text{D}$; $p \leq 0.001$) with mutant eyes being highly myopic. Age correlated to refractive error weakly in mutant (0.11) and moderately negative in normal dogs (-0.55). In contrast, correlation between AXL and age was much weaker in normal (0.08) vs. mutant dogs (0.49).

Conclusions: Mutant eyes are significantly longer than normal eyes due to a deeper VCD resulting in high degree of myopia even before the increase in IOP. Weak correlation between refractive error and biometric parameters suggest that lens position may have an important role in myopia. The increased LT may be due to ADAMTS10-mutation-related lens zonular dysplasia and weakness.

CONTROL ID: 3546413

SUBMITTER (NAME ONLY): Kennedy Johnson

TITLE: Assessment of the Inclusion of Novel Autoantibodies into a Prediction Model to Screen Dry Eye Patients for Sjogren's Syndrome: Preliminary Findings

SESSION TITLE: Dry eye and microbiome clinical

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To determine if the addition of novel Sjogren syndrome (SS) autoantibody data improves the performance of a previously reported algorithm to screen dry eye patients for SS.

Methods: Inclusion criteria were age ≥ 18 years, no history of autoimmune disease, and dry eye complaints for ≥ 3 months. Ocular and systemic symptoms were assessed using a questionnaire. Subjects underwent an ocular surface exam, measurement of unstimulated whole salivary rate, serological testing, and a lip biopsy if indicated to diagnose SS. A participant was diagnosed with SS if they met the 2016 American College of Rheumatology/European League Against Rheumatism criteria. The screening algorithm score was originally determined using questionnaire responses, assessment of tear film break-up time and conjunctival staining with lissamine green (Bunya et al Cornea 2021). The presence or absence of IgG, IgM, or IgA isotypes of the novel SS antibodies (anti-salivary protein (SP), anti-parotid secretory protein (PSP), and anti-carbonic anhydrase isoenzyme VI (CA-VI)) was compared between patients with and without SS, and incorporated into the algorithm.

Results: 89 patients (18 SS, 71 no SS) were enrolled, 82% of them female with a mean age (\pm SD) of 57 (\pm 17.6) years. There was no significant association between the presence of any one novel antibody and a positive SS diagnosis (Table 1). The percent of positive subjects in the following specific immunoglobulin groups: SP IgA, PSP IgM or CA-VI IgM, was higher in those with SS than those without SS (61.1% vs. 25.4%, $p=0.0009$, Table 1). The area under the ROC curve (95% CI) for SS screening was 0.68 (0.55-0.81) with the likelihood score alone, and significantly ($p=0.04$) improved to 0.77 (0.65-0.89) when using both the novel antibodies and the likelihood score (Figure 1).

Conclusions: We found that the inclusion of specific novel autoantibodies (SP IgA, PSP IgM and CA-VI IgM) significantly improved the performance of our previously reported SS screening tool. This likelihood scoring system can be implemented using the brief series of questions alone, or combined with standard ocular surface signs and novel SS antibody testing for improved performance. Once validated, the algorithm may serve as an effective screening tool to determine the likelihood of SS in dry eye patients, potentially allowing for earlier diagnosis and treatment.

CONTROL ID: 3546414

SUBMITTER (NAME ONLY): Katie Williams

TITLE: Axial lengths in a cohort of patients with a range of inherited retinal disease

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRDs) are frequently associated with refractive error, usually resulting from an abnormally long or short axial length (AL). We investigated AL distributions in patients with particular IRD subtypes.

Methods: We analyzed axial lengths measured by partial coherence interferometry (IOLMaster optical biometer, Carl Zeiss Meditec AG, Jena, Germany) from patients recruited from the IRD clinics of Moorfields Eye Hospital London as part of a wider imaging study. Patients had a clinical IRD diagnosis with molecular confirmation in most cases. Distributions of AL for each IRD (where measurements >10 patients were available) were examined and comparison made against a normative database of AL from a cohort with a similar median age (Raine Study, Australia). Firth's logistic regression models for an AL greater than or equal to 26mm and less than or equal to 21mm were constructed with adjustment for age and sex in unrelated individuals, and only inclusive of males in the case of X-linked IRDs.

Results: 342 patients from 51 families with sixteen different IRDs were examined (median age 19.2yrs IQR 13.1-30.5; 63% male; mean AL 24.11mm SD 1.94). For 7 IRDs, we had data on >10 individuals: ABCA4 (n=74, mean AL 23.68mm), Blue Cone Monochromatism (BCM) (n=12, mean AL=26.02), Bornholm Eye Disease (BED) (n=13, mean AL = 26.54), CNGA3 (n=23, mean AL =23.91), CNGB3 (n=39, mean AL =23.19), RPE65 (n=25, mean AL = 23.27), and RPGR(n=58, mean AL = 24.75). The Raine Study included 1335 unrelated individuals (median age 19.9yrs IQR 19.7-20.3; 51% male; mean AL 23.60mm SD 0.93). Compared with this cohort, significantly increased odds for longer AL were observed for BCM (OR 34.7 p<0.001), BED (OR 80.4 p<0.001), RPGR (OR 6.1 p<0.001) and RPE65 (OR 6.7 p=0.004). Patients with variants in RPE65 also had increased odds for short AL (OR 12.5 p<0.001).

Conclusions: We identified longer mean ALs in patients with BED, BCM and RPGR-associated disease. Interestingly patients with RPE65-associated disease had increased odds for both longer and shorter AL (although the average AL of these patients was shorter than that for the reference cohort). Exploration of axial lengths in patients with specific defects in retinal signaling can shed light on processes driving development of refractive error as well as yielding a more complete description of disease phenotypes and visual impairment.

CONTROL ID: 3546415

SUBMITTER (NAME ONLY): Tharindu de silva

TITLE: Deep-learning based sequence modelling of the dark adaptation curve for noise reduction and parameter prediction in patients with AMD

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. de silva, P. Grisso, S. Mukherjee, B.G. Jeffrey, H. Wiley, T.D. Keenan, E.Y. Chew, C. Cukras, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dark adaptation (DA) has shown to reveal early functional changes in eyes with age-related macular degeneration (AMD). This work aims to translate recent advances in deep learning sequence modelling to robustly estimate DA curves from sparse, noisy measurements and forecast late phase of the curve to reliably estimate parameters in shorter test times.

Methods: The data was collected in a clinical study involving AMD patients (NCT01352975). The DA test involved 82% focal bleach and recordings of log thresholds using a 3-down/1-up modified staircase threshold estimate procedure. 1496 DA curves were acquired from multiple annual study visits from 207 patients. During analysis, the sparse data points were interpolated within a 1.5 log unit reduction (Δ LU) and 3.1 Δ LU range using isotonic regression to obtain a monotonically-decreasing fit to the data. A recurrent neural network with long-short term memory (LSTM) autoencoder model was then devised to estimate the DA curve minimizing the curve fluctuations due to noise. The same model was then trained to forecast the latter part of the curve using the sequence of measurements up to different early portions of the curve ranging from 2 Δ LU – 2.9 Δ LU. The models were developed using 1271 train, 150 validation, 75 test curves. In each model, rod intercept time (RIT) was measured as the time required to reach 3 Δ LU and evaluated by comparing the model predicted RIT to ground truth.

Results: RIT measurements in the acquired data set varied between 3.6–39.9 min. When the entire curve was estimated from the model, the model successfully mitigated noisy fluctuations and the measured RIT had error (mean \pm stdev) = 0.3 ± 0.4 min (range=0.0–2.8 min) compared to ground truth. When the curve was forecasted at 2.5 Δ LU the predicted RIT had error = 1.2 ± 1.3 min whereas at 2 Δ LU the predicted RIT error degraded to 3.1 ± 3.1 min. Even at 2 Δ LU, 78.7% cases reported error < 5 min.

Conclusions: LSTM autoencoder modelling provides a useful method to estimate and predict DA curve utilizing patterns of variation and mitigating noise. The ability to forecast from early phase of the DA curve suggests that the trends in the curve could help estimate the parameters from patients who are unable to complete the test and could lead to the development of shorter tests and identification of additional curve parameters to serve as useful endpoints.

CONTROL ID: 3546417

SUBMITTER (NAME ONLY): Flavius Beca

TITLE: Endophthalmitis caused by Burkholderia cepacia: Clinical features, antibiotic susceptibility, and outcomes

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Beca, J. Sengillo, P. Iyer, D. Miller, N.A. Yannuzzi, H.W. Flynn, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To report the clinical features, antibiotic sensitivities, and outcomes of Burkholderia cepacia associated endophthalmitis in three patients.

Methods: The study design was a retrospective, observational case series.

Clinical and microbiology records were reviewed for patients evaluated at the Bascom Palmer Eye Institute and diagnosed with culture confirmed endophthalmitis due to B. cepacia. Antibiotic susceptibility profiles were generated using standard microbiologic protocols via an automated VITEK system.

Results: Of 3 patients identified, endophthalmitis occurred in the setting of post penetrating keratoplasty (P1), following cataract surgery (P3), and after glaucoma filtering surgery (P2). Time from surgical procedure to presentation with endophthalmitis occurred on post-operative day 14 (P1) and month 5 (P2). In P3, infection occurred several years after cataract surgery but in the context of a possible direct orbital trauma. Presenting visual acuity (VA) ranged from hand motion to light perception. Initial treatment strategies were intravitreal ceftazidime and vancomycin injection together with fortified topical antibiotics (n = 2), and surgical repair of corneal defect and fortified topical antibiotics (n = 1). VA outcomes ranged from hand motion to no light perception, with two eyes ultimately requiring enucleation (P1 and P2), and P3 developing early phthisis bulbi at last follow up.

Conclusions: Endophthalmitis caused by B. cepacia is a rare clinical entity with generally poor visual outcomes.

CONTROL ID: 3546418

SUBMITTER (NAME ONLY): Geertje van der Sterre

TITLE: Intergenerational utility in parents of children with amblyopia

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. van der Sterre, H. van der Meulen-Schot, H.J. Simonsz, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|E. Abma-Buistraan, Reinier de Graaf Gasthuis, Delft, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: The cost-effectiveness of screening and treatment for amblyopia is uncertain. Gain of quality of life in adulthood is experienced long after amblyopia has been detected and treated. Possible functional loss of the only good eye occurs even later in life. There are few immediate benefits for the child when its amblyopia is treated. Yet the detection and treatment of amblyopia is not abolished because the parents decide on this. We think that the reduction of quality of life of the parents because of the amblyopia of their child, should be included in the cost-utility analysis.

We measured the loss of disease-related quality of life in parents whose child was treated for amblyopia.

Methods: In our study we ask the parents of a child who has had occlusion therapy for six weeks two questions. Two questions that measure their loss of utility. First, how many years of their life they are willing to give up (Time Trade-Off), and secondly, how much risk of unilateral blindness they are willing to take (Standard Gamble) in exchange for their child having good vision in both eyes.

Results: So far we have been able to interview 10 parents.

Against expectations, the responses to the Time Trade-Off question showed parents were willing to give up the maximum of 5 years of their life in exchange for the amblyopic eye of their child to be healthy. Clearly a ceiling effect had occurred.

This result was the reason to expand the options in the Time Trade-Off method by 10 years, 20 years and 30 years.

As we initially had not included the Standard Gamble question, only three parents have been interviewed with this question. One parent who was willing to risk 10% had amblyopia himself.

Conclusions: These highly surprising results necessitate an inventory of possible confounders.

We are considering:

- desire to give socially acceptable answers
- innate striving for reproductive success
- religious beliefs about sacrificing your own life
- social context and family structure: can others care for the child
- co-morbidity of the child

CONTROL ID: 3546419

SUBMITTER (NAME ONLY): Chelsea Bender

TITLE: Evaluation of founder effect burden on recurrent variants in X-linked retinoschisis

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Pathogenic variants in the RS1 gene cause X-linked retinoschisis (XLRS), a rare inherited disease that results in childhood vision loss. Variants may be transmitted through multiple generations of unaffected carrier females before an affected male is discovered. Notably, certain RS1 variants are repeatedly reported in seemingly unrelated probands. Here, we investigate recurrent pathogenic variants to determine whether this phenomenon represents founder alleles or multiple mutation events.

Methods: Patients were consented and blood-derived DNA was obtained for analysis. Three polymorphic short tandem repeat (STR) markers and four single nucleotide polymorphism (SNP) markers surrounding the RS1 gene (~2 cM) were selected. Custom STR primers were designed with 5'6 FAM. Proband DNA was amplified with STR primers by Polymerase Chain Reaction (PCR) and analyzed by capillary electrophoresis. Alleles were called based on marker sizes. SNP markers were analyzed by Sanger sequencing. Visualization of haplotype geographical distribution was mapped by Zone Improvement Plan (ZIP) code using Python.

Results: XLRS probands (n=114) with one of the 13 most prevalent RS1 variants were analyzed. Nine variants (69%) had at least two probands with common variant-specific haplotypes over 7/7 markers (~2 cM). Twelve variants (92%) had two or more probands with shared alleles across at least 3/7 markers bilaterally adjacent to RS1 (~0.4 cM). Eleven variants (85%) demonstrated one or more geographic clusters for probands sharing variant-specific haplotypes. Recurrent variants with shared haplotype showed varying degrees of geographic clustering. Overall, 19 unique haplotypes of at least ~0.4 cM surrounding the RS1 gene comprised 87/114 (76%) of reportedly unrelated probands. Additionally, 65/87 (75%) probands with shared haplotypes of ~0.4 cM or more clustered in specific regions of the United States.

Conclusions: Examination of this large XLRS cohort for common RS1 haplotypes supports that the majority are explained by founder effect rather than multiple equivalent mutation events. This is beneficial for clinical variant classification and may be generalizable to other X-linked disorders.

CONTROL ID: 3546424

SUBMITTER (NAME ONLY): Mark Simcoe

TITLE: Genetic analyses identify the first two genetic loci associated with sporadic pigment dispersion syndrome and indicate myopia is a causal factor for disease onset

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Pigment dispersion syndrome (PDS) affects 2.45% of people of European ancestry and is highly correlated with myopia. In some cases, PDS can progress to pigmentary glaucoma (PG) leading to irreversible loss of vision with a relatively young average age of onset. The purpose of this study was to identify genetic variants associated with PDS risk, providing greater understanding of its genetic aetiology, and subsequently investigate whether myopia plays an active role in PDS and PG development.

Methods: GWAS was performed by meta-analysing four cohorts with a total of 574 PDS cases, and 52,627 controls all of European ancestry. Two-sample Mendelian randomisation was utilised to determine a causal relationship between myopia and PDS; uncorrelated variants, significantly associated ($p < 5 \times 10^{-8}$) with myopia in an independent analysis were selected as instrumental variables.

Results: Variants clustered at two distinct genomic loci were associated with PDS with genome-wide significance ($p < 5 \times 10^{-8}$). Associations at these loci implicate two previously unreported genes involved in human PDS development. The strongest association was within the gamma-secretase activator protein (GSAP) ($p = 6.0 \times 10^{-10}$), which participates in the same pigmentation pathways as PDS associated genes previously identified in familial studies. Significantly associated SNPs account for 3.1% of PG risk ($p = 1.9 \times 10^{-7}$), which is 6.9% of the total PG SNP heritability (0.45). Two-sample Mendelian randomisation analyses indicated that myopia exerts direct, causal effects over PDS risk ($p = 8.9 \times 10^{-7}$) with each decrease in spherical equivalent by one dioptre translating to an odds ratio of 1.4 for PDS risk.

Conclusions: Common genetic variants account for a considerable proportion of risk for PDS and PG. This is the first study to identify specific genetic risk factors for these conditions among unrelated cases outside of familial studies and provides insight into the genetic pathways of these conditions. Though myopia is known to correlate with PDS and PG, this study provides strong evidence that this correlation is a consequence of myopia exerting causal effects over PDS.

CONTROL ID: 3546427

SUBMITTER (NAME ONLY): Jacobi Robertson

TITLE: Risk and Assessment of COVID-19 in a Retina Ophthalmologic Setting

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Robertson, M.T. Moore, J.M. Coney, S. Platt, L.J. Rao, D.G. Miller, S.D. Pendergast, J.P. Schartman, M.A. Novak, S.A. Lewis, M.K. Adams, A.F. Nothnagel, T.P. Hull, T.J. Tsai, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|J.A. Robertson, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|M. Abdulaal, University Hospitals, Cleveland, Ohio, UNITED STATES|M.T. Moore, University of Maryland Baltimore, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the risks and impact of COVID-19, SARS-CoV-2, on a private ophthalmology practice in Ohio and analyze the fluctuation in patient visits and surgeries before and during the COVID-19 pandemic.

Methods: A retrospective analysis was performed using outpatient clinic logs for patients seen during the first 10 weeks of 2020 and compared to outpatient clinic logs for 10 weeks during the COVID-19 pandemic. During the twenty-week period, the number of appointments, intravitreal injections, and surgeries, most commonly retinal detachments, epiretinal membrane (ERM), and vitreous hemorrhages, were compared. Additionally, consideration was given to potential measures to reduce the spread and maintain pre-pandemic clinical care levels. The number of appointments, injections administered, and surgeries completed or postponed were analyzed before and during the COVID-19 pandemic. The practice implemented additional precautions for patients and staff. These included, but were not limited to, temperature checks, hand sanitizer availability, required use of face masks, and asking patients to come alone to appointments; with the exception of patients that were wheelchair bound, suffered from dementia, were under the age of 18, or required a translator.

Results: During the first 10 weeks of 2020, the practice saw an average of 2,205 visits a week. In week one of the pandemic, the average was 1,147 patients per week, a 54% drop. An overall 40% drop was seen in surgical cases; vitreous hemorrhage surgeries decreased by 35%, retinal detachment surgeries decreased 25%, and ERM peels reduced by 60%. The drop in ERM's were mostly due to rescheduling. Intravitreal injections during the first 10 weeks averaged 1,025 (SD±112) per week. During the start of the 10 COVID-19 weeks, intravitreal injections averaged 852 (SD±122) per week and by the last weeks injections averaged 972 (SD±142) per week.

Conclusions: In the early stages, the initial number of outpatient visits declined by 54%, the average number of intravitreal injections did not change in a similar pattern. This represents the importance of patients' triage and prioritizing urgent cases.

CONTROL ID: 3546428

SUBMITTER (NAME ONLY): Shaili Patel

TITLE: Characterization of early eye developmental defects in a new Rbm24 conditional knockout mouse model

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Patel, S. Dash, S.A. Lachke, Department of Biological Sciences, University of Delaware, Newark, Delaware, UNITED STATES|S.A. Lachke, Center for Bioinformatics and Computational Biology, University of Delaware, Newark, Delaware, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early eye development involves regulatory interactions between the optic vesicle and the overlying surface ectoderm that are necessary for formation of the lens and the correct placement of the retina. While signaling and transcriptional regulation in early eye development is well characterized, the significance of RBPs and post-transcriptional gene expression control, is less clear. Germline deletion of the RNA-binding protein (RBP) gene, Rbm24, in mice (Rbm24^{-/-}) perturbs these regulatory events, resulting in severe early eye defects such as microphthalmia (small eye) and anophthalmia (absence of eye). Rbm24 is expressed in both the optic vesicle and the presumptive lens ectoderm and how its activities in these tissues impacts eye development. Therefore, as a first step toward dissecting the tissue-specific role of Rbm24, Rbm24 compound conditional knockout mice were generated and characterized.

Methods: Rbm24^{cKO} (Rbm24^{+/-}-Rax-CreER^{T2}:Rbm24^{flox/flox}; termed Rbm24^{cKO}) mice were generated by crossing Rbm24^{flox/flox} mice with the tamoxifen-inducible Rax-Cre line that supports Cre expression in optic vesicle. Phenotypic characterization of the ocular defects was performed by marker analysis using immunofluorescence and confocal microscopy.

Results: Rbm24^{cKO} mice exhibit fully penetrant early eye defects exhibiting features of microphthalmia and anophthalmia, similar to that of Rbm24^{-/-} mice. The lens tissue in Rbm24^{cKO} mice appears abnormal from early stage at E10.5. Further, Rbm24^{cKO} mouse exhibit abnormal expression of key ocular transcription factor-encoding genes such as Sox2, Pax6, and Lhx2 in early eye development.

Conclusions: This work reports the development of a new Rbm24 compound conditional knockout mouse line. Phenotypic characterization of these mice show that Rbm24 is required in the optic vesicle for early eye and lens development. Further, these findings define a new layer of regulatory mechanism in early eye development, that involving Rbm24 and its downstream targets the key ocular transcription factors Pax6, Sox2, and Lhx2. Because these transcription factors are linked to anophthalmia/microphthalmia, this work also uncovers a potential mechanism for the eye defects observed in Rbm24 deficient mice.

CONTROL ID: 3546430

SUBMITTER (NAME ONLY): Ashley Radparvar

TITLE: The Combined Effects of Diabetes Mellitus and Sickle Cell Disease on Retinopathy and Vascular Comorbidities

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Curtis, C. Minniti, Hematology-Oncology, Montefiore Medical Center, Bronx, New York, UNITED STATES|U. Mian, Ophthalmology, Montefiore Medical Center, Bronx, New York, UNITED STATES|A. Radparvar, R. Muhtadi, N. Jackson, J. Wu, Yeshiva University Albert Einstein College of Medicine, Bronx, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect on retinopathy, hypertension (HTN) and kidney disease in sickle cell disease (SCD) patients with an added diagnosis of Diabetes Mellitus (DM).

Methods: This is a cross-sectional study of 743 adult patients with SCD seen at Montefiore Medical Center (Bronx, NY) from January 2014 to June 2020. Patients were categorized as having SCD without DM (n=703) or having SCD and DM (SCD-DM, n=40). Demographics, genotype of SCD (HbSS (SS) or HbSC (SC)) lab values, comorbidities, and ophthalmic complications were collected from the Montefiore electronic medical record (Epic, Verona, WI). Presence of DM, ophthalmic diagnoses and HTN were based on clinical diagnosis in the EMR. Ophthalmic diagnoses were collected in patients who had at least one ophthalmology visit (n= 434). A Chi-Squared test was used for total categorical data, while a Fisher's Exact test was used for genotype categorical data. A Wilcoxon Two-Sample test was used for continuous variables.

Results: While there was an increased percentage of retinopathy and proliferative disease in SCD-DM compared to SCD, this relationship was not statistically significant, as seen in Table 1. Increased retinopathy was also noted in patients with SS + DM and in patients with SC + DM compared to the SS and SC group, respectively. While there was an increase in proliferative disease in SS + DM, there was a decrease in proliferative disease in SC + DM, as compared to SS or SC, respectively.

SCD-DM was significantly correlated to increased rate of HTN, higher BMI, and lower GFR in both genotypes, as seen in Table 2. Comparing SS + DM and SS patients, SS + DM had a significantly significant increase in HTN, higher BMI, and lower GFR. A similar statistically significant relationship was seen in patients with SC + DM who had increased rates of HTN, increased BMI, and lower GFR, compared to SC.

Conclusions: SCD patients with DM were more likely to have a higher BMI, increased rates of HTN and lower GFR than those with SCD alone. While retinopathy remains an important complication in both SCD and DM, there appears to be no statistical difference in retinopathy in SCD-DM versus SCD patients.

CONTROL ID: 3546432

SUBMITTER (NAME ONLY): Alejandra Daruich

TITLE: Higher protein concentrations are toxic for photoreceptors and correlate with lower functional recovery after rhegmatogenous retinal detachment

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Rhegmatogenous retinal detachment (RRD) is a threatening visual condition. Despite successful reattachment surgery, vision does not fully recover, due to subretinal fluid (SRF) accumulation and subsequent photoreceptor cell death. Various molecular components of SRF could exert toxicity on retinal neurons. With increased RRD duration, SRF protein concentration increases and visual prognosis worsens, but the direct effect of proteins on photoreceptors has not been evaluated. The aim of this study is to analyze the effect of proteins on photoreceptors as well as the role of protein concentration in SRF on functional outcome in RRD patients.

Methods: First, human cones cell line were treated by albumin from 2.5 to 40 g/L and cultured during 24 hours. Cell Titer was assessed to determine viable cells. Secondly, SRF from 21 consecutive patients underwent vitrectomy for RRD repair were collected and protein concentration was measured by Micro BCA protein assay. Clinical data was recorded at baseline and at 6 months after surgery. Finally, rat retinal explants were created to mimic retinal detachment and treated by albumin at 12 mg/ml. LDH release was measured in medium after 6 hours of culture.

Results: Albumin reduced cone viability in dose-dependent manner. Albumin concentrations higher than 5g/L significantly reduced viability of cone cells, when compared to the control ($p < 0.05$, Mann-Whitney test). At 20 mg/ml, albumin reduced 40% of cone cells viability.

Mean protein concentration in SRF from patients with RRD was 3.1 ± 2.9 mg/ml (range: 0.6-12.1 mg/ml). The protein concentration, measured in the SRF at the time of surgery correlated with lower best-corrected visual acuity (BCVA) at baseline ($r = 0.5$, $p = 0.0004$, Spearman correlation), as well as with lower BCVA recovery 6 months after surgery ($r = 0.6$, $p = 0.0001$, Spearman correlation).

Rat retinal explants treated by albumin, at concentration ranges found in SRF of patients, showed significantly higher LDH release in culture medium compared to control retinas ($p = 0.01$, Mann-Whitney test).

Conclusions: Lower visual outcome in RRD patients is associated with higher protein concentration in SRF that could be explained by a direct toxic effect of albumin on photoreceptors.

CONTROL ID: 3546435

SUBMITTER (NAME ONLY): Jason Myers

TITLE: Enhanced Hammerhead Ribozymes as Synthetic Nucleic Acid Ocular Therapeutics

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Myers, J.M. Sullivan, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|J. Myers, J.M. Sullivan, Medical Research, VA Western New York Healthcare System Buffalo VA Medical Center, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: We are investigating structure/function potential with enhanced hammerhead ribozymes (EhhRzs), discovered in this lab, that exceed the turnover rate of historical minimal hhRzs (mhhRzs) (1/min) by at least two log-orders. Therapeutic potential is enhanced because less EhhRz is needed to affect strong levels of target mRNA cleavage vs. a mhhRz. Gene and/or synthetic nucleic acid therapeutics become feasible. Synthetic RNA therapeutics require stabilization against nucleases for intraocular injection.

Methods: Substrate RHO-266 RNA is 15 nt long with 5' FAM and 3' BHQ1 (IDT); cleavage at CUC 266 results in liberation of quenched fluorescence which is quantified optically in real time. EhhRzs are transcribed (MegaShortScript) from PCR templates or generated synthetically (IDT). RNA Thermostability Enhancer Set (TriLink) was utilized to evaluate modified nucleotides. Anti-Reverse Cap Analog (ARCA) and poly(A) tailed transcripts were transcribed with mMESSAGE mMACHINE T7 Ultra (ThermoFisher). Reactions are initiated by mixing EhhRz with substrate RNA in buffer (10 mM Tris-HCl, pH 7.5) at 0.5 mM Mg^{2+} and optically measured at 37°C in a qRT/PCR machine. Data are analyzed in Origin 8.

Results: Site-specific chemical modifications (2'-O-Methyl) of the antisense flanks and the first three residues of the stem-II loop allow enhanced turnover activity (Model 1: 712/min vs unmodified 282/min $p=9.4E-17$, Model 2: 882/min vs unmodified 746/min $p=7.1E-5$), whereas modifications in the enzyme core are not tolerated (ANOVA $F=386.9$, $p\approx 0$). ARCA and addition of poly(A) tail to a model EhhRz supports enhanced turnover activity (ANOVA $F=363.2$, $p=2.07E-11$). Replacement of all A residues (2-aminoadenosine-5'ppp) obviates activity, whereas replacement of all U residues (5-methyridine-5'ppp) or replacement of all C residues (5-methylcytidine-5'ppp) permits strong enhanced turnover rate of the model EhhRz (U=389/min, C=206/min).

Conclusions: Efforts to stabilize EhhRz RNA with established synthetic chemistries by modifications of the antisense flanks and parts of the stabilizing stem-II loop region, or 5' capping and 3' polyadenylation has shown preservation of strong turnover rate activity, under substrate excess conditions and physiological Mg^{2+} levels. Certain enzyme core modifications are tolerable, but other residues critically involved in the reaction mechanism will require alternative chemistries from those already evaluated.

CONTROL ID: 3546438

SUBMITTER (NAME ONLY): Maryam Mousavi

TITLE: Evaluation of Tear Film Surface Quality Non-Invasively During Soft Contact Lens Wear

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mousavi, K.K. Nichols, The University of Alabama at Birmingham, Alabama, UNITED STATES|M. Mousavi, I. Garaszczuk, D. Iskander, The Wroclaw University of Science and Technology, POLAND|

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ABSTRACT BODY:

Purpose: To evaluate tear film surface quality (TFSQ) over 12 months of soft daily disposable contact lens (CL) wear using non-invasive method.

Methods: Fifty healthy subjects aged (mean \pm standard deviation) 25.7 ± 4.3 years were prescribed with silicone hydrogel (SiHy) or hydrogel (Hy). The protocol consisted of baseline visit including first(F)/mean(M) non-invasive keratometry break-up times (F/MNIKBT, K5M, Oculus Optikgeräte GmbH, Wetzlar, Germany), fluorescein tear film break-up time (FBUT), and corneal and conjunctival staining. At the end of the fitting day (day 2), the preferred lens was chosen based on objective measurements of contact lens fit, reported subjective comfort after four hours of wear and pre-lens TFSQ measurements. Thereafter, visits occurred at 2 weeks (CL check) and at 3, 6, and 12 months. TFSQ was measured over this period and differences between SiHy (n = 34) and Hy (n=16) fitted group were assessed.

Results: FNIKBT showed statistically significant differences between baseline (pre-fitting) and other visits: ($P < 0.001$ for Day 2 and at 3, 6, and 12-month visit, $P < 0.001$ for Day 2 and at 3, 6, and 12-month visit, respectively) and in MNIKBT between baseline (pre-fitting) and other visits ($P=0.004$, $P<0.001$, $P<0.001$, $P<0.001$ for Day 2 and at 3, 6, and 12-month visit, respectively). Across all visits, there were no significant differences in the measurements associated with both lens types for FBUT, corneal staining, conjunctival staining, FNIKBT, and MNIKBT. Measurements with F/M NIKBT were found to be the same and stable from Day 2, which indicates that TFSQ can be assessed and monitored reliably with NIKBT.

Conclusions: Throughout the course of the study, TFSQ was unaffected during CL wear and NIKBT showed to be the same after a four-hour and 12-month period. Therefore, NIKBT can be a promising indicator to evaluate TFSQ and furthermore improving CL wear success rate.

CONTROL ID: 3546440

SUBMITTER (NAME ONLY): Eric Weh

TITLE: HK2 and PKM2 deletion leads to outer segment shortening and photoreceptor degeneration

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Weh, K.X. Li, H. Hager, S. Sheskey, T.J. Wubben, C.G. Besirli, Ophthalmology and Visual Sciences, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptor (PR) metabolism is unique among other neurons in that they primarily process glucose into lactate via aerobic glycolysis. This unique adaptation allows maintenance of the highly-specialized PR cell structure under basal conditions and provides a survival advantage during prolonged nutrient deprivation. The main drivers of aerobic glycolysis, HK2 and PKM2, are expressed primarily in PRs in the retina. We have previously demonstrated that the conditional knockout (cKO) of HK2 from rods sensitizes PRs to cell death following retinal detachment whereas cKO of PKM2 protects PRs from cell death during acute nutrient deprivation. Here we present data from animals lacking both HK2 and PKM2 in rod PRs.

Methods: Mice harboring a floxed Hk2 allele were crossed to mice carrying a floxed Pkm2 allele. Homozygotes for both floxed genes were generated and crossed to animals harboring a cre recombinase gene under the control of the rhodopsin promoter to create animals with conditional deletion of both Hk2 and Pkm2 from rods specifically. OCT was performed monthly and ERG was performed at specific time points. Whole eyes were fixed, and sectioned for H&E staining. The total number of PRs at each time point were counted using a custom macro in ImageJ and normalized to inner retinal area. Immunofluorescence was used on sections to verify deletion of HK2 and PKM2 from rods. Whole retinas were extracted for protein, RNA, or metabolite purification for Western blotting, qRT-PCR, or metabolomics analysis, respectively. Experimental retinal detachment was induced and whole eyes were collected at 3 days for TUNEL analysis and at 1 month for PR viability assessment.

Results: OCT analysis showed shortening of outer segments by 4 months of age and thinning of the outer nuclear layer (ONL) by 5 months of age. Western blotting and immunofluorescence confirmed successful deletion of both HK2 and PKM2 from rods and a compensatory upregulation of HK1 and PKM1. Total cell counts of H&E stained retina showed a significant loss of photoreceptors at 10 months of age compared to control animals.

Conclusions: Our data demonstrate that loss of both HK2 and PKM2 in double cKO retinas leads to outer segment shortening followed by PR degeneration, a phenotype different from the conditional deletion of HK2 or PKM2 alone. Early shortening of outer segments suggests metabolic, structural, and functional deficits prior to loss of PRs.

CONTROL ID: 3546441

SUBMITTER (NAME ONLY): Andrew Smith

TITLE: The cost, components and affordability of eye examinations in optometry practices in Western Nova Scotia, Canada.

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.F. Smith, Department of Ophthalmology, King's College London, London, London, UNITED KINGDOM|A.F. Smith, Medmetrics Inc., Wolfville, Nova Scotia, CANADA|

Commercial Relationships Disclosure (Abstract): Andrew Smith: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To explore variations in the cost, components and affordability of eye examinations conducted in optometry practices in Western Nova Scotia, Canada.

Methods: A telephone survey was undertaken to assess the cost of obtaining an eye examination provided by a licensed optometrists in a sample of optometry practices in Western Nova Scotia, Canada. Descriptive summary statistics were tabulated for the key variables of interest.

Results: Complete responses were obtained from a total of fourteen (14) unique optometric practices. The mean cost for an eye examination was CDN \$ 121 (SD: \$17.92; Range: \$95 to \$140). The mean waiting time to the first available appointment was 4.14 weeks (SD: 2.4 weeks; Range: 1 to 9 weeks). All eye examinations included an overall assessment of the health of the eye, an intra-ocular pressure (IOP) test and the provision of a prescription if required. 85% (n=12) of the eye examinations also included some sort of retinal imaging, most commonly via Optical Coherence Tomography (OCT), while only 14% (n=2) included visual field perimetry as part of the eye examination. 50% (n=6/12) of optometry practices who did not include visual fields as part of the eye exam, however, responded that they could arrange for visual field testing at an additional mean cost of CDN \$ 45.50 (SD: \$ 11.69; Range: \$ 25 to \$ 56) if required. The mean number of hours worked at a minimum wage of CDN \$12.55 to afford an eye examination was 9.68 hours (SD: 1.48 hours; Range: 7.57 to 11.16 hours).

Conclusions: The cost of accessing an eye examination was found to be high, particularly among lower wage earners in Nova Scotia. Either increasing the supply of optometrists across Nova Scotia or reducing the cost of obtaining an eye examinations may assist in increasing the affordability of eye exams, thus potentially preventing avoidable vision loss and blindness.

CONTROL ID: 3546444

SUBMITTER (NAME ONLY): Gislin Dagnelie

TITLE: Hand-Eye Coordination in Virtual Reality under Simulated Ultra-Low Vision Conditions

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Dagnelie, A. Kartha, S. Lee, Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|R. Sadeghi, Biomedical Engineering, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|T. Swanson, W. Gee, BaltiVirtual LLC, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop calibrated measures of hand-eye coordination for ULV individuals in virtual reality (VR), allowing objective quantification of visual ability in realistic activities of daily living (ADLs).

Methods: Based on an inventory of ADLs valued by ULV individuals (Adeyemo et al., TVST 2017) and prior data from visual information gathering ADLs in VR (Kartha et al., ARVO 2019/2020), we created 20 scenes with hand-eye coordination ADLs; examples include locating and flipping a light switch, giving a high five to an avatar, picking up common objects, building a block tower, sorting pills, putting on a mitt, and baking cookies and a pancake. Most scenes were implemented at 3 visibility levels by varying contrast or size, for a total of 55 activities. Scenes were presented in a Vive Pro Eye VR headset using a Leap Motion hand tracker to visualize the subject's hand. Subjects were allowed to practice manipulating objects in normal vision (NV). Simulated ULV (sULV) was achieved in these normally sighted subjects through Bangerter foils, reducing visual acuity to 2.0 LogMAR. Performance was compared across observers and across vision status (NV vs. sULV).

Results: All four subjects were able to complete 98% of activities in NV and 81% in sULV. Completion times in NV were 4.0 s [2.0,9.7] (median[IQR]), in sULV 6.4 s [3.7,17.8]; 67% of completed activities required (on average 33%) more time in sULV than in NV, with 20 of 55 requiring significantly more time (by ANOVA);. Rank correlations of completion times between NV and sULV within observers ranged from 0.62 to 0.71, suggesting that task difficulties were unequally affected by vision degradation. Rank correlations between observers ranged from 0.81 to 0.89 for NV, and from 0.65 to 0.89 for sULV, suggesting subjects were unequally affected, despite equal vision degradation levels.

Conclusions: Most of these activities, representative of ADLs valued by individuals with ULV, could be completed by individuals with sULV equivalent to 20/2000. The wide range of completion times in sULV suggests that these activities cover a broad difficulty range, required to cover the full spectrum of ULV. They will be validated in our population with ULV due to a wide variety of conditions.

CONTROL ID: 3546446

SUBMITTER (NAME ONLY): Catherine Lee

TITLE: 3D-printed ABCB5-positive stem cells for treating bilateral limbal stem cell deficiency

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Lee, Y. Sasamoto, N. Frank, Division of Genetics, Brigham and Women's Hospital Department of Medicine, Boston, Massachusetts, UNITED STATES|W. Lee, J. Kunes, S. Yoo, Brigham and Women's Hospital Department of Radiology, Boston, Massachusetts, UNITED STATES|B. Ksander, Schepens Eye Research Institute, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|C. Lee, Y. Sasamoto, M.H. Frank, N. Frank, Nephrology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|M.H. Frank, Harvard University Harvard Stem Cell Institute, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limbal stem cells (LSC) residing in the limbus continually repopulate the corneal epithelium. Limbal stem cell deficiency (LSCD) occurs when these LSC are damaged (due to trauma such as burns) or missing (due to genetic conditions). Patients with LSCD are unable to regenerate the corneal epithelium, resulting in blindness due to invasion of the conjunctiva and neovascularization. For patients with unilateral LSCD, transplantation of autologous limbal tissue or ex vivo expanded limbal cells from the unaffected eye can be used to treat LSCD. However, patients with inflammation as well as those with severe pathologies resulting in total, bilateral LSCD have no source of autologous LSC and must rely on allogeneic transplants, associated with poor outcomes and requiring lifelong immunosuppression. Such patients would greatly benefit from an alternative autologous source of stem cells and reconstructed LSC niche to sustain donor stem cells. We previously demonstrated that human ABCB5+ LSC were capable of restoration of the corneal epithelium in an NSG mouse model of LSCD. We found that ABCB5 is also expressed by skin stem cells and hypothesized that these dermal cells could provide an alternative source of stem cells for corneal epithelial regeneration.

Methods: Human ABCB5+ dermal stem cells (DSC) expanded in vitro and purified by cell sorting were cultured in corneal differentiation media to determine their ability to transform into corneal epithelial cells. ABCB5+ DSC were also transplanted onto NSG mice with mechanically induced LSCD. In vitro, a 3D bioprinter was used to layer collagen and precisely deliver ABCB5+ DSC to the peripheral rim of human central corneas, their normal anatomical location, which we predict will enhance reconstruction of the LSC niche.

Results: Human ABCB5+ DSC were induced in vitro to express significant levels of PAX6 and KRT12 and mice transplanted with human purified ABCB5+ DSC had clearer corneas compared to mice transplanted with carrier only or ABCB5- cells (Fig 1). Bioprinted ABCB5+ DSC surrounding a human central cornea (Fig 2).

Conclusions: Our results support the use of 3D-printed ABCB5+ DSC as an alternative autologous source of stem cells to regenerate the corneal epithelium and reconstruct the LSC niche in patients with bilateral LSCD.

CONTROL ID: 3546449

SUBMITTER (NAME ONLY): Nagarajan TN

TITLE: Blue light-induced alterations in visual cortex layer 5 pyramidal neuron and amelioration by Blue light blocking lenses (BBLs) in Wistar rats

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. TN, S. Ballae Ganeshrao, Department of Optometry, MCHP, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA | S. S, Anatomy, MMMC, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA | J. Manjunath B, MSLS, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA | M. Valiathan, Pathology, KMC, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA |

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ABSTRACT BODY:

Purpose: This study aims to investigate the influence of blue LED light on the visual cortex layer-5 pyramidal neurons (L5PN) and the protective efficacy of 2 commercially available blue blocking lenses (BBL) namely Crizal Previsiona (CP) and Duravision Blue (DB).

Methods: This study was approved by animal ethics committee of The Manipal Academy of Higher Education, Kasturba Medical College (IAEC/02/2017). 24 male Wistar rats divided into 4 groups: 1 light exposure (LE), 2 BBL group (CP and DB) and 1 control group (NC). In LE group, rats were exposed to blue LED (400-490nm), in CP and DB group, BBL was fitted on top of LED, in NC group, rats were in normal lab illumination. In all groups, rats were exposed for 28 days, 12:12 hours of light:dark cycles and a uniform (450-500 lux) light intensity. Rats were sacrificed at the end of 28 days; brain was embedded in Golgi-cox stain. Brain tissues of 150 microns sections were obtained using sledge microtome. Golgi stained L5PN were identified using the 20X objective of a wide-field microscope and images were captured using a Moticam 580-5.0 mp. Totally 30 photomicrographs were obtained from each neuron and they were separated by 5 μ m in the z-plane. All photomicrographs were projected to a calibrated Sholl's grid. Dendrites were manually traced in a masked fashion. For apical and basal dendrites, the number of branching and intersections with 20 μ m concentric circles up to 140 μ m from the soma were quantified using Sholl analysis.

Results: The L5PN of NC had significantly more intersections compared to LE, CP and DB. LE group had significant ($p < 0.001$) loss of dendritic branches (13.72 ± 3.2) compared to NC (21.3 ± 0.3). Similarly, the CP (10.69 ± 1.93) and DB (15.58 ± 3.88) group had significantly less ($p < 0.05$) dendritic branches compared to NC group (21.3 ± 0.3) (Figure:1). Although, not statistically significant the number of dendritic branches and intersections were higher in CP and DB compared to LE group.

Conclusions: Exposure to blue LED damages the L5PN of visual cortex. BBL may offer moderate protection from blue LED.

CONTROL ID: 3546450

SUBMITTER (NAME ONLY): Pirro Hysi

TITLE: Exploration of associations between a prevalent Stargardt disease-associated variant in ABCA4 and retinal thickness in the general population

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.G. Hysi, M.J. Simcoe, O.A. Mahroo, King's College London, London, London, UNITED KINGDOM|M.J. Simcoe, G. Arno, P.J. Patel, A. Webster, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|T. Ko, 4.Topcon Healthcare Solutions, Inc., Fremont, California, UNITED STATES|G. Arno, P.J. Patel, O.A. Mahroo, A. Webster, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Pathogenic variants in ABCA4 are associated with Stargardt disease. One particular variant, c.5603A>T, p.Asn1868Ile, has previously been shown to be significantly enriched in Stargardt patients and is regarded as supportive of the diagnoses; however this variant is relatively common (6.3% allele frequency in Europeans). The purpose of this study was to determine whether this variant is associated with effects on macular thickness among the general population.

Methods: Quantitative OCT data using the Topcon 3D OCT-1000 Mk2 machine and genetic data from whole exome sequencing for the c.5603A>T variant was available for 20180 participants of European ancestry in the UK Biobank, following quality control. Of these, 101 were homozygous and 2610 were heterozygous for c.5603A>T. Linear regression analyses, adjusted for age and sex, were performed to test for association between this variant and total retinal thickness as well as three available segmented layer thicknesses (retinal nerve fibre layer, RNFL; ganglion cell-inner plexiform layer, GC-IPL; retinal pigment epithelium, RPE). Further linear regression analyses were performed with eight automated QC measures as the outcome variable to determine whether c.5603A>T is associated with abnormal or scans of low quality.

Results: No association was identified between c.5603A>T and retinal thickness ($p=0.76$) or with any of the three segmented layer thicknesses (RNFL $p=0.16$; GC-IPL $p=0.82$; RPE $p=0.52$). No association was identified between c.5603A>T and any of the eight quality control measures (all $p>0.25$). Participants with the c.5603A>T variant were also no more likely to be excluded during quality control, indicating an absence of pathogenic effects affecting scan quality. Finally, out of 144 homozygotes (pre-QC), only two (1.4%) have been diagnosed with degeneration of macula and posterior pole.

Conclusions: The c.5603A>T variant alone does not appear to affect total retinal thickness in the general population. The variant is likely therefore to require a distinct pathogenic trans-allele to cause retinopathy. Moreover, other cis- or trans-acting modifiers might contribute to pathogenicity of such a c.5603A>T genotype and in part might cause the enrichment seen in Stargardt patients.

CONTROL ID: 3546451

SUBMITTER (NAME ONLY): Nicole Carvajal

TITLE: Impact of COVID-19 Shelter-In-Place orders on pediatric device use, outdoor activity and eye symptoms

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Carvajal, J. Cunningham, A. Tang, W.P. Shibley, A.G. de Alba Campomanes, E.N. Harb, School of Medicine, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic caused the implementation of public health measures globally, including a call to Shelter-In-Place (SIP). In most cases, traditional classroom teaching became remote, pediatric outdoor programs such as organized sports were halted and parks closed. This study primarily aimed to understand the impact of COVID-19 SIP orders on pediatric habitual device use, outdoor activity, and reported eye symptoms.

Methods: Eligible participants included English and Spanish speaking UCSF pediatric ophthalmology patients aged 5-10 years with no history of ocular disease, surgery or trauma. A parental survey was administered electronically or over the phone by a trained examiner. The survey included questions regarding their child's average daily device use, outdoor activity and how often their child typically reported eye symptoms before and during SIP. Statistical analysis was performed using paired t-tests to examine changes in behaviors before and during SIP.

Results: 42 participants (n=17 female, mean age 6.6 ± 1.3 years) were enrolled in the study. 98% (n = 41) of those surveyed reported that their child was in remote online learning during SIP, with the majority (56%) using a laptop as their main device for remote learning. On average, laptop and hand-held device (smartphone or tablet) use increased significantly during SIP for both weekdays and weekends (Laptops: ~3 hour increase weekdays and 1 hour increase weekends, $p < 0.001$; Hand-held devices: ~1 hour increase weekdays and weekends $p < 0.002$). Outdoor activity decreased on average by approximately 1 hour on both weekdays and weekends ($p < 0.008$). Despite the increase in device use, there was only a slight increase in 'eyes feeling uncomfortable or tired' (from never to occasionally, on average). None of the other eye symptoms surveyed (seeing words moving, jumping, swimming, or floating; headache; dry eyes; blurry vision) were reported to change during SIP.

Conclusions: This study provides insights into how COVID-19 SIP orders impact habitual pediatric device use and outdoor activity. Despite children spending significantly increased time on devices during SIP, there was a low prevalence of reported eye symptoms in our cohort. Further work is warranted to determine the potential longer term impacts of these behavior modifications on pediatric eye health.

CONTROL ID: 3546452

SUBMITTER (NAME ONLY): Emmanuel Kofi Addo

TITLE: Association of carotenoid status between mothers and infants in the Lutein and Zeaxanthin in Pregnancy (L-ZIP) clinical trial

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Addo, A. Gorusupudi, P.S. Bernstein, Department of Ophthalmology, Moran Eye Centre, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular pigment (MP), comprised of the dietary carotenoids lutein (L), zeaxanthin (Z), and meso-zeaxanthin (MZ), protects the macula from photo-oxidative damage and enhances visual acuity. MP selective accumulation in the human retina begins before birth, implying a possible physiological and protective role in early visual development. Given the paucity of data on maternal and infants' carotenoid status during pregnancy, we sought to determine associations between postpartum maternal carotenoid status and newborn infants' skin and umbilical cord blood carotenoids.

Methods: We used masked study data from participants who had completed the ongoing L-ZIP study (ClinicalTrials.gov identifier: NCT 03750968; still recruiting). Participants were randomized (1:1 allocation) to consume daily a standard prenatal multivitamins (Spring Valley™ Prenatal Multi + DHA capsule) with an added capsule containing 10 mg L and 2 mg Z in safflower oil (Carotenoid group) or with a capsule containing only safflower oil with no added carotenoids (Control group) for a period of 6 to 8 months. Skin, MP, and serum carotenoids were measured at every study visit (i.e., baseline, before 14 weeks gestational age [GA]; 22-26 weeks GA; 37-39 weeks GA and 0-2 weeks of giving birth). Skin, MP, and serum carotenoid status assessments were by resonance Raman spectroscopy (RRS), dual-wavelength autofluorescence, and high-performance liquid chromatography (HPLC), respectively.

Results: The present sample comprises 12 mother-infant pairs who had completed the ongoing L-ZIP study. Maternal serum L+Z levels significantly correlated with infant cord blood L+Z levels ($r = 0.82$, $p = 0.002$) and skin carotenoid levels ($r = 0.59$, $p = 0.042$). Maternal skin carotenoids significantly associated with infant cord blood L+Z levels ($r = 0.60$, $p = 0.040$). Infant skin carotenoids significantly correlated with cord blood L+Z levels ($r = 0.61$, $p = 0.037$). Maternal skin carotenoid levels correlated with serum L+Z levels ($r = 0.63$, $p = 0.027$).

Conclusions: Our findings indicate that maternal serum carotenoid status associates with carotenoid levels in infants. Hence, increasing maternal carotenoid status during pregnancy may improve infants' carotenoid status and could consequently enhance infant visual development.

CONTROL ID: 3546453

SUBMITTER (NAME ONLY): Rucha Borkhetaria

TITLE: Telemedicine in Pediatric Ophthalmology

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Borkhetaria, M. Chiam, M. Langue, A. Ely, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Telemedicine use has risen in light of the COVID-19 pandemic as many ophthalmologists face barriers to providing in-person eye care. This study aims to describe caregiver experience using telemedicine for managing pediatric eye care at a rural academic medical center.

Methods: An anonymous online survey was distributed to 35 caregivers of pediatric patients who had been contacted to participate in a telehealth eye appointment during the COVID-19 pandemic. Average scores were calculated for statements posed in the form of a five-point Likert scale (1 = strongly disagree, 2 = disagree, 3 = neutral/not applicable, 4 = agree, 5 = strongly agree).

Results: A total of 17 responses were collected, of whom all had participated in telehealth. This was the first telehealth experience for 64.7% (11/15) of participants. The mean child and caregiver ages were 4 and 37 years old, respectively. The preferred telehealth platform was Zoom (15/17, 88.2%). Caregivers reported ease with obtaining at-home exam information including visual acuity and 9gaze motility photos (14/16, 87.5%). Additionally, 64.7% (11/17) of caregivers stated a telehealth appointment was more convenient than an in-person appointment. Overall, caregiver satisfaction with their child's telehealth appointment was high with an average satisfaction score of 4.18/5.00.

Conclusions: The telemedicine model for managing pediatric eye health was met with high levels of patient satisfaction at one rural academic medical center. This care approach should be considered for clinical management of pediatric eye health in the presence of barriers to in-person care, such as COVID-19.

CONTROL ID: 3546454

SUBMITTER (NAME ONLY): Lauren Jeang

TITLE: Comparison of Gortex Sutured and Fibrin-Glued Secondary Intraocular Lenses, including Visual Acuity, Lens Tilt, and Adverse Events

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Jeang, L. Vander Woude, A. weaver, S.S. Iyer, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Surgical techniques vary significantly for Gortex sutured intraocular lenses (IOL) and fibrin-glued IOLs and the type of lens is often chosen based on surgeon preference. However, the sutured vs glued IOLs have 4 points vs 2 points of fixation, respectively, which may result in different positioning and stability of the IOL. The purpose of this retrospective chart review is to analyze the long-term stability of these IOL implantation techniques and their impact on best corrected visual acuity (BCVA), IOL tilt, and adverse events.

Methods: This study examines 63 patients over a 2-year follow up period at the University of Florida from 1/1/2011 to 5/1/2020. Patients were included if they were implanted with a Gortex sutured B&L Akreos A060 or Alcon CZ70BD (with cow-hitch technique) or Alcon MA60AC fibrin-glued IOL. Patients were excluded if they had concurrent macular pathology, required a second surgery for any reason, or had less than one month follow up. The primary outcomes measured were BCVA, IOL tilt, as measured by change in cylinder on refraction over time, and adverse events, as listed in Table 1.

Generalized estimating equations and Wald Chi-squared test were used to compare logMAR VA between sutured and glued IOLs. An independent t-test was used to analyze lens tilt. A Chi-squared test was used to analyze the difference in adverse events measured as categorical variables.

Results: There was no significant difference in BCVA between the Gortex sutured ($M=0.73$, 95% CI 0.59 – 0.87) and fibrin glued IOLs ($M=0.74$, 95% CI 0.55 – 0.93) with the Wald $\chi^2 = 0.01$ and $p=0.94$. With “M” being marginal means of logMAR where 0.73 and 0.74 are equivalent to the Snellen values of 20/107.4 and 20/109.9, respectively. There was also no significant difference in IOL tilt between the Gortex 4-point and glued 2-point fixated IOLs (mean=0.409, 95% CI -1.08 – 2.63, $p=0.225$), nor significant differences in adverse events (Table 1).

Conclusions: There was no significant difference in BCVA, IOL tilt, or adverse events between our studied IOLs. With a 2 year-follow up period, this study has the longest observational study to the authors’ knowledge. Clinically, this provides evidence that a surgeon may implant their preferred choice of studied IOL.

CONTROL ID: 3546456

SUBMITTER (NAME ONLY): Emily Dosmar

TITLE: COMSOL Multiphysics 3D modeling of drug diffusion to the vitreous following subconjunctival injection

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Dosmar, X. Su, Biology and Biomedical Engineering, Rose-Hulman Institute of Technology, Terre Haute, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Build a 3D model of the eye to simulate the diffusion of Vancomycin (VAN) delivered via subconjunctival injection and predict VAN profile and concentration buildup in the vitreous.

Methods: COMSOL Multiphysics was used to simulate VAN diffusion through the vitreous, where a “Time Dependent” and “Transport of Diluted Species” study was constructed.

The model was created by establishing three 2D work planes for each tissue layer in the eye. In each work plane, a curve with a diameter and thickness of the tissue layer was created and revolved around the central axis. In addition, the bottom of the sclera layer was made flat to represent a site where VAN diffusion begins. After the three layers were constructed, a solid sphere with the diameter of the vitreous was created to represent the vitreous humor. COMSOL's “Form Union” method was employed to create a single geometry object composed of many different domains.

Material properties and transport properties were applied to each layer. The initial concentration for the compartments were assume zero. The initial concentration of the flattened bottom of the eye was assumed to be 1 mg/ml in the subconjunctival space. After all parameters were set, the element size in Mesh was set to “Normal” to discretize the geometry. The simulation was executed over 1440 minutes (24 hours) and data were collected at 144 minute increments.

Results: Final results from the simulation were displayed as a diffusion profile over a period of time (24 hours). The concentration of the eye was illustrated as both Streamline (with slices) and Surface (Figure 1).

The simulation suggests the steady build-up of VAN in the center of the vitreous over time where 12% of the initial VAN concentration is present in the vitreous after 24 hours and diffuses at a rate of ~0.005mg/ml per hour. Based on these findings, a therapeutic concentration (0.007 mg/ml) of VAN in the vitreous is achieved after 2 hours following injection. This preliminary model suggests potential to predict minimum drug loading requirements for sustained release drug delivery systems meant to be placed in the subconjunctival space.

Conclusions: This model predicts drug build-up in the vitreous following a subconjunctival injection and can be expanded to predict sustained release drug delivery system drug loading requirements.

CONTROL ID: 3546457

SUBMITTER (NAME ONLY): Pei-An Lo

TITLE: Ultrasound-directed, microbubble-assisted Crispr/Cas9 delivery in RPE cells

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Lo, M.S. Humayun, L. Yue, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|P. Lo, J. Castillo, M.S. Humayun, L. Yue, Ginsburg Institute for Biomedical Therapeutics, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Crispr/Cas9 is a popular gene editing tool whose therapeutic potential in ophthalmology is being actively explored. Our goal is to develop a microbubble (MB)-assisted sonoporation method to deliver the Crispr/Cas9 constructs into the eye for the treatment of hereditary retinal diseases with minimal invasiveness and high spatial precision. This study investigates the feasibility of sonoporating Crispr/Cas9 plasmids into cultured human retinal pigment epithelial (RPE) cells, a cell type that is heavily involved in the pathology of the outer retinal degeneration.

Methods: Sonoporation was tested in ARPE-19 cells and HEK cells. The GFP plasmid and the RPE65 Crispr/Cas9 knockout plasmid with a GFP tag were employed to fluorescently label the transfected cells. The GTS Sonoporation System equipped with a plane wave transducer (center frequency of 1 MHz) was used as the ultrasound (US) source. The cell monolayer cultured on a cover slip was placed in a customized polydimethylsiloxane (PDMS) well supplied with the MBs and the DNA plasmids. US was delivered from the transducer placed ~35 mm below and the entire system was submerged in heated distilled water. Transfection under variations of sonoporation parameters was examined by fluorescence microscopy. The trypan blue assay was employed to test cell viability.

Results: Our in vitro experimental setup successfully introduced the GFP plasmid and the commercial Crispr/Cas9 plasmid into the HEK and the ARPE-19 cells. Among the sonoporation parameters examined, increase of the acoustic intensity from 2 to 4 W/cm² enhanced the GFP delivery by 1.6 fold and increase of the MB concentration from 0.4 to 4% (V/V) resulted in a 6.8 fold enhancement. However, the transfection efficiency of the Crispr/Cas9 plasmid was substantially lower than that of the GFP under similar sonoporation conditions, either at 100 Hz or 1000 Hz pulse repetition frequency (PRF). All sonoporation experiments did not lead to increased cell death.

Conclusions: This study shows the possibility of sonoporating an all-in-one Crispr/Cas9 plasmid into cultured human HEK cells and RPE cells at 1 MHz acoustic frequency. The lower delivery efficiency of Crispr than GFP may stem from the bulky size of the all-in-one Crispr plasmid that encodes both the Cas9 nuclease and the guide RNA (gRNA). Further studies are underway to investigate the microbubble-assisted sonoporation of more versatile Cas9 and gRNA constructs.

CONTROL ID: 3546460

SUBMITTER (NAME ONLY): Sonal Dalvi

TITLE: Proteomic analyses of extracellular matrix and basal deposits in iPSC-RPE models of macular dystrophies

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Dalvi, M. Roll, P.P. Barbosa, R. Singh, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|C. Galloway, Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York, UNITED STATES|C. Galloway, R. Singh, Biomedical Genetics, University of Rochester, Rochester, New York, UNITED STATES|G. Jang, J.S. Crabb, J.W. Crabb, Ophthalmic Research, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|J.S. Crabb, J.W. Crabb, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Induced pluripotent stem cell-retinal pigment epithelium (iPSC-RPE) in vitro models of maculopathies such as Sorsby's fundus dystrophy (SFD) and Doyme honeycomb retinal dystrophy (DHRD) display drusen-like basal deposits that appear consistent with the human diseases. The purpose of this study was to evaluate the proteomic relatedness of the basal deposits in the SFD and DHRD iPSC-RPE cultures with the human drusen proteome.

Methods: Extracellular matrix (ECM) and/or basal deposits were isolated from parallel patient-derived SFD and DHRD iPSC-RPE cultures and control (unaffected family member and/or gene-corrected line) iPSC-RPE cultures that were grown in culture for 40-100 days. ECM/basal deposit proteins were extracted in SDS, and digested with trypsin. Peptides were fractionated by reversed-phase high performance liquid chromatography (RPHPLC) at pH 10 then analyzed by Liquid chromatography-mass spectrometry (LC MS/MS) and proteins identified using the human UniProt database. Bioinformatic analyses was performed using PANTHER and Ingenuity Pathway analysis software.

Results: Proteome analyses identified 1689 and 2237 number of total proteins with 2 or more unique peptides in the ECM of SFD and DHRD cultures respectively. Of note, 61 proteins present in ECM/basal deposit underlying SFD iPSC-RPE cultures and 56 proteins present in ECM/basal deposit underlying in DHRD iPSC-RPE cultures were common with the 123 proteins previously reported in human AMD drusen (2002 PNAS, (23) 14682-14687). Furthermore, 49 of the previously identified drusen proteins in the AMD eyes were seen in both SFD and DHRD iPSC-RPE cultures. Notably, cytoskeletal, calcium-binding, and inflammation associated proteins constituted the majority of proteins detected in the ECM/basal deposits from SFD and DHRD cultures.

Conclusions: LC MS/MS analyses demonstrate overlap between the proteome of drusen from AMD donor eyes and basal deposits in SFD and DHRD iPSC-RPE cultures. The results further support the utility of these in vitro models for mechanistic studies of macular degeneration.

CONTROL ID: 3546464

SUBMITTER (NAME ONLY): Steffi Daniel

TITLE: Species and age-related changes to fibulin-3 expression in the retina and RPE of a series of mammals

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Daniel, J. Hulleman, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|J. Hulleman, Pharmacology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Steffi Daniel: Commercial Relationship: Code N (No Commercial Relationship) | John Hulleman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Fibulin-3 (F3), a secreted ECM glycoprotein, has been linked to retinal pathologies, namely Malattia Leventinese (ML) and age-related macular degeneration (AMD), with evidence supporting association of F3 with drusen deposits in both of these diseases. Mouse models of ML form basal laminar deposits after extensive aging, but do not appear to form other pathological characteristics of AMD (drusen, RPE atrophy, etc). This may simply be due to physiological differences in expression levels, timing of expression, or localization of key contributing factors (like F3) between mice and humans within the eye. To address this, we examined and compared the expression levels and localization of F3 and another fibulin family member, fibulin-5 (F5), in the posterior eye cups of mice, pigs, non-human primates (NHP), and humans. Finally, we assessed the potential for age-related changes in fibulin expression in mice.

Methods: qPCR was performed to determine levels of F3 and F5 in neural retina (NR) and RPE of mice, pigs, NHPs, and humans. Immunohistochemistry (IHC) was performed to determine the localization of fibulins in the different retinal layers of mice and compared to NHPs and human tissues. qPCR studies to assess age-related changes in F3 and F5 were also performed in mice at 2, 6, 15, and 18 months of age.

Results: qPCR revealed a surprisingly low level of F3 in the RPE compared to the NR in mice (~1.25 fold). In contrast, F3 expression was found to be much higher in RPE for pigs (~15 fold), NHPs, and human donors (~70 fold) compared to their respective NR. IHC showed localization and higher expression of F3 in the ganglion cell layer and inner retina of mice, while F3 labeling of NHP and human tissues revealed higher expression in the RPE, corroborating the gene expression data. Gene expression studies also showed that F3 expression in the RPE increases with age (albeit slightly, N=4, p=0.02 (2 vs 18 mo)) while F5 levels are similar across ages.

Conclusions: These studies suggest that there are differences in expression of F3 in mice compared to other higher-order mammals, specifically in the RPE, where the primary disease pathology of ML and AMD occurs. These observations may partially explain the need for aging ML mice to obtain a phenotype. More closely matching the expression of F3 in mouse RPE to that of humans may result in a model with an earlier onset and better fidelity to human disease.

CONTROL ID: 3546465

SUBMITTER (NAME ONLY): O'Rese Knight

TITLE: Examining Cantilever Induced Epithelial Damage

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.J. Knight, H. Mei, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|D. Hubbard, Biomedical Engineering, University of North Carolina System, Chapel Hill, North Carolina, UNITED STATES|N. Ziebarth, Biomedical Engineering, University of Miami, Coral Gables, Florida, UNITED STATES|N. Ziebarth, Physiology and Biophysics, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Atomic force microscopy (AFM) cantilevers have been used to measure the biomechanical properties of the full-thickness cornea ex vivo. In this study we examine the effect of repetitive cantilever indentations on corneal epithelial integrity to assess the utility of cantilevers for in vivo applications.

Methods: Human cadaveric corneas prepared for research purposes were obtained from the Miracles in Sight Eye Bank (Winston-Salem, NC) without apparent epithelial or stromal defect and mounted in a custom-designed holder, which enabled complete submersion of the corneas in Optisol GS (Bausch + Lomb, Rochester, NY) at room temperature. The corneal bath was placed in the Puima nanoindenter (Optics 11 Life, Amsterdam, Netherlands). Standard AFM cantilevers (4.59 N/m, 45.5 μ m diameter, Optics 11 Life) were used to complete 1000 indentations in the same location with a 5 μ m indentation depth over 4 hours. The cornea was sectioned for histology and expression of apoptotic/stress markers. Hematoxylin and eosin staining was used to compare epithelial integrity in indented and adjacent non-indented areas of the cornea. Expression of apoptotic/stress markers, including cleaved Caspase-3 (Asp175), phospho-HSP27 (Ser82), phospho-c-Jun (Ser73), and phospho-SAPK/JNK (Thr183/Tyr185), were compared between indented and adjacent non-indented areas.

Results: Young's modulus of elasticity was 14.6kPa with drift towards lower values over the duration of the trial. Hematoxylin and eosin staining of the indented cornea demonstrated epithelial deformation and partial stromal edema without epithelial denuding. There was no expression of the four apoptotic/stress markers observed in the indented area, which was comparable to the adjacent non-indented area from the same cornea.

Conclusions: AFM cantilevers can accurately assess Young's modulus of elasticity without significant damage to the corneal epithelium. This suggests that cantilevers can be used in in vivo applications to assess biomechanical properties.

CONTROL ID: 3546467

SUBMITTER (NAME ONLY): Masoumeh Ashouri

TITLE: Dynamic Transcriptional and Translational Profiling of Reactive Muller Glia Following Retinal Injury

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ashouri, M.B. Bhuckory, M. Nahmou, S. hay, C.M. Knasel, E.G. Cameron, S. Wang, D.V. Palanker, J.L. Goldberg, Spencer Center For Vision Research, Byers Eye Institute, Stanford University School of Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Muller glia (MG) respond to retinal injury through a process referred to as reactive gliosis, driven by changes in gene expression that promote both neuroprotective and neurotoxic functions. Differences in the MG reactivity induced by inner and outer retinal injury suggest MG locally respond to insults via differential gene expression and local translation. Here, we describe a novel molecular approach to label newly synthesized mRNA in vivo to characterize transcriptional changes in MG associated with glaucomatous injury and photoreceptor degeneration. Further, we show inner and outer MG processes can be isolated by laser ablation to assess local transcriptional and translational changes.

Methods: Thiol uracil (TU) tagging of nascent mRNA is facilitated by introduction of the uracil salvage enzyme uracil phosphoribosyltransferase (UPRT) that converts 4-thio-uracil (4sU) to 4-thio-uridine-5'-monophosphate (4TU). A transgenic mouse line, UPRT/GFAPcre25/TdTom, was used to express the UPRT enzyme in MG cells specifically. UPRT-expressing mice were injected with 4-sU every 3 hours over a 6-hour period and assessed TU-tagged RNA (TU-RNA) levels by HPLC. TU-RNA was treated with iodoacetamide to alkylate, enabling identification of labeled transcripts by RNA seq. To assess translational changes, a transgenic line, Ribo/GFAPcre25/TdTom, was used to obtain Ribo-Tag expression in MG and an excimer laser was used to ablate the inner or outer retina to isolate MG processes.

Results: Comparison of 4sU/RNA sequencing and MG single cell sequencing reveals that 85% of identified genes overlap in both RNA sequencing results. Inner and outer retinal injury were induced by optic nerve crush and photocoagulation, respectively. Both optic nerve injury and photocoagulation resulted in MG reactivity and peak GFAP expression was detected 4 days after insult. The inner and outer retina were successfully ablated using an excimer laser with a desirable precision. Tissue sections confirmed the ablation of the inner nuclear layer. Eight excimer treated retinas were required to obtain the minimum amount of RNA for sequencing

Conclusions: Identifying transcriptional and translational changes in MG after various types of retinal insult provides insights into the molecular mechanisms that underlie MG reactivity and may ultimately lead to new approaches to prevent vision loss associated with retinal injury or disease.

CONTROL ID: 3546468

SUBMITTER (NAME ONLY): James Akula

TITLE: Modeling Refractions and Eye Lengths in the Periphery

SESSION TITLE: Refractive control: Molecular and Anatomical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.D. Akula, A.K. Curran, J. Szczygiel, R. Ramamirtham, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|J.D. Akula, A.B. Fulton, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|R. Grytz, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|R. Ferguson, FergusonRD, LLC, Melrose, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To measure refractions and eye lengths in the periphery of eyes with a range of refractive errors and to devise numerical models of these eyes consistent with both sets of measurements.

Methods: Central and peripheral cycloplegic refractions were obtained (Grand Seiko Open-field Autorefractor) in 22 healthy subjects (12–39 years old) at eccentricities from 40° nasal (N) to 40° temporal (T), by directing their gaze using a fixation target at 1 m. Then, eye lengths and corneal curvatures were measured (LenStar Optical Biometer) at N/T horizontal eccentricities 0°, 10°, 20°, and 30°; optical path lengths of the cornea, anterior chamber, lens, vitreous, and retina were exported and transformed into geometrical lengths using custom software. A complete optical model was developed (Zemax optical design code) that incorporated all of these parameters.

Results: Relative to central refractive errors, eccentric peripheral refractive errors were hyperopic in myopes (0.49 ± 1.10 D at 30° T), but myopic in emmetropes (-0.93 ± 0.47 D at 30° T) and hyperopes (-1.96 ± 1.62 D at 30° T). These refractions corresponded to central and peripheral axial length measures (myopes at 0°: 25.24 ± 1.73 mm, 30° T: 24.65 ± 1.68 mm; emmetropes 0°: 23.46 ± 1.06 mm, 30° T: 23.02 ± 1.14 mm; hyperopes 0°: 23.81 ± 0.23 mm, 30° T: 23.10 ± 0.01 mm). For one hyperope, one emmetrope, and one myope, optimized Zemax eye models, supplied with the measured corneal curvatures, path lengths, and individual refractions, captured most of the optical behavior of the eye with only (1) a small tilt ($\sim 2^\circ$) on the lens and (2) a fitted posterior lens curvature. With a finite diameter (2 mm) refractor beam, coma was the dominant remaining aberration. In the examined cases, significant differences were found in the "shape-factor" (ratio of anterior to posterior curvature at given optical power) of the lens.

Conclusions: In the modeling, a single fitted parameter, representing the posterior curvature of the lens, produced substantial agreement among off-axis refractive profiles and eye lengths. Thus, the resultant, self-consistent model eyes can derive previously unmeasurable lenticular parameters that may be helpful in clinical studies. The shape factor for the lens appears to depend upon the refractive state of the eye which, in turn, may be implicated in refractive development; longitudinal study of refractive development will be needed to determine the predictive validity of such an indicator.

CONTROL ID: 3546470

SUBMITTER (NAME ONLY): Peter Koulen

TITLE: Synergism of mechanisms underlying early-stage changes in retina function after experimentally induced dyslipidemia and hyperglycemia

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Koulen, G. Edwards, T.P. Johnston, Vision Research Center, Department of Ophthalmology, School of Medicine, University of Missouri Kansas City, Kansas City, Missouri, UNITED STATES|P. Koulen, Department of Biomedical Sciences, School of Medicine, University of Missouri Kansas City, Kansas City, Missouri, UNITED STATES|T.P. Johnston, Division of Pharmacology and Pharmaceutical Sciences, School of Pharmacy, University of Missouri Kansas City, Kansas City, Missouri, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Peter Koulen: Commercial Relationship: Code N (No Commercial Relationship) | Genea Edwards: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Johnston: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The study was designed to quantify retina function in a genetic mouse model of diabetes, in which sustained dyslipidemia was induced chemically. The goal of the study was to identify if dyslipidemia in the presence of hyperglycemia resulted in either a synergistic, or merely additive, exacerbation of retinopathy in the context of the two most clinically-relevant components or features of the metabolic syndrome.

Methods: Two cohorts of mice, C57BL/6 and C57BL/KsJ-db/db mice were divided into two groups each. One group of each strain received the triblock copolymer, poloxamer 407 (P-407), administered by intraperitoneal injection ("P-407" and "P-407 db/db" groups) with saline as a control in the remaining two groups ("saline" and "db/db" groups). Blood glucose, total cholesterol (TC) and total triglyceride (TG) levels were quantified using enzyme-based colorimetric assays. Retina function was measured using electroretinography (ERG) and visual acuity was determined behaviorally.

Results: TC and TG levels were normal in both saline controls and db/db mice, but were significantly elevated in the P-407 group ($P < 0.05$), while levels of the same lipids were further elevated in the P-407 db/db group when compared to the P-407 group levels ($P < 0.0001$). ERG measurements of scotopic retina function showed a significant decline in the b/a wave ratio of the P-407 and db/db groups and a further reduction for the P-407 db/db group when compared to controls ($P < 0.01$). Similarly, behavioral assessment of the optomotor reflex indicated reduced visual acuity for both the P-407 and db/db groups and was further reduced in the P-407 db/db group when compared to either the P-407 or the db/db groups ($P < 0.001$).

Conclusions: Dyslipidemia in the presence of hyperglycemia synergistically exacerbated disease severity of diabetic retinopathy. P-407 administration significantly elevated plasma TC and TG levels in wild-type and diabetic mice (db/db), but the resulting hyperlipidemia was more significantly pronounced in the diabetic mice. While elevated plasma lipid and blood glucose levels were individually correlated with a decline in retinal function, the combination of both exacerbated retina dysfunction. This model of combined hyperglycemia and dyslipidemia can be used to dissect individual contributions of features of the metabolic syndrome to the pathogenesis of diabetic retinopathy.

CONTROL ID: 3546471

SUBMITTER (NAME ONLY): Kara Quealy

TITLE: Stride length in different luminance in non-advanced age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Quealy, E. Bensinger, K. Theberge, M.B. Abelson, Ora, Andover, Massachusetts, UNITED STATES|M.B. Abelson, Ophthalmology, Harvard University, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kara Quealy: Commercial Relationship(s);Ora:Code E (Employment) | Ethan Bensinger: Commercial Relationship(s);Ora:Code E (Employment) | Kelly Theberge: Commercial Relationship(s);Ora:Code E (Employment) | Mark Abelson: Commercial Relationship(s);Ora:Code E (Employment)

ABSTRACT BODY:

Purpose: Detecting early stage age-related macular degeneration (AMD) needs clinical tests that correspond to impacts on activities of daily living. The purpose of this study is to determine if stride length is affected in early AMD subjects under different luminance levels.

Methods: Six participants with non-advanced AMD (grade 1 to 4 on AREDS simplified scale) and 9 age-matched normal controls (AREDS grade 0) with best visual acuity (VA) 20/25 or better during their baseline visit were included. Stride length was measured using the 16 feet long GAITRite electronic walkway system. The testing room was set up to test under 3 luminance levels, high (about 300 Lux), moderate (about 20 Lux) and low (mesopic, about 5 Lux). A practice session was done prior to recording the test conditions. For each luminance condition, foot falls were automatically detected, stride length was measured and averaged across 4 trials. Best corrected visual acuity (BCVA) was recorded.

Results: For all light levels, stride length trended shorter in the non-advanced AMD group compared to the normal control group, although statistical significance was not reached. Stride length did not considerably alter with change in luminance for either normal or non-advanced AMD groups. For all subjects combined, the mean stride length was 105.5 ± 14.6 cm at high luminance, 104.8 ± 15.6 cm at moderate luminance and 104.3 ± 14.7 cm at low luminance (mesopic). Stride length at moderate and low luminance mesopic testing did not significantly differ from high luminance photopic testing ($p=0.32$ for moderate vs high, $p=0.16$ for low luminance vs high comparisons). LogMAR BCVA was also not significantly different between AMD (mean 0.05 ± 0.10) and normal group (mean 0.02 ± 0.12) ($p=0.65$).

Conclusions: Subjects with non-advanced AMD trend towards smaller stride length than age-matched normal controls. An effect of change in stride length in response to luminance was not observed in this small cohort, possibly due to a combination of small sample size and less challenging test conditions. An additional study with larger sample size and alterations in test conditions is currently in progress.

CONTROL ID: 3546474

SUBMITTER (NAME ONLY): Budd Tucker

TITLE: Development and biological characterization of a clinical gene transfer vector for the treatment of MAK-associated retinitis pigmentosa.

SESSION TITLE: Gene therapy in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B.A. Tucker, E.R. Burnight, C.M. Cranston, J.L. Fick, A.J. Reutzel, M.R. Devore, L.A. Wiley, I. Han, R.F. Mullins, E.M. Stone, Institute for Vision Research/Ophthalmology and Visual Science, The University of Iowa, Iowa City, Iowa, UNITED STATES|T. Westfall, C. Scott, A. Marsden, D. Slusarski, Biology, University of Iowa, Iowa City, Iowa, UNITED STATES|K.N. Gibson-Corley, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: By combining next generation whole exome sequencing and induced pluripotent stem cell (iPSC) technology we found that an Alu repeat inserted in exon 9 of the MAK gene results in a loss of normal MAK transcript and development of human autosomal recessive retinitis pigmentosa (RP). The purpose of this study was to determine if a viral gene augmentation strategy could be used to safely restore functional MAK protein as a step toward a treatment for early stage MAK-associated RP.

Methods: Patient-specific iPSC-derived photoreceptor precursor cells were transduced with the MAK gene transfer vector, and immunocytochemistry, rt-PCR and western blot analysis were performed to evaluate the effect on MAK expression. To demonstrate transgene function, cilia length assays were performed using patient-derived fibroblast cells in vitro and mak knockdown zebrafish in vivo. In addition, visual function testing was also performed in the zebrafish. Local and systemic toxicity studies of cGMP clinical grade MAK vector were performed via subretinal injection into wildtype rats.

Results: MAK mutant iPSC-derived photoreceptor cells harboring the previously identified Alu insertion (Tucker et. al., 2011) were generated and transduced with viral vectors containing the retinal MAK transcript. One week after transduction, normal retinal MAK transcript and protein could be detected via rt-PCR and western blotting respectively. Using patient-derived fibroblast cells and mak knockdown zebra fish we demonstrate that over-expression of the retinal MAK transgene restored primary cilia length in both MAK RP patient-derived fibroblasts and mak knockdown zebrafish. In addition, the visual defect in mak knockdown zebrafish was mitigated via treatment with the retinal MAK transgene. There was no evidence of local or systemic toxicity at 1-month or 3-months following subretinal delivery of clinical grade vector into wild type rats.

Conclusions: We developed a MAK gene replacement strategy and validated it in human iPSC-derived photoreceptor precursor cells in vitro as well as mak knockdown zebra fish and wildtype rats in vivo. The findings reported here provide the efficacy and safety data required for initiation of a phase 1 clinical trial for the treatment of patients with MAK-associated RP.

CONTROL ID: 3546475

SUBMITTER (NAME ONLY): Isaac Vidal Paredes

TITLE: Evaluation of pirfenidone and pirfenidone-loaded liposomes for treating chemical corneal injury

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Vidal Paredes, J. Navarro Partida, A. Santos, Instituto Tecnológico y de Estudios Superiores de Monterrey Campus Guadalajara, Zapopan, Jalisco, MEXICO | C.D. Diaz Palomera, J. Armendariz Borunda, Universidad de Guadalajara Centro Universitario de Ciencias de la Salud, Guadalajara, Jalisco, MEXICO |

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ABSTRACT BODY:

Purpose: An aberrant fibrotic repair process after a chemical corneal burn may lead to corneal opacity, inflammation and neovascularization and, therefore, vision impairment. Pirfenidone is clinically approved antifibrotic and anti-inflammatory drug for the treatment of idiopathic pulmonary fibrosis. We evaluated the effect of pirfenidone on human corneal fibroblast (HCF) treated with TGF β . We also tested the effect of pirfenidone and pirfenidone-loaded liposomes against alkali burn-induced corneal damage in mice.

Methods: HCF primary cultures were established from human donor corneas. HCFs were treated with TGF β 1 (5ng/ml) to induce myofibroblastic transformation and fibrosis for 7 days under serum-free conditions. Cultures were treated with pirfenidone at two concentrations (100 and 300 μ M) α -SMA mRNA expression levels were measured using Real-time quantitative PCR.

C57BL/6 mice were treated with 0.5 N NaOH to the cornea for 30 seconds. Pirfenidone (100 μ M) and pirfenidone-loaded liposomes (100 μ M) were administered topically to damaged corneas four times a day during 14 days. Corneal opacity and neovascularization were clinically evaluated at 24, 48 hours, and 2 weeks after chemical burn injury. Histology of corneas was performed after day 14 and corneal thickness, neovascularization, inflammatory infiltrate, edema and goblet cell differentiation of corneal epithelium was evaluated with hematoxylin and eosin and Masson stains.

Results: Pirfenidone at 100 μ M significantly reduced α -SMA mRNA levels ($p < 0.5$) in HCF cultures. Both pirfenidone and pirfenidone-loaded liposomes reduced corneal opacity and neovascularization, as well as histologic corneal thickness, neovascularization, inflammatory infiltrate, edema and goblet cell differentiation of corneal epithelium in mice models, however, liposome-free pirfenidone showed a more pronounced improvement.

Conclusions: Pirfenidone and pirfenidone-loaded liposomes have the potential to treat chemical corneal injury, however, further evaluations of liposome effectiveness are warranted.

CONTROL ID: 3546476

SUBMITTER (NAME ONLY): Mihyun Nam

TITLE: Peptains block retinal ganglion cell death in mouse models of ocular hypertension

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Nam, S. NANDI, R.B. Nahomi, R.H. Nagaraj, Sue Anschutz-Rodgers Eye Center and Department of Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|R.H. Nagaraj, Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Aurora, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: The death of retinal ganglion cells (RGCs) is a primary cause of irreversible blindness in glaucoma. In this study, we determined the neuroprotective effect of chaperone peptides (peptain-1 and peptain-3a) against RGC death in two models of ocular hypertension in mice.

Methods: The chaperone activity of peptain-1 and peptain-3a was tested in protein aggregation assays. Two mouse models were employed to simulate ocular hypertension. In the first, microbeads were injected into the anterior chamber. After 3 weeks, peptains were injected intravitreally at 1 µg each in PBS and subsequently once a week for 3 weeks. In the second model, silicone oil (2 µl, 1,000 mPa.s) was injected into the anterior chamber; after 2 weeks the oil was removed and peptains were injected intravitreally at 1µg each in PBS. In both models, the control group received PBS alone.

Results: The in vitro assays showed both peptain-1 and peptain-3a possess robust chaperone activities. The injection of microbeads into the anterior chamber elevated the IOP to 30 mmHg (from 12 mmHg in control) within a week. IOP progressively declined over the following 6-week period, but the levels were still significantly higher than controls ($p<0.05$). The number of Brn3a-positive RGCs decreased by 31% following microbead injection as compared to contralateral eyes. Injection of peptain-1 and peptain-3a significantly decreased RGC death by 4 and 12%, respectively, when compared to PBS-treated eyes. Flat-mounted retinas immunostained for β III-tubulin showed that peptains were able to inhibit axonal degeneration. In eyes injected with silicone oil, the number of Brn3a-positive RGCs decreased by 39% at 2 weeks post-injection compared to contralateral eyes. Two weeks after silicone oil removal, the number of RGCs further decreased even though IOP returned to normal levels (48.3% reduced at 2 weeks post-oil removal). However, the injection of peptain-1 and peptain-3a significantly reduced RGC loss by 26.6% and 25.3%, respectively ($p<0.05$).

Conclusions: Peptain-1 and peptain-3a both protect RGC somas and axons against ocular hypertension and suggest that they could be developed as neuroprotective agents for the treatment of glaucoma.

CONTROL ID: 3546479

SUBMITTER (NAME ONLY): Karteek Kunala

TITLE: Adaptive optics fluorescence lifetime ophthalmoscopy of iGlucoSnFR-TS suggests increased glucose in RPE of $\rho^{-/-}$ compared to healthy mice

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Kunala, K. Huynh, Q. Yang, K. Parkins, J.J. Hunter, Center for Visual Sciences, University of Rochester, Rochester, New York, UNITED STATES|Y. Xue, C.L. Cepko, Departments of Genetics and Ophthalmology, Blavatnik Institute, Harvard Medical School, Boston, Massachusetts, UNITED STATES|Y. Xue, C.L. Cepko, Howard Hughes Medical Institute, Boston, Massachusetts, UNITED STATES|K. Huynh, Department of Biomedical Engineering, University of Rochester, Rochester, New York, UNITED STATES|S. Steven, Institute of Optics, University of Rochester, Rochester, New York, UNITED STATES|S. Steven, A. Dubra, Ophthalmology, Stanford University, Stanford, California, UNITED STATES|J.J. Hunter, Flaum Eye Institute, University of Rochester, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: A potential consequence of outer retinal degeneration is an accumulation of glucose in the retinal pigment epithelium (RPE). iGlucoSnFR-TS (GS), a fluorescence lifetime-based sensor for cellular glucose, presents a powerful new tool to study disease mechanisms in the living eye. We developed adaptive optics fluorescence lifetime imaging ophthalmoscopy (AOFLIO) to image GS in healthy mice and those with outer retinal degeneration.

Methods: A custom adaptive optics scanning light ophthalmoscope (4-6° square field of view, 25 Hz frame rate, 180 s exposure) was used for two-photon excitation of fluorescence (790 nm, ~55 fs pulse width, 80 MHz repetition rate, 7 mW mean power). We performed AOFLIO of RPE at multiple locations in one healthy C57BL/6J (B6/J) mouse and 3 GS-labeled mice (2 B6/J, 1 $\rho^{-/-}$) injected subretinally at birth with an adeno-associated viral vector encoding GS driven by the Best1 promoter. The fluorescence lifetime decay histograms were measured using time-correlated single-photon counting (SPC-160, Becker & Hickl GmbH) across emission bandwidth 380-550 nm. A two-component exponential function was fit to each decay curve from which the mean fluorescence lifetime (τ_m) was calculated.

Results: AOFLIO can measure the lifetimes of both intrinsic fluorophores and extrinsic GS at cellular resolution. In GS-injected mice, we observed patches of RPE cells with high and low fluorescence intensity, which we interpret as high (GS+) and low expression. Additionally, some RPE appeared to have no expression (GS-). In GS-injected B6/J mice, there was a significant ($p < .0001$) difference in τ_m between GS+ (162 ± 16 ps) and GS- (96 ± 16 ps) RPE. τ_m of GS- B6/J RPE was not significantly ($p = 0.11$) different from the uninjected mouse (79 ± 3 ps). Similar trends were observed for τ_m in $\rho^{-/-}$ mice (GS+ 331 ± 61 ps; GS- 194 ± 105 ps). The τ_m of GS+ RPE in $\rho^{-/-}$ mice was significantly longer than in B6/J mice ($p < .0001$).

Conclusions: The longer lifetimes observed in labeled cells of $\rho^{-/-}$ mice suggest an increase in cellular glucose of RPE compared to the labeled B6/J. However, we have not determined the optical impact on fluorescence lifetime due to blur or disease-related photoreceptor loss. Two-photon AOFLIO will allow longitudinal assessment of fluorescence lifetime markers, such as GS, in vivo to track metabolism at cellular-scale in RPE of healthy and diseased mice.

CONTROL ID: 3546481

SUBMITTER (NAME ONLY): Sudan Puri

TITLE: Trigeminal ganglion neurons directly modulate leukocyte migration via chemotactic mediators

SESSION TITLE: Corneal immunology and neovascularization II

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Puri, B. Kenyon, V.G. Sendra, F. Qiu, Y. Seyed-Razavi, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center; Department of Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|B. Kenyon, Program in Neuroscience, Tufts University School of Graduate Biomedical Sciences, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: An association between corneal nerves and resident leukocytes during steady state and their dissociation following injury has previously been shown. We hypothesize that corneal nerves may directly modulate leukocyte migration via chemotactic mediators. Thus, our aim was to assess the migration of leukocytes and characterize alterations in chemotactic neuropeptide and chemokine expression within the trigeminal ganglion (TG), following corneal nociceptor stimulation.

Methods: Expression of select chemotactic neuropeptides/chemokines in the TG was assessed by RT-qPCR. TG neurons were co-cultured with plasmacytoid dendritic cells (pDCs) in a modified Boyden chamber, using transwell inserts with 3-mm pore size for the cell migration assay. To investigate the effect of nociceptor stimulation in the absence of injury, CO₂ was applied to the central cornea of adult C57BL/6 mice in a series of 3 pulses every hour over 4 hours, using a modified Belmonte CO₂ esthesiometer. TGs were excised at 30 minutes or 24 hours following final CO₂ application and RNA isolated for RT-qPCR analysis for candidate molecules.

Results: RT-qPCR results indicated that TG neurons directly express various chemotactic neuropeptides and chemokines, including CGRP, Substance P, ADM, and CXCL12. Higher density of TG neurons co-cultured in the modified Boyden chamber (10⁴ and 10⁵ cells) had higher percentage of pDCs migrating through the transwell membrane after 24 hours (1.67±0.72% vs. 6.67±1.44%) and 48 hours incubation period (2.08±0.72% vs 9.58±2.60%) (p<0.05) compared to no migration in the absence of neurons. Following corneal nociceptor stimulation with CO₂, the cornea had elevated inflammatory cytokine IL-1β expression (4-fold; p<0.05). In the TG, there was significant 12.83-fold increase in CGRP (p<0.05), 4.35-fold increase in Substance P (p<0.05), 0.11-fold decrease in NGF (p<0.05), 0.02-fold decrease in Urocortin (p<0.05) and no significant change in ADM and CXCL12 expression compared to naïve controls.

Conclusions: Our study demonstrates that TG neurons express chemotactic molecules and have a direct chemotactic effect on leukocytes, and that changes in expression levels of pro-inflammatory and anti-inflammatory neuropeptides in the TG following CO₂-induced pain may further mediate leukocyte chemotaxis.

CONTROL ID: 3546483

SUBMITTER (NAME ONLY): Denise Valente

TITLE: Assessing the functional response of photoreceptors in the fovea using AO-FF-OCT

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Valente, K.V. Vienola, R.J. Zawadzki, R.S. Jonnal, Department of Ophthalmology and Vision Science, University of California Davis, Davis, California, UNITED STATES|R.J. Zawadzki, Department of Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A high-speed full-field (FF) swept-source (SS) optical coherence tomography (OCT) was implemented incorporating an adaptive optics (AO) subsystem to image the human retina in vivo. It has been previously reported that digital aberration correction (DAC) permits visualization of cones with FF-SS-OCT, but only in the perifovea and periphery. By combining hardware AO with FF-SS-OCT this system is able to resolve foveal cones and measure their functional responses. With the reference arm blocked, the system is a high speed (kHz) AO flood illumination (FI) fundus camera.

Methods: The FF-SS-OCT imaging system is arranged as a Mach-Zehnder interferometer with tunable source (Superlum BS-840-2-HP). In the sample arm the light that is backscattered from the retina is imaged at a CMOS sensor (Photron NOVA S12 Fastcam). The reference arm hits the camera with an angle of $\approx 1^\circ$ with respect to the sample arm to suppress common path artifacts. In parallel, a deformable mirror (ALPAO DM-97-15) is operated by custom software in closed-loop with a Hartmann-Shack wavefront sensor for real-time aberration correction. The system also incorporates a stimulus channel based on a green (555 nm) LED, used to elicit optoretinographic (ORG) responses. Two subjects were imaged at eccentricities between 1° and 2° TR.

Results: With closed-loop AO correction, diffraction-limited FI and OCT images of the retina were successfully collected at rates of 1 kHz and 200-1000 Hz, respectively. Cones were laterally resolved in the FI images and resolved in 3D in the OCT images. ORGs were collected at 2° TR and 200-400 vol/s, showing a characteristic, stimulus-evoked pattern of initial rapid contraction followed by slower elongation of the outer segment, similar to what was previously reported by others using FF-OCT in the periphery or confocal scanning AO-OCT in the fovea.

Conclusions: The system was demonstrated to be capable of producing multimodal images and measuring ORG responses in the foveal cone mosaic. Future plans include incorporation of a DMD-based visible stimulus channel and modification of the AO system to permit higher correction speed and dynamic range. Comparison of images acquired with AO with images acquired with DAC is also of interest.

CONTROL ID: 3546485

SUBMITTER (NAME ONLY): Sindhu Saraswathy

TITLE: Pharmacological Sub-conjunctival Lymphatic Manipulation In Lymphatic Reporter Mice

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Saraswathy, J. Lee, A.S. Huang, Doheny Eye Institute, Los Angeles, California, UNITED STATES|J. Lee, Gachon University Gil Medical Center, Incheon, Incheon, KOREA (THE REPUBLIC OF)|Y.G. Seong, Y. Hong, Department of Surgery, University of Southern California, Los Angeles, California, UNITED STATES|S. Saraswathy, A.S. Huang, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blebs from bleb-forming glaucoma surgeries utilize sub-conjunctival lymphatics for aqueous outflow and intraocular pressure (IOP) reduction. Here, we test the ability to pharmacologically manipulate sub-conjunctival lymphatics as a way to modulate bleb biology

Methods: Lymphatics are natively visible in reporter mice that express GFP under a Prox-1 promoter. Superior sub-conjunctival injections were performed (vascular endothelial growth factor-C [VEGFC; n=11 at 0.36 mg/ml], mitomycin-C [MMC, n=10 at 0.25 mg/ml and n=9 at 0.5 mg/ml], 5-fluorouracil [5FU; n=10 at; 50 mg/ml]), control (BSS; n=10), and non-injected controls (n=10). Three sub-conjunctival injections were given (every other day), and eye were harvested and fixed in 4% PFA on the 7th day. Anterior segment flat mounts were visualized by fluorescent microscopy. Sub-conjunctival lymphatic length and branch number were quantified. Comparisons were made by Mann-Whitney U test.

Results: Sub-conjunctival lymphatics were readily visible. Many comparisons were made and main results included increased lymphatic branch number ($p=0.007$) with trending increase in length ($p=0.06$) after BSS injection, demonstrating the impact of trauma. VEGFC increase lymphatic length and branch number compared to all conditions ($p<0.001$ - $p=0.004$). 5FU demonstrated decrease in lymphatic branch number and length (both $p=0.015$) to BSS control. MMC also demonstrated a significant or trending decrease in lymphatic branch and length ($p<0.001$ - 0.075) to BSS control. A mild dose-dependent effect was seen for MMC with trending lesser lymphatic length at the higher dose ($p=0.079$). These overall changes were further less significant on the temporal/nasal to inferior portions of the eye as the injections were superior.

Conclusions: Sub-conjunctival lymphatic presence can be pharmacologically manipulated. Enhanced presence may be useful for improving aqueous outflow and IOP reduction after performing bleb-forming glaucoma surgeries. Limiting sub-conjunctival lymphatic presence may improve the sub-conjunctival space as a drug delivery depot by diminishing lymphatic drainage from that space.

CONTROL ID: 3546492

SUBMITTER (NAME ONLY): Shuang-An Yang

TITLE: Trends and Usage Patterns of Minimally Invasive Glaucoma Surgery (MIGS) in the US: IRIS Registry Analysis 2013-2018

SESSION TITLE: Surgery and Wound Healing

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Yang, W.G. Mitchell, Harvard University T H Chan School of Public Health, Boston, Massachusetts, UNITED STATES|S. Yang, W.G. Mitchell, N. Hall, T. Elze, A.C. Lorch, J.W. Miller, N. Zebardast, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|A.C. Lorch, J.W. Miller, N. Zebardast, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Understanding trends and patterns in the use of minimally invasive glaucoma surgery (MIGS) as well as patient profiles undergoing each procedure is important given their relative expense and unknown long-term safety and effectiveness.

Methods: We used the American Academy of Ophthalmology (AAO) Intelligent Research in Sight (IRIS®) Registry between 2013-2018 (inclusive) to measure adjusted annual number of MIGS and standard surgical techniques (trabeculectomy or glaucoma drainage device (GDD)) performed in the US, stratified by demographic characteristics. Secondary analyses of concurrent surgeries and of subsequent surgeries for MIGS and standard surgical technique were also conducted.

Results: 202,574 eyes and 232,537 unique procedures had associated, documented ICD 9/10 codes for glaucoma and were included in final analyses. Those receiving either iStent or endoscopic cyclophotocoagulation (ECP) were more likely to be female, while those receiving GDDs were more likely to be younger and male ($p < 0.05$). Those receiving either iStent or Xen Gel stent were more likely to be White, while those receiving GDD, goniotomy or trabeculectomy were more likely to be Black ($p < 0.001$). There was an increase in annual MIGS procedures over the study period (from 7,586 in 2013 to 39,677 in 2018), and a reciprocal decrease in standard glaucoma procedures (from 16,215 to 13,701). The proportion of iStent procedures tripled during the study period (from 14% to 40%), and by 2017 accounted for 43.7% of all glaucoma surgeries in the US. 21,524 (10.6%) of all eyes received multiple procedures; 7,381 (34.3%) on the same day and 14,143 (65.7%) on subsequent days. ECP and iStent were the most common concurrent procedures (58.9% of all concurrent procedures). Trabeculectomy and GDD were most commonly followed by another standard glaucoma surgery.

Conclusions: There was a significant increase in MIGS use over the recent six-year period despite limited evidence of their long-term safety or effectiveness, highlighting the need for studies comparing safety and outcomes of novel MIGS vs traditional surgical treatments for glaucoma.

CONTROL ID: 3546493

SUBMITTER (NAME ONLY): Alexis Stefaniak

TITLE: Racial Disparities in Outcomes of Cataract Vs. Cataract Plus iStent in Open-Angle Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Stefaniak, S. Kirk, Ophthalmology, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, UNITED STATES|S. Griffin, N. Chung, M. Li, M. Henry, M. Chaku, Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|M. Henry, Ophthalmology, University of Illinois Hospital and Health Sciences System, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The benefit of cataract and cataract plus iStent[®] (Glaukos Corp. Laguna Hills, CA) surgeries in reducing intraocular pressure (IOP) has been noted in open-angle glaucoma (OAG), yet the impact of race has not been studied. The purpose of our study is to compare intraocular pressure (IOP) and number of glaucoma medications (meds) in cataract extraction alone (CE) vs. cataract extraction plus iStent (CE+iStent) in Caucasians (CA) vs. African Americans (AA) at 1 year.

Methods: 88 OAG patients (58 CA, 30 AA) who underwent CE and 147 (99 CA, 48 AA) who underwent CE+iStent at Edward Hines, Jr. VA and Loyola University Medical Center from 2015 to 2019 were retrospectively reviewed. IOP and meds were recorded at baseline and postoperative months 1, 3, 6, and 12. IOP spikes (>21 mmHg) on postoperative day 1 were recorded. Independent samples t-test analyses were performed.

Results: In the total patient sample, baseline IOP was significantly higher in CE+iStent group vs. CE ($p=0.0001$). IOP at 1 year was significantly higher after CE+iStent vs. CE ($p=0.013$). Meds at 1 year were significantly less after CE+iStent vs. CE ($p=0.019$).

Regarding race, baseline IOP was significantly higher in CE+iStent group vs. CE ($p=0.039$ CA; $p=0.0005$ AA). CE resulted in a significant decrease in IOP at 1 year in CA ($p=0.001$). CE+iStent resulted in a significant decrease in IOP at 1 year in both CA ($p<0.0001$) and AA ($p=0.012$). Comparing CE+iStent to CE at 1 year, IOP was higher after CE+iStent for both races ($p=0.178$ CA; $p=0.011$ AA).

CE+iStent resulted in a significant decrease in meds at 1 year in CA ($p=0.002$) but not AA ($p=0.082$). Comparing CE+iStent to CE at 1 year, meds were significantly reduced with CE+iStent in CA ($p=0.004$) but not AA ($p=0.841$).

29.2% of AA and 14.4% of CA had severe OAG in CE+iStent group vs. only 16.7% of AA and 13.8% of CA in CE group.

39.7% of CA and 36.7% of AA had an IOP spike on postop day 1 in CE group compared to 20.2% of CA and 33.3% of AA in CE+iStent group.

Conclusions: This study shows significant benefit in lowering pressure and medication burden after cataract extraction alone and with iStent. Racial differences are seen in postoperative outcomes, and further research is needed to understand how race impacts these surgical outcomes. A limitation of the study is smaller sample size.

CONTROL ID: 3546494

SUBMITTER (NAME ONLY): Michael Goldstein

TITLE: Incidence of Endophthalmitis Following Routine or Complex Cataract Surgery in Practices With and Without Access to Hydrogel Sealant: Retrospective Study Using the IRIS Registry

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Goldstein, J.L. Metzinger, S. Vantipalli, N. Oliynyk, Ocular Therapeutix Inc, Bedford, Massachusetts, UNITED STATES|H. Fevrier, Verana Health, San Francisco, California, UNITED STATES|A.A. Moshfeghi, Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endophthalmitis after cataract surgery is a vision-threatening but rare event with an incidence of ~0.5 to 3 per 1,000, thus necessitating a large sample size to conduct meaningful studies. As of Sep. '20, the IRIS® Registry (Intelligent Research in Sight) includes data from >60 M (million) unique patients, making it an ideal data source to assess rare events. Hydrogel Sealant (ReSure Sealant) creates an in situ temporary soft surface barrier to prevent wound leakage of any clear corneal incision after cataract surgery. Here, we evaluate the incidence of endophthalmitis following any cataract surgery (routine or complex) between sites with and without access to ReSure Sealant.

Methods: This retrospective study analyzed patient data from the IRIS Registry from Jan 1, 2016 to Dec 1, 2019 on the incidence of endophthalmitis following cataract surgery in practices with & without access to hydrogel sealant. Inclusion criteria for patients included having cataract removal via phacoemulsification with intraocular lens insertion, ≥1 visits within 30 days after surgery, & being at least 22 years. Practices must have provided data for at least 30 days after each surgery.

Results: Approximately 6 M eyes of 4 M patients were eligible for inclusion. Mean age was 70.91 (SD: 8.95). Overall endophthalmitis incidence was 0.644 (all incidence rates calculated per 1,000 cataract surgeries; 95% Confidence Interval: 0.625, 0.663). Endophthalmitis rate at practices with ReSure Sealant access was 0.619 (0.59, 0.64) vs. without 0.671 (0.64, 0.7) (P=0.01). Endophthalmitis rate (87% cases) after routine cataract procedures was 0.582 (0.56, 0.61) at practices with Sealant access vs. without 0.625 (0.60, 0.65) (P=0.03). Endophthalmitis rate (13% cases) after complex cataract procedures at practices with Sealant access was 1.097 (0.97, 1.22) vs. without 1.227 (1.09, 1.37) (P=0.18).

Conclusions: To our knowledge, this is the largest reported recent review of endophthalmitis cases after cataract surgery. Overall endophthalmitis rate was low (0.644 per 1,000 cataract surgeries). Patients undergoing complex cataract surgery had a higher incidence of endophthalmitis. Sites with access to ReSure Sealant had a statistically significant lower rate of endophthalmitis than sites without access. This difference was not clinically meaningful.

CONTROL ID: 3546496

SUBMITTER (NAME ONLY): Maryam Rezaei

TITLE: A new functional test sensitive to a reduction in light absorption by photoreceptors

SESSION TITLE: Assessing human vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Rezaei, G.N. Chamaa, C. Rodrigue, J. Renaud, R. Allard, School of optometry, Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: The amount of light absorbed by photoreceptors likely drops at early stages of retinal diseases (e.g., age-related macular degeneration) although basic visual functions like visual acuity (VA) and contrast sensitivity (CS) remain normal. The current study adapted a psychophysical paradigm to create a novel psychophysical test (photon noise test) presumably sensitive to the amount of light absorbed by photoreceptors. This experimental study tested the hypothesis that the photon noise test is better at detecting a reduction in the amount of light absorbed by photoreceptors compared to current standard functional tests: ETDRS (VA), Pelli-Robson (CS) and MARS (CS).

Methods: Twenty-one young healthy adults participated in this study comparing the capability of the photon noise test and three standard clinical tests (ETDRS, Pelli-Robson, MARS) to discriminate the baseline viewing condition from a reduction of light absorbed by photoreceptors. To simulate a reduction of light absorbed by photoreceptors, neutral density (ND) filters of 0.5, 1.0 and 1.5 reducing the amount of light by a factor of 3.1, 10 and 31, respectively were used. The capability of each test to detect a reduced absorption of light was quantified by measuring the area under the ROC curve (AUC). Then, the capability of the photon noise test was compared to the capability of each clinical test using a chi-square test.

Results: The figure shows the AUC for the four tests and three levels of light reduction. Even for the smallest amount of simulated reduction in absorption rate tested (ND filter=0.5), the capability of the photon noise test was outstanding (AUC=.95) and significantly higher ($p<.015$) than the three clinical tests, which were poor or acceptable (AUC of .66, .75 and .73 for ETDRS, Pelli-Robson and MARS tests, respectively).

Conclusions: The photon noise test is better at detecting a small decline in light absorption than standard functional tests. The photon noise test may be useful to detect early signs of retinal diseases affecting the photoreceptors.

CONTROL ID: 3546500

SUBMITTER (NAME ONLY): Abigail Strauss

TITLE: Therapeutic contact lens use in patients with thyroid eye disease at a tertiary care center

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Strauss, C. Kocasarac, S. Akella, P. Setabutr, V.K. Aakalu, E. Shorter, Illinois Eye and Ear Infirmary, Department of Ophthalmology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe visual outcomes and characteristics of thyroid eye disease patients undergoing therapeutic contact lens use at a tertiary care center.

Methods: Records were identified and reviewed of consecutive patients with a diagnosis of thyroid eye disease utilizing billing records with ICD 9 code 242.0, 376.21 or ICD 10 code E05.00. Eligible patients were those evaluated in the contact lens service of the Illinois Eye and Ear Infirmary at the University of Illinois at Chicago between July 1st 2015 and July 1st 2020. Demographics, history of orbital decompression, eyelid/orbital surgery, orbital radiation, clinical findings, visual acuity and contact lens parameters were recorded. Snellen visual acuities were converted to LogMAR for analysis. Descriptive statistics are presented as well as paired T tests.

Results: Fourteen patients met inclusion criteria with a mean age of 59.6 years [15.3, 30-80]. The majority were female (78.6%). About one third of the patients had undergone orbital decompression surgery (n=5/14) and 3 had non-healing corneal epithelial defects. Clinical findings in these patients included punctate keratitis 78.6%, eyelid retraction 50.0%, bulbar conjunctival injection 42.9%, corneal scarring 35.7% and corneal thinning and steepening consistent with keratoconus 14.3%. There were 7 patients fit with soft lenses, 1 with corneal gas permeable lenses, 1 with hybrid and 5 with scleral lenses.

Vision in the right eye improved from baseline mean LogMAR 0.41 [0.47, 0.0-1.46; n=13] to 0.07 [0.11, 0.0- 0.30) with contact lenses (difference in means 0.34, 95%CI[0.076 to 0.598], t(12)=2.81, P=0.016).

One left eye was limited to light perception; however the other eyes improved from mean baseline LogMAR 0.55 [0.58, 0.0-1.83; n=13] to 0.065 [0.12, 0.0- 0.40) with contact lenses (difference in means 0.49, 95%CI[0.188 to 0.789], t(12)=3.55, P=0.004).

Conclusions: This series of patients demonstrates the characteristics of patients with thyroid eye disease. Moreover, therapeutic lenses, including soft and scleral lenses, were utilized most often and associated with visual improvement.

CONTROL ID: 3546501

SUBMITTER (NAME ONLY): William Johnson

TITLE: Impact of master bacterial virulence regulators on the host response to *Staphylococcus aureus* keratitis

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.L. Johnson, C. Woeller, R. Wozniak, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|P. Chatterjee, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|M. Chojnacki, Microbiology and Immunology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bacterial keratitis (BK) is a major cause of blindness worldwide. *Staphylococcus aureus* is the predominant organism implicated in BK and causes considerable ocular tissue damage largely due to the ability to significantly modulate the host immune response via secreted virulence factors. In *S. aureus*, Agr and Sae are two important virulence regulators, yet their role in BK is yet unknown. This study investigated the role of Agr and Sae in host cytokine production in a murine model of BK.

Methods: *S. aureus* isolates USA300 (WT), USA300 Δ saePQRS, and USA300 Δ agr, were used to inoculate the corneas of BLALB/c mice. At 24 and 48 hours, eyes were harvested, homogenized and evaluated for the abundance of a panel of cytokines including interleukin 6 (IL6), interleukin 12 (IL12), and tumor necrosis factor alpha (TNF α) using standard sandwich ELISA assays. Three biological replicates were assayed for each strain and time point.

Results: IL-6 was significantly elevated in mice infected with *S. aureus* USA300 Δ saePQRS at 24 h post infection compared to USA300 (WT) or USA300 Δ agr (ANOVA, $P = 0.005$; Tukey-Kramer post hoc test, $P = 0.021$ and $P = 0.005$, respectively). Production of IL6 at 48 h post infection was not significantly different between the three strains (ANOVA, $P = 0.34$). No significant differences were detected between strains at 24 or 48 hours for IL12 (ANOVA, $P = 0.1753$ and $P = 0.1951$, respectively) or TNF α (ANOVA, $P = 0.5440$ and $P = 0.3663$, respectively).

Conclusions: Agr and Sae are well-known virulence factor regulators in *S. aureus* yet their downstream effectors and resulting host response is not well characterized in BK. Here we demonstrate that Sae significantly impacts IL-6 production in a murine model of BK in the early stages of infection. Targeting bacterial factors that modulate the host immune response may provide a therapeutic approach to treating this blinding disease.

CONTROL ID: 3546502

SUBMITTER (NAME ONLY): Hendrik Scholl

TITLE: ALK-001 (C20-D3-Vitamin A) slows the growth of atrophic lesions in ABCA4-related Stargardt Disease: Results of a Phase 2 placebo-controlled clinical trial (TEASE study)

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: G. DeBartolomeo, I. Washington, L. Saad, Alkeus Pharmaceuticals, Massachusetts, UNITED STATES|H.P. Scholl, Institute of Molecular and Clinical Ophthalmology Basel (IOB), SWITZERLAND|H.P. Scholl, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Hendrik Scholl: Commercial Relationship(s);Astellas Institute for Regenerative Medicine:Code C (Consultant);Gensight Biologics:Code C (Consultant);Gyroscope Therapeutics Ltd.:Code C (Consultant);Janssen Research & Development, LLC (Johnson & Johnson):Code C (Consultant);Pharma Research & Early Development (pRED) of F. Hoffmann-La Roche Ltd:Code C (Consultant);Novartis Pharma AG :Code C (Consultant);Boehringer Ingelheim Pharma GmbH & Co:Code C (Consultant);Novo Nordisk :Code C (Consultant);Gerson Lehrman Group:Code C (Consultant);Guidepoint:Code C (Consultant) | Gabrielle DeBartolomeo: Commercial Relationship(s);Alkeus Pharmaceuticals:Code E (Employment) | Ilyas Washington: Commercial Relationship(s);Alkeus Pharmaceuticals:Code P (Patent) | Leonide Saad: Commercial Relationship(s);Alkeus Pharmaceuticals:Code E (Employment)

ABSTRACT BODY:

Purpose: To study the effects of ALK-001 on the progression of Stargardt disease (STGD1). STGD1 is the most prevalent inherited macular dystrophy and results from defects in the ABCA4 gene that cause accelerated formation of vitamin A dimers in the retina. No treatment exists.

Methods: The TEASE study is a multicenter two-year Phase 2 double-masked, randomized, placebo-controlled clinical trial that randomized 50 subjects with STGD1 and a well-delineated area of RPE atrophy. The investigational drug ALK-001 is a selectively deuterated vitamin A used as vitamin A replacement and taken orally once-a-day. Deuterium slows vitamin A dimer formation 4-5 fold without inhibiting the visual cycle. Subjects were randomized 2:1 ALK-001:placebo during the first year, with 50% of placebo subjects randomly crossed over to ALK-001 for the second year of treatment. The prespecified primary efficacy outcome measure is the rate of growth of the square root of atrophic lesions, as measured on short wavelength fundus autofluorescence imaging, and evaluated using a linear mixed model. The study was performed at 7 centers in the USA. 50 subjects (38 white; 28 female) were randomized. Median age was 46 years (range, 18-60) and disease duration 9 years (0-36). Atrophic lesions at baseline were bilateral in 74% of cases with a $\sim 5 \text{ mm}^2$ median area.

Results: The growth rate of the square root of atrophic lesions in the ALK-001 treated group was 21% slower than in the untreated group ($p < 0.001$). When using areas, the growth rate was 28% slower in the ALK-001 arm than the placebo arm. There were no significant changes in BCVA in either treated and untreated arms after 2 years as expected in this patient population. On average, $\sim 90\%$ of vitamin A was replaced with deuterated vitamin A, which was maintained over time. ALK-001 was well-tolerated with no unexpected adverse reactions, no report of night blindness or impaired dark adaptation, and no clinically-significant increases in liver enzymes.

Conclusions: These data represent the first time that a therapeutic intervention slows the progression of STGD1 in a clinically and statistically meaningful way. In addition, the data provides clinical evidence that vitamin A dimers contribute to the pathophysiology of STGD1, and that slowing vitamin A dimerization is beneficial even in advanced stages of STGD1.

CONTROL ID: 3546503

SUBMITTER (NAME ONLY): Sara Jamal

TITLE: A non-invasive imaging method to detect retinal hypoxia in a rat model of 50/10 oxygen-induced retinopathy using HYPOX4

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Jamal, J. Penn, M.I. Uddin, ophthalmology, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Neovascularization a condition that might arise due to retinal hypoxia is a leading cause of vision loss in a variety of retinopathies. The development of hypoxia detecting probes will provide a platform for early disease diagnosis and therapy monitoring. This study demonstrates the utility of HYPOX4 which is a hypoxia sensitive fluorescein-based imaging probe for early detection of retinal hypoxia in a 50/10 rat model of oxygen-induced retinopathy (OIR) in real-time.

Methods: OIR rat model was induced by exposing newborn Brown Norway rats (BN) to a 24 hrs alternate cycle of 50% and 10% oxygen for 14 days. The pups were returned to normoxia for 2 hrs and HYPOX4 was injected intraperitoneally for in vivo imaging of retinal hypoxia in 50/10 OIR model compared to age-matched control (exposed to normoxia throughout the duration of the experiment). A Separate group of OIR pups were injected with pimonidazole and sacrificed 90 min post-injection. Retinas were harvested and immune-stained for pimonidazole-adducts as an established method for ex vivo detection of retinal hypoxia. Post in vivo imaging, HYPOX4 injected pups were euthanized after 24 hrs for ex vivo imaging of retinal hypoxia. Vascular structures were counterstained using Isolectin B4 (IB4).

Results: Retinal hypoxia was observed within the avascular area in the peripheral retina that was detected with HYPOX4. The observation was validated using pimonidazole immune-staining. Confocal imaging allowed us to detect this retinal hypoxia in the inner retina hypoxic region.

Conclusions: Retinal hypoxia plays a major role in the onset and progression of neovascularization. HYPOX-4 was successfully used as a highly sensitive molecular imaging probe to detect retinal hypoxia in BN 50/10 OIR. Thus, HYPOX-4 could be utilized as a promising and noninvasive imaging tool for early-stage diagnosis and tracing of hypoxia in OIR and potentially in other vascular diseases.

CONTROL ID: 3546505

SUBMITTER (NAME ONLY): Salman Sadiq

TITLE: The ILUVIEN implant in DME – are we leaving it too late?

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.N. Sadiq, M. Habib, Sunderland Eye Infirmary, Sunderland, Tyne and Wear, UNITED KINGDOM|S.N. Sadiq, Royal Victoria Infirmary, Newcastle upon Tyne, Newcastle upon Tyne, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Salman Sadiq: Commercial Relationship: Code N (No Commercial Relationship) | Maged Habib: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Optimising medicines usage remains a focus as healthcare resources continue to shrink. We performed a retrospective, observational study in diabetic macular edema (DME) patients treated with the ILUVIEN (0.2µg/day fluocinolone acetonide; FAc) implant to understand the impact of disease duration on outcomes.

Methods: We analysed DME patient records treated with the FAc implant between 02/2014 and 11/2017. Baseline parameters included the duration of DME, prior intravitreal therapies, history of vitrectomy and tractional pathologies, and retinopathy status. We analysed changes in visual acuity (VA, Early Treatment Diabetic Retinopathy Study [ETDRS] letters), central macular thickness (CMT, µm), maximum macular thickness (MMT, µm), intraocular pressure (IOP, mmHg), and recorded any further treatment for DME or ocular hypertension (OHT). Two sub-groups were compared: those with baseline DME duration below the mean of 25 months (shorter DME duration), or ≥25 months (longer DME duration). Groups were compared using unpaired tests: Student's t-test, Wilcoxon (Mann-Whitney U test) and Fischer's exact test.

Results: Of the 84 eyes treated, 59.5% had shorter DME duration and 40.5% had longer DME duration; the duration of follow-up for each group was 28.7 months ±10.9 (mean ±standard deviation) and 26.1 months ±10.3, respectively. At last observation, shorter DME duration was associated with larger VA gains (+5.4 vs -1.5 letters, P=0.0566, see image 1), a greater reduction in central (-151.7 vs. -88.1 microns, P=0.0141) and maximum macular thickness (-157.6 vs. -91.9 microns, P=0.008) from baseline, and higher rates of anatomical response (defined as a reduction of ≥20% from baseline) for CMT (P=0.0132) and MMT (P=0.0110). Supplementary treatments were given in a lower percentage of patients with shorter compared with longer DMO duration (34.0% vs 50.0%). Furthermore, there were lower rates of surgical intervention for OHT observed in the shorter DMO duration sub-group (n=1 and 3, respectively). See Table 1.

Conclusions: Our results demonstrate the anatomical and functional benefits of considering earlier treatment with FAc implant in the course of DME disease, or earlier conversion of treatment to the use of slow release steroid implants. These results could help optimise future management plans for DME. Limitations of the study include being retrospective and the differences in baseline characteristics that may have impacted on results.

CONTROL ID: 3546507

SUBMITTER (NAME ONLY): Eman Alzghoul

TITLE: Induced Peripheral Blur and its Effect on Visual functions

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.A. Alzghoul, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

Commercial Relationships Disclosure (Abstract): Eman Alzghoul: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Peripheral hyperopic defocus has been considered to be a contributing factor to myopic progression. Thus, it has been suggested that reducing peripheral blur may slow down myopia progression. However, how the eye recognizes optical blur in different meridians and responds to change in peripheral visual functions is not fully understood. This prospective study hypothesized that inducing myopic peripheral blur using utilized multifocal contact lenses will improve detection visual function and may be involved in reducing myopia progression. In this study, we quantified the impact of peripheral blur on visual function which may provide further insights on myopia development

Methods: 20 myopic subjects (Mean age 21 ± 2 years) were fitted with Proclear multifocal lenses of distance center design in one eye. All subjects were with a central spherical equivalent myopic refraction of -1.00D or more, $\leq 0.75\text{DC}$ cylindrical power, and 1.00D or more peripheral blur at the horizontal visual field. Peripheral refraction and detection acuity were measured with the contact lens on the eye. All measurements were taken along the horizontal meridian at $\pm 10^\circ$, $\pm 20^\circ$, $\pm 30^\circ$, and $\pm 35^\circ$, and under three conditions; no blur, $+0.50\text{D}$, and $+1.00\text{D}$. Linear mixed model and Post-hoc t-tests were used for statistical analysis; to assess changes in visual functions under different peripheral defocus conditions

Results: Compared to the baseline, peripheral refraction was significantly more hyperopic at all points along the horizontal meridian when compared to the center except at nasal and temporal 10° ($p < 0.05$). No significant difference was found in detection ability with varying amounts of peripheral blur at different locations ($p=0.764$). However, detection acuity was highest centrally (± 10 degrees) and gradually started to decrease peripherally with the lowest acuity at location ± 35 degrees

Conclusions: The results of this study showed that inducing optical blur changed peripheral refraction across horizontal meridian when compared to spherical contact lenses. Further, the results showed that inducing optical defocus does not change peripheral detection ability along the horizontal visual field which contradicts our hypothesis that improvement in peripheral visual function may be involved in reducing myopia progression. However, more studies need to be conducted to comprehensively establish the impact of hyperopic blur on peripheral detection abilities

CONTROL ID: 3546509

SUBMITTER (NAME ONLY): Zaynab Sajjadi

TITLE: Outcomes of The Cancer Genome Atlas (TCGA) Classification in Uveal Melanoma by Patient Age in 1001 Eyes

SESSION TITLE: Advances in Diagnosis and Treatment of Uveal Melanoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Sajjadi, Z. Bas, E.L. Mayro, C. Shields, Wills Eye Hospital Ocular Oncology Service, Philadelphia, Pennsylvania, UNITED STATES|A. Ganguly, Genetics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The Cancer Genome Atlas (TCGA) is a genetic based classification of 33 types of cancer including uveal melanoma and is highly predictive of uveal melanoma-related metastasis and death. We performed a retrospective, cohort study to evaluate TCGA classification and outcomes for uveal melanoma based on patient age at presentation.

Methods: Retrospective analysis of patients with uveal melanoma at a single ocular oncology center treated with plaque radiotherapy or enucleation from 1998 to 2020 and who completed genetic testing of chromosome 3 and 8 after fine needle aspiration biopsy. Patients were classified by age group (<21 years vs. 21-40 years vs. 41-60 years vs. >60 years) at presentation. Categorical variables were compared using χ^2 tests or Fisher's exact tests. Kaplan-Meier analysis was performed for metastasis (liver metastasis, any metastasis) and death from uveal melanoma.

Results: Of 1001 eyes with uveal melanoma, 9 (1%) were <21 years, 104 (10%) were 21-40 years, 420 (42%) were 41-60 years and 468 (47%) were >60 years of age at presentation. By comparison, the older age group had higher frequency of class D tumor (0% vs. 4% vs. 10% vs. 14%, $p<0.001$) and greater tumor basal diameter (11.6 vs. 12.0 vs. 11.7 vs. 12.6, $p=0.02$) and the younger age group had higher frequency of 20/400-no light perception (NLP) vision (56% vs. 8% vs. 8% vs. 11%, $p<0.001$). By Kaplan-Meier analysis (10 years), the older age group had higher rate of liver metastasis (0% vs. 14% vs. 11% vs. 14%, $p=0.017$), any metastasis (0% vs. 14% vs. 12% vs. 14%, $p=0.033$), and uveal melanoma-related death (0% vs. 2% vs. 1% vs. 3%, $p=0.049$).

Conclusions: Uveal melanoma diagnosis at an older age is associated with more advanced TCGA classification, larger tumor size, and higher metastasis and death rate.

CONTROL ID: 3546511

SUBMITTER (NAME ONLY): Elizabeth Crabtree

TITLE: Prevention of experimental autoimmune uveitis by intravitreal AAV-EqIL-10

SESSION TITLE: Cytokines, growth factors, anti-inflammatory

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Crabtree, B.C. Gilger, S. Smith, B. Salmon, L. Song, Clinical Science, North Carolina State University College of Veterinary Medicine, Raleigh, North Carolina, UNITED STATES|B.C. Gilger, M. Hirsch, J. Bower, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Non-infectious uveitis (NIU) is an intractable and painful disease that is a significant cause of vision loss in humans and horses. Current treatments of NIU are non-specific and have serious side effects which limits them to short-term use. As NIU necessitates long-term immunosuppression to prevent vision loss, a single dose treatment that mediates long-term immunosuppression without side effects is desired. The purpose of this work was to develop an effective long-term therapy for NIU in horses. We investigated the use of adeno-associated virus (AAV) gene therapy as a vehicle for delivering anti-inflammatories to the uveal tract. The ciliary body was the targeted ocular tissue for gene therapy as it is the location of the blood ocular barrier break down. We exploited the use of an endogenous anti-inflammatory protein, Equine-IL10.

Methods: To simulate the prevention of NIU, naïve Lewis rats received a single intravitreal injection of a low dose or high dose AAV particles harboring codon-optimized cDNAs encoding Equine-IL10 one week prior to experimental autoimmune uveitis (EAU) induction. Daily blinded biomicroscopy examination and optical coherence tomography (OCT) examinations were performed. Genome biodistribution and transduction efficiency were characterized using Q-PCR for ocular tissues. Blinded histological examinations were performed and the level of inflammation was scored. To determine if intravitreal injection of AAV vectors resulted in an antibody response to the injected capsid, neutralizing antibody assays were performed.

Results: Intravitreal injection of AAV-EqIL-10 successfully mediated expression of Equine-IL-10 in the ciliary body of both treatment groups. There was a dose dependent influence of viral expression in other ocular tissues. There was a significant decrease in clinical and histological inflammatory scores in both treatment groups compared to control EAU eyes ($p < 0.5$). Mean cellular infiltrative scores were significantly less in treated eyes compared to control eyes on days 10, 12 and 14 post EAU induction ($p < 0.5$).

Conclusions: Localized gene delivery of Equine-IL10 establishes a long-term anti-inflammatory effect, that would be a novel therapeutic strategy for refractory and recurrent uveitis as well as other ocular autoimmune inflammatory diseases in both human and veterinary patients.

CONTROL ID: 3546512

SUBMITTER (NAME ONLY): Giulia Corradetti

TITLE: Risk Factors for Development of iRORA in Eyes with Nonneovascular Intermediate Age-related Macular Degeneration

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Corradetti, F. Corvi, M. Nittala, S.R. Sadda, Doheny Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the relationship between optical coherence tomography (OCT) features and demographic characteristics on the development of incomplete retinal pigment epithelial and outer retinal atrophy (iRORA) in eyes with nonneovascular intermediate age-related macular degeneration.

Methods: Fifty eyes from fifty subjects with nonneovascular intermediate age-related macular degeneration and no history of atrophy or macular neovascularization (MNV) in the study eye, were enrolled in this retrospective cohort study. OCT B-scans data and electronic medical records were reviewed for all subjects. The visit with first evidence of intermediate age-related macular degeneration on OCT was labeled as “baseline”. Baseline OCT B-scans from the study eye were annotated for previously described high-risk biomarkers including intraretinal hyperreflective foci (IHRF), subretinal drusenoid deposits (SDD), hyporeflective foci within core drusen (hDC), while the fellow eye was assessed for presence of atrophy and/or MNV. Electronic medical records were reviewed for socio-demographic characteristics including age, gender, ancestry, use of AREDS supplements and treatment with statins. OCT B-scans from the study eye obtained at month 6, 12, 18, 24, 30 and 36 were reviewed by masked graders for evidence of incident iRORA. The appearance of iRORA was plotted as a survival curve over a period of 36 months. Cox proportional hazards regression analysis was used to assess the factors associated with the development of iRORA.

Results: By month 36, 70% of eyes (35/50) demonstrated evidence of iRORA. The overall mean time to development of iRORA was 23.2 (1.4) months. Baseline socio-demographic factors showed no significant association with the development of iRORA. Among baseline OCT features, only IHRF showed a statistically significant association with the development of iRORA (HR 3.06; 95% confidence interval [CI] 1.69 – 7.94; p = 0.001).

Conclusions: A substantial proportion of intermediate eyes, particularly those with IHRF, can progress to demonstrate evidence of iRORA over a three year period. These findings may be of value in risk stratification and study design in early intervention trials of dry AMD.

CONTROL ID: 3546513

SUBMITTER (NAME ONLY): Pablo De Gracia

TITLE: Microsaccade Frequency, Magnitude, and Peak Velocity when using Multifocal Contact Lenses

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. De Gracia, M. McGee, B. Helmetag, A. Stein, Chicago College of Optometry, Midwestern University, Downers Grove, Illinois, UNITED STATES|Z. Goodman, Midwestern University Chicago College of Osteopathic Medicine, Downers Grove, Illinois, UNITED STATES|T. Whitescarver, Walter Reed National Military Medical Center, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe microsaccade magnitude, microsaccade peak velocity, and number of microcrossades when using distance center multifocal contact lenses in emmetropic and myopic subjects.

Methods: Binocular microsaccades were measured on 22 subjects using a custom developed binocular optical system with a field of view of 1.25 degrees coupled to an Eye Link 1000 eye tracker. The main components of the optical system were two Badal systems, two high luminance pico-projectors, and two diaphragms placed in conjugated planes to the subject's pupils. Badal systems allowed for the correction of refractive error between the powers of +5.00D and -10.00D without inducing magnification. External pupil diaphragms were used to maintain constant retinal illumination on all subjects by setting the artificial pupil size to 4mm. Each participant was measured under three different conditions: Naked Eye (NE), Biofinity Multifocal "D" +1.50D (BM1), and Biofinity Multifocal "D" +2.50D (BM2). Within each condition nine levels of defocus were presented, +4.00D to -4.00D in one diopter steps, using the Badal system. Each participant performed a total of 27 trials (total 3 hours). A single trial consisted of a subject fixating on the center of a Maltesse Cross for two minutes with breaks allowed as necessary. The NIMO instrument from Lambda-X was used to perform the analysis of BM1 and BM2 and coupled with custom developed software (Matlab) in order to evaluate the VSOTF for a 4 mm pupil.

Results: In the graph below, each row represents a viewing condition (71,012 binocular microsaccades, Engbert and Kliegl method). The upper row shows Naked Eye trials, the middle row shows Biofinity +1.50 D trials, and the bottom row shows Biofinity +2.50 D trials. The data for myopes (n=18) is in blue and data for emmetropes/hyperopes (n=4) is in orange. Lines represent moving averages (period 2). The optical profile and the VSOTF of the Biofinity +1.50 "D" and the +2.50 "D" for a 4 mm pupil can also be found on the left panels.

Conclusions: Emmetropic patients modify their average microsaccade size to a larger extent in comparison to myopic patients in the presence of induced blur. The use of BM1 significantly decreases the average size and the peak velocity of the microsaccades produced by myopic subjects when exposed to myopic blur. The number of microcrossades of myopic subjects is higher than in emmetropic.

CONTROL ID: 3546515

SUBMITTER (NAME ONLY): Carolina Rovarotto

TITLE: Delineating temporal and spatial recruitment of systemically administered RPE65-programmed bone marrow-derived cells to the retina in a mouse model of age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Rovarotto, X. Qi, M.E. Boulton, Ophthalmology, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|J. Godoy, Hospital Albert Einstein, Sao Paulo, Sao Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: We have previously reported that the intravenous injection of bone marrow-derived cells (BMDC) programmed with the RPE65 gene promoted visual recovery in a mouse model of AMD. Because of that, the aim of this study was to characterize the spatial and temporal recruitment of those programmed cells to the RPE layer.

Methods: 2-month old C57BL/6J female mice received a subretinal injection of AAV1-SOD2 ribozyme to induce the AMD mouse model. One month after the injection, systemic intravenous injection of 50,000 GFP⁺ RPE65-programmed mouse bone marrow-derived cells (BMDC)/animal was performed. Animals were terminated at different time-points from one to 60 minutes after cell injection and the localization of GFP⁺ cells was determined by fluorescence microscopy in RPE/retinal flat mounts and sections.

Results: The analysis of RPE/retina flat mounts showed that the majority of the GFP⁺ cells were found exclusively in the RPE layer. In the first two time-points, the cells were found especially in the proximity of ora serrata (peripheral) region of the RPE flat mount while few cells were observed in the center, near the optic nerve. In the following time-points, up to one hour after cell injection, the number of cells in the peripheral area was reduced while in the central area the number was increased. The neural retina showed cells scattered in the center of the tissue that presented a higher density in the first 2 minutes which decreased in the following time-points after cell injection. These findings were confirmed by immunofluorescence analysis of retinal sections, where we observed individual cells expressing both GFP and RPE65 markers.

Conclusions: In this study our group shows that the reprogrammed BMDC, administrated systemically, are capable of migrating to the eye, enter the retina via both the central retina and posterior ciliary arteries and migrate to the injured RPE layer.

CONTROL ID: 3546516

SUBMITTER (NAME ONLY): Kristyn Hake

TITLE: LOXL1-AS1 regulates extracellular matrix remodeling, mechanotransduction responses, and cellular morphology in human outflow cells.

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Hake, H. Schmitt, W. Johnson, M. Gomez-Caraballo, K. Perkumas, M.A. Hauser, D.W. Stamer, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pseudoexfoliation glaucoma (PEXG) is a form of open angle glaucoma that is characterized by outflow resistance dysregulation and elevated intraocular pressure (IOP). The LOXL1-AS1 gene codes for a long non-coding RNA, whereby polymorphisms decrease its expression and are associated with risk of PEXG. Since LOXL1-AS1 influences the transcription of many genes, we hypothesize that LOXL1-AS1 in outflow cells regulates the expression of gene-products known to participate in outflow resistance regulation, including extracellular matrix (ECM), cell adhesion and mechanotransduction signaling proteins.

Methods: Knockdown of LOXL1-AS1 expression was achieved in primary cultures of human trabecular meshwork (TM) and Schlemm's canal (SC) cells using a targeted Ad-shRNA, or by introducing targeted siRNA into HLE-B3 cells. Knockdown efficiency of LOXL1-AS1 and ECM gene expression was assessed using qPCR. Western blots were used to monitor ECM and mechanotransduction protein expression after LOXL1-AS1 knockdown, comparing to scrambled controls. Lastly, morphological changes due to LOXL1-AS1 knockdown in HLE-B3, SC, and TM cells were evaluated by calculating semi-axis ratios using FIJI.

Results: Knockdown of LOXL1-AS1 in HLE-B3 cells significantly altered the expression of seven ECM proteins ($p < 0.05$, $n = 3$), but did not change phosphorylation status of candidate mechanotransduction proteins AKT, MAPK, FAK ($p > 0.05$, $n = 3$). Experiments in one TM cell strain show that knockdown of LOXL1-AS1 results in dysregulation of ECM target genes including, but not limited to, MMP2, MMP14, MMP28, and MYC. In SC cells, knockdown of LOXL1-AS1 led to significant expression changes in ECM target genes including neuronal adhesion protein, vascular adhesion protein, integrin alpha 2, and laminin gamma 1 ($p < 0.05$, $n = 4$). With LOXL1-AS1 knockdown, SC cells significantly increased the proportion of phosphorylated AKT ($p = 0.008$, $n = 4$), but no changes were observed with phosphorylation status of FAK or MAPK. Knockdown of LOXL1-AS1 resulted in a shortening of the major axis of SC cells ($p = 0.006$, $n = 3$).

Conclusions: LOXL1-AS1 regulates genes involved in ECM remodeling and mechanotransduction signaling in human ocular cells. These data indicate that LOXL1-AS1 has a regulatory role in outflow resistance homeostasis, and represents a potential target for PEXG therapies.

CONTROL ID: 3546520

SUBMITTER (NAME ONLY): Deepak Shukla

TITLE: Optineurin is a novel host defense factor against viral infections of the eye and infection-associated nerve damage

SESSION TITLE: Pathobiology of Ocular Infections

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Shukla, J. Ames, T. Yadavalli, R.K. Suryawanshi, J. Hopkins, A. Agelidis, Illinois Eye and Ear Infirmary, Chicago, Illinois, UNITED STATES|T. Valyi-Nagy, Pathology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our main goal was to identify intrinsic host factors responsible for defending against viral infections of the eye. We used herpes simplex virus-1 (HSV-1) as a model virus to characterize a mammalian protein, optineurin. Optineurin is a glaucoma-associated gene, and mutations in this gene are also commonly reported in many other neurodegenerative diseases.

Methods: Cell types including human corneal epithelial, HeLa, Vero cells as well as primary cultures of neurons were used for infection with various HSV-1 strains. Viral plaque assays, viral genome counts by real-time PCR, and virus growth was estimated over time using time lapse fluorescence microscopy. TIRF/Super-resolution microscopy was used to demonstrate degradation of HSV-1 proteins and HSV-1 xenophagy. Immunohistochemistry was performed to detect optineurin localization in postmortem human nervous system tissues from patients with HSV encephalitis and ALS disease. Flow cytometry was performed to estimate cell death. Novel object recognition test was used to determine cognitive decline in mice.

Results: We provide the very first evidence that lack of optineurin results in measurably enhanced HSV-1 infection of the cells of ocular and non-ocular origins. We demonstrate that optineurin selectively binds to and degrades HSV-1 viral proteins via autophagy. In addition to selective degradation of HSV-1 proteins, optineurin may potentially participate in xenophagy of HSV-1 virions, which significantly restricts viral spread in wild-type compared to optineurin knockout cells. Loss of optineurin in intact animals demonstrates a more robust effect on nerve damage and potential loss of optimal vision in HSV-1 infected eyes. These animals show significantly reduced corneal sensitivity and succumb to HSV-1 infection due to rapid onset of encephalitis. Most interestingly, HSV-1 infected animals lacking optineurin show significantly lower scores in object recognition tests, suggesting a rapid loss of cognitive functions compared to wild-type animals

Conclusions: Optineurin is an important host defense factor that prevents severe damage to corneal cells and innervating nerves as well as the brain upon HSV-1 infection. Ours may be the first demonstration to explain an important protective role for this protein in infection as well as neurodegeneration.

CONTROL ID: 3546523

SUBMITTER (NAME ONLY): Prabhavathi Maddineni

TITLE: Effect of ocular hypertension on synaptic function and plasticity during the progression of glaucomatous neurodegeneration.

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Maddineni, R. Kasetti, G. Zode, Department of Pharmacology and Neuroscience, North Texas Eye Research Institute, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary Open Angle Glaucoma (POAG), the most common form of glaucoma, is characterized by progressive loss of retinal ganglion cells (RGCs) and their axons. Elevated intraocular pressure (IOP) is the major risk factor for POAG. The neurodegeneration in POAG extends beyond the eye into the visual centers of the brain (VCB). Unfortunately, the underlying pathological mechanisms responsible for IOP-induced glaucomatous neurodegeneration still remain unclear. To this end, we have developed a novel glucocorticoid (GC)-induced mouse model of glaucoma, and determined the role of GC-induced ocular hypertension (OHT) on synaptic dysfunction, and how alterations in synaptic plasticity contribute to glaucomatous neurodegeneration in the VCB.

Methods: C57BL/6J mice were injected with either Dexamethasone (Dex) or Vehicle (Veh) via periocular-route, once a week for 10-weeks. IOP was measured every week and glaucomatous neurodegeneration was examined using pattern ERG (pERG), whole mount retina staining with RBPMS antibody and PPD staining for optic nerve (ON) degeneration. The electrical response of the brain's primary visual cortex was measured using visually evoked potential (VEP). Expression of synaptic markers in the VC of the brain were assessed by immunostaining.

Results: Dex-induced sustained OHT led to glaucomatous neurodegeneration in 10-weeks Dex treated mice compared to Veh treated mice. Glaucomatous neurodegeneration was associated with significant functional and structural loss of RGCs as evident from reduced pERG amplitudes (10 μ V v/s 25 μ V), with ~33% RGC loss and ~62% axonal loss. We observed RGC hyper excitability during the early stages of axonal damage with significantly increased VEP amplitudes with decreased latencies in 5-weeks Dex treated mice (32 μ V; 73ms) compared to Veh mice (26 μ V; 79ms). Interestingly, we observed complete collapse of neuronal excitability, with decreased VEP amplitudes and increased latencies in 10-weeks Dex treated mice (12 μ V; 132ms) due to chronic IOP elevation. Also, we observed an altered synaptic plasticity with decreased expression of both pre and post synaptic markers (VGLUT-2 and PSD-95 respectively) in the VC of the 10-weeks Dex treated mouse brain.

Conclusions: These data highlights that OHT alters neurotransmission and axonal synaptic plasticity in the VC of the brain during the progression of glaucomatous neurodegeneration.

CONTROL ID: 3546524

SUBMITTER (NAME ONLY): Leina Lunasco

TITLE: Comparative Assessment of Long-Term Longitudinal Multi-Layer Retinal Dynamics in Non-neovascular Age-Related Macular Degeneration in Eyes Progressing to Subfoveal Geographic Atrophy and Eyes without Progression

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Lunasco, J.R. Abraham, K. Sarici, D. Sevgi, A. Hanumanthu, H. Cetin, M. Hu, S. Srivastava, J. Reese, J.P. Ehlers, The Tony and Leona Campane Center for Excellence in Image-Guided Surgery and Advanced Imaging Research, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|L. Lunasco, J.R. Abraham, K. Sarici, D. Sevgi, A. Hanumanthu, H. Cetin, S. Srivastava, J. Reese, J.P. Ehlers, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|M. Hu, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study evaluates the longitudinal retinal and sub-retinal pigment epithelium (RPE) dynamics on spectral domain optical coherence tomography (SD-OCT) and their associations with the long-term development of subfoveal geographic atrophy (sfGA) in non-neovascular age-related macular degeneration (AMD).

Methods: This retrospective cohort study compared eyes with non-neovascular AMD without sfGA using macular cube SD-OCT scans available at baseline, year 1, and year 5. Based on disease status at year 5, eyes were classified into one of two subgroups: non-conversion or sfGA converter. Macular cube scans at baseline and year one were evaluated using a machine learning-enhanced multi-layer segmentation software followed by manual verification by expert readers. Outer retinal integrity (e.g., ellipsoid zone (EZ)) and the sub-RPE compartment metrics were exported for comparative assessment. T-tests and Wilcoxon signed-rank test were used to compare sfGA converters and non-converters.

Results: One hundred and seventeen eyes were included in this analysis. Baseline mean EZ-RPE volume (i.e., surrogate for photoreceptor outer segment volume) was significantly smaller in the sfGA converter group compared to the non-converter group ($0.017 \pm 0.008 \text{ mm}^3$ vs $0.027 \pm 0.006 \text{ mm}^3$, $p=0.003$). In the first year, mean EZ-RPE volume decreased significantly in the sfGA converter group ($-0.0067 \pm 0.008 \text{ mm}^3$, $p<0.001$) but unchanged in the non-converter group ($-0.0007 \pm 0.003 \text{ mm}^3$). Baseline total EZ attenuation was significantly higher in the sfGA converter group compared to the non-converter group (4.14% vs 0.64%, $p<0.001$). The baseline RPE-BM volume (i.e., drusen burden) was significantly higher in the sfGA converter group (compared to the non-converter group ($0.045 \pm 0.024 \text{ mm}^3$ vs. $0.021 \pm 0.013 \text{ mm}^3$, $p=0.001$).

Conclusions: Higher order assessment of targeted retinal layer compartments identified significant differences in eyes that developed sfGA compared to eyes that did not over a 5-year period. Specific anatomic features, such as photoreceptor integrity are associated with development of sfGA and should be further explored as potential predictive biomarkers.

CONTROL ID: 3546525

SUBMITTER (NAME ONLY): Raymond Zhou

TITLE: Development of a platform to explore associations between single nucleotide polymorphisms and diabetic retinopathy

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zhou, R. Haliyur, S. Angaramo, N.G. Morales, J.B. Hatcher, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|D.A. Padovani-Claudio, Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|S.L. Mitchell, J.N. Hellwege, Division of Genetics, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) is the leading cause of blindness in 20-74 year-old U.S. adults. Genetic factors, including single nucleotide polymorphisms (SNPs), have been correlated with DR susceptibility and progression. Our goal is to develop a platform to explore novel associations between DR phenotypes and genetic variants.

Methods: We queried the Synthetic Derivative (SD), a de-identified database from VUMC's electronic health record linked to DNA samples. A combination of ICD and CPT codes was used to classify all SD records by presence of diabetes mellitus (DM), DR, non-proliferative and proliferative DR (NPDR, PDR), and diabetic macular edema (DME). We used Quanto software to calculate the expected statistical power of this platform to detect associations between vision threatening DR (VTDR) and SNPs of varying allele frequencies (AF). To confirm the accuracy of our code-based search criteria, presence of DM, DR, NPDR, PDR and DME was confirmed by manual review for a random sub-sample. Data regarding additional characteristics (risk factors, comorbidities, diagnostics, therapeutics) were also manually collected. We used Pearson's analysis to correlate the prevalence of these characteristics with DR susceptibility and progression (control vs DR, NPDR vs PDR, and no DME vs DME) in our sub-sample.

Results: A total of 5447 controls, 1168 NPDR, 734 PDR, and 441 DME cases met ICD/CPT code-based search criteria. This platform has >80% power to detect odds ratios >1.4 for SNPs with AF >35% using pre-existing genetic data, and for SNPs with AF >10% among all records. DR status and clinical characteristics were confirmed by manual review of 155 controls, 134 NPDR, 178 PDR, and 188 DME cases. Among these, Type 1 DM, nephropathy, and neuropathy were more prevalent in DR cases than controls ($p<0.00001$) and in PDR than NPDR cohorts ($p<0.05$). Type 2 DM, obesity, and hypertension were more prevalent in cohorts with DME than without ($p<0.05$) but had no evidence of association with progression to PDR. There was no evidence of association between gender, smoking, mortality, and hyperlipidemia with DR susceptibility or progression.

Conclusions: Our platform is clinically relevant and adequately powered to detect associations between SNPs and VTDR. We will use this resource to explore novel associations that may provide insights into DR pathophysiology, diagnosis, and management.

CONTROL ID: 3546527

SUBMITTER (NAME ONLY): Giovanna Guidoboni

TITLE: Physiology-enhanced data analytics to evaluate the effect of altitude on intraocular pressure

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Guidoboni, Electrical Engineering Computer Science, Mathematics, University of Missouri, Columbia, Missouri, UNITED STATES|M. Szopos, MAP5 UMR CNRS 8145, Universite de Paris, Paris, FRANCE|A. Verticchio Vercellin, B.A. Siesky, A. Harris, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|A. Verticchio Vercellin, C. Bruttini, I. Riva, L. Quaranta, Department of Surgical and Clinical, Diagnostic and Pediatric Sciences, Section of Ophthalmology, Universita degli Studi di Pavia, Pavia, Lombardia, ITALY|C. Bruttini, I. Riva, L. Quaranta, IRCCS Fondazione Policlinico San Matteo, Pavia, ITALY|

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ABSTRACT BODY:

Purpose: While it is known that altitude affects intraocular pressure (IOP), the underlying mechanisms remain unclear. Mean arterial pressure (MAP) and osmotic pressure difference (OPD) are considered important factors governing the IOP change with altitude. Herein we use a novel physiology-enhanced approach to analyze data from the Mont Blanc Study (MBS) (Bruttini et al. 2020), with the goal of assessing the relative roles of MAP and OPD on IOP.

Methods: In MBS, IOP and MAP were measured in 33 healthy volunteers at 77 m above sea level (a.s.l.) (Pavia, PV, Italy), at 1,300 m a.s.l. (Courmayeur, CM, Italy) and 3,466 m a.s.l. (Pointe Helbronner, PH, Mont Blanc Mountain, Italy), in addition to other systemic factors. A validated mathematical model for aqueous humor (AH) circulation (Szopos et al 2016) was used to analyze the MBS data. In the model, IOP is predicted as the result of the balance between AH production and drainage, with MAP and OPD included as parameters regulating AH production.

Results: A first analysis is conducted using measured MAP as an individualized model input to predict the corresponding IOP and compare it with IOP measured at different altitudes (PV, CM, PH). Fig.1 shows that changes in MAP are not sufficient to explain the measured IOP differences, since the measured IOP decreases with altitude while the model-predicted IOP increases. A second analysis is conducted by using the measured MAP and IOP as an individualized model inputs and estimates the OPD that would be necessary to have AH flow balance at different altitudes (PV, CM, PH). Fig. 2 shows that changes in OPD, in conjunction with MAP, capture the decreasing trend of IOP with altitude as observed in MBS.

Conclusions: Physiology-enhanced data analytics based on mathematical modeling suggests OPD plays an important role in regulating IOP with changes in altitude. Modeling factors that are conjectured to be relevant such as OPD may provide insights into parameters that cannot be measured directly. Future model analytics will include the effect of temperature and central corneal thickness for enhanced specificity.

CONTROL ID: 3546528

SUBMITTER (NAME ONLY): Hanna De Bruyn

TITLE: The Development of Retinal Function and Refractive Error in Retinopathy of Prematurity

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. De Bruyn, N. Mergia, V. Selian, R. Hansen, J.D. Akula, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|R. Hansen, J.D. Akula, A.B. Fulton, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the association of development of retinal function with refractive error in those with a history of retinopathy of prematurity (ROP).

Methods: Rod-mediated thresholds for detecting blue, 2°-diameter, 50-ms duration spots at both 10° and 30° were estimated in dark-adapted subjects (N=140) aged 10 weeks post-term through adulthood using a two-alternative, forced-choice, transformed up-down staircase method. Preterm-born subjects were stratified according to maximum severity of acute phase ROP: (1) Never developed ROP, None (n=32); (2) Mild ROP, resolved without treatment (n=67); and (3) Severe ROP that required ablative treatment (n=13). Healthy Term-born subjects (n=28) served as controls. Additionally, maturation of visual acuity [VA, expressed as log₂(cycles/degree)] and spherical equivalent (SE, diopters) were summarized; a single value for VA and SE at age 10 years was predicted using linear mixed-effects modeling. Each subject's course of threshold maturation was expressed relative to normal threshold development (De Bruyn et al., ARVO 2020) at both 10° and 30°. These parameters were evaluated as significant predictors of SE at age 10 years using stepwise linear regression, by: (1) Group (None, Mild, Severe), (2) threshold at 30°, (3) threshold at 10°, (4) difference (Δ 10–30), and (5) VA.

Results: In accord with previous reports, threshold development at 10° was significantly delayed in those with ROP. Developmental increase in VA proceeded most rapidly in None and most slowly in Severe. Likewise, all preterm groups showed progression of SE from hyperopia to myopia, slowest in None and most rapid in Severe. Preterm group (None, Mild, Severe) was a predictor of SE. Of the threshold parameters, only threshold development at 10° was a significant predictor of SE at age 10 years. Threshold development at 30° was not.

Conclusions: Given that the retina is a controller of refractive development, that VA is a measure of central retinal function, and that threshold development at 10° and 30° are respective measures of retinal function at nearer and farther peripheral retina, these data suggest that the nearer periphery (i.e., 10°) mediates refractive development. These results dovetail with the demonstration that retinal control of simian eye growth and refractive development is greatest at near-peripheral retinal eccentricities (Smith III et al., IOVS 2020).

CONTROL ID: 3546531

SUBMITTER (NAME ONLY): Radhika Malhotra

TITLE: Ocular Injuries Caused by Intimate Partner Violence Using an Emergency Room Database – a Gender-Based Analysis

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Malhotra, Y. Shah, N. Bhagat, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Radhika Malhotra: Commercial Relationship: Code N (No Commercial Relationship) | Yash Shah: Commercial Relationship: Code N (No Commercial Relationship) | Neelakshi Bhagat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intimate partner violence (IPV) is a leading cause of visits to the emergency department (ED), estimated in up to 35% cases. Literature suggests that orbital fractures are highly suggestive of domestic violence injuries and can often go underreported. It is important for emergency room physicians and ophthalmologists to be able to recognize ocular injuries caused by IPV. The aim of our study is to determine the epidemiologic trends of IPV related-ocular injuries presenting to the emergency department.

Methods: The National Electronic Injury Surveillance System-All Injury Program (AIP) (NEISS–AIP) was queried for injuries specifically involving the eyeball for the years 2006 to 2016. IPV was defined by sexual or other assault conducted by a spouse or a partner. Cases were weighted per the SUDAAN protocol, and statistical analysis was conducted with weighted data for frequency of injury by gender. Frequencies of race, incident locale, disposition from ED, reason for assault, precipitating injury, diagnosis, hospital size, and treatment month were conducted.

Results: Females were more likely to experience ocular injury as a result of IPV than males (n=18748 vs n=6667) at a younger average age (32.8 vs 36.7). By race, Black males and females were more likely than their white counterparts to have ocular injury as a result of IPV (black men 47.5% vs white men 18.1%, black females 35.5% vs white females 27.2%). The most common ocular injury in both genders involved ocular contusion/abrasions (males 43.4% vs females 53.4%), and subjects were most likely to be treated and released home. In males, the precipitating cause of injury was either being struck by an object or injury by fire (struck 66.1% vs fire 30.6%), whereas females were overwhelming injured by a striking injury (90.4%). Both males and females were most likely to be diagnosed with a contusion or abrasion injury.

Conclusions: Females are more likely to present with ocular injuries as a result of IPV, especially younger females. However, our study shows that men can also be victim to IPV, and are more likely to present with ocular injuries due to fire or burns as a result of intimate partner violence. The Black population is at higher risk of intimate partner violence. Consideration of IPV when a patient presents with a contusion or abrasion injury is important as IPV patients are likely to present to the ER again due to abuse.

CONTROL ID: 3546534

SUBMITTER (NAME ONLY): Daniel Flitcroft

TITLE: The SF properties of European, Middle-Eastern and Asian text and the potential implications for myopia development.

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.I. Flitcroft, B. Fitzpatrick, J. Loughman, Centre for Eye Research, Technological University Dublin, Dublin, Dublin, IRELAND|D.I. Flitcroft, Ophthalmology, Children's Health Ireland at Temple Street, Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: Reading and education are a well-recognised risk factors for myopia development, furthermore there are marked geographical differences in myopia prevalence in school age children. This study analyses the spatial frequency (SF) attributes of the printed text in a range of different alphabets/languages to determine the potential implications for myopia development.

Methods: Texts in 12pt font in English (Roman alphabet), Russian (Cyrillic script), Greek, Hebrew, Arabic, Chinese (simplified and traditional characters), Korean and Japanese were analysed at a 30cm viewing distance. The page layout was identical for each language. A photopic luminance image was generated and analysed to generate rotationally averaged SF spectra. The slope of the log amplitude vs log SF relationship (SF slope) was the calculated for each text sample at low (0.5-2 c/deg), intermediate (2-8 c/deg) and high (8-32 c/deg) spatial frequencies.

Results: Printed text has SF properties that differ markedly from natural or man-made images, yet the very different alphabets shared similar spatial characteristics. The log amplitude vs log SF relationship was highly non-linear with three distinct quasi-linear segments in low, intermediate and high SF ranges. This was most marked in Chinese text. There were also narrow spectral peaks corresponding to line spacing and/or character spacing. The slope of the low and intermediate SF segment was much flatter than natural images (low: mean -0.39, sd 0.30; intermediate: mean -0.27, sd 0.19) but the high frequency segment was much steeper, comparable to those reported for indoor environments (mean -1.76, sd 0.16) (See Table 1). There was a significant difference between low/intermediate and high SF slopes ($P < 0.0001$). All Asian languages showed a significantly steeper high SF slope than European/Middle Eastern languages ($P < 0.0005$). No significant differences were observed between serif and sans-serif fonts in English text.

Conclusions: The printed word has very different spatial properties to natural scenes with increased contrast at low/intermediate SF, but reduced high SF content which resembles man-made environments. At high spatial frequencies Asian languages show a significantly steeper log amplitude vs log SF relationship than European/Middle Eastern languages. Spatial properties of the written word may potentially contribute to regional variations in myopia.

CONTROL ID: 3546535

SUBMITTER (NAME ONLY): Imaan Kherani

TITLE: The Impact of Inherited Retinal Diseases on Canadian Patients: A Mixed Methods Study

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.Z. Kherani, Termerty Faculty of Medicine, University of Toronto Temerty Faculty of Medicine, Toronto, Ontario, CANADA|C. Andrews, L.S. Moniz, Fighting Blindness Canada, Ontario, CANADA|J. Pereira, JRL Research & Consulting, Ontario, CANADA|C.X. Qian, Ophthalmology, Universite de Montreal, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Inherited retinal diseases (IRDs) are a group of rare genetic conditions that lead to degenerative vision loss. Current literature gaps exist around the lived experience of Canadian individuals with IRDs and the associated impacts on health usage, policy, and care. This study aims to understand the physical, psychosocial, and practical challenges faced by those with lived experience, and to identify areas of need and reform from a medical, health policy, and social care perspective.

Methods: This sequential mixed method study comprised an online survey of Canadians living with or caring for someone with an IRD. Survey data fields included demographics, self-reported vision, genetic testing, information needs and preferences, healthcare management and experiences, treatment goals, and disease impact on productivity and social functioning. Recruitment occurred through Fighting Blindness Canada's patient database, filtering by disease-type. Survey dissemination also occurred via social media, newsletters, and not-for-profit stakeholder organizations to their constituents. A subset of respondents also participated in telephone interviews to more deeply explore the burden of their condition.

Results: Between March and June 2020, 408 individuals (mean age = 51.4 yrs \pm 16.7; male = 45.7%) participated in our survey. Respondents identified having one of over 14 IRDs, with 72% specifying retinitis pigmentosa. 68% reported being legally blind. Having an IRD had significant impacts on daily functioning, with 53% of participants indicating affected employment or education and 43% specifying a severe or very severe impact on mobility. Psychological burdens were evident: >70% worried about coping with daily life and 68% indicated frequent feelings of depression and hopelessness. Interviewees described their most significant disease impacts being loss of independence and challenges with social interaction. Despite this, the majority of respondents had not accessed support services, including counseling, mobility training or career support, due to a lack of awareness and/or access.

Conclusions: Our study describes the Canadian IRD community, including support network and impact of vision loss on daily activities and wellbeing. This data highlights the pronounced psychosocial burden that IRDs have on Canadian patients and families while elucidating unmet need for treatments, awareness, and support.

CONTROL ID: 3546537

SUBMITTER (NAME ONLY): Walter Sze Tung Lam

TITLE: Handheld chromatic pupillometry detects functional retinal loss in patients with retinal dystrophies

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.W. Lam, National University of Singapore, Singapore, SINGAPORE|R. Mathur, C. Chan, D. Milea, R. Najjar, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|R. Mathur, P. Chougule, D. Milea, R. Najjar, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To evaluate the ability of handheld chromatic pupillometry (HCP) to characterise and evaluate functional loss in patients with inherited retinal dystrophies (IRD).

Methods: In a cross-sectional study, we included 47 patients with IRD and 26 age-matched controls (44.5 ± 14.2 years, 53.8% males). The IRD population included 27 patients with rod-cone dystrophies (RCD, 50.7 ± 16.9 years, 55.6% males) and 20 patients with cone or cone-rod dystrophies (CRD, 53.8 ± 15.8 years, 50% males). Prior to an extensive ophthalmic examination that included electroretinography, participants underwent monocular evaluation of the pupillary response to 9 seconds of ramping-up blue (469nm) and red (640nm) light stimuli (45° field, 12.5-14 log photons/cm²/s). Pupillary light responses (PLRs) were assessed using a custom-built handheld pupillometer. Baseline-adjusted pupillary constriction traces were calculated for each participant and pupillometric features were extracted and compared between groups using a one-way ANOVA followed by a Holm-Sidak pairwise comparison.

Results: PLRs were altered in IRD patients (Fig. 1) who displayed a reduction in phasic constriction to blue and red lights compared to controls ($P < 0.05$). RCD patients showed a greater reduction in the phasic constriction to blue light compared to CRD patients ($P = 0.03$). Maximum constrictions to both lights were also reduced in IRD groups compared to controls. The early pupil redilation slope, calculated within 1.7s from blue light offset, an indicator of outer retinal contribution to the predominantly melanopsin-driven post-illumination pupillary response (PIPR), was decreased in IRD patients compared to controls ($P < 0.001$). Consequently, the Net PIPR (blue PIPR - red PIPR) was increased in IRD patients, yet, this increase was not statistically significant ($P = 0.09$) (Fig. 2).

Conclusions: Pupillometric features mainly driven by rods and cones (e.g., phasic constriction, early redilation slope) are altered in IRD patients. HCP can identify outer-retinal dysfunction and may provide a rapid method for detecting eyes with IRD.

CONTROL ID: 3546538

SUBMITTER (NAME ONLY): Alicia Gómez Sánchez

TITLE: Effects of cigarette smoke extract on the zebrafish visual system

SESSION TITLE: Retinal physiology

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Cigarette smoke is composed of hundreds of chemical products. Chronic smoking can damage human vision and is linked to development of age-related macular degeneration, cataract, glaucoma, diabetic retinopathy and dry eye syndrome. Here, we investigate the acute effect of cigarette smoke extract on the visual system of zebrafish larvae (*Danio rerio*).

Methods: Cigarette smoke extract (CSE) was tested at 10 and 20 µg/ml by adding directly to zebrafish embryo medium at 3 days post fertilisation (dpf). At 5 dpf, visual behavioural assays were conducted using a rotating striped drum which evokes saccadic eye movements known as the optokinetic response. Heartbeats were manually counted in one minute by direct observation. Startle response to touch was measured by touching larval caudal fins and manual observation. Retinal sections were imaged by light microscopy.

Results: There were no differences in gross morphology between vehicle control and the CSE treated larvae. However, CSE treatment resulted in a significantly ($p=0.0001$) lower number of saccades (10/minute) than 0.05% DMSO controls (19/minute) at standard frequency of 0.02 cycles per degree (cpd). Visual acuity data indicates CSE treated larvae exhibit a significant ($p=0.047$) deficit (0 saccades/minute) compared to control larvae (5 saccades/minute) at the highest frequency of 0.2 (cpd). Images of retina sections revealed no obvious effects of CSE on retina histology. The heartbeat rate of CSE treated larvae was within standard range and locomotor activity evoked by touch response was indistinguishable from 0.05% DMSO larvae.

Conclusions: Acute CSE treatment affects zebrafish visual function but retina histology remains intact. CSE has no adverse effects on zebrafish heart rate or startle response. Zebrafish offer an *in vivo* model to investigate the effects of CSE on vision.

CONTROL ID: 3546539

SUBMITTER (NAME ONLY): Soobin Song

TITLE: Anatomical and Physiological Effects of Nocturnal Normobaric Hyperoxia Treatment in Patients with Diabetic Macular Edema

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Song, C. Lemire, P. Atreay, B. Seto, K. Yamada, J.G. Arroyo, Beth Israel Deaconess Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes Mellitus can lead to ocular complications that include retinal ischemia and macular edema. Current common practices to treat patients with such conditions often include anti-vascular endothelial growth factor (VEGF) injections or focal lasers, which target the production of angiogenic factors such as VEGF and vascular leakage, respectively. This retrospective study explored the supplemental effects of Nocturnal Normobaric Hyperoxia (NNBH) treatment in patients with Diabetic Macular Edema (DME).

Methods: Of 9 patients diagnosed with diabetic retinopathy and presenting macular edema, 7 adhered to self-administering 3 to 5 LPM normobaric hyperoxia (40% FiO₂) overnight for at least 180 days. Macular Optical Coherence Tomography (OCT) imaging and ETDRS Visual Acuity measurements were taken for each eye (n=14) periodically for 180 days before NNBH and a following 180 days while on NNBH. Subjects' measurements during the control time period were compared with those from the time period on NNBH using Wilcoxon Rank Sum Test. The number of anti-VEGF injections administered to each eye during each time period was also analyzed.

Results: On average, patients saw decreases in the number of anti-VEGF injections needed while on NNBH ($p<0.05$). Additionally, the length of time between injections increased on average. Variability in macular thickness and volume while on NNBH was also shown to be decreased when compared to measurements collected while off NNBH.

Conclusions: The data suggests that oxygen therapy may be beneficial in minimizing the progression of edema and its detrimental effects to visual acuity as evidenced by the more stable values of macular thickness and volume in patients with DME. NNBH is a low-cost therapy that may reduce the burden of treatment for diabetic retinopathy by lessening the need for anti-VEGF injections. These results also suggest further long-term studies may be necessary to delineate the comprehensive effects and elucidate the mechanism of supplemental oxygen in patients with DME.

CONTROL ID: 3546540

SUBMITTER (NAME ONLY): David Buickians

TITLE: A novel device for descemetorhexis creation: 3D Printed Prototype Design and Ex Vivo Evaluation

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Corneal transplantation over the last decade has increasingly shifted towards selectively addressing pathologic layers as opposed to full-thickness tissue replacement. Such procedures include DMEK (Descemet's membrane endothelial keratoplasty), DSAEK (Descemet Stripping Automated Endothelial Keratoplasty), and DSO (Descemet's Stripping Only). In many cases, these newer procedures have led to improved final visual acuity, faster recovery times, and decreased incidence of graft rejection. Proper descemetorhexis is a critical step in these surgeries to avoid potential complications such as graft detachment, and stromal scarring.

Methods: Several variants of a handheld surgical device apparatus were designed to allow insertion into the anterior chamber through a standard 2.4 mm corneal incision. Parametric device designs were created using computer-aided design (CAD) software. An SLA 3D printer (Form 2, Formlabs ©) was used for prototyping using a commercially available, biocompatible resin. Prototypes were evaluated for their potential descemetorhexis application using ex vivo porcine eyes. The quality of descemetorhexis creation and relative ease of use were assessed. Results from empirical testing were then used to iterate and refine the design.

Results: Several prototypes were created, each evaluated based on intraocular manipulation stability, ease of use, and ability to create a circular descemetorhexis at the appropriate depth. Current device iterations— which include magnetically controlled, mechanically controlled, and a combined magnetic and mechanically controlled scoring of Descemet's membrane— resulted in successful descemetorhexis creation with minimal damage to neighboring anatomic structures.

Conclusions: A novel surgical device for descemetorhexis creation was created with a 3D printer for rapid prototyping, using an iterative design process. Prototypes were successfully used to create a circular descemetorhexis in ex vivo porcine eyes. Future work will be directed toward necessary design improvements and testing in vivo.

CONTROL ID: 3546541

SUBMITTER (NAME ONLY): David Sidhom

TITLE: Disparities in Eye Care Utilization During the COVID-19 Pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Sidhom, C. Andrews, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|P. Ugoh, Baylor College of Medicine, Houston, Texas, UNITED STATES|P. Newman-Casey, M.A. Woodward, L. De Lott, A. Elam, Kellogg Eye Center, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Telemedicine utilization has risen dramatically during the COVID-19 pandemic, particularly during the state-wide shut down, but multiple factors contribute to its potential inaccessibility to different populations. To explore these factors, we conducted a prospective mixed-methods study to assess the relationship between telemedicine utilization and socio-demographic factors among patients seeking eye care. We also assessed patient satisfaction with eye care using a health disparities lens.

Methods: We conducted phone interviews with a stratified random sample of 1,720 patients who had a visit scheduled at the University of Michigan Kellogg Eye Center in Ann Arbor, Michigan from 4/30/20-5/25/20 to ascertain patient perception of care received during the COVID-19 pandemic. The participant data was stratified by visit type and then analyzed by demographic variables. A Chi-square test was used to assess for association between categorical variables. Associations between visit type were determined using a multinomial logistic regression model. Open ended questions were stratified by race and analyzed using grounded theory to identify whether themes varied through a disparities lens.

Results: Non-white patients had lower odds of having an in-person visit ($p < 0.02$). Older patients had lower odds of having a video visit ($p = 0.007$) and higher odds of having an in-person visit ($p = 0.023$) compared to younger patients. The mean neighborhood median household income varied significantly ($p < 0.0001$) by race with Blacks having the lowest estimated mean. Access to broadband signal with faster download speeds compared to slower was associated with lower odds of an in-person visit ($p = 0.022$). No differences between races were identified in patient satisfaction or perception of care.

Conclusions: Disparities existed in how patients accessed eye care during the COVID-19 pandemic with non-white patients less likely to access care. Coupled with other barriers such as lower income, which, on a population level, may limit access to broadband internet, reimbursing telemedicine solely through broadband internet connection may further exacerbate disparities in access to eye care. Insurers should consider continued reimbursement of telemedicine delivered via phone to prevent further marginalization of underserved communities.

CONTROL ID: 3546542

SUBMITTER (NAME ONLY): Pieter Norden

TITLE: Delineating the role of neural crest- and endothelial-derived FOXC2 in Schlemm's Canal morphogenesis

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.R. Norden, T. Kume, Feinberg Cardiovascular and Renal Research Institute, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|L. Beckmann, Z. Cai, X. Zhang, D.A. Miller, H. Zhang, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Impaired development and maintenance of the Schlemm's Canal (SC) vasculature, characterized by both venous and lymphatic identity, is associated with impaired aqueous humor outflow regulation and the progression of glaucoma and loss of vision. Several key molecular regulators, such as Angpt/TEK, VEGFC/VEGFR3, and PROX1, were demonstrated to regulate SC development and maintenance, but mechanisms of paracrine signaling from neighboring tissues and cells contributing to SC development are poorly understood. Human forkhead box (FOX) FOXC2 variants were identified as modifier factors in congenital glaucoma (Medina-Trillo et al. PLoS One 2019) and our laboratory demonstrated that neural crest (NC)-derived periocular mesenchymal cells require expression of Foxc2 for development of the anterior segment (Seo et al. IOVS 2017). However, the role of Foxc2 in contribution to the development of the SC has yet to be investigated.

Methods: Using Foxc2-Cre^{ERT2}; mTmG reporter mice, we identified positive FOXC2 expression in both NC-derived trabecular meshwork and SC endothelium. Foxc2 was deleted from NC-derived cells by crossing Foxc2^F mice with Wnt1-Cre mice. Eyes of NC-Foxc2-KO and control mice were imaged in vivo using a visible light optical coherence tomography (Vis-OCT) system as previously described (Zhang et al., IOVS 2020). Inducible deletion of Foxc2 from endothelial cells (EC) was achieved by administering tamoxifen postnatally to Cdh5-Cre^{ERT2}; Foxc2^F mice. Immunohistochemistry for characterization of SC morphology was performed on flatmounted eyes where the lens and retina were removed.

Results: Vis-OCT image volumes showed different levels of narrowed and discontinuous SC morphology in NC-Foxc2-KO mice while OCT angiography showed various levels of corneal neovascularization. Immunostaining of CD31 identified abnormal SC morphology, or the absence of SC, in NC-Foxc2-KO compared to Cre-negative mice, which was accompanied by reduced PROX1, VEGFR-3, and TEK expression. Additionally, deletion of Foxc2 in the endothelium resulted in impaired SC morphogenesis at postnatal day 7, which was accompanied by reduced TEK expression compared to littermate controls.

Conclusions: Both Foxc2 expression in the NC lineage and ECs is required for morphogenesis of the SC vasculature. NC-derived Foxc2 expression is key for maintenance of SC identity and EC-derived Foxc2 expression regulates SC TEK expression.

CONTROL ID: 3546543

SUBMITTER (NAME ONLY): Marion Chiariglione

TITLE: Genome-wide association analyses identify novel loci influencing age-at-onset of glaucoma

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Chiariglione, D. Reed, S.E. Moroi, X.R. Gao, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|X.R. Gao, Department of Biomedical Informatics and Division of Human Genetics, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is an insidious, asymptomatic and progressive eye disease that damages the optic nerve, and is one of the leading causes of blindness worldwide. People over the age of 60 are at highest risk, but it can occur in younger adults as well. Our research aims to identify novel loci influencing the age-at-onset (AAO) of glaucoma. Previous studies have identified susceptibility genes for glaucoma, i.e. those associated with glaucoma as a binary trait. Here, we examine a large dataset to identify specific genes that might influence the variation of AAO of glaucoma.

Methods: With large amounts of data available from the UK Biobank, a cohort of half a million individuals, we selected participants of European ancestry that presented with AAO for glaucoma as a case-only design study (n = 13,000). Over 800,000 genotyped and 92 million imputed single nucleotide polymorphisms were available in the dataset. We used Bayesian mixed-model association analysis (BOLT-LMM) to test for associations between the AAO and genotypes. Genetic variants with $P < 5 \times 10^{-8}$ were declared genome-wide significant.

Results: We identified two novel associations to AAO on chromosomes 9 and 18. SNPs rs7866318 at GLIS3 and rs72899117 at LINC01477 both show significant association with AAO of glaucoma, $P = 2.4 \times 10^{-8}$ and $P = 1.4 \times 10^{-8}$ respectively. Mutations in GLIS3 (GLI-similar zinc finger protein family, chr9), which encodes a protein involved in the development of the eye, have been previously associated with many diseases, such as neonatal diabetes, congenital hypothyroidism, Alzheimer's, and congenital glaucoma. LINC01477 (Long Intergenic Non-Protein Coding RNA 1477, chr18) has no known associated eye disorders, but it has been associated with mathematical ability and intelligence.

Conclusions: These discoveries further our understanding of the genetic loci influencing AAO of glaucoma, and shed new light on the biological processes underlying glaucoma.

CONTROL ID: 3546544

SUBMITTER (NAME ONLY): Victor Wang

TITLE: Inhibition of TNF- α and NF- κ B decreases epithelial-mesenchymal transition in cigarette smoke-induced proliferative vitreoretinopathy

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Wang, University of Rochester Medical Center, Rochester, New York, UNITED STATES|A. Heffer, E. Roztocil, S.E. Feldon, C. Woeller, A.E. Kuriyan, University of Rochester David and Ilene Flaum Eye Institute, Rochester, New York, UNITED STATES|A.E. Kuriyan, Retina Service, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proliferative vitreoretinopathy (PVR) is the growth and contraction of cellular membranes within the vitreous cavity and on both surfaces of the retina and is the most common cause for recurrent retinal detachments. Cigarette smoke is associated with higher rates of PVR and our lab previously demonstrated elevations in proinflammatory cytokines TNF- α , IL-6, and IL-8 when RPE cells were exposed to cigarette smoke. Prior studies have shown that TNF- α induces RPE cells to upregulate epithelial-mesenchymal transition (EMT). The purpose of this study was to assess the effect of anti-inflammatory drugs on EMT pathogenesis in vitro and of cigarette smoke exposure on EMT markers in vivo.

Methods: Human ARPE-19 cells were pre-treated with a direct TNF- α inhibitor (Cas 1049741) or Bay-11, an NF- κ B inhibitor, before culture with concentrations of cigarette smoke extract (CSE) ranging from 0% to 1%. Cells were harvested after 24 hours and analyzed by quantitative PCR (qPCR) for known markers of inflammation and EMT, with at least 3 replications. In vivo mouse eyes were injected with ARPE-19 cells alone or ARPE-19 cells treated and resuspended in 0.5% CSE and sacrificed at 4 weeks for histologic analysis and immunohistochemistry staining (n=25). T-test and qualitative analysis were performed for in vitro and in vivo assays, respectively.

Results: ARPE-19 cells pre-treated with direct TNF- α inhibitor showed no significant differences in TNF- α expression but significantly decreased expressions of Snail (by 53%), IL-6 (by 50%), and IL-8 (by 82%) mRNA ($p < 0.05$). Bay-11 pre-treatment resulted in 78% decreased TNF- α as well as decreased expressions in Snail (by 77%), IL-6 (by 74%), and IL-8 (by 93%) ($p < 0.05$). Our in vivo studies showed a significantly higher mean PVR grade in mice injected with CSE-treated RPE cells (4.82 \pm 1.08) compared to mice injected with RPE cells alone (3.43 \pm 1.45, $p < 0.05$). Immunohistochemistry data showed that intravitreal injection of CSE-treated RPE resulted in significantly elevated vimentin and α -SMA protein expression in mouse retinal tissue, compared to RPE cells alone.

Conclusions: We demonstrate that inhibiting TNF- α or the NF- κ B pathway in RPE cells exposed to CSE also inhibits downstream proinflammatory and EMT pathways, suggesting that the TNF- α /NF- κ B/Snail pathway may be a viable target for inhibiting EMT pathogenesis and PVR progression.

CONTROL ID: 3546545

SUBMITTER (NAME ONLY): Bindu Kodati

TITLE: Cell Permeable Peptain for Neuroprotection in Glaucoma

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kodati, V. Krishnamoorthy, R.R. Krishnamoorthy, D.L. Stankowska, Pharmacology and Neuroscience, North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|R.B. Nahomi, M. Nam, R.H. Nagaraj, Department of Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|R.M. Chaphalkar, Department of Ophthalmology, School of medicine, University of California San Francisco, San Francisco, California, UNITED STATES|K.J. Beall, A.K. Brodrick, Texas College of Osteopathic Medicine, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if intravitreal administration of the core peptide of α -B crystallin, peptain-1 (P1) conjugated to a cell permeable peptide CPP (P1-CPP) could inhibit retinal ganglion cell (RGC) loss and functional decline in a rodent model of glaucoma.

Methods: Primary RGCs were isolated from post-natal day 4-6 rat pups. The cultured RGCs were deprived of neurotrophic factors for 48 h in the presence of either P1-CPP (12.5 μ g/ml) or vehicle, following which RGC survival was assessed by CytoCalcein™ Violet 450. In a different set of experiments, intraocular pressure (IOP) was elevated in one eye of Brown Norway (BN) rats and intravitreally injected with 2 μ l of either P1-CPP (2 μ g per eye) or vehicle, once in a week for a period of 6 weeks. RGC function was assessed by the pattern electroretinogram (PERG) amplitude and compared between all the treatment groups. Following the treatments, the rats were euthanized by approved methods, retinal flat mounts obtained were stained with an antibody to the RGC marker, Brn3a, to assess RGC counts. Retinal flat mounts were imaged and surviving RGCs were counted.

Results: In primary RGCs neurotrophic factor deprivation treatment for 48h led to 83% of RGC loss compared to cells grown in complete medium ($p < 0.0001$). P1-CPP treatment significantly lowered the neurotrophic factor-mediated RGC loss by 64% ($p < 0.0001$). IOP elevated and vehicle injected animals had 1192 ± 279 per mm^2 surviving RGCs in eccentricity 2 and 700 ± 246 per mm^2 in eccentricity 3, while P1-CPP treated rats had significantly higher RGC counts (1482 ± 388 and 1054 ± 343 respectively; $**p < 0.01$). P1-CPP treatment also promoted axonal protection during IOP elevation. IOP elevation caused 63% decline in the PERG amplitude ($*p < 0.03$) in comparison with naïve rats, which was sustained by P1-CPP treatment.

Conclusions: Intravitreal administration of P1-CPP provides cellular as well as functional protection of RGCs, and has the potential to facilitate neuroprotection in glaucoma.

CONTROL ID: 3546546

SUBMITTER (NAME ONLY): Sathishkumar Chandrakumar

TITLE: Mechanical Control of AGE/RAGE Signaling in Retinal Vascular Inflammation

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Chandrakumar, M. Agarwal, K. Ghosh, Ophthalmology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, UNITED STATES|S. Chandrakumar, I. Santiago Tierno, N. Matisioudis, M. Agarwal, K. Ghosh, Ophthalmology, Doheny Eye Institute, Los Angeles, California, UNITED STATES|I. Santiago Tierno, Molecular, Cellular, and Integrative Physiology Interdepartmental PhD Program, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Advanced glycation end products (AGEs) promote retinal endothelial cell (EC) activation, a hallmark of early diabetic retinopathy (DR). We recently reported that lysyl oxidase (LOX)-dependent subendothelial matrix stiffening mediates the inflammatory effect of AGEs on retinal ECs. Yet, precisely how matrix stiffening promotes AGE-mediated retinal EC activation remains unknown. Addressing this question is the main objective of this study.

Methods: Human retinal endothelial cells (HRECs) were treated with methylglyoxal (MGO, 10 μ M) for 10 days. AGE (MG-H1) and RAGE levels were measured by ELISA and western blotting (WB), respectively while EC activation was determined by ICAM-1 expression (WB) and monocyte-EC adhesion. LOX expression and collagen IV (Col IV) deposition were assessed by WB and immunofluorescence, respectively, while the stiffness of decellularized matrix was measured using atomic force microscope. The direct effect of matrix stiffness on RAGE and ICAM1 mRNA was assessed by plating the fresh ECs on decellularized matrices. Finally, the role of LOX and RAGE in AGE-mediated effects was confirmed by adding LOX inhibitor BAPN and RAGE-antagonist in these studies.

Results: Our findings revealed that MGO-treated HRECs exhibit significant increase in AGE formation (MG-H1, $p < 0.001$), RAGE ($p < 0.01$), and ICAM-1 ($p < 0.01$) expression while simultaneously increasing LOX, Col IV deposition, and matrix stiffness. Importantly, inhibition of LOX-dependent matrix stiffening suppressed the AGE-induced ICAM-1 expression/clustering ($p < 0.0001$) and monocyte-EC adhesion ($p < 0.0001$). Crucially, we found that inhibiting LOX-dependent matrix stiffness blocks the inflammatory effects of AGEs by decreasing RAGE expression. Finally, pharmacological inhibition of RAGE prevented AGE-induced LOX expression ($p < 0.001$). Collectively, these studies indicate that although RAGE signaling is upstream of LOX-dependent matrix stiffness, the latter feeds back to regulate RAGE expression. Ongoing in vivo studies aim to confirm the role of LOX-dependent vascular stiffening in controlling RAGE-mediated retinal vascular inflammation in diabetes.

Conclusions: These findings reveal a previously unknown and potentially crucial role of LOX-dependent vascular stiffening in AGE/RAGE signaling and associated retinal EC activation and provide the basis to examine this pathway as a novel anti-inflammatory strategy for effective DR management.

CONTROL ID: 3546547

SUBMITTER (NAME ONLY): Miranda Scalabrino

TITLE: Time-dependent changes in ON bipolar cell transcriptomes before and after genetic rescue from rod degeneration

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Scalabrino, M. Thapa, E. Davis, G. Field, Neurobiology, Duke University, Durham, North Carolina, UNITED STATES|A.P. Sampath, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|J. Chen, Cell & Neurobiology, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Photoreceptor death induces remodeling of bipolar cell (BC) dendrites. This remodeling is accompanied by changes in gene expression, but the gene networks that are involved in this rewiring are poorly understood. Furthermore, gene therapies are being developed to halt and rescue photoreceptors from degeneration. The halting of photoreceptor death at different timepoints in the degeneration process is likely to have distinct consequences on the morphologies and gene expression patterns of postsynaptic BCs. The purpose of this study was to examine how progressive photoreceptor degeneration impacts the transcriptomes of BCs and how these transcriptomes are altered by the genetic rescue of rods from degeneration.

Methods: Mice with a floxed neomycin cassette inserted into the Cngb1 locus (Cngb1^{neo/neo}) were crossed with UBC-cre and Grm6-GFP mice to create a triple transgenic line. These mice express green fluorescent protein (GFP) in BCs and exhibit a slow form of rod degeneration (all rods are lost ~6 months). Also, this line allows for genetic rescue of rods by tamoxifen-induced cre-recombination that triggers the expression of Cngb1 from the endogenous locus. Littermates heterozygous for the neomycin cassette were used as controls. At designated ages, mice were sacrificed, retinas dissociated using papain, and FACS sorted into GFP+ and GFP- cell populations, which yielded relatively pure populations of sorted BCs for RNA extraction and transcriptomic analysis.

Results: We found significant BC gene expression differences between groups that depended on the amount of rod degeneration and the time-point of rod rescue: WT vs degenerating (P30, P90, P210), untreated vs treated, and early treatment (Tx at P30) vs late treatment (Tx at P90). There were fewer differentially expressed genes between late-stage degenerating bipolar cells (P90 untreated) and late treated bipolar cells (Tx at P90, sac at P150), indicating that late therapy is not fully reversing pathology.

Conclusions: These results identify gene networks in postsynaptic BCs that respond to rod degeneration and death. These results also point toward the development of novel therapies to ameliorate blinding conditions and increase the effectiveness of vision restoration.

CONTROL ID: 3546552

SUBMITTER (NAME ONLY): Aoife Smyth

TITLE: Elevated Expression of ADAM 12 and 19 in Human Glaucoma Lamina Cribrosa Cells

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Smyth, C.J. O'Brien, Dept of Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|A. Smyth, M. Irnaten, S.K. Powell, C.J. O'Brien, Clinical Research Centre, University College Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: The lamina cribrosa (LC) of the optic nerve head is a key site of damage in glaucoma. A disintegrin and metalloproteinase (ADAM) 12 & 19 are members of a family of transmembrane, multidomain proteins implicated in a variety of cellular activities including proteolysis, cell adhesion, signalling and the regulation of growth factors through ectodomain shedding. Both ADAM 12 & 19 have been shown to be upregulated in numerous cancers and fibrotic processes. Stimulation of renal cells with TGF β , a key mediator of fibrosis, upregulates ADAM 12/19 expression via Smad2/3 phosphorylation. MiR29b, a microRNA which is believed to play an antifibrotic role, blocks the TGF β -induced overexpression of ADAM12. Our lab has previously shown that glaucoma LC cells have elevated pro-fibrotic gene expression. Here, we investigate the expression of ADAM12 & 19 in normal and glaucoma lamina cribrosa cells and examine their role in extracellular matrix gene production.

Methods: LC cells were obtained from 2 normal and 2 glaucoma age matched human eye donors. Cells were cultured under physiological conditions. Quantitative real time reverse transcriptase Polymerase Chain Reaction (qRT-PCR) was performed to measure the expression level of ADAM 12 and 19 mRNA in normal LC cells compared to glaucoma LC cells. The relative expression of both genes of interest ADAM 12 & 19 was calculated using $\Delta\Delta C_t$ method. The ribosomal gene 18S was used as housekeeping gene.

Results: ADAM 12 and ADAM 19 transcription levels are significantly ($p < 0.05$) enhanced in glaucoma LC cells compared to normal LC cells. The relative transcription level of ADAM 12 increased from 0.48 ± 0.049 in NLC to 0.76 ± 0.067 in GLC, and the relative expression level of ADAM 19 increased from 0.61 ± 0.058 in NLC to 0.82 ± 0.077 in GLC. The relative expression level of genes was determined using the $\Delta\Delta C_t$ method, with data normalized to the internal reference gene 18S.

Conclusions: Here we have shown ADAM 12 and 19 to be significantly upregulated at the lamina cribrosa in glaucoma. We are currently investigating whether mir29b may play a role in suppressing the upregulation of ADAM 12/19 in glaucoma LC cells and therefore, may represent a potential future therapeutic target for the prevention of fibrotic transformation at the lamina cribrosa in glaucoma.

CONTROL ID: 3546553

SUBMITTER (NAME ONLY): Menaka Thounaojam

TITLE: Differential bile acids biosynthetic pathways in the developing retina and in the oxygen-induced model of retinopathy of prematurity

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Thounaojam, S. Rajpurohit, H. Abouhish, M. Bartoli, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|J. Zou, Chemistry, Augusta University, Augusta, Georgia, UNITED STATES|R. Jadeja, P.M. Martin, Biochemistry and Molecular Biology, Augusta University, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently reported the differential ability of various secondary conjugated bile acids (BAs) in ameliorating pathological neovascularization in a mouse model of oxygen-induced retinopathy (OIR). Several studies have also shown the existence of primary BAs synthetic pathways in extrahepatic tissues, such as brain and retina, however no information is available on this metabolic pathway in the postnatal developing retina. Here, we have investigated retinal BAs synthesis in mice during normal postnatal development and in response to the OIR model of retinopathy of prematurity (ROP).

Methods: OIR was induced in mouse pups by subjecting them to different oxygen tensions, according to the protocol of Smith et al. Changes in sterol and BAs metabolic pathways in control and OIR mice were evaluated by RNA sequencing(RNAseq) using an Illumina HiSeq 2500 sequencer. Retinal expression of key enzymes of the classical (CYP7A1) and alternate (CYP46A1 and CYP27A1) BAs synthetic pathways were analyzed at different postnatal days (7, 12, 14, 17, and 23) in control mice and age-matched mice subjected to OIR by immunostaining (cell-specific localization), qPCR and immunoblotting. Retinal BAs content was evaluated using LC-MS/MS assay.

Results: RNAseq data, followed by validation with QPCR and immunoblotting analyses, showed a significant increase in mRNA and protein levels of CYP46A1 (at P12, 14, 17 & 23) and CYP27A1 (at P14, 17 and 23) in normal postnatal retina. On the contrary, CYP7A1 was progressively down-regulated (at P14, 17 and 23). Dual immunofluorescence staining of these enzymes with neuronal (NeuN) and endothelial (CD31) cell markers revealed that while CYP27A1 is immunolocalized in endothelial cells, CYP46A1 is co-localizing with neuronal and endothelial cell markers. A significant dysregulation in retinal sterol and BAs synthetic pathways was found in OIR mice retinas in comparison to control. This was characterized by a significant loss of CYP46A1 and CYP27A1. LC-MS/MS assay further confirmed a significant dysregulation of BAs profiles content in OIR mice compared to control.

Conclusions: In summary, we have found that the developing retina relies primarily in the alternate BAs synthetic pathway. However, in the OIR condition BAs synthesis is significantly down-regulated, thus potentially implicating these signaling molecules also in ROP pathogenesis.

CONTROL ID: 3546558

SUBMITTER (NAME ONLY): James Deom

TITLE: In Vitro Potency of Tobramycin Against Common Bacterial Pathogens Implicated in Blepharitis

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Deom, Hazleton Eye Specialists, Hazle Township, Pennsylvania, UNITED STATES|M.E. Cavet, C.M. Sanfilippo, H.H. DeCory, Medical Affairs, Bausch + Lomb, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although the etiology of blepharitis is not fully understood, bacteria are commonly implicated. Combination topical antibiotic/corticosteroid medications are often used as a short-term therapy with or without lid hygiene. We evaluated the in vitro potency of the anti-infective in the combination product loteprednol etabonate 0.5%/tobramycin 0.3% (Zylet[®], Bausch + Lomb) against common bacterial pathogens implicated in blepharitis.

Methods: The antibacterial activity of tobramycin was tested against 487 isolates from 14 genera (67 species) known to be associated with blepharitis. Minimum inhibitory concentrations (MICs) were determined by broth microdilution or agar dilution as appropriate per CLSI M07 and M11 guidelines. ATCC strains were included for quality control (QC) testing.

Results: The MIC range, MIC₅₀ (MICs for 50% of isolates) and MIC₉₀ (MIC for 90% of isolates) for tobramycin are shown in the table. The MIC₅₀/MIC₉₀ against the subset of methicillin-sensitive and methicillin-resistant staphylococci were, respectively, 0.25/0.5 and 0.5/>64 for *Staphylococcus aureus* and 0.12/0.25 and 0.12/16 for *Staphylococcus epidermidis*. All QC data were within CLSI approved ranges.

Conclusions: Tobramycin demonstrated low MICs against most bacterial species associated with blepharitis, including staphylococci and most methicillin-resistant strains thereof. Together with previous published clinical studies, these data support the use of combination loteprednol etabonate 0.5%/tobramycin 0.3% in the treatment of blepharitis, including in staphylococcal blepharitis.

CONTROL ID: 3546559

SUBMITTER (NAME ONLY): Sara Aghajari

TITLE: Development of a gaze-contingent electroretinogram system

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Aghajari, F.A. Vera-Diaz, T. Panorgias, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P. Bex, Northeastern University College of Science, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The presence of eye movements during multifocal electroretinograms hinders the spatial resolution and location specificity that can be achieved. A solution to this problem could be a gaze-contingent display coupled with an ERG system. Here, we present the early development of such a system that could potentially improve the diagnostic value of ERG recordings.

Methods: Eye movements were recorded using an Eyelink 1000 plus eye tracker with a 2KHz sampling rate (SR Research CA). Simultaneously, single channel ERG signals were recorded from one eye using a 1902 amplifier and a 1401 data acquisition system (CED UK) with 100K gain and frequency bandwidth 0.2 - 100Hz. Stimuli were generated using Psychtoolbox and MATLAB, and were presented onto a monitor with a refresh rate of 120Hz through the Bits# stimulus generator (CRS UK). We recorded electroretinograms (ERG) with and without gaze-contingency. The stimulus, a white 10 degree disk (330 cd/m^2) on a neutral background (165 cd/m^2), was on for one monitor frame, and for the gaze-contingent mode its location was updated based on an average gaze location sampled over 30 ms before the stimulus onset. The ERG acquisition system was time-locked with the stimulus presentation via a TTL trigger generated by the Bits#. The gaze-contingent system's latency was measured with a modified method described before (Saunders & Woods 2013). Briefly, an Arduino Duo board that controlled an infrared LED generated artificial blinks and disrupted the eye tracking causing a luminance change on the monitor. With a high-speed camera (1000 fps) the frame difference between the onset of a blink and the onset of the monitor luminance change, i.e. the system latency, was estimated.

Results: The latency of the gaze-contingent system based on 34 measurements was calculated to be $10.79 \pm 2.9 \text{ ms}$. Qualitative comparison of the ERG responses recorded with a gaze-contingent and a fixed stimulus suggests that the recordings are similar, in terms of the ERG components, but also latency and amplitude.

Conclusions: Using a video-based eye tracker and a data acquisition system we created a gaze-contingent ERG system. The use of our system in future studies using a multifocal stimulus could potentially improve the spatial resolution and location specificity that can be achieved without the need of spatial averaging.

CONTROL ID: 3546560

SUBMITTER (NAME ONLY): Elise Heon

TITLE: Patient-reported visual functioning in persons with bi-allelic USH2A variants

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Heon, Ophthalmology and Visions Sciences, The Hospital for Sick Children, Toronto, Ontario, CANADA|E. Heon, University of Toronto, Toronto, Ontario, CANADA|B.M. Melia, L.E. Bocchino, A. Ayala, Jaeb Centre for Health Research, Tampa, Florida, UNITED STATES|J.L. Duncan, University of California San Francisco, San Francisco, California, UNITED STATES|C. Bradley, G. Dagnelie, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|C.Y. Weng, Baylor College of Medicine, Houston, Texas, UNITED STATES|M.E. Pennesi, Oregon Health & Science University, Portland, Oregon, UNITED STATES|T. Jayasundera, Kellogg Eye Center, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|N. Jain, Emory Eye Center, Atlanta, Georgia, UNITED STATES|C. Hoyng, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|J.K. Cheetham, T. Durham, Foundation Fighting Blindness Inc, Columbia, Maryland, UNITED STATES|I. Audo, Institut de la vision, Paris, Île-de-France, FRANCE|I. Audo, Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Paris, Île-de-France, FRANCE|

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ABSTRACT BODY:

Purpose: To describe a patient-reported visual functioning outcome (PRO) at baseline in RUSH2A participants and explore relationships between PRO, visual acuity (VA) and hill of vision (V_{TOT}).

Methods: The Rate of Progression of USH2A-related Retinal Degeneration (RUSH2A) is a multicenter, international, longitudinal natural history study of individuals with biallelic disease-causing variants in USH2A. History of hearing loss and baseline audiology exams were used to assign a clinical diagnosis of Usher syndrome type 2 (USH2) or autosomal recessive non-syndromic retinitis pigmentosa (ARRP). The VALVVFQ-48 was administered verbally in the local language of participants ≥ 18 years. ETDRS VA was measured in both eyes. V_{TOT} was determined from full-field static perimetry in the study eye (better VA). Baseline PRO measure was calculated using the method of successive dichotomizations, a type of Rasch analysis.

Results: Median age of the 120 participants at enrollment was 41 years (range: 19 to 80); 65 (54%) were female. Clinical diagnosis was USH2 in 75 participants and ARRP in 45. Median age of onset was 16 years [IQR: 13-22] in USH2 and 32 [IQR: 20-41] in ARRP, and median duration of disease was 17 [IQR: 10-27] and 13 years [IQR: 6.8-18], respectively. Median VA was 80 letters (interquartile range (IQR): 75, 85) in the study eye and 75 letters (IQR: 69, 82) in the fellow eye, and median V_{TOT} in the study eye was 20 dB-sr (IQR: 5.4 – 45). A wide range of PROs was seen with person measures ranging from -2.0 to 7.4 logits (median (IQR): 2.9 (1.5-3.8)). ARRP participants had similar PRO to USH2, both before (mean (95% CI): 2.8 (2.3-3.4) and 2.7 (2.3-3.2), respectively), and after adjusting for baseline differences in age, VA, duration of VA loss, and V_{TOT} [mean (95% CI): 2.5 (2.1-3.0) and 2.9 (2.6-3.3), respectively; $p=0.25$]. VA and V_{TOT} , separately, accounted for 29% and 26% of variation in PRO, respectively; ($p<0.001$ for each). Together, they accounted for 36% of variation in PRO.

Conclusions: Bi-allelic USH2A variants are associated with a large range of PRO using VALVVFQ-48. PRO in ARRP and in USH2 were similar, despite concomitant hearing loss in USH2. VA and V_{TOT} appear to be significant and approximately equal contributors to PRO in this population. However, these 2 measures account for less than $\frac{1}{2}$ of variation in PRO.

CONTROL ID: 3546566

SUBMITTER (NAME ONLY): Souska Zandi

TITLE: Introduction of a novel animal model of subretinal fibrosis after choroidal neovascularization

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Subretinal fibrosis can develop in the course of neovascular age-related macular degeneration (AMD) and can lead to further vision loss of AMD patients. Intravitreal anti-VEGF treatment can reduce the choroidal neovascularization (CNV), but not the subretinal fibrosis. Until now, there is no successful treatment nor established animal model for subretinal fibrosis. We aim to introduce a novel animal model of subretinal fibrosis that might facilitate the development of novel therapeutic strategies for the reduction or inhibition of subretinal fibrosis.

Methods: C57BL/6J mice underwent laser photocoagulation to induce CNV-related fibrosis. Mice were anesthetized, and pupils were dilated with 5% phenylephrine and 0.8% tropicamide. Using a 532-nm laser, a slit-lamp delivery system, and a cover glass as a contact lens, six spots (100 mW, 50 mm, 100 ms) were placed in each eye. Volume of CNV and fibrosis was quantified with optical coherence tomography (OCT) measurements and confocal microscopy of choroidal flat mounts stained with isolectin B (CNV) and type 1 collagen (fibrosis) every week after laser injury (d7, d14, d21, d28, d35, d42, d49, n=6 per timepoint). Additionally, we performed autofluorescence and fluorescence angiography at every timepoint to document CNV and fibrosis changes over time.

Results: From day 21 to day 49 after laser injury of mice eyes the CNV and leakage decreased and the subretinal fibrosis increased in OCT and fluorescence angiography. The expression of collagen 1 in lesions of choroidal flat mounts increased, whereas isolectin B decreased.

Conclusions: The current results indicate that the CNV-related fibrosis model can be used for screening of anti-fibrotic treatment of subretinal fibrosis in neovascular age-related macular degeneration.

CONTROL ID: 3546567

SUBMITTER (NAME ONLY): Hongmin Yun

TITLE: Sensory nerve retraction and sympathetic nerve innervation are involved in the immunopathology of murine recurrent Herpes Stromal Keratitis (HSK)

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: H. Yun, A. St. Leger, Department of Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|A. St. Leger, Department of Immunology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|X. Yin, P. Stuart, Department of Ophthalmology, Saint Louis University, Saint Louis, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: HSK is a potentially blinding corneal disease caused by herpes simplex virus type 1 (HSV-1) infection, which manifests in both humans and mice as corneal edema, opacity, neovascularization, and hypoesthesia. After primary corneal infection, the virus gains access to the trigeminal ganglion through the ophthalmic branch of the trigeminal nerve and establishes lifelong latency. The virus can reactivate under certain circumstances and travel to the cornea to cause recurrent HSK (rHSK). We have found that the replacement of corneal sensory nerves with sympathetic nerves in murine primary HSK led to severe and diffuse inflammation, and CD4⁺ T cells and myeloid cells, through the production of vascular endothelial growth factor A, maintained the disrupted corneal nerve landscape. Here, we aimed to identify whether this mechanism governs rHSK.

Methods: Male and Female C57BL/6 and NIH mice were infected with HSV-1 McKrae strain and were protected from primary infection by intraperitoneal injections of pooled human serum. The eyes were then exposed to 170 (NIH mice) or 250 (C57BL/6 mice) mJ/cm² of UV-B light. Groups of mice received anti-CD4 antibody (150ug, once a week) to deplete CD4⁺ T cells or appropriate control. Mice were monitored for corneal opacity, neovascularization, and blink reflex. Virus reactivation was determined by eye swabbing for live virus and IHC staining for HSV-1 antigens. Corneal whole mounts were stained for β III tubulin, tyrosine hydroxylase, and substance P to define sympathetic and sensory nerves, respectively.

Results: No virus was detected in mice that did not receive U.V. irradiation. Live virus was detected in 30% of both strains of mice after U.V. irradiation. IHC study detected HSV-1 antigens in 100% of the corneas. Mice developed progressive HSK and eventually lost blink reflex with a significant reduction in corneal sensory nerve density. Different from the primary HSK, the invasion of sympathetic nerves in the rHSK cornea was sectorial. Finally, depletion of CD4⁺ T cells correlated with less severe disease, more sensory nerve retention, and less dense sympathetic innervation of the cornea.

Conclusions: U.V. light-mediated viral reactivation from latency is more consistent than previously realized. CD4⁺ T cell-dependent induction of sympathetic innervation of the cornea acts both in the primary HSK and rHSK.

CONTROL ID: 3546568

SUBMITTER (NAME ONLY): Anthony St. Leger

TITLE: Genetic engineering to identify microbial factors responsible for colonization and immunity at the ocular surface.

SESSION TITLE: Microbiota and the Gut-Eye Axis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. St. Leger, Y. Rigas, J. Shane, R.M. Shanks, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|A. St. Leger, B. Treat, Immunology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recently, our lab discovered that the eye harbors a resident ocular microbiome that includes *Corynebacterium mastitidis* (C. mast), which can stimulate local immunity to protect the eye from infection. We know that C. mast remains associated with the ocular surface indefinitely and can stimulate protective immunity. Our studies are now focused on better understanding the microbial factors that govern colonization of the ocular mucosa and stimulation of the host immune response. To achieve the study goals, we performed transposon mutagenesis on C. mast to generate a library of mutants for the purpose of identifying microbial genes critical for colonization and immunogenicity of C. mast.

Methods: We created a transposon mutant library containing ~1,500 candidates with distinct insertion sites and varying phenotypes. To do this, we used the EZ-Tn5 kit (Lucigen) to generate transposomes that contained genes encoding the fluorescent protein, mCherry, and a kanamycin-resistance cassette. Tn mutants were initially selected on kanamycin-treated plates. Functional mutants were then screened for desired phenotypes.

Results: We found several mutant candidates of interest. First, a mutant constitutively expressed mCherry in vitro and in vivo when associated with the ocular mucosa. This candidate colonized the eye and induced immunity similar to that observed with the parental C. mast strain. A separate candidate lost the ability to colonize the ocular mucosa and failed to elicit an immune response in vivo; however, it still induced the production of cytokines in vitro. A final candidate corresponded with a reduced immune response both in vitro and in vivo compared to the parental strain.

Conclusions: We have demonstrated that an ocular commensal, C. mast, can be mutated. Using in vivo imaging and Tn-C. mast mutants, we can conclude that C. mast only colonizes the conjunctiva and does not associate with the cornea. Furthermore, we can conclude from our library of transposon mutants that simple exposure to C. mast does not induce a measurable immune response, but colonization of the ocular surface is required for in vivo immunity. These studies are the first steps towards understanding what makes an ocular commensal bacterium what it is, and from this, we can begin to engineer ocular bacteria to promote ocular health to limit disease and pathogenesis.

CONTROL ID: 3546571

SUBMITTER (NAME ONLY): Vincent Monnier

TITLE: Lens crystallin destabilization by ascorbylation: Mapping of glycation sites associated with protein insolubilization

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V.M. Monnier, G. Hom, S. Dong, D.R. Sell, Pathology, Case Western Reserve University School of Medicine, Cleveland, Ohio, UNITED STATES|K. Zientek, L.L. David, Proteomics Shared Resource, Oregon Health & Science University, Portland, Oregon, UNITED STATES|S. Dong, College of Food Science and Engineering, Ocean University of China, Qingdao, Shandong, CHINA|

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ABSTRACT BODY:

Purpose: The aging human lens accumulates protein modifications that are dramatically elevated in cataracts. Among chemical processes involved ascorbylation protein adducts carboxymethyl-lysine (CML), carboxyethyl-lysine (CEL) and methylglyoxal hydroimidazole (MG-H1) (Fan et al Aging Cell 2020) are thought to destabilize the proteins based on Ortwerth(1968) who showed that crystallins incubated with ascorbate precipitate under both aerobic and anaerobic conditions. Here we determined ascorbylation sites present solely in insoluble protein exposed to ascorbate.

Methods: Calf lens crystallin homogenate was fractionated by Sephadex G200 gel filtration into Pool 1-4 (P1-P4) corresponding to alpha-, beta-H, beta-L and gamma crystallin, respectively. Pool 3 and 4 were incubated sterile in 50 mM K+/PO4 buffer for 7days with 10 mM ascorbate or dehydroascorbate and centrifuged. Precipitates and supernatants were processed for proteomics analysis. Electrospray MS/MS spectra were obtained and tryptic peptides were analyzed for modified lysine (CML (m/z: +58), CEL (m/z: +72)) and arginine residues by MG-H1 (m/z: +54).

Results: 30-40% of P3 proteins precipitated upon incubation with ASA or DHA. Presence of chelator DTPA suppressed precipitation from DHA, but not ASA. Precipitation of P4 proteins was suppressed by DTPA suggesting ASA/DHA fragmentation are necessary for precipitation. Robust CML modifications sites were K88 (CRYAA), K23 (CRYBB1), K168 (CRYBB2) and K163 (CRYGD). For CEL K168 (CRYBB2). For MG-H1: R188 (CRYBB2), R147 (CRYGC) and R10 (CRYGD). Multiple other sites were also modified, but deemed less important for insolubilization. The significance of the ascorbylation sites for cataract remains to be established. However, K88 is in the minichaperone domain of CRYAA, K23 in the highly conserved sequence GPDGKGK(23)G of CRYBB1, K168 in the conserved QYLLEKGD domain of CRYBB2. R188 in CRYBB2 is in the last strand of β B2-crystallin Greek-key motif 4 and its mutation to R188H promotes β B2-crystallin aggregation via perturbation of the dynamic equilibrium by dissociating the dimer and stabilizing the tetramer (Zhang et al. BBA 1842, 2014). R10 in CRYGD is highly conserved and so is the positive charge at K/R163.

Conclusions: The uncovered robust ascorbylation sites in various bovine crystallins are hypothesized to play a destabilizing role in age-related human cataract.

CONTROL ID: 3546574

SUBMITTER (NAME ONLY): Heuy-Ching Wang

TITLE: Automating the Detection of Retinal Tears from Vascular Deformation using Machine Learning

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.H. Wang, A. Peitzsch, L. Martinez, S. Tewolde, S. Cardin, Combat Casualty Care & Operational Medicine, Naval Medical Research Unit San Antonio, Fort Sam Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the modern combat environment, ocular trauma is becoming more common while the detection of retinal tears still requires a limited number of trained professionals to detect. In this study, we investigated whether automated image processing systems using machine learning could detect subtle changes in the retinal vasculature that are indicative of retinal tearing.

Methods: Full color fundus images were taken from nine rabbits with penetrating eye injury (Figure 1). MATLAB® programming toolbox was used to analyze a total of 704 images taken before and after retinal tearing. The images were segmented using a combination of color filtering, difference of Gaussian functions, and k-means clustering to isolate the retinal vessels. These images were used to train convolutional neural network and support vector machine (SVM) models to classify individual images based on the presence or absence of a tear. Models were compared using sensitivity, specificity, and the area under the receiver operating characteristic curve.

Results: A SVM Gaussian kernel performed better than the other machine learning models used in this study. This model had a true positive classification rate of 85.53% and a true negative classification rate of 91.11%.

Conclusions: Our study shows that machine learning models are able to detect retinal tear features at a rate comparable to and even exceeding human diagnosis.

CONTROL ID: 3546575

SUBMITTER (NAME ONLY): Scott Schachter

TITLE: Clinical Manifestations of Demodex Blepharitis

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Yeu, Virginia Eye Consultants, Norfolk, Virginia, UNITED STATES|M.J. Holdbrook, Tarsus Pharmaceuticals, Inc., Irvine, California, UNITED STATES|S.N. Baba, Tarsus Pharmaceuticals, Inc., Irvine, California, UNITED STATES|P.J. Gomes, Ora Inc, Ora Inc, Andover, MA, US, corporate/medsupport, Andover, Massachusetts, UNITED STATES|S. Schachter, Ocular Surface Academy, Pismo Beach, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blepharitis affects approximately 20 million Americans, of whom about 45% have an associated Demodex mite infestation. We analyzed a large data set of patients with confirmed Demodex blepharitis to characterize the population affected by this condition and to better understand their symptoms and motivations for seeking care.

Methods: Adult patients (age ≥ 18) with Demodex blepharitis were examined clinically and asked questions about their ocular symptoms, diagnoses, and history. These 311 patients had objective signs of Demodex blepharitis, including the presence of Demodex mites, presence of collarettes (cylindrical dandruff) on the lashes, and lid margin erythema. Questionnaire responses from these 311 patients with confirmed Demodex blepharitis were analyzed.

Results: Among these Demodex blepharitis patients, 38% were male; 62% female. The mean age was 67 (range: 23 to 92). Over half of them (51%) had been experiencing signs and symptoms of blepharitis for at least 4 years, but most (58%) had never been diagnosed with blepharitis. There was a high degree of overlap with other ocular surface conditions, including those having been previously diagnosed with dry eye (81%), rosacea (3%), or both (16%). The most bothersome symptoms for patients were itchy eyes, dry eyes, foreign body sensation, and eyes tearing (Fig 1). The majority experienced symptoms of dryness, itching, and ocular irritation frequently or all of the time in the past month. 28% had first seen an optometrist about their symptoms, while 61% had seen an ophthalmologist and 11% had gone to a primary care physician. Although most had seen a doctor only once, 33% had made at least 2, and sometimes more than 6, visits to a doctor for this condition. 81% of patients seek some type of treatment for the condition. Of those who discontinued treatment, 43% discontinued due to ineffectiveness, tolerability issues, or other reasons. Women were more likely than men to have tried medication to treat their symptoms (90% vs. 66%).

Conclusions: The symptom burden of blepharitis is considerable and leads patients to seek treatment and medical care, mostly unsuccessfully. Proven safe and effective treatments for Demodex blepharitis are needed.

CONTROL ID: 3546576

SUBMITTER (NAME ONLY): Aman Kumar

TITLE: Elucidating cytokine-mediated immunomodulation of NK cells in uveitis patients

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kumar, P.R. Nath, J.W. Lee, M. Maclean, V.V. Agashe, M. Yakin, H. Sen, National Eye Institute, Bethesda, Maryland, UNITED STATES|A. Kumar, Albany Medical College, Albany, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Natural killer (NK) cells are a subset of lymphocytes that participate in the innate immune defense via their cytotoxic effector functions and cytokine secretion. NK cells play a role in the development of uveitis such as Behçet's uveitis. Additionally, several cytokines have been associated with promoting inflammation and contributing to the development of uveitis in both animals and humans. The purpose of this study is to understand the effect of cytokines relevant to human uveitis on NK cells.

Methods: Peripheral serum cytokines for 126 uveitis patients and 34 healthy controls were investigated using SOMAScan, an aptamer-based proteomics platform that measures over 1300 analytes. Human NK-92 cells were incubated with recombinant human cytokines that were relevant from the SOMAScan studies at previously titrated concentrations for 24 and 48 hours. At each timepoint, expression levels of several activation and inhibitory markers were characterized using a Cytoflex flow cytometer.

Results: SOMAScan proteomic analysis of serum showed elevated levels of certain cytokines, including interleukin (IL)-8, IL-9, IL-18Bpa, and IL-23 in the sera of uveitis subgroups. Flow cytometry from the peripheral blood of the same subgroup of patients also showed NK cell expansion. NK-92 cells demonstrated increased activation upon exposure to IL-12, IL-23 and IL-18, as indicated by elevated CD69 and CD314 expression after 24 hours. Additionally, there was a change in inhibitory receptor expression between the control and ED₅₀ MFI, but to a lesser extent, illustrated by the level of CD94 expression.

Conclusions: The subset of cytokines previously identified to be associated with uveitis may play a role in immunomodulation of effector cells. We plan to further characterize the effect of these cytokines on human PBMCs and NK cells from uveitis patients and healthy controls.

CONTROL ID: 3546578

SUBMITTER (NAME ONLY): Ellen Shorter

TITLE: Evaluation of Optometrist's Perspectives of Artificial Intelligence in Eye Care

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Shorter, C. Kinnaird, S. Kravets, J. Hallak, T. Al-Khaled, E. Cole, N. Valikodath, T. McMahon, R.V. Chan, A.C. Scanzera, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|C. Kinnaird, Jesse Brown VA Chicago Health Care System, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: The application of artificial intelligence (AI) in diagnosing and treating disease has gained popularity in all areas of medicine including eye care. There has been considerable amount of work dedicated to utilizing AI to improve the practice of eye care and patient outcomes. The objective of this study was to survey optometrists on their perspectives of AI in eye care.

Methods: Members of the American Academy of Optometry were sent an electronic invitation to complete a 17-question survey administered via Qualtrics between September 30, 2020 and November 30, 2020. Participants were included if they indicated they were an optometrist. Survey items assessed perceived advantages and concerns regarding AI using a 5-point Likert scale ranging from "strongly agree" to "strongly disagree." Descriptive statistics were used to analyze perceptions surrounding AI.

Results: There were a total of 400 optometrists that completed the survey. The participant's mean years from graduating optometry school was 25 ± 15.08 , and over half were male (54.5%). The majority of participants (55.8%) self-reported completing a residency, most commonly focused on ocular disease (34.6%) or primary care (17.6%). The most common practice setting was private (33.0%) or optometry school (20.0%). The majority of participants reported they were familiar with AI (66.8%) and felt AI should be incorporated into the optometry school or residency curriculum (80.3%). Some participants felt that there was concern for AI to replace providers (25.1%). When selecting what role participants believed AI should play in the future of eye care, optometrists indicated: disease screening (86.8%), monitoring disease progression (69.0%), triage (61.8%), diagnosis (35.3%), and management of decisions (27.0%) or determining refractive error (27.0%). Though half of participants had concerns about the diagnostic accuracy of AI (53.0%), most believed it would improve the practice of optometry (72.0%). Interestingly, participants reported willingness to incorporate AI into practice increased from 53.3% before the pandemic to 65.5% after the onset of the pandemic ($p < 0.001$).

Conclusions: The findings from this study suggest that optometrists are optimistic about the use of AI in eye care. Future studies will be aimed at better understanding optometrist's knowledge of AI and best practices when integrating AI into clinical practice.

CONTROL ID: 3546581

SUBMITTER (NAME ONLY): Roksana Sadeghi

TITLE: Comparing threshold estimation methods for the psychometric function of electrically induced perception

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sadeghi, M.P. Barry, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|C. Bradley, A. Kartha, S. Lee, G. Dagnelie, Ophthalmology, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|P. Troyk, Armour College of Engineering, Illinois Institute of Technology, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Controlling the dynamics of electrically induced perception in neural prostheses requires threshold estimation for each electrode, which becomes burdensome for high electrode counts. In this study, we compared four common threshold estimation methods in terms of speed of convergence and accuracy for epiretinal Argus II visual implants.

Methods: Threshold testing methods that are compared here are 1) the standard hybrid (H) method for Argus II epiretinal implants — a combination of the method of constant stimuli (non-adaptive) and maximum likelihood estimation (MLE; adaptive); 2) stochastic approximation staircase (SC; adaptive); 3) minimizing the variance (MV; adaptive); and 4) maximizing the information (MI; adaptive). Data were collected concurrently across all electrodes for adaptive methods, but by groups of 6 electrodes for the H method.

Weibull psychometric function thresholds were estimated in a yes/no experiment for two Argus II users for 24 and 56 electrodes respectively using the four methods. For each subject, data were collected in one session per adaptive method, and two sessions for the hybrid method. Subject responses across all sessions were used offline to estimate the thresholds and confidence intervals (CI) with MLE. To test method accuracies, we computed the average normalized root mean square error (RMSE) between estimated thresholds and MLE thresholds.

Results: Fig.1 shows that hybrid threshold testing requires more trials compared to adaptive methods and only 25% of the thresholds estimated by H were within MLE estimated CI, compared to SC 35%, MV 58%, and MI 61%. The adaptive methods were also more accurate compared to H (RMSE for H: 11%, SC: 10%, MV: 6%, and MI: 6%).

Conclusions: Our results show that the adaptive methods provide more accurate threshold estimates within fewer trials. Adaptive methods enable threshold estimation for a greater number of electrodes concurrently in a session, which is important for neural prostheses with a high number of electrodes.

CONTROL ID: 3546586

SUBMITTER (NAME ONLY): Zoe Love

TITLE: Dynamics of pro-inflammatory microglia activation across multiple mouse models

SESSION TITLE: Glial Cells

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Love, N. Nasraty, N.B. Haider, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M.M. DeAngelis, Ophthalmology, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is a leading form of inherited blindness impacting more than 1 million individuals across the globe. RP is characterized as a progressive loss of photoreceptor cells. However, RP is a heterogeneous disease involving over 100 mutations and genes with various disease mechanisms. While microglia activation in RP patient retinas has been reported, the role that microglia play in the progression of disease is not well understood. Microglia, the myeloid cells of the central nervous system (CNS) typically have a tolerogenic function that is lost in neurodegenerative diseases like RP. This study aims to understand the role of microglia in RP disease. Due to the differing mechanisms that underlie RP, each of these mouse models will provide an opportunity to identify how retinal microglia change phenotypically through the varied progressions of disease.

Methods: We evaluated 11 mouse models recapitulating disease phenotypes for RP, including $rd1^{-/-}$, $rd7^{-/-}$, $Rho^{-/-}$, $RhoP347S^{-/-}$, $RhoP23H$, $Nrv1$, $Nrv2$, $Cep290$, $BBS1^{-/-}$, $Abca4^{-/-}$, and $ApoE^{-/-}$ through immunohistochemistry to determine the distribution of retinal microglia at early, mid, and late stage of disease progression compared to C57BL/6J (B6) wild-type control. IPA analysis was also performed looking at the genes involved in microglia activation as well as their function in both inflammatory and neurodegenerative pathways.

Results: Microglia, including those that indicated disease phenotype, were observed in varying amounts across multiple models of retinal degeneration. Immunohistochemistry also indicated increased microglia activity in degenerative retinas. These changes, likely mediated by activation of inflammatory pathways and possibly the presence of chronic inflammation, create microglia with cytotoxic neurodegenerative function rather than neuroprotective.

Conclusions: Microglia activation has implications for many diseases involving neurodegeneration, including RP. This study enhances current understanding of how microglial altered morphology impacts disease pathology in various degenerative models. Additionally, these results add to the current knowledge of the therapeutic potential for patients with retinal degeneration to protect photoreceptors through the inhibition of neurotoxic microglia and reversion to the wild-type homeostatic microglia state.

CONTROL ID: 3546590

SUBMITTER (NAME ONLY): Seth Miller

TITLE: Relationship Between Dry Eye Symptoms and Aging

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Miller, M. Watson, D. Narayanan, G.W. Ousler, Ora, Inc, Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) is a common ocular condition known to impact everyday activities. Examining the relationship between subject and disease characteristics like age, disease duration, ocular symptoms etc., without the confounding effects of therapies, are critical for better understanding the disease process.

Methods: Data from 1154 subjects who came for study screening prior to initiation of any therapeutic intervention were included for this analysis. The mean age (\pm SD) was 57.4 ± 15.5 years; 70% of the subjects were females and 30% were males. Subject symptoms were captured using the Ocular Surface Disease Index (OSDI) questionnaire which comprises of 12 questions and overall OSDI score, ranging from 0 to 100, was calculated. Relationship between subject symptom based on OSDI overall score and subject age was assessed by correlation of the continuous variables. In addition, subjects were divided into 4 groups based on overall OSDI score; Normal:0 to 12 (N=123), Mild:13 to 22 (N=200), Moderate:23 to 32 (N=201), or Severe: 33 to 100 (N=630). ANOVA was used to compare outcomes between the groups. For each subject, data from only the right eye was included for analysis.

Results: For all subjects, the overall OSDI score showed significant, mild to moderate negative correlation with age ($R = -0.20$, $p < 0.0001$), indicating that the OSDI scores were showing improvement with increasing age. Consistently, subjects in mild, moderate and severe OSDI group were younger when compared to those in the normal OSDI group. Mean age in normal OSDI group was 63.3 ± 14.8 years compared to mild group (mean 60.8 ± 14.3 years, $p = 0.30$); Mean age in moderate OSDI group was 57.3 ± 15.8 years ($p = 0.0018$ vs normal group) and in the severe group was 55.2 ± 15.7 years ($p < 0.0001$ vs normal group). More severe groups, based on OSDI scores, also showed longer DED duration when compared to normal group. Mean DED duration was 7.9 years in normal, 9.5 years in mild, 10.9 years in moderate and 11.3 years in severe ($p = 0.01$ for moderate vs normal and $p = 0.0006$ for severe vs normal comparisons).

Conclusions: Subjects with dry eye show reduced symptoms with increased aging and increased duration of the disease. This could be attributed to reduced sensitivity that occurs as a consequence of increased aging and long-standing disease.

CONTROL ID: 3546591

SUBMITTER (NAME ONLY): Christina Ohnsman

TITLE: Pilot Study of Novel Optokinetic Nystagmus-Based Visual Acuity Test in Children with CLN2 Disease

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.M. Ohnsman, Clinical Development, REGENXBIO Inc, Rockville, Maryland, UNITED STATES|Y. Atiskova, J. Wildner, A. Schulz, S. Dulz, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Hamburg, GERMANY|B. König, Objective Acuity, Ltd., Auckland, NEW ZEALAND|A. Schulz, University Children's Hospital, Hamburg, GERMANY|

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ABSTRACT BODY:

Purpose: Vision loss is a prominent feature of neuronal ceroid lipofuscinosis Type 2 (CLN2) Batten disease, developing after cognitive, motor and language impairments are already present. While progressive, symmetrical loss of central retinal thickness (CRT) has been well characterized in CLN2 disease, measurement of visual acuity (VA) using standard methods is difficult and unreliable in this population, resulting in lack of natural history data on the range, severity and impact of visual impairment. We conducted a pilot study of a novel VA test using optokinetic nystagmus (OKN) detection technology (Threshold Visual Acuity Test, Objective Acuity, Ltd., Auckland, NZ) to determine its usefulness in children with CLN2 disease.

Methods: 23 children ages 3 to 9 with classic CLN2 disease followed at University Medical Center Hamburg-Eppendorf (UKE) were included. Binocular and monocular VA testing using Threshold Visual Acuity Test and binocular VA testing using preferential looking (PL) were performed at two consecutive visits two weeks apart. CRT was measured under anesthesia using SD-OCT. VA testing results were correlated with CRT.

Results: Seventeen children (74%) tested with the Threshold Visual Acuity Test had measurable binocular VA, while 6 (26%) had no detectable OKN, indicating VA>1.3 logMAR. Binocular VA ranged from 0.3 to >1.3 logMAR and was strongly correlated with CRT ($R = -0.93$; Figure 1). Eighteen children (78%) had measurable VA with PL and 5 (22%) were unresponsive. VA measured by PL was poorly correlated with CRT ($R = -0.44$). Monocular VA measured by OKN was obtained in 12 right eyes and 11 left eyes; 9 children cooperated with monocular testing in both eyes. Monocular VA was highly symmetric between right and left eyes ($R = 0.95$) and correlated with CRT ($R = -0.84$ OD; $R = -0.88$ OS).

Conclusions: The novel, OKN detection-based Threshold Visual Acuity Test appears to be useful in children with CLN2 disease. Results demonstrate the high correlation between CRT and VA as well as symmetrical VA between eyes in this population. More longitudinal data are needed to characterize the pattern and progression of VA loss in CLN2 disease. Additional validation studies with an expanded range of VA are underway.

CONTROL ID: 3546593

SUBMITTER (NAME ONLY): Behnam Tayebi

TITLE: Pore Shape Variation in Glaucomatous Lamina Cribrosa

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Tayebi, Z. Ghassabi, J.S. Schuman, P. Alexopoulos, M. Wu, R. Zambrano, H. Ishikawa, G. Wollstein, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES| B. Tayebi, Tech4Health and Neuroscience Institutes, NYU Langone Health, New York, New York, UNITED STATES|J.S. Schuman, H. Ishikawa, G. Wollstein, Departments of Biomedical Engineering and Electrical & Computer Engineering, New York University, New York, New York, UNITED STATES|M. Wu, Departments of Population Health and Environmental Medicine, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The lamina cribrosa (LC) is considered to play an important role in the pathogenesis of glaucoma. In this study, we investigate the shape variation (SV) of the LC pores as a potential biomarker for quantifying the morphological irregularity in vivo.

Methods: 36 healthy and 14 glaucomatous (GL) eyes (total: 39 subjects) underwent a comprehensive ophthalmic examination and scanning of the optic nerve head with swept-source OCT (Table 1). Images were converted to isotropic and pores were segmented using ImageJ. SV was defined as the mean-squared error of the pore pattern with respect to a solid circle (Figure 1(a)) with SV of a circle marked as zero, and higher SV value with increasing shape irregularity. SV of each pore was automatically calculated by a MATLAB code. The overall SV value was generated as the average of SV in the stack of individual slices. Age effect on SV was examined in all healthy eyes and a subset of 14 eyes was selected for age-matched comparison with the glaucomatous eyes (Table 1).

Results: No significant correlation was detected between SV and age ($p=0.145$; Spearman correlation) in all healthy subjects. Examining the effect of depth on the difference between SV of glaucomatous and healthy eyes, the posterior third of the LC had significantly lower than other sections ($p=0.007$; Figure 1(b)). SV in glaucoma eyes was significantly higher than in the healthy group ($p=0.008$; Figure 1(c)).

Conclusions: We demonstrated morphological differences in pore shape variation between healthy and glaucoma eyes that is mostly affecting the anterior 2/3 of the LC. Further studies are warranted to assess the use of SV as a structural biomarker in glaucoma.

CONTROL ID: 3546594

SUBMITTER (NAME ONLY): Céline Portal

TITLE: Differential role of the Hedgehog pathway and the primary cilium in Meibomian gland development

SESSION TITLE: Lacrimal gland and Meibomian gland

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Portal, C. Iomini, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|C. Portal, C. Iomini, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Meibomian gland (MG) dysfunction is considered the leading cause of dry eye disease, a common, multifactorial disease with a global prevalence ranging from 5 to 50%. MG are modified sebaceous glands (SG) that secrete lipids at the ocular surface which increase the stability of the tear film. MG are composed of several acini organized around a central duct similar to a hair follicle (HF) without a hair shaft. It is well known that the hedgehog (Hh) pathway is required for the growth of HF and implicated in SG differentiation. However, its role in MG development remains unknown. In this study, we investigate how components of the Hh pathway interplay during MG development.

Methods: To assess the role of Hh signaling in MG development we ablated Smoothed (Smo), required to activate Gli transcription factors, and Ift88, a component of the intraflagellar transport required for trafficking Hh pathway components within the primary cilium. Smo and Ift88 were selectively deleted in keratin 14 (K14)-expressing epithelial cells to generate K14cre;Smo^{fx/fx} and K14cre;Ift88^{fx/fx} mice. To monitor the Hh activity, we utilized the Gli1-LacZ reporter mouse line. MG morphology was evaluated by lipid staining, histology, immunostaining, and two-photon microscopy.

Results: First, we showed that meibocytes are ciliated, mainly in the developing part of the MG central duct and in the ductules at the junction between the central duct and the acini. Using the Gli1-LacZ reporter mouse, we found that in wild-type (WT) mice, Gli1 is highly expressed so the Hh pathway is highly activated in developing MG between E18.5 and P3, but dramatically decreased at P5 and in older mice. Surprisingly, the conditional ablation of the primary cilium in the K14-positive cells (K14cre;Ift88^{fx/fx} mice) leads to an increase of MG size when compared to WT mice, mostly due to the development of supernumerary acini. In contrast, MG size was significantly reduced when Smo is conditionally deleted in K14-positive cells (K14cre;Smo^{fx/fx} mice).

Conclusions: Our data suggest that the Hh pathway is required for MG development and could have implications in the regenerative process of MG. Moreover, ablation of primary cilia or Smo leads to opposite phenotypes during MG development suggesting a possible novel role of primary cilia in Hh regulation in MG tissue.

CONTROL ID: 3546597

SUBMITTER (NAME ONLY): Fiona McDonnell

TITLE: Vasoregulator Effects on Outflow Resistance, Flow Patterns and Distal Vessels in the Conventional Outflow Pathway of Mouse and Human Eyes

SESSION TITLE: Aqueous humor dynamics and IOP

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F.S. McDonnell, T. Fleming, M. Kuhn, H. Schmitt, K. Perkumas, D.W. Stamer, Duke University, Durham, North Carolina, UNITED STATES|J. van Batenburg-Sherwood, D.R. Overby, Imperial College London, London, London, UNITED KINGDOM|A.S. Huang, Doheny Eye Institute, Los Angeles, California, UNITED STATES|A.S. Huang, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vessels distal to Schlemm's canal (SC) play a significant role in outflow resistance generation, contributing up to 50% of total resistance. Regulatory regions within distal vessels and their contribution to IOP are not well understood. We hypothesize that vasomotion of distal vessels are control points for outflow resistance generation.

Methods: We used two models to test our hypothesis. The first was OCT imaging of human anterior segments (hAS) in organ culture under constant flow conditions (2.5µl/min). Distal vessel behavior was monitored post treatment with the vasoconstrictor ET-1, or the vasodilator DETA-NO. The treatment protocol was repeated post-trabeculotomy in the same eyes to visualize collector channels (CCs). In the second model, enucleated eyes from C57BL/6 mice were perfused ex vivo with fluorescein tagged soy bean agglutinin lectin, immediately or 24 hrs post enucleation. One eye was treated with 10nM ET-1, while the paired eye received perfusion media. The outflow pathway was visualized in PECAM1-labeled limbal flat mounts by confocal microscopy. Masked analysis of images was conducted using ImageJ. Data are presented as Mean±SD (hAS) or Mean±CI (mice).

Results: The cross-sectional area (CSA) of intrascleral vessels decreased by 60.3±20.2% in hAS treated with ET-1 compared to baseline (p=0.003), while CSA increased by 79.5±121.4% (p=0.02) with DETA-NO treatment compared to ET-1. The SC lumen CSA increased with ET-1 by 68.7±29.1%, p=0.003 and decreased with DETA-NO by 21.8±11.8%, p=0.01. Post-trabeculotomy, neither ET-1 (3.4±16.3% decrease p=0.98) nor DETA-NO (16.1±22.7% increase p=0.17) had a significant effect on CC CSA. In C57BL/6 mice, ET-1 decreased outflow facility (C) (4.6±1.6 to 2.7±1.5 nl/min/mmHg, p=0.04) in freshly enucleated eyes, and decreased C (4.1±1.8 to 3.0±2.0 nl/min/mmHg, p=0.12) 24 hrs post enucleation. Interestingly, lectin staining was largely located in the SC lumen with less lectin distal to CCs in ET-1 treated eyes compared to control.

Conclusions: Vasomodulator (NO and ET-1)-mediated changes in intrascleral vessel diameter was easily visualized by OCT in perfused human eyes, while ET-1 effects on behavior of CC ostia was better visualized indirectly using lectin as a flow tracer in perfused mouse eyes. Taken together, there are at least two vasoactive control points that regulate distal outflow resistance.

CONTROL ID: 3546598

SUBMITTER (NAME ONLY): Xiaoyi Gao

TITLE: Polygenic risk scores and machine learning improve glaucoma prediction

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X.R. Gao, Y. Lin, M. Chiariglione, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Columbus, Ohio, UNITED STATES|X.R. Gao, Department of Biomedical Informatics and Division of Human Genetics, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a chronic, degenerative optic neuropathy, and the leading cause of irreversible blindness. It affects about 70-90 million people worldwide. Primary open-angle glaucoma is the most common form of glaucoma. At present, there is no cure for glaucoma. Early detection and treatment are crucial for preventing vision loss from this blinding disease. Polygenic risk scores (PRSs) enable disease early prediction based on an individual's genetic makeup. We constructed PRSs and utilized advanced machine learning for glaucoma prediction.

Methods: We conducted this study using participants from the UK Biobank cohort, a population-based prospective study of 500,000 individuals. All study subjects were 40 years of age and older. The participants were genotyped and further imputed to 92 million genetic markers. About 118,000 study subjects participated in the eye and vision component of the study, where numerous ocular measurements were obtained, including intraocular pressure (IOP). Glaucoma information was extracted from electronic medical records and self-reported medical history (cases n = 13,712). We constructed PRSs for multiple diseases/traits, such as glaucoma and IOP, and evaluated their predictive power using XGBoost (an efficient machine learning algorithm) and cross-validation. To avoid overfitting in predictive models, we used independent datasets for model training and testing.

Results: The glaucoma PRS was significantly associated with glaucoma disease risk ($P = 4.69 \times 10^{-24}$) in our testing dataset, after adjusting for covariates, such as age and sex. Subjects in the top 10% of PRSs were 10.28 times more likely to have glaucoma, compared to those in the bottom 10% category ($P = 7.5 \times 10^{-27}$). The area under the receiver operating characteristic curve (AUC) for glaucoma risk prediction was 0.82. Furthermore, the XGBoost method gave better prediction accuracy than traditional logistic regression.

Conclusions: We determined that an ensemble of PRSs and advanced machine learning improve the prediction of glaucoma.

CONTROL ID: 3546599

SUBMITTER (NAME ONLY): Pooja Mohanty

TITLE: Rod pathway signaling has protective effects on myopia susceptibility in dim, but not bright light.

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Mohanty, D. Brown, M.T. Pardue, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|P. Mohanty, D. Brown, R. Mazade, M.T. Pardue, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Bright ambient light has protective effects on the development of myopia. Recently, we have shown that in addition to bright light, dim ambient light is also protective in a mouse model of myopia, while intermediate, indoor ambient light was not (Landis et al., IOVS 2021). Since rod photoreceptor pathways can still be active in bright light conditions (Tikidji-Humburyan et al., Nature Comm 2017), we investigated the role of the rod pathway signaling in the protective effects of dim and bright light against lens-induced myopia (LIM) using transgenic mice that only have functional rods.

Methods: We developed an in-house breeding colony that produced mice with a “rod only” genotype: rod transducin α Gnat1^{+/+}, cone transducin α Gnat2^{-/-}, and melanopsin Opn4^{-/-}. Myopia was induced by affixing a -10D lens over the right eye starting at postnatal day 28; naïve left eyes were used as contralateral controls. Mice were housed in dim (1 lux), indoor (50 lux), or bright (10,000 lux) lighting for the entirety of lens wear. In each light group, we compared LIM mice (n=3) to naïve littermate controls (n=4). Refractive error, corneal curvature, and ocular axial parameters were measured weekly until 3 weeks post-LIM.

Results: Under all light levels, “rod only” mice with LIM developed significant refractive shifts (difference in refractive error between right and left eye) compared to naïve controls (p<0.02). However, the ambient light level significantly influenced the magnitude of LIM development (two-way RM ANOVA, p<0.001). Similar myopic shifts developed in the indoor (-6.95±0.05D) and bright light (-6.69±0.61D) groups (p=0.99). However, mice housed in dim light had a reduced myopic shift (-4.22±0.32) that was significantly different from mice housed in indoor lighting (p=0.04). No differences were found between groups for corneal curvature or ocular axial parameters.

Conclusions: “Rod only” mice were able to respond to lens defocus under all ambient light conditions, suggesting that rod pathways are sufficient to detect the myopigenic signal. In the absence of cone and melanopsin function, bright light was not found to be protective on myopia development. However, rod pathways appear to underlie the protective effects of dim light on myopia. Future research will determine the selective contribution of cone and melanopsin pathway signaling in the protective effects of bright light on myopia.

CONTROL ID: 3546600

SUBMITTER (NAME ONLY): Alejandro Ochoa III

TITLE: Erythrocyte parameters and their associations with glaucoma

SESSION TITLE: GL- Predictive Biomarkers

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Ochoa III, Internal Medicine, University of California Riverside, Riverside, California, UNITED STATES|A. Ochoa III, K. Kitayama, F. Yu, V. Tseng, A.L. Coleman, Center for Community Outreach & Policy, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|K. Kitayama, A.L. Coleman, Epidemiology, UCLA Fielding School of Public Health, Los Angeles, California, UNITED STATES|L. Chen, F. Yu, Biostatistics, UCLA Fielding School of Public Health, Los Angeles, California, UNITED STATES|A. Frederes, Community Health Sciences, UCLA Fielding School of Public Health, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anemia may contribute to increased local hypoxia, leading to optic nerve head cupping seen in glaucoma. The purpose of this study was to examine possible associations between erythrocyte parameters and glaucoma in a nationally representative sample of non-institutionalized civilian adults in the United States.

Methods: This was a cross-sectional study of participants in the 2005-2008 National Health and Nutrition Examination Survey (NHANES) dataset who had optic disc photos and erythrocyte parameter laboratory tests performed, including hemoglobin concentration (Hgb), Hematocrit concentration (Hct), and red blood cell count (RBC). A binary variable for anemia was also created based on sex specific Hgb cutoffs defined by the World Health Organization (WHO). The outcome of interest was diagnosis of glaucoma based on ophthalmologist grading of optic disc photos for characteristic features of glaucoma. Logistic regression modeling was performed to assess for associations between each of the individual erythrocyte parameters and glaucoma, controlling for demographic information, including age and race/ethnicity. All analyses were weighted according to the NHANES multistage sampling design.

Results: A total of 4,396 sampled participants were included, of whom 41 had prevalent glaucoma (0.9%). The sample represented a weighted estimate of 90,577,744 participants with a weighted glaucoma prevalence of 0.5%. After adjusting for covariates, a 1 gram/deciliter increase in Hgb resulted in a 26% reduction in odds of glaucoma (odds ratio [OR]: 0.74, 95% confidence interval [CI]: 0.63-0.88), a 1% increase in Hct resulted in a 10% reduction in odds of glaucoma (OR: 0.90, 95% CI: 0.84-0.97), and a 1 million cell increase in RBC resulted in a 68% reduction in odds of glaucoma (OR: 0.32, 95% CI: 0.17-0.60). The presence of anemia was associated with a non-significant 2.26 increased odds of glaucoma (OR: 2.26, 95% CI: 0.76-6.71) after adjusting for covariates.

Conclusions: In the 2005-2008 NHANES adult population, increases in erythrocyte parameters (Hgb, Hct, RBC) are associated with decreased odds of glaucoma; however, the presence of anemia is not statistically significantly associated with glaucoma. It may be that the WHO cutoff value for anemia does not have direct impact on the pathogenesis of glaucoma. Further population-based studies are needed to examine associations between additional erythrocyte parameters and glaucoma.

CONTROL ID: 3546601

SUBMITTER (NAME ONLY): Rafael Widjajahakim

TITLE: Prediction of AMD Progression Within Eye-Specific Baseline Severity Scales, and Attributable Fraction for Modifiable Factors and a Genetic Risk Score

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Widjajahakim, J.M. Seddon, Dept. of Ophthalmology and Visual Sciences, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|B. Rosner, Channing Division of Network Medicine, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine modifiable and genetic factors associated with progression to advanced age-related macular degeneration (AMD) for eyes with different baseline severity scales, and to assess population attributable fraction of these factors.

Methods: An eye that progressed was defined as a transition from no AMD or non-advanced AMD (AREDS severity scales 1-8) to any advanced AMD (scales ≥ 9) at 2 consecutive visits during 12 years of follow up. Eight genetic variants were associated with progression, adjusting for age, sex, education, smoking history, BMI, baseline severity scale, and AREDS treatment. A Genetic Risk Score (GRS) was calculated. Kaplan-Meier survival curves were constructed for the impact of GRS and smoking on rate of progression within categories of the baseline AMD scales, and population attributable fractions were calculated for specific factors.

Results: Among 5421 eyes, 948 progressed to advanced AMD. Genetic variants associated with progression included genes in the complement, immune, inflammatory, lipid, extracellular matrix, DNA repair and protein binding pathways. Eyes from subjects with GRS in the upper tertile had three times higher risk of progression than the lowest tertile (HR=3.03, 95% CI: 2.31-3.97) (Fig. 1). For overall advanced AMD, as well as the neovascular and atrophic subtypes, there was a strong effect for GRS among eyes with baseline intermediate level severity scales 6-8, while the differences were smaller among eyes starting with severity scales 1-5. As shown in Fig. 2, for eyes among past smokers with baseline severity scale 8, the 12 year probability of progression was 55% for GRS 1 vs. 90% for GRS 3, while among current smokers, the corresponding progression rates were 80% vs. > 95%. Calculation of population attributable fraction showed that the percent of disease prevented if smoking and body weight behaviors changed to past or never smoking and BMI < 25, was about 15%. In a similar calculation, if GRS tertiles changed from higher levels to the lowest risk, the percent prevented would be 37%, holding severity scale constant.

Conclusions: Carriers with higher GRS have higher risk of progression for eyes with the same level of baseline severity scale, and smoking further increases risk. Changing to healthier behaviors could reduce risk of progression from non-advanced to advanced stages of AMD.

CONTROL ID: 3546603

SUBMITTER (NAME ONLY): Vimal Prabhu Pandiyan

TITLE: Variation of human cone spectral composition with eccentricity

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: V. Pandiyan, S. Schleufer, H. Yan, X. Jiang, J. Kuchenbecker, M. Neitz, J. Neitz, R. Sabesan, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|S. Schleufer, Graduate Program in Neuroscience, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: The cone mosaic sets the primary limit on the fidelity of luminance and color vision. Here we describe the spectral composition of the cone mosaic in the parafovea using an adaptive optics (AO) line-scan OCT-based optoretinogram (ORG) and compare the modality against AO retinal densitometry and flicker-photometric electroretinogram (ERG).

Methods: Two subjects were imaged in an AO line-scan OCT from at 1.5 to 10 deg temporal eccentricity (ecc.) after 3-4 min. of dark adaptation. OCT volumes were recorded after a 10-20 ms 660±10 nm LED flash. The B-scan rate was 6 to 12 kHz and field of view was 1 to 1.6 deg. The stimulus-induced optical phase change was computed between individual cone inner/outer segment junctions and outer segment tips in registered and segmented volumes and converted to optical path length (OPL). The change in OPL was subjected to Gaussian mixture model clustering to distinguish the three cone types. In one subject, cone spectral identities so obtained with ORG were compared against AO retinal densitometry at 1.5 deg ecc. and the nature of disagreements explored. ERG was conducted on both subjects with a 35 deg stimulus for comparison against ORG.

Results: Depending on cone type, bleach strength and ecc., OPL amplitudes vary from 10 - 700 nm, thus offering up to ~2 log units of sensitivity for separating cone types in ORG. Thus, high probability and low uncertainty in LMS assignments were obtained for both subjects across a large population of cones at each ecc. The cone types obtained from ORG and densitometry had ~90.5 % agreement, tested over 813 cones at 1.5 deg ecc. Disagreement of spectral-type assignments included incidence of cones with normal reflectivity in one system but not the other, typed as "dysflective". Of the disagreements, ~44% of mismatches were between L vs. M, ~5% were between LM vs. S, and ~51% involve instances of dysflectivity. For subject 1, the L:M ratio was 2.2, 3.0, 3.0 and 2.4 at 1.5, 3.5, 4.75, and 10 deg ecc., respectively. For subject 2, the L:M ratio was 2.2, 2.0, 2.1 at 1.5, 4.75 and 10 deg ecc. For both subjects, % S-cones increased with ecc., from 4 - 7.6%. The L:M ratios derived from ERG were 2.2 and 2.7 respectively.

Conclusions: Cone spectral composition based on ORG aligned well with densitometry and ERG. The L:M cone ratio remained relatively uniform in the parafovea.

CONTROL ID: 3546604

SUBMITTER (NAME ONLY): Paul Taylor

TITLE: Emulated trial comparing the effectiveness of Bevacuzimab vs Aflibercept using an external control arm

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Taylor, D. Thomas, Institute of Health Informatics, University College London, London, London, UNITED KINGDOM|A.Y. Lee, University of Washington, Seattle, Washington, UNITED STATES|P.L. Mueller, R. Schwartz, A. Olvera-Barrios, A. Warwick, P.J. Patel, T. Herren, C. Egan, A. Tufail, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: There have been no randomised controlled trials comparing off-label bevacizumab to aflibercept for treating neovascular Age-related Macular Degeneration (nAMD). Recent advances in the emulation of target trials suggests that the standard-of-care arms can be approximated with real-world cohorts. Given that the treatment of retinal disorders with inhibitors of Vascular Endothelial Growth Factor accounts for 12% of Medicare expenditure, evidence for the non-inferiority of bevacizumab relative to licensed therapies could have implications for on the cost of treating nAMD.

Our hypothesis was that the visual acuity at 54 weeks of nAMD eyes treated with bevacizumab (q6w pro re nata) would not be inferior relative to aflibercept (q8w fixed-interval).

Methods: We emulated a target trial using the bevacizumab arm (n 65) of the ABC trial — a prospective, double-masked, randomised controlled trial — with external synthetic control arms derived from real-world cohorts receiving aflibercept as part of routine healthcare in the United Kingdom. Analyses were pre-specified and undertaken in accordance with the Target Trial Framework. External real-world cohorts were restricted to eyes that would have been eligible for the ABC trial and, to overcome the non-random treatment assignment in the real-world, we undertook conditional randomisation via 1:1 exact matching (EM), 1:1 propensity score matching (PSM), and inverse probability of treatment weighting (IPTW) on hypothesised confounding (age, sex, baseline read). Ordinary least squares regression was modelled on the change in visual acuity from baseline to week 54, stratified by treatment in eyes that received three loading doses within 70 days. Non-inferiority was declared if the lower confidence interval bound was \geq than a non-inferiority margin of -4 ETDRS letters.

Results: Of 31,151 eyes that started aflibercept treatment for nAMD, 4,471 (14%) fulfilled the ABC and target trial eligibility criteria. Eyes included in the bevacizumab trial & aflibercept synthetic arms were, respectively: 131 & 8,506 for IPTW (pseudo-population); 43 & 43 for EM; and 65 & 65 for PSM. The results show, with exception of PSM, that bevacizumab is not inferior to aflibercept, on a noninferiority margin of 4 ETDRS letters.

Conclusions: We found off-label bevacizumab to be non-inferior to licensed aflibercept. We show the potential of real-world cohorts as external control arms.

CONTROL ID: 3546607

SUBMITTER (NAME ONLY): Shin Ae Park

TITLE: Correlation between in vivo imaging parameters of the optic nerve head and axon counts in canine open-angle glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Park, Purdue University, West Lafayette, Indiana, UNITED STATES|C. Harman, K. Leary, V.A. Raphtis, K. Jongnarangsin, A.M. Komaromy, Michigan State University, East Lansing, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Quantifying optic nerve (ON) axons is the gold standard method of disease progression in glaucoma animal models; however, this can only be done after enucleation. Optical coherence tomography (OCT) and scanning laser ophthalmoscopy (SLO) have been used to monitor pathological changes of the optic nerve head (ONH) and retinal nerve fiber layers in patients with glaucoma. In this study, we report the relationship between the number of ON axons and OCT parameters of the ONH at different disease stages in a clinically relevant canine open-angle glaucoma model (OAG).

Methods: Dogs with moderate- and advanced- stage OAG due to an ADAMTS10 mutation (6 eyes, 6 dogs) and one normal control (2 eyes, 1 dog) were included. Ages of the dogs with OAG ranged from 3 to 7 years (median of 4 years old); the control dog was 6 years old. An equal number of mutant males (n=3) and females (n=3) were included while the control dog was male. High-resolution spectral-domain OCT and SLO (Spectralis®, Heidelberg Engineering) imaging of the ONH and the peripapillary retina were performed. ONs were collected and embedded in epoxy resin. Semi-thin cross-sections were stained with 1% p phenylenediamine and digitally scanned (Aperio digital pathology slide scanner, Leica). The number of axons in the entire ON was counted manually. An image analysis software (Image J, National Institute of Health) was used to measure the OCT parameters and count ON axons.

Results: A strong positive correlation was found between ON axon numbers and neuroretinal rim ($r=0.91$, $p<0.01$) and ONH area[KA1] s ($r=0.73$, $p=0.04$). There was a moderate positive correlation between ON axon number and ONH diameter ($r=0.52$, $p=0.19$). A strong negative correlation was found between ON axon numbers and optic cup area ($r=-0.75$, $p=0.03$) and a moderate negative correlation between ON axon numbers and the age of dogs[KA2] with OAG ($r=-0.70$, $p=0.12$).

Conclusions: OCT and SLO parameters of the ONH area showed a moderate to a strong correlation with ON axon numbers in the canine ADAMTS10-OAG model.

CONTROL ID: 3546609

SUBMITTER (NAME ONLY): Suneel Gupta

TITLE: Mechanism associated with acrolein's toxicity to the cornea in vitro

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Gupta, N.R. Sinha, P. Balne, R. Tripathi, N. Hesemann, P.R. Sinha, R.R. Mohan, Harry S Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|S. Gupta, N.R. Sinha, P. Balne, R. Tripathi, P.R. Sinha, R.R. Mohan, College of Veterinary Medicine and Surgery, University of Missouri, Columbia, Missouri, UNITED STATES|N. Hesemann, MU Health Care Mason Eye Clinic-University Hospital, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acrolein, a volatile organic compound, was used as a warfare agent in World War I and has the potential viable public threat worldwide. Recently, we studied the impact of acrolein exposure to the cornea and other ocular surface tissues in vivo using a rabbit model. The study sought to uncover the mechanisms of acrolein's toxicity to the cornea using an in vitro model.

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Methods: Primary human corneal stromal fibroblasts cultures (h-CSFs) from donor human corneas were used. Presto blue and MTT assays were used to determine the dose of acrolein, N-acetyl cysteine (NAC), and Buthionine sulfoximine (BSO) for h-CSFs. Different biochemical assays using standard commercial kits and qRT-PCR analysis were performed to understand the mode of acrolein toxicity.

Results: The MTT and PrestoBlue assays defined that 100 μ M dose of acrolein represents IC_{50} , for h-CSFs an acute level at 4h ($p < 0.001$). The biochemical assays revealed that acrolein exposure to h-CSFs led to oxidative stress and a compromised level of glutathione. These biochemical variations led to mitochondrial dysfunction via changes in the mitochondrial membrane potential ($\Delta\Psi_m$). The mRNA data, TUNEL, and caspase-3/7 assays showed that acrolein induces apoptosis in h-CSFs. Treatment with NAC; a precursor of glutathione, in h-CSFs decreased the oxidative stress, elevated the GSH level, regulated the mitochondrial membrane potential ($\Delta\Psi_m$), and rescued h-CSFs from apoptosis under acrolein-exposed conditions.

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Conclusions: Acrolein's exposure to human corneal fibroblasts induced alterations in phenotype, and cell death through oxidative damage at least in part of toxicity, in vitro.

CONTROL ID: 3546610

SUBMITTER (NAME ONLY): Rupesh Singh

TITLE: Longitudinal retinal image analysis of diabetic Akita mice

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Singh, M. Ali, J.C. Batoki, B. Anand-Apte, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|B. Anand-Apte, Cleveland Clinic Lerner Research Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the changes in the retinal structure and retinal vasculature in type-1 diabetic mice (C57BL/6-Ins2^{Akita}/J) over time.

Methods: Fluorescein angiography (FA), Indocyanine green angiography (ICGA) and OCT imaging was performed on Akita mice at 3 months and 6 months of age. The confocal scanning laser ophthalmoscopy (cSLO) images were analyzed for FA and ICGA. OCT images were evaluated for thickness measurement of distinct layers of the retina. A total of 25 (male) animals were used in the study. FA was performed after IP injection of Na- fluorescein, and images were collected at ~three mins and ~six mins for early and late phase of dye circulation. ICG was administered via tail vein. Statistical comparison were made using non-parametric two tailed t-test with significance at P<0.05.

Results: Using ImageJ, a simple thresholding protocol was developed, which uses IsoData algorithm, and fixed lower and upper threshold values for all the FA and ICG images. Both FA and ICGA showed significantly increased retinal vasculature leakage (92% increase in FA and 101.9 % increase in ICGA) in 6-month old Akita mice compared with age matched WT (Fig. 1). OCT based total retinal thickness was significantly reduced in Akita mice at both three (2.8%) and six (2.5%) months of age. The middle retinal layer thicknesses, OPL and ONL were significantly different in mice in the 6-month age group (Fig.2). However, at three months, only the OPL layer had thinning in the outer and middle retinal region (Fig. 2). No observable changes were observed in the outer retinal layers (IS/OS and RPE).

Conclusions: Aging diabetic mice exhibit clear imaging biomarkers such as retinal fluid leakage and inner retinal layer degeneration.

CONTROL ID: 3546611

SUBMITTER (NAME ONLY): Anse Vellappally

TITLE: Normative OCT optic nerve head parameters of rhesus macaques

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Rhesus macaques are a common animal model in ophthalmology because of the high similarity of their eyes and visual pathway to human. The characterization of optic nerve head (ONH) and peripapillary region in monkeys reported so far mostly involved a manual process which is laborious and subjected to operator errors. It is also usually generated from a cohort of similar age group. In this cross-sectional observational study, we deploy automated and manual segmentations to evaluate the OCT retinal nerve fiber layer (RNFL) thickness, ONH and lamina cribrosa (LC) microstructure parameters in a cohort of free roaming macaques.

Methods: In-vivo ONH spectral-domain OCT scans (Leica, Chicago, IL) were obtained by a single experienced operator after excluding eyes with any retinal pathologies. The margins of the optic disc were drawn manually and the resultant scans were analyzed using an automated segmentation software of our own design. The LC microstructure parameters were obtained through a previously described segmentation algorithm. The other parameters of ONH, namely the cup-to-disc (C/D) ratio and minimum rim width (MRW) were assessed manually. Wilcoxon rank sum test was used to test the association of LC parameters, C/D ratio and MRW with age, while the rest of the parameters were analyzed using mixed effects model accounting for age, sex and intra-subject correlation.

Results: 29 eyes from 19 monkeys (11 females, 8 males) with age ranging from 4.2 to 23.8 years were analyzed. Males were overall bigger and significantly heavier than females in our cohort (Table 1). Superior RNFL was thicker in male and is the only RNFL parameter that was associated with age or sex in this healthy cohort. No significant association was detected for any of the ONH parameters with age or sex. LC was more visible and thicker in male with higher beam to pore ratio and connective tissue fraction than in female.

Conclusions: The characterization of normal macaque eyes from a cohort of free roaming animals is useful as a standard reference to assess pathological changes in future experimental studies.

CONTROL ID: 3546612

SUBMITTER (NAME ONLY): Kirill Zhurenkov

TITLE: Prospects of lower lip mucosa stem cells in corneal restoration

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Chemically burned cornea requires appropriate measures for preventing inflammation and tissue damage, as well as for being repaired. Here we investigated an artificial corneal graft (ACG) based on lower lip mucosa stem cells (LMSC). The aim of this study was to characterize cells derived from lower lip mucosa in two species, including human and rabbit, as well as to understand if ACG can promote corneal restoration.

Methods: Both human and rabbit LMSCs were characterized by several criteria, especially in terms of their proliferation capacity, differentiation ability, genomic stability, and immunophenotypic characterization. The proliferation rate of LMSCs was evaluated by producing their growth curves. Osteogenic, chondrogenic, and adipogenic differentiation potential was examined by culturing LMSCs in differentiation media for several weeks and after that von Kossa, safranin-O, and Oil Red O staining, respectively. Genomic stability was evaluated by producing their karyotypes, and the percentage of chromosomal rearrangements was assessed. The abundance of ABCB5, ABCG2, ALDH3A1, CK3, CK14, and CK15 was examined by immunocytochemistry. Finally, a decellularized human amniotic membrane (HAM) was used as a scaffold, and rabbit LMSCs were seeded on it in a density of 100000 cells/cm². In vivo, the ability of ACG to repair damaged cornea was evaluated in a limbal stem cell deficiency (LSCD) rabbit model. Inflammation and corneal wound healing were examined by histological analysis. Untreated cornea and cornea with total LSCD acted as a control.

Results: LMSCs were characterized at 6 passages. Among both human and rabbit LMSCs grew at the highest speed. The population doubling time of human and rabbit LMSCs was 36.22±0.57 and 54.78±1.3 hours (p<0.05), respectively. It was found that LMSCs were able to differentiate toward osteogenic, chondrogenic, and adipogenic lineages. However, rabbit LMSCs differentiation potential was slightly lower. The genome of both human and rabbit LMSCs was stable with the chromosomal rearrangements number of 6.67% and 10%, respectively. Immunocytochemistry showed that both human and rabbit LMSCs expressed epithelial and stem cell markers. In vivo, it was found that the transplantation of ACG promoted corneal reepithelization via 1 month.

Conclusions: Thus, our results suggest that ACG based on HAM and LMSCs are able to repair the corneal structure and decrease inflammation after being wounded.

CONTROL ID: 3546613

SUBMITTER (NAME ONLY): Ryan McNabb

TITLE: Robotically aligned OCT enables physically distanced imaging and relevant measurements in a retina clinic population

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optical coherence tomography (OCT) is a ubiquitous ophthalmic imaging technology. However, currently patients are required to position themselves in chin/forehead rests for stabilization with the system operator in close proximity. Introducing a robot to the clinic enabled distanced, no-contact imaging of a retina clinic population.

Methods: We developed a custom robotically (UR3e) aligning swept source OCT (RAOCT; 1040nm) system with a low mass (2.4kg) sample arm utilizing 70mm diameter achromatic lenses with 3D printed optomechanics providing a clinically relevant 32° view on the retina (Fig. 1A&B). During acquisition, face and pupil tracking cameras triangulated 3D eye and pupil motion which were compensated in real-time by the robot and OCT system (Fig. 1C&D). We acquired B-scans and volumes in triplicate from the right eyes of 20 subjects from the Duke Eye Center clinics (10 normal, 10 diseased; 25 - 91 years old) with RAOCT and Heidelberg Spectralis under an IRB approved protocol. Differences between device foveal thickness maps were tested using two-tailed t-tests.

Results: Subjects were seated and free of any head restraints (no forehead strap or chin rest, Fig. 1A). The system automatically aligned on the subject's eye allowing for motion compensated OCT B-scans and volumes of the retina (Fig. 2). There was a mean paired inter-device $1.2 \pm 5.9\mu\text{m}$ difference ($p = 0.53$) in healthy retinal thickness and $3.7 \pm 7.5\mu\text{m}$ ($p = 0.13$) difference in diseased retinal thickness (Fig. 2E).

Conclusions: In a clinic population, we demonstrated a robotically aligned OCT system that provides retinal views and measurements comparable to current clinical OCT.

CONTROL ID: 3546614

SUBMITTER (NAME ONLY): Varun Kumar

TITLE: Loss of NQO1 generates genotoxic estrogen byproducts and causes increased female susceptibility to UVA in Fuchs dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Purpose: Fuchs endothelial corneal dystrophy (FECD) is a genetic, female predominant, and late-stage oxidative disorder characterized by progressive loss of corneal endothelial cells (CEnCs). Previously, we have reported a decrease in [NAD(P)H: quinone oxidoreductase 1 (NQO1)], an estrogen metabolite detoxifying enzyme, and altered estrogen metabolism in FECD. In this study, we have investigated the role of reactive estrogen metabolites in the estrogen genotoxic pathway for FECD.

Methods: Methods: NQO1^{+/+} and NQO1^{-/-} male and female mice were irradiated with UVA (500 J/cm²). CEnCs were imaged using a Heidelberg Retinal Imaging Rostock Corneal module (HRT-RCT) and quantified manually at weeks 1, 2 and 4 post-UVA. At week 4 post-UVA, toxic estrogen metabolites (4-OHE_{1/2}, 2-OHE_{1/2}), depurinating DNA adducts, and neutralized protective estrogen conjugates (4-OCH₃E_{1/2} and 2-OCH₃E_{1/2}) were analyzed by Ultraperformance Liquid Chromatography/Tandem Mass Spectrometry (UPLC/MS) in the cornea and reactive oxygen species (ROS) was analyzed in the aqueous humor.

Results: Results: At week 2 post-UVA, when compared to the baseline, UVA irradiation led to the greatest decrease in HCEncs in NQO1^{-/-} female mice (45.7%), followed by NQO1^{-/-} males (25%), NQO1^{+/+} females (24.8%) and then NQO^{+/+} males (6.8%). UPLC/MS-based metabolites analysis demonstrated that NQO1^{-/-} females had a 4.2-fold increase (p<0.05) in the ratio (OD/OS) of 4-OHE_{1/2}, a 7.4-fold increase (p<0.05) in 2-OHE_{1/2}, a 10.1-fold increase (p<0.05) in 4-OHE_{1/2} DNA adducts compared to NQO1^{-/-} males, a 10-fold increase (p<0.05) in 2-OHE_{1/2} for NQO1^{+/+} female compared to NQO1^{+/+} male. Thus, increased reactive estrogen adducts may lead to increased susceptibility to CEnC loss in NQO1^{-/-} females. For 4-OCH₃E_{1/2} and 2-OCH₃E_{1/2}, NQO1^{-/-} females had a 5-fold and 2.7-fold decrease (p<0.05, respectively) compared to NQO^{-/-} males, explaining the conversion of most estrogen metabolites to toxic byproducts in females. NQO1^{-/-} females had a 3-fold increase in ROS compared to NQO1^{-/-} males and unaltered in NQO1^{+/+} females and males.

Conclusions: Conclusions: Our study indicates that NQO1 deficiency accelerates UVA-induced CEnC loss in females due to increased reactive toxic estrogen DNA adducts. This novel study highlights the potential role of NQO1-mediated estrogen metabolite genotoxicity in explaining the higher incidence of FECD in females.

CONTROL ID: 3546618

SUBMITTER (NAME ONLY): Wesam Shalaby

TITLE: The Effect of Phacoemulsification on the Functioning Tube Shunts in Open Angle Glaucoma

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.S. Shalaby, A. Garg Shukla, N.N. Kolomeyer, D. lee, L. katz, M. Moster, J. Myers, R. Razeghinejad, Glaucoma Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|W.S. Shalaby, Ophthalmology, Tanta University, Tanta, EGYPT|S. Lam, S. Patel, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|A. Ganjei, Drexel University College of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate intraocular pressure (IOP) following phacoemulsification in eyes with prior tube shunts.

Methods: Retrospective chart review of consecutive open angle glaucoma patients with a prior tube shunt and IOP \leq 21 mmHg, who underwent phacoemulsification and had \geq 24 months of follow-up following cataract surgery. The main outcome measure was cumulative surgical failure at post-operative month 24, which was defined as IOP $>$ 21 mmHg, progression to no light perception (NLP) vision, glaucoma reoperation, or removal of the implant. Additional analysis of surgical failure defined as IOP $>$ 18 and $>$ 15 mmHg (for eyes with baseline IOP below these cutoff points) was performed. Changes in visual acuity (VA), IOP, and medications number were also assessed.

Results: 27 eyes of 27 patients with mean age of 64.2 ± 10.8 years and 2-year follow-up duration were included. The average interval between the tube shunt and cataract surgeries was 28.8 ± 25.0 months. All patients had moderate to severe glaucoma. At month 24, 4 (14.8%) eyes met the failure criteria, and mean time to failure was 19.3 ± 3.8 months. Reasons for failure were high IOP in 2 (50.0%) and glaucoma reoperation in 2 (50.0%) eyes. No eyes progressed to NLP vision. Additional analyses of surgical failure defined as IOP $>$ 18 and $>$ 15 mmHg showed increasing failure rate (18.5% and 48.5%, respectively). Kaplan-Meier survival analysis showing the cumulative rate of surgical failure at 24 months using the main and alternate failure criteria is displayed in Figure 1. The mean IOP and number of glaucoma medications remained stable at month 24 compared to baseline ($P=0.131$ and $P=0.302$, respectively). VA showed initial improvement at month 6 ($P=0.001$), but at month 24 this improvement was not significant ($P=0.430$).

Conclusions: IOP remained controlled in most eyes with prior tube shunt surgery 2 years following phacoemulsification.

CONTROL ID: 3546619

SUBMITTER (NAME ONLY): Rebecca Deffler

TITLE: Perceptions of Advanced Driver Assistance Systems by People with and without Age-Related Macular Degeneration

SESSION TITLE: Visual Impairment - Driving and Mobility

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Advanced driver assistance systems (ADAS), including blind spot warning and forward collision warning, are becoming widely available in many new cars. It has been reported that these systems improve the driving safety of elderly and normally sighted drivers. The purpose of this study was to assess exposure to, perceived safety with and interest in using ADAS among older drivers with age-related macular degeneration (AMD).

Methods: Current drivers aged 60+ years were recruited at four sites (the Ohio State University, University of California, Los Angeles, New England College of Optometry, and Envision Research Institute) to complete a cross-sectional survey about driving habits and use of: forward collision warning, forward collision avoidance, blind spot warning, lane departure warning, rearview camera, cruise control, adaptive cruise control, and GPS. If subjects had a particular ADAS in their vehicle, they completed survey items about frequency of use and improvements in safety associated with the system. If participants did not have a particular ADAS, they completed survey items about knowledge and anticipated benefits.

Results: One hundred twelve participants completed the survey (69 with AMD vs. 43 without, 54% female). Subjects with AMD were older (77 ± 8 years vs. 71 ± 7 years, $p < .001$), had poorer self-rated vision (64% good to excellent rating vs. 98%), and drove significantly fewer miles per week (55 ± 74 miles vs. 85 ± 64 miles, $p = .032$) than those without. A majority of participants used cruise control (AMD 54%, non-AMD 72%), rearview camera (AMD 54%, non-AMD 63%), and GPS (AMD 70%, non-AMD 77%). Subjects with AMD believed their safety was improved with use of rearview camera (89%), GPS (72%), and cruise control (54%). Of the less common systems, most drivers with AMD who did not have them believed their safety would be improved by: blind spot warning (83%), forward collision warning (72%), lane departure warning (64%), adaptive cruise control (59%), and forward collision avoidance (57%).

Conclusions: Many drivers with AMD utilize common ADAS, which subjectively improve their road safety. They are inclined to believe a variety of less common ADAS would further improve their driving safety, particularly the use of forward collision warning and blind spot warning. Further work is needed to objectively assess whether road safety actually improves as a result of these systems.

CONTROL ID: 3546620

SUBMITTER (NAME ONLY): Satoshi Hirose

TITLE: IL-17 is involved in a CNS demyelination model of optic neuritis

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Hirose, S. Wang, H. Ghiasi, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We previously reported that ocular infection of different strains of mice with a recombinant HSV-1 constitutively expressing murine IL-2 (HSV-IL-2) but not wild-type HSV-1 causes CNS demyelination and optic neuropathy. Interleukin-17 (IL-17) pathway plays an important role in host defense and various inflammatory diseases. However, the relationship between IL-17 pathway and CNS demyelination is not well established. Thus, we investigated the role of IL-17 pathway in HSV-IL-2 model of optic neuritis and multiple sclerosis.

Methods: We studied the role of IL-17 on CNS demyelination in IL-17A^{-/-} and IL-17 receptor -deficient (IL-17RA^{-/-}, IL-17RC^{-/-}, IL-17RD^{-/-}, and IL-17RA^{-/-}RC^{-/-}) mice. These female mutant mice were ocularly infected with HSV-IL-2 or parental virus and demyelination in brain, spinal cord and optic nerves of infected mice were determined on day 14 post infection using Luxol Fast Blue staining.

Results: Regions of demyelination were not found in the brain, spinal cord or optic nerves of HSV-IL-2-infected IL-17A^{-/-} mice, while demyelination was observed in mice lacking IL-17RA, RC, RD or both RA and RC. However, mice lacking both RA and RC had lower level of demyelination than mice lacking RA, RC, or RD. Both focal and diffuse regions of demyelination were detected in WT mice infected with HSV-IL-2 but not with WT virus. Transfer of T cells from IL-17A^{-/-} mice to Rag^{-/-} recipient mice induced CNS demyelination. Similarly, transfer of T cells from WT mice to IL-17A^{-/-} recipient mice induced CNS demyelination.

Conclusions: Our results suggest that the absence of IL-17A blocks CNS demyelination in ocularly infected mice. Presence to at least one receptor is sufficient to cause demyelination, suggesting a level of redundancy between the three receptors. In addition, T cell transfer experiments suggested that both T cell and non-T cell producing IL-17 are contributing to CNS pathogenesis. Thus, this study shows that IL-17 plays an important role in induction of CNS demyelination, and provides insight towards the mechanism of IL-17 pathway in induction of demyelination.

CONTROL ID: 3546622

SUBMITTER (NAME ONLY): Reanna Rodriguez

TITLE: Acrolein and Hypoxia Induced VEGF Secretion by 661W Cone Photoreceptors

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.R. Rodriguez, A.T. Tsin, K. Lowe, Molecular Science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|M. Keniry, Molecular Science, The University of Texas Rio Grande Valley School of Medicine, Edinburg, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR) is a leading cause of blindness in the United States with vascular endothelial growth factor (VEGF) being one of the main hallmarks that exacerbates this condition. In this study, we will determine the effects of acrolein and hypoxia on VEGF secretion under different glucose concentrations in mouse cone photoreceptors (661W) to study the molecular mechanisms of DR.

Methods: 661W cells were cultured in P100 dishes and then seeded in 6 wells plates at 300k cells/per well. Upon confluency of 80%, cells were subjected to the appropriate treatments consisting of complete culture media with normal (NG; 5.5mM) or high glucose (HG; 30 mM). Hypoxia was induced chemically by using cobalt (II) chloride hexahydrate solution of 300ug/ml. Acrolein concentrations consisted of low (25uM and 50uM) and high (100uM and 200uM). Elisa was used to measure the VEGF protein in conditioned media.

Results: Hypoxia had a significant impact by increasing the amount of VEGF secretion (NG=234 pg./ml, NG + hypoxia=658, HG=246, HG+ hypoxia =630; p=0.002 and 0.0275 respectively) and decrease number of viable cells (NG=2,200,000, NG + hypoxia=762,333, HG=2,230,000, HG+ hypoxia =1,040,000; p=0.003 and 0.037 respectively). Additionally, acrolein played a significant role in decreasing cell viability (p=0.035 in HG with 25uM acrolein=1,470,000, 50uM =760,200, 100uM =95,833, 200uM =76,233 and p=0.0064 in NG with 25uM acrolein=1,500,000, 50uM =1,290,000, 100uM =228,500, 200uM =58,600) and decreased VEGF secretion (p=0.05 in HG with 25uM acrolein=204 pg./ml, 50uM =112, 100uM =27.4, 200uM =18 and p=<0.0001 in NG with 25uM acrolein =272, 50uM =283, 100uM =56.6, 200uM =19.4) in 661W photoreceptor cells.

Conclusions: Hypoxia exerted significant effects to reduce 661W cell viability and increase VEGF secretion. However acrolein induced a reduction in cell viability, along with a decrease VEGF secretion. Since hypoxia (low oxygen) and acrolein (a highly reactive aldehyde) are known to affect significantly oxidative pathways, it is possible that their effects may be mediated by the TGFb pathway. Further experiments will be conducted to determine the underlying molecular mechanism.

CONTROL ID: 3546623

SUBMITTER (NAME ONLY): Steven Zhang

TITLE: Gathering Non-traditional, 15 Year, Real-World Patient Insights into Dry Eye Flares

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Zhang, D.V. Owen, K. Brazzell, Medical Affairs, Kala Pharmaceuticals, Watertown, Massachusetts, UNITED STATES|K.K. Nichols, The University of Alabama at Birmingham College of Arts and Sciences, Birmingham, Alabama, UNITED STATES|B. Joshi, C. Pandian, A. Shaw, Syneos Health Inc, Morrisville, North Carolina, UNITED STATES|W. Isenburg, Bentley University, Waltham, Massachusetts, UNITED STATES|C. Oh, School of Pharmacy, Shenandoah University, Winchester, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry Eye Disease (DED) is a symptomatic, chronic inflammatory disease. Most DED patients are thought to suffer from episodic exacerbations of their signs and symptoms (DED flares). However, very limited clinical data and patient insights exist on DED flares in the literature. We collected and analysed real-world patient insights into DED flares from unsolicited, self-reported and publicly available online data sources using internet technology driven data collection approaches from a 15-year period.

Methods: Real-world data patient- and HCP-reported information (English language) were collected from 2005 to 2020. Collected and analyzed patient experiences included DED flares symptoms, comorbid conditions, treatment usage, lifestyle behaviors and quality of life impact using an array of keywords associated with DED flares and a combination of technology driven approaches like natural language processing, machine learning, artificial intelligence (AI) and manual curation techniques used to standardize patient reports from real world data. SPEC-R (Social, Physical, Emotional, Cognitive and Role activity), an analytical framework was used to categorize functional impairments and symptoms from unstructured patient, caregiver and provider narratives.

Results: A total of 116,450 internet posts about DED flares and a population of 12,743 patient profiles were identified, collected and analysed from 75 data sources during the 15-year period. The identified DED flare patient population was predominately female (88%) and fell between the ages of 35 and 70 (86%). The most reported symptoms associated with reported DED flares were eye discomfort, pain and redness. Majority (78%) of the patients suffered DED flare resurgence within 2 months suggesting an annual occurrence of ~6 flares. Allergy and depression were most mentioned comorbidities and laser in-situ keratomileusis (LASIK) was the most common trigger for DED flares. SPEC-R analysis revealed that social and family life, work and the ability to concentrate were impacted the most by DED flares

Conclusions: This novel approach to collect a multitude of patient-reported, real-world insights revealed a wealth of data, which may help improving diagnosis, treatment and patient education on DED flares and quality of life.

CONTROL ID: 3546624

SUBMITTER (NAME ONLY): Mircea Mujat

TITLE: Large area choroidal and retinal vasculature maps in rats

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Mujat, A. Patel, N. Iftimia, Physical Sciences Inc, Andover, Massachusetts, UNITED STATES|R. Ferguson, FergusonRD LLC, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mircea Mujat: Commercial Relationship(s);Physical Sciences Inc.:Code E (Employment) | Ankit Patel: Commercial Relationship(s);Physical Sciences Inc.:Code E (Employment) | R. Daniel Ferguson: Commercial Relationship(s);Physical Sciences Inc.:Code P (Patent) | Nicusor Iftimia: Commercial Relationship(s);Physical Sciences Inc.:Code E (Employment)

ABSTRACT BODY:

Purpose: Examination of the ocular vasculature plays an important role in diagnosing eye diseases including age-related macular degeneration, diabetic retinopathy, and glaucoma. We developed a new imaging platform to visualize the vasculature without additional contrast agents and over large areas. The purpose of the current study was to identify vascular differences between rats with retinal degeneration and healthy rats.

Methods: A choroidal and retinal hemodynamic imager (CHARMER) has been developed enabling measurements of retina/choroid structure and ocular blood flow based on optical coherence tomography (OCT) and line-scanning Doppler flowmetry (LSDF). Ten rats with retinal degeneration (RD - eight Royal College of Surgeons rats and two heterozygous transgenic P23H rats) and ten age-matched Sprague-Dawley healthy controls (CD) have been imaged following an IACUC approved protocol.

Results: Large area Velocity maps have been obtained with the LSDF channel in CHARMER as shown in Fig. 1. The retinal blood vessels originating at the ONH are more visible and distinguishable in CD rats (left column in Fig. 1) than in RD rats (right column) indicating a reduced retinal flow in RD rats. On the other hand, the choroid vasculature is more visible in RD rats than in CD rats and with much better contrast than the retinal vasculature. As confirmed with OCT, the retina is thinner in RD rats as compared to CD rats and the LSDF light can penetrate deeper into the tissue and interrogate the choroid, less affected by scattering in the inner retina. The same trend is noticed between younger and older normal rats, the older ones (bottom left) have slightly thinner retina than the younger ones (top left) and therefore, a more visible choroidal vasculature. The choroidal vasculature is similarly visible in younger and older RD rats indicating that thinning of retina has already occurred in the younger ones, as confirmed with OCT.

Conclusions: Large area mapping of retinal and choroidal blood flow using LSDF can be used to investigate retinal and choroidal vascular changes due to disease. Such an advanced diagnostic imaging system will help understanding hemodynamic processes in the eye as a response to disease or treatment.

CONTROL ID: 3546625

SUBMITTER (NAME ONLY): Marvin Cruz

TITLE: Assessment of erythrocyte velocities in the retina and nailfold of glaucoma subjects and controls

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Cruz, J. Pottenburgh, V.Y. Chen, C. Le, O. Saeedi, Ophthalmology, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Blood flow is important to multiple ocular diseases and has been shown to be impaired in patients with glaucoma. Nailfold capillaroscopy visualizes peripheral capillaries and their blood flow while erythrocyte mediated angiography (EMA) precisely and accurately quantifies retinal blood flow. The purpose of this study is to compare the velocities of erythrocytes in the retina and nailfold.

Methods: We conducted a cross-sectional study using EMA in twenty-six patients to determine retinal venular, arteriolar, and capillary velocities, and a subset of seven patients underwent nailfold capillaroscopy. EMA uses ICG loaded erythrocytes to directly visualize blood flow in the retina and find erythrocyte velocities via a scanning laser ophthalmoscope (Tracey et al., Scientific Reports, 2019). Nailfold video capillaroscopy is a non-invasive approach to visualize capillaries at the fingernail base (Cousins et al., British Journal of Ophthalmology, 2019). By tracking blood gap displacement in the capillaries through the image frames, erythrocyte velocities were obtained.

Results: Average retinal arteriolar velocities for control (7.60 ± 2.16 mm/s), glaucoma suspect (6.82 ± 1.67 mm/s), and glaucoma subjects (7.84 ± 2.62 mm/s) were not significantly different from each other ($p = 0.30$). However, average retinal venular velocities for control (5.00 ± 1.57 mm/s), glaucoma suspect (6.78 ± 1.63 mm/s), and glaucoma subjects (6.41 ± 1.46 mm/s) significantly differed ($p = 0.0016$). Average nailfold capillary velocity was not significantly different ($p = 0.11$) among control (0.301 ± 0.119 mm/s), glaucoma suspect (0.242 ± 0.103 mm/s), or glaucoma subjects (0.394 ± 0.153 mm/s). Retinal capillary velocities were obtained in seven subjects with a mean of 1.54 ± 0.35 mm/s.

Conclusions: Retinal capillary velocities are markedly higher than nailfold capillary velocities, consistent with the high metabolic rate of the retina. While nailfold capillary velocities are more accessible, a higher degree of precision may be necessary to detect differences given the lower velocities. Our nailfold capillary velocities were within range of what is reported in literature. Future work will compare nailfold capillary velocities to retinal capillary velocities in controls, glaucoma, and glaucoma suspects.

CONTROL ID: 3546627

SUBMITTER (NAME ONLY): Mishek Thapa

TITLE: Cone-mediated encoding of natural stimuli is robust in Cngb1 mouse model of advanced retinitis pigmentosa

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Thapa, M. Scalabrino, E. Davis, E. Zhang, G. Field, Neurobiology, Duke University, Durham, North Carolina, UNITED STATES|J. Chen, Cell and Neurobiology, University of Southern California, Los Angeles, California, UNITED STATES|A.P. Sampath, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|M. Thapa, J. Xu, Statistical Science, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is an inherited blinding disease that causes degeneration of rod photoreceptors. Rod death causes many second-order changes in retinal circuits including the remodeling of bipolar cell dendrites and cone death. For treating vision loss from RP, a critical issue is determining how the fidelity of cone-mediated visual signaling depends on the amount of rod death.

Methods: We measured responses of retinal ganglion cells (RGCs) to artificial and natural visual stimuli under mesopic and photopic conditions using a mouse model of Cngb1-RP. In this model, rod death is a relatively slow process: rods progressively die until all are lost at 6-7 months. We measured RGC responses in animals at 1 month intervals from 1-7 months and compared responses to RGCs from WT mice. Ex vivo retinal recordings were performed using a 512 electrode array. Retina were placed RGC side down on the array, spikes were identified and sorted while presenting visual stimuli to the photoreceptors. The fidelity of signaling was examined in two ways. First, checkerboard noise was used to estimate the spatial and temporal receptive fields (RFs) of the RGCs. Second, repeated sequences of checkerboard noise or a natural movie were presented. These two approaches allowed an examination of the visual features encoded by the RGCs and the fidelity of this encoding process.

Results: Under both mesopic and photopic conditions, RF structure was relatively robust to the loss of rods out to 6 months of age (<10% rods surviving). Despite this relative stability in RF structure, the fidelity of visual signaling, measured by the mutual information (MI) between stimulus and response, was strongly impacted by rod loss. MI rates under mesopic conditions rapidly deteriorated when 50-80% of the rods remained. Under photopic conditions, MI rates were higher and less impacted by rod loss. Surprisingly, MI rates to natural movies were minimally impacted by rod loss and did not deteriorate significantly until after nearly all rods were lost and cones began to die.

Conclusions: Our results indicate that cone-mediated signaling of natural stimuli are minimally impacted by rod loss. This indicates that therapies for RP are likely to result in useful cone-mediated vision so long as rod photoreceptor death is halted.

CONTROL ID: 3546629

SUBMITTER (NAME ONLY): Miguel Miron Mendoza

TITLE: Vimentin as Regulator of Spreading and Migration of Corneal Fibroblasts in 3D Collagen Matrices

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Miron Mendoza, K. Poole, H. Hassaniardekani, M. Petroll, Ophthalmology, The University of Texas Southwestern Medical Center, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The intermediate filament (IF) vimentin has been associated with myofibroblast transformation of corneal keratocytes and the development of fibrosis in vivo. Studies in other systems suggest it can play a central role in regulating key aspects of cell mechanical behavior, including mechanosensing, polarization, and migration. In this study, we investigate the role of vimentin in mediating spreading and migration of corneal fibroblasts in 3D collagen matrices.

Methods: To assess 3D cell spreading, human corneal fibroblasts were embedded in fibrillar collagen matrices. To assess 3D cell migration, compacted cell-populated collagen matrices were embedded in cell-free collagen matrices. Once polymerized, samples were cultured for 24h in serum-free media (S-), S- plus PDGF (50 ng/ml), or S- plus TGF β (5 ng/ml). Withaferin A (WFA), a vimentin polymerization inhibitor, was added at a concentration of 2 μ M based on initial dose response experiments. 3D and 4D imaging were used to assess cell-matrix mechanical interactions, global matrix contraction, and live cell spreading and migration. F-actin labeling was used to assess cell morphological changes.

Results: During initial cell spreading in PDGF, corneal fibroblasts randomly extended and retracted dendritic processes; these protrusions disappeared over time as cells elongated. When WFA was present, cells maintained their protrusive activity but did not elongate. As shown in Figure 1, cells treated with WFA had a significant decrease in both length and area, and a less elongated morphology (as indicated by a higher shape factor). In contrast, during culture in S- or TGF β (which do not induce cell elongation or migrational polarity), WFA induced an increase in cell length and area. Global matrix contraction in response to PDGF was reduced by 39% when WFA was present ($P < 0.035$), and cell migration assays showed a reduction of 40%.

Conclusions: Our results suggest that cells cultured with WFA are unable to polarize and elongate in response to PDGF, which results in a reduction in migration through 3D collagen matrices. In addition, inhibition of cell-induced matrix reorganization by WFA suggests that polymerization of IFs is important for development of cell tractional forces. Overall, vimentin may mediate key aspects of cell mechanical activity during corneal wound healing.

CONTROL ID: 3546630

SUBMITTER (NAME ONLY): Camiel Boon

TITLE: X-linked retinoschisis: Long-term follow-up and genetic spectrum in 340 patients

SESSION TITLE: Macular diseases excluding AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.J. Boon, L. Hahn, M.J. van Schooneveld, Ophthalmology, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|C.J. Boon, Leids Universitair Medisch Centrum, Leiden, Zuid-Holland, NETHERLANDS|R.J. Florijn, J.B. ten Brink, A.A. Bergen, Clinical Genetics, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|I. Strubbe, B.P. Leroy, Ophthalmology, Universitair Ziekenhuis Gent, Gent, Oost-Vlaanderen, BELGIUM|M.H. Hof, Clinical Epidemiology, Biostatistics and Bioinformatics, Amsterdam UMC Locatie AMC, Amsterdam, North Holland, NETHERLANDS|M. Meester-Smoor, C.C. Klaver, A.A. Thiadens, Ophthalmology, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|J. Ossewaarde-van Norel, Ophthalmology, Universitair Medisch Centrum Utrecht, Utrecht, Utrecht, NETHERLANDS|L. van den Born, Oogziekenhuis Rotterdam, Rotterdam, South Holland, NETHERLANDS|C. Hoyng, Ophthalmology, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|M.J. van Schooneveld, M.M. van Genderen, Bartiméus Diagnostic Centre for Complex Visual Disorders, NETHERLANDS|A.A. Bergen, Nederlands Herseninstituut, Amsterdam, Noord-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Detailed knowledge regarding genetic and clinical characteristics of X-linked retinoschisis (XLRs) is necessary to provide patients with a more accurate prognosis, but also to identify clinical endpoints and optimal patient selection for (gene) therapy. This study aims to improve clinical counseling and acquire crucial information for the development process of treatment by evaluating the largest cohort of XLRs patients to this date.

Methods: This multicenter retrospective study reviewed medical records for medical history, symptoms, best-corrected visual acuity (BCVA), ophthalmoscopy, full-field electroretinography and retinal imaging (fundus photography, spectral-domain optical coherence tomography (SD-OCT), fundus autofluorescence).

Results: In total, 340 patients from presumably 178 different families were included with a mean age of 28.6 ± 19.3 years at last visit. The median BCVA of the better-seeing eye at last examination was 0.52 logarithm of the minimum angle of resolution (logMAR) (Interquartile range, Q1: 0.30, Q3: 0.70 logMAR). Severe visual impairment below 1.0 logMAR was predominantly present in patients above 40 years old, with a prevalence of 13.5% in that age group. Linear mixed models revealed a slow annual decline of 0.39% in BCVA ($P < 0.001$), with a relatively stable visual acuity until the age of 20 years. The integrity of the ellipsoid zone (EZ) as well as the photoreceptor outer segment (PROS) length on SD-OCT were significantly correlated with visual acuity (Spearman's $r = -0.604$, $P < 0.001$; $r = -0.759$, $P < 0.001$; respectively). Fifty-three different RS1 gene mutations were found. The most common variants were two founder mutations: c.214G>A (p.Glu72Lys; 102 subjects, 38.2%) and a deletion of exon 3 (38 subjects, 14.6%). There was no significant difference in decline of BCVA between mutations that were predicted to be severe and mild ($p=0.852$).

Conclusions: In general, XLRs showed a slow progression starting around the age of 20, suggesting an optimal window of opportunity for treatment within the first two decades of life. The integrity of EZ as well as the PROS length on SD-OCT may be important potential clinical endpoints in future therapeutic studies. No clear genotype-phenotype

correlations were found.

CONTROL ID: 3546636

SUBMITTER (NAME ONLY): Davide Ortolan

TITLE: The human retinal pigment epithelium has five morphometrically distinct subpopulations which present differential disease vulnerability

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Ortolan, R. Sharma, A. Volkov, A. Maminishkis, J. Ferrari Escoto, K. Bharti, National Eye Institute, Bethesda, Maryland, UNITED STATES|N. Hotaling, National Center for Advancing Translational Sciences, Bethesda, Maryland, UNITED STATES|S. Di Marco, Istituto Italiano di Tecnologia, Genova, Liguria, ITALY|S. Bisti, Universita degli Studi dell'Aquila Dipartimento di Medicina Clinica Sanita Pubblica Scienze della Vita e dell'Ambiente, L'Aquila, Abruzzo, ITALY|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) cells present geographical differences across human eyes. In the macula, RPE cells are smaller in size and present distinct shapes of apical processes, in comparison to peripheral RPE. In addition, there are functional and molecular differences in these two RPE populations, such as RPE metabolism and expression of specific transporters. Moreover, selective death of macular RPE cells occurs during retinal degenerative diseases, such as age-related macular degeneration (AMD). Currently, there is no thorough description of human regional RPE diversity and vulnerability, thus limiting the understanding of regional degenerative diseases. This study aims to provide a detailed and comprehensive morphometric map of the entire human RPE.

Methods: RPE/choroid flatmounts were generated from more than 20 human non-AMD and AMD eyes. The entire flatmounts were stained for RPE cell borders and imaged. An open-source software for image analysis, based on machine learning, was developed to quantify RPE morphometry. Spreadsheets with raw data and color-coded images were generated to compare regional RPE differences.

Results: Human RPE cell shape analysis of non-AMD eyes revealed the presence of 5 morphometrically different RPE subpopulations, which we named as P1 to P5, going from the macula toward the periphery. RPE cell area increases with eccentricity; in the mid-periphery (P3), RPE cells are almost double the size of macular RPE (P1) (median: $238.7 \mu\text{m}^2$ ($\pm 18.9 \mu\text{m}^2$ sd) vs $149.6 \mu\text{m}^2$ ($\pm 16.7 \mu\text{m}^2$ sd)). In addition, a peripheral ring of smaller RPE cells (P4) was discovered (median: $181.8 \mu\text{m}^2$ ($\pm 19.8 \mu\text{m}^2$ sd)). So far, the nature of P4 population remains elusive. RPE lesions were detected in the periphery of non-AMD eyes, revealing selective vulnerability of peripheral RPE populations (P4 and P5). Quantification of RPE lesions from AMD eyes and ultra-widefield retinal images of patients with monogenic disorders shows differential susceptibility of RPE subpopulations to degeneration.

Conclusions: Overall, the study provides the first comprehensive morphometric map of the human RPE and it provides a geographic reference of RPE subpopulations for other researchers in the field. Finally, studying the nature of each RPE subpopulation might help to understand regional retinal degeneration.

CONTROL ID: 3546637

SUBMITTER (NAME ONLY): Rupalatha Maddala

TITLE:

Growth/Differentiation factor 15 (GDF-15) induced effects on intraocular pressure in mouse models

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Maddala, C. Eldawy, W. Bachman, V. Rao, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the role of GDF-15, a divergent member of the transforming growth factor beta superfamily in trabecular meshwork physiology and homeostasis of intraocular pressure (IOP).

Methods: Telomerase inhibitor, lipopolysaccharide (LPS), and tunicamycin were used to determine whether cellular senescence, inflammation, and ER (endoplasmic reticulum) stress, respectively, influence the expression of GDF-15 in human trabecular meshwork (TM) cells, utilizing ELISA and immunoblot analyses. To determine the role of GDF-15 in regulation of IOP, mildly anesthetized human GDF-15 overexpressing transgenic mice (C57BL/6J) and GDF-15 null mice (C57BL/6J) were monitored for changes in IOP using a rebound tonometer.

Results: Treatment with telomerase inhibitor (20 μ m BIBR1532, 24 hrs) and Tunicamycin (one μ g/ml for 48 hrs) but not LPS (1-5 μ g/ml for 24 hrs) significantly increased GDF-15 levels in human TM cells. Transgenic mice expressing human GDF-15 exhibited significantly elevated human GDF-15 levels in both serum and aqueous humor compared to age-matched control mice. GDF-15 transgenic mice also exhibited a significant increase in IOP (~24 % $P < 0.01$; $n = 16$) compared to control mice. On the other hand, the GDF-15 null mice ($n = 15$) maintained normal IOP.

Conclusions: The increase in GDF-15 levels under senescence and ER stress and elevated IOP in GDF-15 overexpressing transgenic mice, when considered together with the known effects of GDF-15 on TM contractile/cell adhesive characteristics and elevated levels of GDF-15 in the aqueous humor of glaucoma patients, suggests that dysregulation of GDF-15 levels may be linked to ocular hypertension and glaucoma.

CONTROL ID: 3546638

SUBMITTER (NAME ONLY): Thomas Swain

TITLE: Left turn driving performance and association with visual function

SESSION TITLE: Visual Impairment - Driving and Mobility

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.A. Swain, G. McGwin, C. Owsley, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|T.A. Swain, G. McGwin, Department of Epidemiology, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|J.F. Antin, Vulnerable Road User Safety, Virginia Tech Transportation Institute, Blacksburg, Virginia, UNITED STATES|J.M. Wood, Centre for Vision and Eye Research, School of Optometry and Vision Science, Queensland University of Technology, Brisbane, Queensland, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To examine the association between visual impairment and driving performance at left turns at four-way intersections with traffic control among drivers aged ≥ 70 .

Methods: A 6-month prospective cohort study focused on drivers aged ≥ 70 years with eye conditions which could cause impairment using naturalistic driving methods was completed. After enrollment, participants completed a battery of visual and visual-cognitive function assessments including visual acuity, contrast sensitivity, visual field sensitivity, visual processing speed, and motion perception. To objectively collect driving information, a data acquisition system (DAS) was installed in participant vehicles. The DAS recorded continuous data streams from accelerometers, vehicle network, GPS, and 5-channel video camera system. Left turns were identified using accelerometer and GPS data and mapped to identify the location. To obtain 500 turns for data reduction, turns were randomized by participant and the location assessed to choose the first 3 or 4 turns for each participant occurring at a four-way intersection with traffic control. Trained analysts coded two outcomes: safe versus unsafe traversal and normal versus improper turn behavior. Generalized estimating equations, which account for repeated measures, were used to calculate age-adjusted odds ratios (ORs) and 95% confidence intervals (95% CIs) for the outcomes and association with visual impairment.

Results: A total of 473 left turns were assessed among 151 participants. Impaired visual processing speed (Trails B) was associated with 46% reduced odds of unsafe traversal (OR: 0.54, 95% CI: 0.34-0.85). Visual field sensitivities (overall, peripheral, lower, left) were significantly associated with 42-44% reduced odds of unsafe traversal. Similar significant protective associations were seen for those with impaired contrast sensitivity, visual processing speed (Trails B), and visual field sensitivities (peripheral, upper, lower, left) and improper turn behavior.

Conclusions: Older adults with vision impairment had reduced odds of unsafe traversal and improper behavior. While this finding could seem counterintuitive, it is consistent with self-report literature indicating that older drivers are aware of challenging driving situations and therefore could be more cautious. As this is the first examination of these associations, future work should further explore these findings continuing to use objective means.

CONTROL ID: 3546639

SUBMITTER (NAME ONLY): Kyuyeon Han

TITLE: Development of small molecule inhibitors against the corneal neovascularization via MMP14

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Han, H. LEE, D.T. Azar, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore the potentiality of quinoline based small molecules for matrix metalloproteinase 14 (MMP14) inhibitors.

Methods: We optimized and established to identify specific and unique MMP14 inhibitors through two-stage assays. Primary high-throughput (HTS) by fluorescence-based enzymatic assay was performed to determine IC_{50} value. We determined dissociation equilibrium constant (K_D) between cat-MMP14 with candidate compounds using surface plasmon resonance (SPR) to validate selected hit compounds. cat-MMP14 was immobilized on a CM5 sensor chip using the standard amine-coupling method using a Biacore 8K instrument. Compound solutions with a series of increasing concentrations (0 to 50 μ M at 1.5-fold dilution) were applied to all channels at a 30 mL/min flow rate at 25 °C. The K_D values were determined by fitting the data with either steady-state affinity or 1:1 Langmuir kinetic fitting. To investigate the potentiality to develop MMP14 inhibitors, we determined a structure-activity relationship (SAR) with twelve quinoline analogs using a fluorescence-based enzymatic assay.

Results: Three compounds (clioquinol, chloroxine, and folic acid) containing quinoline as a base structure showed inhibitory effects of MMP14. We found that two compounds (clioquinol and chloroxine) directly bound to act-MMP14 using SPR analysis. Clioquinol, chloroxine, and folic acid did not show cytotoxicity on corneal epithelial and fibroblast cells.

Conclusions: Our results show that quinoline containing small molecules inhibited MMP14 enzymatic activity. Based on these findings, we propose that the unique MMP14 inhibitors can specifically inactivate the MMP14 enzyme activity, leading to inhibition of corneal neovascularization via MMP14.

CONTROL ID: 3546640

SUBMITTER (NAME ONLY): Frank Jakobs

TITLE: Assessment of Stereo Deficiency and its Epidemiological Determinants in a Large-Scale Cohort of Military Recruits

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.M. Jakobs, D. Hering, J. Frischmuth, F. Weber, L. Bressem, Ophthalmology, German Air Force Centre of Aerospace Medicine, Muenchen, Bavaria, GERMANY | R. Schimmel, Ophthalmology, Bundeswehr Hospital Ulm, Ulm, Baden-Wuerttemberg, GERMANY |

Commercial Relationships Disclosure (Abstract): Frank Jakobs: Commercial Relationship: Code N (No Commercial Relationship) | Diana Hering: Commercial Relationship: Code N (No Commercial Relationship) | Rudolf Schimmel: Commercial Relationship: Code N (No Commercial Relationship) | Joerg Frischmuth: Commercial Relationship: Code N (No Commercial Relationship) | Frank Weber: Commercial Relationship: Code N (No Commercial Relationship) | Lothar Bressem: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Multiple studies have investigated the mechanisms of infant adaptation to visual stimulus as well as the residuals of developmental misadaptation in adults. Considerably less is known about the respective dissemination of factors and dynamics in juvenile populations. The purpose of this study was to assess the occurrence of stereo deficiency and its determinants in adolescents and young adults.

Methods: Routine eye examination data of 224,604 military recruits aged 17 to 21 yrs were retrospectively assessed and analyzed using standard statistical software. Data were assigned to either stereonormal or stereo-deficient individuals and substratified by grade of stereopsis. Presumed determinants were addressed on three levels (low, moderate, high) and included myopia (≤ -0.5 ; < -2.0 ; < -5.0 D), hyperopia ($\geq +0.5$; $> +2.0$; $> +5.0$ D), astigmatism (≥ 0.5 ; ≥ 2.0 ; > 3.0 D), anisometropia (≤ 1 ; ≤ 2 ; > 3 D), amblyopia (BCVA < 1.0 ; < 0.6 ; ≤ 0.2), and residual strabism. For each subset, logistic regression was performed using iterative log-likelihood approximation for calculation of odds ratios (OR) and confidence intervals (0.95 CI).

Results: A total of 20,762 cases of stereo deficiency was identified relating to 9.2% of the population analyzed in this study. Of these, 26.8% displayed myopia, 13.8% hyperopia, and 23.8% astigmatism. Correctable refraction error was present in 46.6% of cases, as compared to 29.7% in stereonormal individuals. Rates of uncorrectable refractive error increased dependent on the extent of stereo deficiency, with the left eye persistently displaying amblyopia at rates 1-2% higher than the right eye. Risk factor analysis identified strabism (OR 26.8 [0.95 CI: 25.2; 28.5]) and high hyperopia (OR 10.3 [0.95 CI: 8.9; 11.9]) being the predominant determinants, while interaction with anisometropia (OR 3.75 [3.57; 3.94]), astigmatism (OR 2.45 [2.38; 2.53]), and myopia (OR 1.21 [1.18; 1.24]) was much less pronounced ($p < 0.0001$).

Conclusions: Our results might be useful in bridging the gap between pediatric and adult-related research in developmental ophthalmology. Given the hyperdominance of motor deficiency and the over-representation of left eye visual deficiency found in this study, we hypothesize that the adaptive expression of higher binocular functions such as depth perception and ocular rivalry may not be fully understood.

CONTROL ID: 3546641

SUBMITTER (NAME ONLY): Laura Campello

TITLE: Alternative Promoter Use in Photoreceptors: Implications for Cell Signaling?

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Campello, H. Mast, L. Dong, A. Swaroop, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Laura Campello: Commercial Relationship: Code N (No Commercial Relationship) | Hannah Mast: Commercial Relationship: Code N (No Commercial Relationship) | Lijin Dong: Commercial Relationship: Code N (No Commercial Relationship) | Anand Swaroop: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Transcriptome analyses of photoreceptors have identified numerous genes with alternative promoter usage. Importantly, many of these alternate promoters are regulated by NRL and CRX, suggesting a crucial role in photoreceptors. However, how alternative promoter usage confers photoreceptor-specific regulation and function to widely expressed genes is not well-characterized. In the present work, we have explored the regulation and function of Hcls1 (hematopoietic cell-specific Lyn substrate 1), implicated in actin remodeling and receptor tyrosine kinase (RTK) signaling in immune cells but with unknown function in the retina.

Methods: RNA-seq analyses of mouse retina and flow-sorted photoreceptors identified genes with putative alternative promoter usage in photoreceptors. ATAC-seq, epigenetic marks (H3K4me3, H3K27ac) as well as NRL and CRX ChIP-seq data analyses predicted new transcription start sites. 5'-RACE was used to identify novel Hcls1 photoreceptor-specific transcripts. Expression of these transcripts was examined by in situ hybridization. Electrophoretic mobility shift assays (EMSA) were used to validate the NRL and CRX binding sites.

Results: We identified by 5'-RACE analysis a novel photoreceptor specific isoform of Hcls1 (Hcls1r), generated by alternative promoter usage. The expression of Hcls1r is concordant with photoreceptor morphogenesis and maturation trajectory. The protein encoded by this new transcript does not include the N-terminal domain involved in actin remodeling but retains signaling elements associated with receptor tyrosine kinase (RTK) signaling, which drives essential cellular processes in response to extracellular cues. In situ hybridization analysis confirmed the enrichment of this novel Hcls1 transcript in the photoreceptor layer. EMSA demonstrated the binding of Nrl and Crx to conserved Hcls1 intronic sequences, close to the transcription start site of the alternate Hcls1r transcript and contained open chromatin regions.

Conclusions: We propose that Hcls1r is a part of the regulatory network associated with photoreceptor function. Specifically, we predict an important function of Hcls1r in RTK signaling to modulate responses to the retinal microenvironment in photoreceptors and maintenance of homeostasis. We hypothesize that alternative promoter usage contributes to highly specialized structural and functional complexity of retinal photoreceptors.

CONTROL ID: 3546642

SUBMITTER (NAME ONLY): Matthew McPheeters

TITLE: Imaging murine corneal nerves in vivo using genetically-encoded calcium indicators

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. McPheeters, B. Blackburn, A.M. Rollins, M.W. Jenkins, Biomedical Engineering, Case Western Reserve University Case School of Engineering, Cleveland, Ohio, UNITED STATES|W.J. Dupps, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Numerous diseases detrimentally affect corneal nerves. Corneal nerve dysfunction has been linked to dry eye syndrome onset, neurotrophic keratopathy, and other diseases. The morphology and histology of corneal nerves in health and disease has been extensively studied. However, studies of corneal nerve function have been limited (e.g., electrical recordings of ciliary nerves or calcium reporter dyes in ex vivo corneas). Here, we present a non-contact method for functional imaging of corneal nerves. This tool has great potential to improve understanding of diseases of corneal nerves and the development of therapies for diminished neural function.

Methods: We made a cre-lox murine line expressing a genetically encoded calcium indicator, GCaMP6f, against the Nestin promoter for expression in the cornea nerves. We built a custom confocal imaging system with an air objective to image the corneal nerves while excluding autofluorescence from the lens. We designed various stereotactic and imaging apparatus to minimize motion of the mouse cornea relative to our imaging system (see Figure 1).

Results: Figure 1 shows our cornea imaging setup and Figure 2 shows a demonstration of in vivo corneal functional neuro-imaging. Using this technique, we were able to stably image the murine corneal nerves over long periods (e.g., 10 minutes). We have also demonstrated longitudinal imaging of the same field of nerves through multiple successive experiments.

Conclusions: Our developed tools and methods can enable study of the relationship between corneal nerve function and diseases of the ocular surface. The use of an in vivo system potentially allows for the study of factors that could slow the development of neuropathies and help develop new clinical interventions and therapies, which is a major goal of this work.

CONTROL ID: 3546643

SUBMITTER (NAME ONLY): Adam Faranda

TITLE: The the Influence of Sex on the Aging Lens Transcriptome

SESSION TITLE: Lens Physiology and Transport

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Faranda, M.H. Shihan, Y. Wang, M.K. Duncan, University of Delaware, Newark, Delaware, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Adam Faranda: Commercial Relationship: Code N (No Commercial Relationship) | Mahbubul Shihan: Commercial Relationship: Code N (No Commercial Relationship) | Yan Wang: Commercial Relationship: Code N (No Commercial Relationship) | Melinda Duncan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Age is a major risk factor for cataract. However, the influence of aging on the lens transcriptome is under studied. While age related cataract affects both sexes, it is more prevalent in women than men. While estrogen withdrawal at menopause is implicated in this observation, how sex influences lens gene expression is unknown. Here, we elucidate the effect of sex and age on the lens transcriptome of inbred mice.

Methods: Lens epithelial (LEC) and fiber cells (LFC) were isolated from young (3 month) and aged (24 month) old C57Bl/6J mice of both sexes, RNA prepared, and subjected to RNAseq. EdgeR was used to estimate differential gene expression in pairwise contrasts, with Advaita's lpathway guide and custom R scripts to evaluate the biological significance of differentially expressed genes (DEGs).

Results: RNAseq revealed age dependent decreases in lens differentiation marker expression in both LECs and LFCs, with gamma crystallin transcripts downregulating nearly 50 fold in LFCs. Aged LECs upregulate genes controlling the immune response, complement pathways, and cellular stress responses, including glutathione peroxidase 3 (GPX3). Aged LFCs exhibit broad changes in the expression of genes regulating cell communication, and upregulate genes involved in antigen processing/presentation, cholesterol metabolism, and calcium signaling, while changes in the expression of mitochondrial respiratory chain genes are consistent with mitochondrial stress. While young LECs only differentially express genes known to be associated with sex determination (i.e Xist in females, and Ddx3y in males), female LECs do not reduce crystallin transcription with age to the same extent as males nor do they upregulate GPX3 expression as dramatically as males. In contrast, young LFCs from males and females differentially express nearly fifty genes, many of which remain differentially expressed in aged LFCs. Notably, female LFCs retain substantially greater gammaD crystallin expression with age compared to males while also exhibiting enhanced upregulation of NDufa4l2, which encodes an alternate electron transport chain protein and is a marker of mitochondrial stress.

Conclusions: Lens cells downregulate the expression of lens markers with age while upregulating markers of inflammation, complement pathways, and cellular stress. Sex does not have a large impact on the young LEC transcriptome, but it does have a modest influence on gene expression in the aging lens.

CONTROL ID: 3546648

SUBMITTER (NAME ONLY): Lydia Sauer

TITLE: FLIO in MacTel patients with and without diabetes

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Sauer, A.S. Vitale, N.K. Modersitzki, P.S. Bernstein, Ophthalmology, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macular telangiectasia type 2 (MacTel) is a vision-altering retinal disease with a high prevalence of diabetes. Fluorescence lifetime imaging ophthalmoscopy (FLIO) was used to further investigate differences between MacTel patients with and without diabetes.

Methods: 89 eyes from 89 patients with MacTel (mean age 59 ± 12 years) were investigated at the Moran Eye Center, with the diagnosis of MacTel confirmed by the Moorfields reading center. 40 patients (45%) did not have diabetes, 16 eyes (18%) were prediabetic, and 33 patients (37%) were diabetic. Of these, 5 patients had diabetic retinopathy. A prototype Heidelberg Engineering FLIO was used to obtain autofluorescence lifetimes in short (SSC, 498-560 nm) and long (LSC, 560-720 nm) spectral channels from different areas of interest within the MacTel zone and in the periphery.

Results: FLIO lifetimes did not show significant differences in any area when comparing diabetic to nondiabetic eyes (MacTel zone SSC diabetic: 265 ± 57 ps, nondiabetic: 259 ± 49 ps, $p=0.59$; LSC diabetic: 333 ± 64 ps, nondiabetic: 317 ± 52 ps, $p=0.23$). When comparing nondiabetic eyes to eyes with diabetic retinopathy, significant differences were only found in the periphery ($P<0.01$) but not within the MacTel zone ($P=0.22$). Longitudinal changes in FLIO within the MacTel zone were similarly unrelated to the diabetes status.

Conclusions: Although MacTel has a high prevalence of diabetes, FLIO lifetimes from the MacTel zone seem to be unrelated to diabetes. This indicates that FLIO retains diagnostic abilities in patients with MacTel even in the presence of prediabetes, diabetes, and advanced diabetic retinopathy.

CONTROL ID: 3546651

SUBMITTER (NAME ONLY): Jeffrey Gemi

TITLE: Comparing Schirmer's test with other clinical outcomes in dry eye

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gemi, M. Watson, D. Narayanan, G.W. Ousler, Ora, Inc., Andover, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dry eye disease (DED) can be a debilitating disease of the eye. With several clinical tools available to evaluate severity and impact of the disease, it is often unclear how outcomes assessed using one test relates to others, specifically outside the context of therapeutic interventions. In this study, several different clinical tests were compared to examine their relationships.

Methods: Subjects (N=1149), who were brought in for screening prior to any therapeutic intervention were included for this analysis. The mean age (\pm SD) was 57.4 ± 15.5 years; 70% of the subjects were females and 30% were males. Subjects were divided into three groups based on results from unanesthetized Schirmer's Test; Normal group: Schirmer's >10 mm, Borderline: Schirmer's = 6 to 10mm, Severe DED: Schirmer's ≤ 5 mm. Several outcomes including corneal fluorescein staining (CFS) total and regional (NEI grading), Ocular Surface Disease Index (OSDI) overall score, disease duration and age were compared between the groups. For CFS, each region was graded on a scale of 0 to 3, with a total possible maximum score of 15. Correlation coefficient (R) was calculated for continuous variables. ANOVA was used for group comparisons. Only data from the right eye was included for analysis.

Results: Schirmer's scores showed significant moderate correlation with total CFS ($R = -0.29$, $p < 0.0001$). CFS was progressively worse in groups with reduced Schirmer's score. Total CFS was 9.2 ± 2.4 in severe Schirmer's group and 8.9 ± 2.4 in the borderline group compared to 7.4 ± 2.7 in normal group ($p < 0.0001$ for both comparisons vs normal). These results were also consistent for all 5 sub-regional staining analysis. Inferior CFS was 2.1 ± 0.6 in severe group, 2.0 ± 0.6 in borderline group and 1.8 ± 0.7 in the normal group ($p < 0.0001$ for both comparisons vs normal). Schirmer's score showed significant mild correlation with age ($R = -0.11$, $p = 0.0001$) with severe subjects being significantly older (mean 61.1 ± 13.4 years) than those with normal Schirmer's (mean 54.7 ± 16.6 years) ($p < 0.0001$). Severe subjects also had significantly longer DED duration (mean 11.5 ± 9.2 years) than those with normal Schirmer's (mean 9.8 ± 8.8 years) ($p = 0.02$).

Conclusions: Schirmer's score captures DED intensity that aligns with total and regional corneal staining measures as well as age and duration.

CONTROL ID: 3546652

SUBMITTER (NAME ONLY): Sanjib Saha

TITLE: Solubilized Ubiquinol Improves Reactive Oxygen Species Scavenging in Donor Corneal Endothelial Cells

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Saha, Y. Naguib, T. Aciri, K. Ebeid, S. Abdel-rahman, S. Kesh, A. Salem, Pharmaceutical Sciences and Experimental Therapeutics, The University of Iowa, The University of Iowa, Iowa City, IA, US, academic, Iowa City, Iowa, UNITED STATES|Y. Naguib, K. Ebeid, Pharmaceuticals, Minia University, EGYPT|J. Skeie, D. Nishimura, M.A. Greiner, Ophthalmology and Visual Sciences, The University of Iowa, The University of Iowa, Iowa City, IA, US, academic, Iowa City, Iowa, UNITED STATES|J. Skeie, G. Schmidt, D. Nishimura, M.A. Greiner, Iowa Lions Eye Bank, Coralville, Iowa, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress in corneal endothelial cells (CECs) preserved under hypothermic conditions is thought to be a major driver of cell death prior to surgery as well as decreased graft survival after keratoplasty. To mitigate oxidative damage and reactive oxygen species (ROS) in CECs, we aimed to develop a highly dispersible and stable formulation comprising a complex of ubiquinol and gamma-cyclodextrin (γ -CD) for use in aqueous-phase ophthalmic products including corneal storage media, intraocular irrigation solution, and topical eye drops.

Methods: Molecular docking study in AutoDock Vina indicated that γ -CD has the strongest binding affinity with ubiquinol. Ubiquinol/ γ -CD complex (UBCD) was prepared using the kneading method and its physiochemical properties were characterized. Stability of UBCD in Optisol-GS®, balanced salt solution, and Refresh® artificial tear eye drops for up to 1 week was determined by HPLC. High ROS-generating cells (A549) and B4G12 human corneal endothelial cells (HCEC-B4G12) were exposed to antimycin A, and UBCD ROS scavenging activity was measured using DHE fluorescence. Cytotoxic effect was determined up to 72 hours using MTS reagent. A NaviCyte vertical diffusion chamber was used to assess transcorneal penetrance of topically applied UBCD in human donor corneas. Lastly, UBCD penetrance of stored CECs was assayed using human corneas preserved for 7 days in Optisol-GS®.

Results: UBCD showed significantly higher stability compared to free ubiquinol by HPLC analysis. UBCD was more effective at lowering ROS at far lower concentrations compared to free ubiquinol. No evidence of cellular toxicity was detected in B4G12 cells. Topically applied UBCD penetrated the entire thickness of human donor corneas with significantly greater ubiquinol retention in the endothelium compared to free ubiquinol ($p=0.059$). UBCD demonstrated higher amounts of ubiquinol retained in the corneal endothelium of preserved donor corneas compared to free ubiquinol ($p<0.05$).

Conclusions: Findings indicate that UBCD can better preserve human CEC function during cold storage, and may be useful in preventing post-keratoplasty cell loss, increasing donor cornea preservation time, and reducing graft failure by scavenging ROS. UBCD's higher bioavailability and stability in the aqueous phase will allow its incorporation into a variety of products for ophthalmic use to protect CECs against oxidative damage.

CONTROL ID: 3546654

SUBMITTER (NAME ONLY): Erika Ellis

TITLE: Synaptic transmission in rod bipolar dendrites is desensitized and does not support significant TRPM1 responses in the degenerating retina

SESSION TITLE: Inner retinal function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Ellis, A.P. Sampath, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|H. Xu, J. Chen, Physiology and Neuroscience, University of Southern California, Los Angeles, California, UNITED STATES|G. Field, Neurobiology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: During the early stages of retinal degeneration rod photoreceptors begin to functionally uncouple from downstream rod bipolar cells, retracting their synaptic terminals. Previous studies have shown that rod bipolar cells lack a light-evoked response under these conditions even though some synaptic puncta remain at their dendritic tips. We tested whether the lack of rod bipolar response is due to impaired glutamate release from rods, or deficient mGluR6 transduction in bipolar dendrites.

Methods: Voltage clamp recordings from rod bipolar cells were made with patch electrodes in dark-adapted retinal slices from 1- and 2-month-old CNGB1^{neo/neo} mice, which display gradual retinal degeneration over 6 months. Light responses were evoked by an LED ($\lambda_{\text{max}} \sim 405\text{nm}$). Responses in the absence of light were evoked with puffs of the weak mGluR6 antagonist, CPPG, onto their dendrites while the retina was bathed in Ames' media with and without the strong mGluR6 agonist, DL-AP4.

Results: Light-evoked responses in 1- and 2-month-old CNGB1^{neo/neo} rod bipolar cells were largely absent, consistent with previous studies. In these same bipolar cells, puffs of the glutamate receptor antagonist CPPG (1 mM) also evoked either a minimal or no inward current. The size of the inward current increased in some rod bipolar cells when the solution bathing the retina also contained 5 mM DL-AP4. Puffs of CPPG in control retinas produced an inward current, which was also increased in the presence of DL-AP4.

Conclusions: Rod bipolar cells largely lack light-evoked responses in the degenerating retina, and under these conditions support minimal responses to puffs of CPPG. The increased response size to CPPG in the presence of DL-AP4 suggests that the molecular machinery remains in place to support responses, but that reduced rod glutamate release causes this mGluR6 machinery to be strongly desensitized. The retained ability of mGluR6 transduction to open TRPM1 channel during degeneration may explain why rod-to-rod bipolar cell synapses can be strengthened following the rescue of rod function.

CONTROL ID: 3546655

SUBMITTER (NAME ONLY): Julia Staverosky

TITLE: Knockout of the mechanotransducer, Integrin- α 7, in trabecular meshwork cells affects signaling through Akt and mTOR

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Staverosky, J.A. Vranka, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, UNITED STATES|V. Raghunathan, Optometry, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is a primary risk factor in the development and progression of glaucoma. The trabecular meshwork (TM) is responsible for maintaining homeostatic IOP. However, specific molecular regulators of IOP remain elusive. Integrin- α 7 (ITGA7) binds laminin and acts as a mechanotransducer in muscle tissue. We previously demonstrated that ITGA7 is upregulated in TM in response to elevated pressure, that the integrin α 7- β 1 heterodimer is expressed in the TM, and that signaling in response to plating on laminin is primarily through Akt. Here we investigate the expression of the three isoforms of Akt in hTM. We further elucidate the impact of ITGA7 on hTM cell signaling by knocking out ITGA7 and measuring its effect on downstream molecules in response to stretch.

Methods: Knockout of ITGA7 in hTERT-GFP immortalized (CL-27) and primary (2020-1183) hTM cells was achieved via lentiviral CRISPR. Percent knockout was determined using Western blotting post puromycin selection. hTM cells were plated on laminin coated Flexcell plates and stretched for 5, 15 or 30 minutes (n = 3 replicates). Protein expression levels and phosphorylation activity was determined by Western blot with protein and phospho-specific antibodies to the following downstream molecules: Akt, p38, JNK, Erk, mTOR, p70S6K, GSK3b, BAD, and 4EBP1.

Results: Knockout in the immortalized CL-27 hTM cell line was complete whereas it was approximately 50% in the primary cell strain. In immortalized hTM cells Akt activation in response to stretch on laminin was more pronounced in the absence of ITGA7. This correlated with increased mTOR phosphorylation. The results in primary cells were similar but less pronounced. There was no notable effect of stretch on the phosphorylation of JNK or Erk. We also demonstrate that all three isoforms of Akt are robustly expressed in hTM cells.

Conclusions: In the absence of ITGA7 Akt activity is increased in hTM cells in response to stretch on laminin. We previously showed that Akt is activated in response to laminin binding, the primary ligand of the integrin α 7- β 1 heterodimer. Thus an increase in Akt phosphorylation in the absence of ITGA7 is unexpected and suggests a key role in modulating signaling pathways in the TM. Further studies in primary hTM cells will provide insight into whether this effect is shared or specific to immortalized hTM cell lines.

CONTROL ID: 3546657

SUBMITTER (NAME ONLY): Yesha Raval

TITLE: Defining clinically meaningful improvement in ocular itching following treatment with reproxalap in an allergic conjunctivitis field trial

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Raval, P.J. Gomes, Allergy, Ora, Inc., Andover, Massachusetts, UNITED STATES|B. Cavanagh, T.C. Brady, Aldeyra Therapeutics, Inc., Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The clinically minimally important difference (MID) has not been defined for the commonly used 9-point ocular itching scale (0 – 4 with half-unit increments). Based on results from an allergic conjunctivitis (AC) field trial evaluating topical reproxalap compared to vehicle, the ocular itch score MID was calculated using a quality of life anchor-based approach and distributional statistics.

Methods: In a double-masked, multi-center field trial, 60 patients with AC were randomized 1:1:1 to receive topical ocular solutions of either 0.25% reproxalap, 0.5% reproxalap, or vehicle four-times daily for one month during allergy season. Ocular itching scores (Ora Calibra™, 0-4 scale) were compared to the Allergic Conjunctivitis Quality of Life Questionnaire (ACQLQ), comprised of 15 sub-scales (0-6) to quantify how bothersome symptoms and signs are across a variety of parameters. Assessments were obtained at baseline (Day 2) and at the end of the trial (Day 28). Average MID across all sub-scales was calculated by subtracting improvement in itching score for subjects that did not improve on the bother scale from improvement in itch score for subjects that improved on the bother scale by one point (mean difference method). Baseline standard deviation (SD) and standard error of measurement (SEM) were used to confirm the anchor-based findings.

Results: The MID was calculated to be 0.42 (95% CI 0.21, 0.64). Half of the baseline SD was 0.43, and the SEM was 0.48. The correlation of itch bother to ocular itch score was statistically significant ($p < 0.0001$), with an r value of 0.8.

Conclusions: Clinically meaningful change in the ocular itching scale was determined to be between 0.42 and 0.48 units, approximately the smallest unit of the itch score scale. The results provide clinically relevant context for the interpretation of AC clinical trials using the 9-point itching scale.

CONTROL ID: 3546659

SUBMITTER (NAME ONLY): Robert Shanks

TITLE: Bacterial metalloproteases inhibit epithelial cell migration and wound healing

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.M. Shanks, M. Al Higaylan, N. Stella, K.M. Brothers, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|R.M. Shanks, P.H. Thibodeau, Microbiology and Molecular Genetics, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of bacterial proteases in upon microbial pathogenesis of the cornea has been well studied; however, little work has gone into the effect these proteases have on corneal wound healing and cell migration. *Serratia marcescens* secretomes (proteins, lipids and other molecules) efficiently inhibit corneal cell migration, but no secreted proteins have been identified as being responsible for the phenotype. In this study we investigated the bacterial factors required to inhibit wound healing using an in vitro corneal epithelial model, specifically by analyzing the impact of bacterial metalloproteases.

Methods: Stratified layers of human corneal limbal epithelial cells were exposed to normalized and filter sterilized culture supernatants of *Serratia marcescens*, *Pseudomonas aeruginosa*, and *Klebsiella aerogenes*. Purified metalloproteases and the *P. aeruginosa* metalloprotease inhibitor AprI were also used to test wound healing.

Results: Mutation of individual *S. marcescens* metalloprotease genes prtS, slpB, and slpE did not affect this phenotype; however, mutation of all three genes eliminated the inhibitory phenotype. This suggested that the three metalloproteases had redundant function. Consistently, plasmid-based expression of each of the individual protease genes restored inhibition ability. Furthermore, exogenous addition of purified PrtS, SlpB, and SlpE metalloproteases was sufficient to inhibit cell migration, and the metalloprotease inhibitor protein, AprI, from *Pseudomonas aeruginosa* restored migration. The role of similar metalloproteases from other important pathogens was addressed.

Conclusions: Bacterial metalloproteases can inhibit cellular migration and our results suggest that protease inhibitors may be useful in experimental therapeutic approaches for chronic wounds or to promote wound healing.

CONTROL ID: 3546660

SUBMITTER (NAME ONLY): Emery Jamerson

TITLE: The Rainbow Brow in Thyroid Eye Disease

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Jamerson, C. Yang, Ophthalmology, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|A.Q. Tran, A.A. Tooley, M. Kazim, L.R. Dagi Glass, Oculoplastic and Orbital Surgery, Edward S Harkness Eye Institute, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe a novel physical exam finding in thyroid eye disease (TED) – the “Rainbow Brow (RB)” – and quantify the finding mathematically

Methods: Eyebrows of subjects with TED and controls were analyzed, and the presence of RB appearance was determined by unanimous agreement of 3 oculoplastic surgeons. Eyebrow curvature was assessed by plotting 15 points along the eyebrow (figure 1A). The quadrinomial was fitted to each eyebrow in Excel.¹ Mann-Whitney U analysis was performed on the five coefficients (a, b, c, d, & e) of the quadrinomial in the form $ax^4 + bx^3 + cx^2 + dx + e$ to evaluate for a difference in brow curvature. TED eyes with RB appearance were compared to age-sex-matched normal controls and other TED eyes without RB appearance. Univariable and multivariable logistic regression were performed to evaluate anatomical features that predicted RB appearance in TED eyes.

Results: A total of 271 eyes were analyzed (200 TED and 71 control). The majority of TED patients were female (82.5%) with a mean age of 53 ± 16 years. A Rainbow Brow was identified in 42% of TED patients, with 13% of TED patients having only unilateral RB appearance. Mann-Whitney U analysis of the quadrinomial coefficients yielded significant differences between RB eyes and controls for the coefficients a ($p = 0.034$), b ($p = 0.003$), c ($p = 0.001$), and d ($p = 0.000$). Similar analysis between TED eyes with and without RB appearance showed differences in coefficients a ($p = 0.034$) and b ($p = 0.041$). Features that were found to increase the odds of RB appearance included age greater than 50 (OR 2.307, $p = 0.009$, 95% CI 1.229 – 4.328) and the presence of brow fat expansion (OR 3.555, $p = 0.000$, 95% CI 1.935 – 6.529). When considering the contribution of these features in a multivariable analysis, only the brow fat expansion was a statistically significant contributing factor for RB appearance ($p = 0.009$).

Conclusions: The Rainbow Brow is a distinct entity in TED and is likely a consequence of the expansion of the brow fat pad. Eyes with RB have a statistically significant difference in eyebrow curvature compared to those of TED without RB and controls.

CONTROL ID: 3546661

SUBMITTER (NAME ONLY): Emma Finburgh

TITLE: The effects of fibroblast growth factor-10 on primary corneal and lacrimal gland human epithelial cell cultures

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.N. Finburgh, T. Noguchi, A.A. Abbas, D.F. Hakim, N.A. Afshari, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|H.P. Makarenkova, The Scripps Research Institute, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Emma Finburgh: Commercial Relationship: Code N (No Commercial Relationship) | Takako Noguchi: Commercial Relationship: Code N (No Commercial Relationship) | Anser Abbas: Commercial Relationship: Code N (No Commercial Relationship) | Dominic Hakim: Commercial Relationship: Code N (No Commercial Relationship) | Natalie Afshari: Commercial Relationship: Code N (No Commercial Relationship) | Helen Makarenkova: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Fibroblast growth factor-10 (FGF10) is a member of the fibroblast growth factor family-7 (FGF7), which controls epithelial morphogenesis and proliferation. This suggests that FGF10 signaling is necessary for the development of functional lacrimal glands. Several recent studies have implicated the in vitro biological functions of FGFs for the regeneration of different organs. However, little is known about the proliferative effects of FGF10 on human corneal and lacrimal glands. We aimed to study the proliferative effects of fibroblast growth factor-10 (FGF10) on human primary corneal and lacrimal gland epithelial cells.

Methods: Epithelial cells were derived from donor transplant tissue by incubating the corneoscleral rims in dispase for 1 hour and then gently scraping the cells from the epithelia. Cultures were expanded in growth-factor-containing medium for two passages and plated on 96-well plates. When the cells reached 50-70% confluency, the medium was replaced with a growth-factor-free base medium with FGF10 (30 ng/mL), with two different added supplements, or with combinations of FGF10 and each individual supplement. Cell viability/proliferation was examined by ATP quantification 72 hours after application. Similarly, human lacrimal gland cells cultured in defined medium were treated with FGF10 (20ng/ml), and cell proliferation was estimated 48-72 hours later.

Results: We found that FGF10, as well as the supplements, increased corneal cell proliferation by $23 \pm 20\%$, $32 \pm 16\%$, and $43 \pm 13\%$, respectively (\pm SD), compared to defined medium alone (N=8). However, combinations of FGF10 and each of the two supplements increased proliferation by $64 \pm 20\%$ and $66 \pm 27\%$, respectively (N = 8). Similarly, FGF10 resulted in increased lacrimal gland cell proliferation ($71 \pm 18\%$) cultured in defined medium with the second supplement compared to the defined medium with the second supplement on its own.

Conclusions: FGF10 is an effective proliferative factor for human corneal and lacrimal epithelial cells. Moreover, the synergistic effects of FGF10 in combination with specific growth supplements suggest the role of FGF10 in cell survival and as a potential use for expansion of human corneal and lacrimal gland epithelial cells.

CONTROL ID: 3546662

SUBMITTER (NAME ONLY): Santiago Delgado-Tirado

TITLE: Topical nanoemulsion of a RUNX1 inhibitor for the treatment of corneal neovascularization

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Delgado-Tirado, L. Gonzalez-Buendia, M. An, L.A. Kim, J. Arboleda-Velasquez, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|J. Ruiz-Moreno, Department of Ophthalmology, Castilla La Mancha University, Puerta de Hierro-Majadahonda University Hospital, SPAIN|

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ABSTRACT BODY:

Purpose: Runt-related transcription factor 1 (RUNX1) inhibition is a novel therapeutic strategy in ocular neovascularization and has previously been shown to be safe and effective for the treatment of retinal and choroidal neovascularization in animal models. Furthermore, topical application of RUNX1 inhibitor, Ro5-3335, as a nanoemulsion (eNano-Ro5) has demonstrated efficacy in experimental proliferative vitreoretinopathy. This study assessed the preclinical efficacy of topical RUNX1 inhibition in alkali burn-induced corneal neovascularization

Methods: 6-8-week-old C57BL/6J male and female mice were used for this study. eNano-Ro5 was administered topically four times a day after alkali burn-induced corneal neovascularization. To induce the corneal injury, a 2-mm paper disc soaked in 1M NaOH was placed on the surface of the central cornea for 30 seconds followed by a thorough washing with saline solution for 60 seconds. Animals were evaluated with slit lamp examination at days 1, 3, 7 and 14. Corneal defect, corneal opacity and corneal neovascularization were analyzed after treatment with either eNano-Ro5 (n=22) or vehicle (n=23) for 14 days after alkali burn. We also included another group treated with Dexamethasone 0.1% (n=9)

Results: RUNX1 positive cells were observed after injury by immunofluorescence within the corneal tissue. We found a significant reduction in corneal defect in the eNano-Ro5 treated group compared to control at day 14 ($P<0.05$). In addition, corneal opacity was significantly improved at day 1, 7 and 14 in the eNano-Ro5 treated animals ($P<0.05$, $P<0.05$ and $P<0.01$, respectively). Corneal neovascularization was also significantly reduced at day 14 compared to control ($P<0.01$). In the dexamethasone group, we found persistent corneal defect ($P<0.001$), improved corneal transparency at day 3, 7 and 14 ($P<0.001$, $P<0.01$ and $P<0.001$) and reduced neovascularization at day 7 and 14 ($P<0.05$ and $P<0.001$)

Conclusions: The severe reduction in corneal thickness observed in the dexamethasone-treated group may explain the reduced corneal opacity and neovascularization. Taken together, these findings suggest a beneficial effect of RUNX1 inhibition with topical eNano-Ro5 in preventing the blinding effects of alkali burn injury. This could be a potential therapy to treat this sight-threatening condition

CONTROL ID: 3546663

SUBMITTER (NAME ONLY): Kendra Johnson

TITLE: Caspase-8 plays an apoptosis-independent role in retinal angiogenesis.

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Johnson, M. Choi, C. Troy, Pathology and Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|C. Troy, Neurology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Previous studies have shown certain caspases to be activated in the course of vascular development, but the specific roles of these proteases remain unclear. In this study, we investigate previously unexplored mechanisms and signaling pathways involved in the outgrowth and subsequent remodeling of the retinal vasculature. We hypothesize that caspase-8 (Casp8) modulates signaling pathways involved in retinal angiogenesis.

Methods: Retina flatmounts from C57BL/6 pups aged P2-P21 were stained for Casp8 and TUNEL. Vascular development was assessed in retinas isolated from inducible endothelial cell specific Casp8 knock mice (EC Casp8 KO) and inducible microglia-specific casp8 knock out mice (mG Casp8 KO) at P7, P10 and P14. At P7 cytokine array was performed and at P10 biocytin-TMR was used to assess barrier establishment in EC Casp8 KO mice. Student's T-test was used for statistical analysis.

Results: Casp8 was expressed in endothelial cells and microglia during early retinal angiogenesis, with expression peaking between P7-P10. Casp8 was selectively activated in microglia. TUNEL assay revealed few apoptotic cells during angiogenesis. At P7, EC Casp8 KO resulted in a significant decrease in vascular outgrowth ($66.90 \pm 2.52\%$ in EC Casp8 KO vs. $83.92 \pm 1.76\%$ controls; $p < 0.0001$), vessel area ($59.96 \pm 2.75\%$ in EC Casp8 KO vs. $78.45 \pm 2.09\%$ controls; $p < 0.0001$) and vascular density ($49.23 \pm 1.90\%$ in EC Casp8 KO vs. $49.23 \pm 1.33\%$ in controls; $p < 0.0001$). The delay in vascular outgrowth persisted up to P14, however barrier establishment was not affected. EC Casp8 KO also resulted in premature vessel regression and increased microglia localization at the vasculature, likely associated with an increase in proinflammatory cytokines. mG Casp8 KO did not affect vascular outgrowth or remodeling, however this did result in a significant decrease in microglia associated with the vasculature and a change in microglia morphology.

Conclusions: Casp8 function during early retinal angiogenesis is independent of apoptosis. EC Casp8 KO resulted in delayed vascular outgrowth and premature vascular remodeling, however mG Casp8 KO had no effect on vascular development indicating cell specific roles of the protease. Microglia localization and activation was also perturbed with EC Casp8 KO indicating a role of caspase-8 in the cell-to-cell communication between endothelial cells and microglia.

CONTROL ID: 3546665

SUBMITTER (NAME ONLY): Alexandra Vitale

TITLE: A phenotypic analysis of uveitic diseases using Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO)

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Vitale, L. Sauer, N.K. Modersitzki, M.B. Larochelle, A. Shakoor, A.T. Vitale, P.S. Bernstein, John A. Moran Eye Center, University of Utah Health, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveitis is a group of ocular inflammatory diseases that can derive from both infectious and noninfectious causes. This study investigates patients diagnosed with a variety of uveitic diseases utilizing Fluorescence Lifetime Imaging Ophthalmoscopy (FLIO).

Methods: 49 eyes of 49 subjects with varying uveitic diseases (mean age 48 ± 19 years) and 49 age-matched healthy subjects ($p=0.899$) were investigated in this study. Clinical grading of uveitic disease subtypes were confirmed by uveitis specialists (ATV, AS, MBL). FLIO images of a 30° retinal field centered at the fovea were acquired using a prototype Heidelberg Engineering Spectralis-based FLIO. FLIO lifetimes were recorded in short (498-560 nm, SSC) and long (560-720 nm, LSC) spectral wavelength channels, with mean autofluorescence lifetimes (t_m) calculated and analyzed.

Results: FLIO is able to categorize uveitic diseases based on phenotype, and lifetimes of patients with uveitic diseases showed significant prolongation in central, inner and outer ring regions of the ETDRS grid compared to age-matched controls ($p=0.03$, $p=0.006$, $p=0.003$, respectively). FLIO lifetimes were variable depending on the type of disease with shortened lifetimes correlating to regions of active inflammation or in areas adjacent to lesions.

Conclusions: FLIO can effectively discriminate between various uveitic diseases with high specificity. While prolonged FLIO lifetimes were found in regions of atrophy or scarring, shortened FLIO lifetimes were observed in regions adjacent to lesions and in patients with clinically active ocular inflammation. FLIO may provide insight into understanding these complex diseases, as well as monitoring disease activity, progression, and remission.

CONTROL ID: 3546666

SUBMITTER (NAME ONLY): Meaghan McGowan

TITLE: Intrauterine Growth Restriction (IUGR) as a Risk Factor for Retinopathy of Prematurity (ROP) Severity in a Population of Black Infants

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Although the two major risk factors for the development of retinopathy of prematurity (ROP) are premature birth and low birth weight, there is a question as to whether intrauterine growth restriction (IUGR) may be an important risk factor for ROP. A previous study that investigated this relationship found no correlation, however the study population consisted of only non-Black subjects. This retrospective cohort study aims to further explore whether IUGR impacts the development of ROP and its severity in a subset of Black infants to see how the inclusion of these demographics impact any correlation that may exist.

Methods: This is a single center retrospective chart review of all infants admitted to the UI Hospital and Health System NICU between 1/1/2010 and 1/1/2020 with a birth weight less than or equal to 1500g who had a pupillary dilation event. Infants were excluded if they died or were transferred before an ROP exam or had missing data in the chart. IUGR was defined as less than the 10th percentile for gestational age using the Fenton growth chart. Statistical analyses included single variable analysis, Spearman correlation and cumulative logistic regression analysis for predicting ROP stage from IUGR, Black ancestral background, and the interaction of these two parameters.

Results: The study population consisted of 518 infants, with 341 (66%) Black infants. In this subset of Black infants, 47 (14%) had IUGR and 149 (44%) were diagnosed with ROP. Within the Black population, IUGR vs. non-IUGR did not significantly impact the risk of an ROP diagnosis (0.56 OR, 95% CI 0.029 – 1.08, P=0.08) or the stage of ROP should it exist (Spearman Rho= 0.16, P=0.05). In contrast, within the subset of all infants with IUGR, we found a significant association between IUGR and ROP stage between Black and non-Black patients (P=0.01). Black infants with IUGR and ROP are more likely to have a more severe stage of ROP than their non-Black counterparts.

Conclusions: Our results illustrate that although IUGR is not a significant risk factor for ROP in Black infants, those that do develop ROP are at a higher risk for more severe disease compared to non-Black infants. Further analysis into the differences between these two populations is warranted.

CONTROL ID: 3546669

SUBMITTER (NAME ONLY): Khulan Batsuuri

TITLE: Genetic Ablation of Cx43 in Astrocytes is Neuroprotective in Experimental Glaucoma and Optic Nerve Injury

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Batsuuri, A. Toychiev, M. Srinivas, SUNY College of Optometry, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reactivity of astrocytes in the retina and optic nerve head (ONH) is observed in glaucoma and other optic nerve injuries. Astrocytes are densely interconnected by gap junction (GJs) formed by connexin 43 (Cx43). The role of astrocytic connectivity on glial reactivity and RGC survival in optic nerve degeneration is not fully understood. Here, we assessed expression of Cx43 with sustained intraocular pressure (IOP) elevation and after optic nerve crush injury. We also examined whether deletion of Cx43 in astrocytes impacted RGC loss and ONH astrocyte reactivity in the two injury models.

Methods: The astrocyte-specific Cx43 knockout (KO) mouse was established using the Cre-loxP recombination system. Experimental glaucoma was induced in C57BL/6 (WT) and Cx43KO mice by intracameral injection of polystyrene microbeads. Optic nerve of one eye was crushed for 10 seconds using fine curved forceps ~ 1 mm behind the eyeball. Immunohistochemistry was used to assess Cx43 expression, RGC survival (using Brn3a labeling), and astrocyte reactivity in the ONH (using GFAP labeling), after 4 and 8 weeks of IOP elevation and 7 days post nerve crush. Student's t-test was used for statistical analyses.

Results: IOP elevation for 8 weeks produced a 35% increase in astrocytic Cx43 expression in the retina (n=5, p=0.001) and ONH (n=3, p=00001). Similarly, Cx43 expression was increased by 30% after optic nerve crush injury (n=5, p=0.0001). Deletion of Cx43 in astrocytes was neuroprotective in glaucomatous injury, with RGC survival increasing by 57% at 4 weeks (n=5-8, p=0.03) and 63% by 8 weeks (n=7-8, p=0.0003) compared to control eyes. The absence of Cx43 also increased viable RGCs after optic nerve crush by twofold compared to control eyes (n=8, p=0.003). Finally, Cx43 deletion caused a decrease in astrocytic reactivity in the ONH of bead injected eyes compared to WT (n=3, p<0.05). However, astrocyte reactivity in the retina was unaffected by Cx43 deletion (n=5-6, p=0.55).

Conclusions: Results in two different models of optic nerve injury indicate that astrocytic Cx43 channels contribute significantly to RGC death. There is an upregulation of Cx43 in astrocytes in both models, and a reduction in astrocyte reactivity in the ONH upon Cx43 deletion, suggesting that GJ coupling might lead to the spread of signals associated with astrocyte reactivity.

CONTROL ID: 3546670

SUBMITTER (NAME ONLY): Alex Gauthier

TITLE: The Role of NQO1 in the Increased DNA Damage Response in Fuchs Endothelial Corneal Dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Gauthier, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|A. Gauthier, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Alex Gauthier: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Fuchs Endothelial Corneal Dystrophy (FECD) is an oxidative stress disorder characterized by accelerated loss of corneal endothelial cells (CEnCs) and high amounts of DNA damage, mediated partly by loss of NAD(P)H:quinone oxidoreductase 1 (NQO1). Ataxia Telangiectasia Mutated (ATM) is a major DNA damage response (DDR) kinase in post-mitotically arrested cells, which orchestrates the modulation of cell cycle checkpoints, DNA repair, and/or apoptosis. In this study, we investigate the role of NQO1 on ATM -mediated DDR in FECD pathogenesis.

Methods: Immortalized normal CEnC line HCEnC-SV-67F-16 and FECD patient-derived cell line FECD-SV-73F-74 (with TCF4 CTG repeat expansion) were treated with or without 25 μ M menadione (MN). Additionally, wild-type and NQO1 null CEnCs were irradiated with UVA (10 or 25 J/cm²) and then lysed at 1, 3, and 24 h post UVA. The phosphorylation status and levels of pATM (Ser1981) and its downstream effectors pCHK2 (Thr68), γ H2AX (Ser139), and binding partner, pNBS1 (Ser343), were evaluated by Western blotting.

Results: In HCEnC-SV-67F-16 cells, MN induced a time-dependent increase in DNA damage markers γ H2AX and pATM. FECD-SV-73F-74 cells exhibited increased activation of pATM (6.9-fold), which was significantly greater compared to HCEnC-SV-67F-16 (4.3-fold) after 1 hr of MN treatment. There were no significant differences observed in downstream effectors pCHK2 and γ H2AX between FECD-SV-73F-74 and normal CEnCs. Similarly, 10 J/cm² UVA-irradiation-induced a significant increase in the phosphorylation of pATM (3.03-fold), γ H2AX (4.23-fold), pCHK2 (1.77-fold) in NQO1 null cells compared to WT CEnCs. UVA-irradiated NQO1 null cells maintained the phosphorylation of pATM after 3 h (2.44-fold), whereas WT cells returned to baseline (0.98-fold).

Conclusions: These results indicate there is increased activation of ATM-mediated DDR upon ROS induction in FECD. NQO1 null CEnCs exhibit enhanced and prolonged activation of ATM-mediated DDR compared to WT cells after irradiation with UVA. Thus, NQO1 deficiency in CEnCs may play an important role in pathogenesis of FECD.

CONTROL ID: 3546671

SUBMITTER (NAME ONLY): Anser Abbas

TITLE: Evaluating the accuracy and utility of a cataract simulation video for relieving patient anxiety

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Abbas, R. Sella, R. Lian, S.D. Fuller, S.S. Bentley, H. Fukuoka, N.A. Afshari, Shiley Eye Institute and Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patient anxiety about cataract surgery can lead to undesired outcomes before and during surgery. We performed a cross-sectional survey-based study to test whether a point-of-view cataract simulation video could (1) accurately represent what patients see during surgery and (2) help relieve patient anxiety.

Methods: In follow-up clinical visits, 100 cataract surgery patients were shown a video depicting cataract surgery from a patient's point of view. The patients were then given a multiple-choice questionnaire about their recollections of visual experiences from surgery. They were asked to evaluate how well the video matched their experience, whether they would have wanted to see the video before their operations, and whether they would recommend the video to other patients.

Patients received surgery with monitored anesthesia care (MAC). Patients younger than 18 years or with a post-operative best-correct visual acuity worse than 20/50 in both eyes were excluded. The simulation video was created in by performing cataract surgery on a porcine eye.

Results: Of patients surveyed (n=100), 78% (n=78) recalled visual experiences during surgery, (65%, n=65) saw bright lights and flashes, 18% (n=18) saw instruments or other objects.

Of patients who recalled visual experiences (n=78), 47.4% (n=37) said that the video was the same or similar to what they experienced overall. Of patients who saw bright lights and flashes (n=65), 46.1% (n=30) said that the video was the same or similar. Of patients who saw objects (n=18), 72.2% (n=13) said that the video was the same or similar.

Thirty-six percent of patients surveyed (n=36) said that seeing the video before their procedures would have helped them relax, and 48% of patients (n=48) would recommend the video to future patients.

Conclusions: Reported visual experiences during surgery differ widely and a simulation video may be helpful in reducing anxiety in patients undergoing cataract surgery.

CONTROL ID: 3546673

SUBMITTER (NAME ONLY): Katy Liu

TITLE: Macrophage Ontogeny and Distribution within the Conventional Outflow Tract

SESSION TITLE: Microglia and other Macrophages in Health and Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Liu, D. Schuman, G. Li, W. Stamer, D.R. Saban, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macrophages reside in tissues throughout the eye and their phenotypes and functions are shaped by both their sub-anatomic location in tissue as well as their respective developmental origins (ontogeny). Developmentally, macrophages are mostly either (a) derived prenatally and are long-lived; or, (b) from circulating monocytes and are short-lived. The purpose of this study was to characterize the presence and distribution of long-lived versus short-lived macrophages in the conventional outflow tract.

Methods: We took advantage of Cx3cr1-YFP^{CreER/+} transgenic mice with various Cre reporters to tamoxifen-induce conditional labeling of tissue resident macrophages in anterior segment tissues. Mice were tamoxifen pulsed (60 mg/kg) and rested. Fixed anterior segment whole mounts were prepared. Tissues were labelled with antibodies against cluster of differentiation 31 (CD31), alpha-smooth muscle actin (Sma-1) and DAPI, along with their isotype controls in separate cohorts. We categorized long-lived macrophages as YFP⁺ cells that retained the Cre reporter labeling (>2 weeks post tamoxifen pulse), whereas short-lived macrophages did not (O’Koren, 2019). Immunolabelled tissue samples were imaged by confocal microscopy.

Results: Macrophages were found throughout the conventional outflow tract, including the trabecular meshwork (TM), Schlemm’s canal (SC), collector channels and surrounding distal vessels (DVs). Macrophage density was measured in the DVs (84 ±42 cells per high-powered field (HPF), 40X magnification) and in the SC and TM (103 ± 32 cells per HPF). Macrophages were counted and averaged over 6-7 randomly selected HPFs imaged from anterior segment whole mounts from 3 mice. Long-lived macrophages comprised a subpopulation of macrophages in the TM, SC, and around the DVs. In the SC and TM, macrophages generally retained a dendritic morphology, whereas DV-associated macrophages were largely elongated or rounded in appearance and in close apposition to the vessels.

Conclusions: Macrophages are present throughout the conventional outflow tract of TM, SC and DVs. The presence of short-lived and long-lived or tissue resident macrophages suggests two distinct populations of macrophages reside in the outflow tract.

CONTROL ID: 3546674

SUBMITTER (NAME ONLY): Heba Altarawneh

TITLE: LONGITUDINAL ANALYSIS OF RETINAL AND BRAIN ATROPHY IN MULTIPLE SCLEROSIS

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Altarawneh, I.N. Petropoulos, G. Ponirakis, A. Khan, H.Y. Gad, F. Al-Shibani, M.H. Rehman, D. Al-Merekhi, K. John, R. Malik, Research Division, Weill Cornell Medicine - Qatar, Doha, QATAR|A. El-Sotouhy, A. Own, D. Dirk Deleu, B.C. Canibano, N. Akhtar, Hamad Medical Corporation, Doha, Ad Dawhah, QATAR|A. Shuaib, Medicine, University of Alberta Faculty of Medicine & Dentistry, Edmonton, Alberta, CANADA|

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ABSTRACT BODY:

Purpose: Non-invasive quantification of retinal axonal and neuronal loss have been proposed as surrogate markers of axonal loss in multiple sclerosis (MS). We assessed their longitudinal relationship with measures of brain atrophy and disability.

Methods: Retinal nerve fiber layer (RNFL) thickness and total macular volume (TMV) were estimated in patients with MS (n=60) and age-matched, healthy controls (n=52) by optical coherence tomography (OCT) at baseline and 24-month follow-up. Brain volumes were quantified from cranial magnetic resonance imaging using NeuroQuant®. Neurological disability was assessed by means of the expanded disability status scale.

Results: In patients with MS compared to controls there was a significant reduction in RNFL ($p<0.0001$) and TMV ($p=0.0004$) at baseline. Specifically, RNFL was significantly reduced in the temporal-superior ($p<0.0001$), temporal ($p<0.0001$), temporal-inferior ($p<0.0001$), nasal-inferior ($p=0.0005$) and nasal-superior ($p=0.001$) aspects of the optic nerve. Patients with secondary progressive MS (SPMS) showed a greater reduction in RNFL ($p=0.003$) and TMV ($P<0.0001$) compared to patients with relapsing-remitting MS (RRMS). RNFL / TMV were significantly correlated (Pearson's r) with grey matter (GM) ($p=0.0003/p=0.0287$), temporal lobe (TL) ($p=0.0007/p=0.0287$), thalamus (TH) ($p=0.0001/p=0.0012$), putamen (PU) ($p<0.0001/p=0.0006$) and whole brain (WB) ($p=0.0028/p=0.0206$) volumes at baseline. At follow-up, there was a further significant reduction in temporal-inferior RNFL ($p=0.009$) and TMV ($p=0.009$). Patients with SPMS had significantly more advanced loss of RNFL ($p=0.01$) and TMV ($p=0.02$) compared to patients with RRMS. RNFL / TMV were significantly correlated with GM ($p=0.0143/p=0.0449$), TL ($p=0.0141/p=0.0381$), TH ($p=0.0004/p=0.0019$) PU ($p<0.0001/p=0.0012$) and WB ($p=0.0015/p=0.0211$) volume at follow-up. Patients with baseline TMV $< 25^{\text{th}}$ percentile ($n=12$) showed a further significant reduction at follow-up in GM ($p=0.02$), TL ($p=0.03$), caudate ($p=0.009$), TH ($p=0.0003$), PU ($p=0.009$) and WB ($p=0.001$) volume. There was no significant relationship between retinal measures and clinical disability at baseline or follow-up.

Conclusions: There is a strong longitudinal relationship between retinal and brain atrophy in MS which further underpins the viability of OCT as a surrogate measure of axonal loss.

CONTROL ID: 3546675

SUBMITTER (NAME ONLY): David Peprah

TITLE: Diabetes and Diabetic Retinopathy in African-born Blacks Living in America: A Cross-sectional Study

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Working with African-born Blacks living in America, the aims were to: (1) determine the prevalence and risk factors associated with diabetic retinopathy (DR) (2) evaluate for other ocular abnormalities

Methods: This was a cross-section evaluation of 265 African-born blacks living in the United States (male 62%, age 39.7 ± 10.2 y (mean \pm SD), BMI 27.8 ± 4.5 kg/m²) who self-identified as healthy. Participants had oral glucose tolerance test (OGTT) to determine glucose tolerance status, comprehensive eye exams, spectral domain optical coherence tomography (OCT) and fundus photos. In addition, A1C, glycated albumin (GA) and fructosamine levels were determined, allostatic load score (ALS) as a measure of physiologic stress was calculated and visceral adiposity was assessed with abdominal CT scan.

Results: Newly diagnosed diabetes mellitus (DM) occurred in 10.2% (27/265), preDM in 40.0% (106/265), normal glucose tolerance (NGT) in 49.1% (130/265). Retinopathy was present in 1.5% (4/265) overall, 18.5% (3/27) in those with DM, 1.0% (1/104) with preDM, and 2.3% (3/130) with NGT. The 3 NGT cases with retinopathy had hypertension and were excluded from analysis. Among diagnostic testing modalities, on univariate analyses, statistical significant associations with DR were found in fasting plasma glucose ($P < 0.002$), 2h glucose from the OGTT ($P = 0.010$), and fructosamine ($P = 0.025$) but no associations were found with A1C or GA ($P = 0.089$, $P = 0.142$, respectively); and higher visceral adipose tissue and allostatic load score were associated with DR ($P = 0.049$ and $P = 0.025$, respectively). The number of participants affected with DR is too low for meaningful analyses with multivariate regression. Additional ocular features evaluated showed 34.7% of all participants had 0.5 or greater cup/disc ratio while the mean intraocular pressure was 15 ± 3 mmHg. The mean visual acuity was 20/25 for those without retinopathy and 20/36 for those with retinopathy ($P = 0.037$). The retinal thickness measured by OCT demonstrated no differences in the inner retinal thickness when comparing glycemic status.

Conclusions: In conclusion, the overall combined prevalence of DM and preDM was high (50.2%) in this population, DR was present in 18.5% with DM. There is relatively high proportion of the participants with large cup/disc ratios. Multivariate regression was not performed. These findings warrant further exploration in this population.

CONTROL ID: 3546677

SUBMITTER (NAME ONLY): Ishrat Ahmed

TITLE: Tele-Ophthalmology Screening for Sickle Cell Retinopathy Using Ultra-Widefield Fundus Photography

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This is a proof-of-concept study to determine the accuracy of non-mydriatic ultra-widefield (UWF) fundus photography taken by clinic personnel in screening for sickle cell retinopathy (SCR) in a non-ophthalmology clinic setting.

Methods: This prospective study compared SCR findings on UWF fundus photography to the gold standard dilated fundus exam (DFE). Adults 18 years or older with sickle cell disease and a DFE within two years of acquisition of fundus photos were included. An UWF fundus camera was used to obtain bilateral non-mydriatic fundus photos by clinic personnel during the participants' routine hematology appointment. These photos were graded by two separate masked retina specialists to assess image quality, visualization of peripheral retina, presence of non-proliferative SCR, and presence of proliferative sickle retinopathy (PSR). A third retina specialist reviewer assessed photos in instances of disagreement.

Results: Forty-five participants (88 eyes) met inclusion criteria. The average age was 37.2 ± 10.8 years. Hemoglobin SS disease was the most common genotype ($n = 30$), followed by hemoglobin SC ($n = 9$) and sickle cell beta thalassemia ($n = 6$). Non-proliferative SCR and PSR were documented in 31.8% and 21.6% of eyes, respectively, on DFE. When comparing UWF grading to DFE for the presence of non-proliferative SCR, 54.4% of eyes were graded accurately and 20.5% were graded inaccurately ($p = 0.014$). For the 18 eyes graded inaccurately by UWF imaging, most were false positives ($n = 16$). UWF image quality was insufficient for grading in 18 eyes. No consensus was reached for 4 eyes. When assessing for PSR, 65.9% of eyes were graded accurately and 4.5% were graded inaccurately by UWF imaging, all as false negatives. UWF image quality was insufficient for grading for 23 eyes and there was no consensus for 3 eyes. When UWF image quality was sufficient, UWF grading was accurate for non-proliferative SCR and PSR in 72.7% and 93.5% of eyes, respectively ($p < 0.001$ for both). Of note, one participant had active sea-fan neovascularization detected on UWF imaging and DFE, and was treated with laser photocoagulation.

Conclusions: UWF imaging provides a useful screening modality for SCR, particularly for proliferative PSR. Tele-ophthalmology-based SCR screening in a hematology clinic may improve adherence to SCR screening recommendations and identify patients with PSR who may require treatment.

CONTROL ID: 3546678

SUBMITTER (NAME ONLY): Mi Zhou

TITLE: Extracellular vesicles from R345W-Fibulin-3 retinal pigment epithelial cells induce epithelial-mesenchymal transition in recipient cells.

SESSION TITLE: Retinal diseases: molecular and biochemical disease mechanisms

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Our previous studies found that expression of R345W-Fibulin-3 induces retinal pigment epithelial (RPE) cells to undergo epithelial-mesenchymal transition (EMT). In the current study we investigated the effect of the R345W-Fibulin-3 mutation on the size, cargo and function of extracellular vesicles (EVs) derived from RPE cells, as well as the role of these EVs in regulating RPE cell dysfunction.

Methods: EVs were isolated from the media of ARPE-19 cells by conventional ultracentrifugation or density gradient ultracentrifugation. The amount and size distribution of EVs were determined by Nanoparticle Tracking Analysis (NTA). EV protein concentrations were quantified using the DCTM Protein Assay (Bio-Rad). EV cargo were analyzed by unbiased proteomics using LC-MS/MS with subsequent pathway analysis (Advaita). The EV-associated TGF- β 1 protein was measured by ELISA. The effect of EV transplantation on ARPE-19 migration was evaluated using a scratch-injury assay.

Results: TEM imaging revealed concave-appearing vesicles, while cryo-EM imaging showed spherical vesicles with two subpopulations of EVs: a small group with diameters around 30nm and a large group with diameters around 100nm. Imaging also indicated a greater number of small EVs (~30 nm) in the mutant group compared to the WT group. This result was further confirmed by NTA showing that, in the mutant group, the particle size distributions were smaller than those of the WT EVs. The protein concentration per EV in the mutant group was not significantly different from that of the WT group. Proteomics identified critical members of sonic hedgehog (SHH) signaling and ciliary tip components in the EVs derived from WT ARPE-19 cells, whereas EVs derived from mutant ARPE19 cells contained EMT mediators. ELISA confirmed the elevated TGF- β 1 associated with mutant EVs compared to WT EVs. Critically, EV transplant studies showed that treatment of recipient cells with EVs derived from mutant cells was sufficient to increase migration and elevate EMT markers in RPE cells after scratch-injury.

Conclusions: The protein cargo of EVs is determined by the phenotype of their parental cells. Expression of R345W-Fibulin-3 mutation also alters the size and autocrine function of EVs. Notably, EVs derived from RPE cells expressing R345W-Fibulin-3 are sufficient to induce EMT in wild-type RPE cells.

CONTROL ID: 3546680

SUBMITTER (NAME ONLY): Timothy P.H. Lin

TITLE: Assessment of risk of normal tension glaucoma progression via deep-learning based retinal-vessel caliber measurement

SESSION TITLE: Deep Learning and Ocular Blood Flow

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Lin, H. Hui, P. Chan, Y. Wang, R. Shen, C. Tham, C. Cheung, Ophthalmology and Visual Sciences, The Chinese University of Hong Kong Faculty of Medicine, Hong Kong, HONG KONG|P. Chan, C. Tham, Hong Kong Eye Hospital, Hong Kong, HONG KONG|T.Y. Wong, Singapore Eye Research Institute, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Vascular insufficiency has been suggested to be of pathogenic role in normal tension glaucoma (NTG). This study evaluated the associations between baseline retinal-vessel caliber measured by an automated deep-learning system to the risk of NTG progression.

Methods: In this longitudinal cohort study, 390 eyes from 253 NTG patients with a follow-up period of ≥ 24 months were included. Central retinal arteriolar equivalent (CRAE) and central retinal venular equivalent (CRVE) were measured from retinal photographs by a validated deep-learning system (SIVA-DLS). We assessed the agreement of retinal vessel caliber measurements between SIVA-DLS and humans, and used the Cox proportional-hazards model to examine the relationships between baseline retinal vessel caliber and subsequent NTG progression. We further assessed the incremental value of adding the retinal vessel caliber for prediction of NTG progression beyond previously reported risk factors. NTG progression was defined as progressive retinal nerve fiber layer (RNFL) thinning over time on Cirrus HD-OCT detected by its built-in guided progression analysis.

Results: Agreement of retinal vessel caliber measurement between SIVA-DLS and human was good to excellent, with intraclass correlation coefficients of retinal vessel caliber between SIVA-DLS and human ranging from 0.87 to 0.90. Sixty-nine eyes (17.7%) developed NTG progression over the follow-up period. Narrower CRAE (hazard ratio [HR] 1.36 [95%CI 1.05, 1.76]) and CRVE (HR 1.38 [95%CI 1.03, 1.84]) at baseline were independently associated with NTG progression in the multivariable model. Addition of baseline CRAE and CRVE improved the discrimination (C-statistic 0.703 vs 0.695, $p=0.038$ and 0.704 vs 0.695, $p=0.038$, respectively) of NTG progression risk beyond previously reported risk factors.

Conclusions: This study demonstrated significant associations between baseline retinal vessel caliber and risk of NTG progression. These findings provided evidence to support the hypothesis of vascular insufficiency in NTG pathogenesis and the utility of a high-throughput deep-learning system for risk assessment in NTG.

CONTROL ID: 3546682

SUBMITTER (NAME ONLY): Augustine Bannerman

TITLE: Contrast Sensitivity Function in Cataract Disease measured with Active Learning

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Bannerman, M. Kasetty, F. Vingopoulos, I. Garg, R. Silverman, Z. Luo, J. Cho, R. Katz, A.C. Lorch, L.A. Lesmes, J.B. Miller, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize contrast sensitivity function (CSF) in cataract and pseudophakia compared to healthy control eyes using a novel quick CSF test with active learning algorithms.

Methods: CSF was prospectively measured in eyes with visually significant cataract, at least 2+ nuclear sclerosis (NS) and visual acuity (VA) more than 20/50 (cataract group), as well as in pseudophakic eyes (pseudophakic group) and in healthy control eyes with no more than 1+ NS and no visual complaints (control group), using the novel Manifold Contrast Vision Meter (Adaptive Sensory Technology, San Diego, CA). Outcomes included Area under the Log CSF (AULCSF), contrast acuity (CA), and CS thresholds at 1, 1.5, 3, 12, and 18 cycles per degree (cpd). A subgroup analysis as performed on cataract eyes with good acuity ($VA \geq 20/25$)

Results: A total of 167 eyes were included, 58 eyes in the cataract group, 77 controls, and 32 pseudophakic eyes with respective AULCSF of 1.053 (0.352) vs 1.228 (0.318) vs 1.256 (0.360). When controlling for VA and age in our multivariate regression model, the presence of cataract was associated with significantly reduced AULCSF ($P=0.04$, $\beta=-0.11$) and contrast threshold at 6 cpd ($P=0.01$, $\beta=-0.16$) compared to controls. Of note, contrast threshold at 6 cpd was significantly reduced even in the subgroup of cataract eyes with $VA \geq 20/25$ ($P=0.02$, $\beta=-0.16$). The presence of cataract was not associated with significantly reduced CSF threshold at lower (1, 1.5, 3 cpd) or higher (12, 18 cpd) spatial frequencies. Pseudophakia was not associated with significantly different contrast outcome measures compared to control eyes.

Conclusions: The novel qCSF test was able to detect disproportionate significant contrast deficits at 6 cpd in cataract eyes, that remained significant even in the cataract eyes with $VA \geq 20/25$.

CSF testing may be a valuable addition to standard cataract evaluation to enhance surgical decision-making, particularly in patients with subjective visual complaints despite good VA.

CONTROL ID: 3546683

SUBMITTER (NAME ONLY): Mojtaba Falahati

TITLE: Oblique Multi-periscopic Prism for Field Expansion in Homonymous Hemianopia Driving

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Falahati, N.M. Kurukuti, K. tang, E. Peli, J. Jung, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M. Falahati, N.M. Kurukuti, K. tang, E. Peli, J. Jung, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Peripheral prisms have been used for field expansion in homonymous hemianopia (HH). We recently developed multi-periscopic prism (MPP) using half-penta prisms, which provided higher prism power (45°) with wider eye scanning (15°) and better image quality. For a useful field expansion through a car windshield, we further develop oblique peripheral MPP that provides a vertical shift as well as a horizontal shift.

Methods: Five half-penta prisms that provide 45° angular shift through a double internal reflection were arranged in a cascade to enable 45° wide field expansion into the blind side. Since the peripheral prisms are located 20° above and below the horizontal midline, we designed the oblique MPP to achieve 18° vertical shift toward the horizontal midline by rotating the half-penta prisms (20° relative to the vertical meridian). This reduces the lateral shift to 42°. To minimize the obscuration scotoma, the half-penta prisms were also tilted (pitch) 20° to match the line of sight. A 3D printed module was developed to mount the prisms at the required position and orientation in front of the carrier lens (Fig. 1). Field expansion through the oblique MPP was verified using optical simulations (LightTools and KeyShot) and also measured (Goldmann perimetry) for a patient with right HH.

Results: Monocular perimetry demonstrated about 36° field expansion with almost 17° vertical shift. The oblique MPP provided the desired field expansion to the blind side through the car windshield (Fig 2). The slight deviation from the optical simulation results may be attributed to the prototyping process and perimetry measurement errors.

Conclusions: The oblique peripheral MPP provides vertically shifted field expansion toward the horizontal midline. The expanded field covers the view through the car windshield, necessary for HH driving. The current configuration of the oblique peripheral MPP may be improved to reach even wider field expansion.

CONTROL ID: 3546685

SUBMITTER (NAME ONLY): Samuel Wachamo

TITLE: Characterization of Temperature-Dependent Kinetics of Oculocutaneous Albinism-Causing Mutant of Tyrosinase

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Wachamo, P. Varghese, M.B. Dolinska, Y.V. Sergeev, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human tyrosinase (Tyr) is a glycoenzyme that catalyzes the first and rate-limiting steps in melanin production and its gene (TYR) is mutated in many cases of oculocutaneous albinism type 1 (OCA1). The mechanisms by which individual mutations contribute to the diverse pigmentation phenotype in patients with OCA1 has only begun to be examined and remains to be delineated. Here, we analyze the temperature-dependent kinetics of wild type Tyr (WT) and R422Q mutant using Michaelis-Menten and van't Hoff analysis.

Methods: Recombinant truncated human WT and R422Q mutant proteins (residues 19-469) were expressed in baculovirus and produced in whole insect *Trichoplusia*. Ni larvae. Proteins were purified by immobilized metal affinity chromatography followed by size-exclusion chromatography. Diphenol oxidase activities of WT and R422Q were measured using 0.05 mg/ml protein and L-DOPA as substrate at 28, 31, 37, and 43 degrees Celsius at physiological pH 7.4. Absorbance measurements of dopachrome formation were measured at 475 nm and converted to concentration. For Michaelis-Menten kinetics, absorbance measurements were performed at 0.09, 0.19, 0.38, 0.75, 1.5, 3, and 6 mM L-DOPA. Kinetic parameters of WT and R422Q catalyzed reactions were determined using nonlinear polynomial fit on OriginPro 7.5. The thermodynamic signature of dopachrome production was determined by measurement of Michaelis-Menten constant (K_m) followed by an analysis using the van't Hoff equation.

Results: The Michaelis-Menten kinetics showed an increasing K_m (WT: $R^2 = 0.87$; R422Q: $R^2 = 0.88$) and V_{max} (WT: $R^2 = 1.00$; R422Q $R^2 = 1.00$) as the temperature increased. It also revealed that the V_{max} , k_{cat} , and k_{cat}/K_m are significantly higher for the WT compared to R422Q. The van't Hoff analysis displayed a negative trendline for both the WT and R422Q. Subsequently, the ΔH (kJ/mol) and ΔS (kJ/mol*K) values were calculated (WT: $\Delta H = 21.25 \pm 6.37$, $\Delta S = 0.11 \pm 0.02$; R422Q: $\Delta H = 21.14 \pm 6.09$, $\Delta S = 0.11 \pm 0.02$), which resulted in a $\Delta G < 0$ for both WT and R422Q.

Conclusions: Overall, the analysis of the temperature-dependent kinetics showed that R422Q is less active than WT at all temperatures examined here. Elucidating the thermodynamics and kinetics of both the WT and mutant Tyr is indispensable for understanding the molecular mechanism of OCA1 to discover drugs that may treat OCA1.

CONTROL ID: 3546686

SUBMITTER (NAME ONLY): Jacob Sterling

TITLE: Inflammatory adipose activates nutritional immunity leading to retinal dysfunction

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is the most common cause of irreversible blindness in the United States among those older than 50. Dysfunction and death of retinal pigment epithelial (RPE) cells are key to the pathogenesis. Previous work has shown that iron accumulates in the RPE of AMD eyes, and iron overload is sufficient to trigger RPE cell death in vitro and in vivo. However, the mechanism of RPE iron accumulation in AMD is unknown.

Methods: Herein, we use in vitro primary human RPE and in vivo mouse RPE studies, in addition to human single-cell RNAseq data from AMD cases and controls, to study an inflammatory mechanism of iron accumulation.

Results: Herein we show that high fat diet, an AMD risk factor, drives systemic and local inflammatory circuits upregulating interleukin 1 β (IL-1 β). IL-1 β upregulates RPE iron importers and downregulates iron exporters. This, in turn, triggers RPE iron accumulation, oxidative stress, and dysfunction. We term this maladaptive, chronic activation of a nutritional immunity pathway the cellular iron sequestration response, or CISR. Single cell RNAseq analysis of choroid and neurosensory retina from human donors revealed that hallmarks of this pathway are present in AMD microglia and macrophages.

Conclusions: Together, these data suggest that obesity, through CISR, can lead to RPE iron accumulation in AMD.

CONTROL ID: 3546689

SUBMITTER (NAME ONLY): Pooja Biswas

TITLE: Identification of unique variants as the underlying cause of IRD in pedigrees that remained unresolved after initial whole genome sequence analysis.

SESSION TITLE: Genetics of Retinal dystrophies

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To identify the molecular basis of disease in 4 pedigrees with IRD that remained unresolved after the initial analysis of WGS data.

Methods: Two pedigrees of Indian origin and one each of Hispanic and European American (EA) origin were analyzed. WGS was done on one affected individual and two unaffected siblings from each pedigree using Illumina HiSeq X Ten. Initial analysis by mapping reads to hg19 and variant calling using GATK did not identify disease causing variants. The data was further analyzed using two methods: (1) the reads were re-aligned to hg38 and variants were called using GATK; (2) read alignment and variant calling was done using the Illumina DRAGEN Bio-IT platform. Validation of a large inversion identified was performed by isolating high molecular weight DNA from the patient and unaffected family members using the Bionano DLS kit and analyzed on Bionano Saphyr. Segregation analysis was done by PCR followed by Sanger sequencing.

Results: Re-analysis using the hg38 reference genome identified 2 novel compound heterozygous variants p.[Pro3Ser;Thr1749Ala] in ALMS1 in one Indian pedigree. Analysis of remaining pedigrees using Illumina DRAGEN Bio-IT identified unique pathogenic variants in known IRD genes. In the second Indian pedigree, uniparental isodisomy (UPiD) involving a 39Mb homozygous region on chromosome-15 that included a novel pathogenic homozygous NR2E3 variant, p.Trp257Ser, was observed. In the EA pedigree, a heterozygous nonsense mutation p.Gln874* and a large inversion in the EYS gene were detected. This inversion (Chr6: g.65986120_67623958inv) was further characterized by analyzing the samples of the patient and unaffected family members using Bionano Saphyr. This analysis confirmed the presence of a 1.6Mb inversion on chromosome-6, which includes exons 1 to 12 of EYS. In the third Hispanic family with 1 affected female and 2 unaffected female siblings, a previously reported p.Glu746ArgfsTer23 mutation in RPGR was identified. All detected mutations segregated with IRD in all 4 families.

Conclusions: Analysis using the hg38 reference genome identified causative variants in one pedigree among four. Additional analysis using Illumina DRAGEN identified a 39Mb segmental UPiD, a mutation in RPGR and mutations in the EYS gene including a large inversion.

CONTROL ID: 3546693

SUBMITTER (NAME ONLY): Koushik Mondal

TITLE: N-3 polyunsaturated fatty acids (n-3 PUFA) prevent traumatic brain injury (TBI)-mediated visual and motor deficits in mice by suppressing ceramide biosynthesis

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Traumatic brain injury (TBI) causes neuroinflammation and neurodegeneration leading to various pathological complications such as motor, and sensory (visual) deficits, cognitive deficit, and depression. N-3 polyunsaturated fatty acid (n-3 PUFA) containing lipids are known to be anti-inflammatory, whereas sphingolipid, ceramide (Cer) is an inducer of neuroinflammation and degeneration. The purpose of this study was to understand whether the presence of an elevated systemic level of n-3 PUFA in the Fat1-transgenic mice is associated with the prevention of TBI-mediated sensory-motor deficits by preventing Cer generation.

Methods: We used Fat1-transgenic mice and their WT littermates and subjected them to mild TBI using left side focal cranial air blast (50-psi) or sham blast (0-psi, control). We conducted visual functional tests, histological, and molecular assays in the brain tissue at 30-days post-blast.

Results: Among different heterogeneous complications, visual function is one of the major sensory parameters affected by TBI. By Optokinetic Nystagmus (OKN) recording, we found that visual acuity decreased, whereas contrast sensitivity increased significantly in WT-blast animals compared to their pre-blast values but not in Fat1-blast animals. By rotarod and open-field studies, we also found Fat1-blast mice were resistant to the declining of motor functions from blast injury. Immunohistochemical labeling of oculomotor nucleus motoneurons for choline acetyltransferase (CHAT) showed a significant reduction in the area of the oculomotor nucleus in WT-blast mice, and immunostaining for IBA1 in the optic tract showed significantly higher numbers of activated microglia of WT-blast mice. Further LC-MS/MS analysis confirmed an elevated level of n-3 PUFA, eicosapentaenoic acid (EPA) in the plasma and brain of the Fat1-transgenic animals. TBI increased Cer level in the brain of the WT mice, which was decreased significantly in the brain of Fat1-blast mice. We further demonstrated that expression of Cer biosynthetic and inflammatory genes was significantly lower in the brain of Fat1-blast mice compared to their WT littermates.

Conclusions: Our result demonstrates that suppression of ceramide biosynthesis and inflammatory factors in Fat1-transgenic animals is associated with significant protection of visual and motor deficits caused by mild TBI.

CONTROL ID: 3546694

SUBMITTER (NAME ONLY): Nancy Aychoua

TITLE: Cone-driven electroretinogram responses to flashes delivered on a dim rod-saturating background: prevalence of negative waveforms

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The dark-adapted electroretinogram (ERG) response to a standard bright flash contains rod and cone components. Negative waveforms usually indicate loss of post-receptoral signals. However, when rod responses are lost completely, the waveform reflects the dark-adapted cone system response (usually not seen due to a larger superimposed rod system response). In order to explore the possible form of the dark-adapted cone system response, we recorded ERGs to flashes delivered on a dim rod-saturating background.

Methods: ERGs to white xenon flashes ($13 \text{ photopic cd m}^{-2} \text{ s}$, similar to the standard DA 10 stimulus), delivered on a dim blue background (1.0 photopic and $30 \text{ scotopic cd m}^{-2}$), were recorded in 211 healthy adults from the TwinsUK cohort, as part of a wider study. Recordings were made with conductive fibre electrodes in the lower fornix following mydriasis. The background was designed to achieve rod saturation, but minimal cone desensitisation, so that the cone system might resemble the dark-adapted state. The standard ISCEV background is much brighter ($30 \text{ photopic cd m}^{-2}$) and significantly light-adapts the cones. A-wave and b-waves were extracted, and the b:a amplitude ratio calculated. Ratios <1 indicated a negative waveform.

Results: Mean (SD) age was 62.5 (11.3) years. 93% were female. Following exclusion of traces with noise artefact, ERGs from 199 right eyes and 208 left eyes were included. Mean (SD) b:a ratio was 1.22 (0.27) and 1.20 (0.30) for right and left eyes respectively; medians were 1.19 and 1.18. Coefficient of inter-ocular correlation was 0.70. ($p < 0.0001$). No significant correlation with age was found. Proportions of eyes with negative waveforms were 22% and 26% for right and left eyes respectively.

Conclusions: Over 20% showed negative waveforms, consistent with this being a feature of the dark-adapted cone system response to standard bright flashes in many people. The majority did not show negative waveforms. In patients with complete loss of rod function, a negative ERG (with reduced a-wave) could reflect the normal dark-adapted cone system response. Our study suggests that it might also be possible for complete loss of rod function to occur without a negative ERG. A limitation is that the blue background might elicit some cone system adaptation, and this will affect our estimate of the true dark-adapted cone-driven ERG.

CONTROL ID: 3546696

SUBMITTER (NAME ONLY): Jie Ni

TITLE: Systems Genetics Analyses of Optic Nerve Axon Health

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is the primary cause of irreversible blindness worldwide. There are various subtypes of glaucoma – primary open angle (POAG), primary angle closure (PACG), and normal tension glaucoma – that share the common clinical pathologies of retinal ganglion cell (RGC) degeneration, optic nerve damage (ON), and subsequent loss of vision. Although intraocular pressure (IOP) is a major risk factor for the development and progression of glaucoma, the relationship is complex and not fully understood. Our goal was to identify genomic regions that modulate the number of healthy axons in the ON and to probe its relationship with IOP using the BXD family of mice.

Methods: IOP data was collected on a large cohort of BXD family aged > 13 months. ONs from 74 strains and the DBA/2J (D2) parent were harvested, sectioned, and stained with p-phenylenediamine. The number of healthy axons per ON cross-section were counted and strain means and standard errors were uploaded to GeneNetwork, a set of systems genetics tools for multi-layered data analysis. Using our previous methods (Stiemke et al, 2020), we mapped the trait using the GEMMA mapping tool and applied stringent criteria to narrow the list of positional candidates. The relationship between the number of healthy axons and IOP was assessed using regression analysis.

Results: The number of healthy axons per nerve varied 2.3-fold in older (> 13-month) BXD strains, and ranged from a low of 28,000 healthy axons/nerve in BXD98 to a high of 64,900 healthy axons/nerve in BXD6.

Identical to our findings on the regulation of the number of necrotic axons in the optic nerve, *Tyrp1* and *Gpnmb*, the two genes that are responsible for pigmentary dispersion glaucoma of the D2 parent, do not influence the endophenotype of the number of healthy axons in the ON. We identified two QTLs with genome-wide significance, one each on chromosomes 3 and 9. Using our inclusion criteria, we narrowed the list of 140 positional candidates to eight genes that could modulate the number of healthy axons in ONs of the BXD family. Lastly, IOP and the phenotype of healthy axons in the ON have no significant correlation.

Conclusions: We identified two genomic regions that modulate the number of healthy axons in the ON. Additional studies are underway to narrow the list of plausible candidate genes. We also demonstrated IOP is not indicative of ON health, thus adding to the complexity of glaucoma-associated endophenotypes.

CONTROL ID: 3546700

SUBMITTER (NAME ONLY): Raj Maturi

TITLE: A Randomized Trial of Intravitreal Anti-VEGF for Prevention of Vision Threatening Complications of Diabetic Retinopathy (Protocol W)

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.K. Maturi, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|R.K. Maturi, Midwest Eye Institute, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Raj Maturi: Commercial Relationship(s);Allergan:Code F (Financial Support);Boehringer-Ingelheim:Code F (Financial Support);Genentech:Code F (Financial Support);Unity Biotechnology:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Eyes with moderate to severe non-proliferative diabetic retinopathy (NPDR) are at high risk for disease progression and development of vision-threatening complications. The DRCR Retina Network Protocol W aimed to determine if aflibercept can prevent the development of proliferative diabetic retinopathy (PDR) and center-involved diabetic macular edema (CI-DME) over 2 years and if so, whether there is an associated visual benefit at 4 years.

Methods: In this multi-center randomized clinical trial, eligible eyes had moderate to severe NPDR (ETDRS severity levels 43-53), without center-involved diabetic macular edema. Eyes were randomly assigned to intravitreal 2.0-mg aflibercept or sham injections performed at baseline, 1, 2, and 4 months and every 4 months through 2 years. Thereafter, through 4 years, treatment was deferred if the eye had no worse than mild NPDR. Aflibercept was provided in both groups if CI-DME with vision loss or high-risk PDR developed. Time to development of PDR or CI-DME with vision loss (primary outcome) were analyzed with marginal Cox regression models, and 2-year change in visual acuity was analyzed with a linear mixed model.

Results: We enrolled 328 participants (mean age 56 years; mean HbA1c 8.8%; 42% female; 47% White, 30% Hispanic and 15% Black) with 399[KJ1] study eyes across 64 clinics in the U.S. and Canada[KJ2]. There were 200 eyes assigned to aflibercept and 199 eyes assigned to sham. At enrollment, 17% of study eyes had moderate NPDR (level 43), 32% had moderately severe NPDR (47A), 27% had moderately severe NPDR (level 47B-D), and 24% had severe NPDR (level 53). Mean baseline visual acuity was 87.6 [KJ3] letters and mean baseline central subfield thickness was 281 μ m [KJ4] (Heidelberg Spectralis equivalent). All available data by the time the last participant completed the 2-year visit will be presented. Results have been analyzed and reviewed by the Data and Safety Monitoring Committee, but per National Eye Institute requirements for NIH-funded clinical trials, primary results cannot be made publicly available before publication. Publication is anticipated shortly before or at the time of presentation.

Conclusions: Conclusions will follow from the results presented.

CONTROL ID: 3546703

SUBMITTER (NAME ONLY): George Maiti

TITLE: Single-cell RNA-seq analysis of human cornea and corneal organoid

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: To establish a well-defined 3D corneal organoid model that will be useful in studying ocular surface diseases, their genetic modeling and screening of pharmaceutical drugs. We performed single-cell RNA sequencing (scRNA-seq) of a human donor cornea and a cornea organoid developed in culture from induced pluripotent stem cells (iPSC) to elucidate corneal cell populations represented in the organoid.

Methods: One cornea organoid (7 month old), and a healthy donor (41 year old) cornea (Lions Eye Institute for Transplant and Research, FL) were digested for 5 h with Collagenase type I (2 mg/ml) in complete DMEM-F12 containing 5% FBS followed by Accutase treatment for 20 min, washed and re-suspended in PBS with 0.04% BSA. Live cells were counted by trypan-blue exclusion in a Countess® II automated cell counter. For scRNA-seq, the cells were captured and libraries generated using Chromium Single Cell 3' Library & Gel Bead Kit v2 (10x Genomics). Libraries were run on an Illumina HiSeq 4000 as 150-bp paired-end reads. The Cell Ranger Single-Cell Software Suite v3.01 was used to perform sample demultiplexing, barcode processing and single-cell 3' gene counting. Quality control filtering was applied to remove any cells with fewer than 1000 reads or greater than 15% mitochondrial reads. The 10x Chromium Single Cell 3' Library & Gel Bead Kit v2 was used to capture cells from the donor cornea (10,000 cells) and the organoid (2792 cells). The Loupe Browser 4.2.0 was used to analyze and visualize the data.

Results: We detected 11 and 18 cell clusters in the cornea organoid and donor cornea, respectively. Among these, the cornea organoid revealed clusters of epithelial cells expressing MUC1 and MUC16, a small set of TP63⁺ cells and a stromal cell cluster expressing COL1A1, COL5A, and a small subset of these expressing LUM and KERA. Unlike the cornea, the organoid also contained cells expressing KRT13 and MUC4, indicative of cornea atypical epithelial differentiation. We also found the expression of SARS-CoV2 receptors (ACE2 and TMPRSS2) in the organoid and the donor cornea.

Conclusions: The cornea organoid displayed considerable overlap with the cornea with respect to stromal cell and some epithelial cell markers. However, the organoid also harbored a cluster indicative of dermal and conjunctival differentiation.

CONTROL ID: 3546704

SUBMITTER (NAME ONLY): Kari Vienola

TITLE: OCTA with active retinal tracking and wavefront sensing

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To test UC Davis 2nd generation multimodal retinal imaging system equipped with tracking scanning laser ophthalmoscope (TSLO) to stabilize the optical coherence tomography angiography (OCTA) acquisition in real-time. In parallel, ocular aberrations are recorded with a custom Shack–Hartmann wavefront sensor (SHWS). The system has two key applications: production of stabilized OCT angiograms of retina and choroidal microvasculature and screening of patients for adaptive optics (AO) imaging, based on OCT image quality, fixation stability, and aberration severity.

Methods: The system schematic is shown in Fig. 1. All three subsystems (OCTA, TSLO and SHWS) are optically coupled with a use of dichroic mirrors before entering the eye. The wavefront detection path is then separated using a beams splitter as the ophthalmic lens is translated to correct for the patient's refractive error and thus would move the pupil plane. The TSLO uses 840 nm light to image the retina at 30 Hz frame rate with a 5° field-of-view with 960 Hz bandwidth for motion detection. The OCTA uses a 1060 nm swept laser operating at 100 kHz sweep frequency to image the retina and the wavefront sensing is done with a 755 nm superluminescent diode. The real-time motion correction from TSLO to the OCTA is done by combining voltage signals controlling the scanning mirrors and the TSLO-generated correction (motion) signal using an analog summing amplifier.

Results: The proposed system has been tested on several subjects without known retinal disease. OCT images and angiograms have been collected with and without active tracking, and the performance of tracking system has been validated using galvanometer-based moving model eye. Data from all three subsystems have been collected from subjects who were later imaged using AO-OCT and data from the wavefront sensor has been used to exclude some patients from AO-OCT imaging.

Conclusions: Real-time eye tracking provides two-fold benefit for the combined system. First, as OCT angiograms are generated from the volumes, eye motion produces OCT artifacts due to spurious decorrelation, which are suppressed by real-time tracking. Second, OCTA with motion tracking further improves visualization by permitting averaging of images without computational motion correction. In addition, subjects' wavefront error can be quantified to determine whether it is suitable for the dynamic range of the sensors and correctors in the AO systems.

CONTROL ID: 3546706

SUBMITTER (NAME ONLY): Justin Migacz

TITLE: Quantitative Choriocapillaris Vessel Analysis of Age-Related Macular Degeneration Patients with Ultrahigh-Speed OCTA

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.V. Migacz, B. Musheyev, E. Zhong, O. Otero, T.Y. Chui, R.B. Rosen, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|I. Gorczynska, Physics, Astronomy and Informatics, Uniwersytet Mikolaja Kopernika w Toruniu, Torun, Kujawsko-Pomorskie, POLAND|B. Marsh-Armstrong, R.J. Zawadzki, R.S. Jonnal, J.S. Werner, Ophthalmology and Vision Science, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To quantitatively assess, in-vivo, the choriocapillaris (CC) vessels of patients with age-related macular degeneration (AMD) in regions under and near pathological features such as drusen.

Methods: Imaging was performed with a custom swept-source OCTA prototype, operating at 1.65MHz A-scan rate. Between 2 and 7 volumes were acquired, centered at the fovea or a nearby region of interest, with a field of view of 2x2mm across. Each volume required a 1 second capture time. En face projections of the choriocapillaris (CC) and retinal vessels were generated for each volume, and the images were averaged to create a high-contrast angiogram. Images were then registered to angiograms from a commercial OCT system () to account for motion distortions. The lateral scale was adjusted using a separate eye length measurement. CC images were binarized and skeletonized using a previously published algorithm (PMID: 31646049). Image portions affected by projection artifacts from retinal vessels were removed from analysis and the vessel density (VD), the number of vessel branches per area, was calculated. These metrics were computed for areas outside and directly below manually segmented pathological features such as drusen and CNV.

Results: Five dry AMD subjects, one suspected wet AMD subject, and 4 age-matched normal subjects were imaged and the CC vessel images skeletonized for quantitative analysis. Fig. 1 shows an example of an AMD subject with the commercial images (a-b), the equivalent images shown with our custom system (c-d), the skeleton segmentation of the CC vessels (e), and the CC vessel map with an overlaid vessel density color map (f). Drusen areas are outlined in magenta. Another example of an AMD subject with drusen and pseudodrusen is shown in Fig. 2, in which more obscuration of the underlying vessels is possible due to eye dryness or blurring caused by the drusen. The scalebars are 1mm.

Conclusions: The ultrahigh-speed OCTA system demonstrated clear visibility of most CC vessels in the CC layer, allowing for effective vessel quantification. Images with this system may provide more insight into the manifestation and progression of AMD pathology.

CONTROL ID: 3546707

SUBMITTER (NAME ONLY): Parisa Emami-Naeini

TITLE: Long-term maintenance of vision required to drive in patients with neovascular age-related macular degeneration (nAMD) and diabetic macular edema (DME) following anti-VEGF intravitreal therapy (IVT)

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Visual acuity (VA) requirements for drivers in the US vary, with most states requiring a minimum Snellen VA of 20/40 in the better-seeing eye. We compared treatment (tx) patterns and VA outcomes in patients (pts) with nAMD or DME receiving anti-vascular endothelial growth factor (VEGF) IVT, and characterized the likelihood of pts to maintain vision following yr 1, specifically VA needed to drive over 4yrs.

Methods: Electronic health record data (Vestrum Health; 01-01-2014 to 06-30-2020) for tx naïve pts at index (i.e. first tx) were analyzed. Number of IVT and VA yr over yr (YoY) were evaluated for pts with nAMD and DME, and by baseline VA. A Kaplan Meier curve was used to assess likelihood of losing “driving vision”, defined as first VA <20/40 sustained for ≥6 months in the treated, better-seeing eye (≥20/40). Pts were censored at end of follow up or date of event and grouped into high frequency IVT (HFI; ≥8) and low frequency IVT (LFI; 1–7) groups.

Results: On average, nAMD pts received ~1.5 more injections vs DME pts in any given yr. In yr 1, pts with nAMD and DME gained 8.5 and 9.5 Early Treatment Diabetic Retinopathy Study letters, respectively. In yrs 2-4, nAMD pts experienced YoY losses of 1.9, 2.2 and 2.5 letters, respectively, while DME pts lost 1.1, 0.7 and 0.9 letters. Overall, from yr 1 to yr 4, pts with nAMD and DME lost 6.6 and 2.7 letters, respectively. nAMD and DME pts with ≥20/40 VA at index gained 1.4 and 2.3 letters, respectively, while those with <20/200 gained >20 and >30 letters. However, pts with ≥20/40 VA maintained better overall vision throughout the study. After 4 yrs, 69% and 72% of pts with nAMD and DME were able to maintain driving vision. When stratified by number of IVTs received in yr 1, the HFI group was more likely to maintain driving vision vs the LFI group in pts with nAMD (Fig 1) and DME (Fig 2).

Conclusions: Pts with nAMD and DME experience similar VA gains, which peak at yr 1, but consistently lose vision beyond yr 1. While nAMD pts had roughly their baseline VA at 4 yrs, pts with DME were able to maintain most vision gained. In pts with nAMD and DME, receiving ≥8 anti-VEGF IVTs reduced the risk of losing driving vision by 5-10% in following yrs.

CONTROL ID: 3546712

SUBMITTER (NAME ONLY): Jessica Pottenburgh

TITLE: Determination of blood flow velocity in retinal capillaries using Erythrocyte Mediated Angiography

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Pottenburgh, O. Saeedi, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jessica Pottenburgh: Commercial Relationship: Code N (No Commercial Relationship) | Osamah Saeedi: Commercial Relationship(s);Heidelberg Engineering:Code F (Financial Support);Heidelberg Engineering:Code R (Recipient);NIH/NEI:Code F (Financial Support);Vasoptic Medical, Inc.:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Through the use of fluorescently-labeled erythrocytes, Erythrocyte Mediated Angiography (EMA) allows for direct observation of retinal blood flow in vivo (Tracey et al., Scientific Reports, 2019). We present a novel technique for quantifying capillary blood flow velocity (BFV) in the superficial vascular plexus (SVP), the intermediate capillary plexus (ICP), and the deep capillary plexus (DCP) in humans and non-human primates (NHPs) using EMA.

Methods: Human red blood cells (RBCs) loaded with 1 mM indocyanine green and rhesus macaque RBCs loaded with up to 10 mM carboxyfluorescein succinimidyl ester (CFSE) were prepared for autologous injection. RBCs were injected intravenously, and a Heidelberg Spectralis was used to acquire angiograms and perform optical coherence tomography angiography (OCTA) at the macula. High intraocular pressure (IOP) was induced in the NHPs by using a tight lid speculum. RBCs in capillaries were tracked using a custom MATLAB script. To identify the corresponding vascular plexus, overlays were made using a time-lapse stack of EMA frames and en-face OCTA images of the SVP, ICP, and DCP (Figure 1). Two-tailed, unpaired t-tests were used to compare velocities in different plexuses or conditions.

Results: Mean retinal capillary BFV in each plexus was quantified in 6 eyes of 4 humans and 4 eyes of 2 NHPs (Table 1). Mean BFV in the NHPs was significantly lower when IOP was increased as compared to the baseline velocities for the SVP, ICP, and DCP ($p < 0.01$, $p < 0.01$, and $p < 0.01$, respectively).

Conclusions: Adequate capillary blood flow is essential to supporting the metabolic functions of retinal tissue. However, our understanding of flow dynamics in the various retinal capillary networks is limited. To our knowledge, we are the first to measure absolute retinal capillary BFV in the SVP, ICP, and DCP in humans and NHPs. Additionally, we found a significant decrease in BFV across the three vascular plexuses when IOP was increased in the NHPs. Retinal capillary velocities are highly dependent on ocular perfusion, both IOP and blood pressure. The ability to quantify blood flow in retinal capillaries may further the understanding of disease progression as a result of impaired ocular flow.

CONTROL ID: 3546713

SUBMITTER (NAME ONLY): Richard Rosen

TITLE: Automated Cell Density Mapping of Macular Surface Macrophages in Diabetic Maculopathy

SESSION TITLE: Diabetic retinopathy - diagnosis and therapies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R.B. Rosen, O. Otero, M.V. Castanos Toral, D.B. Zhou, R. Weitz, J.V. Migacz, T.Y. Chui, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|R.B. Rosen, O. Otero, M.V. Castanos Toral, D.B. Zhou, J.V. Migacz, T.Y. Chui, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal macrophages play key roles in vascular inflammatory regulation and angiogenesis. A novel automated density mapping technique and clinical OCT was used to examine the relationship between surface macrophages density and perfused capillary density in the maculae of healthy and diabetic eyes.

Methods: 49 patients with diabetic retinopathy (DR) and 14 controls were imaged using clinical SD-OCT(Avanti RTVue-XR; Optovue). Ten 3x3mm scans centered at the fovea were acquired and averaged (PMID: 28068370). Ocular magnification of each image was corrected for axial length . Foveal avascular zone (FAZ) border was outlined manually on the OCT-A scan. Automated surface macrophage cell density measurements within the FAZ were performed on the 3µm OCT-Reflectance (OCT-R) slab above the ILM surface using MATLAB (Fig. A1 & B1) (PMID: 32574351). Surface macrophage cell density maps were also generated for each subject. OCT-Angiography (OCT-A) full vascular slab, from the ILM to 9µm below the posterior boundary of the outer plexiform layer OPL, was used to measure capillary density (Fig. A2 & B2) (PMID: 31106029).

Results: Maculae of control eyes revealed a few slender, ramified surface macrophage cells . Diabetic maculae showed more cells which were rounder with fewer protrusions, irregularly distributed. Surface macrophage cells within the FAZ were found in 14% of controls and 80% of diabetic eyes (Fig. A3 & B3). Statistically significant differences were observed between control and DR groups in surface macrophage cell density (Kruskal-Wallis tests, $P=0.0005$) with mean±SDs of 1 ± 4 , 12 ± 16 , 15 ± 12 , and 17 ± 16 cells/mm² in the controls, diabetes without DR, NPDR, and PDR, respectively. Linear regression showed significant correlation between surface macrophage cell densities within the FAZ and surrounding perifoveal perfused capillary densities ($R=-0.36$, $P=0.005$).

Conclusions: Clinical OCT is capable of detecting and mapping the density of macular surface macrophage cells in control and diabetic eyes. Our findings suggest that these cells migrate towards the center of the FAZ in diabetic eyes as compared to control eyes. Higher surface macrophage cell density within the FAZ appears to correlate with progressive reduction of perfused capillary density as DR worsens. Density mapping of surface macrophage cells may provide a useful clinical biomarker of progressive retinal vascular disease or response to therapy.

CONTROL ID: 3546714

SUBMITTER (NAME ONLY): Thangal Yumnamcha

TITLE: Tranilast protects against endoplasmic reticulum stress-induced cell death in retinal pigment epithelial cells: Implications for age-related retinal diseases

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Yumnamcha, M. Guerra, E. Abdul-Shukkur, E.A. Berger, L.S. Pukhrambam, A.S. Ibrahim, Ophthalmology, Visual, and Anatomical Sciences, Wayne State University, Detroit, Michigan, UNITED STATES|A.S. Ibrahim, Pharmacology, Wayne State University, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal pigment epithelium (RPE) plays an important role in maintaining outer blood-retinal barrier integrity. RPE function declines with age due to endoplasmic reticulum (ER) stress, which results in age-related macular degeneration (AMD). Tanilast, a specific NLRP3 inflammasome inhibitor, has been shown to possess anti-inflammatory potential that so far untested in RPE dysfunction under ER stress. Therefore, the objective of this study is to test the efficacy of tranilast on ER stress-induced RPE dysfunction and cell death.

Methods: ER stress was induced in a RPE cell line ARPE-19 in culture by adding tunicamycin (TM, 1µg/mL) in the presence or absence of 10 µM tranilast for 48 h. Mitochondrial function and membrane potential ($\Delta\psi_m$) were measured by cellular ATP level and JC1 assay, respectively. Cell death was determined by measuring the release of lactate dehydrogenase (LDH) into media and by MTT assay. RPE barrier integrity was evaluated by transepithelial electrical resistance (TER) using an electric cell-substrate impedance sensing (ECIS) system and immunostaining of ZO-1, a tight junction protein. 2D gel protein electrophoresis was performed, then stained with SyproRubyTM dye to determine differential protein profiles. Statistical analysis was performed using One-way ANOVA followed by Bonferroni post-hoc test. $p < 0.05$ was considered statistically significant.

Results: TM treatment of ARPE-19 causes mitochondrial dysfunction ($\Delta\psi_m \downarrow$ and ATP \downarrow) and cell death (LDH leakage and reduced MTT activity). These deleterious effects of TM on ARPE-19 are alleviated by treatment with tranilast. Furthermore, we show that TM-induced mitochondrial dysfunction and cell death are associated with a significant reduction in TER suggesting ARPE-19 barrier breakdown, which is prevented by tranilast. In addition, TM-treatment reduces ZO-1 immunostaining accompanied by changes in proteomic profile compared to controls without TM.

Conclusions: Our results show that ER-stress causes mitochondrial damage and RPE barrier dysregulation. The beneficial effects of tranilast on RPE function and cell viability under stress may represent a new interventional therapy to ameliorate early pathological pathways that occur in age-related retinal diseases and vision loss.

CONTROL ID: 3546715

SUBMITTER (NAME ONLY): Cristina Sánchez Fernández

TITLE: Distal nerve degeneration in the cornea is initiated by oxidative stress.

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Martin, L. Quirós, Instituto Universitario Fernández-Vega, Oviedo, SPAIN|C. Sánchez Fernández, C. Suarez-Barrio, S. del Olmo Aguado, J. Merayo-Lloves, I. Alcalde, Instituto Universitario Fernández-Vega - Fundación de Investigación Oftalmológica - Universidad de Oviedo, Oviedo, Asturias, SPAIN|C. Martin, L. Quirós, J. Merayo-Lloves, Universidad de Oviedo, Oviedo, Asturias, SPAIN|L. Fernandez-Vega-Cueto, Instituto Oftalmologico Fernandez Vega, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Apart from its function in perception of stimuli, the sensory innervation of the cornea is important for the maintenance of hydration and homeostasis of the ocular surface. Corneal nerve degeneration is progressive during normal aging. Aging reduces the ability of mitochondria to get rid of free radicals and oxidative stress. The aim of this work is to study the effect of induced oxidative stress on the corneal sensitive innervation.

Methods: Oxidative stress was induced by intense light exposure to trigeminal ganglion cell cultures from adult Wistar rats (blue light: 470 nm and 500 lux, 4 hours a day for 10 days). Also, rats were exposed to a source of blue light under the same conditions and corneas and trigeminal ganglia were collected. An equivalent group of animals and cultures were maintained in the dark during light exposure cycles and were used as controls. A group of rats and cultures were treated with antioxidants before light exposure.

Immunofluorescence analysis and qPCR for β tubulin III, tau-p, CaMKII, Hemoxigenase-1, Tomm 20 and Cytochrome C Oxidase, were performed to evaluate oxidative stress and axonal cytoskeleton degeneration. Alexa Fluor 594 and 488 secondary antibodies were used to visualize the results. WST-1 assay was performed to evaluate cell viability. Whole mounted cornea preparations were immunolabeled with β tubulin III and imaged under a Leica SP8 confocal microscopy. FIJI software (ImageJ 1.49d, NIH) was used to analyze nerve loss on the subbasal plexus.

Rats were handled and cared following ARVO statements for the use of animals.

Results: Exposure to intense light caused expression of HE-1 (oxidative stress inducible) and cleavage of Cit C from the mitochondrion membrane. Activated α CaMKII participated in tau phosphorylation and axonal microtubule disassembly. This cascade of events caused the rupture of neurites in cultured trigeminal neurons without affecting severely to neuronal survival. Distal degeneration was also observed as a reduction of corneal subbasal nerve plexus density.

Conclusions: Axonal distal degeneration of sensory nerve terminals in the cornea may be initiated by oxidative insults, such as intense light exposure or normal aging. Reduction of corneal nerve density is associated with ocular diseases such as age-related dry eye. Reducing oxidative stress may prevent axonal loss and functionality.

CONTROL ID: 3546717

SUBMITTER (NAME ONLY): Thomas Strong

TITLE: Ephrin Forward Signaling as A Therapeutic Target in Hereditary Optic Neuropathy

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Optic neuropathies are a major cause of irreversible blindness worldwide. While we know many risk factors, the molecular progression towards synaptic instability, neurite retraction, and, ultimately, neuronal loss has yet to be fully elucidated. The first step in halting or reversing this progression is to identify potential molecular targets for intervention. Studies show that ephrin signaling is one of the most dysregulated signaling pathways in the pathophysiology of optic neuropathies. We hypothesize that synaptic instability, neurite retraction, and subsequent neuronal apoptosis are initiated by the anachronic reactivation of the Eph-receptor forward signaling.

Methods: To investigate the correlation between Eph-receptor reactivation and RGC loss we will use the DBA/2J (D2J) mouse model along with its genetically matched control, the DBA/2J-Gpnmb+/SjJ mouse. A semi-quantitative immunoblot-based assay to profile the phosphorylation in Eph-receptors will characterize receptor activation temporally. Immunofluorescence confocal microscopy (IF) will identify Eph-receptors localization within the inner retina, and the interplay between retina neuronal and glial compartments.

Results: Our results show an age-dependent increase in the activation of several Eph receptors in the retina of D2J mice, with the majority of Eph receptors present in a hyperphosphorylated state at age 23mo. Interestingly, results show that EphA1, EphA3, EphA6, EphA7, EphB1, EphB2, and EphB6, are significantly phosphorylated as early as 2mo of age ($p < 0.05$). IF of 2mo and 10mo D2J retinas shows an overall increase in phosphorylation temporally in both EphA and EphB classes. Both EphA and EphB class receptors are observed to be localized within the GCL with suspected localization within the OPL and the IPL for both Eph classes.

Conclusions: These preliminary results indicate that Eph receptor activation may play a role in the neuropathic progression of hereditary optic neuropathy. These results demonstrate that Eph activation can be observed as early as 2mo of age and is localized within the inner retina, indicating their potential interactions with glial components within the retina. Together these results underscore the need to explore this pathway in early optic neuropathies and it provides a glimpse of the number of receptors that are present in the retina of mice and which are engaged in neuropathic states.

CONTROL ID: 3546718

SUBMITTER (NAME ONLY): Sabrina Bergeron

TITLE: Optical biopsies of peri-ocular skin cancers: how OCT imaging can heighten accessibility to specialized healthcare by telemedicine.

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Basal cell carcinoma (BCC) is the most common peri-ocular skin cancer. It is a slow growing tumour and early clinical diagnosis is often challenging. Admittedly, patients presenting with BCC report having the lesion for several years, having seen many health professionals before they are referred to oculoplastics.

In an era where telemedicine is the new norm, and in addition to stay-at-home orders in effect, patients are reluctant to seek medical attention in large specialized care centers. In attempt to facilitate referral of patients with suspicious lesions, primary eye care providers may benefit from an additional diagnostic tool.

Our team has previously shown how optical coherence tomography (OCT), a well-established and broadly available imaging modality, may facilitate the diagnostic of peri-ocular skin cancers. The aim of this project is to highlight common OCT features observed in BCC.

Methods: This is part of an ongoing prospective study assessing patients with peri-ocular cancers; OCT images and clinical photos are obtained prior to surgical excision of the lesion. For this specific study, 51 patients with histopathologically confirmed BCC were selected. For each, OCT images were compared to their respective histopathological tissue sections.

Results: A total 994 OCT images were obtained. The dermal-epidermal junction nearing the lesion is disrupted in 100% of malignancies. Hypo-reflective tumour nests underneath the epithelium are observed in 82% of BCC, while they are seldom observed in other malignancies. When present, hyperkeratosis and telangiectasia can also be viewed on OCT, however they are not pathognomonic of BCC.

The presence of sub-epithelial hypo-reflective nests on OCT appears to be a hallmark feature of nodular BCC, allowing to rule-in the diagnostic. This hypothesis is supported by a tight correlation between the OCT image and the microscopic histopathological findings for each lesion.

Conclusions: Basal cell carcinoma on OCT shows a distinctive signature consisting of sub-epithelial hypo-reflective tumour nests with a neighboring disrupted epidermal-dermal junction.

Facilitating the early recognition of this slow-growing, often asymptomatic cancer provides eye care professionals with an additional tool to increase their confidence in the diagnosis of BCC and to encourage and expedite referral to a surgical specialist.

CONTROL ID: 3546719

SUBMITTER (NAME ONLY): Robert Ricciardi, PhD

TITLE: Infection by Herpes Simplex Virus-1 in human primary corneal epithelial cells is blocked by an antiviral stapled peptide

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.P. Ricciardi, PhD, H.P. Guan, M. Nuth, C.H. Mitchell, W. Lu, Basic and Translational Sciences, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|R.W. Scott, M.H. Kulp, III, A.B. Reitz, Fox Chase Chemical Diversity Center, USA, Pennsylvania, UNITED STATES|V. Lee, C. Lin, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acyclovir is most commonly used for treating ocular Herpes Keratitis, a leading cause of infectious blindness. However, increasing resistance to Acyclovir in treating ocular Herpes Keratitis has prompted the need for new therapeutics directed against a different viral protein. One novel target is the HSV-1 Processivity Factor which is essential for tethering HSV-1 Polymerase to the viral genome to enable long-chain DNA synthesis.

Methods: A series of peptides, based on the crystal structure of the C-terminus of HSV-1 Polymerase, were constructed with hydrocarbon staples to retain their alpha-helical conformation. The stapled peptides were tested for blocking both HSV-1 DNA synthesis and infection. The most effective peptide was further optimized by replacing its negative N-terminus with two hydrophobic valine residues. This di-valine stapled peptide was tested for inhibiting HSV-1 infection of human primary corneal epithelial cells.

Results:

The stapled peptides blocked HSV-1 DNA synthesis and HSV-1 infection. The unstapled control peptide had no inhibitory effects. Specificity of the stapled peptides was confirmed by their inability to block infection by an unrelated virus. Significantly, the optimized di-valine stapled peptide effectively blocked HSV-1 infection in human primary corneal epithelial cells.

Conclusions: Hydrocarbon stapled peptides that simulate the α -helix from the C-terminus of HSV-1 DNA polymerase specifically block DNA synthesis and infection of HSV-1 in human primary corneal epithelial cells. These stapled peptides provide a foundation for developing a topical therapeutic for treating human ocular Herpes Keratitis.

CONTROL ID: 3546722

SUBMITTER (NAME ONLY): Anthony Musolf

TITLE: Novel genes are associated with refractive error in Indo-Europeans and East Asians using rare variant aggregation tests

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Musolf, D.D. Lewis, J.E. Bailey-Wilson, National Human Genome Research Institute, Baltimore, Maryland, UNITED STATES|A. Haarman, V.J. Verhoeven, C.C. Klaver, Erasmus MC, Rotterdam, Zuid-Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Refractive error is one of the most common eye diseases in the world. While genome-wide association studies (GWAS) have identified many potential risk loci for refractive error, these variants have been common with moderate to small effect on the disease trait. The aggregated Cauchy association test (ACAT) allows for the combination of single variant p-values into an overall gene p-value, providing increased power on rare variants (RV) compared to single marker tests.

Methods: We jointly analyzed exome-based genotype data and quantitative mean spherical equivalent (SER) measurements in diopters (D) on 13 population-based cohorts. These cohorts were combined and then split into two ancestry groups, Indo-Europeans (13,037 subjects) and East Asians (4,867 subjects), for analysis. Three additional European cohorts: the Raine Eye Health Study, the Beaver Dam Eye Study, and the EPIC-Norfolk study were used as replication sets, giving a total of five cohorts analyzed.

We performed single variant association analysis (one RV at a time with the SER phenotype) using EMMAX, which accounts for cryptic relatedness and ancestry differences. Variants were filtered to $MAF \leq 0.01$; only exonic variants were included. We used ACAT to combine the single variant p-values in a given gene into a single p-value for that gene. This is distinct from burden style tests, such as the variable threshold test, which combines RVs into a single, new marker on which association analysis is performed. Different approaches have different strengths and weaknesses, which is beneficial when searching for candidate genes. Fisher's method was further used to combine the gene p-values.

Results: The meta-analysis across the five cohorts identified 28 genome-wide significant genes using a significance threshold of 1×10^{-5} . The most significant gene was MUC16 ($p=9.61 \times 10^{-10}$). 11 of the 28 genes were found to be significant in one cohort and replicated in another. Good candidate genes for causality include GDF15 ($p=1.95 \times 10^{-9}$), which is known to be overexpressed in myopic eyes, ST6GALNAC5 ($p=9.03 \times 10^{-10}$), which may stimulate new rod development in zebrafish, and PER3 ($p=1.08 \times 10^{-6}$) located near the known myopia locus MYP14 on 1p36.

Conclusions: We have identified 28 novel genes that are associated with refractive error using gene-based RV tests. Further validation studies are planned to confirm these results.

CONTROL ID: 3546723

SUBMITTER (NAME ONLY): Syed Mahmood Shah

TITLE: Management and cost differences in patients with Transient Visual Loss and Transient Ischemic Attack presenting to the Emergency Department in the United States: A 9-year trend analysis.

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.A. Shah, B. Usmani, S. Mukhtar, T. Gao, J. Ong, A. Yan, K.K. Dansingani, I. Zaydan, T. Shazly, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe patient characteristics and Emergency Department (ED) disposition between patients presenting with transient vision loss (TVL) and transient ischemic attack (TIA).

Methods: Data was sourced from the Nationwide Emergency Department Sample (NEDS) dataset (2006-2015). ICD-9-CM codes were used with a diagnosis of TVL, Amaurosis Fugax (AF), and TIA to identify cases, aged 18 years and older. These were compared for patient characteristics and management differences in the ED. Statistical analyses included descriptive statistics, trends analyzed using national incidences using US population.

Results: Patient characteristics and demographics were similar amongst type of diagnosis and disposition. Majority of patients were elderly (44.1% TVL, 66.5% TIA) with female preponderance (>50% both). There was a trend toward routine discharge in the TVL group (51.9%) versus TIA group (34.1%) with length of stay, if admitted, being longer in TVL group (4.2 days (Standard deviation (SD)= 4.8) versus 3.2 days (SD=3.9) in the TIA group), resulting in higher inpatient costs (\$181 million vs \$68 billion). CCI differed between groups, which was normal/mild (86.8%) in TVL group and mild/moderate (94.4%) in TIA group. 12.1% of TVL encounters and 16.5% of TIA encounters resulted in ED procedures.

Conclusions: This study highlights the difference in patient characteristics, procedural care, cost, and discharge practices from the ED with diagnosis of TVL compared to TIA. It shows discrepancies in management between patients with primary diagnosis of TVL compared to TIA, which highlights the current clinical dilemma amongst neurologists, ophthalmologists, and emergency medicine physicians in how to best manage patients with transient neurologic deficits without acute infarction. This needs to be addressed better with need for coherent guidelines to be established.

CONTROL ID: 3546724

SUBMITTER (NAME ONLY): Ernie Hixon

TITLE: Transcriptional profiling of glaucoma donor retina using axon analysis for sample stratification

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Hixon, A. Banks, N. Vo, Y. Qiu, G. Prasanna, A. Chen, Ophthalmology, Novartis Institutes for BioMedical Research Inc, Cambridge, Massachusetts, UNITED STATES|L. Fan, O. Iartchouk, CBT, Novartis Institutes for BioMedical Research Inc, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is an optic neuropathy which includes retinal ganglion cell (RGC) death and cupping of the optic nerve head. The underlying mechanisms of RGC degeneration is not well understood. Studying differentially expressed retina genes from glaucoma donor samples offers the opportunity to understand the disease biology and identify key drivers of disease. The lack of detailed clinical records from sample donors complicates the data analysis. Here we describe the use of histological methods to qualitatively rank corresponding optic nerves for the loss of myelination then stratify samples for differential gene expression analysis from retinal transcriptional profiling studies.

Methods: Frozen optic nerves corresponding to RNAseq profiled human glaucomatous (per medical record) and non-glaucomatous donor retinæ (n = 15 each; age: 65-97) were prepared for cryosections and sectioned at 7µm thickness on a cryotome. For myelin detection, sections were fixed with 2% Osmium Tetroxide, and stained with p-phenylenediamine (PPD). For other markers sections were fixed with isopropanol and probed with neurofilament or GFAP antibodies. Severity of axon degeneration was ranked in a masked manner and divided into 4 bins – no apparent change, mild, moderate, and severe myelin loss. The differential gene analysis of RNAseq data was analyzed using these groups for comparison.

Results: Demyelination of the optic nerve assessed by PPD, mirrored the loss and disorganization of neurofilament. GFAP signaling in general was more condensed and intense in damaged samples but did not specifically correlate with myelin loss. Samples designated by medical record as glaucomatous were enriched in groups 3 and 4. RNAseq expression data were analyzed either by combined groups 1/2 compared with groups 3/4 or glaucomatous vs non-glaucomatous groups per medical records. More differentially expressed genes were identified in the comparison between groups 1/2 vs the groups 3/4, particularly known RGC markers.

Conclusions: We have a protocol for analyzing glaucomatous optic nerve tissue from human donor samples for myelin loss offering an alternative method for donor sample stratification to potentially overcome limited donor medical records. We have observed an increased sensitivity in detection of differentially expressed genes in a transcriptional profiling study based on binning optic nerves at different stages of glaucoma.

CONTROL ID: 3546732

SUBMITTER (NAME ONLY): Sandip Basu

TITLE: A Novel Topical Formulation of FTY720 Protects Photoreceptors in Animal Model of Light Induced Retinal Degeneration

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: FTY720 (Fingolimod) is an FDA approved drug for Multiple Sclerosis. It is a structural analog of the bioactive sphingolipid sphingosine, but also inhibit the enzyme Ceramide Synthase (CS) thereby inhibiting ceramide biosynthesis. Increase in ceramide levels had been associated with photoreceptor apoptosis and reducing ceramide levels by FTY720 have been shown to prevent their degeneration in multiple animal models. This study was aimed to develop a novel topical formulation of FTY720 and test its efficacy in preventing photoreceptor degeneration in animal models.

Methods: Sprague-Dawley rats (8-10 weeks) raised in dim (~50 lux) cyclic light (12 hours ON/OFF) from birth receive eye drops of a novel nano-particle based formulation with or without 0.3% FTY720 (w/w) twice a day. After three days, they were subjected to light induced retinal degeneration (LIRD) by exposure to white fluorescent light (~3000 lux) for 12 hours, and the treatment were continued for another seven days. Same age littermates either treated with placebo formulation or without LIRD served as control. At the conclusion of the treatment, retinal functions were measured by Electroretinography (ERG) and the retinas were used for histochemical and lipidomic analysis.

Results: We were able to identify formulation #1003-92, as a stable proprietary formulation that does not cause any ocular inflammation, irritation to the eye or visible distress, in the treated animals. FTY720 can be detected in picomole levels in the retina of the treated animals after ten days of treatment. Histochemical analysis showed preservation of photoreceptors in FTY720 treated animals compared to the placebo treated animals after LIRD. Eye drops with FTY720 protects the retinal functions after LIRD as observed by scotopic and photopic ERG.

Conclusions: Our study identified a novel proprietary ocular eye-drop formulation that can deliver the drug of interest to the retina without causing any distress to the eye. Our results also confirmed that reducing ceramide level by FTY720 prevents photoreceptor apoptosis and preserve retinal function. Our data established FTY720 as a potentially promising drug candidate for ocular diseases that causes photoreceptor apoptosis. It also emphasizes the fact that reducing ceramide levels could be a potential therapeutic approach for preventing photoreceptor degeneration in multiple human retinal diseases.

CONTROL ID: 3546733

SUBMITTER (NAME ONLY): Patrick Leavey

TITLE: The impact of ectopic expression of the Kruppel-like Factors on mammalian retinal development

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Leavey, C. Santiago, L. Jiang, S. Blackshaw, Solomon H Snyder Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The seven neuronal cell types of the retina arise in a well defined sequence of temporal windows from retinal progenitor cells (RPCs). Over the course of neurogenesis, RPCs express different transcription factors predicted to control gene regulatory networks guiding cell fate decisions and pluripotency capacity. The Kruppel-like factor (KLF) family is enriched within the late stage RPC population. We hypothesize that the KLF family members dictate cell cycle exit and cell lineage within the developing retina, and maintain this capacity outside their developmental expression window.

Methods: All procedures with animals were conducted in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. CD-1 wildtype E14 and P0 (representing early and late stages of neurogenesis) retinas were harvested and electroporated with pCAGIG overexpression plasmids encoding just the IRES-GFP cassette (control) and KLF3/6/9/13. Retinal explants were cultured for two days and subsequently dissociated into a single cell suspension. GFP positive cells were obtained by flow sorting and prepared for single cell RNA sequencing (scRNA-Seq). Cell suspensions for control and KLF3/6/9/13 electroporated E14 and P0 retinas were process on the 10x Genomics Chromium Single Cell System to assess the KLF family's impact on the transcriptional profile at a single cell level after two days of overexpression. Downstream analysis was performed using the Seurat package in R.

Results: Clusters of retinal neurogenic cells and retinal neurons were identified by the expression of marker genes for each timepoint for the control and KLF3/6/9/13 scRNA-seq profiled cells. In addition, when comparing the gene expression patterns within the RPC and neurogenic precursors between the control and KLF samples, changes were observed in genes dictating cell cycle and neurogenesis.

Conclusions: Determining which transcription factors control the transition from early and late-stage RPCs as well as the temporal patterning dictating cell fate and divisions is paramount to understanding how certain cell types arise within the mammalian retina. By establishing the KLF family as a group of transcription factors regulating retinal neurogenesis, this work can potentially inform the design of stem cell-based therapies for retinal dystrophies.

CONTROL ID: 3546734

SUBMITTER (NAME ONLY): Jeremy Hatcher

TITLE: Ophthalmic service utilization and out-of-pocket cost for Affordable Care Act Marketplace plan beneficiaries

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.B. Hatcher, N.G. Morales, J. Lindsey, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|L. Sulieman, Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|J.B. Hatcher, N.G. Morales, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|J. Lindsey, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: A decade after the Affordable Care Act (ACA) became law, the ACA and its marketplace exchanges remain highly politicized. Lack of aggregated exchange claims data has made it difficult to assess the marketplaces' success in achieving their central aims (promotion of high-value care, protection against catastrophic out-of-pocket cost, etc.). We performed a cross-sectional study to understand how beneficiaries on ACA marketplace plans are utilizing ophthalmic care and experiencing out-of-pocket cost for ophthalmic services.

Methods: We analyzed claims data from Wakely Consulting Group's proprietary WACA 2018 data set, containing detailed claims, eligibility, and premium data from national EDGE Servers. Among 3.9 million 2018 beneficiaries, we used the data set to identify all claims and beneficiaries with an ophthalmology-specific ICD-10 diagnosis or CPT procedure code. Medication analysis was performed with National Drug Codes (NDCs) in claims for ophthalmology beneficiaries identified in the above manner. We then analyzed cost by service to calculate total allowed cost and member out-of-pocket cost.

Results: Among all beneficiaries in the WACA 2018 data set (median age of 40), roughly 12% (459,000 beneficiaries, median age 50) had claims related to Ophthalmology services and/or diagnoses. Most commonly, refractive error was seen in 45 per 1000 beneficiaries, cataract in 25 per 1000, and glaucoma in 16 per 1000. Ophthalmology claims generated \$242 million (M) in total cost, with \$24M in medications, \$69M in diagnostics and imaging, and \$150M due to procedures and surgery. The highest total procedural costs were due to cataract surgery (\$50M), glaucoma procedures (\$45M), and retina surgery/procedures (\$42M). \$70M (29%) were paid out-of-pocket on ophthalmic services after premiums, amounting to a mean of \$153 among such beneficiaries.

Conclusions: Despite a much younger population than that covered by Medicare, ophthalmic care for beneficiaries on ACA marketplace exchange plans nonetheless generated substantial cost (nearly \$250M) in 2018. Nearly 30% of total ophthalmic cost was paid out-of-pocket by the beneficiary. In order to identify potential disparities or gaps in affordable ophthalmic care, further analysis is needed to understand how ophthalmic care is being utilized and translating to out-of-pocket cost for various ophthalmic conditions, metal plan tiers, and income levels.

CONTROL ID: 3546737

SUBMITTER (NAME ONLY): Qiang Zhou

TITLE: Characterization and application of a hydrogel derived from acellular porcine corneal stroma

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Zhou, V.H. Guaiquil, A. Escobar, M. Wong, E. Ivakhnitskaia, G. Yazdanpanah, M. Sun, J. Sarkar, Y. Luo, M. Rosenblatt, Ophthalmology and Visual Science, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|H. Jing, Obstetrics and Gynecology, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hydrogels may be an advantageous alternative to the clinically used fibrin gel in the treatment of corneal wounds. In this study, we created an acellular porcine corneal stroma hydrogel (APCS-gel) and evaluated its physical and regenerative properties.

Methods: The optimized APCS-gel was prepared by adjusting the concentration of acellular porcine corneal stroma (APCS). We evaluated its turbidimetric gelation kinetics, light transmittance and protein content using spectrophotometry, SDS-gel electrophoresis and mass spectrometry. Surface ultrastructure, biomaterial permeability and cellular infiltration of the APCS-gel were evaluated by scanning electron microscopy, permeability, H&E staining and tissue culture, respectively. Additionally, the cellular biocompatibility was evaluated by MTT, live/dead assays, and corneal epithelium reconstruction in vitro, using rabbit corneal epithelial (RCEC) and stromal keratocyte (RCSC) cells seeded on the APCS-gel. In vivo, the APCS-gel was transplanted onto the mouse cornea subjected to epithelium debridement and the injury recovery was evaluated by slit-lamp imaging and fluorescence immunostaining.

Results: The APCS-gel was successfully prepared by using APCS concentrations ranging from 10-30 mg/ml. The APCS-gel prepared from 20 mg/ml APCS demonstrated the highest light transmittance and fastest gelation kinetic properties. It retained most collagens, proteoglycans, glycoproteins and growth factors of native cornea. Compared with fibrin gel, the APCS-gel demonstrated a higher porosity ratio, increased permeability, and deeper RCSC cellular infiltration. Additionally, the APCS-gel showed better biocompatibility as evidenced by higher cellular survival and proliferation. After 7 days of culture, 3-4 layers of RCEC were formed on APCS-gel versus 1-2 layers on fibrin gel. We also found higher RCEC stem/progenitor cell phenotypes (K3-, p63+, ABCG2+) and proliferation phenotypes (Ki67+) on the APCS-gel. In vivo, the APCS-gel demonstrated faster corneal reepithelization after corneal epithelium debridement than both untreated mice and mice treated with fibrin gel.

Conclusions: APCS-gel demonstrated similar properties of native cornea, maintained corneal epithelial stemness, enhanced corneal epithelial proliferation in vitro and in vivo. It may be a promising therapeutic intervention for the treatment of corneal wounds in the future.

CONTROL ID: 3546739

SUBMITTER (NAME ONLY): Lloyd Aiello

TITLE: Integrating Macular Optical Coherence Tomography with Ultrawide Field Imaging in a Diabetic Retinopathy Telemedicine Program Using a Single Device

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.P. Aiello, C.M. Jacoba, J.K. Sun, P.S. Silva, Joslin Diabetes Center Beetham Eye Institute, Boston, Massachusetts, UNITED STATES|L.P. Aiello, C.M. Jacoba, J.K. Sun, P.S. Silva, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lloyd Aiello: Commercial Relationship(s);KalVista:Code F (Financial Support);Novo Nordisk:Code F (Financial Support);KalVista:Code I (Personal Financial Interest) | Cris Jacoba: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Sun: Commercial Relationship(s);Optovue:Code F (Financial Support) | Paolo Silva: Commercial Relationship(s);Optomed:Code F (Financial Support);Hill-rom:Code F (Financial Support);Optos plc:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To determine the effect of integrating point-of-care macular spectral domain optical coherence tomography (SDOCT) within a diabetic retinopathy (DR) ultrawide field (UWF) retinal imaging telemedicine program using Monaco device (Optos, plc).

Methods: This retrospective, comparative cohort study evaluated consecutively imaged patients from 1/8/2020 to 3/16/2020 at an UWF image-based DR teleophthalmology program. Both UWF photos and SD-OCT images were acquired using the same instrument at the same session. UWF photos were assessed for DR and DME by a centralized reading center grader masked to SDOCT findings. OCT images were evaluated using standardized templates by a grader masked to UWF photos and findings. Normative OCT measures are currently not available for the Monaco, thus SDOCT scans were evaluated qualitatively for macular pathology (DME, epiretinal membrane [ERM], pigment epithelial detachment, neovascular macular degeneration, tractional retinal detachment). Reliability indices were calculated with SDOCT as gold standard.

Results: 422 eyes from 211 diabetic patients were evaluated. Severity by UWF grading: No DR 57.8%, mild NPDR 30.3%, moderate 7.1%, severe 1.7%, proliferative 2.4%, ungradable 0.7%; no DME 93.4%, non-ciDME 5.2%, ciDME 0.7%, ungradable 0.7%. SDOCT was ungradable in 0.5%. The distribution of macular pathology observed on UWF and SDOCT is shown in Table 1. SDOCT identified 5 (25%) non-ciDME, 9 ciDME (75%) and 28 (97%) ERM eyes that were undetected on UWF. SDOCT did not confirm 14 (56%) non-ciDME, 2 ciDME (67%) and 9 (90%) ERM eyes identified on UWF. Reliability indices are presented in table 2.

Conclusions: Addition of SDOCT increased the identification of macular pathology by 62%. DME and ERM represented 36% and 53% of SD-OCT identified referable macular pathology, respectively. Only 27.3% of eyes with ciDME and only 3.4% with ERM present on SDOCT were identified on UWF imaging. The integration of SDOCT with UWF imaging markedly increased detection and reduced false positive assessments of DME and ERM in a large-scale DR screening program. Given the reduced effort, compact footprint and reduced overall cost of integrated SDOCT/UWF devices, their use in large DR screening programs could substantially improve disease identification and improve visual outcomes.

CONTROL ID: 3546740

SUBMITTER (NAME ONLY): Felix Bock

TITLE: Basement membrane integrity maintains blood vessel networks in inflamed corneas

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: F. Bock, V.N. Le, Department of Ophthalmology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|M. Koch, Center for Biochemistry, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|M. Koch, Institute for Dental Research and Oral Musculoskeletal Biology, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|F. Bock, Center for Molecular Medicine, Universitat zu Koln, Koln, Nordrhein-Westfalen, GERMANY|R. Reuten, Biotech Research and Innovation Centre (BRIC),, Kobenhavns Universitet, Kobenhavn, DENMARK|

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ABSTRACT BODY:

Purpose:

The basement membrane is a specialized extracellular matrix sheet mainly composed of collagen IV and laminins. Laminins are heterotrimeric proteins forming a network which is directly linked to the cell surface via cell adhesion molecules. The secreted extracellular matrix protein netrin-4 is able to intercalate into the network via binding to the laminin $\gamma 1$ chain. The resulting complex of netrin-4 and laminin $\gamma 1$ disrupts the laminin network and the entire basement membrane. The functional role of the laminin network during angiogenesis and vessel maintenance in inflammatory eye diseases has not been addressed so far. We hypothesis that laminin networks are necessary for blood vessel maintenance in the inflamed cornea.

Methods: Three interrupted 11-0 nylon sutures were placed into the corneal stroma of Balb/C mice (6 weeks old) and left in place for 14 days to induce neovascularization. Two weeks after suture placement sutures were either removed (supportive regression) or left in place for another 7 days (active regression). At that time, to disrupt laminin networks, the treatment group (n=10) received eye drops (3 μ l/3x/day; 7 days) of either Netrin-4 (1mg/ml), a laminin-binding mutant of Netrin-4 (Net4^{E195A,R199A}, 1mg/ml) or PBS as negative control. For immunohistochemistry, corneal flat mounts were stained with CD31 as pan endothelial marker and laminin $\gamma 1$. Image analysis was performed by fluorescence and confocal microscopy.

Results: Netrin-4 eye drops significantly supported the regression of preexisting corneal blood vessels compared to the control group (p= 0.0010; Net4: 13.03 \pm 1.7%; control: 21.7 \pm 5.9%) where as Net4^{E195A,R199A}, which is unable to disrupt preexisting laminin networks, could not support vessel regression (p= n.s.; Net4^{E195A,R199A}: 17.45 \pm 3.1%; control: 21.7 \pm 5.9%). Furthermore, destabilization of the laminin network by Netrin-4 actively induced blood vessel regression (p= 0.0156; Net4: 14.29 \pm 2.3%; control: 19.2 \pm 5.4%) whereas Net4^{E195A,R199A} could not induce blood vessel regression (p=n.s.; Net4: 16.07 \pm 2.8%; control: 19.2 \pm 5.4%). Immunohistochemistry revealed that the target structure Laminin $\gamma 1$ is co-localized with corneal CD31+ blood vessels.

Conclusions: We show that the basement membrane is pivotal to guarantee blood vessel maintenance in the inflamed cornea. Moreover, our data identify the laminin network as a promising therapeutic target for angiogenesis associated diseases.

CONTROL ID: 3546743

SUBMITTER (NAME ONLY): Jonas Jarutis

TITLE: Validation of a novel artificial intelligence (AI) machine learning algorithm for quantification of vascular pathology in preclinical models

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To validate a novel artificial intelligence (AI) machine learning algorithm for the automated quantification of lesion size in the mouse choroidal neovascularization (CNV) model.

Methods: CNV was induced in male C57Bl/6JRj mice using a diode laser. The progression of CNV was monitored using live in vivo imaging: fluorescent angiography and spectral-domain optical coherence tomography (SD-OCT). SD-OCT scans covering the whole retina were analyzed by a proprietary algorithm, which uses a combination of convolutional neural network (CNN) and traditional computer vision algorithms. The neural network was trained to recognize and quantify CNV lesions using a transfer learning approach.

Results: We used the Dice coefficient to evaluate AI algorithm-derived results. Dice coefficient comparing predicted lesion volume with volume from the manually annotated data was 0.87 and 0.89 for follow-up day 3 and day 7, correspondingly.

Conclusions: Our data provide evidence that our novel AI algorithm can successfully detect and quantify CNV lesions in the mouse CNV model. Notably, the algorithm accurately recognized temporal changes in retinal structure and pathology over a one-week experimental period. Automated vs. manual analysis resulted in approx. 90% congruence. The novel AI algorithm will provide automated computational analysis of phenotypes in the commonly-used CNV model for age-related macular degeneration, and offer complementary quantitative and bias-free data to accelerate and support drug discovery efforts.

CONTROL ID: 3546745

SUBMITTER (NAME ONLY): Xiuqian Mu

TITLE: The shifting epigenetic landscape along the developmental trajectory of retinal ganglion cells

SESSION TITLE: Applications of single-cell RNA-seq and Transcriptome Studies to Retinal Cell Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Mu, Y. Ge, M. Cheng, F. Wu, Ophthalmology/Ross Eye Institute, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|J. Bard, J. Kann, NYS Center of Excellence in Bioinformatics and Life Sciences, University at Buffalo, Buffalo, New York, UNITED STATES|T. Liu, J. wang, Biostatistics & Bioinformatics, Roswell Park Comprehensive Cancer Center, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The formation of retinal ganglion cells (RGCs) is a stepwise process subject to tight genetic control. Our purpose in this study is to use single cell ATAC-seq (scATAC-seq) to investigate how the epigenetic landscape changes along the RGC developmental trajectory.

Methods: We used two knock-in mouse lines, Atoh7-zaGreen and Pou4f2-tdTomato, to enrich different cell populations by FACS. scATAC-seq and scRNA-seq libraries were then generated using the 10X Chromium platform and sequenced on an Illumina sequencer. The sequence data were then analyzed using Cell Ranger, Seurat, and archR. We also used CRISPR and RNAscope in situ hybridization to investigate the function of one candidate enhancer of Pou4f2, a key gene for the RGC lineage.

Results: We first performed UMAP clustering and gene score calculation of the scATAC-seq data and were able to cluster the cells into the same groups as achieved by scRNA-seq. We next identified enriched accessible peaks in individual clusters, which represented potential enhancers for each developmental stage/cell types. We further performed DNA motif enrichment and footprinting analysis which revealed stage/cell type-specific motif binding by key transcription factors. Further, we performed peak-to-gene linkage analysis by integrating scATAC-seq data with the scRNA-seq data and assigned the stage/cell type-specific enhancers to the genes they likely regulate, thus generating a global enhancer-gene linkage map for the developing retina at E14.5 and E17.5. We also compared the wild-type and Atoh7-null scATAC-seq data and identified peaks (enhancers) that were dependent on Atoh7. Finally, as a pilot validation, we used CRISPR to delete one of the candidate enhancers of Pou4f2, a key gene involved in RGC genesis, and confirmed by RNAscope in situ hybridization that the enhancer indeed played a critical role in the expression of Pou4f2.

Conclusions: Using scATAC-seq, we identified stage/cell-specific enhancers in the developing retina, assigned them to genes they likely regulate, and identified DNA-motifs in them likely bound by key transcription factors. Our results shed significant new light on the shifting epigenetic landscape along the developmental trajectory of the RGC lineage.

CONTROL ID: 3546746

SUBMITTER (NAME ONLY): Nana Yaa Nsiah

TITLE: Prolonged HIF-1a Stabilization Impairs Retinal Metabolism

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Nsiah, D.M. Inman, Pharmaceutical Science, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|G. Johnson, Pharmacology and Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Chronic hypoxia accompanied by decreased glycolysis in the retina and ON has been observed in retinal cells following long-term ocular hypertension. Declines in glycolysis despite its hypoxia-associated promotion suggest the retina may transition into a pseudohypoxic state, with HIF-1 α stabilization despite sufficient oxygen. This project investigates the role of chronic HIF-1 α stabilization in metabolic dysfunction in mouse eyes.

Methods: To induce chronic HIF-1 α stabilization, the prolyl hydroxylase inhibitor Roxadustat (Roxa) was injected into CAG-creERT2-ODD HIF-1 α reporter mice for 2 or 4 weeks. These mice express tdTomato protein when HIF-1 α is stabilized. Protein and mRNA isolated from retina and optic nerve was used to analyze glucose transporters, metabolic enzymes, and mitochondrial proteins. We also used the Seahorse XFe24 Analyzer to measure dependency and flexibility of Roxa retina on glycolysis.

Results: Roxa injection resulted in tdTomato expression in the retina, confirming the stabilization of HIF-1 α . Chronic HIF-1 α stabilization was associated with significant changes in the levels of key metabolic proteins. There was a progressive decrease in the mitochondrial protein TOM20 and metabolic enzymes pyruvate dehydrogenase and succinate dehydrogenase. The antioxidant protein SOD2 levels also decreased over time. Glucose transporter 1 (GLUT-1), specific for glial cells, significantly decreased after 4 weeks; however, the levels of glucose transporter 3 (GLUT-3), specific for neurons, did not change. Seahorse results indicated Roxa-injected mouse retinas were less dependent on glycolysis than control retinas. More relevant for function and perhaps indicative of pseudohypoxia, chronic HIF-1 α stabilization reduced the flexibility of retinas to use other metabolic substrates.

Conclusions: Our results show that chronic hypoxia leads to significant decline in mitochondrial function in mice retinas. This is expected because hypoxia promotes glycolysis. However, the limit on glycolysis dependence along with limited metabolic flexibility indicates HIF-1 α stabilization may contribute to metabolic dysfunction in glaucoma. These indicate that chronic hypoxia, as we observe in glaucoma, possibly impairs the primary metabolic pathways in mice retina and cellular response to metabolic stress.

CONTROL ID: 3546747

SUBMITTER (NAME ONLY): Chirag Shah

TITLE: Large Operative Case Series of Degenerative Lamellar Macular Holes

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Shah, T. Murphy, V. Chaturvedi, Ophthalmology, Rush University Medical Center, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Chirag Shah: Commercial Relationship: Code N (No Commercial Relationship) | Terrence Murphy: Commercial Relationship: Code N (No Commercial Relationship) | Vivek Chaturvedi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: This study examines the anatomic and visual outcomes of pars plana vitrectomy with membrane peeling for degenerative lamellar macular holes.

Methods: A retrospective chart review was conducted on 5 years of vitreoretinal surgeries performed at a large hybrid retina practice in the Chicagoland area. All pre- and post-operative OCTs over the study period were examined for all patients who had vitrectomy with a concomitant diagnosis of a lamellar hole. These OCTs were used to codify lamellar holes as degenerative as opposed to tractional or pseudoholes. Pre-operative best corrected visual acuity (BCVA) and post-operative BCVA (6 to 12 months after membrane peel), as well as hole closure, were documented. Student's two-tailed T-test was used to compare pre- and post-operative visual and anatomic outcomes with an alpha of 0.01.

Results: 23 degenerative lamellar holes in 22 patients, 59 tractional lamellar holes in 55 patients, and 9 pseudoholes in 9 patients were operated on over the study period. The degenerative holes were found to have an statistically significant improvement of 2.5 lines in BCVA ($p < 0.01$). Only 2 patients had a one line loss in BCVA in the post-operative period, and 100% of the degenerative lamellar holes closed post-operatively.

Conclusions: Degenerative lamellar holes have been postulated to have a unique pathophysiology in contrast to tractional lamellar holes and pseudoholes. Previous, smaller-sample case series have shown mixed visual outcomes after vitrectomy with membrane peel for degenerative lamellar holes. To our knowledge, this is the largest series of surgical cases of degenerative lamellar holes published to date, and our results suggest a significant visual benefit to peeling. Further study of our dataset will include comparison to outcomes of surgeries done on tractional holes and pseudoholes.

CONTROL ID: 3546749

SUBMITTER (NAME ONLY): Sydney Sterben

TITLE: The Impact of Deep Learning Architecture on Fluid Segmentation and Classification on SD-OCT

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sterben, J. Whitney, D. Sevgi, J.M. Bell, J. Hach, S. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose:

Manual fluid segmentation in SD-OCT is tedious and subject to variability. This study compared machine learning (ML) model architecture performance in fluid segmentation and classification to understand the optimal model architecture for use in automated segmentation.

Methods:

A deep convolutional neural network was tested modifying parameters such as batch normalization, kernel size (10x10 compared to a 5x5), and dilation (rate = 2 compared to rate = 0). The training set was composed of 1369 SD-OCT slices for classification, and 1593 slices for segmentation and included retinal disorders, such as diabetic macular edema and age-related macular degeneration. The segmentation model detected “all fluid” whereas the classification model categorized the type of fluid [e.g., intraretinal fluid (IRF), subretinal fluid (SRF)] present in ground truth segmented “generic” fluid. Performance was evaluated using F-scores.

Results:

Segmentation F-scores ranged from 0.00 (when batch normalization not performed) to 0.72. The optimal model architecture for segmentation was the 5x5-kernel, with batch normalization, and no dilation. This may be caused by reduced training data dilution when using smaller kernels. Classification F-scores varied from 0.78 to 0.87. The optimal classification architecture used 5-kernel with batch normalization and a dilation rate of 2. This 5x5-kernel model took the same amount of spatial context as a 10x10-kernel model, using fewer nodes. This efficiently incorporates contextual information from relative location and retinal features.

Conclusions:

Model architecture impacts fluid segmentation and classification performance. Optimizing architecture to incorporate contextual information efficiently is key to high performance in spatial problems with limited datasets.

CONTROL ID: 3546750

SUBMITTER (NAME ONLY): Siebren Faber

TITLE: Dissecting the disease mechanism of Leber congenital amaurosis type 5 (LCA5) using retinal affinity proteomics

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Faber, S. Letteboer, R. Collin, R. Roepman, Human Genetics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|A. Garanto, Pediatrics, Radboudumc, Nijmegen, Gelderland, NETHERLANDS|K. Junger, T. Beyer, M. Ueffing, K. Boldt, Experimental Ophthalmology and Medical Proteome Center, University of Tübingen, GERMANY|J. Bennett, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the LCA5 gene disrupt its cognate ciliary protein lebercilin, causing Leber congenital amaurosis (LCA), one of the most severe forms of inherited blindness. Previous proteomics studies performed in non-retinal cells (HEK293T) identified a lebercilin interactome that contained several submodules, including the ciliary intraflagellar transport (IFT) complex. This suggested that defective ciliary trafficking underlies the congenital blindness in LCA5 patients. In this study, we set out to identify the retina-specific interactome of lebercilin by applying two complementary retinal affinity proteomics approaches.

Methods: To optimize an ex vivo affinity purification of lebercilin interactors from bovine retinal extracts, we first purified correctly processed recombinant N-TAP tagged lebercilin bait-proteins, both wild-type (WT) and mutant (LCA5 p.P493TfsX1), from HEK293T cells employing an SDS 'bait-purification' procedure. These purified lebercilin baits were then used to pull-down specific interactors from bovine retinal lysates, followed by mass spectrometry (MS) analysis. For an in vivo approach, we used the AAV serotype AAV7m8 to intravitreally deliver a 3xFLAG-tagged human LCA5 cDNA in the eyes of Lca5^{+/gt} mouse pups (P2). After four weeks, retinas were isolated and subjected to affinity purification of lebercilin followed by MS analysis.

Results: Ex vivo, we found that all IFT-B proteins, two members of the multi subunit C-terminal to LisH (CTLH) complex, and the dynein light chain 1 complex are significantly enriched in purifications of lebercilin WT versus control. However, only the IFT-B and CTLH proteins were lost from the interactome due to the mutation. In vivo, we found that two specific IFT-B proteins and four CTLH complex proteins were significantly enriched in AAV/3xFLAG-lebercilin purifications from mouse retinas compared to controls. Analysis of additional potential interactors is currently ongoing.

Conclusions: Our results indicate that the IFT complex and the CTLH complex, previously identified in HEK293T cells, are conserved in the retinal context. Furthermore, we identified that the interaction of all IFT-B proteins and several CTLH complex proteins is lost when lebercilin is mutated. Overall, these findings highlight the potential contribution of these protein complexes to the disease mechanism.

CONTROL ID: 3546759

SUBMITTER (NAME ONLY): Ruchi Shah

TITLE: Wnt5a promotes diabetic corneal epithelial wound healing and limbal stem cell expression

SESSION TITLE: Corneal Epithelial Repair and Corneal Neuropathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Shah, T.M. Spektor, S. Turjman, S. Ghiam, J. Kim, S. Tolstoff, C. Amador, S.T. Chun, M. Saghizadeh, A.A. Kramerov, A.V. Ljubimov, Eye Program, Cedars-Sinai Medical Center Board of Governors Regenerative Medicine Institute, Los Angeles, California, UNITED STATES|V. Punj, D.J. Weisenberger, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|R. Shah, T.M. Spektor, S. Turjman, S. Ghiam, C. Amador, S.T. Chun, A.A. Kramerov, Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|M. Saghizadeh, A.V. Ljubimov, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetes mellitus appears to be an epigenetic disease with DNA methylation and histone acetylation changes. It causes persistent corneal epithelial alterations including impaired wound healing, which may occur due to the dysfunction of limbal epithelial stem cells (LESC). Previously, DNA methylation analysis showed WNT5A gene to be hypermethylated in diabetic primary cultured human limbal epithelial cells (LEC) enriched in LESC. Our purpose was to examine the effect of Wnt5a on diabetic corneal epithelial wound healing and limbal stem cell expression.

Methods: LEC were isolated from age-matched autopsy non-diabetic and diabetic limbal rims and eyes with IRB approval. Scratch wound healing was carried out in LEC treated with recombinant Wnt5a (200 ng/mL) or DNA methylation inhibitor, zebularine (1, 5, 10 μ M), or transfected with siRNA to WNT5A or with miR-203a mimic or inhibitor. Healing of epithelial wounds created with 1-heptanol was monitored in organ-cultured diabetic corneas with or without the addition of exogenous Wnt5a. Protein expression was determined in these LEC and corneas using Western blot and immunostaining.

Results: Diabetic LEC and corneal epithelium showed significantly decreased expression of Wnt5a protein apparently due to hypermethylation of WNT5A gene. Wnt5a treatment significantly stimulated wound healing in cultured cells and organ-cultured corneas and increased the expression of putative stem cell markers, K15 and K17. In contrast, siRNA knockdown of WNT5A in non-diabetic LEC decreased wound healing vs. control. Zebularine significantly decreased the expression of DNA methyltransferase DNMT1 and 5-methylcytosine and increased Wnt5a expression with an acceleration of wound healing in diabetic LEC. siRNA experiments suggested that demethylating effect was directly related to Wnt5a level changes. Transfection of LEC with Wnt5a-suppressing miR-203a significantly retarded wound healing in non-diabetic LEC, whereas miR-203a inhibitor increased Wnt5a expression and promoted wound healing in diabetic LEC.

Conclusions: In summary, this study confirms the epigenetic changes in diabetic limbal epithelium with reproducible differential methylation in non-diabetic and diabetic primary LEC. Wnt5a is a new diabetic marker in the cornea that appears to be under dual inhibition in diabetic corneas by DNA hypermethylation and miRNA action.

CONTROL ID: 3546761

SUBMITTER (NAME ONLY): Amber-Lee Curran

TITLE: Electroretinographic Responses to Full Field Stimuli in Children with a History of Retinopathy of Prematurity (ROP) Treated with Anti-VEGF

SESSION TITLE: Retinopathy of prematurity

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Curran, L. Ambrosio, D. Vanderveen, I. Mantagos, C. Wu, J.D. Akula, A.B. Fulton, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|L. Ambrosio, D. Vanderveen, I. Mantagos, C. Wu, J.D. Akula, A.B. Fulton, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate dark adapted, full field electroretinographic (ffERG) response parameters in children with a history of retinopathy of prematurity (ROP) treated only with an anti-vascular endothelial growth factor (anti-VEGF) therapy and those in which anti-VEGF treatment was subsequently supplemented with laser photocoagulation.

Methods: Full field electroretinography (ffERG) was performed in patients (N=18) who had ROP treated with anti-VEGF therapy. The subjects were born at median gestational age of 24 weeks (range 23 - 29 weeks) and median birth weight at 645 g (range 410 - 960g). The median corrected age at ffERG test was 41.9 weeks (range 8 to 83 weeks). None had a retinal detachment. In every patient, the ffERG was performed following anti-VEGF treatment. In one group (n=9), the anti-VEGF treatment was deemed adequate (i.e., the ROP required no further treatment); in the other group, subsequent retreatment with laser photocoagulation was administered following inadequate anti-VEGF treatment (n=9). Sensitivity and saturating response amplitude parameters were calculated from the a-wave, b-wave, and oscillatory potentials (OPs), respectively, to provide information about rod mediated photoreceptor, post-receptor, and inner retinal function. Linear mixed modeling was used to evaluate response parameters for differences between those in the anti-VEGF adequate versus inadequate groups.

Results: Neither gestational age at birth nor birthweight differed significantly between the group wherein anti-VEGF treatment was adequate and the group requiring additional laser treatment. Furthermore, there were no significant differences in any amplitude or sensitivity parameter between these groups.

Conclusions: These ffERG results indicate no evidence that dark adapted ffERG photoreceptor and post-receptor activity parameters differ between children with ROP for whom anti-VEGF is adequate and those who will require additional laser treatment. This is despite the strong evidence that photo receptor activity instigates the vascular abnormalities that are the clinical hallmark of ROP (Akula et al., ExER 2010).

CONTROL ID: 3546763

SUBMITTER (NAME ONLY): Qitong Gao

TITLE: A deep learning-based automated tool for the identification of referable retinal pathology from multi-modal imaging sources

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Q. Gao, M. Pajic, Electrical and Computer Engineering, Duke University, Durham, North Carolina, UNITED STATES|J. Amason, S. Cousins, M. Hadziahmetovic, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a fully-automated, learning-based system to identify referable retinal pathology in different imaging modalities obtained remotely at the primary care clinic.

Methods: We used a dataset of 1148 Optical Coherence Tomography (OCT) and color fundus (CFP) retinal images obtained from 647 diabetic patients using Topcon's Maestro care imaging unit. A Convolutional-Neural Network (CNN) with dual-modal inputs (OCT and CFP images) was developed to identify retinal pathology. We developed a novel alternate gradient descent algorithm to train the CNN that allowed for the use of uninterpretable images (i.e., images that do not contain sufficient image biomarkers to conclude a definitive diagnosis). Specifically, a 9:1 ratio to split the training and testing dataset was used for training and validating the CNN. The CFP/OCT inputs obtained from a patient's single eye were grouped as retinal pathology negative (RPN, 924 images) in the absence of retinal pathology in both imaging modalities, or if only one of the imaging modalities was uninterpretable and the other without retinal pathology. If any imaging modality exhibited referable retinal pathology, the corresponding inputs were deemed retinal pathology positive (RPP, 224 images). Additionally, if both imaging modalities were uninterpretable, the inputs were labeled retina pathology potentially present (RPPP).

Results: We achieved $88.60 \pm 5.84\%$ (95% CI) accuracy in identifying referable retinal pathology, along with the false-negative rate of $12.28 \pm 6.02\%$, the sensitivity of $87.72 \pm 6.03\%$, the specificity of $89.47 \pm 6.13\%$, and area under the curve of the receiver operating characteristic (AUC-ROC) of $92.74 \pm 4.76\%$.

Conclusions: Our newly developed learning-based approach can be successfully used in clinical practice to facilitate the presence of referable retinal pathology.

CONTROL ID: 3546765

SUBMITTER (NAME ONLY): Mohamed Abdouh

TITLE: Effects of Spectrum of Wavelengths of Blue-Light on Retinal Pigment Epithelial Cells

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Abdouh, A.A. Goyeneche, E. Youhnovska, R. Denis, P. Garcia de Alba Graue, J.V. Burnier, M.N. Burnier, McGill University Ocular Pathology and Translational Research Laboratory, McGill University Health Centre, Montreal, Quebec, CANADA]

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is a major cause of blindness in the elderly population. It is characterized by loss of central vision due to damaged retinal pigment epithelium (RPE) cells and photoreceptors. Blue Light (BL) is recognized as a risk factor for AMD as it triggers RPE cell death. As BL covers a large light spectrum, we undertook this study to determine the exact range of BL wavelengths that affect the behaviour of RPE cells.

Methods: RPE cells (ARPE-19 and h-TERT-RPE1 cells) were exposed or not to BL (400 – 500 nm) under a Solar Simulator (TSS-156R, OAI) set at 50 mW/cm². RPE cells were analyzed for (i) their growth (using the Incucyte live imaging system to assess cell confluence, and the CCK8 assay to assess cell metabolic activity), and (ii) their oxidative stress by measuring mitochondrial reactive oxygen species (mROS) (using the MitoSox probe). All experiments were performed at least 3 times, and data were compared using an ANOVA followed by the Dunnett post-hoc test for multiple comparisons with one control group. A p value < 0.05 was considered statistically significant.

Results: We observed that BL exposure significantly decreased the proliferation of RPE cells (58 +/- 4% decrease in cell confluence), and their metabolic activity (51 +/- 5% reduction). To get an insight on the mechanisms underlying the observed effects, we analysed the effects of BL on oxidative stress. We noted that although non-exposed RPE cells displayed a baseline level of mROS, BL significantly increased the amount of mROS production (3 times increase). Using a set of filter cut-offs, we noticed that BL at wavelengths above 460 nm did not affect RPE cell behavior. In contrast, BL at wavelengths ranging from 400 to 460 nm was responsible for the deleterious effects observed on exposed RPE cells.

Conclusions: Our data show that BL at wavelengths below 460 nm are deleterious to RPE cells due to increased oxidative stress. The use of lenses with a filtering potential below 460 nm may reduce the harmful effects of these radiations on RPE cells and delay the onset of AMD.

CONTROL ID: 3546767

SUBMITTER (NAME ONLY): Christina Mastromonaco

TITLE: Drusen Quantification of Eye Bank Eyes Implanted with or without Blue-Light Filtering IOLs: a Histopathological Study

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Mastromonaco, S. Bergeron, J. Coblenz, M. Abdouh, M.N. Burnier, MUHC-McGill University Ocular Pathology & Translational Research Laboratory, Quebec, CANADA|J.V. Burnier, McGill University Health Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration(AMD) is a disease that affects central vision and is the leading cause of blindness in the developed world. Despite the lack of a clear understanding of AMD pathogenesis, growing evidence suggests a link between photooxidative stress caused by short-wavelength(blue) light and subretinal drusen accumulation. This study examines the relationship between blue-light filtering intraocular lens(IOL) implants and drusen development through the histopathology of post-mortem eyes.

Methods: A total of eighty donor eyes with IOL implants(Forty with clear IOL and 40 with yellow IOL) were obtained from the Minnesota Lions Eye Bank and examined at the MUHC-McGill University Ocular Pathology Lab. The age, sex, ocular history, clinical history, time from IOL implantation(cataract surgery) to enucleation, and lens model type were obtained for each eye. Eyes were sectioned in their sagittal axis, and formalin-fixed paraffin embedded macular cross sections were obtained H&E stained sections were digitalized using the Zeiss Axio Scan.Z1 scanner.Drusen were identified and classified according to the following criteria: type (soft, cuticular, hard), size (small, medium, large, flat ovoid), and quantity (none, few, multiple, zonal, multiple zonal or extensive).

Results: The presence of soft drusen is observed in 51.32% (n=39) of our samples, while cuticular is observed in 10.53% (n=8) of cases and hard drusen in 14.47% (n=11). The remaining 23.68% does not show macular drusen (n=18). The presence of soft drusen is greater in the group implanted with a clear IOL implant (61.5%, n=24) when compared to the yellow IOL implant. In addition, the number of eyes without apparent drusen is greater in the yellow IOL implant group.The ratio of soft drusen for clear vs yellow IOL is 16:9 for the initial five years after implantation and 22:15 for a ten-year period. Soft drusen accounts for 80% of the aggregate in the 90-99 years old group, while only 42.31% of the drusen in the 70-79 years old group are categorized as soft drusen.

Conclusions: We observe a lesser presence of drusen of all groups of patients with a yellow IOL implant. The presence of soft drusen, which is known for its relationship with macular disease, is also markedly less in patients with yellow blue-light filtering IOL implant when compared to the clear one. This effect is observed across all age groups.

CONTROL ID: 3546768

SUBMITTER (NAME ONLY): Warren Campbell IV

TITLE: Endocannabinoids reduce NF- κ B signaling in Müller glia and promote the formation of Müller glia-derived progenitor cells in damaged retinas

SESSION TITLE: Glial Cells

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W.A. Campbell IV, S. Blum, A. Reske, A. Fischer, Neuroscience, The Ohio State University, Columbus, Ohio, UNITED STATES]

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ABSTRACT BODY:

Purpose: Endocannabinoids (eCB) are lipid-based neurotransmitters that are known to influence visual function and perception. Additionally, eCBs are known to reduce inflammatory signaling in pathological states. However, little is known about the role of the eCB system in modulating inflammation after damage and during reprogramming Müller glia (MG) into progenitor cells (MGPCs).

Methods: Chick retinas after excitotoxic damage were implemented as a model of partial retinal regeneration. The expression of eCB signaling genes were analyzed using single cell RNA sequencing (10X Genomics) in postnatal chicks (P7-P21) with intravitreal injection of NMDA (2 μ mol/dose). Small molecule drugs targeted the CNR1 receptor and eCB synthesis and degradation. MGPCs were identified via 5-ethynyl-2'-deoxyuridine incorporation. Microglia morphology was characterized via Sholl Analysis (ImageJ). Retinal NF- κ B activation was determined using cis-NF- κ B EGFP reporter mice. Statistical Significance was assessed via a Student's T test, Wilcoxon Rank Sum test with Bonferroni correction, one-way ANOVA, and Tukey's test.

Results: MG express eCB signaling and synthesis genes (CNR1, PLCB, NAPELPD, DAGLB, MGLL). Intravitreal injections of eCB increased numbers of MGPCs after damage ($n = 8$, $p < 0.05$). The CNR1 agonist win55, 212-2 ($n = 8$, $p < 0.05$) and inhibition of eCB-degradation with JJKK048 ($n = 8$, $p < 0.05$) resulted in comparable increases in numbers of MGPCs. The CNR1 antagonist rimonabant ($n = 8$, $p < 0.05$) and lipase inhibitor Orlistat ($n = 8$, $p < 0.05$) reduced MGPC formation. However, chick microglia reactivity (proliferation, accumulation, area, CD45 intensity, morphology) after damage was unaffected by all treatment conditions ($n = 8$, $p > 0.05$). In damaged mouse retinas, numbers of NF- κ B-GFP⁺ MG increased after rimonabant treatment ($n = 4$, $p < 0.05$) and decreased with win55, 212-2 ($n = 4$, $p < 0.05$) and eCBs ($n = 4$, $p < 0.05$).

Conclusions: MG respond to inflammatory signaling factors, which influence the capacity of MG to transition into a proliferative state. eCBs result in fewer MG with NF- κ B activation in mouse, and promote MGPC formation in the chick, without significant changes to microglia reactivity. These findings suggest that eCB inhibits NF- κ B signaling in MG which promotes MPGC formation.

CONTROL ID: 3546770

SUBMITTER (NAME ONLY): Puja Brahmabhatt

TITLE: Lipid Layer Thickness, Blink Parameters, and Meiboscore in Patients with Dry Eye Disease: A Retrospective Cohort Study

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Brahmabhatt, S. Khanna, W. Adams, B.I. Gaynes, C.S. Bouchard, Loyola University Health System, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although meibomian gland structure and function can be assessed through meibography and measurement of lipid layer thickness (LLT), the role of blink parameters on the tear film has not yet been fully elucidated. Blink frequency and completeness may impact the lipid layer thickness measurement. In this retrospective cohort study, the relationship between LLT, meiboscore, blink rate, partial blink rate, and inter-blink interval were investigated.

Methods: This is a single-center, retrospective cohort study at the Loyola University Medical Center. We analyzed 2 years of data (2018-2020) generated from the LipiView Interferometer device for 456 eyes. The meiboscore of each eye was graded using the (4 point) Heiko Pult meiboscore. Inter-blink interval was determined from the Lipiview report using the measuring tool application on Adobe Acrobat DC. Linear mixed-effects models were used to analyze the relationship between LLT, meiboscore, blink rate, partial blink rate, and inter-blink interval.

Results: For every 1-point increase in the Pult meiboscore, the average LLT declined by -1.31 units (95% CI: -3.57 to 0.95; $p = .26$) and the total blink rate decreased by 4% (RR = 0.96; 95% CI: 0.91 – 1.03; $p = .26$). Both measures were not statistically significant. LLT and inter-blink interval did not differ significantly between disease states (floppy eyelid syndrome, obstructive sleep apnea, meibomian gland dysfunction, ocular graft vs host disease, Stevens-Johnson Syndrome). There was no statistically significant difference in LLT in patients with a partial blink rate >50% as compared to a partial blink rate <50%. However, there was an association between inter-blink interval (in seconds) and partial blink rate (%). That is, a partial blink rate between >0% to 50% had an inter-blink interval that was -0.73 (95% CI: -1.33 to -0.13) seconds shorter on average than with a 0% partial blink rate ($p = .01$).

Conclusions: A decrease in LLT is associated with increased meibomian gland dropout (meiboscore). Patients who blink more completely (have an incomplete blink rate less than 50% of the time) have a shorter inter-blink interval (time between blinks). We speculate that in patients with an increase in partial blinks, the longer inter-blink interval results from impaired corneal sensation related to the chronic exposure.

CONTROL ID: 3546771

SUBMITTER (NAME ONLY): Abbi Engel

TITLE: Crispr/Cas9 correction of the TIMP3 S204C mutation in Sorsby fundus dystrophy iPSC-derived RPE

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Engel, R. Lim, K. Gonzalez, J.R. Chao, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sorsby fundus dystrophy (SFD) is an early onset macular degenerative disease that is defined by a mutation in the TIMP3 gene. Retinal pigment epithelial (RPE) cells are important in the pathogenesis of age-related macular degeneration and SFD. Cell culture models show promise in reproducing some prominent disease features. By correcting the TIMP3 mutation, we propose to determine the role of TIMP3 in disease phenotype and identify factors that might be independent of the mutation.

Methods: Induced pluripotent stem cells (iPSCs) derived from SFD patients with the Ser204Cys TIMP3 mutation were electroporated with a ribonucleoprotein (RNP) complex of Cas9 and gRNA with donor ssDNA using Amaxa nucleofactor in the presence of ROCK inhibitor and HDR enhancer. Individual colonies were selected and plated into 96-well plates. DNA was extracted and nested PCR was performed. The purified PCR product was sent for Sanger sequencing analysis and karyotype. Clones were differentiated into RPE, which were then cultured on filter membranes to determine structural and functional characteristics using TEM or IHC analysis. RPE cultured on chambered slides were stained with Alizarin Red S. Western blot was performed to determine changes in protein expression.

Results: The Crispr/Cas9-corrected SFD iPSC-derived RPE have typical RPE cobblestone morphology and form tight junctions as observed by ZO-1 staining. Cell polarization and maturation is demonstrated by the presence of apical microvilli, basal infoldings, and tight junction formation visualized by TEM. We previously reported a significant increase in TIMP3 accumulation in the extracellular matrix (ECM) of SFD RPE. CRISPR/Cas9-corrected iPSC RPE were noted to have decreased basal TIMP3 accumulation. SFD iPSC-derived RPE form basal calcium deposits that stain for Alizarin Red S, while Crispr/Cas9-corrected SFD RPE demonstrate decreased calcium deposition ($p < 0.0001$), similar to control levels.

Conclusions: CRISPR/Cas9 correction of the TIMP3 mutation in SFD RPE results in reduced accumulation of extracellular TIMP3 and reversal of the formation of calcium-staining sub-RPE deposits.

CONTROL ID: 3546776

SUBMITTER (NAME ONLY): Melodyanne Cheng

TITLE: Foveal Topographic and Volumetric Measures: New Biomarkers for Detection of Early Glaucoma

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To test the hypothesis that newly developed topographic and volumetric foveal outcome measures can discriminate patients with early perimetric glaucoma from normal subjects.

Methods: We used new measures defining inner foveal shape and central macular volume that were recently developed based on parametric modeling of central macula with cubic Bézier (Figure). Global, hemiretinal, and quadrant parameters were calculated for a group of 50 glaucoma eyes (50 patients) with MD of -6 dB or better and 181 eyes of 96 normal subjects. 8×8 arrays of ganglion cell layer (GCL) and inner plexiform layer (IPL) measurements within 3°×3° superpixels were exported and GC IPL thickness parameters were estimated for 5 macular sectors in the superior and inferior hemiretinas. Multivariate logistic regression and area under ROC curves were used to compare the performance of foveal topographic and volumetric measures to that of thickness measurements.

Results: The average (±SD) visual field mean deviation was -3.6 (±1.5) in the glaucoma group. The main global parameters discriminating glaucoma from normal eyes were the macular rim volume and the area of the maximum foveal slope (AUC:0.786). Among the regional topographic/volumetric parameters, a combination of four temporal hemiretinal parameters (rim height, inner rim volume, foveal pit depth, and pit volume) performed best for discrimination of glaucoma from normal eyes (AUC:0.903; 95% CI=0.858-0.948). A combination of 13 regional parameters selected with elastic net regression resulted in AUC of 0.931 (95% CI:0.899-0.966). In comparison, the AUC for the best GC IPL thickness parameter (inferior sector 2) was 0.895 (95% CI:0.844-0.946).

Conclusions: The newly defined topographic and volumetric foveal biomarkers are able to detect early perimetric glaucoma with clinically relevant performance. Such biomarkers do not depend on segmentation of intraretinal layers and may be helpful where adequate segmentation of macular layer cannot be achieved; they may be used to define macular phenotypes in glaucoma and could assist for detection of disease progression in the later stages of glaucoma.

CONTROL ID: 3546777

SUBMITTER (NAME ONLY): Nazarul Hasan

TITLE: Restoration of cone ON bipolar cells signalplex expression and function in a mouse model of cCSNB

SESSION TITLE: Inner retinal function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Hasan, R.G. Gregg, Biochemistry and Molecular Genetics, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|B.G. Borghuis, Anatomical Sciences and Neurobiology, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|R.G. Gregg, Ophthalmology and Visual Sciences, University of Louisville School of Medicine, Louisville, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adeno-associated virus (AAV) mediated gene delivery is showing great potential for treating genetic diseases that disrupt retinal structure and function. The human disease, complete congenital stationary night blindness (cCSNB) is a genetically heterogeneous disorder of the retina characterized by impairment of low light vision and loss of the b-wave of the electroretinogram (ERG). In mouse models of cCSNB the normal ON retinal ganglion cell responses are absent. Synaptic function requires proper alignment of pre- and postsynaptic elements, including alignment of signaling molecules that govern neurotransmitter release and reception. LRIT3 is a presynaptic, leucine rich repeat protein that when absent causes loss of the postsynaptic TRPM1 and Nyctalopin expression from the dendritic tips of rod bipolar cells, and in addition mGluR6, GPR179 and the RGS complex of proteins from dendritic tips of cone ON bipolar cells. Here we investigate whether LRIT3 expression in cone photoreceptors regulates the cone ON bipolar cells signalplex expression and localization.

Methods: To express LRIT3 in cone photoreceptors we used a human GNAT2 promoter to selectively express LRIT3 in cones. The construct GNAT2::Lrit3, was packaged in rAAVs, which were injected subretinally into adult mice. We characterized overall retinal function of GNAT2::Lrit3 rAAVs in Lrit3^{-/-} mice using ERG, and retinal ganglion cell (RGC) responses by patch-clamp recording. Expression and localization of synaptic proteins were examined by immunohistochemistry.

Results: We show that expression of LRIT3 in cones restores cone mediated retinal function. Light adapted ERGs from 12 GNAT2::Lrit3 mice showed restoration of the b-wave to between 32% and 72% of WT values. Recordings from ON alpha RGCs showed recovery of light responses and synaptic current oscillations characteristic of Lrit3^{-/-} retina were absent or negligible. Immunohistochemistry showed that LRIT3 expression was restored to cone terminals, as were the post-synaptic signalplex proteins, TRPM1, Nyctalopin, mGluR6, and GPR179.

Conclusions: Our data show that LRIT3 functions in a trans-synaptic manner and controls the expression and localization of the cone ON bipolar cell signalplex proteins. These data also show the potential for gene therapy of cCSNB patients with mutations in LRIT3 by AAV mediated gene delivery.

CONTROL ID: 3546779

SUBMITTER (NAME ONLY): Edward Bloch

TITLE: Macular subfield thickness measurements in Alport syndrome

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Bloch, K.M. Clarke, Z. Shalchi, M. Shunmugam, C.J. Hammond, M. Mohamed, Department of Ophthalmology, Guy's and St Thomas' NHS Foundation Trust, London, London, UNITED KINGDOM| E. Bloch, K.M. Clarke, Z. Shalchi, M. Shunmugam, C.J. Hammond, M. Mohamed, Ophthalmology Section, King's College London, London, London, UNITED KINGDOM|H. Storey, Department of Molecular Genetics, Viapath, Guy's and St Thomas' NHS Foundation Trust, London, London, UNITED KINGDOM|F. Flinter, Department of Clinical Genetics, Guy's and St Thomas' NHS Foundation Trust, London, London, UNITED KINGDOM|O.A. Mahroo, Institute of Ophthalmology, University College London, London, London, UNITED KINGDOM|O.A. Mahroo, Genetics Service, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Temporal macular thinning has been shown in patients with Alport syndrome (AS), particularly in X-linked males (XLM). We investigated macular retinal thickness measurements in a cohort of AS patients (including females with X-linked disease (XLF) and patients with autosomal recessive (AR) disease), making comparisons with matched control subjects and exploring association with visual acuity (VA).

Methods: Patients underwent macular optical coherence (OCT) imaging (3D OCT-1000, Topcon Corporation, Japan). One eye was included per subject. Data collected included age, genotype, VA, average retinal thickness (AvRT) and ETDRS 9-subfield thickness (outer (O), inner (I); superior (S), inferior (I), nasal (N) temporal (T) and central (C)). Temporal thinning index (TTI) was calculated using the formula $((ON+IN)-(OT+IT))/(IN+ON) \times 100$. Data were compared using Mann-Whitney-U tests and associations measured with robust logistic or linear regression models. OCT measurements were compared with similar data from 30 age and sex-matched control participants.

Results: 30 patients (15 XLM, 10 XLF, 5 AR genotypes) were included. Comparison with controls revealed a significant difference for TTI, AvRT and all EDTRS subfields (all $p \leq 0.01$), except for the IN region ($p = 0.162$). On subgroup analysis, only OT and OS subfield thickness remained significantly different from controls in each AS subgroup (all $p < 0.05$), while TTI only remained significantly different in XLM ($p \leq 0.001$). XLM subjects had significantly greater TTI than XLF subjects ($p < 0.001$). Age-adjusted logistic regression demonstrated significant association between AvRT, OT and OS with each AS subgroup (all $p < 0.05$), and TTI with XLM phenotype (OR: 3.85 [95%CI: 1.68-8.84], pseudo- R^2 0.79, $p = 0.001$). OT thickness was most strongly predictive of XLF or AR genotypes (AUC 0.89), while TTI was most strongly predictive of XLM genotype (AUC 0.99). In the XLM group, age-adjusted VA was significantly associated with all retinal thickness measurements (all $p \leq 0.02$), except the ON subfield ($p = 0.078$).

Conclusions: Alport syndrome is associated with generalized macular thinning, which is detectable in all EDTRS subfields, with the exception of the IN region. We found that retinal thickness metrics varied by subgroup, but numbers were small. In addition, most OCT thickness metrics demonstrated correlation with VA in the XLM subgroup.

CONTROL ID: 3546780

SUBMITTER (NAME ONLY): Munevver Burcu Cicekdal

TITLE: Targeted deletion of a cis-regulatory element of abca4 using a paired guide RNA CRISPR/Cas9 system in *Xenopus tropicalis*

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: ABCA4-retinopathy (including Stargardt disease, STGD1) is by far the most common single-gene inherited retinal disease (IRD). Entire ABCA4 sequencing in a large cohort of over 1,000 STGD1 cases demonstrated the importance of non-coding, mainly deep intronic splicing variants in ABCA4-associated disease pathogenesis. This raises the hypothesis that variants in other non-coding regions, such as cis-regulatory elements (CREs), may be implicated in missing heritability of ABCA4-associated disease. Previous studies have shown that CRISPR/Cas9 editing can be used to disrupt CREs in model organisms. *Xenopus (X.) tropicalis* is an interesting model organism for IRD, having the major cell types of the human eye, thousands of eggs that are easy to manipulate for CRISPR/Cas9 injections, and a true diploid genome. Here, we aimed to map and functionally study CREs of the abca4 region in *X. tropicalis*. Moreover, we aimed to generate and characterize a stable knock-out of a CRE of abca4 in *X. tropicalis* using CRISPR/Cas9 editing.

Methods: Putative CREs of abca4 were determined according to epigenetic markers H3K4me1 and Pol II in *X. tropicalis* whole embryo. Regulatory activity of putative CREs was tested using in vitro luciferase assays. Paired guide RNAs (gRNA) and Cas9 in *X. tropicalis* embryos was used to create a deletion of a selected CRE.

Results: A putative CRE of abca4, showing around 2-fold increase in luciferase activity compared to empty vector was selected as a target for disruption. Two gRNAs were designed as flanking the target CRE of abca4. The genomic region flanking the CRISPR target site was amplified and sequenced. Genome editing using a paired gRNA CRISPR/Cas9 system showed the deletion of the target CRE compared to using one gRNA and/or non-injected embryos. Further assessments including histology, immunohistochemistry, TUNEL assays and electroretinography to characterize the disease phenotype are ongoing.

Conclusions: In conclusion, regulatory elements can be disrupted in model organisms using paired gRNAs. Regulatory animal models may contribute to the annotation of the non-coding genome and provide insights into the regulation of IRD genes such as abca4.

CONTROL ID: 3546781

SUBMITTER (NAME ONLY): Andrew Tirsi

TITLE: Macular Vascular Integrity is Associated with Retinal Ganglion Cell Dysfunction in Pre-perimetric Glaucoma

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Most studies have focused on abnormalities in large vessels and capillaries that supply the optic nerve head (ONH) in glaucoma but there is little evidence on macular microvascular abnormalities in pre-perimetric glaucoma (PPG) and their effects on retinal ganglion cells (RGC) function. The purpose of this cross-sectional prospective study was to determine the relationship between foveolar avascular zone (FAZ) area, a biomarker for macular vascular integrity and RGC function assessed by pattern electroretinogram (PERG)

Methods: Twenty consecutive PPG participants (31 eyes) with normal visual fields tests and suspicious glaucomatous ONH appearance were enrolled in this study conducted at Manhattan Eye Ear & Throat hospital and underwent a complete ophthalmologic examination, standard automated perimetry, optical coherence tomography-angiography (OCTA) and PERG. FAZ area was measured using ImageJ software, with ICC of 0.99 between 2 raters. Mediation analysis Process by Andrew Hayes was tested using the Sobel test, and the bias corrected nonparametric bootstrapping procedure with 5000 bootstrapped samples, at 95% CI. The indirect effect (IE) was significant if the CI did not contain zero. $p < 0.05$ was used

Results: After controlling for risk factors for glaucoma [age, sex, intraocular pressure (IOP), central corneal thickness (CCT) and refractive error (RE)], PERG parameters Magnitude (Mag), and MagnitudeD (MagD) were significantly correlated with FAZ ($r > -0.503$, $p < 0.028$), all PERG parameters correlated with superior quadrant RNFL ($r > 0.498$, $p < 0.030$), with superior (S), superior temporal GCL-ILP thickness ($r > 0.545$, $p < 0.016$); MagD and MagD/Mag ratio with average and minimum GCL-IPL thicknesses ($r > 0.495$, $p < 0.031$). Mediation analysis revealed that FAZ area was a significant mediator in the relationship between MagD and S GCL-ILP thickness, independent of CCT and RE (effect = 4.92, $p = 0.0033$, 95% CI [0.41-9.44]). While the direct effect of MagD remained significant (effect = 4.92, $p = 0.033$, 95% CI [0.41-9.44]), the indirect effect was also significant, indicating that FAZ area partially mediated the effect of MagD on S sector GCL+IPL (effect = 2.71, 95% CI [0.22-6.06]).

Conclusions: RGC dysfunction is associated with structural thinning of the GCL-IPL layer, and this effect is partially mediated by the disruption of the macular vascular integrity and FAZ enlargement

CONTROL ID: 3546782

SUBMITTER (NAME ONLY): Simran Mangwani Mordani

TITLE: Short-Term Effects on Corneal Endothelial Cell Density and Morphology After Deep Small Incision Lenticule Extraction (SMILE)

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mangwani Mordani, E.O. Graue-Hernandez, A. Navas Perez, A. Ramirez Miranda, Cornea and Refractive Surgery, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To identify the effect of deep SMILE (160µm Cap depth) on corneal endothelium cell density (ECD) and morphology.

Methods: Retrospective, single arm pre-post study that included 30 eyes. During September-December 2020, 15 patients were identified as candidates for refractive surgery. Before surgery, measurements of endothelial cell density (ECD), coefficient of variation (CV) and hexagonality (HEX) were performed with specular microscopy. Follow up measurements of ECD, CV and HEX were repeated a week and month after SMILE surgery.

Results: All patients were within the age range of 22-42 years. Paired T-Student tests were performed to compare preoperative and postoperative measurements for ECD, CV and HEX individually, at one week and month follow up. Mean values for HEX showed no change, while ECD (2971.2 vs. 2952.1, $p=0.59$) and CV (31.9 vs. 30.5, $p=0.11$) presented a slight non-significant decrease after a week when compared to preoperative values. Compared to basal measurements, follow up mean values after a month of surgery showed a small increase in ECD (2986.9 vs. 3008.8, $p=0.49$), CV (31.9 vs. 32.3, $p=0.66$) and HEX (64.1 vs. 64.4 $p=0.79$). The same pattern was identified comparing week one and month results for ECD (2952.1 vs. 3008.8, $p=0.18$), CV (30.53 vs. 32.2 $p=0.003$) and HEX (64.2 vs. 64.4 $p=0.90$). No complications were observed.

Conclusions: Deep SMILE has no statistically significant effect on ECD and morphology. The 160µm Cap depth has no adverse effects on corneal endothelial cells and no correlation with the amount of myopia or astigmatism treated.

CONTROL ID: 3546784

SUBMITTER (NAME ONLY): Liyun Zhang

TITLE: Inducible Poly (ADP-Ribose) Polymerase Dependent Cell Death in a Zebrafish Model of Retinitis Pigmentosa

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Zhang, T. Kam, M.T. Saxena, J.S. Mumm, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is an inherited retinal degenerative disease characterized by rod cell death followed by cone loss. Recently, non-apoptotic cell death mechanisms have been implicated in RP. In a comprehensive biochemical analysis of ten mammalian RP models, evidence of non-apoptotic cell death, such as activation of Poly (ADP-ribose) Polymerase (PARP), was common across all models while apoptosis was implicated in only one. Previously, our lab generated a nitroreductase (NTR)/metronidazole (Mtz) based transgenic zebrafish model enabling inducible rod cell death to study rod cell regeneration. However, relevance of NTR/Mtz-induced cell death to retinal degeneration was unclear. The purpose of this study was to investigate the cell death mechanism of NTR/Mtz-induced rod photoreceptor degeneration.

Methods: Five day old zebrafish larvae expressing yellow fluorescent protein (YFP) and NTR in rod photoreceptors were pre-treated with cell death pathway inhibitors for four hours followed by Mtz addition to induce rod cell death. After two days, rod cell survival was assessed using an established plate reader assay. Genes encoding key factors for three cell death pathways were knocked down using CRISPR/Cas9 and rod cell survival assessed following NTR/Mtz-induced cell death. Targeted genes included parp1 (parthanatos pathway), receptor (TNFRSF)-interacting serine-threonine kinase 1 like (ripk1l; necroptosis) and caspase 3a/3b (casp3a/3b; apoptosis). qPCR was performed to confirm reduced expression of targeted genes and western blots used to assess PARP activation, i.e., accumulation of poly (ADP-ribose) (PAR) polymers.

Results: Increased rod cell survival was observed in larvae treated with PARP/parthanatos inhibitors and a necroptosis inhibitor, but not an apoptosis inhibitor. Similarly, knock down of parp1 and ripk1l, but not casp3a/3b, improved rod cell survival. Moreover, PAR polymers accumulated in Mtz-treated fish compared to controls, indicating PARP activation, a signature of parthanatos.

Conclusions: Mtz/NTR induced rod cell death involves both the PARP1/parthanatos and ripk1l/necroptosis. As both of these pathways have been implicated in neurodegeneration, including RP, we conclude that the NTR/Mtz system serves as an inducible model of RP providing a useful tool for exploring neuroprotective therapeutics.

CONTROL ID: 3546785

SUBMITTER (NAME ONLY): Hua Mei

TITLE: Identification Of Putative Limbal Stem Cells By Analyzing Label-Retaining Cells In H2B-GFP Mice Using Single-Cell RNA Sequencing

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Mei, Z. Song, Ophthalmology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|D. Wu, B. Chen, Oral - Craniofacial Health Sci, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limbal stem cells (LSCs) lack specific markers. This study is to identify putative LSC markers by analyzing label-retaining cells (LRCs) from limbus of H2B-GFP mice at single-cell level.

Methods: H2B-GFP mice express H2B-GFP under doxycycline (dox). Mice were fed with dox for 4 weeks, followed by 2 rounds of wound healing on corneal epithelium. Limbal epithelium and anterior stroma from wounded and unwounded eyes was collected and GFP⁺ cells (LRCs) were obtained by FACS followed by single-cell RNA sequencing. Data were analyzed by Seurat to partition cells into clusters based on expression similarity. The characteristic markers for each cluster were calculated by Seurat and used to identify the nature of cluster. To find correlation among clusters from wounded and unwounded eyes, the clusters from both samples were ranked in a dendrogram by hierarchical clustering.

Results: All limbal epithelial cells were GFP⁺ with dox, and no limbal epithelial cell was GFP⁺ without dox, indicating no false-negative or false-positive expression. Wounded corneas showed GFP⁺ migration from limbus to cornea, suggesting healing property of LRCs and inclusion of LSCs within LRCs. In total 11 clusters from 3136 cells were obtained from unwounded eyes and 12 clusters from 4967 cells obtained from wounded eyes. Epithelial clusters were identified by expressing epithelial-specific cytokeratins and non-epithelial clusters fell into the categories of stromal cells (Dcn, Col1a2, Col3a1) and 2 types of immune cells (Lyz2, C1qa, Trdc). Epithelial clusters were divided into stem, progenitor, and differentiated groups based on low, medium, and high expression of maturation markers (Krt12, Krt13). From dendrogram, 2 clusters in stem group were closely related to 2 clusters in progenitor group in unwounded eyes and gave rise to a new cluster in progenitor group in wounded eyes, indicating the possibility of putative LSCs. The 2 putative LSC clusters expressed a comparable high levels of progenitor markers (e.g. Krt14, Trp63). Their characteristic markers showed a specific labeling on discrete basal limbal epithelial cells.

Conclusions: Two putative LSC clusters were identified from the LRCs based on their low expression of maturation markers, close correlation to progenitor clusters, ability to produce progenitor cluster upon wounding, and discrete location on basal limbal epithelium.

CONTROL ID: 3546786

SUBMITTER (NAME ONLY): Yizi Lin

TITLE: Whole-exome sequencing study identifies rare variants associated with intraocular pressure

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Lin, K. Williams, S.E. Moroi, X.R. Gao, Department of Ophthalmology and Visual Sciences, The Ohio State University, Columbus, Ohio, UNITED STATES|X.R. Gao, Department of Biomedical Informatics and Division of Human Genetics, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genome-wide association studies (GWAS) have identified numerous common genetic variants associated with intraocular pressure (IOP), the only modifiable risk factor for glaucoma treatment. However, these common variants typically show small effect sizes. Rare variants may provide important information in furthering our understanding the IOP genetic regulation and suggest potential therapeutic targets for glaucoma. We carried out a genome-wide rare-variant analysis for IOP.

Methods: We conducted this study using data from the UK Biobank, a cohort of half a million individuals. We used 62,810 individuals of European ancestry who had both whole-exome sequencing and IOP data for this study. We performed single-variant and gene-based analyses to identify rare variants with minor allele frequency (MAF) < 1% and their corresponding genes associated with IOP using the variant-Set Test for Association using Annotation information (STAAR) method.

Results: We confirmed the known association of rs28991009 (MAF = 0.007), a nonsynonymous variant located on chromosome 1p36.22 in ANGPTL7, with IOP ($P = 2.98 \times 10^{-8}$). The gene-based analysis also showed a significant association for ANGPTL7 ($P = 1.6 \times 10^{-10}$). We identified a candidate novel nonsynonymous variant, rs372786669 (MAF = 0.0001, GRCh38/hg38 position 13613559) located on chromosome 4p15.33 in BOD1L1, that is significantly associated with IOP ($P = 3.76 \times 10^{-8}$). The gene-based association p-value for BOD1L1 was 1.6×10^{-4} . BOD1L1 was previously reported to have an association with ovarian carcinoma.

Conclusions: We confirmed known and identified candidate novel rare variants and genes associated with IOP. Our findings provide insights into the genetics of rare variants affecting IOP.

CONTROL ID: 3546787

SUBMITTER (NAME ONLY): William Erb

TITLE: New Ophthalmic Viscosurgical Device (OVD) with Enhanced Hydroxyl Radical Scavenging Activity

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.J. Erb, Bausch and Lomb Rochester, Rochester, New York, UNITED STATES|W.J.

Erb, M. Ayyagari, G. Lau, Bausch Health Companies Inc, Laval, Quebec, CANADA|

Commercial Relationships Disclosure (Abstract): William Erb: Commercial Relationship: Code N (No Commercial Relationship) | Madhu Ayyagari: Commercial Relationship: Code N (No Commercial Relationship) | George Lau: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In-vitro evaluation of increased hydroxyl radical scavenging activity of a new dispersive ophthalmic viscosurgical device (ClearVisc OVD, Bausch and Lomb, Inc.).

Methods: Using the 2-deoxy-D-ribose oxidation method, hydroxyl radicals (OH) are formed for detection via high-performance liquid chromatography (HPLC) with UV detection. Various OVD components such as buffer and additives as well as other OVD formulations have been utilized to measure their ability to scavenge free radicals that are typically formed during phacoemulsification.

Results: The results of testing provide a comparison of water as control as well as standard sodium hyaluronate formulations to the ClearVisc OVD. The results show the effectiveness of the new buffer and sorbitol additive capabilities to scavenge free radicals.

Conclusions: Hydroxyl free radicals generated during phacoemulsification in cataract surgery can contribute to corneal endothelial damage. The overall results in this study show the effectiveness of the combination of buffer and additives in this new dispersive OVD in hydroxyl free radical inhibition.

CONTROL ID: 3546791

SUBMITTER (NAME ONLY): Muhammad Sohail Halim

TITLE: Measuring Anterior Chamber Flare using Novel Slit-Lamp Imaging Technique

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Halim, N.L. Onghanseng, M. Hassan, M.S. Ormaechea, M. Hasanreisoglu, W. Matsumiya, G. Uludag, A.N. Tran, Y.J. Sepah, Q.D. Nguyen, Byers Eye Institute, Stanford University, Stanford, California, UNITED STATES|M. Halim, Ocular Imaging Research and Reading Center (OIRRC), Sunnyvale, California, UNITED STATES|A.D. Chakravarthy, M. Subramaniam, University of Nebraska Omaha, Omaha, Nebraska, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Muhammad Sohail Halim: Commercial Relationship(s); Ocular Imaging Research and Reading Center (OIRRC): Code E (Employment) | Adithi Chakravarthy: Commercial Relationship: Code N (No Commercial Relationship) | Neil Onghanseng: Commercial Relationship: Code N (No Commercial Relationship) | Muhammad Hassan: Commercial Relationship: Code N (No Commercial Relationship) | Maria Ormaechea: Commercial Relationship: Code N (No Commercial Relationship) | Murat Hasanreisoglu: Commercial Relationship: Code N (No Commercial Relationship) | Wataru Matsumiya: Commercial Relationship: Code N (No Commercial Relationship) | Gunay Uludag: Commercial Relationship: Code N (No Commercial Relationship) | Anh Tran: Commercial Relationship: Code N (No Commercial Relationship) | Yasir Sepah: Commercial Relationship: Code N (No Commercial Relationship) | Mahadevan Subramaniam: Commercial Relationship: Code N (No Commercial Relationship) | Quan Nguyen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Accurate measurement of anterior chamber (AC) flare requires a lot of experience and skill. There is a need for widely accessible tool to objectively detect and measure AC flare. The purpose of this study is to assess the use of novel imaging technique employing slit-lamp camera to reliably measure anterior chamber (AC) flare by utilizing artificial intelligence.

Methods: Subjects from a tertiary care uveitis clinic were enrolled in the study. Each subject underwent ophthalmic examination including measurement of AC flare using SUN scale, followed by imaging using a slit-lamp camera. The images were processed to extract regions of interest (ROI) between the cornea and lens indicative of presence or absence of flare (Fig. 1B-D). Next, the image was converted to the HSV (hue, saturation, value) color space; a 50×50 sample of color values resulting in 2,500 features from the ROI were organized as the feature set for that image for training and validation using a 10-fold cross validation (1E-1H). We evaluated the use of HSV color space and machine learning techniques such as support vector machines (SVM) and decision trees. Principal component analysis (PCA) was utilized to reduce the number of features without information loss and to improve model performance by addressing multi-collinearity and removing redundant features. Classification models were built using decision trees, and SVMs to classify images as with and without flare on 60 principal components (PCs) and ground truth labels with a 10-fold cross validation in R.

Results: Twenty-three (23) subjects (57% female) were enrolled in the study. Mean age was 50 years. Ninety-three (93) images (30 eyes/15 subjects) were analyzed. Slit-lamp images from eight patients were excluded due to poor image quality or ambiguous image captures (1A). PCA demonstrated that 60 components result in variance close to ~98% (1I). Table 1 outlines the results of classification models using 60-PCs as features. The model built using the HSV color space and SVM classifier showed the highest accuracy, specificity of 0.936 and 0.905 respectively, while the C5.0 classifier showed the highest sensitivity of 0.965.

Conclusions: Artificial intelligence-based image analysis of slit-lamp photographs of anterior chamber can reliably assess anterior chamber flare with high accuracy in uveitic eyes.

CONTROL ID: 3546792

SUBMITTER (NAME ONLY): Alicia Goyeneche

TITLE: Deleterious genotoxic, metabolic, and oxidative stress effects of sunlight exposure on keratinocytes and fibroblasts

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Goyeneche, M. Abdouh, E. Youhnovska, P. Garcia de Alba Graue, C. Mastromonaco, M. Caruso McDonald, J.V. Burnier, M.N. Burnier, Pathology, Research Institute of the McGill University Health Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Basal cell carcinoma and squamous cell carcinoma, the two most common non-melanoma skin cancers, are epidemiologically and molecularly linked to ultraviolet radiation (UVR) exposure. Keratinocytes and fibroblasts are the major targets of UVR within the epidermis and dermis respectively. In this study, we assessed the impact of solar radiation exposure on keratinocytes and fibroblasts in respect to genotoxic, metabolic, and oxidative stress effects.

Methods: Cells of human origin were used: primary epidermal keratinocytes (normal adult; HEKa) and normal diploid fibroblasts (Malme-3). Cells were exposed to 1-SUN by a Tri-Sol Solar Simulator (300-1800 nm), or under long path filters that gradually reduced exposure to the UVR wavelengths. Acute direct DNA damage was assessed through the accumulation of cyclobutane pyrimidines dimers (CPDs). Photo-oxidative stress was evaluated by the capacity of UVR to induce mitochondrial superoxide production. Metabolic activity was assessed by the CCK8 assay and on cell viability and toxicity by the Live/Dead assay.

Results: Solar exposure induced CPD formation in both keratinocytes and fibroblasts. Notably, a proportion of non-exposed normal adult keratinocytes were positive for CPDs, while fibroblasts were CPD negative. 1-SUN exposure caused a decrease in metabolic activity in both cell types when compared to non-exposed cells, but more markedly in fibroblasts. Viability and cell death were not affected by light exposure. Blockage of artificial sunlight spectrum by a 355 nm filter prevented the formation of CPDs, but not a decrease in metabolic activity—this was only prevented by a 380 nm filter. The production of mitochondrial superoxide was higher in solar-exposed compared to non-exposed keratinocytes and fibroblasts. Keratinocytes under the long path filters of 355, 380, 395, and 400 nm maintained a non-exposed basal level of superoxide production.

Conclusions: Exposure to wavelengths from 300 to 355 nm is enough to cause DNA damage via CPD formation in both keratinocytes and fibroblasts. Moreover, light exposure at 355-380 nm causes a reduction in metabolic activity without CPD induction. Decreased UVR stimuli resulted in increased oxidative stress in fibroblasts. Our data suggests that there is a degree of stimuli within the UVR spectrum that causes genotoxic, metabolic, and oxidative stress effects on keratinocytes and fibroblasts.

CONTROL ID: 3546793

SUBMITTER (NAME ONLY): Mandkhai Molomjamts

TITLE: Identification of reference genes for the normalization of retinal gene expression in oxygen induced retinopathy, anemia and erythropoietin administration

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Molomjamts, E. Ingolfssland, Pediatrics, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mandkhai Molomjamts: Commercial Relationship: Code N (No Commercial Relationship) | Ellen Ingolfssland: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The role of anemia on retinopathy of prematurity (ROP) is unclear; however, gene expression studies of phlebotomy induced anemia (PIA), its treatment with recombinant human erythropoietin (EPO) and oxygen induced retinopathy (OIR) may shed new light on the underlying molecular mechanism of ROP. Quantitative polymerase chain reaction (qPCR) is a sensitive technique for estimating the gene expression changes at the transcript level; however, there is no current consensus on reference genes for qPCR analysis of neonatal rat retinal tissue with PIA and OIR. We hypothesize that s18 is an unstable reference gene across these experimental conditions. In this interest, we carried out an evaluation of 8 commonly used reference genes, Ppia, Mapk1, Rplp0, S18, Hprt, Tbp, Rpp30 and Gapdh, and identified the most stable genes.

Methods: 4 groups of Sprague Dawley newborn rat pups with the following experimental conditions were generated: normoxia (control), normoxia with PIA, OIR, and OIR with PIA and EPO. The Penn et al. rat 50/10 model of OIR was used. PIA groups reached their hematocrit target of 15-20% (a 50% reduction from baseline) by P14-15. EPO groups received IP injections from P10-P20. At target timepoint, P14.5 or P20, pups were euthanized, followed by immediate whole retinal dissection. Retinas from 4-6 pups/group underwent RNA extraction, cDNA synthesis, and qPCR with 8 candidate reference genes selected from the literature. qPCR was run in duplicate. Cycles threshold (Ct) values were analyzed by RefFinder which combines ΔCt , geNorm, Normfinder, and BestKeeper algorithms to determine and rank stability of each reference gene.

Results: The three most stable reference genes were Rpp30 (stabilization index (S.I.) 1.316), Tbp (S.I. 1.732) and Ppia (S.I. 2.828). S18 and Gapdh showed the lowest stability (Figure 1). Variation of reference gene Ct values is shown in Figure 2.

Conclusions: Rpp30, Tbp and Ppia expression is least affected by experimental conditions of OIR, PIA and EPO administration, therefore suitable to use for qPCR data normalization across any of these experimental conditions.

CONTROL ID: 3546795

SUBMITTER (NAME ONLY): Ramesh Ayyala, MD

TITLE: Optimizing drug release in sterilized drug delivery devices to prevent post-operative fibrosis

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Ayyala, MD, Ophthalmology, University Of South Florida, Tampa, Florida, UNITED STATES|K. Freer, M. Fullerton, D. Blake, Biochemistry and Molecular Biology, Tulane University School of Medicine, New Orleans, Louisiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ramesh Ayyala, MD: Commercial Relationship(s);Elutimed, Inc:Code I (Personal Financial Interest);Tulane University:Code P (Patent);Elutimed, Inc:Code S (Non-remunerative) | Katherine Freer: Commercial Relationship: Code N (No Commercial Relationship) | Mitchell Fullerton: Commercial Relationship: Code N (No Commercial Relationship) | Diane Blake: Commercial Relationship(s);Tulane University :Code P (Patent);Elutimed, Inc:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Glaucoma drainage device (GDD) implantation has a 5-year failure rate of ~50% because of post-operative fibrosis. Our group has developed two drug delivery devices that reduced fibrosis after GDD implantation in an animal model (TVST 2015;4(3)4). This study advances these devices toward clinical trials by characterizing the effects of FDA-approved sterilization methods on drug release.

Methods: We compared drug release in unsterilized (US), gamma sterilized (GS), and e-beam sterilized (EBS) PHEMA and PLGA devices (n=8). Devices were manufactured and lyophilized in a GMP facility, then sterilized using gamma or e-beam irradiation. The PHEMA-device contained mitomycin C (MMC) and the PLGA device contained 5-fluorouracil (5-FU). We used UV/Vis spectroscopy to quantify drug release into saline over a 30-day period.

Results: Plots of 5-FU released vs time in the PLGA device had sigmoidal character and were fitted to a variant of the Hill equation, where " K_A " was redefined as " $T_{1/2}$ ", the time of 50% drug release, and the "Hill coefficient" was redefined as the "sigmoidicity coefficient" (SC). A lower SC indicates that similar quantities of drug are released over equal time intervals. Mean values of the $T_{1/2}$ for GS, US, EBS sterilized PLGA were 23.04, 27.67, 29.55 days. The $T_{1/2}$ of the GS product was significantly lower ($p<0.0001$) than the US or EBS material. We hypothesize that GS (at 15 kGy) introduced free radicals that enhanced PLGA degradation. Lower energy (10.5 kGy) EBS provided a product with an SC significantly lower ($p<0.013$) than that of the GS or the US product (4.57, 6.32 and 7.92, respectively). The slower, more gradual drug release provided by the EBS product may be advantageous, since optimal drug release from this product would extend over 20-30 days in order to attenuate the post-op wound-healing response. MMC release from PHEMA followed a one-phase exponential decay. GS and EGS increased polymer crosslinking, which significantly slowed drug release ($p<0.0001$). $T_{1/2}$ was 2.12, 4.17, and 5.79 days for the US, EBS and GS PHEMA, respectively

Conclusions: PHEMA and PLGA devices respond differently to sterilization. EBS led to a more gradual drug release from PLGA. Both GS and EBS slowed drug release from PHEMA. Both devices can be manufactured in a GMP facility, which provides a path for these devices to enter clinical trials.

CONTROL ID: 3546796

SUBMITTER (NAME ONLY): Lucia Le Roux

TITLE: In Vivo Neural Imaging: The Impact of Retinal Neuropathy on Axonal Transport

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Le Roux, Cancer Systems Imaging, The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES|L. Le Roux, Neuroradiology, The University of Texas MD Anderson Cancer Center, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lucia Le Roux: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The goal of this study was to illustrate retinal axonal transport with a fluorescent nerve imaging tracer based on fast axonal transport in control and neuropathic eyes. Our hypothesis was that loss of axonal transport could be an early event in the development of neuropathy.

Methods: Neuropathy was induced in Norway brown rats eyes by injecting N-methyl-D-aspartic acid (NMDA) into the vitreous of one eye and PBS into the contralateral eye as a control. 48 Hours after the NMDA injection, a fluorescently labeled neural imaging probe based on the non-toxic, C-fragment of Tetanus Toxin (TTc) was injected into the vitreous of both the treated and control eyes. In vivo imaging of the distribution of TTc was performed using retinal ophthalmoscopy. Retinas were harvested at 3 hours after TTc injections, followed by whole retinal flat mount microscopy and immuno-histology.

Results: Axonal TTc co-localizes with the retinal axonal (RA) neurofilament marker (SMI32) while a selective cytoplasmic marker (RBPMS) for retinal ganglion cells (RGC), confirmed the presence TTc endovesicles in the RGC neural somas. In contrast, neuropathic eyes showed a marked reduction in the RA TTc uptake. Plotting circular transects around the optic nerve head at a radius of 500 μ m demonstrated that axonal strand crossings were markedly reduced in retinopathic eyes at 365 ± 41.46 vs control eyes 479 ± 48.41 ($P=0.003$). There is co-localization (Pearson's $r = 0.7 \pm 0.05$) between TTc and the neurofilament marker in the control eye RAs. A relative loss of RA fluorescence in retinopathic eyes showed a reduction in co-localization (Pearson's $r = 0.4 \pm \text{SD}$) between neurofilament marker and the neural probe.

Conclusions: The retinal uptake and transport of the neural tracer, TTc, could be observed using ophthalmoscopy, and was markedly different between the normal and neuropathic state. These findings were confirmed to be specific with specific histologic markers for RAs and RGCs. NMDA induced retinopathy decreases neuronal uptake and transport of TTc, indicating that abnormalities of neuronal uptake and transport are early events in the development of retinal neuropathy.

CONTROL ID: 3546797

SUBMITTER (NAME ONLY): Stuart Mangel

TITLE: Role of circadian clock-controlled increase in GABA inhibitory feedback to cones at night.

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.C. Mangel, H. Choi, Neuroscience, The Ohio State University, Columbus, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Stuart Mangel: Commercial Relationship: Code N (No Commercial Relationship) | Heejoo Choi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Following maintained (30 min) darkness, repetitive mid-mesopic stimulation for 5-20 min increases the cone ERG by ~50%, while the rod ERG is rapidly suppressed in seconds (Bui, Fortune, 2006). This phenomenon, which has been called a “suppressive rod-cone interaction” (SRCI) (Eysteinnsson, Frumkes, 1989) (aka a “dark-light switch” (Morgan, Boelen, 1996)), has been observed in many vertebrate species including humans. Because 1) GABA inhibitory feedback from horizontal cells to cones is strongest at night in the dark, reduces the size of cone light responses, and is suppressed by light (Mangel, 2019, ARVO), and 2) closing of rod-cone electrical synapses by repetitive mid-mesopic stimulation contributes to SRCI (Heikkinen et al., 2011), we studied whether GABA inhibitory feedback to cones also mediates SRCI.

Methods: Following maintained darkness, the effects of 10 min of repetitive (0.1 Hz) mid-mesopic stimulation on goldfish cone light responses were studied in day and night using whole-cell patch-clamp recording. Because inhibitory feedback to cones is dependent on cone dopamine D_4 Rs and GABA_ARs (Mangel, 2019), we studied the effects of spiperone (SPI; D_4 R antagonist), gabazine (GBZ; GABA_AR antagonist) and/or meclofenamic acid (MFA; gap junction blocker) on SRCI.

Results: We found that after maintained darkness repetitive mid-mesopic stimulation increased cone light responses and input resistance at night but not in the day. Prior application of SPI for 30 min blocked the nighttime effect. Also, following 30 min of SPI, application of MFA or GBZ increased cone response size, and following 30 min of both SPI and MFA, GBZ increased cone response size.

Conclusions: These results indicate that the retinal circadian clock, by modulating cone D_4 Rs, enhances the GABA_AR-gated chloride conductance of cones at night so that SRCI is stronger at night than in the day. The findings suggest that as mid-mesopic illumination and/or the retinal clock gradually increase dopamine release and D_4 R activation at dawn, the resultant decrease in GABA_AR-mediated inhibition of cone terminals enhances the size of cone light responses. Conversely, the slow increase in GABA_AR inhibition of cones at dusk gradually reduces cone light response size. Because rods do not express GABA_ARs in day or night, circadian clock control of GABA inhibitory feedback to cones speeds up the transitions between rod and cone vision at dawn and dusk.

CONTROL ID: 3546801

SUBMITTER (NAME ONLY): Caitlin Collin

TITLE: CRISPR/Cas9-based genome editing approaches for RP1 associated autosomal dominant Retinitis Pigmentosa

SESSION TITLE: Gene therapy in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Collin, Q. Liu, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES]

Commercial Relationships Disclosure (Abstract): Caitlin Collin: Commercial Relationship: Code N (No Commercial Relationship) | Qin Liu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Developing a gene therapy for autosomal dominant Retinitis Pigmentosa (adRP) is extremely challenging, since suppression of the mutant protein may be required, in addition to delivery of a healthy gene. Furthermore, overexpression of many IRD genes can also lead to retinal degeneration, therefore it is necessary to maintain wild-type protein expression at endogenous levels. Around 35% of RP is caused by autosomal dominant mutations, with mutations in RP1 accounting for around 5-10% of cases. The CRISPR/Cas9 system can distinguish target sequences differing by a single base pair, thus we propose to develop a haplotype based approach to specifically ablate mutant RP1 alleles which bear any dominant frameshift or nonsense mutation in exon 4

Methods: Three common RP1 haplotypes carrying distinct SNPs were identified from the 1000 Genome Project. sgRNAs for SNPs on each of the three haplotypes were synthesized and cotransfected with Cas9 expressing plasmids into human cell lines that are heterozygous or homozygous for the RP1 haplotypes. Editing efficiency and allele-specificity was determined by PCR and amplicon sequencing. The most efficient sgRNAs were then tested in combination with a non-allele specific sgRNA targeting intron 3. Dual DSBs and deletion of a fragment of RP1 genome were analysed and quantified by qPCR. The expression level of the targeted RP1 allele was quantified by qPCR in modified RP1-expressing Hap1 cells.

Results: A non-allele specific sgRNA with high editing efficiency was tested in pair-wise combinations with allele specific sgRNAs targeting intron 1, or exon 4. These dual Cas9/sgRNAs were able to delete 3.5-6 kb of genomic DNA, encompassing either exons 2 and 3, or a large portion of exon 4 of RP1 in an allele specific manner. Deletion of the large fragment of RP1 genome led to reduction of RP1 expression in edited Hap1-EF1a-RP1 cells

Conclusions: This proof-of-concept study is an important step towards the application of CRISPR/Cas9 gene editing technology in the treatment of patients with RP1 associated dominant IRDs. Our haplotype-based approach greatly enhances the feasibility of using the CRISPR-Cas9 system because a small number of sgRNAs are necessary to specifically target relatively large sets of mutant alleles. Furthermore, it paves the avenue of its application in human RP1 patients

CONTROL ID: 3546803

SUBMITTER (NAME ONLY): Pablo Galarza

TITLE: Survival of uveal melanoma patients with additional malignancies.

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.E. Galarza, J. Pe'er, S. Frenkel, Ophthalmology, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|S. Frenkel, The Wohl Institute for Translational Medicine, Hadassah Medical Center, Jerusalem, Jerusalem, ISRAEL|

Commercial Relationships Disclosure (Abstract): Pablo Galarza: Commercial Relationship: Code N (No Commercial Relationship) | Jacob Pe'er: Commercial Relationship: Code N (No Commercial Relationship) | Shahar Frenkel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Patients with uveal melanoma (UM) may also develop other tumors before or after being diagnosed with UM, but there is little characterizing data in the literature. We assessed the survival of UM patients with second malignancies in Israel.

Methods: A retrospective review and analysis of a cohort of 927 uveal melanoma patients at the Ocular Oncology Service of the Hadassah University Hospital from 1982 to 2017.

Results: Seventy-four (7.9%) patients (42 (57.5%) women) had second tumors. In 37 (50.7%) patients UM was diagnosed 69.5 months before a second malignancy, while in the rest it appeared 128.3 months after another malignancy. The most common malignancies in descending order were: breast (32%), colon (16%), renal cell carcinoma (9%), cutaneous melanoma (8%), basal or squamous cell carcinoma (8%), and other tumors (27%). The mean (\pm SE) survival for UM patients without and with second malignancies was similar (230.4 (\pm 7.5) vs. 200.9 (\pm 16.9) months, respectively, Log-Rank $p=0.48$). Survival was also similar whether UM was diagnosed first or after another malignancy (205.5 (\pm 19.6) vs. 159.1 (\pm 16.8) months, respectively, Log-Rank $p=0.52$). There is a trend for a higher chance to develop UM metastases if patients did not have a second malignancy (16.7% vs. 9.5%, respectively, Likelihood ratio $p=0.083$). Whether UM was diagnosed first did not impact that chance (Likelihood ratio $p=0.50$).

Conclusions: Second malignancies in UM patients are uncommon and do not affect the overall survival.

CONTROL ID: 3546804

SUBMITTER (NAME ONLY): Kayvan Barekattain

TITLE: Impact of Anti-VEGF therapy on Swept Source OCTA measurements in Diabetic Retinopathy

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Barekattain, S. Sharma, K. Baynes, C. Chen, J. Bhangu, N. Karthik, P. Le, M. Ramos, M.A. McDonald, D. Burton, P.M. Kaiser, A. Rachitskaya, P.K. Kaiser, J.P. Ehlers, S. Srivastava, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kayvan Barekattain: Commercial Relationship: Code N (No Commercial Relationship) | Sumit Sharma: Commercial Relationship(s);Alimera:Code C (Consultant);Allergan:Code C (Consultant);Bausch and Lomb:Code C (Consultant);Clearside:Code C (Consultant);Eyepoint:Code C (Consultant);Genentech:Code C (Consultant);Regeneron:Code C (Consultant) | Kimberly Baynes: Commercial Relationship: Code N (No Commercial Relationship) | Cindy Chen: Commercial Relationship: Code N (No Commercial Relationship) | Jasmin Bhangu: Commercial Relationship: Code N (No Commercial Relationship) | Naveen Karthik: Commercial Relationship: Code N (No Commercial Relationship) | Phuoc-Hanh Le: Commercial Relationship: Code N (No Commercial Relationship) | Michael Ramos: Commercial Relationship: Code N (No Commercial Relationship) | Megan McDonald: Commercial Relationship: Code N (No Commercial Relationship) | Danielle Burton: Commercial Relationship: Code N (No Commercial Relationship) | Peter Kaiser: Commercial Relationship: Code N (No Commercial Relationship) | Aleksandra Rachitskaya: Commercial Relationship(s);Genentech:Code C (Consultant);Alcon:Code C (Consultant);Allergan:Code C (Consultant);Novartis:Code C (Consultant);Zeiss:Code C (Consultant) | Peter Kaiser: Commercial Relationship(s);Alcon:Code C (Consultant);Allegro:Code C (Consultant);Allergan:Code C (Consultant);Bayer:Code C (Consultant);Boehringer Ingelheim:Code C (Consultant);Kodiak:Code C (Consultant);Novartis:Code C (Consultant);Oxurion:Code C (Consultant);Regeneron:Code C (Consultant) | Justis Ehlers: Commercial Relationship(s);Aerpio:Code C (Consultant);Alcon:Code C (Consultant);Allergan:Code C (Consultant);Genentech:Code C (Consultant);Novartis:Code C (Consultant);Regeneron:Code C (Consultant);Oxurion:Code C (Consultant);Allegro:Code C (Consultant);Leica:Code C (Consultant);Roche:Code C (Consultant);Santen:Code C (Consultant);Zeiss:Code C (Consultant) | Sunil K. Srivastava: Commercial Relationship(s);Eyepoint:Code C (Consultant);Regeneron:Code C (Consultant);Allergan:Code C (Consultant);Santen:Code C (Consultant);Novartis:Code C (Consultant);Regeneron:Code C (Consultant);Bausch and Lomb:Code C (Consultant);Eyepoint:Code C (Consultant);Eyeevensys:Code C (Consultant);Abbvie:Code C (Consultant);Zeiss:Code C (Consultant)

ABSTRACT BODY:

Purpose: To evaluate the utility of Swept-Source Optical Coherence Tomography Angiography (SS-OCTA) in non-invasively assessing change in perfusion and density after anti-VEGF therapy in diabetic retinopathy (DR) when compared to ultra-widefield Fluorescein Angiography (UWFA) leakage metrics.

Methods: This is a retrospective review of consecutive DR patients who had received repeated SS-OCTAs (Zeiss Plex Elite) and UWFAs (Optos California). 6mm x 6mm and 3mm x 3mm images of non-proliferative and proliferative DR eyes were analyzed. Both perfusion density (total area of perfused vasculature per unit area ranging from 0-1) as well as vessel density (total perfused vasculature per unit area) were obtained. UWFA metrics were quantified using a customized feature analysis platform that detected leakage indices automatically (3-disc diameter and 6-disc diameter areas of leakage centered on the macula). Statistical analysis was performed using MS-Excel.

Results: 20 eyes were included in the 6x6 SS-OCTA non-treatment group while 8 eyes were in the treatment group. Of these, 16 also had 3x3 SS-OCTA for the non-treatment group and 4 had treatment. UWFA analysis was available for 15 of the eyes without treatment and 6 of those with treatment. Average follow up was 12.1 months.

In the 3x3 non-treatment group there was significant reduction in superficial and deep perfusions and densities over time within the average field of view ($p<.05$). Superficial perfusion density averaged at 0.314 at baseline and decreased 12.1%. Deep perfusion density averaged 0.184 at baseline and reduced by 23.5%. No significant difference was seen in the treatment group ($p>0.1$). Similar associations were seen in the 6x6 SS-OCTA non-treatment ($p<0.1$) vs treatment groups ($p>0.1$).

Findings of UWFA showed similar trends, with leakage indices worsening in those not treated vs treated. 6-disc diameter macula centered leakage area showed an average baseline leakage of 1.8% that increased 50.7% in the non-treatment group ($p=0.056$) and had insignificant change in the treatment group $p>0.1$.

Conclusions: SS-OCTA and UWFA can quantify the impact of anti-vegf therapy in DR patients over time. Using both modalities, trends towards better perfusion metrics in those treated vs non treated were seen. Further larger investigations will verify whether SS-OCTA can quantify a difference from anti-VEGF treatment over time in DR patients.

CONTROL ID: 3546805

SUBMITTER (NAME ONLY): Katharine Bunch

TITLE: Arginase Isoforms and Diabetic Retinopathy in the db/db Mouse

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.L. Bunch, R.W. Caldwell, Pharmacology and Toxicology, Augusta University, Augusta, Georgia, UNITED STATES|R.B. Caldwell, Research, Charlie Norwood VA Medical Center, Augusta, Georgia, UNITED STATES|R.B. Caldwell, Vascular Biology Center, Augusta University, Augusta, Georgia, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Katharine Bunch: Commercial Relationship: Code N (No Commercial Relationship) | Ruth Caldwell: Commercial Relationship: Code N (No Commercial Relationship) | Robert Caldwell: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The obese, type 2 diabetic db/db mouse has been established as suitable model for the pathogenesis of human diabetic retinopathy (DR), but the role of arginase in this model is unknown. Given the association of arginase isoforms, A1 and A2, in several models of retinopathy, we hypothesize that A1 and A2 are associated with the pathophysiology of DR in the db/db mouse. A1/A2 compete with nitric oxide synthase (NOS) for L-arginine and increased A1/A2 decreases nitric oxide (NO) levels. NO is imperative for tissue perfusion in many pathologic disease states, including stroke, DR, and cardiovascular disease (CVD). Increased NO has been shown to be protective in murine models of stroke, CVD, and DR, while A2^{-/-} mice were protected against western diet-induced DR.

Methods: Whole eyes, retinas, and plasma were collected from 16 (n=8) and 23 week-old (n=6) female db/db mice and their DB/db (control) littermates (#000642). Globes were sectioned and immunofluorescence (IF) was performed for A1, A2, markers of inflammation, and neuroglial activation, including GFAP and IL-6. Retinas were used to western blot for proteins in the NLRP3 inflammasome cascade, products of reactive oxygen species, and hypoxia, including A1, A2, GFAP, HIF-1 α , and IL-1 β . Western blot signals were quantified by densitometry using ImageJ software and normalized to loading controls. Plasma was used for A1 ELISA analysis, reported in ng/mL. GraphPad Prism 9 was used to implement unpaired t-test analyses. Values of p<0.05 were considered significant.

Results: A1 levels were markedly increased in both the plasma (16 weeks p=0.011, 23 weeks p<0.0001) and retina lysates (p=0.005) of the db/db mice compared to controls. Retinal A2 was also significantly increased (p=0.0332). Markers of inflammasome activation were significantly increased in db/db retinas (Eg: IL-1 β p=0.008). Hypoxia marker HIF-1 α , a VEGF transcription factor, was also markedly elevated in db/db retinas (p=0.027). IF of GFAP, an indicator of neurodegeneration, showed increased expression in db/db retinas compared to controls.

Conclusions: These results are consistent with our hypothesis that A1 and A2 are linked to the pathophysiology of DR in the db/db mouse, as elevated A1 and A2 correlate with increased markers of hypoxia, inflammation, neurodegeneration in db/db mouse retina compare to controls. Further investigation is needed to elucidate the mechanistic effects of A1/A2 on the pathogenesis of db/db DR.

CONTROL ID: 3546806

SUBMITTER (NAME ONLY): Wanyi Jia

TITLE: Neuronal Activity-Dependent Myelin Plasticity during Adulthood

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Jia, R.T. Karadottir, Cambridge Stem Cell Institute, Cambridge, Cambridgeshire, UNITED KINGDOM|W. Jia, T. Khatib, Clinical Neurosciences, John van Geest Centre for Brain Repair, Cambridge, Cambridgeshire, UNITED KINGDOM|K.R. Martin, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Oligodendrocytes in the central nervous system (CNS) produce myelin, which is essential for ensuring fast signal transmission in neurons, providing synchronization of neuronal impulses, and maintaining axonal health. Unlike previously believed, increasing evidence show that myelin changes throughout life. Oligodendrocyte precursor cells differentiate into myelinating oligodendrocytes until old age. Several studies demonstrate that de novo myelination onto previously unmyelinated axons and myelin remodeling of existing sheaths' length, thickness, and number occurs in many CNS regions. Both human and murine studies suggest that neuronal activity plays a role in de novo myelination and myelin remodeling, the two components of myelin plasticity. In light of this, we asked how neuronal activity regulates myelin plasticity, and whether bidirectional changes could occur.

Methods: Using designer receptor exclusively activated by designer drugs (DREADDs), we increased and decreased neuronal activity of retinal ganglion cells via the Gq (hM3Dq) and Gi (hM3Di) pathways to observe myelin plasticity in the optic nerve. Recent studies showed that the inert DREADD ligand clozapine N-oxide does not cross the blood brain barrier, and that its metabolite clozapine is responsible for DREADD activation in vivo. Since clozapine is an antipsychotic drug that affects multiple endogenous receptors at high concentration, we performed a dose-response curve to determine the optimal concentration for long-term neuronal activity change without affecting endogenous receptors. Using the PDGFR α -CreER^{T2}:Tau-mGFP and OPALIN-iCreER^{T2}:Tau-mGFP mouse lines, which label newly myelinating and currently existing OLs, we quantified how neuronal activity regulates de novo myelination and myelin remodeling during adulthood.

Results: We demonstrated that clozapine has greater affinity to DREADDs in vivo than CNO and at low concentrations, clozapine does not cause off-target effects. Moreover, we showed that neuronal activity bidirectionally affects the rate of differentiation of OPCs as well as the morphology of existing and newly myelinating oligodendrocytes.

Conclusions: Our data suggest that myelinating glia can detect functional activity in axons and respond with adaptive change. Additionally, these findings indicate that activity-dependent communication may stretch beyond synaptic transmission.

CONTROL ID: 3546807

SUBMITTER (NAME ONLY): Nate Pappenhagen

TITLE: Metabolic changes in optic nerve head astrocytes following glaucoma-associated deformation

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pappenhagen, K. Zaman, L. Prokai, D.M. Inman, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|N. Pappenhagen, Biomedical Sciences, Kent State University, Kent, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: The astrocytes of the optic nerve head are in a unique position in glaucoma as the predominant glial cell in the unmyelinated portion of the optic nerve. We tested the metabolic changes these cells face in glaucoma by exposing them in vitro to degrees of deformation/stretch that these cells would similarly experience from increased intraocular pressure in order to better understand the role of metabolism in glaucomic degeneration.

Methods: Primary astrocytes were cultured from the cortices of P1 mouse pups or P7 optic nerve head explants then seeded on collagen-coated FlexCell plates. The astrocytes were then biaxially stretched by 12% for 24 hours using the FX-6000T FlexCell system. Conditions were chosen to mimic the forces applied to optic nerve head astrocytes (ONHAs) during glaucoma. ONHA glycolytic rates and mitochondrial fuel preferences were measured using the Seahorse XFe24 Analyzer, while changes in the proteome were measured using mass spectroscopy.

Results: Stretched cortical astrocytes showed at least twofold increases in metabolic proteins such as glutamate dehydrogenase 1, isocitrate dehydrogenase 1, and aldolase fructose-bisphosphate c (n=3, p=0.00024, p=0.022, and p=0.00065). There was also a twofold decrease in citrate synthase, a 10-fold decrease in isocitrate dehydrogenase 2, and 2.5-fold decreases in glycogen phosphorylase B and adenylate kinase 1. In the Seahorse Analyzer, stretched ONHAs showed an increased glycolytic extracellular acidification rate (ECAR), maximal ECAR, and baseline oxygen consumption rate (n=18, p=0.0032, p=0.0070, and p=0.0203). Stretched astrocytes showed no difference in their dependence on pyruvate compared to controls, but a significant decrease in their capacity for mitochondrial respiration from pyruvate (n=18, p=0.0828 and p=0.0001).

Conclusions: Exposing astrocytes, both cortical and ONHAs, to glaucoma-associated deformation altered their metabolism in ways that indicated increased glycolytic activity compared to control astrocytes. The increase in glutamate dehydrogenase 1 combined with a decrease in isocitrate dehydrogenase 1 and citrate synthase suggest a shift away from mitochondrial energy production. The decrease in pyruvate-based mitochondrial respiration capacity is consistent with these findings.

CONTROL ID: 3546808

SUBMITTER (NAME ONLY): Ram Nagaraj

TITLE: Advanced glycation endproducts are not elevated in human diabetic lens capsules when compared to age-matched nondiabetic lens capsules

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Nagaraj, J. Rankenberg, B. Wagner, J. Patnaik, A. Lynch, Ophthalmology, University of Colorado School of Medicine, Aurora, Colorado, UNITED STATES|S. Rakete, Institute and Clinic for Occupational, Social and Environmental Medicine, University Hospital LMU, GERMANY|M. Glomb, Institut für Chemie - Lebensmittelchemie, Martin-Luther-Universität Halle-Wittenberg, Halle, Sachsen-Anhalt, GERMANY|

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ABSTRACT BODY:

Purpose: Formation of advanced glycation endproducts (AGEs) in tissues with negligible protein turnover, such as the lens capsule, leads to their accumulation with aging. We have previously shown that AGEs in the lens capsule exacerbate TGF β 2-mediated mesenchymal transition of lens epithelial cells and proposed that capsule AGEs could play a role in posterior capsule opacification (PCO) after cataract surgery (Raghavan et al., Aging Cell, 15, 465, 2016). To determine the effects of diabetes on capsule AGEs, in this study we measured the levels of AGEs in capsulorhexis specimens collected from non-diabetic and diabetic [with or without retinopathy (DR)] cataract patients.

Methods: Capsulorhexis specimens were obtained at the time of cataract surgery from consented patients at the Sue Anschutz-Rodgers Eye Center. Following removal of adherent epithelial cells and fiber cell mass, capsulorhexis specimens were hydrolyzed with enzymes or 6N HCl to measure AGEs. We measured 14 AGEs using an LC-MS/MS multimethod and reference compounds. Means and 95% confidence intervals of each AGE were compared across the three patient groups.

Results: Patients included 48 non-diabetic, 42 diabetic without DR and 30 diabetic with DR. Among the AGEs measured, the levels of CMA were highest for all patient groups but did not significantly differ; 205.9 ± 21.4 , 246.7 ± 22.8 and 217.1 ± 27.8 pmoles/ μ mol OH-proline equivalent in nondiabetics, diabetics and diabetics with DR, respectively. The levels of other AGEs were < 50 pmoles/ μ mol OH-proline equivalent. When adjusted for age and gender, the levels of most AGEs were similar between diabetics (with or without DR) and nondiabetics, although glucosepane was significantly lower for non-diabetics.

Conclusions: Our data show that the AGE levels are similar in non-diabetic and diabetic (with or without DR) capsules and provide a biochemical basis for the similar incidence of PCO in nondiabetic and diabetic cataract patients, observed in some studies.

CONTROL ID: 3546810

SUBMITTER (NAME ONLY): Alan Marmorstein

TITLE: Identification and validation of ZSCAN10 as a marker of iPSC impurities in cultures of iPSC-derived RPE.

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.D. Marmorstein, M. Hill, C. Andrews-Pfannkoch, J. Pulido, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: iPSC derived RPE transplants potentially offer a treatment for macular degeneration. The clinical use of iPSC-derived RPE cells requires testing of the final product for the presence of contaminating iPSCs. While LIN28A has been suggested as a marker of iPSC contamination in RPE, it is likely that regulatory bodies will require redundant testing with additional markers. To accomplish this we sought to identify and validate a new marker of pluripotency that could be used to identify contaminating iPSCs in a preparation of iPSC-derived RPE cells.

Methods: We performed RNASeq on iPSC's and iPSC-derived RPE from the same donor and screened for mRNAs that were in the iPSC dataset and not the RPE dataset. To confirm the RNASeq data we performed SybrGreen reverse transcription PCR on ZSCAN10 a candidate gene identified from the RNASeq dataset. qPCR was used to determine relative levels of expression of ZSCAN10 across iPSC clones from different donors and from clones isolated from the same donor. Publicly available databases were screened to determine expression of ZSCAN10 in tissue.

Results: Of the top 10 genes identified by our RNASeq screen, ZSCAN10 was the only gene identified that is a known marker of pluripotency. Using RT-PCR we observed ZSCAN10 expression in 15 of 15 iPSC cell clones from 6 different donors, but not in RPE cultures derived from those donors. Using qPCR the ZSCAN10 signal was observed in similar amounts in all iPSC tested regardless of donor. ZSCAN10 was only observed in the iPSC cells and was absent from all iPSC-RPE preparations tested. Screening of publicly available databases identified very low levels of expression in human tissue, predominantly in brain and kidney.

Conclusions: ZSCAN10 is a strong marker of undifferentiated iPSC impurities in a population of iPSC-derived RPE.

CONTROL ID: 3546813

SUBMITTER (NAME ONLY): Devy Deliyanti

TITLE: ROR γ inhibition attenuates vasculopathy in mice and rats with diabetic retinopathy by reducing Th17 cells and increasing the functionality of Tregs

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Deliyanti, V. Suphapimol, J.L. Wilkinson-Berka, Anatomy and Neuroscience, The University of Melbourne, Melbourne, Victoria, AUSTRALIA]

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ABSTRACT BODY:

Purpose: Purpose: The vision-threatening vascular pathology that can develop in diabetic retinopathy (DR) is highly influenced by angiogenic factors such as vascular endothelial growth factor (VEGF). There is evidence that retinal inflammation also promotes vascular injury in DR, but the mechanisms involved are not fully understood. We previously reported that increasing the number of anti-inflammatory Foxp3 regulatory T cells (Tregs) reduced inflammation and vasculopathy in mice with proliferative retinopathy. Tregs exist in balance with pro-inflammatory Th17 cells via the retinoic acid receptor-related orphan receptor (ROR) γ . Here, we hypothesised that ROR γ inhibition would attenuate retinal inflammation and vasculopathy in DR by reducing the abundance of Th17 cells and increasing Treg functionality.

Methods: Methods: Female Sprague Dawley rats were made diabetic with streptozotocin (STZ) and then studied for 8 weeks. To evaluate Tregs, male Foxp3^{rfp} mice (C57Bl6/J background) expressing Foxp3 as a red fluorescent protein (rfp) were administered STZ and studied for 26 weeks. Comparisons were made to non-diabetic controls, and animals administered the ROR γ inhibitor, SR2211 (3mg/kg) intraperitoneally one week after STZ and once every three days until the end of the studies. Twenty-four to 36 animals were studied per group, and data were analysed by unpaired t-tests or one-way ANOVAs. Statistical significance was defined as $p < 0.05$.

Results: Results: SR2211 had no effect on body weight and blood glucose and Hba1c levels. In rats with DR, the number of Th17 cells was increased compared to non-diabetic rats and reduced with SR2211. In mice with DR, SR2211 did not alter the number of Tregs in blood, lymph nodes and spleen, but did increase the number of effector Tregs (CD44⁺CD62L⁻) in lymph nodes. Importantly, in both rats and mice with DR, SR2211 reduced retinal vascular leakage and VEGF protein levels compared to diabetic controls. In diabetic rats, the mRNA levels of the inflammatory factors, tumour necrosis factor (TNF) and intracellular adhesion molecule (ICAM)-1 in retina were reduced by SR2211.

Conclusions: Conclusion: ROR γ inhibition attenuates DR by reducing pro-inflammatory Th17 cells and boosting the functionality of Tregs.

CONTROL ID: 3546814

SUBMITTER (NAME ONLY): Kathleen Chirco

TITLE: Establishing an in vitro human Leber congenital amaurosis model system

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.R. Chirco, S. Chew, J.L. Duncan, A.T. Moore, D.A. Lamba, Department of Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dominant cone-rod homeobox (CRX)-associated Leber congenital amaurosis (LCA7) is a severe retinal degenerative disease for which no treatments are currently available. Disease-causing variants in CRX typically result in the production of a dominant negative form of the protein, which disrupts normal photoreceptor maturation. To gain further insight into LCA7, we aimed to establish an in vitro model system to investigate CRX variant-specific disease mechanisms.

Methods: Human iPSC lines were generated from LCA7 patient whole blood samples, which harbor dominant mutations in CRX (CRX^{T155ins4/+} and CRX^{K88Q/+}). The patient-derived hiPSC lines were differentiated to generate retinal organoids, and immunohistochemistry, TEM, qPCR, and single-cell RNA sequencing were utilized to characterize photoreceptor cell development and maturation up to day 240 (D240) of differentiation.

Results: Retinal organoids were successfully generated from patient iPSCs, and both lines exhibit retinal tissue thickness and photoreceptor cell numbers comparable to those of CRX^{WT} organoids throughout differentiation. Morphologically, both CRX^{T155ins4/+} and CRX^{K88Q/+} organoids remain identical to CRX^{WT} until D240, when they fail to develop outer segments, similar to what has been reported in LCA7 patients and mouse models. Although both CRX^{T155ins4/+} and CRX^{K88Q/+} organoids exhibit similar levels of OTX2 protein and mRNA compared to control, CRX^{T155ins4/+} organoids show an increase in total CRX, while CRX^{K88Q/+} organoids show a decrease. CRX^{T155ins4/+} and CRX^{K88Q/+} organoids both reveal a reduction in RCVRN, AIPL1, ARR3, RHO, OPN1SW, OPN1MW, and OPN1LW compared to CRX^{WT} organoids (p<0.05), suggesting a decrease in expression of key photoreceptor genes. Variant-specific differences in levels of NRL, NR2E3, SAG, and cone opsins were also observed through D240 of differentiation, highlighting intriguing differences in disease mechanisms between variants.

Conclusions: Here, we have established an early photoreceptor cell-specific LCA phenotype in our patient organoids, and these data provide promise for a reliable in vitro model system which can be used to study variant-specific disease mechanisms. Future work will focus on studying disease mechanisms and therapeutic approaches in our organoid model system.

CONTROL ID: 3546815

SUBMITTER (NAME ONLY): Zohreh Hosseinaee

TITLE: Non-contact, in-vivo, functional, and structural ophthalmic imaging using dual-modal photoacoustic remote sensing microscopy and optical coherence tomography

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Hosseinaee, N. Abbasi, L. Khalili, L. Mukhangaliyeva, A. Mei, N. Pallegirino, P. Haji Reza, System Design Engineering, University of Waterloo, Waterloo, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: To provide complementary imaging contrast of optical absorption and optical scattering through a completely non-contact imaging system. For the first time, photoacoustic remote sensing (PARS) microscopy is combined with a swept-source optical coherence tomography (SS-OCT) system and applied for non-contact, in-vivo functional and structural imaging of the murine ocular tissue.

Methods: Multi-wavelength, photoacoustic remote sensing microscopy is combined with swept-source optical coherence tomography. The PARS subsystem has a 532-nm nanosecond-pulsed fiber laser which is co-focused with an 830-nm interrogation beam within the tissue. Stimulated Raman Scattering (SRS) happening inside the excitation fiber was used to implement multiwavelength imaging. The difference in optical absorption of oxy and de-oxy hemoglobin at different wavelengths is utilized to evaluate oxygen saturation inside ocular tissue and reconstruct the oxygen saturation (SO₂) map. The OCT subsystem consists of a swept-source laser centered at 1060 nm with 100 nm spectral bandwidth and frequency swept at 60 kHz.

Results: Figure A represents a cross-sectional OCT image acquired from the anterior segment in the mouse eye which provides depth-resolved scattering contrast over the anterior part of the eye. Figure B is acquired from iris vasculature in the mouse eye using PARS microscopy covering an area of 2 mm × 2mm. Figure C represents the SO₂ map in the iris vasculature acquired using PARS microscopy using 532 nm and 545nm wavelengths.

Conclusions: The presented dual-modal system can provide complementary imaging contrast of optical absorption and optical scattering. The non-contact imaging ability of the system makes it a favorable technology for clinical ophthalmic imaging applications. The system is a major step toward non-invasive, simultaneous, and accurate measurement of the metabolic rate of oxygen (MRO₂) in the ophthalmic tissue and can assist ophthalmologists with the diagnostics and treatment of major eye diseases.

CONTROL ID: 3546816

SUBMITTER (NAME ONLY): Chengxin Zhou

TITLE: Safety and efficacy of a novel injectable anti-TNF- α /anti-VEGF drug delivery system for corneal and retinal protection after injury.

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Zhou, P. Hui, N. Wolkow, C.H. Dohlman, D.G. Vavvas, E.I. Paschalis, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|N. Wolkow, David G. Cogan Laboratory of Eye Pathology and Ophthalmic Plastic Surgery Service, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|C. Zhou, P. Hui, C.H. Dohlman, E.I. Paschalis, Boston Keratoprosthesis Laboratory, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|D.G. Vavvas, Angiogenesis Laboratory, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a novel therapy to suppress acute and long-term ocular complications after injury by using an injectable thermosensitive drug delivery system (DDS) for sustained subconjunctival delivery of anti-TNF- α and anti-VEGF reagents.

Methods: A thermosensitive, biodegradable hydrogel DDS (PLGA-PEG-PLGA triblock) loaded with 2mg of infliximab and aflibercept (1:2; Infli/Afli) was injected subconjunctivally in 3 Dutch-belted rabbits after corneal alkali injury. Control rabbits received human IgG loaded DDS (n=4) or only aflibercept DDS (n=3). Animals were followed for 3 months and assessed in vivo for tolerability, corneal neovascularization (CoNV), re-epithelialization, and ex vivo for retinal ganglion cell (RGC) loss, optic nerve axon loss, and expression of inflammatory markers. Drug release kinetics was assessed in-vitro by using fluorescein-dextran as a model drug, and in-vivo by aqueous humor analysis.

Results: Infli/Afli DDS treatment led to complete suppression of CoNV for over 3 months without adverse effects or reactions by the eye, while aflibercept DDS showed mild CoNV (~10% of cornea) and IgG DDS significantly more CoNV (~30% of cornea). Eyes treated with Infli/Afli DDS showed minimal corneal epithelial defect (0-2% of cornea) over 3 months, while IgG DDS treated eyes exhibited epithelial defect up to 11% of the cornea area albeit wound closure at 3 months. Aflibercept DDS group exhibited persistent corneal epithelial defects (~7% at 3 months). Histologically, Infli/Afli DDS reduced CD45⁺ immune cell accumulation (92%, P<0.05) and ameliorated TNF- α expression (70%, P<0.05) in the cornea, as compared to IgG DDS. Subconjunctival administration of infli/afl DDS achieved sustained retinal drug diffusion, and prevented RGC loss as compared to the other two groups at 3 months which exhibited 33-63% RGC loss. Quantification of IgG content in the aqueous humor using ELISA assay demonstrated that the DDS provided sustained, first-order drug release for over 3 months.

Conclusions: Sustained subconjunctival administration of infliximab and aflibercept using a thermosensitive biodegradable DDS that targets TNF- α and VEGF signaling pathways is an extremely effective therapy for preventing post-injury corneal inflammation and neovascularization, while providing the much needed retinal protection against RGC loss. Further studies are warranted.

CONTROL ID: 3546817

SUBMITTER (NAME ONLY): Rebhi Abuzaitoun

TITLE: The prevalence, visual significance, and genotype-phenotype associations of foveal hypoplasia in inherited retinal diseases

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Abuzaitoun, K. Branham, D. Schlegel, T. Jayasundera, A.T. Fahim, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the prevalence, visual significance, and genotype-phenotype associations of foveal hypoplasia (FH) in inherited retinal degenerations (IRDs).

Methods: In this retrospective case-control study, the case group of 285 patients (492 eyes) consisted of genetically-confirmed IRDs while the control group contained 256 IRD-free patients (444 eyes). Exclusion criteria were age less than four, poor-quality/absent optical coherence tomography (OCT), or loss of retinal OCT lamination. LogMAR Best corrected visual acuity (BCVA), OCT, and demographic data were obtained. Published FH grading was used.

Results: Foveal hypoplasia was significantly prevalent in retinitis pigmentosa (RP; 110/351, 31.33%, $p < 0.001$), as well as IRDs overall (135/492, 27.44%, $p < 0.001$), compared to controls (20/444, 4.50%). In RP, LogMAR BCVA in FH grade 1 (0.18) was not different from age and gender matched patients with fully-developed fovea (0.18) ($p = 0.06$). Similarly, in controls BCVA of FH grade 1 (-0.01) was not different from age/gender-matched eyes with fully-developed fovea (0.02) ($p = 0.06$). RPGR (21/50, 42%) and USH2A (16/75, 21.33%) were significantly associated with FH compared to controls ($p < 0.001$, $p < 0.001$).

Conclusions: FH is associated with IRDs, and RP in particular. Genotypes RPGR and USH2A are each individually associated with FH. Although grade 1 FH is associated with IRDs that may reduce visual function, grade 1 FH is not associated with reduced visual acuity within the IRD cohort, indicating visual insignificance of persistent inner retinal layers. The presence of grade 1 or atypical grade FH in a patient with reduced vision should prompt consideration of an IRD diagnosis.

CONTROL ID: 3546821

SUBMITTER (NAME ONLY): Eric Kawulok

TITLE: Multicenter Review of Indications for Scleral Lens Wear

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Kawulok, Ophthalmology, Mayo Clinic Arizona, Scottsdale, Arizona, UNITED STATES|M. Schornack, C.B. Nau, Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, UNITED STATES|C. Guier, Ophthalmology, Mayo Clinic's Campus in Florida, Jacksonville, Florida, UNITED STATES|C. Wentz, Illinois College of Optometry, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Survey research has defined primary indications for scleral lens wear as corneal irregularity (74%), ocular surface disease (16%), and uncomplicated refractive error (10%). Data on secondary indications or specific conditions for lens wear have not been systematically reported. This multicenter study reports primary and secondary indications and specific conditions for which scleral lenses were prescribed within a single health care system from 2006 through 2019.

Methods: A retrospective chart review collected demographic information, primary and secondary indications for scleral lens wear, and specific conditions treated of patients who completed scleral lens fitting from 2006 through 2019. Descriptive statistics are reported.

Results: Scleral lenses were prescribed for 850 patients. The mean age at the time of scleral lens fitting was 53.5 [16.4] years of age (range 6-93 years). Male/female distribution was 372/478. Primary indications were corneal irregularity (434 patients, 51%), ocular surface disease (407 patients, 48%) and refractive error (9 patients, 1%). The numbers of patients with specific conditions causing corneal irregularity were: keratoconus (138), S/P keratoplasty (87), S/P RK (56), S/P LASIK (42), S/P trauma (30), S/P keratitis (29), pellucid marginal degeneration (22), S/P PRK (7), Terrien's marginal degeneration (2), unspecified corneal scarring (9), and unspecified irregular astigmatism (12). The numbers of patients with specific ocular surface conditions were: exposure keratopathy (103), unspecified dry eye syndrome (89), neurotrophic keratopathy (58), chronic GvHD (53), Sjogren syndrome (34), Salzmann degeneration (18), cicatrizing conjunctivitis (16), anterior basement membrane dystrophy (11), dry eye syndrome related to refractive surgery (11), limbal stem cell deficiency (11), congenital disorder (2), and superior limbic keratoconjunctivitis (1). A secondary indication was noted for 129 (30%) patients with corneal irregularity. A secondary indication was noted for 87 (21%) patients with ocular surface disease. A secondary indication was noted in only 1 patient with refractive error.

Conclusions: Ocular surface disease was the primary indication for lens wear in almost 50% of patients within this cohort, compared to less than 20% in previous studies. A secondary indication for scleral lens wear was noted in 20-30% of these patients, which may suggest that complex disease can be managed with scleral lenses.

CONTROL ID: 3546823

SUBMITTER (NAME ONLY): Yuhua Zhang

TITLE: High-order hemodynamic properties of erythrocyte flow in human retinal capillaries

SESSION TITLE: Highlights of angiographic imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Zhang, X. Wang, B. Gu, Doheny Eye Institute, Los Angeles, California, UNITED STATES|Y. Zhang, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yuhua Zhang: Commercial Relationship: Code N (No Commercial Relationship) | Xiaolin Wang: Commercial Relationship: Code N (No Commercial Relationship) | Boyu Gu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Purpose: To characterize retinal hemodynamics and identify sensitive biomarkers for quantifying age-related changes in retinal microcirculation, we investigate high-order dynamic characteristics relating to the time derivatives of the velocity of erythrocyte flow in human retinal capillaries, using high speed adaptive optics ophthalmoscopy.

Methods: Erythrocyte flows in retinal capillaries were imaged in human subjects with normal healthy retinae using an adaptive optics near-confocal ophthalmoscope (AONCO) at a frame rate of 800 Hz. Continuous pulsatile velocity of the erythrocytes flowing in the capillary was measured from the consecutive frames. In addition to conventional measures of the velocity (Figure 1), such as the maximum (V_{max}), the minimum (V_{min}), the mean velocity (V_m), the amplitude (V_d), and the pulsatility index (PI), we proposed new metrics, including the maximum acceleration (A_{max}), the acceleration time index (T_p), the rising rate (Rr). We further introduced the acceleration change index (AI) of the second order derivative of the velocity for estimating the acceleration change. This metric has been used to assess age-related vascular stiffness in photoplethysmography. Hemodynamic characteristics were measured in human subjects in normal physical health in 2 age groups: 24-25 years old ($n = 8$) and 50-60 years old ($n = 4$).

Results: Conventional measures pertaining to the velocity (V_{max} , V_{min} , V_m , V_d , and PI) showed no difference between the 2 age groups. In contrast, high-order characteristics disclosed significant differences (Figure 2). The prolonged T_p for cells to reach peak velocity in one cardiac cycle may indicate that the capillary or the erythrocytes have higher rigidness that increases the friction between the cell and the capillary, thereby delaying the time to reach the maximum velocity. Likewise, increased stiffness may increase the Rr and reduced A_{max} as well as AI.

Conclusions: High-order hemodynamic characteristics of the erythrocyte flow in the retinal capillary provide new and sensitive biomarkers for assessing age-related changes in the retinal microcirculation that cannot be differentiated by conventional metrics. These metrics may reflect the mechanical properties of the erythrocyte-capillary system.

CONTROL ID: 3546824

SUBMITTER (NAME ONLY): Hsuan-Yeh Pan

TITLE: Expression and regulation of TFEB in ATP Binding Cassette Subfamily A Member 4 (ABCA4) knockout retinal pigment epithelium

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Pan, M. Valapala, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Hsuan-Yeh Pan: Commercial Relationship: Code N (No Commercial Relationship) | Mallika Valapala: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: RPE is one of the most phagocytic cells in the body, both autophagy and phagocytosis are highly active in the RPE. The terminal events of both autophagy and phagocytosis involve degradation in the lysosome. Lysosome plays a crucial role in the proper functioning of both autophagy and phagocytosis in the RPE. Imbalances in lysosomal function can lead to the accumulation of undegraded autophagy and phagocytic substrates in the RPE. Transcription factor EB (TFEB) is identified as a master of the regulator of autophagy and lysosomal function. Decrease expression and activity of TFEB is known to increase the pathological accumulation of cellular substrates in different cell types. In this study, we investigated the expression and regulation of TFEB in the ABCA4 knockout (KO) RPE.

Methods: ABCA4 KO RPE cells were isolated and the expression of TFEB was monitored using immunoblotting analysis and quantitative real-time PCR (qRT-PCR) analysis. The expression of TFEB regulated coordinated lysosomal expression and regulation (CLEAR) network genes was studied by qRT-PCR analysis. The cells were also transfected with a constitutively active TFEB S142AS211A and the expression of TFEB and CLEAR network gene, Cathepsin D (CTSD), Lysosomal-associated membrane protein 1 (LAMP1), Beclin-1(BECN1), UV radiation resistance-associated gene (UVRAG), Sequestosome 1(SQSTM1), Microtubule Associated Protein 1 Light Chain 3 Beta (MAP1LC3B) by qRT-PCR. Cathepsin D activity was also measured using the Cathepsin D activity assay kit.

Results: Our result shows that both mRNA and protein levels of TFEB were downregulated in the ABCA4 KO RPE compared to age-matched WT RPE. The expression of TFEB regulated CLEAR network genes were rescued upon overexpression of constitutively active TFEB in the ABCA4 KO RPE. Our results also show rescue of Cathepsin D activity in ABCA4 KO RPE upon overexpression of constitutively active TFEB in the ABCA4 KO RPE.

Conclusions: Our study shows that decreased expression of TFEB in the ABCA4 KO RPE is accompanied by downregulation of TFEB-regulated CLEAR network genes. TFEB-regulated transcriptional program is rescued by overexpression of constitutively active TFEB in the ABCA4 KO RPE. These results suggest that TFEB plays a crucial role in the regulation of cellular clearance in the ABCA4 KO RPE.

CONTROL ID: 3546828

SUBMITTER (NAME ONLY): Lea Bennett

TITLE: L-DOPA Stimulates Neurite Outgrowth during Early Retinal Organoid Development

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.D. Bennett, B. Radojevic, Ophthalmology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|L.D. Bennett, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lea Bennett: Commercial Relationship: Code N (No Commercial Relationship) | Bojana Radojevic: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Human retinal organoids made from inducible pluripotent stem (iPS) cells mimic retinogenesis and have been crucial for uncovering diseases mechanisms that cannot be recapitulated in animal models. However, mature retinal organoids are disorganized and unlike fetal retina, do not express important cellular pathways (circadian entrainment and axon guidance). Therefore, the goal of this study was to evaluate a key regulator of circadian entrainment, dopamine (DA) in developing retinal organoids.

Methods: At day 30 (D30) and D60, human retinal organoids were dissociated and grown on laminin-coated coverslips for neurite outgrowth assay. At D30, L-DOPA with ascorbic acid was added to the media for 2-3 hours to stimulate DA synthesis. Cells were stained with neuron-specific marker TUJ1 (β III tubulin) and MAP2 to visualize axon outgrowth. Axon-guiding signals (e.g. *Irx4*, *Foxg1*, *Nfil3*) and cell type-specific markers were quantified with RT-qPCR.

Results: Exogenous L-DOPA with ascorbic acid induced expression of the penultimate enzyme, tyrosine hydroxylase (TH) and DA synthesis prior to the appearance of dopaminergic amacrine cells (DACs). Cells treated with L-DOPA and ascorbic acid at D30 modified neurite outgrowth in early retinogenesis and showed increased axon lengths as well as expression of axon guiding genes (RT-qPCR). Expression of TH was 3 fold higher in the cells treated with L-DOPA and ascorbic acid at D30 compared to cells that were not treated with L-DOPA.

Conclusions: This work aimed to determine how developing retinal neurons respond to DA to ultimately create functional retinal organoids that mimic the structure and physiology of human retina which will have broader potential for ophthalmic research.

CONTROL ID: 3546829

SUBMITTER (NAME ONLY): Dominic Hakim

TITLE: Effect of anti-inflammatory eye drops on cultured porcine corneal endothelial cell viability

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.F. Hakim, T. Noguchi, A.A. Abbas, E.N. Finburgh, N.A. Afshari, University of California at San Diego Department of Ophthalmology at the Shiley Eye Institute, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Dominic Hakim: Commercial Relationship: Code N (No Commercial Relationship) | Takako Noguchi: Commercial Relationship: Code N (No Commercial Relationship) | Anser Abbas: Commercial Relationship: Code N (No Commercial Relationship) | Emma Finburgh: Commercial Relationship: Code N (No Commercial Relationship) | Natalie Afshari: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the effect of three commonly used anti-inflammatory eye drops: cyclosporin (0.05%), lifitegrast (5%), and tacrolimus (0.1%) on porcine corneal endothelial cell viability.

Methods: We harvested porcine eyes and separated their corneascleral rims. Corneal endothelial cells were scraped from Descemet membrane after 0.5% trypsin treatment for 15 min. Cells derived from pig eyes were first plated into one well of a 12 well plate, proliferated to confluency in a low growth factor medium, passaged to a well of 6-well plate, and then passaged to a 96 well plate for drug treatment. Wells were separated into the following three treatment groups: cyclosporine 0.05%; lifitegrast 5%; tacrolimus 0.1%, as well as two control groups: a balanced salt solution (BSS) group and no treatment group. The cells were exposed to medium containing 20% cyclosporin (original 0.05% diluted to 0.01%), 20% lifitegrast (original 5% diluted to 1%), and 10% tacrolimus (original 0.1% diluted to 0.01%) and washed out after 1h, 2h, 4h, and 24h (N = 6 wells for each condition derived from 3 pig eyes). The survival rates of corneal endothelial cells were assessed by ATP quantification 48 h after the beginning of eye drop application.

Results: Measurements of porcine endothelial cell viability after application of cyclosporine, lifitegrast, and tacrolimus revealed a statistically significant decrease down from 100±10% survival in the untreated group to 75±6%, 42±21%, and 0±0% (mean ± SD, N = 6), respectively. Compared to non-treated control group, decreases in viability after application of cyclosporine became statistically significant at 24h [75±6% (mean ± SD, N = 6)]. After application of lifitegrast, decreases became statistically significant at 1h and 24 hours [67±22% at 1h, 42±21% at 24h (mean ± SD, N = 6)]. After application of tacrolimus, decreases became statistically significant at 1h, 2h, 4h and 24h [58±21% at 1h, 61±10% at 2h, 16±13% at 4h, 0±0% at 24h (mean ± SD, N = 6)].

Conclusions: Porcine endothelial cell viability decreased progressively across application of cyclosporin, lifitegrast, and tacrolimus containing anti-inflammatory eye drops. These findings may serve as a resource for appropriate selection of anti-inflammatory eyedrops in the clinical setting and provide further insight into the study of inflammatory signaling and cell death pathways.

CONTROL ID: 3546830

SUBMITTER (NAME ONLY): Joel Papay

TITLE: Quantification of number of scattering defects detected using a Digital Light Ophthalmoscope vs OCT

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Papay, M.S. Muller, A.E. Elsner, T. Gast, Aeon Imaging, Bloomington, Indiana, UNITED STATES|J.A. Papay, A.E. Elsner, C.A. Clark, R. Gilbert, T. Gast, Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joel Papay: Commercial Relationship(s);Aeon Imaging:Code F (Financial Support);Aeon Imaging:Code E (Employment) | Matthew Muller: Commercial Relationship(s);Aeon Imaging:Code F (Financial Support);Aeon Imaging:Code I (Personal Financial Interest);Aeon Imaging:Code E (Employment);Aeon Imaging:Code P (Patent) | Ann Elsner: Commercial Relationship(s);Aeon Imaging:Code F (Financial Support);Aeon Imaging:Code I (Personal Financial Interest);Aeon Imaging:Code E (Employment);Aeon Imaging:Code P (Patent) | Christopher Clark: Commercial Relationship: Code N (No Commercial Relationship) | Robert Gilbert: Commercial Relationship: Code N (No Commercial Relationship) | Thomas Gast: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare the reliability of visualizing scattering defects as seen on the Digital Light Ophthalmoscope (DLO) vs on OCT images.

Methods: Twenty subjects (53.1 +/- 13.7 yrs, range 27-73 yrs) were imaged using both the DLO (Aeon Imaging, Bloomington, IN, USA) and OCT (Spectralis, Heidelberg, Germany). The DLO uses 860 nm light in a line scan to collect retinal images over a 37 deg field of view at 20 Hz. Multiply scattered light imaging suppresses superficial light scatter and reveals scattering disruptions in the deeper retina. Thus, we used a mode that offsets the scanning beam from the camera aperture by 51µm, leading and lagging, for collecting multiply-scattered light in equal but opposite directions. These pairs of images were automatically aligned and then processed to obtain images of differences to emphasize scattering defects. Three graders independently marked the center of each region with scattering defects. The DLO has a digital resolution of 10.8 µm/pixel.

One reviewer marked the center of the defects found in vertical OCT B-scans, which were taken with 870nm light. OCT scans were spaced 11 µm apart, and only the center of drusen or other sufficiently large scattering defects in the outer retina was marked. The en face scan provided by the Spectralis was aligned to the DLO image. The OCT scan boundary rectangle provided on the en face scan was used to compare the defect coordinates between the OCT scans and DLO images.

Results: Ten subjects were fully analyzed with both OCT and DLO, and 26 light-scattering defects were found on both instruments, with agreement in locations of at least two of the DLO image graders. Regions where OCTs were taken comprised of a smaller area than the total area imaged with the DLO, thus, a larger number of defects were found on the DLO, because of the larger field of view.

Conclusions: There was good agreement between the marked defects on the DLO and OCT B-scan images. The DLO images covered a larger region of the retina than the dense OCT scans, and numerous small defects were immediately and simultaneously observable from a single composite image, making it a promising device for detecting early signs of AMD.

CONTROL ID: 3546832

SUBMITTER (NAME ONLY): Jeffrey Messinger

TITLE: Multiscale clinicopathologic correlation of canonical and non-canonical intraretinal neovascularization in age-related macular degeneration (AMD)

SESSION TITLE: CNV

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.D. Messinger, L. Chen, A. Berlin, D. Kar, C.A. Curcio, Ophthalmology, 1.University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|L. Chen, Ophthalmology, 2. First Affiliated Hospital of Chongqing Medical University China, Chongqing, Sichuan, CHINA|A. Berlin, Ophthalmology, 3.University Hospital Würzburg Germany, Würzburg, GERMANY|T. Bacci, K. Freund, Ophthalmology, 4.Vitreous Retina Macula Consultants of New York, New York, New York, UNITED STATES|C. Balaratnasingham, Ophthalmology, 5.Centre for Ophthalmology and Visual Science, University of Western Australia, Perth, Australia, Perth, Western Australia, AUSTRALIA|C. Balaratnasingham, Ophthalmology, 7.Sir Charles Gairdner Hospital, Western Australia, Australia, Nedlands, Western Australia, AUSTRALIA|R. Mendes, Ophthalmology, 8.Canberra Retina Clinic, Australia, Deakin, Western Australia, AUSTRALIA|D. Ferrara, 9.Genentech, South San Francisco CA, San Francisco, California, UNITED STATES|K. Freund, Ophthalmology, 10.LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear and Throat Hospital, New York, NY, USA, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: Intraretinal macular neovascularization (MNV) is often preceded by hyperreflective foci (HRF) attributed to ectopic retinal pigment epithelium (RPE) and non-RPE. RPE migration may reflect a response to choroidal ischemia. We investigated with histology clinically documented HRF in fellow eyes, each with 3 MNV.

Methods: Methods: A white woman receiving anti-VEGF was monitored by optical coherence tomography (OCT) and angiography (OCT, dye-based) (OD, n=37; OS, n=6; last visits 3 and 2 months, respectively, before death). Eyes were recovered 4:05 hours after patient death at age 97 years. Eye-tracking (Heidelberg Engineering) aligned clinical and ex vivo imaging of the preserved eye prior to epoxy embedding for high-resolution light microscopic and transmission electron microscopic (TEM) investigation. Horizontally oriented 12 mm wide sections, 30 µm apart, were interleaved with 30 µm-thick slabs re-embedded for TEM.

Results:

Results: In OD, 2 MNV were investigated via TEM. In the first MNV, a hyperreflective triangle, with base-down and apex disrupting outer retinal and RPE layers correlated to an intraretinal vascular complex with numerous pericytes, ensheathed by collagenous material. Fully pigmented RPE distributed upward along this complex, entering but not contacting vessels. The complex rested on persistent basal laminar deposit overlying a completely calcified druse. Bruch's membrane was intact. In the second MNV, a hyperreflective column atop a soft druse correlated to a column of RPE emerging from the top of intact RPE covering a lipid-rich druse. Cells at the column tip encircled a vessel dipping into the Henle fiber layer from the deep capillary plexus. Pericytes were not seen.

Conclusions:

Conclusion: The components and morphology of the first MNV resembled our recent description of treated type 3 MNV and added new observations of pericytes, and lack of penetration into the sub-RPE-BL space, which contained calcified drusen. The second MNV did not resemble the first MNV or others in either eye. It may represent another entity such as perifoveal exudative vascular anomalous complex (PEVAC; PMID 29079450), which is non-responsive

to anti-VEGF. Recognition of different intraretinal MNV morphologies through clinicopathologic correlation may assist management decisions for neovascular AMD.

CONTROL ID: 3546833

SUBMITTER (NAME ONLY): William Boucenna

TITLE: Phenotype screening and genotype exclusion in Map-dot-fingerprint corneal epitheliopathy

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Boucenna, Université de Picardie Jules Verne, Amiens, Hauts-de-France, FRANCE|S. Valleix, Service de génétique moléculaire ; Assistance Publique-Hôpitaux de Paris ; Hôpital Cochin., Paris, FRANCE|W. Boucenna, Amiens University Hospital Center, Paris, FRANCE|J. Bourges, Université de Paris, Centre de recherche des Cordeliers, INSERM 1138 équipe 17, Paris, France, Paris, FRANCE|J. Bourges, Service d'ophtalmologie, Assistance Publique-Hôpitaux de Paris, Ophtalmopôle ; Hôpital Cochin., Paris, FRANCE|

Commercial Relationships Disclosure (Abstract): William Boucenna: Commercial Relationship: Code N (No Commercial Relationship) | Sophie Valleix: Commercial Relationship: Code N (No Commercial Relationship) | Jean Louis Bourges: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate pedigrees, clinical phenotype and TGFB1 mutational status in patients with corneal epithelial basement membrane dystrophy (EBMD) patterns.

Methods: Patients displaying sub epithelial bleb-like micro cysts, geographic map-like lines, dots or fingerprint lines at slit lamp examination were prospectively included between April 2018 and September 2019. We gathered both medical history and pedigree. We confirmed phenotypic patterns from biomicroscopic examination by anterior segment optical coherence tomography (OCT). We collected blood samples from patients and submitted to molecular genetics to investigate TGFB1 mutations.

Results: We included 22 eyes with typical patterns of EBMD from 13 patients. Anamnesis failed to report any case or symptom in relatives. All patients reported clinical symptoms. The main complaint associated a foreign body sensation, pain linked to recurrent epithelial erosions and/or visual symptoms. Over the 22 eyes, 9 eyes (7 patients) displayed the typical map-dot-fingerprint triad. Other patterns were "map-dot" (3 eyes, 2 patients), "dot-fingerprints" (3 eyes, 2 patients), "maps" (3 eyes, 2 patients), "dot" (2 eyes, 2 patients), "map-fingerprint" (one eye) and "fingerprint" (one eye). Split EBM was observed with OCT in all eyes. All patients failed to respond to medical lubricant and underwent excimer laser phototherapeutic keratectomy (PTK). We did not identify any TGFB1 mutation in our patients.

Conclusions: EBMD phenotype is heterogeneous in the absence of familial history. In our patients, EBMD was not related to an anomaly of TGFB1 gene, and compatible with an ill-understood degenerative process. Some work is still mandatory to discriminate hereditary and degenerative EBMD.

CONTROL ID: 3546834

SUBMITTER (NAME ONLY): Weiming Mao

TITLE: Small molecule Wnt signaling activators inhibit TGF β signaling in the trabecular meshwork

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Mao, C.K. Sugali, N.P. Rayana, J. dai, M. Peng, Ophthalmology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Weiming Mao: Commercial Relationship: Code N (No Commercial Relationship) | Chenna Sugali: Commercial Relationship: Code N (No Commercial Relationship) | Naga Rayana: Commercial Relationship: Code N (No Commercial Relationship) | jiannong dai: Commercial Relationship: Code N (No Commercial Relationship) | Michael Peng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Elevated TGF β 2 is found in the aqueous humor and trabecular meshwork (TM) of glaucoma patients. TGF β 2 induces excessive accumulation of extracellular matrix, alters cytoskeleton, and increases intraocular pressure in various experimental models. We previously reported that the Wnt signaling is able to inhibit TGF β signaling in the TM at transcriptional level. Here, we determined if small molecule Wnt signaling activators are able to inhibit TGF β 2 signaling.

Methods: GTM3 cells were transfected with Wnt signaling reporter luciferase vectors. The cells were treated with different GSK3 β inhibitors (Wnt activators) at different concentrations, and luciferase levels were measured using a plate reader. After determination of the optimal concentration, TM cells were transfected or transduced with TGF β signaling reporter luciferase vectors. These cells were treated with 5ng/ml TGF β 2 with or without GSK3 β inhibitors, and luciferase levels were measured. Primary human TM (pHTM) cells were also treated with or without TGF β 2 and/or GSK3 β inhibitors to study fibronectin and collagen I using Western immunoblotting and immunofluorescent microscopy.

Results: We found that the optimal concentration of the GSK3 β inhibitors in TM cells was 1uM for 6-bromoindirubin-3'-oxime (BIO), 10uM for SB216763 (SB), and 5uM for CHIR-99021 (CHIR). Also, these compounds were more potent compared to Wnt3a recombinant proteins in Wnt signaling activation. At these concentrations, they inhibited TGF β 2-induced TGF β signaling activation in the TM. They also inhibited TGF β 2-induced expression of fibronectin and collagen I in pHTM cells.

Conclusions: Small molecule Wnt signaling activators inhibit TGF β signaling in the TM and may have potentials for therapeutic use in treating glaucoma.

CONTROL ID: 3546835

SUBMITTER (NAME ONLY): Jeffrey Peterson

TITLE: Predictive modeling for singlet oxygen generated during Rose Bengal Photodynamic Antimicrobial Therapy

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Peterson, Y. Chang, F. Manns, J.A. Parel, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|J.C. Peterson, Y. Chang, F. Manns, Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|I. Kochevar, Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, UNITED STATES|J.A. Parel, Brien Holden Vision Center, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Rose Bengal Photodynamic Antimicrobial Therapy (RB-PDAT) has been shown to effectively treat antimicrobial resistant and atypical infectious keratitis. RB-PDAT works by generating antimicrobial singlet oxygen ($^1\text{O}_2$) by exciting Rose Bengal (RB) photosensitizer with 525 nm light. While the cumulative $^1\text{O}_2$ dose distribution generated during RB-PDAT is currently unknown, this project aims to create a predictive model to calculate this distribution under clinical conditions. This model will eventually enable optimization of $^1\text{O}_2$ dose by optimizing RB-PDAT treatment parameters.

Methods: A chemical kinetics model was previously developed (Wang et al., 2010) for modeling $^1\text{O}_2$ dose distributions in tumors treated with photodynamic therapy. To describe ground-state oxygen (O_2) supply specific to the cornea, the oxygen supply term was adapted to include the model described by Larrea & Büchler (2009) and Castillo et al. (2014). RB distribution was modeled using Fick's second law, and 525 nm excitation light distribution by a time-dependent application of Beer's law. Rate constants for RB diffusion were then derived from experimental data describing RB corneal penetrance (Naranjo, Pelaez, et al., 2019; Peterson et al., 2018; Wertheimer et al., 2019). Lateral variation of all species was assumed to be minimal to allow for one-dimensional modeling. The resulting system of partial differential equations was solved numerically in MATLAB. Cumulative $^1\text{O}_2$ dose was calculated for RB-PDAT during typical conditions (6 mW/cm², 5.4 J/cm², 0.1% RB), as well as for conditions of pulsed and increased light dose, and addition of 90% supplemental O_2 .

Results: Under typical RB-PDAT conditions, calculated O_2 decreases to approximately 0 beyond 10 μm depth in the first 1 min of treatment. In this scenario, $^1\text{O}_2$ dose distribution was calculated to be limited to the first 10 μm of the cornea. Adding supplemental O_2 increases $^1\text{O}_2$ dose depth by approximately 5–10 μm . Increasing the light dose from 5.4 J/cm² to 10 J/cm² while adding 1s on, 1s off pulsing increases calculated $^1\text{O}_2$ surface dose 1.85x. Adding supplemental O_2 to the 10 J/cm² scenario, $^1\text{O}_2$ surface dose is 1.7x the dose seen in the 5.4 J/cm² condition.

Conclusions: We demonstrate a proof-of-concept predictive model for $^1\text{O}_2$ dose generated during RB-PDAT, capable of testing a range of experimental parameters. This model can be used for optimizing RB-PDAT clinical efficacy.

CONTROL ID: 3546839

SUBMITTER (NAME ONLY): Lora Waybright

TITLE: Unbiased omics analyses of the sigma-2 antagonist CT1812 in age-related diseases and models

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Waybright, C. Rehak, E. Watto, A. Caggiano, M.E. Hamby, Cognition Therapeutics Inc, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: CT1812, now in Ph2 clinical trials for Alzheimer's disease (AD), is an orally bioavailable, brain penetrant small molecule antagonist of the sigma-2 receptor, which contributes to key pathways involved in age-related diseases including autophagy, lipid trafficking, and amyloid- β (A β) toxicity. Human genetics points to a role of the sigma-2 receptor in dry age-related macular degeneration (dAMD); namely, a SNP in the chief sigma-2 receptor constituent TMEM97 locus confers an increased risk for dAMD (Fritsche et al., 2016). In support, CRISPR knockdown of TMEM97 in retinal pigment epithelial (RPE) cells significantly ameliorates oxidative stress-triggered cell death (Wang et al., 2020). We hypothesized that CT1812 will alter dAMD-relevant biologies in patients and in human iPSC-RPE cells treated with disease-relevant stressors.

Methods: Proteomics analysis was performed with plasma and cerebrospinal fluid (CSF) from AD patients treated with CT1812 or placebo for 28 day (N=14) or 6 mo (N=18). Unbiased pathway analyses were performed using Metacore to identify the pathways significantly altered in AD patients treated with CT1812 compared to placebo, and data were compared to publicly available dAMD proteomic datasets to identify significantly altered proteins linked to dAMD. Human iPSC-RPE cells were exposed to hydrogen peroxide, TNF- α and IFN- γ , A β oligomers, or vehicle to assess the effect of CT1812 under physiological and pathophysiological conditions. RNAseq analysis, including differential expression and pathway analysis, was performed to evaluate the transcriptomic changes elicited by CT1812 in vehicle- or stressor-treated cultures.

Results: Unbiased pathway analysis of AD clinical trial CSF proteomics indicated that geographic atrophy was the most significantly altered functional disease ontology by CT1812 compared to placebo ($p < 0.05$), and comparative analyses to publicly available AMD datasets illuminated a subset of dAMD-relevant proteins altered by CT1812 ($p < 0.05$). In iPSC-RPEs (n=3-4), transcriptomic analyses revealed highly regulated genes and pathways ($p < 0.05$) altered by oxidative stress, inflammation, and A β oligomers and by CT1812 vs vehicle data, illuminating the role of sigma-2 signaling in RPE cells under physiological and pathophysiological conditions.

Conclusions: In sum, data indicate a key role of sigma-2 in AMD and suggest CT1812 may be a promising therapeutic approach for dAMD.

CONTROL ID: 3546843

SUBMITTER (NAME ONLY): Berzhan Kurmanov

TITLE: Identification of causative mutations in ten pedigrees with inherited retinal degeneration by whole genome analysis (WGS)

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Analysis of 10 pedigrees with a diagnosis of IRD to identify the underlying cause of pathology

Methods: DNA isolation was performed on 24 affected and 29 unaffected individuals from 10 pedigrees with IRD. WGS was performed on 21 individuals using Illumina HiSeq X Ten. The sequence alignment and variant calling was done with the Illumina DRAGEN Bio-IT Platform, BWA-MEM+GATK-HC software with high accuracy for both SNPs and INDELs. Annotation of variants included SpliceAI and PrimateAI. Segregation analysis of all identified candidate variants was performed by PCR followed by Sanger sequencing.

Results: The pedigrees analyzed belonged to four different ethnic groups: one each of Ashkenazi Jewish, Hispanic and Pakistani origin, while the remaining 7 are of European American (EA) origin. Our analysis detected 12 pathogenic variants in 9 genes associated with IRD. Two novel compound heterozygous nonsense variants (p.[Glu526*;p.Gln1629*]) segregated with disease in one EA pedigree. A set of known compound heterozygous mutations c.5012+5G>A and p.Arg1752Trp in CEP290 were observed in another EA pedigree. Interestingly, two large structural variants were identified in the PRPF31 gene in two unrelated EA pedigrees. A known heterozygous mutation p.Ser212Gly in the PRPH2 gene segregated with IRD in an EA family with dominant IRD. A novel homozygous variant in DRAM2 (p.Ser234Tyr) and a reported nonsense mutation in RLBP1 (p.Tyr111*) were detected in the remaining two EA pedigrees. A known homozygous CRB1 mutation, p.Arg764Cys was detected in the Pakistani pedigree, while a previously reported nonsense mutation p.Gly723* in RP1 was found in the Ashkenazi Jewish pedigree. In the Hispanic pedigree, a novel intronic homozygous variant c.1107+3A>G in PDE6B was identified as a disease-causing variant.

Conclusions: Our analysis detected 4 novel and 8 previously reported mutations segregating with IRD in 10 pedigrees. These mutations include 4 nonsense, 2 intronic, 4 missense and two large structural changes in ALMS1, PDE6B, CEP290, DRAM2, RLBP1, PRPF31, RP1, PRPH2 and CRB1.

CONTROL ID: 3546844

SUBMITTER (NAME ONLY): Mitchell Kirby

TITLE: Elastic anisotropy of the cornea: comparison of non-contact A μ T-OCE with mechanical tests

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kirby, I. Pelivanov, H. Liou, R. Wang, M. O'Donnell, Bioengineering, University of Washington, Seattle, Washington, UNITED STATES|R. Wang, T.T. Shen, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal stiffness, along with intraocular pressure (IOP), determines corneal shape, providing a majority of the refractive power to the human visual system. We demonstrate non-contact acoustic micro-tapping (A μ T) optical coherence elastography (OCE) of porcine cornea to quantify the shear moduli which contribute to corneal refraction using a nearly-incompressible transversely isotropic (NITI) model based on corneal microstructure.

Methods: The cornea contains layered collagen sheets (lamellae) arranged mostly parallel to the surface, which suggests a transversal isotropy of its mechanical properties. Consequently, corneal shear and tensile behavior (Fig.1) are described by different moduli. We introduce a shear modulus, G , to quantify out-of-plane shear modulus and tensile elastic modulus, E , responsible for corneal deformation.

We perform non-contact A μ T-OCE measurements in ex vivo porcine cornea to reconstruct both shear moduli using a nearly incompressible transversally isotropic (NITI) model and compare OCE results with parallel-plate rheometry and strip extensimetry.

Results: Figure 2a shows modulus estimates from A μ T-OCE under varying IOP. The OCE test in an exemplary sample yielded a mean Young's modulus of 16.8 – 33 MPa and shear storage modulus of 50.4 - 120.5 kPa (IOP 5mmHg- 20mmHg). Tensile tests yielded a Young's modulus (E) of ~2 -25 MPa (1-9% strain) (Fig. 2c). Shear rheometry yielded a storage modulus (G') of 100- 148 kPa and loss modulus (G'') of 15.7- 31.5 kPa over the low-frequency (1-10Hz) regime (Fig. 2b).

Conclusions: Both A μ T- OCE and destructive mechanical tests performed on ex vivo cornea reveal anisotropic elastic behavior with the tensile modulus E differing by orders of magnitude from the shear modulus G . However, mechanical tests are destructive, and each test type measures either G or E , but not both moduli together. On the other hand, A μ T-driven OCE is non-contact and non-destructive and is capable of in vivo measurement of both moduli simultaneously.

CONTROL ID: 3546845

SUBMITTER (NAME ONLY): Akosua Boateng

TITLE: RNA-sequencing profile of Lenses of β A3 Δ G91 Mice: A Model for Pediatric Congenital Nuclear Cataract

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Boateng, R. Joseph, O.P. Srivastava, Optometry and Vision Science, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: G91-deletion (Δ G91), a mutational hotspot in β A3-crystallin (CRYBA3/A1), causes pediatric congenital cataract in several families worldwide. However, the molecular mechanism of β A3 Δ G91-induced cataract is presently unknown. The purpose of the study to understand the molecular mechanism through comparative analysis of gene expression profiles in lenses of β A3 Δ G91- and wild-type mice.

Methods: Methods: We have generated β A3 Δ G91 mouse model by the CRISPR-Cas9 methodology using the UAB Transgenic & Genetically Engineered Models Core (TGEMs) facility. Lenses from 1-month-old β A3 Δ G91- and wild-type mice were examined for cataract development using Micron IV slit-lamp analysis. The relative protein profile by SDS-PAGE and the differential gene expression (transcriptome) followed by Ingenuity pathway analyses were performed in the 1-month old lenses of β A3 Δ G91- and wild-type mice.

Results: Results: β A3 Δ G91 mice showed congenital cataract relative to wild-type mice. SDS-PAGE analysis showed that β A3-crystallin level was relatively reduced in lenses of β A3 Δ G91 mice compared to the wild-type mice, which seems to be due to its insolubilization. The transcriptome analysis identified 93 dysregulated genes (q-value<0.05), out of which 11 genes were upregulated and 82 genes were downregulated. Biological function analysis revealed that the major affected genes were associated with protein synthesis, RNA damage and repair and cellular compromise. EIF2 signaling was identified as the top canonical pathway affected, showing that during congenital cataract development, ribosomal proteins (RPL, RPS) and genes involved in cellular stress (GADD34) were downregulated.

Conclusions: Conclusions: Our study provides informative data about the potentially affected candidate genes and biological mechanisms during β A3 Δ G91-induced congenital cataract development. Taken together, targeting EIF2 signaling might be a stepping-stone in developing therapeutic strategies to mitigate the congenital cataract.

CONTROL ID: 3546847

SUBMITTER (NAME ONLY): Daniel Choi

TITLE: Improvement in mask utilization with 3D-printed ear protectors

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Choi, E. Meer, B.J. Nguyen, J.M. O'Brien, V.M. Addis, P.J. Tapino, Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Face masks have been associated with significant discomfort for health care workers. Face mask ear protectors (EP) may reduce discomfort by allowing ear loop masks to be worn without tension. In Ophthalmology, given the close proximity required for the exam, appropriate mask usage and fit is essential. There is evidence of higher COVID-19 disease burden in ophthalmology compared to other specialties. This study aims to assess how a simple, attachment may decrease discomfort and increase compliance in an academic institution's Ophthalmology department.

Methods: EPs were distributed to the Ophthalmology department. A validated questionnaire was administered before and 2 weeks after EP usage, which surveyed demographics, likelihood of wearing a mask during select activities, and degree of mask usage (measured as number of times mask was removed/hour) during these activities. Descriptive statistics were performed with Fischer's t test to assess for a change in face mask utilization pre- and post-EP distribution.

Results: Although changes in mask usage post-EP were not statistically significant, post-EP responses demonstrated increased likelihood of mask usage across all activities. The greatest change was seen during outdoor activities with a 14.3% increase in those responding as "very likely" to wear a mask after using the EP. There was a 7.3% increase in responders who were likely to wear a mask in the workplace. EP decreased noncompliance while visiting friends. Nearly no subjects reported mask removal of >15 times/hr post-EP. 91.9% reported improved comfort, 91.9% improved fit, and 81.6% increased mask usage.

Conclusions: Our results suggest that simple 3D-printed EPs may improve fit, comfort, and overall mask compliance. This has potential implications not only for healthcare workers, but for the larger population as well. The statistical significance of this study may be limited due to the small subset of healthcare workers who were already high mask utilizers pre-EP, and thus may not truly appreciate the effect of EPs on the general population. The results of this study should drive broader public health efforts to further investigate whether mask attachments can improve overall mask compliance through better comfort and fit.

CONTROL ID: 3546848

SUBMITTER (NAME ONLY): Jimmy Le

TITLE: Cognitive Impairment and Progression to Late Age-Related Macular Degeneration in the Age-Related Eye Disease Study 2 (AREDS2) 10-year Follow-on

SESSION TITLE: Retina and AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.T. Le, E. Agron, T.D. Keenan, E.Y. Chew, National Eye Institute, Bethesda, Maryland, UNITED STATES|T.E. Clemons, The Emmes Company LLC, Rockville, Maryland, UNITED STATES|W.D. Brenowitz, K. Yaffe, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cognitive impairment and age-related macular degeneration (AMD) are progressive, often irreversible causes of disability. Using 10-year longitudinal data from the Age-Related Eye Disease Study 2 (AREDS2), a multi-center randomized trial of nutritional supplements in older people, we investigated bidirectional associations between cognitive impairment and late AMD.

Methods: AREDS2 participants received annual eye exams and regular testing of cognitive function, which included the Modified Telephone Interview for Cognitive Status (TICS-M). A centralized reading center reviewed fundus photographs to assign severity ratings using the AREDS AMD severity scale (i.e., a score ≥ 7 indicated worse AMD severity) and determine progression to late AMD (i.e., development of geographic atrophy or choroidal neovascularization). Proportional hazards regression was used to examine associations between cognitive impairment (i.e., a TICS-M score < 30) and progression to late AMD by the end of the trial (5-years) and extended follow-up (10-years). Associations between having worse AMD severity at baseline and development of cognitive impairment was also examined. Models were adjusted for baseline age, gender, and risk factors (e.g., smoking status).

Results: The analysis included 5189 eyes (3157 participants from 82 US clinics). Most participants were female (57%) older adults (mean 73 years), who never smoked (43%) or were former (50%) smokers at baseline. Eyes of cognitively impaired participants were more likely to progress to late AMD at 5 years (HR, 1.24; 95%CI, 1.08-1.43) and 10 years (HR, 1.20; 95%CI, 1.05-1.37), compared with eyes of those who were not cognitively impaired (Figure). No associations were observed between worse AMD severity at baseline and development of cognitive impairment at 5 years (HR, 1.13; 95%CI, 0.89-1.44) or 10 years (HR, 1.10; 95%CI, 0.92-1.32).

Conclusions: Our finding that people with cognitive impairment were more likely to progress to late AMD calls for greater awareness of the importance of eye care for people with cognitive impairment. Cognitive impairment may impede on a person's ability to identify changes in their vision, or that individual may not have adequate access to eyecare services because of more obvious issues linked to impaired cognition.

CONTROL ID: 3546849

SUBMITTER (NAME ONLY): Charles Zhang

TITLE: Allele-Specific Expression in Normal and Diseased Donor Eyes Reveals Potential Therapeutic Targets for Intermediate AMD

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Zhang, J. Lillvis, M.H. Farkas, M.M. DeAngelis, Ophthalmology, University at Buffalo, Buffalo, New York, UNITED STATES|Q. Li, L. Owen, A. Shakoor, D.A. Nix, University of Utah Health, Salt Lake City, Utah, UNITED STATES|I.K. Kim, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is considered one of the most well genetically defined complex disorders; however, the mechanisms underlying disease pathophysiology are poorly understood. Current therapies address advanced AMD when vision loss is largely irreversible. Interventions directed towards earlier disease stages are desperately needed to prevent AMD blindness. Our analysis of allele-specific expression (ASE) profiles in AMD diseased tissues offers a robust approach toward identification of candidate gene and gene variants relevant to local pathophysiology and environmental risk.

Methods: Well characterized donor eye tissue (postmortem time of less than 6 hours) of 14 patients over the age of 70 years (6 with intermediate stage AMD and 8 healthy age-matched controls) were surveyed using whole exome sequencing, RNA sequencing and whole genome genotyping using illumina chips. To generate ASE profiles, Exome Seq Fastq data was processed and merged with SNP chips and RNA sequencing data to build "personal" alignment indexes using Lofreq and STAR. Using these alignments, differential gene analysis was performed on high quality SNPs to calculate an ensemble prioritization score for each gene using the data from the imprinted gene, eQTL and GTEx databases. ASE candidates were then selected given a specific prioritization score cutoff which was compared to the prioritization score distribution of known AMD genes and genes not associated with AMD using a Kolmogorov-Smirnov test. Validation of identified candidate genes was performed using drop-seq PCR of macular neural retina and RPE/choroid from AMD patients versus normal patient tissues.

Results: After initial identification using our novel pipeline and subsequent validation as described, our analysis identified three novel genes, EOC1, FMN1 and TF, to be statistically associated with intermediate AMD within the local diseased tissues. Statistical analysis using a Kolmogorov-Smirnov test further showed a significant difference between the distributions, $p < 0.05$.

Conclusions: Using our ASE pipeline to identify disease mechanisms could pinpoint novel therapeutic targets for intermediate AMD with relevance to local disease mechanisms and therefore, potential to slow or stop disease progression.

CONTROL ID: 3546850

SUBMITTER (NAME ONLY): Anil Chekuri

TITLE: A novel exon-specific U1snRNA therapeutic strategy to prevent retinal degeneration in familial dysautonomia

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Familial dysautonomia (FD) is an autosomal recessive neurodegenerative disorder caused by a splice mutation in the gene encoding Elongator complex protein 1 (ELP1). A T-to-C base change in the 5' splice site of ELP1 gene results in exon 20 skipping with tissue specific reduction of ELP1 protein predominantly in the nervous system. In addition to a complex neurological phenotype, FD patients also exhibit progressive retinal degeneration severely affecting their quality of life. To test novel splicing-targeted therapeutic approaches, we have developed a phenotypic mouse model, TgFD9; Ikbk^{Δ20/flox} which exhibits most of clinical features of the disease while displaying the same tissue specific mis-splicing observed in patients.

Methods: Spectral domain optical coherence tomography (SD-OCT) was used to evaluate thickness of the retinal layers. Retinal whole mounts were performed to count the number of retinal ganglion cells (RGCs). Immunohistochemical staining was performed to detect degeneration of the optic nerve in FD mice. Adeno Associated Viral (AAV) vectors expressing ExspeU1s were generated to correct ELP1 splicing.

Results: We have comprehensively characterized the retinas of our FD mouse using SD-OCT and immunohistochemical assays during disease progression. Our findings showed a significant decrease in the thickness of the retinal nerve fiber layer (RNFL) and the ganglion cell layer (GCL) starting from 3 months of age ($p < 0.009$ and 0.005). Retinal whole-mount analysis showed reduction of RGC cell counts from 6 months of age ($p < 0.002$). Neurofilament (NF) staining analysis of the optic nerve from FD mice indicated diffuse degeneration of axonic bundles, demonstrating that our mouse model correctly recapitulates the retinal degeneration observed in patients. To correct ELP1 splicing defect, we have designed a novel splice targeted therapy using modified version of the spliceosomal U1 snRNAs (ExSpeU1s) that permit targeted binding to intronic sequences downstream of the mutant 5' splice site enabling efficient recruitment of spliceosomal machinery. In vivo delivery of FD ExSpeU1 using AAV led to successful correction of ELP1 splicing.

Conclusions: Our findings demonstrate that our novel FD mouse model exhibits most of retinal degeneration pathology observed in FD patients and highlight the valuable therapeutic potential of ExSpeU1 delivery to treat retinal degeneration in FD.

CONTROL ID: 3546852

SUBMITTER (NAME ONLY): Catharina Grubaugh

TITLE: The role of a novel scaffold protein in mediating RPE phagocytosis of photoreceptor outer segment

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Grubaugh, B.T. Kendrick, G.D. Aguirre, K.E. Guzewicz, Division of Experimental Retinal Therapies, Department of Clinical Sciences & Advanced Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|A. Dhingra, K. Boesze-Battaglia, Department of Biochemistry, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|D. Sinha, D. Gamm, McPherson Eye Research, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|B.A. Bell, Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|H. Tang, Proteomics and Metabolomics Facility, The Wistar Institute, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The efficient diurnal RPE-mediated phagocytosis of photoreceptor outer segment (OS) relies on a tightly coordinated cascade of extra- and intracellular events that includes OS binding and internalization, followed by phagosome maturation and degradation. However, many aspects of phagocytic machinery, including mechanisms linking cytoskeleton-dependent temporal events with maturation of newly formed phagosomes remain elusive. We used previously established model systems of defective phagocytosis (cBEST1 and MREG/LC3B) to uncover molecular factors contributing to RPE phagocytic clearance in health and disease.

Methods: A combination of LC-MS/MS, Western blot, and co-IP analyses were used to explore the molecular signature of RPE and validate protein-protein interactions. In vivo (UHR-OCT) and ex vivo (H&E/IHC) assessments were performed to characterize retinal phenotype of Ahnak^{-/-} mouse. Subcellular localization, spatial and temporal association of AHNAK with OS were determined in vitro in primary human and mouse RPE cells using phagosome uptake and maturation assays.

Results: Expression of a giant protein AHNAK (~630kDa) was confirmed across mammalian retina, co-localizing with actin filaments at the RPE apical aspect, suggesting AHNAK's involvement in regulating RPE cell membrane cytoarchitecture. In vivo imaging revealed a spectrum of abnormalities in Ahnak^{-/-} eyes, predominantly associated with RPE-photoreceptor and RPE/choroid complexes, which was further confirmed by H&E, IHC, and ex vivo study in Ahnak^{-/-} retinal flat-mounts. The involvement of AHNAK in OS processing was examined using in vitro OS uptake model, which showed AHNAK-OS phagosome co-localization at the apical surface of hRPE and accumulation of phagosomes in the RPE of Ahnak^{-/-} model. Notably, proteomic study exposed association of AHNAK with MREG and its binding partner LC3B, linking temporal regulation of OS to MREG/LC3B-dependent machinery mediating OS phagosome maturation.

Conclusions: We report a new molecular regulator of RPE phagocytic machinery, AHNAK, and show an essential role of this scaffold protein in temporal regulation of OS phagocytosis and MREG/LC3B-mediated phagosome maturation. Further study is required to better understand the extensive signaling network of the AHNAK-MREG nexus, which ultimately will lead to identification of new therapeutic targets for inherited as well as age-related retinopathies.

CONTROL ID: 3546854

SUBMITTER (NAME ONLY): Kevin Schneider

TITLE: The influence of microRNA 135b-5p and 148a-3p on ARPE19 cybrids

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Schneider, M. Chwa, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|M. Saghizadeh, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of microRNA in age-related macular degeneration (AMD) is of great interest for understanding disease progression, and the development of possible treatment(s). This study investigates microRNA modulation in our in vitro AMD model. The “personalized” transmitochondrial cybrids are cell lines that have identical nuclei, but mitochondria from different individuals. Previously we showed that AMD cybrids express higher mir135b-5p and mir148a-3p compared to age-matched normal cybrids, and that inhibition of these microRNA can alter gene expression in our cybrids. We hypothesize that in addition to gene expression changes, modulation of these microRNAs can potentially altar cellular health.

Methods: Cybrids were generated from AMD (n=5) and aged-matched normal (n=5) subjects by fusing platelets from clinically well-characterized patients with human retinal pigmented epithelial cells (ARPE-19) lacking mitochondria (Rho0). Since all cell lines have identical nuclei, differing responses between AMD and age-matched normal cybrids can be attributed to mitochondrial influence. MicroRNA inhibition was achieved through transfection of antisense miRNA inhibitors. Caspase 3/7 assays used the IncuCyte live cell imager. Statistical analyses were by paired t-test.

Results: Inhibition of mir135b-5p in AMD cybrids decreased expression of pro-apoptotic genes, BAX, BCL2L13 and CASP3 (0.85*, 0.7*, 0.82* fold) and decreased Casp3/7 staining by 40%*. In contrast, inhibition of mir148a-3p increased expression of pro-apoptotic CASP9 gene (1.3* fold) ER Stress gene DDIT3 (4.6* fold), autophagy genes ATG5 and ATG12 (1.75*, 1.73* fold) and inflammatory genes IL6 and IL1B. (12.3*, 4.4* fold). Inhibition of mir148a-3p also increased expression of mitochondrial biogenesis genes TFAM, POLG, TFB2M. (1.5*, 1.98*, 2.0* fold), and decreased ROS levels by 15%*. (*=p<0.05)

Conclusions: This study shows that inhibition of mir135b-5p decreases expression of apoptotic genes, and decreased Caspase 3/7 staining in AMD cybrids, supporting our hypothesis that modulation of this microRNA may improve ARPE cybrid cell health. In contrast, inhibition of mir148a-3p was associated with increased expression of cell death, inflammation, ER stress, and interestingly an increase in mitochondrial biogenesis genes as well as decreased cellular ROS levels. This data demonstrates that manipulation of specific microRNA can have dramatic effects on many pathways relevant to AMD.

CONTROL ID: 3546855

SUBMITTER (NAME ONLY): Charles DeYoung

TITLE: Human retinal pigment epithelium secretes insulin-like growth factor 2 in vitro

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. DeYoung, C. Zhang, A. George, K. Bharti, T. Cogliati, B.P. Brooks, Ophthalmic Genetics and Visual Function Branch, National Institutes of Health, Bethesda, Maryland, UNITED STATES|C. DeYoung, A. George, T. Cogliati, B.P. Brooks, Pediatric, Developmental & Genetic Ophthalmology Section, National Institutes of Health, Bethesda, Maryland, UNITED STATES|T. Pfister, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Functional retinal pigment epithelium (RPE) cultures can be derived from human induced pluripotent stem cells (iPSCs) to investigate the molecular mechanisms underlying human disease via an in vitro model. The RPE secretes various molecules and growth factors which can play a critical role in eye development. Retrospective analysis from RNA-sequencing and gene expression data (<https://eyeintegration.nei.nih.gov/>) showed that insulin-like growth factor 2 (IGF2) is expressed in RPE at the transcript level. IGF2 is a peptide hormone known to regulate cell proliferation, growth, migration, differentiation, and survival (Bergman et al., 2013). We aimed to validate the data via protein studies and investigate whether IGF2 could be a growth factor secreted by the RPE.

Methods: Human iPSC lines were derived from unaffected individuals and differentiated toward RPE cells. The RPE cells were cultured on a 2-D trans-well system for 6-8 weeks to mature and form an epithelial monolayer. All experiments were performed after 6-8 weeks of post-selection maturation. Western blot was performed to study IGF2 protein levels in RPE. Immuno-fluorescence followed by confocal microscopy (Zeiss 880) was performed to study cellular localization of IGF2. ELISA was performed using cell-culture supernatant media to quantify secreted levels of IGF2 from the apical and basal sides of RPE monolayers.

Results: A 20 kDa band was consistently observed in RPE monolayer lysates from three different RPE sources when incubated with anti-IGF2 antibody (ab9574). Immuno-fluorescence staining of RPE monolayers was performed using the same anti-IGF2 antibody and counter stained with ZO1 and nuclear stain (Hoechst333142). ZO1 staining was observed on the apical cell borders, and IGF2 staining localized in the apical portion of the cells just basal to the ZO1 staining.

To confirm IGF2 protein is secreted from the RPE monolayer, we performed ELISA using the apical and basal media sides of the RPE monolayer 24 hours after media change. We consistently observed IGF2 in the range of 200-400 pg/mL in the supernatant media.

Conclusions: IGF2 is expressed at the transcript and protein levels and secreted from the human RPE monolayer in vitro. This novel finding is important as IGF2 could play a crucial role in the development of the neural retina. Ongoing work is testing this hypothesis through an in vivo mouse model.

CONTROL ID: 3546856

SUBMITTER (NAME ONLY): Sailee Lavekar

TITLE: Modeling neurodegenerative features of glaucoma using human pluripotent stem cell-derived retinal ganglion cells

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.S. Lavekar, C. Fligor, K. VanderWall, K. Huang, Biology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|C. Gomes, J. Meyer, Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|S.S. Lavekar, K. VanderWall, K. Huang, C. Gomes, J. Meyer, Stark Neurosciences Research Institute, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal ganglion cells (RGCs) connect the eye and the brain, allowing for visual perception, and these cells are known to be damaged in various blinding disorders such as glaucoma. The degeneration of RGCs is known to occur in a compartmentalized fashion, with the axonal compartment degenerating via different mechanisms than the somatodendritic compartment. While previous studies have demonstrated the ability to study certain aspects of RGC neurodegeneration with human pluripotent stem cells (hPSCs), they have lacked a focus upon the compartmentalized nature of RGC neurodegeneration. Thus, the goal of this study was to examine how RGC neurodegeneration occurs within different cellular compartments.

Methods: RGCs were differentiated from isogenic control and CRISPR/Cas9 edited OPTN(E50K) hPSCs. RGCs were enriched via Magnetic Activated Cell Sorting (MACS). Initially, RGCs were plated upon laminin-coated coverslips, and studies explored neurodegenerative features within RGCs over the first 4 weeks of maturation including neurite retraction and changes in excitability. Subsequently, RGCs were also plated onto microfluidics slides to allow for the recruitment of RGC axons away from the somatodendritic compartments, which allowed for an analysis of cellular changes within discrete compartments of RGCs.

Results: Glaucomatous OPTN(E50K) RGCs showed reduction in soma size and neurite outgrowth compared to isogenic controls, correlated with an enhanced excitability. Upon growth in microfluidic platforms, RGC axons and dendrites could be readily distinguished, and changes in the complexity of these processes were analyzed and compared for significant changes. Overall, OPTN(E50K) RGCs demonstrated morphological and functional deficits, mimicking some aspects of the phenotypes observed during the progression of glaucomatous neurodegeneration.

Conclusions: The results of this study demonstrate the ability to study neurodegenerative phenotypes in RGCs differentiated from human stem cells, including those with a glaucoma-associated OPTN(E50K) mutation along with the further application of microfluidic platforms that allows for the analysis of neurodegenerative changes in separate neuronal compartments. The results of this study will expand our understanding of the cellular changes that occur in human RGCs, and will support future studies including disease modeling and drug screening.

CONTROL ID: 3546858

SUBMITTER (NAME ONLY): Manuela Bartoli

TITLE: Diabetes-induced HDAC6-miR-34a pathway downregulates SIRT-1-miR-146a axis to promote stress-induced premature senescence and diabetic retinal microangiopathy

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Bartoli, H. Abouhish, S. Rajpurohit, M. Thounaojam, Ophthalmology, Augusta University, Augusta, Georgia, UNITED STATES|R. Jadeja, F.L. Powell, P.M. Martin, Biochemistry and Molecular Biology, Augusta University Medical College of Georgia, Augusta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose:

We have previously shown that stress-induced premature senescence (SIPS) is a key pathogenic component of diabetic retinal vascular dysfunction. Here we have investigated the reciprocal role of histone deacetylase 6 (HDAC6) and sirtuin 1 (SIRT-1) in diabetes-induced SIPS. These two HDACs have been shown to play opposing roles in regulating SIPS, however their reciprocal interaction in this process was not investigated before.

Methods: We used streptozotocin-induced diabetic rats at 8 weeks of hyperglycemia (STZ-rats) and age-matched normoglycemic rats. Human retinal endothelial cells (HREC) were cultured for 48 hours in different glucose conditions (HG=25mM D-glucose). Senescence was determined by senescence-associated-beta-galactosidase activity assay. Extracellular vesicles (EVs), were isolated from HREC supernatants using ultracentrifugation. Inhibition of HDAC6 was achieved in STZ-rats by treatment with the specific inhibitor Tubastatin (TS;10mg/Kg/day) and in HREC by 5µM TS. HDAC6 expression in HuREC was also halted using human specific gRNA and compared to negative controls. MicroRNA arrays were conducted on HREC extracts and in EVs in response to the different treatments.

Results: Hyperglycemia stimulated HDAC6 while downregulating SIRT1 retinal expression and activity. TS prevented diabetes-induced loss of SIRT-1 in rats and significantly reduced senescence markers. In HuREC, HG treatment inhibited and TS treatment restored SIRT-1 while decreasing the number of senescent cells. MiRNA arrays of HREC extracts and EVs collected from the cells supernatants showed the up-regulation of miR-34a and down-regulation of miR-146a. Treatments of the cells with TS or transfection with HDAC6-specific gRNA, halted HG-induced cells senescence while restoring SIRT-1 expression and activity. Loss of HDAC6 (TS and gRNA) also down-regulated miR-34a expression while restoring miR-146a. Finally, transfection of HREC with miR-34a mimic overrode the effects of TS in blocking HG-induced loss of SIRT-1 and miR-146a.

Conclusions: We have identified in the HDCA6-miR-34a axis a key molecular event leading to diabetes-induced retinal vascular senescence and diabetic microangioapthy through loss of SIRT1 and of miR-146a. Overall, our results suggest the potential therapeutic use of HDAC6 inhibitors for diabetic retinopathy

CONTROL ID: 3546859

SUBMITTER (NAME ONLY): Lindsay Rhodes

TITLE: Telemedicine quality assessment by eye clinic patients at the outset of the COVID-19 pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Rhodes, P. Balakrishnan, T.A. Swain, A. Atik, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|J. Cho, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has placed unprecedented challenges on the provision of eye care. This study assessed patient attitudes about eye care with relation to visit type at the outset of the coronavirus pandemic when eye care offices were limiting patient visits to urgent and emergent care based on recommendations from the American Academy of Ophthalmology.

Methods: This is a cross-sectional survey of patients who completed either an in-person or telemedicine visit or who deferred their previously scheduled visit at the Callahan Eye Hospital & Clinics at the University of Alabama at Birmingham during April 2020. Quantitative self-reported responses about eyesight quality, worry about eyesight, and satisfaction were collected. Responses to qualitative questions were categorized positively or negatively by themes of quality, risk, precaution, convenience, trust, and communication. Responses were assessed by visit type and compared using Fisher's exact or the Pearson chi-square test.

Results: 450 patients completed the survey with a mean age 55.1 ± 22.7 years. The majority were female (63.7%) and white (54.7%). A greater number of patients reporting fair to very poor eyesight were seen in-person (25.6%) or by telemedicine (40.0%) compared to those who deferred (19.1%) ($p=0.0005$). Worrying about eyesight some, most or all of the time was significantly greater in patients seen in-person (18.8%) or by telemedicine (14.9%) compared to deferral (9.7%) ($p=0.0002$). When asked about feelings regarding their visit, those who had a telemedicine visit more frequently responded with a positive comment about quality ($p<0.0001$) while those completing in-person visits were more positive regarding precaution ($p<0.0001$). There were no significant differences by visit type with regard to positive or negative comments on risk, trust, and communication. Patients completing a telemedicine visit less frequently reported complete satisfaction (67.8%) compared to deferred (86.3%) and in-person visits (74.4%) ($p=0.0001$).

Conclusions: Patient responses demonstrate that telemedicine may be an acceptable modality for eye health management, especially among patients with fair to poor eyesight. During the COVID-19 pandemic, telemedicine may provide a way for patients worried about their eyesight to feel supported by their eye care provider. Further analysis regarding patient satisfaction with telemedicine is needed.

CONTROL ID: 3546860

SUBMITTER (NAME ONLY): Zhouhuan Xi

TITLE: AAV-mediated Gene Therapy Restores Retinal Function in CRISPR-based Mouse Models of PRPF31 Retinitis Pigmentosa

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Xi, A. Vats, J.A. Sahel, Y. Chen, Department of Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|Z. Xi, Department of Ophthalmology, Xiangya School of Medicine, Xiangya Hospital, Central South University, Changsha, Hunan, CHINA|L. Byrne, Department of Ophthalmology, Department of Neurobiology, Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinitis pigmentosa (RP) is an important cause of visual impairment, characterized by degeneration of retinal photoreceptors (PR). Mutations in pre-mRNA processing factor 31 (PRPF31) are the second most common cause of autosomal dominant RP. Gene therapy holds promise to treat retinal inherited diseases, and AAV-mediated PRPF31 augmentation has been shown to restore critical functions in iPSC-derived PRPF31[±] cells. Currently, there are no satisfying animal models with similar phenotypes to human PRPF31 patients. Our study aims at establishing animal models of this disease by AAV-CRISPR/Cas9 gene editing and testing gene therapy efficiency in vivo in these models.

Methods: Cas9 and/or guide RNA with/without GFP reporter gene targeting early coding exons of PRPF31 were delivered to the retina of WT and SpCas9-expressing transgenic mice using AAV. Different delivery routes including systemic injection, intravitreal injection (IVT), and sub-retinal injection (SRI) were evaluated. AAV-PRPF31 gene augmentation was achieved using SRI. Retinal conditions were evaluated by fundus imaging, OCT, ERG, and histology.

Results: Systemic delivery of knockout (KO) vectors to P0 neonatal mice caused low body weights and high early mortality rates. IVT delivery to the retina resulted in reduced thickness of the inner plexiform layer and reduced amplitude of the ERG b-wave. SRI, which led to higher expression levels of KO vectors in PR, induced retinal pallor and formation of black-brown pigmentation, which spread away from the injection site over time. OCT revealed the disappearance of the inner and outer segment layers, followed by loss of the outer nuclear layer, indicating PR degeneration. ERGs showed notable reductions in a-, b- and c-wave amplitudes, with prolonged c-wave implicit time. Co-injection of PRPF31 therapeutic vectors with KO vectors decreased retinal pallor and pigmentation, improved retinal thickness, as well as a-, b- and c-wave responses compared to PBS and KO vectors co-injected eyes.

Conclusions: PRPF31 RP mouse models with early on-set morphological and functional impairments like those in patients were established, providing new platforms to investigate the pathogenetic mechanisms of PRPF31 and to evaluate treatment efficacy. AAV-mediated gene therapy rescued the function of PRPF31-mutant retinas, further demonstrating proof-of-concept for gene therapy to treat PRPF31 RP.

CONTROL ID: 3546862

SUBMITTER (NAME ONLY): George Ousler

TITLE: Prevalence of hyper-response to CAE challenge in dry eye disease

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.W. Ousler, M. Watson, D. Narayanan, Ora, Inc., Andover, Massachusetts, UNITED STATES|G. Wallstrom, SDC Clinical, Phoenix, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: It has been previously reported that patients with dry eye disease (DED) who exhibit a rapid symptomatic response to the Ora CAE® challenge demonstrate enhanced investigational treatment differences as well as a reduction of placebo effects in clinical studies. The purpose of this study is to report the prevalence of this CAE hyper-response across treatment naïve dry eye patients.

Methods: Data from 1209 DED patients were analyzed. The CAE is a controlled chamber which allows for highly standardized atmosphere of low relative humidity, increased airflow, and constant visual tasking. This controlled environment overcomes a dry eye subject's ability to maintain a stable tear film and allows for reproducible evaluation of signs and symptoms of dry eye. Each subject's ocular discomfort is documented using the Ora Calibra® Ocular Discomfort scale (0 = none to 4 = worst) before and periodically during the 90 minutes CAE challenge. A subject is defined as a CAE hyper-responder if their ocular discomfort worsens to 3 or greater (or to 4 if 3 at time 0) in less than 20 min in CAE (considered a more symptomatic patient or hyper-responder) versus \geq 20 minutes in CAE (i.e. not hyper-responder). For each study, number of subjects identified as hyper-responders were documented and percentage was calculated.

Results: Among the 1209 subjects, 496 (41%) were identified as CAE hyper-responders and 713 (59%) were not hyper-responders to the CAE. Overall reproducibility of subjects meeting these criteria at more than one CAE challenge was 787/1209 (65%). When considering a 10 min. window of the 90 min. challenge for re-qualification, CAE hyper-responders reproduced 79% of the time.

Conclusions: Hyper-response to CAE is a phenomenon well-documented across a large number of patients. An individual DED patient's inherent sensitivity to respond to a challenge might be a contributing factor and indicator of their ability to report symptoms and better distinguish treatment differences. Additional study is ongoing to identify specific individual characteristics that might be related to exhibiting hyper-response on CAE. A hyper-response to the CAE as an inclusion criterion or pre-defined subpopulation may result in patient enrichment in dry eye clinical trials.

CONTROL ID: 3546863

SUBMITTER (NAME ONLY): Emmanuel Ho

TITLE: Modified Exosomes for Extended Intravitreal Drug Delivery

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Ho, D. Chen, Y. Zhao, P. Nekkar Rao, Pharmacy, University of Waterloo Faculty of Science, Waterloo, Ontario, CANADA|E. Ho, D. Chen, Centre for Eye and Vision Research Limited, Hong Kong, HONG KONG|

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ABSTRACT BODY:

Purpose: Intravitreal injection (IVI) is the only feasible method of drug delivery to the retina. However, IVIs are only suitable for drugs with large therapeutic indices and long half-lives, as rapid diffusion mediates clearance and loss of therapeutic effects. There is a need to improve IVI systems to reduce injection frequency and allow for delivery of drugs with unfavorable properties. Nanoparticle encapsulation of a drug can improve drug solubility, stability, and half-life. Exosomes are cell-derived vesicles that can be used as drug delivery nanoparticles. Hyaluronan is an aminoglycan found in high concentrations in the vitreous of the eye. Conjugation of hyaluronan-binding moieties is one strategy that can be used to restricting diffusion and improve the intravitreal half-life of therapeutics. The objectives are to design and evaluate hyaluronan-binding peptides using in silico modeling and in-vitro modeling. Then, peptides are evaluated for their ability to restrict exosomes drugs using an in vitro diffusion model. We hypothesize that presence of hyaluronan solution will decrease the diffusion rate of peptide conjugated exosomes, and thus may be useful for increasing the half-life of therapeutics for retinal drug delivery.

Methods: Exosomes will be isolated from retinal cell culture using differential ultracentrifugation. Exosome cell uptake into retinal cells will be evaluated qualitatively by fluorescence microscopy. Drug loading and release will be evaluated following loading of exosomes with model small molecule drugs. Hyaluronan-binding peptides will be designed using molecular docking techniques. Candidate peptides will be conjugated to the surface of exosomes using click chemistry. Exosome diffusion rates will be evaluated using a diffusion cell model.

Results: Exosomes were positive for CD63, had a mean diameter of 85.0 nm, and had round morphology as imaged by STEM. Molecular docking identified several peptides with strong interaction to hyaluronan. Exosomes displayed time depending uptake into ARPE19 cells in culture.

Conclusions: Exosomes derived from retinal cell culture are a promising nanoparticles system for IVI as they have favorable properties for drug delivery. Molecular docking is a useful tool to design peptide ligands. Future work should evaluate the extent of drug loading and release and evaluate the effect of peptides on diffusion through hyaluronan solution.

CONTROL ID: 3546864

SUBMITTER (NAME ONLY): Alberto Recchioni

TITLE: Impact of the United Kingdom (UK) COVID-19 lockdown measures on air pollution and ocular surface disease symptomatology amongst shielding patients

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Recchioni, N. Poonit, G.R. Wallace, S. Rauz, Academic Unit of Ophthalmology, Institute of Inflammation and Ageing, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|A. Recchioni, Optometry & Vision Sciences Group, School of Life & Health Sciences, Aston University, Birmingham, Birmingham, UNITED KINGDOM|M. Makanvand, W. Bloss, School of Geography, Earth and Environmental Sciences, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Worldwide lockdown reduced global air pollution during the SARS-CoV-2 pandemic. In this study, we evaluate whether the UK lockdown impacted upon dry eye symptoms in severe ocular surface disease (OSD) patients and whether there is a relationship with changes in air pollution levels.

Methods: 35 OSD patients (median age 70 (range 42-85) years; 17(48.5%) females; 22(63%) ocular mucous membrane pemphigoid; 3(9%) high-risk corneal transplant recipients; 4(12%) ulcerative keratitis; 2(6%) Stevens-Johnson syndrome; 3(9%) other (granulomatous polyangiitis, Sjögren's syndrome, pemphigus vulgaris) maintained on systemic immunosuppression including mycophenolate mofetil, azathioprine, tacrolimus, methotrexate and cyclophosphamide achieved a risk stratification score of >3, defined as coronavirus high-risk and fulfilled the government criteria for shielding for a minimum of 12 weeks. Symptoms and air pollutions data were considered from three different time periods categorised as pre, during and post-lockdown. Pre-lockdown symptoms were curated from hospital electronic databases using the OSDI[®] symptom questionnaire (Allergan plc, Irvine, CA) whilst during and post-lockdown data were obtained via postal hardcopy. Air pollution data for patient postcodes were derived from Department for Environment, Food, & Rural Affairs (DEFRA) and from the Automatic Urban and Rural Network (AURN) monitoring network for nitrogen dioxides (NO₂), nitrogen oxides (NOx) particulate matter 10µm (PM₁₀) and 2.5µm (PM_{2.5}).

Results: A 12% increase in symptom scores were observed during versus pre periods (36.11±16.09 vs 32.24±29.17, p=0.381). Similarly, a 19% reduction was observed between the during and post periods (36.11±16.09 vs 29.46 ± 26.29, p=0.144). However, significant reduction of NO₂ (35%, from 17.11±6.87 to 11.17±4.79, p<0.001) and NOx (44%, from 26.06±11.64 to 14.53±7.18, p<0.001) respectively, were observed between pre and during periods. Symptoms and air pollutants were not correlated across all the considered periods.

Conclusions: Despite the reduction of air pollutants due to lockdown measures, dry eye symptoms experienced by immunosuppressed OSD patients were increased. This might be due to a range of environmental factors such as increase use of electronic blue screen electronic devices as well as the psychological impact of lockdown on patient wellbeing.

CONTROL ID: 3546867

SUBMITTER (NAME ONLY): Rashed Kashem

TITLE: Comparison of Heru Visual field as a cloud based artificial intelligence-powered software application downloadable on commercial augmented reality headset with Humphrey Field Analyzer SITA Standard

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Kashem, A.H. Goldbach, F. Mohder, S. Bonyadi, M. Sharma, C. Duque, T. Eleiwa, A.R. Shaheen, M. Abou Shousha, R. Parrish, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|A. Elsayy, University of Miami, Coral Gables, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: 1-To evaluate the comparability of visual field (VF) measurements obtained using Heru VF that uses a cloud based artificial intelligence (AI)-powered software application downloadable on commercial augmented reality headset to those of standard automated perimetry in normal, glaucoma and neuro-ophthalmology patients.

2-To evaluate the reproducibility of Heru VF measurements in normal and pathological eyes.

Methods: This prospective clinical study included 47 eyes (21 healthy and 26 of patients with glaucoma and neuro-ophthalmic diseases). VF results were obtained using Heru VF application that uses a cloud based AI testing algorithm (Heru Visual Field, Miami) downloaded on Magic Leap 1 augmented reality device (Magic Leap, Plantation, FL) and a Humphrey Field Analyzer (HFA) 800 series (Carl Zeiss Meditec, Inc, Dublin, CA, USA) using SITA Standard. Patients underwent 24-2 test point pattern in both devices. Comparing test times and correlations of threshold values (TV) and mean deviations (MD) obtained using both were calculated to determine agreement. Test time (TT) was compared between the two devices. In Heru device, testing is paused when patient is not fixating, thus testing time excludes idle time when patient was not interacting with the test. Pathological VF defects seen were typical glaucomatous VF defects and ring scotomas.

Results: There were strong correlations between Heru VF MD and TV and those of HFA in normal, glaucoma and neuro-ophthalmology patients ($R=0.91$, $P<0.001$ and $R=0.81$, $P<0.001$, respectively). MD and TV of Heru VF in normal and pathologic eyes showed excellent reproducibility with ICC of 0.95 (95%CI 0.86-0.98) and 0.80 (95%CI 0.78-0.82), respectively. Heru VF was statistically significantly faster than the HFA SITA Standard (4.3 vs 5 minutes respectively; $P<0.001$). Mean TT in Heru VF was 15.4% faster than HFA in pathologic eyes (4.7 vs 5.5 minutes, $P<0.001$) and 7.8% faster than HFA in healthy eyes (3.9 vs 4.24 minutes, $P<0.001$).

Conclusions: Central VF measurements from Heru VF that uses a cloud-based AI-powered software application downloadable on commercial augmented reality headset were comparable to HFA in normal, glaucoma and neuro-ophthalmology patients. Heru VF measurements are reproducible in normal and pathologic patients. Heru VF is faster than HFA SITA Standard.

CONTROL ID: 3546869

SUBMITTER (NAME ONLY): Danielle ClarksonTownsend

TITLE: Developmental Circadian Disruption Alters Refractive Development in Mice

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. ClarksonTownsend, Gangarosa Department of Environmental Health, Emory University, Atlanta, Georgia, UNITED STATES|D. ClarksonTownsend, K. Hogan, D. Brown, M.T. Pardue, Center for Visual and Neurocognitive Rehabilitation, Atlanta VA Medical Center, Decatur, Georgia, UNITED STATES|K. Hogan, D. Brown, M.T. Pardue, Department of Biomedical Engineering, Georgia Institute of Technology, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Circadian rhythms in ocular tissues play important roles in homeostasis, photoreceptor disc shedding, and visual function and are also thought to influence ocular growth and emmetropization. To test whether circadian disruption caused by environmental light affects refractive development, we utilized an experimental model of environmental circadian disruption and longitudinally measured refractive error in mice.

Methods: Wild-type C57Bl/6J male and female mice were developmentally exposed throughout gestation and after weaning to either a control light (CL, 12:12 light:dark, n=17-20) or environmental circadian disruption (CD, weekly light:dark inversions, n=16-22) light cycle. Refractive error (photorefractometry), corneal curvature (keratometry), and eye biometry (spectral domain optical coherence tomography) were measured at 4, 5, and 6 weeks of age. A mixed-effects analysis with Sidak's method to control for multiple comparisons (significance threshold $p < 0.05$) was performed to test for differences in refractive error and corneal curvature by treatment group and time. Student's unpaired t-tests (significance threshold $p < 0.05$) were used to evaluate differences in eye biometry measures in a subset of mice (n=14 CL, n=12 CD) at 4 weeks of age.

Results: Mice in the CD group had greater refraction values compared to CL at 4, 5, and 6 weeks of age (Figure 1, main effect of group, $F(1, 41) = 174.7$, $p < 0.001$). Corneal curvature does not appear to significantly differ between groups, but eye biometry measures from a subset of mice suggest trends towards decreased corneal thickness ($p = 0.122$), decreased lens thickness ($p = 0.117$), and shorter axial length ($p = 0.283$), in the CD mice.

Conclusions: These results suggest that the developmental light environment can influence refractive error. We plan to further evaluate eye biometry measures in the remaining mice at all time points. Because mice were kept in the light conditions for the duration of the experiment, it is possible that circadian changes in choroidal dynamics may also play a role in these results.

CONTROL ID: 3546870

SUBMITTER (NAME ONLY): Sachin Anil Ghag

TITLE: Role of Notch Signaling Pathway in Steroid Induced Glaucoma

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Ghag, P.P. Pattabiraman, Department of Ophthalmology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sachin Anil Ghag: Commercial Relationship: Code N (No Commercial Relationship) | Padmanabhan Pattabiraman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Treatment with corticosteroid hormone Dexamethasone (DEX) results in increased fibrogenic stimulus, extracellular matrix (ECM) accumulation in the trabecular meshwork (TM) and elevated intraocular pressure (IOP) leading to steroid induced glaucoma (SIG). Notch signaling pathway is an evolutionarily conserved signaling mechanism contributing to the pathophysiological processes like tissue fibrosis. Here, we investigated the effects of DEX on Notch signaling and ECM remodeling in the TM.

Methods: Primary Human TM (HTM) cells were treated with 100nM DEX in serum free media alone or in combination with- a) N-(N-[3, 5-difluorophenacetyl])-L-alanyl)-S-phenylglycine t-butyl ester - DAPT (Notch signaling inhibitor), b) Phenethyl isothiocyanate - PEITC (Notch signaling activator), and c) RU486 (Glucocorticoid receptor inhibitor) - and investigated for changes in protein expression by immunoblotting for- canonical notch signaling including Notch receptor - Notch1, Notch ligand - Jagged-1, Notch effector - Hes1, ECM proteins - Fibronectin (FN) and Collagen1A (COL1A), pro-fibrogenic marker - α -Smooth Muscle Actin (α -SMA), and pro-fibrotic growth factor - Transforming growth factor β 2 (TGF β 2). Student's t-test and/or one-way ANOVA was used for statistical analysis and results were significant if $p \leq 0.05$ with a sample size of $n \geq 3$ in each experiment.

Results: DEX treatment significantly - downregulated - Notch1 ($p=0.008$), Jagged1 ($p=0.050$), Hes1 ($p=0.001$) and upregulated - a) α -SMA ($p=0.001$), b) TGF β 2 ($p=0.048$), and c) ECM- COL1A ($p=0.018$) and FN ($p=0.024$) proteins. Inhibition of Notch signaling using DAPT mimicked the effect of DEX in upregulating COL1A and FN. Conversely, activation of Notch signaling using PEITC downregulated ECM proteins. Finally, inhibition of DEX signaling by RU486 restored the Notch1 ($p=0.016$) and Hes1 ($p=0.001$) and decreased FN ($p=0.024$) levels similar to PEITC treatment in presence of DEX.

Conclusions: Our preliminary data in TM demonstrates that - 1) canonical Notch signaling pathway is downstream of DEX mediated events, 2) DEX induces ECM production by downregulating the Notch pathway, and 3) activation of Notch signaling mimics inhibition of DEX receptor-mediated signaling. From this study, we speculate that notch signaling plays an important role in ECM remodeling in TM outflow pathway and help maintain the IOP homeostasis. The activation of notch signaling pathway can be a potential therapeutic target for SIG.

CONTROL ID: 3546871

SUBMITTER (NAME ONLY): Paul Chamberlain

TITLE: Measured and Predicted Axial Elongation in the MiSight 1 day Clinical Trial – 6 year results

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Chamberlain, D. Hammond, B. Arumugam, R&D, Coopervision Inc, Pleasanton, California, UNITED STATES|M.A. Bullimore, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: A 6-year clinical trial randomized subjects to MiSight 1 day (Omafilcon A, dual focus design, CooperVision, Inc.; M1d) or Proclear 1 day (Omafilcon A, single vision, CooperVision, Inc.;P1D) contact lenses for the first three years during which M1d significantly slowed axial elongation Chamberlain et al. (2019). This analysis reports annual axial elongation and overall treatment effects over 6 years using a virtual control group.

Methods: Part 1: 144 myopic children (8-12 years of age) were randomized to wear either M1d or P1d. Part 2: After 3 years, the P1d wearers (n=56) were switched to M1d lenses (M1d-3) while the original treatment group (M1d-6; n=52) continued with M1d. All subjects were followed, unmasked, for an additional 3 years. In the absence of a concurrent control group, a virtual control group was created, based on the axial elongation model of Brennan et al. (AAO 2018). Estimated annual elongation (EAE) was calculated using the age and ethnicity of the P1d control cohort and used to quantify the myopia treatment effect of MiSight over the full 6 years.

Results: EAE for the virtual control group agrees well with the experimental control group during years 1-3. The EAE was 0.619 mm and 0.624 mm respectively, validating the virtual control group and its use for estimating EAE for an untreated control group for the final 3 years. The EAE for the virtual control group growth in years 4 to 6 was 0.395 mm. The year 4-6 total elongation in the M1d-3 and M1d-6 groups were 0.190 mm and 0.184 mm indicating 0.205 mm and 0.211 mm treatment effects. The treatment effect for the M1d-6 group when compared to the virtual control group over the full 6 years revealed a 0.529 mm reduction in axial eye growth (six year cumulative growth of 1.014 (control) – 0.485 mm (treatment)).

Conclusions: Using a virtual control group, M1d substantially retards myopia by slowing axial elongation throughout six years of wear. This approach also shows effectiveness in newly treated older subjects in years 4-6.

CONTROL ID: 3546873

SUBMITTER (NAME ONLY): Megan Steinkerchner

TITLE: Relationship between Time spent using Video Display Terminals and Dry Eye Disease

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Steinkerchner, R.R. Sayegh, Ophthalmology, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|R.R. Sayegh, Ophthalmology, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Megan Steinkerchner: Commercial Relationship: Code N (No Commercial Relationship) | Rony Sayegh: Commercial Relationship(s);Allergan:Code R (Recipient);Novartis:Code R (Recipient)

ABSTRACT BODY:

Purpose: To evaluate how time spent viewing video display terminals (VDT) influences ocular surface disease index (OSDI) scores and ocular pain rating scales, and to report VDT users' treatment responses to available dry eye disease (DED) therapies.

Methods: A cross-sectional study evaluated patients presenting for dry eye management in an academic setting. Demographics, ocular and medical history, time spent on VDTs (computers, tablets, and cellphones), OSDI scores, ocular numeric rating scale (NRS) and descriptors, and subjective response to previously tried eye drop, systemic, and non-pharmacologic treatments were collected from the patient population. Statistical analysis was performed to assess the correlation between time utilizing VDTs with OSDI and NRS scores and to examine the treatment response in VDT users.

Results: 144 patients were included in the study, with a mean age of 58.1 years. The average reported daily time spent on all VDT was 5.6±4.5 hours, with an average of 3.2±3.5 hours on computers, 0.8±1.5 hours on tablets, and 1.7±1.6 hours on cellphones. There was a very weak correlation between OSDI score and time spent on computers ($R^2=0.002$), tablets ($R^2<0.001$), cellphones ($R^2=0.01$), and all VDT combined ($R^2<0.001$). The lack of correlation persisted when controlling for age. There was a similarly very weak correlation between NRS score and time spent on computers ($R^2=0.01$), tablets ($R^2=0.001$), cellphones ($R^2<0.001$), and all VDT combined ($R^2=0.006$). Patients with more than four hours of daily VDT use and ocular pain had a response rate of 90.6% with artificial tears, 82.7% with hot compresses, 79.1% with steroid eyedrops, 74.5% with tinted lenses, 63.6% with lifitegrast, and 60.0% with cyclosporine A 0.005%.

Conclusions: Time spent engaging VDT was not related with OSDI or NRS scores, highlighting the need for further investigation of dry eye diagnostic tools in VDT users. There was a trend towards decreased computer usage with increased ocular pain, possibly reflecting the loss of productivity in this group. Available DED therapy has a high rate of efficacy in patients with ocular pain associated with VDT use.

CONTROL ID: 3546874

SUBMITTER (NAME ONLY): Steven Skula

TITLE: Post-Operative Outcomes After Pediatric Cataract Surgery in an Urban Hospital Setting

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Skula, Z. Mendelson, S. Guo, Rutgers New Jersey Medical School Department of Ophthalmology & Visual Science, Newark, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pediatric cataracts remain a challenge throughout all ages. The post-operative management after pediatric cataract surgery continues to be challenging. Advancement in surgical techniques and better long-term post-operative care have improved these outcomes, but there is still more to learn. We performed a retrospective chart review of pediatric cataract surgery outcomes over an 11-year period in an urban inner-city hospital. The goal of our study was to further understand the post-operative outcomes and compare our results to the current literature.

Methods: Data was initially collected from 21 patient charts which accounted for 35 eyes. Inclusion criteria required eyes to have a congenital cataract that was not associated with either trauma or previous ocular disorders or surgery and had postoperative follow up for a minimum of 6 months. Of those 35 eyes identified during the chart review, 32 met our inclusion criteria. Subgroups were stratified based on age at time of surgery (infantile ≤ 18 months, Juvenile > 18 months), unilateral or bilateral cataracts, and aphakic or pseudophakic. Average follow up was for 30 months (2.5 years) with a range of follow up from 6 months to 11 years. Statistical analysis for each group was performed using fisher exact test with an α of 0.05.

Results: Incidence of glaucoma was significantly higher in the group with infantile cataract (50% (6/12)) compared to the juvenile group (0% (0/20), $p=0.001$) and in the aphakic group (35% (6/17)) compared to the pseudophakic group (0% (0/15) $p=0.0192$). Posterior capsular opacity (PCO) was significantly greater in the juvenile group (50% (10/20)) than in the infantile cataract group (8.3% (1/12), $p=0.0232$). In the latter group 11 were left aphakic due to the young age and underwent both primary posterior capsulotomy and anterior vitrectomy at the time of the cataract surgery.

Conclusions: We found that children with infantile cataract were associated with a higher incidence of glaucoma. While aphakia was associated with a greater incidence of glaucoma, we believe that children with infantile cataract often have other associated congenital anterior segment anomaly, which may be more influential in the development of glaucoma. PCO was found to occur more frequently in the juvenile group because all of these eyes had their posterior capsule left intact to support intraocular lens implant. Our findings were consistent with the literature.

CONTROL ID: 3546876

SUBMITTER (NAME ONLY): Alessandro Jammal

TITLE: Social History and Glaucoma Progression: The Effect of Obesity, Tobacco, and Alcohol Consumption on the Rates of Structural Change in Patients with Glaucoma

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.A. Jammal, E.B. Mariottoni, L. Shigueoka, F.A. Medeiros, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although obesity, tobacco and alcohol use have been linked to the development and progression of numerous chronic and degenerative diseases, objective evidence of the association of such aspects of a patient's social history with glaucoma progression is yet to be determined. The purpose of this study was to investigate the effect of the body mass index (BMI) and history of use of tobacco and alcohol on the rates of retinal nerve fiber loss (RNFL) loss over time in patients with and suspected of glaucoma.

Methods: This study included 8,424 eyes of 4,480 patients from the Duke Glaucoma Registry. All patients had at least 2 good-quality optical coherence tomography (OCT) tests over a minimum follow-up of 6 months. Self-reported history of alcohol and tobacco consumption was extracted from electronic health records and the mean BMI was calculated for each individual. Linear mixed models were used to determine the effect of each parameter on the rates of change in RNFL over time, with adjustments for sex, race, age at baseline, mean intraocular pressure, central corneal thickness, baseline RNFL, and follow-up time.

Results: Mean follow-up time was 3.9 ± 2.0 years, with an average of 4.0 ± 1.8 (range: 2 to 13) OCT tests per eye. 41% and 58% of the eyes were from subjects with a history of tobacco or alcohol consumption, respectively, and 71% were classified as overweight or obese ($\text{BMI} \geq 25 \text{ kg/m}^2$). Eyes from subjects with history of tobacco consumption had, on average, $0.072 \mu\text{m/year}$ faster rates of RNFL loss over time than subjects that never used tobacco ($P=0.021$). Higher BMI, however, had a protective effect on the rates of glaucomatous progression over time ($0.005 \mu\text{m/year}$ slower per each 1 kg/m^2 higher; $P=0.047$). Alcohol consumption was not significantly associated with rates of RNFL change over time ($P=0.130$). No significant association was observed between smoking intensity (pack-years) and rates of progression ($P=0.757$). After adjustment for confounding factors, only BMI remained significantly associated with rates of RNFL loss ($\beta=0.012$; $P<0.001$).

Conclusions: Habits of tobacco and alcohol consumption showed no significant effect on the rates of RNFL change in glaucoma. Higher BMI was significantly associated with slower rates of RNFL loss. Future studies should investigate the mechanisms by which BMI may affect structural progression in glaucoma.

CONTROL ID: 3546877

SUBMITTER (NAME ONLY): Nazia Alam

TITLE: Contrast sensitivity assessment in children with brain injury.

SESSION TITLE: Amblyopia and Pediatric Ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.M. Alam, S.W. Mooney, L. Tesfaye, G.T. Prusky, Burke Neurological Institute, White Plains, New York, UNITED STATES|G.T. Prusky, Weill Cornell Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: The contrast sensitivity function (CSF) is a highly valuable measure of visual health, but has generally been difficult or impossible to assess in individuals with cognitive impairment. We show that a rapid gaze-based task can assess contrast sensitivity in children with a range of neurological disorders such as cortical visual impairment (CVI), including non-verbal children.

Methods: We measured CSFs in fifteen child in-patients (age 4 to 18) with varying levels of neurological deficit using the eye-tracking-based task Gradiate. This task displays drifting band-filtered noise targets and determines when the participant is smoothly tracking a target with their eyes, then advances the target's spatial frequency and contrast in real time until it is no longer visible. Five distinct thresholds were measured multiple times over multiple sessions in order to form a CSF. We also measured six-threshold CSFs in the most impaired children with a variant of Gradiate that uses scrolling full-screen noise. In this variant, the tester can manually toggle an attractive cartoon overlay to recapture the participant's attention (a "bait-and-switch").

Results: Well-formed CSFs were obtained from ten out of fifteen children, though different patients required different numbers of testing sessions to overcome their varying cognitive and attentional deficits. The low rate of false positives in the Gradiate task allows us to infer thresholds from the best results across multiple sessions with high confidence. Figures 1 and 2 depict example CSFs from children with severe (non-verbal) and mild traumatic brain injury, respectively. Five children exhibited no tracking behavior in any session and could not be assessed.

Conclusions: Our findings indicate that a non-verbal, gaze-based tracking task makes it possible to measure contrast sensitivity in young and/or impaired participants. Due to the task's inherent low false positive rate, transiently poor performance that is due to cognitive rather than visual impairment is readily detectable. Quantitative contrast sensitivity measurements in these clinical populations would aid in diagnosing specific visual disorders in greater detail than broad-spectrum categories such as CVI. These assessments may also be developed further into potential behavioral therapies, which we are currently exploring.

CONTROL ID: 3546882

SUBMITTER (NAME ONLY): Miguel Flores-Bellver

TITLE: Drusen proteins are released in association with exosomes

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Flores-Bellver, S. Aparicio-Domingo, K. Li, H. Cobb, P. Lenhart, V. Canto Soler, CellSight Ocular Stem Cell and Regeneration Program, Department of Ophthalmology, University of Colorado School of Medicine, Colorado, UNITED STATES|J. Mighty, C. Shi, J. Zhou, S.M. Redenti, Lehman College, Bronx, New York, UNITED STATES|J. Mighty, C. Shi, J. Zhou, S.M. Redenti, Biology Doctoral Program, The Graduate School and University Center, City University of New York, New York, UNITED STATES|G.A. Michelis, S. Becerra, NIH-NEI-LRCMB, Section of Protein Structure and Function, Bethesda, Maryland, UNITED STATES|A. Goodspeed, University of Colorado Denver Department of Pharmacology, Aurora, Colorado, UNITED STATES|A. Goodspeed, University of Colorado Cancer Center, Aurora, Colorado, UNITED STATES|S. Heissel, Proteomics Resource Center, The Rockefeller University, New York, New York, UNITED STATES|C. Coughlan, Dept. Neurology, University of Colorado Alzheimer's and Cognition Center, and Linda Crnic Institute for Down Syndrome, CU-AMC, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Despite our growing understanding of dry AMD, effective treatments remain elusive. In the early stages of AMD, drusen accumulate between the RPE and the Bruch's membrane, leading to RPE atrophy and ultimately, central vision loss. Exosomes, cell-derived extracellular vesicles containing proteins and RNAs have been found in drusen of AMD patients. Exosomes play a role in spreading toxic-aggregated proteins in other diseases. Our goal is to recapitulate key features of AMD in human RPE, including drusen-like deposits and, to characterize the cargo of secreted exosomes under cellular stress.

Methods: We established an efficient protocol to produce functionally RPE cells from hiPSC. We induced oxidative stress in the hRPE by exposure to cigarette smoke extract. To characterize exosomes secreted by hRPE cells, we analyzed the concentration, morphology, and proteomic content of released exosomes. We validated the proteins found in exosomes by western blot. For exosome uptake assays, exosomes released by GFP-hRPE were co-cultured with wt hRPE, followed by PCR and immunofluorescence analysis to evaluate internalized exosomes in the recipient cells.

Results: We have established an efficient strategy to derive functionally RPE monolayers from hiPSC. We introduced a model that combines several key aspects of AMD and then, characterize the directional exosomal protein cargo of hRPE. Proteomic profiling of hRPE exosomal cargo revealed that exosomes were selectively enriched in proteins involved in oxidative stress, immune response, inflammation, and drusen-associated proteins pathways. Interestingly, exosomes secreted by hRPE cells within an AMD environment significantly enhanced the release of AMD-associated proteins. Finally, we confirmed the uptake of exosomal proteins and mRNAs released from hRPE cells by recipient cells.

Conclusions: This work represents the first proteomic profile from exosomes released by hiPSC-derived RPE and the first demonstration that proteins linked to drusen are released in association with exosomes. The exosomal cargo suggests a role for exosomes in both, normal physiology of the retina and the progression of retinal disorders. The

identification of well-known drusen proteins secreted in exosomes also suggests a potential involvement of exosomes during drusen development. The confirmation that exosomes released from hRPE are taken up by target cells opens new avenues for possible therapeutic interventions.

CONTROL ID: 3546883

SUBMITTER (NAME ONLY): Neha Deshpande

TITLE: Defective DNA Repair in Fuchs endothelial corneal dystrophy

SESSION TITLE: Corneal endothelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Deshpande, G. Melangath, S. Vasanth, U.V. Jurkunas, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M. Price, F. Price, Cornea Research Foundation, Indianapolis, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Fuchs endothelial corneal dystrophy (FECD) is a genetic, age-related corneal endothelial (CE) degeneration from lifelong exposure to oxidative stress. We previously reported heightened nuclear (nDNA) and mitochondrial (mtDNA) damage to be a hallmark of FECD. This was recapitulated in the ultraviolet-A (UVA) light-induced FECD mouse model which showed early stage mtDNA and late stage nDNA damage to contribute to degenerative CE phenotype. In this study, we investigated whether impaired DNA repair pathways can cause the build-up of deleterious DNA lesions in FECD

Methods: Differential expression profiles of 84 DNA repair and 5 housekeeping genes were analyzed by real-time (RT)PCR arrays. Total RNA was extracted from Descemet's membrane-CE stripped from age-matched normal donors (n=4) and FECD specimens (n=8). cDNA was subjected to RTPCR on Human DNA Repair RT Profiler plates. A change of <0.5 or >2.0-fold mRNA expression in FECD relative to normal was set as the cutoff for down- and upregulation. Total protein was extracted from CE of 7-9 weeks C57BL/6 mice irradiated with 1000 J/cm² UVA at 1 day and western blotting was carried out to assess LIG3 and XPC levels

Results: FECD specimens differentially expressed (p<0.05) 8 nucleotide excision repair (NER), 5 base excision repair (BER), 4 double strand break (DSB) repair and 4 mismatch repair (MMR) pathway genes compared to normal donors. While the total 11 upregulated (>2-fold; p<0.05) genes were equally distributed between the 4 pathways, the set of 10 downregulated (<0.5-fold; p<0.05) genes predominantly (8 out of 10 genes) belonged to NER or BER pathways. NER gene XPC and BER gene LIG3 were downregulated (0.2-fold; p<0.005 and 0.36-fold; p<0.005) in FECD specimens and were also reduced (0.3-fold; p<0.05 and 0.4-fold; p<0.05) in mouse CE cells after UVA irradiation; correlating to the early time-point of mtDNA damage seen in UVA mouse model of FECD. Differentially expressed DSB and MMR pathways were primarily upregulated (3 out of 4 genes each) in FECD compared to normal donors

Conclusions: Our findings indicate that deficient NER and BER pathways may trigger the accumulation of unrepaired DNA lesions in FECD. Downregulation of XPC and lig3 may contribute to the mtDNA damage and mitochondrial dysfunction seen in FECD. This is the first study to provide evidence that DNA repair pathways are deficient in FECD and may be important when designing therapeutics for degenerative cell loss

CONTROL ID: 3546884

SUBMITTER (NAME ONLY): Elias Pavlatos

TITLE: Detection of Corneal Ectasia Using OCT Maps of Pachymetry and Posterior Surface Mean Curvature

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pavlatos, D. Huang, Y. Li, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Elias Pavlatos: Commercial Relationship(s);Optovue, Inc.:Code F (Financial Support) | David Huang: Commercial Relationship(s);Optovue, Inc.:Code F (Financial Support);Optovue, Inc.:Code I (Personal Financial Interest);Optovue, Inc.:Code P (Patent);Optovue, Inc.:Code R (Recipient) | Yan Li: Commercial Relationship(s);Optovue, Inc.:Code F (Financial Support);Optovue, Inc.:Code P (Patent)

ABSTRACT BODY:

Purpose: To formulate an Ectasia index to quantify the abnormal corneal thinning and posterior surface steepening that is associated with ectatic pathologies such as keratoconus.

Methods: 32 eyes from normal subjects and 131 eyes with varying degrees of keratoconus severity were imaged using a Fourier-domain OCT system (Avanti, Optovue, Fremont, CA). Maps of corneal pachymetry and mean curvature of the posterior corneal surface were generated. All pachymetry and mean curvature maps were converted to pattern deviation (PD) maps to show differences in normalized thickness and curvature relative to the healthy population (Li et al, JCRS, 2016). The minimum value on the pachymetry PD map was located, and a 2D symmetric Gaussian function was fit to a sub-region of the map centered at this location. The average vector between the pachymetry PD map minimum and the mean curvature PD map maximum was calculated using all of the keratoconus eyes. Gaussian fitting of the mean curvature PD map was performed with the center of the fit shifted by this average vector with respect to the location of the pachymetry PD minimum. The Ectasia index was calculated from the product of the two Gaussian fits. K-fold cross-validation was used to compare the diagnostic performance of the Ectasia index compared to minimum pachymetry and maximum mean curvature.

Results: The ectatic pattern of coincident corneal thinning and posterior surface steepening was evident for the keratoconus eyes, but not for the normal eyes (Figure 1). The average Ectasia index value for the normal eyes was $-0.1 \pm 1.0\%$. The Ectasia index was larger for the manifest, subclinical, and forme fruste keratoconus groups, with average values of $-19.4 \pm 6.9\%$, $-13.7 \pm 4.6\%$, and $-3.7 \pm 3.9\%$ respectively (all $p < 0.0002$). The Ectasia index was statistically more sensitive than minimum pachymetry in detecting manifest keratoconus and more sensitive than maximum mean curvature in detecting forme fruste keratoconus. The specificity of the Ectasia index did not differ statistically from the specificity of the two other metrics.

Conclusions: The Ectasia index was effective in differentiating between normal and keratoconic eyes and could therefore be a useful additional metric for clinicians to consider when screening for ectasia.

CONTROL ID: 3546886

SUBMITTER (NAME ONLY): Amanda Lehman

TITLE: Resident Performed MIGS Outcomes at a Veterans Hospital

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Lehman, E. Meer, T. Liu, E. Miller, Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Amanda Lehman: Commercial Relationship: Code N (No Commercial Relationship) | Elana Meer: Commercial Relationship: Code N (No Commercial Relationship) | Tianyu Liu: Commercial Relationship: Code N (No Commercial Relationship) | Eydie Miller: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To explore the comparative safety and efficacy of evolving MIGS procedures/devices, the Hydrus, Kahook, and iStent in the Philadelphia VA population to guide future decision-making about the most suitable glaucoma treatment in a resident-training population with diverse demographics.

Methods: A retrospective chart review was conducted for patients who underwent a Minimally Invasive Glaucoma Surgery (MIGS) operation in conjunction with cataract surgery at the Philadelphia Veterans Administration Medical center from approximately 01/01/2015 – 11/1/2020. Descriptive analyses, ANOVA and chi-squared analyses were performed to compare across MIGS types.

Results: 126 patients undergoing MIGS procedure were included. 96% were male, 69.84% African-American, and 29.36% Caucasian. 46.03% patients received a Hydrus, 31.75% an iStent, and 22.22% a Kahook. The average preoperative maximum intraocular pressure was 23.78 mmHg, with an average preoperative IOP of 15.78 mmHg and an average preoperative drop number (total number of glaucoma medications used per day) of 1.45, not significantly different across MIGS types. When separated out by MIGS used, Hydrus demonstrated the greatest reduction in IOP, on average a reduction of 6.14 mmHg at initial post-operative visit and 4.08 mmHg at final post-operative visit, a statistically significant decrease in intraocular pressure when compared to both the iStent and the Kahook ($p < .05$) at postoperative day 1 and postoperative week 1. However, at the 9-12 months postoperative visit the Hydrus was only statistically significantly better at reducing IOP compared to the iStent, and performed similarly to the Kahook. The Hydrus demonstrated a statistically significant decrease in medication reduction (either frequency or number) when compared to both the Kahook and iStent ($p < .05$). There were no significant differences in complication rates across MIGS types.

Conclusions: Overall, this study suggests that Hydrus may be more efficacious than the iStent and the Kahook initially in decreasing glaucoma medication use and IOP postoperatively, however, this difference may not be statistically significant in longer term follow up. More studies are needed to evaluate outcomes in glaucoma populations of different severities.

CONTROL ID: 3546890

SUBMITTER (NAME ONLY): Sarah Redmon

TITLE: Developing novel TRPV4 antagonists for the treatment of glaucoma

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: A single target in the conventional outflow pathway has been approved for glaucoma treatment but the ubiquitous ocular distribution of Rho kinases (ROCKs) is not ideal in terms of specificity and potential side effects. To obviate this, we sought to determine the upstream driver of ROCK in the trabecular meshwork (TM) and Schlemm's canal and tested the efficacy of its modulation as an IOP lowering strategy in acute and chronic models of ocular hypertension.

Methods: Novel anti-TRPV4 compounds were tested by calcium imaging and electrophysiology in vitro in overexpressing HEK293 (HEK-V4OE) cells and primary trabecular meshwork (pTM) cells. IOP was elevated in mice acutely via cannulation or chronically with the microbead occlusion method. IOP lowering was also tested in beagles that express the ADAMTS10 mutation. IOP was measured tonometrically for roughly 24 hrs (mice) or a week (dogs) following topical antagonist administration.

Results: The calcium-permeable stretch-activated channel TRPV4 was identified as the upstream driver of mechanically induced ROCK activation in the TM. SMC-0151 and SMC-0155 inhibited TRPV4 activity at picomolar concentrations, with dose-dependent suppression of agonist-evoked responses. SMCs, but not the commercial antagonist HC067047, lowered IOP in the acute mouse model. Intraocular injection and topical administration significantly lowered IOP in the chronic model. The IOP-lowering effect in dogs was facilitated by increasing the drug concentration.

Conclusions: We demonstrate that TRPV4 and calcium drive mechanically-induced Rho pathway signaling in the TM. Novel, cornea-permeant TRPV4 antagonists were developed as effective reducers of intraocular pressure in two animal models of glaucoma. These results shed light onto the basic mechanisms of IOP-induced TM injury and expand the roster of potential anti-glaucoma strategies and targets.

CONTROL ID: 3546891

SUBMITTER (NAME ONLY): Anita Penkova

TITLE: Sustained-Release Drug Implants in the Vitreous Humor: Analytical and Computational Modeling

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.N. Penkova, A. Naghdloo, S.S. Sadhal, Aerospace and Mechanical Engineering, University of Southern California, Los Angeles, California, UNITED STATES|A.N. Penkova, S.S. Sadhal, Children's Hospital of Los Angeles Saban Research Institute, Los Angeles, California, UNITED STATES|M. Humayun, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|M. Humayun, Biomedical Engineering, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: For patients requiring regular ocular drug therapy, frequent intravitreal injection is painful, undesirable, and unnecessarily risky, and therefore, sustained delivery is a viable alternative. One type of sustained-release systems includes micro-pellets loaded with the drug, encapsulated in a porous shell that can be injected into the vitreous humor where the released drug diffuses while the physiological flow of water provides the convective transport. The purpose of this work is to quantify the drug release rate from a spherical microcapsule for given drug diffusion and capsule permeability properties in the vitreous. The goal is to provide useful parameters such as capsule half-life for various transport parameters for the system.

Methods: The model consists of a porous microsphere shell encapsulating a specific drug. The fluid flow within the vitreous is described by Darcy's equations for the analytical model and Brinkman flow for the computational analysis, while the drug transport is given by the classical convection-diffusion equation. With the timescale for the drug depletion being quite large, we consider the exterior surrounding the capsule to be quasi-steady and the interior is time dependent. In the vitreous, the fluid-flow process is relatively slow, and meaningful results can be obtained for small Peclet number (Pe) whereby a perturbation analysis is possible. For an isolated capsule, with approximately uniform flow in the far-field around it, the mass-transfer problem requires singular perturbation with inner and outer matching. The computational model, however, allows for fully time-dependent solution and also admits large Peclet numbers.

Results: The analytical/computational modeling provides the drug distribution within and around the microsphere. Additionally, the effective lifetime of the drug capsule is obtained in terms of the shell permeability and the biophysical transport parameters. The perturbation analysis has been carried out to order Pe^2 and agrees very well with the computational model. The results are sufficiently general and may be applied to a range of drugs and capsule permeability.

Conclusions: The release rate diminishes with time as expected since the drug source depletes and lowers the driving potential. The predictive results are applicable to the design of the sustained-release microspheres, especially in terms of selecting the capsule permeability.

CONTROL ID: 3546894

SUBMITTER (NAME ONLY): Aleksandra Mihailovic

TITLE: Evaluation of Away-from-Home Excursion Patterns after Falling among Individuals with Glaucoma

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Mihailovic, C. Garzon, J. E. S.K. West, P.Y. Ramulu, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|L.N. Gitlin, Drexel University College of Nursing and Health Professions, Philadelphia, Pennsylvania, UNITED STATES|D.S. Friedman, Massachusetts Eye and Ear Infirmary Department of Ophthalmology, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the associations between fall status and subsequent away-from-home excursions in older adults with glaucoma.

Methods: Prospective observational cohort of individuals with glaucoma or suspected glaucoma who reported falls prospectively via monthly calendars for 1 year and wore a GPS for 1-week at study baseline and again at follow-up 1 year later. GPS data were utilized to quantify average daily excursions, average daily time away from home, average time per excursion, and percentages of days without excursions. Fall status was defined as fallers (≥ 1 fall), recurrent fallers (≥ 2 falls), injurious fallers (≥ 1 injurious fall), and recurrent injurious fallers (≥ 2 injurious falls) using falls data collected over the first study year. Separate negative binomial regression models were used to evaluate the association between fall status and each excursion parameter at follow-up. Integrated visual field (IVF) sensitivity was evaluated as a potential confounder and effect modifier, and models were adjusted for covariates (Table 1). Generalized estimating equations models accounting for clustering by individual were utilized to evaluate change in excursion parameters comparing follow-up assessment to baseline.

Results: One-hundred and eighty-five individuals participated in the study, and roughly half were males (50.8%) with a mean age of 70.3 years; just over one fourth were Black (28.1%) (Table 2). There were no statistically significant associations between fall status and excursion parameters at the follow-up assessment ($p > 0.52$ for all) and IVF sensitivity did not appear to modify these relationships, at baseline or follow-up ($p > 0.14$ for all). Excursion patterns at the follow-up assessment were not significantly different from those at baseline and did not differ by fall status ($p > 0.131$ for all).

Conclusions: Individuals with poor vision from glaucoma who fell did not modify their away-from-home excursions and did not display any restrictions in their excursion patterns compared to their counterparts who did not fall. Even if participants sustained recurrent or injurious falls, daily excursions patterns were not altered.

CONTROL ID: 3546897

SUBMITTER (NAME ONLY): Talia Tunstill

TITLE: Novel Metrics of Contrast Sensitivity for Glaucoma and Suspects

SESSION TITLE: Visual Fields and Psychophysics

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Glaucoma can cause dramatic reduction in visual field prior to any loss of high contrast visual acuity (VA). However, spatial and temporal contrast sensitivity (CS) and color vision can be impaired early in glaucoma. Our purpose was to quantify novel measures of CS and VA with and without glare in a heterogenous cohort of glaucoma patients to develop new metrics for detection and monitoring.

Methods: 30 subjects (mean age 54 ± 12 , 23 females) with diagnosed or suspected open or narrow angle glaucoma, scheduled to undergo laser peripheral iridotomy, participated in our IRB approved protocol after written informed consent. Measures included high contrast VA with and without glare (BAT; Brightness Acuity Tester, Marco Ophthalmic), CS across four spatial frequencies (3, 6, 12, 18 CPD) with and without glare (Vector Vision/Guardion: VVG CS), and Pelli-Robson CS. Repeated measures ANOVA, t-tests and sensitivity analyses were used to evaluate CS metrics.

Results: Mean VA (n=60 eyes) without glare was 0.053 log MAR and slightly decreased (.084) with glare ($P < .03$). However, two-way ANOVA of VVG CS across spatial frequency and glare showed a significant effect of spatial frequency ($F=71.4$, $P < .0001$) but no significant effect of glare ($F = 2.53$, $P = 0.1$). The VVG CS test did reveal decreased CS in 54% to 79% of eyes across four spatial frequencies with the greatest decrease at 12 CPD (20/50 equivalent). Moreover, the sum of VVG log CS values computed to approximate area under the CS curve showed that 74% of eyes were below age comparable norms, with Pelli-Robson log CS (mean 1.47) below age norms in 68% of eyes (Elliot et al., 1990).

Conclusions: Glare disability did not prove to be a strong index of glaucomatous dysfunction, but CS is often decreased in various types and degrees of glaucoma including suspects. Pelli-Robson large letter (20/700) CS proved sensitive, as did VVG higher spatial frequency CS (20/50) also measurable with small letter CS testing, a potential new metric for glaucoma. Finally, the VVG test can be used to sum log CS across spatial frequencies as a sensitive, expedient metric of overall CS which may prove useful to monitor vision in advanced disease.

CONTROL ID: 3546899

SUBMITTER (NAME ONLY): Harini Gudiseva

TITLE: Single cell sequencing of stem cell derived retinal ganglion cells (iPSC-RGC) reveals distinct molecular signatures and RGC subtypes.

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.V. Gudiseva, V. Vrathasha, J. He, V.R. Chavali, J.M. O'Brien, Dept of Ophthalmology/Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To identify marker genes, differential gene expression and retinal ganglion cell (RGC) subtypes in human induced pluripotent stem cell (iPSC) derived retinal ganglion cells.

Methods: Human pluripotent stem cells were differentiated into RGCs using a novel step-wise differentiation protocol developed in our laboratory (PMID:32678240). Single cell sequencing was performed on mature and functional iPSC-RGCs at day 40 using 10X Genomics Single Cell RNA Sequencing following the Chromium Single Cell 3' V3 protocols. Sequencing libraries were run on Illumina Novaseq to generate 150 PE reads. The demultiplex FASTQ files were mapped to the hg38 ref genome using STAR package, and cluster analysis were performed using the cell ranger single cell software. The qc analysis was performed by removing the reads corresponding to ribosomal and mitochondrial genes, as well as cells that had a mean absolute deviation (MAD) lower than 1X. Sub-populations of single cell clusters were identified using unsupervised clustering. Differential expression gene (DEG) analysis of the identified clusters was performed to characterize subsets of RGCs and RGC markers in the iPSC-RGCs. Results from day 40 were compared and analyzed with single sequencing data obtained from iPSC-RGCs matured till day 35 and day 74.

Results: After filtering for mitochondrial reads (>20%), ribosomal reads (>50%) and 1X MAD, 4705 cells that passed quality control were analyzed. Cells were separated into 11 clusters based on the gene expression normalization via PCA and TSNE analysis in the Seurat tool. Several previously known RGC marker genes like MAP2, RPBMS, TUJ1, BRN3A, SOX4, TUBB3, SNCG, PAX6 and NRN1 were found to be expressed in iPSC-RGC clusters. Differential expression analysis between the separate clusters identified (average log fold change > -0.25 and < 0.25) significant DEG transcripts associated with cell cycle, transcription factor neuron regulatory networks, protein kinases, calcium signaling, growth factor hormones and homeobox transcription factors. Further cluster refinement identified RGC diversity and subtype specification within iPSC-RGCs.

Conclusions: We have identified both known and novel marker genes to distinguish subsets of RGCs. The DEGs can be used as biomarkers for RGC subtype classification that will allow screening model systems that represent a spectrum of RGC damaging disease.

CONTROL ID: 3546900

SUBMITTER (NAME ONLY): Muhammad Ali

TITLE: Pluripotent Stem Cell-derived Corneal Endothelial Cells for Donor-Free Keratoplasty

SESSION TITLE: Corneal tissue engineering and regenerative medicine

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Ali, S.Y. Khan, J. Gottsch, S. Riazuddin, The Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|A. Khan, Interdisciplinary Stem Cell Institute, University of Miami, Miami, Florida, UNITED STATES|E. Hutchinson, Molecular and Comparative Pathobiology, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal endothelial dystrophies are responsible for a large percentage of corneal transplants performed around the world. A number of corneal transplant techniques, full and partial thickness keratoplasties, have been developed that are highly effective in restoring vision. However, in many areas of the world, there is a shortage of transplantable-grade donor corneal tissue. Here, we evaluate the efficacy of cryopreserved human embryonic stem cell (hESC)-derived corneal endothelial cells (CECs) to form a functional monolayer of corneal endothelium (CE) in pre-clinical animal models.

Methods: H9 hESCs were differentiated to generate CECs under xeno-free conditions. A silicone needle was used to remove the resident CECs in an 8 mm diameter area of the central cornea of rabbits and monkeys, and cryopreserved hESC-derived CECs were injected in the anterior chamber. The animals were placed in an eye-down position for three hours to allow the injected cells to settle on denuded Descemets Membrane (DM). The clinical examination of post-operative eyes was performed by evaluating intraocular pressure, corneal thickness, and CEC density at different time points. Immunohistochemical (IHC) analysis was performed to confirm the expression of ZO-1, Na⁺/K⁺ ATPase α 1, and N-cadherin. A detailed necropsy and CBC/blood chemistry examination was completed 9- and 12-months post-injection in rabbits and monkeys, respectively.

Results: The injected corneas became clear within 3-4 weeks post-injection in both rabbits and monkeys accompanied by a negligible difference in the corneal thickness between the injected (right) eye and the untreated (left) eye. Confocal scanning microscopy confirmed an intact layer of hexagonal/polygonal cells in the CE formed from the cryopreserved hESC-derived CECs. IHC analysis illustrated intact tight junctions, pump function, and structural integrity of the injected cryopreserved hESC-derived CECs. Finally, all parameters examined during the CBC/blood chemistry analysis were within the normal physiological range while necropsy examination confirmed no remarkable change in multiple tissues examined for teratoma formation.

Conclusions: We present an alternative to eye bank donor corneal tissue of cryopreserved hESC-derived CECs for restoring vision in corneal endothelial dystrophies.

CONTROL ID: 3546902

SUBMITTER (NAME ONLY): Yasuo Yanagi

TITLE: Causal Association of Serum Cholesterol Efflux Capacity and Polypoidal Choroidal Vasculopathy of Singapore Chinese Population

SESSION TITLE: Pathophysiology of ocular aging and degeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Yanagi, R.Y. Chuan, W.A. Shihabuddeen, K. Teo, A.C. Tan, C. Cheng, T.Y. Wong, G.C. Cheung, Singapore Eye Research Institute, Singapore, SINGAPORE|K. Teo, A.C. Tan, C. Cheng, T.Y. Wong, G.C. Cheung, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate cholesterol efflux capacity (CEC) of serum samples from patients with age-related macular degeneration (AMD), and to analyse the serum lipid subfractions of the lipidomics data obtained by using nuclear magnetic resonance (NMR).

Methods: CEC of the serum and their routine lipoprotein profiles were analysed in control, early AMD, typical neovascular AMD (tAMD), and PCV groups and lipid subfractions were measured using NMR analysis in control, early AMD, and PCV samples (Nightingale Ltd, Helsinki, Finland). Analysis of covariance (ANOVA) was conducted to compare the baseline characteristics and routine lipoprotein profiles of the serum samples among the four groups. Multiple regression analysis was used to investigate the difference in CEC between the four groups. Associations between CEC and the lipid subfractions were examined by Pearson correlation coefficient. $P < 0.05$ was considered to be significant.

Results: Mean (SD) ages were similar across four groups (controls, 66.7 (8.5); eAMD, 67.1 (9.3); tAMD, 69.4 (7.9); PCV, 68.3 (9.2) years old: $P = 0.1515$). Early AMD and PCV had a significantly higher CEC than controls, while that of tAMD was comparable with controls after adjusting for age, gender, and use of lipid lowering drug ($P < .0001$). CEC in PCV was higher than early AMD ($P < .0001$). Using conventional lipid biochemistry, tAMD and PCV had higher levels of HDL and LDL cholesterol compared with controls ($P < .02$), although there was no significant difference of those between tAMD and PCV ($P > .05$). NMR lipidomics demonstrated that mean diameter of HDL and LDL was larger and that of VLDL was smaller in PCV compared to control. In early AMD, the diameter of HDL was higher, whereas the diameter of LDL and VLDL was not different from controls. Lipid subfraction analysis showed that the concentrations of large and medium HDLs and large and medium VLDLs as well as the ratio of ApoB to ApoA1, were significantly associated with PCV ($P < .00022$). However, extra-large HDL and small VLDL were not associated with PCV ($P \geq .00022$).

Conclusions: CEC of the serum samples was higher in PCV and early AMD than controls, while that of typical AMD was comparable to controls. Additionally, the lipid subfractions (especially HDL subfractions) were altered in PCV, suggesting that especially HDL among all lipids has a role in the pathogenesis of PCV.

CONTROL ID: 3546903

SUBMITTER (NAME ONLY): Praveen Balne

TITLE: Cellular and molecular changes in human corneal fibroblasts following hydrogen sulfide exposure in vitro

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.K. Balne, N.R. Sinha, A.C. Hofmann, R. Tripathi, S. Gupta, P.R. Sinha, R.R. Mohan, One-Health Vision Research Program, Departments of Veterinary Medicine & Surgery and Biomedical Sciences, College of Veterinary Medicine, University of Missouri, Columbia, Missouri, UNITED STATES|P.K. Balne, N.R. Sinha, R. Tripathi, S. Gupta, P.R. Sinha, R.R. Mohan, Harry S. Truman Memorial Veterans' Hospital, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hydrogen sulfide (H_2S) is a common environmental pollutant and a chemical warfare agent. H_2S exposure to the eye leads to ocular irritation, pain, and vision loss, however, underlying molecular mechanisms driving its toxicity to the cornea is still unclear. We sought to study changes in cellular and molecular parameters in primary human corneal stromal fibroblasts following H_2S exposure in vitro.

Methods: A total of 30 healthy human donor corneas obtained from the eye bank were used in this study. Primary human corneal stromal fibroblasts (hCSFs) were generated from healthy donor corneas following our standard protocol and passages two to five were used for in vitro experiments. Sodium hydrosulfide (NaSH) was used as a source of H_2S and hCSF cells were exposed to H_2S for up to 72h and the changes in mitochondrial function were assessed using Complex IV (cytochrome c oxidase) Human Specific Activity Microplate Assay Kit (Abcam, Cambridge, MA, USA) according to the manufacturer's guidelines. The mRNA expression of cell death genes - Receptor-interacting serine/threonine-protein kinase 1 (RIP1), Tumor necrosis factor receptor type 1-associated DEATH domain protein (TRADD), Caspase 8, and Mixed lineage kinase domain-like protein (MLKL) was studied using QuantStudio 6 Flex Real-Time PCR System (Applied Biosystems, CA, USA).

Results: H_2S exposure showed dose and duration dependent cytotoxicity to hCSFs in cytotoxicity assays and IC_{50} of H_2S was determined to be 5.35 mM. H_2S IC_{50} exposed hCSFs showed significantly decreased levels of cytochrome c oxidase enzyme activity ($p < 0.01$) and quantity ($p < 0.0001$) compared to healthy cells. The mRNA expression of RIP1, TRADD, Caspase 8, and MLKL genes were significantly altered in H_2S IC_{50} exposed hCSFs compared to control ($p \leq 0.05$).

Conclusions: H_2S exposure to human corneal fibroblasts activates cell death pathways and damages mitochondrial function in vitro.

CONTROL ID: 3546904

SUBMITTER (NAME ONLY): Benjamin Backus

TITLE: Reducing detection time from 24 months to 9 months or less for rapid visual field loss in glaucoma

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.T. Backus, J.J. Blaha, Vivid Vision, Inc., San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Patients with rapidly progressing glaucoma must be identified quickly to receive aggressive treatment to save their vision. Progression is diagnosed with visual field tests, but current tests lack precision, with a test-retest variability of ~1.0 dB in mean sensitivity (MS) for moderate to severe glaucoma. New at-home tests with redesigned psychophysical procedures have recently made it practical to test 10 times in 5-10 days (Deiner, Damato & Ou, 2020. Implementing and Monitoring At-Home VR Oculo-kinetic Perimetry During COVID-19. Ophthal 127:1258). The additional data reduces test-retest variability by a factor of $\sqrt{10}$, to 0.3 dB. We asked how many months are needed to detect rapid progression (-2 dB/year) for a patient taking quarterly clusters of 10 tests, as compared to a conventional test quarterly or twice-yearly.

Methods: Simulations in Matlab modeled progression in 10,000 cases each at rates of 0 dB or -2 dB/year, respectively. Test-retest variability for single tests was 1.0 dB. Specificity was set to 0.95 and sensitivity to 0.8. The testing procedure continued until the fitted rate parameter for progression (the slopes of the regression lines) could be segregated by a boundary, with 95% of non-progressors below, and 80% of progressors above, the boundary.

Results: Detecting progression took 24 months for tests administered twice yearly, 18 mos for quarterly, but only 9 mos for 10-test clusters quarterly. Alternatively, specificity and sensitivity could be 99% and 98% respectively, for time-to-detect of 36, 27, and 12 months, respectively. Many glaucoma patients have test-retest variability < 1.0 dB. In a patient whose test-retest variability is 0.5, time-to-detect is 6 months for quarterly clusters. It is similarly reduced if the new at-home test has better test-retest variability than conventional tests.

Conclusions: Even by itself, at-home testing of visual fields using conventional psychophysical methods would greatly improve treatment of glaucoma. Additionally, new testing procedures that are less fatiguing for the patient mean that 10 tests can be collected at a time, shortening the time to detect progression to as little as 6 months.

CONTROL ID: 3546908

SUBMITTER (NAME ONLY): Xiangrong Kong

TITLE: The design and patient acceptability of NAC Attack a phase-3 clinical trial for retinitis pigmentosa (RP)

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Kong, F. Naufal, P.A. Campochiaro, Wilmer Eye Institute, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|S. trotochaud, USHER 2020, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: NAC Attack is a Phase III multicenter, randomized, and placebo-controlled study to evaluate the efficacy and safety of oral N-acetylcysteine (NAC) in patients with RP and is in the planning phase. It aims to enroll 438 eligible patients who will be randomized to either 1800mg/bid NAC or placebo. This study aimed to learn patients attitudes of participating a clinical trial to facilitate the trial design and assess recruitment potential.

Methods: Crowdsourcing is a method that utilizes social media to quickly involve a group of people for ideas. It was used to survey RP patients attitudes toward a study of over 4 years to test an oral medication to slow or stop vision loss caused by RP. The survey questionnaire was developed by the NAC Attack Study Chair and Coordinating Center in collaboration with the USHER 2020 foundation. The survey required no protected health information. It was administered using Google Form by USHER 2020 from Aug to Nov of 2020. The survey link was sent to various email lists of retinal patient advocacy groups, social media, emails through My Retina Tracker of Foundation Fighting Blindness, and was picked up by other RP patients listserve. The study was approved by the JHU IRB.

Results: There were 1473 responses: 24% were of age 18-40, 60% were 40-69, and 15% were >70 years; female was 56%; 20% patients had genetic testing done before but the genetic cause was not found; 96% used a mobile phone and among them 96% received text messages; 61% were very and 18% somewhat enthusiastic about participating in a trial; 70% were very and 28% somewhat willing to have a clinical visit every 4-5 months for 45 months; 83% were very and 15% somewhat willing to have a tele-visit with a doctor between clinical visits.

Acceptability of a daily text reminder of medication was 60% Yes, 24% No, and 13% don't know; 70% were willing to report any missing dosages or problems related to medication using a text message based system daily or weekly.

Conclusions: Enthusiasm was high for participating a clinical trial that may find an effective treatment for RP. Rates of possession of mobile phones and usage of text messages were high. Using SMS messages to keep patients engaged and to encourage and survey their medication adherence is feasible. NAC Attack will have in-clinic follow-up visits every 9 months and in-between every 4.5 months a televisit with site investigator.

CONTROL ID: 3546910

SUBMITTER (NAME ONLY): S. Swaroop Vedula

TITLE: Economic benefits of cataract surgery: A pilot prospective cohort study

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Vedula, Malone Center for Engineering in Healthcare, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|G. Castro, V. Lansingh, Instituto Mexicano De Oftalmologia, MEXICO|J. Macias, Anterior Segment Department, Instituto Mexicano de Oftalmologia, Queretaro, MEXICO|

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ABSTRACT BODY:

Purpose: Cataract is the most prevalent cause of avoidable blindness worldwide. Poverty and blindness are inextricably linked. We developed a protocol to evaluate the potential economic benefits of cataract surgery for the household in resource-limited settings. This report describes baseline characteristics of the current cohort and lessons learned from following-up patients during the pandemic.

Methods: In this prospective cohort study, patients 40 years or older with symptomatic age-related cataract seeking care at "Instituto Mexicano de Oftalmología" (Queretaro, Mexico) and residing within 30 km of the facility were eligible. Patients with complicated cataracts and coexisting eye conditions were ineligible. Patients received a comprehensive eye exam, assessment of economic status at baseline, and standard clinical care for cataract. Follow-up is planned at 6, 12, and 36 months using surveys on surgical and economic outcomes, including monthly household income and total household budget (USD).

Results: The present cohort includes 42 patients. 61.90% were women and 38.09% were men. The mean age was 71 (standard deviation; SD 10.30). 19.04% were uninsured, 45.23% were covered by the Institute of Health for the Wellbeing and 35.71% were covered by employment-based government insurance entities. 42.85% and 57.14% of patients lived in a rural and urban area, respectively. At baseline, average monthly household income was \$438 (SD = \$377 USD); it was \$330. USD (SD = \$320) for patients in rural areas and \$508 (SD = \$400) for patients in urban areas. The average monthly household budget before cataract surgery (including food basket, health, educational, housing, personal and housing expenses) was \$240 (SD = \$294) and \$144 (SD = \$114) for patients in urban and rural areas, respectively. Of 5 patients followed up at 6 months, the average monthly household income was \$239 (SD = \$46), with a difference of \$199 from baseline. Recruitment was challenging because we restricted eligibility by how far patients lived from the hospital. Follow-up in the context of the Covid-19 pandemic continues to be a challenge, although administering surveys by phone may facilitate it.

Conclusions: Our findings show feasibility of conducting this study. To ensure a representative patient sample, effort is underway to implement the study protocol at multiple centers in Mexico, India and Brazil.

CONTROL ID: 3546911

SUBMITTER (NAME ONLY): Yuanyuan Chen

TITLE: Pharmacological chaperones for RHO-associated retinitis pigmentosa

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Clinger, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|Y. Chen, B. Feng, Y. Xi, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|M. Schurdak, Drug Discovery Institute, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|Y. Chen, Pharmacology and Chemical Biology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Genetic mutations in the RHO gene lead to structural disability of the photopigment rhodopsin, resulting in rod cell death and vision loss accounting for 25-30% of autosomal dominant retinitis pigmentosa cases. The goal of this study is to seek pharmacological strategies for preventing rod cell death by restoring rhodopsin homeostasis.

Methods: A total of 23 single mutations have been generated on the extracellular side of human rhodopsin, and these cDNA constructs were transfected to NIH3T3 cells in 384 wells. Cells were treated with compounds at 24 h after transfection and DMSO was used as vehicle control. Cell-surface immunostaining of rhodopsin was performed after 24 h of treatment, and immunofluorescence images were taken by a high-content imaging system.

Immunofluorescence of rhodopsin per cell was quantified based on the analyses of 400-600 cells per well, averaged by three replicates. Cell viability was quantified by the number of cells per well. A docking calculation was performed by the AutodockVina software using the bovine rhodopsin structure (PDB ID: 1f88) as the structure template. 11-cis-retinal was deleted from the density to leave the chromophore pocket for the docking of small molecules. ΔG s were obtained indicating the stability of the complex of rod opsin with each compound. To test the effect of small molecule chaperone on retinal morphology and function in vivo, we injected YC-001 suspension in PBS intravitreally to the eyes of Rho^{P23H/+} mice at PND15, OCT and ERGs were taken at PND28.

Results: We showed that three rhodopsin chaperones we identified previously improved the transport of multiple, but not all mutants of rhodopsin to the plasma membrane. Scriptaid showed non-selective rescue to all the mutants of rhodopsin, with high cytotoxicity. YC-001 was docked within the chromophore pocket at the ionone side. One intravitreal injection of YC-001 showed improved scotopic ERG responses in the Rho^{P23H/+} mice at PND28.

Conclusions: Our results provide a pharmacological profile of two small molecule chaperones towards misfolding rhodopsin mutants, suggesting the efficacy of pharmacological chaperones are highly dependent on the mutation site and residue of rhodopsin. The short-term efficacy of YC-001 in Rho^{P23H/+} knock-in mice strongly supports that restoring rhodopsin folding can prevent rod cell death caused by RHO mutants that carry mild folding defects.

CONTROL ID: 3546912

SUBMITTER (NAME ONLY): Ignacio Alcalde

TITLE: In vitro study of the generation of anterior subcapsular opacity after mechanical stimuli

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Alcalde, C. Sánchez Fernández, M. Chacon, N. Vázquez, A. Meana, J. Merayo-Llves, Instituto Universitario Fernández-Vega - Fundación de Investigación Oftalmológica - Universidad de Oviedo, Oviedo, Asturias, SPAIN|C. Martin, J. Merayo-Llves, Universidad de Oviedo, Oviedo, Asturias, SPAIN|B. Alfonso, J. Alfonso, Instituto Oftalmológico Fernández Vega, Oviedo, Asturias, SPAIN|C. Martin, Instituto Universitario Fernández-Vega, Oviedo, Asturias, SPAIN|

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ABSTRACT BODY:

Purpose: Lens epithelial cells undergo epithelial to mesenchymal transition (EMT) after injury, resulting in the generation of myofibroblasts and tissue fibrosis in the lens. This process is comparable to the maturation process of a cataract and also to the postoperative features on the anterior capsule after cataract surgery.

In some cases, literature suggests the possibility of an anterior subcapsular cataract after Implantable Collamer Lens (ICL) implantation. This effect is associated with the contact of the ICL with the crystalline lens, especially in older patients and patients with a narrow anterior chamber. The aim of this work is to study the generation of anterior subcapsular opacity in the lens after mechanical stimuli.

Methods: Anterior lens capsules were obtained from cataract surgeries and from healthy donors from the Community Center for Blood and Tissues - CCST.

An explant culture model was performed using the total tissue collected in surgery, usually a 6 mm in diameter disc of the anterior capsule of the lens, containing the anterior subcapsular epithelium.

One group of cultures was exposed to mechanical contact with an sterile ICL with cycles of 2 hours for one week. Control cultures were maintained in normal conditions. Selected cultures from each group were treated with SIS3 inhibitor or with Rapamycin.

The molecular phenotype of the cells in culture was evaluated by means of immunocytochemical techniques in the different phases. Epithelial markers, such as E-Cadherin or β -Catenin, was used, as well as mesenchymal and fibroblast cell markers such as vimentin or smooth muscle actin (α -SMA).

Results: Capsular epithelial cells maintain epithelial morphology and biochemistry in culture. These cells presented the ability to spontaneously express markers of contractile cells, such as α -SMA or vimentin. Expression of α -SMA was increased after mechanical contact with ICL in vitro.

Cultures in which EMT was inhibited showed a lower proportion of SMA cells. Cultures in which ICL contact was interrupted, also exhibited a partial reversion of the fibrotic phenotype.

Conclusions: Contact with implanted collamer lenses in vitro triggered the signaling of contractile fibers production in anterior subcapsular epithelium. This process was partially reversible by removing contact stress.

CONTROL ID: 3546915

SUBMITTER (NAME ONLY): Hans Lemij

TITLE: Building a labeled dataset for training an Artificial Intelligence (AI) algorithm for glaucoma screening

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H.G. Lemij, H. Kliffen, Glaucoma Service, The Rotterdam Eye Hospital, Rotterdam, NETHERLANDS|K. Vermeer, Rotterdams Oogheelkundig Instituut, Rotterdam, Zuid Holland, NETHERLANDS|

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ABSTRACT BODY:

Purpose: Too many people in the world are visually impaired by glaucoma, largely because the disease is detected too late. Aim: to build a labeled dataset for training an AI algorithm for automated glaucoma screening by fundus photography.

Methods: Color fundus photographs of over 110,000 eyes were obtained from EyePACS, California, USA, from a population screening programme for diabetic retinopathy. A tool was developed specifically for efficient grading. Thirty carefully selected graders (ophthalmologists and optometrists) graded the images. To qualify, they had to pass the EODAT¹ stereoscopic optic disc assessment with at least 85% accuracy and 92% specificity. Of 87 candidates, 30 passed. Each image of the EyePACS set was then scored by varying pairs of two randomly matched graders as 'Referable glaucoma', 'No referable glaucoma' or 'Ungradable'. In case of disagreement, a glaucoma specialist ('third grader') made the final grading. 'Referable glaucoma' was scored only if visual field damage was expected.

¹ Reus NJ, Lemij HG et al. Clinical Assessment of Stereoscopic Optic Disc Photographs for Glaucoma: The European Optic Disc Assessment Trial. Ophthalmology. 2009 Dec 31. [Epub ahead of print] Ophthalmology. 2010 Apr;117(4):717-23.

Results: Approximately 14,000 eyes were graded per week. For the first two weeks, the average time per grading was 21.6 sec, but the grading of "Referable glaucoma" took longer, on average 50.3 sec. Approximately 20 % was scored by a third grader. The overall sensitivity and specificity were, initially, 84% and 90%, respectively. The reference standard for these was the final label, i.e., the consensus between the first two graders, or, in case of any disagreement between the two, the label of the third grader. Measures were then taken to improve these scores for the consecutive gradings. Six graders were disqualified for further participation. Both individualized and general feedback was provided to each of the remaining 24 graders. In addition, online meetings were scheduled to discuss difficult cases. Graders with high sensitivity scores were matched with those who showed high specificities. With these measures, the individual scores improved and the overall quality of the labels as well.

Conclusions: Building a labeled dataset is a huge, but quite feasible task, which calls for careful planning, execution, monitoring and refinement.

CONTROL ID: 3546916

SUBMITTER (NAME ONLY): Antonio Jacobo Lopez

TITLE: Retinal organoids generated from rhesus macaque (*Macaca Mulatta*) induced pluripotent stem cells demonstrate mature photoreceptors and rods

SESSION TITLE: Retinal Organoids: Cell Diversity and New Strategies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Jacobo Lopez, S.M. Thomasy, A. Moshiri, Department of Ophthalmology & Vision Science, University of California Davis School of Medicine, Sacramento, California, UNITED STATES|K. Sangbae, J. Rogers, R. Chen, HGSC, Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, UNITED STATES|S.M. Thomasy, Department of Surgical and Radiological Sciences, University of California Davis School of Veterinary Medicine, Davis, California, UNITED STATES|A. Miltner, A. La Torre, Department of Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|T. Stout, Department of Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the development of non-human primate (NHP) derived retinal organoids in comparison to those derived from human embryonic stem cells (hESCs).

Methods: Human embryonic stem cells (hESCs) and induced-pluripotent stem cells (hiPSCs) derived from non-human primates (*Macaca mulatta*) were differentiated into retinal organoids by using a well-established differentiation protocol. Briefly, embryoid bodies were formed from pluripotent stem cells and induced into neural lineage with neural induction media with the addition of BMP4. Thereafter, self-formation of optic vesicles was allowed to form in a 2D culture in retinal differentiation media (RDM). Optic vesicles were then picked off and suspended in 3D-RDM until analysis. Differences in the timing of differentiation and efficiency of retinal organoid development were assessed by light microscopy, electron microscopy, immunocytochemistry, and next-generation sequencing.

Results: Generation of retinal organoids was achieved from both human and several NHP pluripotent stem cells lines. All hiPSC lines resulted in retinal differentiation with the formation of optic vesicle like structures similar to what has been observed in hESC retinal organoids. NHP retinal organoids had defined structure and were composed of mature retinal cells types including cone and rod photoreceptors. Characterization of cell populations in NHP retinal organoids were assessed by single cell RNA sequencing which allowed comparison of expression profiles of retinal neurons to hESC derived retinal organoids and to samples of retinal tissue. Important differences between rhesus and human cells were measured regarding the timing and efficiency of retinal organoid differentiation. While culture of NHP-derived iPSCs is relatively difficult compared to human stem cells, generation of retinal organoids is feasible and may be more time effective due to an intrinsically faster timing of retinal differentiation.

Conclusions: Retinal organoids can be produced from iPSCs derived from rhesus macaque using established protocols. Important species-specific differences exist that warrant further investigation. The production of NHP retinal organoids may be advantageous to reduce experimental time and cost for basic biology in retinogenesis as well as for preclinical trials in NHPs.

CONTROL ID: 3546918

SUBMITTER (NAME ONLY): Julia Khorolskaya

TITLE: Rabbit limbal stem cells in vitro observation and their transplantation to rabbits

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Khorolskaya, O. Aleksandrova, D. Pereplechikova, K. Zhurenkov, N. Mikhailova, M. Blinova, Institute of Cytology of the Russian Academy of Science, St-Petersburg, RUSSIAN FEDERATION | I. Gavril'yik, S. M. Kirov Military Medical Academy, St-Petersburg, RUSSIAN FEDERATION |

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ABSTRACT BODY:

Purpose: Cell technology is one of the most promising approaches to reconstruct the ocular surface and restore the integrity and transparency of the damaged cornea. In the present study, we investigated rabbit limbal stem cells (LSCs) in vitro during several passages in different conditions and used them as a component of the cornea substitute in an animal model of limbal stem cell deficiency (LSCD). The goal was to find a highly proliferative population that can be used for cornea recovery.

Methods: Rabbit LSCs were isolated from rabbit corneoscleral rims using the Dispase II, Collagenase I, and trypsin. Cells were cultured under standard conditions in different media: epithelium growth medium and in DMEM/F12 with serum. LSCs cultured in different media were compared by the main stem markers and markers of differentiation (PAX6, ALDH3A1, ABCB5, p63, cytokeratins 3/12, 14, 15, 19). LSCs at the 6th passage were subjected to air-lifting, cells were cultured in cell culture inserts for 14 days in the epithelial medium. Then cytokeratin 14 and actin were observed. For in vivo study rabbits with previously formed limbal stem cell deficiency were used. LSCs were transplanted inside collagen hydrogel. As a control collagen hydrogel without cells was used. The process of corneal restoration was examined by histological analysis.

Results: It was shown that in DMEM/F12 LSCs have high proliferative potential and after several passages change their morphology and mainly mesenchymal-like cells are observed. In mesenchymal-like LSCs some markers such as $\Delta Np63\alpha$ and PAX6 are present, but change their localization from nucleus to cytoplasm. Even though the population has a mesenchymal-like phenotype, the presence of various cytokeratins was observed in the cytoplasm. Also, it was shown that in LSCs that were subjected to air-lifting, the expression of cytokeratin 14 increased. On the 90th day after transplantation mesenchymal-like LSCs to rabbits with previously formed LSCD, normal corneal epithelium was restored, vascularization, and goblet cells were absent. In the control group opacity and neovascularization of the stroma was observed.

Conclusions: During in vitro cultivation, LSCs may undergo an epithelial-mesenchymal transition. It was shown that mesenchymal-like LSCs are a highly proliferative population and are able to restore corneal epithelium in rabbits.

CONTROL ID: 3546920

SUBMITTER (NAME ONLY): Leah VandenBosch

TITLE: Molecular and Machine Learning in Unexplained Inherited Visual Disorders

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. VandenBosch, K. Luu, A. Timms, T.J. Cherry, CDBRM, Seattle Children's Research Institute, Seattle, Washington, UNITED STATES|Y. Wu, A. Lee, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Prior studies demonstrate the impact of specific cis-regulatory variants in retinal disease. However, genetic variants are common within cis-regulatory elements and determining which variants have a functional impact remains a major challenge. In this study, we develop a machine learning approach, trained on retinal epigenomic data, to systematically quantify the predicted functional impact of cis-regulatory variants.

Methods: We generated 35 human retinal epigenomic datasets to determine a core set of 47k cis-regulatory elements and train a machine learning model utilizing a gapped k-mer support vector machine. In silico saturation mutagenesis was applied in tandem with the model to predict the functional impact of all potential single nucleotide variants within cis-regulatory elements. Impact scores were validated against known TF binding motifs, previously characterized variants, phylogenetic conservation, and population frequencies.

Results: Five-fold cross-validation demonstrates that the model distinguishes between active human retinal regulatory elements and negative test sequences within 95% accuracy. Positively-scoring sequences are enriched for motifs corresponding to transcription factors necessary for retinal function. Additionally, this model quantified the predicted impact of all possible single nucleotide variants (SNVs) within 20k human retinal CREs, yielding a wide range of impact scores. Variant scoring correlates with observed changes in population frequency.

Conclusions: In this study, we demonstrated the use of human retinal epigenomic data to train an effective machine learning model, which can be used to predict the impact of sequence variations. Our model demonstrated the ability to accurately score sequences and identify relevant motifs, which can be used to identify sequence variants of interest. This modeling has potential to expedite the search for and characterization of natural sequence variants in the context of retinal disease.

CONTROL ID: 3546924

SUBMITTER (NAME ONLY): Hannah Yoo

TITLE: Targeting YAP/TAZ mechanoregulation with statins to reverse glaucomatous trabecular meshwork stiffening

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Yoo, H. Li, A.N. Strat, R.W. Weisenthal, P.S. Ganapathy, S. Herberg, State University of New York Upstate Medical University, Syracuse, New York, UNITED STATES|H. Roberts, D.W. Stamer, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|A. Patteson, Syracuse University, Syracuse, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Trabecular meshwork (TM) stiffening in primary open-angle glaucoma (POAG) arises from elevated ROCK-mediated TM cell contraction and extracellular matrix (ECM) deposition/crosslinking. YAP/TAZ play central roles in TM mechanoregulation and increased YAP/TAZ activity has been linked to glaucomatous TM stiffening. Common cholesterol-lowering statins competitively inhibit HMG-CoA reductase (HMGCR), which potently decreases YAP/TAZ activity. Statins also inhibit ROCK activity upstream of YAP/TAZ. Here, we investigate whether statins can reverse glaucomatous TM cell dysfunction using a tissue-engineered TM hydrogel model.

Methods: Normal TM/glaucomatous GTM cells were isolated from surgical discard corneal rims/POAG globes. Cells were plated on glass coverslips or encapsulated in photocrosslinked hydrogels (collagen type I, elastin-like polypeptide and hyaluronic acid). Glaucomatous conditions were induced with DEX/TGF- β 2, then treated with cerivastatin or simvastatin; GTM cells were used for validation and proven ROCK inhibitor Y27632 served as treatment control. Cell morphology and cytoskeletal organization were assessed by phalloidin staining for f-actin. Immunoblot and immunostaining were used to evaluate YAP/TAZ expression/activity and changes in cell contractile force regulation. TM hydrogel contraction and stiffness were determined by longitudinal imaging and oscillatory rheology.

Results: Induced TM and GTM cells exhibited decreased cytoplasmic (inactive) pYAP and increased nuclear (active) YAP/TAZ with increased downstream TGM2 (an ECM crosslinking enzyme) vs. controls ($p < 0.01$); this was significantly reduced with either statin in a dose- and time-dependent manner. These effects were reversed by supplementation of mevalonate, thus bypassing statin-mediated HMGCR inhibition. Statin treatment restored glaucomatous actin stress fibers, and pMLC/ α -SMA levels to baseline. Immunostaining revealed significant statin-mediated reduction of glaucomatous fibronectin deposition. Pathologic TM hydrogel contraction and stiffening were potently rescued with statin treatment; constructs were significantly relaxed and softened ($p < 0.01$), comparable to direct ROCK inhibition.

Conclusions: Our data suggest that indirectly targeting the YAP/TAZ mechanoregulatory axis with statins presents an intriguing avenue for treating glaucomatous TM dysfunction with high translational potential.

CONTROL ID: 3546925

SUBMITTER (NAME ONLY): Dirk-Uwe Bartsch

TITLE: Comparison of adaptive optics scanning laser ophthalmoscopy and high-magnification scanning laser ophthalmoscopy

SESSION TITLE: Adaptive optics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.G. Bartsch, M. Jhingan, Q. Zawaydeh, M. Cavichini Cordeiro, W.R. Freeman, Ophthalmology, Joan and Irwin Jacobs Retina Center, La Jolla, California, UNITED STATES|M. Cavichini Cordeiro, Ophthalmology, Faculdade de Medicina do ABC, Santo Andre, SP, BRAZIL|

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ABSTRACT BODY:

Purpose: Adaptive-optics scanning laser ophthalmoscopy (AOSLO) uses a wavefront detection and a deformable mirror for wavefront correction. These instruments are very expensive and cumbersome to maintain and operate. We have used the high-magnification module objective for a commercial scanning laser ophthalmoscope to image the photoreceptor cone mosaic. We wanted to compare the photoreceptor images captured with both devices.

Methods:

The Heidelberg Engineering High Magnification Module for the Spectralis SLO is a special lens that images an area of 8° x 8° degrees. The normal imaging modes of high-speed and high-resolution are supported. Blue and green imaging are not supported. We imaged 10 subjects with and without glasses. We used proper refraction to allow imaging with proper spherical and cylindrical correction. We used room light to limit the pupil to about 3 mm to achieve diffraction-limited imaging. We compared the photoreceptor images obtained with the HMM lens with images obtained with a custom-built adaptive optics scanning laser ophthalmoscope (AOSLO).

Results: We found that in more than half the subjects we were able to image the photoreceptor mosaic in the patients using 3 mm pupil and proper spherical and cylindrical correction.

We used image steering to confirm that our imaging areas were similar for the AOSLO and HMM imaging.

The photoreceptor density using the High Magnification Module was within 10% of the density as measured in the same region using the AOSLO.

Conclusions: The High Magnification Module was able to image the photoreceptor cone mosaic in more than half the cases. The use of the HMM lens has some limitations. Since the module is a fixed optical element, the module cannot correct for aberrations. Instead, the HMM uses the diffraction-limited 3 mm pupil to achieve optical imaging conditions. The human eye can be considered diffraction-limited up to a pupil diameter of 3 mm. This was confirmed by our experiments. Increase the pupil diameter beyond 3 mm decreased image quality.

We found that we could use the High Magnification Module for pre-screening of patients for imaging with the AOSLO. It is well known that AOSLO imaging is not possible in all subjects due to other optical limitations. If we were able to image the mosaic with the HMM lens, it was also possible to image with the AOSLO.

CONTROL ID: 3546928

SUBMITTER (NAME ONLY): Alex Huang

TITLE: Structural Confirmation of Lymphatic Outflow from Subconjunctival Blebs in Live Human Subjects

SESSION TITLE: Hot Topics in Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.S. Huang, S. Saraswathy, P. Le, G. Heilweil, J. Lee, Doheny Eye Institute, Los Angeles, California, UNITED STATES|A.S. Huang, P. Le, G. Heilweil, Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|J. Lee, Gachon University, Seongnam, KOREA (THE REPUBLIC OF)|

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ABSTRACT BODY:

Purpose: Subconjunctival blebs are utilized in glaucoma surgeries and in drug delivery with lymphatics hypothesized to drain them. Limited direct evidence for lymphatic outflow is available in live human subjects. The purpose of this study is to perform simultaneous subconjunctival outflow imaging and structural assessment to uncover pathway identity in live human subjects.

Methods: Patients were identified who required intravitreal injections to treat retinal disorders. For anesthesia, they receive subconjunctival lidocaine. Subjects were consented for subconjunctival lidocaine injections (1.98%) that also contained indocyanine green (ICG; 0.005%) (UCLA IRB 20-001064) to perform ocular surface lymphangiography. Subjects were angiographically imaged on their ocular surface (Spectralis; Heidelberg Engineering) to visualize the bleb and ICG-labeled outflow pathways. Simultaneous anterior segment optical coherence tomography (OCT) was performed in cross-section or longitudinal to these pathways.

Results: Fourteen subjects were imaged (M/F=6/8; 77.4±2.6 years [mean±SEM]). Subjects (n=4) who were immediately imaged after tracer injection demonstrated fluorescent blebs but no outflow pathways. All subjects who were imaged after completion of the clinical visit (n=10 subjects; 16±1.6 min after subconjunctival tracer injection) showed visible blebs with 7/10 subjects also demonstrating visible outflow pathways. The pathways appeared sausage-shaped (thicker alternating with thinner regions). OCT in cross-section to these pathways clearly demonstrated superficial subconjunctival lumens. OCT longitudinal to these pathways demonstrated the presence of semi-lunar valves or flaps.

Conclusions: Angiographic imaging of subconjunctival outflow demonstrated sausage-shaped outflow pathways that have been described and that are hypothesized to represent lymphatics. Simultaneous OCT imaging demonstrated valves, a lymphatic hallmark. This study provides multimodal outflow/structural imaging evidence confirming the hypothesis that lymphatics drain blebs in live humans.

CONTROL ID: 3546929

SUBMITTER (NAME ONLY): Lawson Ung

TITLE: Performance Evaluation of Commercially Available Swabs for Ocular Microbiology

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Ung, P.J. Bispo, C. Saini, S. Sharifi, S. Han, M.S. Gilmore, J. Chodosh, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|S. Sharifi, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Swabs are the most widely used sampling devices for ocular surface infections, including infectious corneal ulceration. However, no current standards of care exist to inform optimal swab compositions that maximize pathogen yield from the cornea. We evaluated the performance characteristics of a range of commercially available swabs, with a view to improve the sensitivity of culture-based microbiology and emerging molecular diagnostics for corneal infections.

Methods: Candidate swabs were chosen according to the American Academy of Ophthalmology Preferred Practice Pattern for Bacterial Keratitis, including mini-tipped flocked (Puritan® PurFlock and HydraFlock, and Copan FLOQSwab®), and traditional spun-fiber swabs (Puritan® polyester, rayon, calcium alginate and cotton). Swab absorption was determined with serial weights before and after immersion in phosphate buffered saline (PBS), and distribution volumes obtained by applying saturated swabs to tryptic soy agar (TSA) using the roll-plate technique per the Clinical Laboratory Standards Institute (CLSI). Recovery efficiencies were determined using a modified CLSI swab-elution protocol. Swabs were contaminated with a standardized inoculum of log-phase *Staphylococcus aureus* (ATCC 29213), eluted in PBS, and serial dilutions plated in tracks on 0.3% TSA. Viable counts were observed at 18 hours, and recovery efficiency calculated as the ratio of colony forming units (CFU/mL) in swab solutions compared to that of the original liquid culture, corrected for swab absorption.

Results: Flocked swabs had higher mean absorption values than spun-fiber swabs, both in absolute volume (Fig.1A) and per unit mass (1359–1543% vs. 200–578%, respectively). Agar distribution volumes were also greater among flocked swabs (Fig.1B and C). Mean recovery efficiencies (%) for PurFlock, HydraFlock and FLOQSwab were 78.9±10.1, 84.4±9.0, 84.5±13.9, respectively, compared to 52.7±14.4 for polyester, 91.0±17.7 for rayon, 54.0±15.8 for calcium alginate and 8.1±2.6 for cotton (Fig.2, $p<0.001$). Bonferroni-adjusted pairwise comparisons revealed significantly lower recovery efficiencies for calcium alginate compared to each flocked swab (all $p<0.001$).

Conclusions: New-generation flocked swabs outperformed spun-fiber swabs in terms of absorption, distribution, and recovery efficiency. Their use may translate to greater microbial yield, which could aid in diagnosing low-biomass corneal infections.

CONTROL ID: 3546930

SUBMITTER (NAME ONLY): Joy Sarkar

TITLE: Differential Distribution of VEGF Receptor Dimers in Neuronal and Endothelial Cells

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sarkar, Y. Luo, Q. Zhou, E. Ivakhnitskaia, E. Katz, M. Sun, D. Lara, V.H. Guaiquil, M. Rosenblatt, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: VEGF Receptor dimer activation is critical for regulating downstream signaling cascades in angiogenesis. However, not much is known about these processes in corneal nerve repair. Previous studies have shown that the non-angiogenic ligand VEGF-B has potent roles in the peripheral nervous system (PNS). The molecular mechanism of VEGF-B-mediated corneal nerve growth is unclear and may be due to differences in VEGFR1 homo- and heterodimer presence. The purpose of this study was to investigate the presence of VEGFR1 and R2 homo- and heterodimers and characterize similarities and differences in their distribution compared to endothelial cells.

Methods: Rat neuronal (PC12), mouse aortic endothelial (MAE), mouse venous endothelial (MVE) and human umbilical venous endothelial (HUVEC) cell lines were used. Cells were acutely stimulated either with VEGF-A (50 ng/μL; VEGFR1 and VEGFR2 binding) or VEGF-B (50 ng/μL; VEGFR1 binding) or “vehicle” (PBS; control group). We also isolated mouse trigeminal ganglion cells from thy1-YFP neurofluorescent mice. After treatment, cells were used as follows: (i) One group was fixed in 4% paraformaldehyde and processed for VEGFR1 and VEGFR2 immunostaining and visualized using confocal fluorescence microscopy and Total Internal Reflection (TIRF) microscopy; (ii) the second group was harvested in cell lysis buffer (containing anti-protease / anti-phosphatase cocktail), lysed and processed for immunoprecipitation (IP; Thermo Fisher IP kit) and immunoblotting (IB; LI-COR® Systems). Immunoprecipitated proteins were probed either with anti-VEGFR1 or anti-VEGFR2 IgG antibodies to evaluate VEGFR1-R2-heterodimerization; (iii) a third group of cells were also processed for Proximity Ligation Assay (PLA; Sigma) to assess the presence and distribution of VEGF Receptor homo- and heterodimers.

Results: TIRF and fluorescence confocal microscopy showed presence of VEGFR1 co-localized with VEGFR2 in endothelial and neuronal cells. Cell lysates immunoprecipitated with anti-VEGFR1 further validated the existence of VEGFR1-R2 heterodimers in neuronal cells. Neuronal cells showed higher levels of VEGFR1-R2 heterodimers compared to endothelial cells whereas endothelial cells showed higher levels of VEGFR2-R2 homodimers as shown by PLA studies.

Conclusions: Differences in VEGF Receptor homo- and heterodimer distribution may explain the differential role of VEGF ligands in neuronal vs endothelial cell types.

CONTROL ID: 3546931

SUBMITTER (NAME ONLY): Allison Spillane

TITLE: Preclinical Testing of HUB-101, a Potential Gene Therapy for LCA16

SESSION TITLE: Ocular disease models: molecular mechanisms and therapeutic approaches

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Spillane, K. Beverley, P.K. Shahi, Pediatrics, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|A. Spillane, K. Beverley, P.K. Shahi, McPherson Eye Research Institute, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|S. Macdonald, S.M. Hall, J. Sabados, B.R. Pattnaik, Hubble Therapeutics, Boston, Massachusetts, UNITED STATES|B.R. Pattnaik, Pediatrics, McPherson Eye Research Institute, Ophthalmology and Visual Science, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lebers Congenital Amaurosis (LCA16) is a monogenic pediatric blindness caused by point mutations in the KCNJ13 gene. This gene encodes an inwardly rectifying potassium channel (Kir7.1) required for retinal pigment epithelial (RPE) function. Gene augmentation, through lentiviral delivery of healthy KCNJ13 ORF, has been shown to rescue Kir7.1 channel function in patient iPSC-RPE cells and a conditional knockout (cKO) mouse. The rescue of RPE cell function in the cKO mouse also resulted in ERG c-wave recovery and preserved retinal integrity. The present study tested in vitro transgene expression from HUB-101, a gene therapy product in development for Kir7.1 replacement in LCA16.

Methods: Eyes from 4-6-week old wildtype C57BL6 mice were used to culture mature primary RPE cells. After culturing cells in 96-well plates for 0, 7, 14, and 28 days, RNA was isolated and converted to cDNA to assess maturation markers. Maturity of cells was confirmed using qPCR to measure Gapdh, Rpe65, Best1, and Rbp1 gene expressions. HUB-101 is an adeno-associated virus (AAV5) containing KCNJ13 under the control of the VMD2 promoter. Mature RPE cells were transduced with 1×10^8 , 1×10^9 , or 1×10^{10} particles of HUB-101 per well. HUB-101 vehicle served as a negative control. Seven days after transduction of HUB-101, RNA was isolated and converted to cDNA for qPCR assay. Specific molecular expression of HUB-101 in mouse RPE was assessed by measuring hGAPDH, hKCNJ13, and AAV ITR transcripts, along with mGapdh, mKcnj13 serving as experimental controls.

Results: Expression profiles of Rpe65, Best1, and Rbp1 indicated that RPE cells matured as early as 14 days in culture, with characteristic pigmented appearance. The matured primary RPE cells in culture, when transduced with HUB-101, showed dose-dependent expression of both hKCNJ13 and AAV ITR transcripts compared to vehicle-treated controls. In comparison, no changes in expression of mGapdh or mKcnj13 transcripts were detected, as expected.

Conclusions: We established a species-specific detection of candidate gene therapy product as a preclinical validation. Our results further confirm that HUB-101 can transduce mature RPE cells in vitro, with the KCNJ13 gene's dose-dependent expression. These data support the further evaluation of HUB-101 in nonclinical safety and toxicity studies, with the ultimate aims of clinical testing and restoration of sight in patients with LCA16.

CONTROL ID: 3546933

SUBMITTER (NAME ONLY): Dharendra Singh

TITLE: Topical Application of Hydralazine Induces Resistance Against Oxidative Stress In Eye Lenses By Activating Nrf2-mediated Antioxidant Response Genes

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.P. Singh, B. Chhunchha, Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, UNITED STATES|H. Sasaki, E. Kubo, Ophthalmology, Kanazawa Medical University, Kanazawa, Ishikawa, JAPAN|

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ABSTRACT BODY:

Purpose: Deterioration of antioxidant response with advancing age is a leading cause of age-related pathologies. Therapeutic activation of antioxidant pathway has been suggested as an effective strategy to combat aging pathobiologies. Hydralazine (Hyd), an antihypertensive, has been shown to be a potent activator of Nrf2 (NFE2-related factor 2) pathway. Using C57BL/6 mice as a model system, we showed that topical instillation of Hyd in the eye activates Nrf2/ARE (antioxidant response element) pathway, and these lenses gained resistance against oxidative stress-induced insult.

Methods: 16-month old mice (n=12) were used for study, and anaesthetized with an oxygen-isoflurane before Hyd instillation. Buffered saline (n=6) or 25µM/5µl (n=6) of Hyd in buffered saline (pH7.4) was instilled once daily in the eyes for 5 days and lenses were collected. Total RNA and protein were isolated and processed for qPCR and Western analyses to assess levels of Nrf2 and its target genes like Prdx6 and other phase II enzymes expression using probes specific to the molecules. In another set of ex-vivo experiments, Hyd-treated or untreated lenses were exposed to 100µM of H₂O₂ to assess lens opacity. 72h later lenses were photographed (Nikon SMZ 745T) and intensity of lens opacity was determined using densitometry. H2DCF-DA dye measured reactive oxygen species (ROS) levels. Two-tailed Student's t-test and one-way ANOVA were used for statistical analysis.

Results: Hyd instilled lenses displayed significantly increased expression of Nrf2 and its target antioxidant genes mRNA and protein, such as Prdx6, Catalase, SOD1, HO1, Gpx1 and GSTπ (p<0.001) compared to untreated lenses. ROS quantitation showed that Hyd instilled lenses had significantly reduced ROS levels compared to untreated lenses. Untreated lenses developed H₂O₂-induced lens opacity ex-vivo, while Hyd treated lenses showed significantly less opacity; 82% at 48h and 70% at 72h of H₂O₂ exposure in comparison to untreated lenses as analyzed by densitometry.

Conclusions: Our findings, for the first time, reveal that topical instillation of Hyd can activate Nrf2/ARE-pathway in lenses in vivo and these lenses engender resistance against oxidative stress. Our study also provide a foundation for further study of Hyd as a viable therapeutic candidate for the treatment or prevention of age-related diseases, including cataract.

CONTROL ID: 3546934

SUBMITTER (NAME ONLY): Sheri Peterson

TITLE: Complement proteins and myeloid cells support optic nerve regeneration via myelin phagocytosis

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.L. Peterson, C. Sun, A. Catacora, L. Benowitz, Neurosurgery, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|S.L. Peterson, L. Benowitz, Neurosurgery, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Axon regenerative failure in the mature CNS contributes to functional deficits following traumatic injuries, ischemic injuries and neurodegenerative diseases. Although neuro-immune interactions modulate critical CNS functions, potential contributions of the classical complement cascade and myeloid cells to CNS axon regeneration or its failure are largely unknown. Building on our recent finding that classical complement proteins C1q and C3 and CR3⁺ (CD11b⁺) myeloid cells each increase locally following experimental mouse optic nerve injury and are each required for retinal ganglion cell (RGC) axon regeneration, we tested the hypothesis that complement and phagocytic myeloid cells support RGC axon regeneration by altering the local environment of the injured optic nerve.

Methods: We quantified RGC axon regeneration (GAP43 immunolabeled axons 0.5mm past the injury site) in adult mice 14 days after optic nerve crush plus intravitreal injection of pro-regenerative treatment (zymosan + CPT-cAMP) and localized (either intravitreal, intra-nerve, or intraperitoneal) injection of C1q function-blocking antibody or IgG control (N = 8-16/group). We characterized the local environment of the injured optic nerve with regard to inflammatory response and myelin debris in optic nerve sections collected 1, 5, 7 and 14 days after injury and immunolabeled for CR3, CD68, and myelin basic protein (MBP). We assessed MBP⁺ myelin debris levels 5 and 14 days after optic nerve injury in CR3^{-/-} mice and CR3^{+/+} controls, both with and without pro-regenerative treatment (zinc chelation; N = 6-8/group).

Results: Whereas intravitreal anti-C1q injection did not alter RGC axon regeneration, intra-nerve and intra-peritoneal injections of anti-C1q each decreased axon regeneration by ~50%. We observed an MBP-negative area that expanded from the injury site over time and that closely corresponded to a dense CR3⁺ and CD68⁺ myeloid cell area, as well as MBP localized inside these myeloid cells. CR3^{-/-} mice exhibited a 3.3-fold increase in myelin debris remaining in the vicinity of the injury site compared to CR3^{+/+} controls.

Conclusions: Our data demonstrate that classical complement proteins and myeloid cells act within the optic nerve to support RGC axon regeneration, primarily through phagocytic removal of growth-inhibitory myelin debris. These results point to the importance of the innate immune response for CNS repair.

CONTROL ID: 3546935

SUBMITTER (NAME ONLY): Nancy Barrett

TITLE: Retinal Image Curation Using Deep Learning

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Barrett, B. Blodi, A. Domalpally, Department of Ophthalmology and Visual Sciences, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|B. Li, E.T. Dobson, K.W. Eliceiri, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Image curation is one of the fundamental aspects of AI algorithm training, and application of deep learning (DL) and application of DL methods for retinal diseases depends on well-organized, representative images. In this project, we have developed a DL workflow to more efficiently curate retinal photographs, relieving the need for manual evaluation by graders.

Methods: Stereoscopic four-field wide-capture images of the retina are commonly used for evaluating diabetic retinopathy in clinical trials. This entails acquiring red reflex images followed by stereo pair of the disc, macula, a superior, nasal, and inferior field (figure) using 50 – 60-degree camera. Graders review these images in a systematic fashion, one eye at a time, to arrive at a diabetic retinopathy severity level. Submission from clinical sites is not always organized in a manner conducive for grading or for DL training. We designed and trained a neural network to label individual image files in 3 aspects: (1) differentiating red reflex image from a retinal photograph (2) differentiating right eye images from left eye, and (3) identifying the field of the retina. Based on these three parameters, labels were generated by the model and affixed to the image file name. 1631 annotated images from 88 participants were used to train the model, and 404 images from 22 participants were used for validation during training. An independent dataset of 180 images (12 participants) with variable image quality was used for testing the performance of the trained DL model. A human grader independently reviewed the quality of field definition and assigned the field number. This was compared with the DL-generated label. All images were clinical trial submissions for various DR trials across multiple international sites.

Results: Field definition was considered adequate quality in 141 images (78.3%). The labeling model was accurate in 152 / 180 (84.4 %) images in the testing dataset. Of the 28 inaccurately labeled images 18 (64.3%) had poor field definition.

Conclusions: The deep learning model is an accurate automated method that can assist with workflows for organization of images for grader evaluation. This also helps develop well curated training images for future DL development towards disease identification.

CONTROL ID: 3546936

SUBMITTER (NAME ONLY): Abia Ahmed

TITLE: Intraocular Pressure and Rates of Macular Thickness Thinning in Subjects with Glaucoma

SESSION TITLE: Imaging in Glaucoma II: Basic and Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Ahmed, A.A. Jammal, S. Berchuck, F.A. Medeiros, Ophthalmology, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|S. Berchuck, Statistical Science, Duke University Trinity College of Arts and Sciences, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the effect of intraocular pressure (IOP) on the rates of macular thickness (ganglion cell layer [GCL] and ganglion cell and inner plexiform layer [GCIPL]) change over time, measured by spectral-domain optical coherence tomography (SDOCT).

Methods: The study involved 469 eyes of 268 patients from the Duke Glaucoma Registry, a database of electronic medical records of patients with glaucoma and suspected disease followed under routine clinical care at the Duke Eye Center and satellite clinics. All records from patients with a minimum of 6 months of follow-up, at least 2 good-quality Spectralis SDOCT scans, and 2 clinical visits with Goldmann applanation tonometry were included. Rates of change for GCIPL and GCL thickness were obtained using linear mixed models.

Results: Eyes had a mean follow-up of 2.0 ± 1.6 years. Average rate of change in GCL thickness was -0.17 ± 0.22 $\mu\text{m}/\text{year}$ (median -0.17 ; IQR -0.27 to -0.06 $\mu\text{m}/\text{year}$) and -0.15 ± 0.36 $\mu\text{m}/\text{year}$ (median -0.13 ; IQR -0.28 to 0.01 $\mu\text{m}/\text{year}$) in the combined GCIPL thickness. Each 1-mmHg higher mean IOP during follow-up was associated with an additional loss of -0.027 $\mu\text{m}/\text{year}$ of GCL thickness ($P = 0.007$) and -0.048 $\mu\text{m}/\text{year}$ of GCIPL thickness ($P = 0.001$), after adjusting for confounding factors such as baseline age, baseline thickness, sex, race, central corneal thickness and follow-up time.

Conclusions: We quantified the effect of IOP on the rates of macular thickness thinning over time using a clinical population. Higher levels of IOP during follow-up were significantly associated with faster rates of GCL and GCIPL loss over time measured by SDOCT. These findings support the use of SDOCT GCL and GCIPL thickness measurements as biomarkers for the evaluation of the efficacy of IOP-lowering therapies.

CONTROL ID: 3546937

SUBMITTER (NAME ONLY): Sangly Srinivas

TITLE: Ocular surface kinetics of topical fluorescein in Systane Gel

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.P. Srinivas, P.S. Kollbaum, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|H. Farhath Pattan, N. Ravi, P. Padmanabhan, R. Reddi Sudhir, Sankara Nethralaya, Chennai, Tamil Nadu, INDIA|

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ABSTRACT BODY:

Purpose: To determine the Systane gel (SG) effect on the ocular surface kinetics of fluorescein using a custom-made spot fluorometer.

Methods: Experiments were performed with a cohort of healthy subjects with no ocular disease. Informed consent was obtained from all subjects before measurements. Fluorescein (0.5%), formulated in normal saline or SG, was administered as a 30 μ L drop into the lower cul-de-sac. The patients were asked to blink after the drop, and corneal surface fluorescence measurements were begun immediately using a custom-made spot fluorometer. The fluorometer, built to measure fluorescence from any spot in the anterior segment, can record fluorescence at > 1 kHz. The fluorescence measurements, which could be started typically in < 10 seconds after the drop, were continued until baseline levels were observed. The measurements were performed frequently after the drop's administration but at 1-2 samples/min at the later stages. The dynamics of tear fluorescence was fitted to monoexponential decay to determine the elimination rate constant (expressed as half-life) and fluorescence at $t = 0$ (expressed in mV; i.e., initial concentration of fluorescein in tears). The tear meniscus height (TMH) and tear breakup time (TBUT) were also assessed after administration of the drops with a keratograph (Oculus 5M) every 20 mins for 1 hour.

Results: After administration of fluorescein in NS or SG, the tear fluorescence decayed with a single exponential profile. The half-life of tear fluorescence and the fluorescence at zero time after an SG drop were much higher than those with NS ($n = 8$; $p < 0.05$). Fig. 1 shows tear fluorescence vs. time in one subject following SG and NS drops. Although fluorescence vanished from the ocular surface by ~ 20 min (with SG), the mucoadhesive property of SG lasted longer. This was apparent by the keratograph measurements, which showed an increase in TBUT for more than 40 min after an SG drop ($p < 0.05$). NS did increase TBUT significantly, even at 20 min.

Conclusions: The increase in half-life with SG is consistent with increased tear film stability noted with the agent [1-2]. Thus, the half-life of fluorescein on the ocular surface is a measure of the potential efficacy of SG in the artificial tear substitutes employed in the palliative treatment of DED. In conclusion, we have demonstrated a paradigm to assess formulations of artificial tear substitutes for DED with our new custom-made fluorometer.

CONTROL ID: 3546939

SUBMITTER (NAME ONLY): Nicholas Tran

TITLE: Population specific axon regeneration programs mediated by Pten, Socs3, and Cntf revealed by scRNA-seq

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N.M. Tran, W. Yan, R. Schaffer, J. Sanes, Molecular and Cellular Biology, Harvard University, Cambridge, Massachusetts, UNITED STATES|A. Jacobi, Neurobiology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|I. Benhar, Broad Institute, Cambridge, Massachusetts, UNITED STATES|Z. He, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose: Neurons in the central nervous system have a limited ability to survive and regenerate their axons following injury. As a tractable system to study nerve injury, many researchers have turned to the optic nerve crush (ONC) model. In mice, ONC results in the loss of ~85% of retinal ganglion cells (RGCs) within 2 weeks. While many treatments that improve RGC survival and promote axon regeneration have been identified, only a fraction is protected in each case and fewer regenerate. Why do some RGCs respond to interventions while others do not? In this project, we investigated the transcriptional programs mediating survival and axon regeneration in injured RGCs.

Methods: Methods: Targeting the mTor pathway (via Pten deletion) in injured RGCs promotes the survival and regeneration of a subset of RGCs. This effect is broadened when the Jak/STAT pathway is co-targeted (via Socs3 deletion or Cntf overexpression (OE)). Gene expression was characterized by single-cell RNA-seq (scRNA-seq) in >125,000 RGCs following 3 treatments: RGC-specific Pten deletion, Pten deletion with Cntf-OE, or Pten+Socs3 deletion with Cntf-OE at multiple timepoints after ONC. Computational analysis was developed to map cell types, cluster cells, and evaluate expression patterns. Results were validated by immunohistochemistry and in situ hybridization. Candidate genes were tested in vivo using AAV-mediated overexpression or knockdown.

Results: Results: Key results from scRNA-seq expression screens included the following. First, all interventions preserved the expression of cell type markers and suppressed injury-related changes following ONC; much of the effects were observed with Pten deletion alone. Second, each intervention resulted in neuroprotection and axon regeneration with distinct type-specificity. Third, we identified multiple population-specific transcriptional modules correlating with degeneration, survival, and axon regeneration, highlighting the differences among RGCs in their responses to treatment.

Conclusions: Conclusions: Our results gene expression programs that correlate with, and presumably help explain, the enhancement of survival and axon regeneration following targeting of Pten, Socs3, and Cntf in injured RGCs. These findings provide potential therapeutic targets and enhance understanding of why neuronal cell types respond differently to neuroprotective and regenerative treatments.

CONTROL ID: 3546940

SUBMITTER (NAME ONLY): Jong Yeon Lee

TITLE: Bleb-related Lymphatic Outflow is Greater in Subconjunctival Compared to Subtenon Blebs.

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Current glaucoma surgeries utilize stents placed in the subconjunctival or subtenon space to create blebs for eye pressure lowering. However, choice of placement has long been debated in terms of clinical benefit and biological principles. The purpose of this ex-vivo experimental study is to evaluate the subconjunctival vs. subtenon space accessibility for lymphatic outflow pathways after creation of tracer-filled blebs at each location.

Methods: Post-mortem porcine eyes received a subconjunctival (n =10) or subtenon injection (n=10) of 500kD fixable fluorescent dextran tracers. Angiographic bleb and bleb-related outflow pathway images were obtained (Spectralis HRA+OCT; Heidelberg Engineering). Bleb-related outflow pathways were counted as lymphatics only if the lumens showed valve-like structures using near simultaneous anterior segment OCT. We also compared the number of outflow pathways arising from subconjunctival and subtenon blebs in different locations (superior/inferior/temporal/nasal). As the tracers could be fixed in place, histologic analysis of the exact pathways seen on angiographic imaging was performed to confirm imaging results.

Results: Subconjunctival blebs showed a greater number of lymphatic outflow pathways compared to subtenon blebs in every quadrant. (superior, 6.10 ± 1.18 vs. 0.50 ± 0.27 [mean \pm SEM], temporal, 2.30 ± 0.40 vs. 0.10 ± 0.10 , nasal 5.30 ± 0.60 vs. 0.30 ± 0.21 , inferior, 6.00 ± 1.29 vs. 0.1 ± 0.1 ; $p < 0.001$, $p < 0.001$, $p < 0.001$, $p = 0.001$, respectively). For subconjunctival blebs, the temporal location gave rise to fewer pathways compared to nasal ($p = 0.005$). Histological sectioning confirmed these pathways. For subtenon blebs, no quantitative difference in the number of pathways was found comparing locations. Further, histological sectioning around subtenon blebs did not demonstrate the presence of deep pathways that could have been missed on angiographic imaging owing to the increased depth.

Conclusions: Subconjunctival blebs accessed greater lymphatic outflow compared to subtenon blebs

CONTROL ID: 3546941

SUBMITTER (NAME ONLY): Sumit Sharma

TITLE: Safety of Suprachoroidal Injection Procedure Utilizing a Microinjector across Three Retinal Disorders

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Suprachoroidal injection (SCI) via SCS Microinjector[®] is an investigational ocular injection providing high, compartmentalized drug concentrations to chorioretinal layers via the suprachoroidal space (SCS). This post hoc study evaluated safety of SCIs across multiple clinical trials involving an investigational proprietary suspension of triamcinolone acetonide (CLS-TA), focusing on events occurring peri-procedurally.

Methods: Datasets from 8 clinical trials involving three disease states: noninfectious uveitis (NIU), diabetic macular edema (DME) and retinal vein occlusion (RVO) and included patients who received one or more SCI, either as monotherapy or with intravitreal (IVT) anti-VEGF. Procedure-related ocular serious adverse events (SAEs) assessed, occurring rarely with intraocular injections, included lens injury, suprachoroidal hemorrhage, retinal tear, retinal detachment, endophthalmitis, and reduced visual acuity. Treatment emergent adverse events (TEAEs) assessed included eye pain on the day of the procedure. Outcomes were compared to control eyes randomized to receive IVT anti-VEGF monotherapy and sham SCI.

Results: 621 patients received one or more SCI, either as monotherapy (N=161) or with IVT aflibercept (N=460). 3 of 621 patients experienced 3 SAEs of interest, all occurring in patients receiving multiple injections. One NIU monotherapy patient had a retinal detachment, and 2 RVO patients receiving combination therapy had reduced vision; each were deemed not related to treatment by a masked Investigator. There were no SAEs involving lens injury, suprachoroidal hemorrhage, endophthalmitis, or retinal tear in patients receiving SCIs, either alone or in conjunction with anti-VEGF. 449 control patients received IVT anti-VEGF in conjunction with a sham SCI. Three RVO patients experienced 3 SAEs of interest, including retinal detachment, vitreous hemorrhage and endophthalmitis. Each were deemed not related to treatment by a masked Investigator. Of 621 patients undergoing SCIs (161 as monotherapy, and 460 in conjunction with IVT injection), 37 (6%) experienced a TEAE related to eye pain, compared to control, 7 of 449 (1.6%) undergoing IVT injection.

Conclusions: Across 8 clinical trials involving NIU, DME and RVO, the safety profile of SCI, either as monotherapy or in conjunction with IVT injection, is comparable to IVT injections alone for events occurring at or after the procedure.

CONTROL ID: 3546943

SUBMITTER (NAME ONLY): Lucia Carichino

TITLE: Effect of altitude on retinal hemodynamics: A physiology-enhanced theoretical analysis

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Glaucoma is a leading cause of blindness worldwide with elevated intraocular pressure (IOP) being the major risk factor and its reduction being the only approved treatment. In many patients, impaired ocular hemodynamics has also been shown to be involved in its pathogenesis. While it is known that IOP is affected by altitude, the relationship between elevation and ocular hemodynamics is unclear. Here we use mathematical modeling for a physiology-enhanced analysis of the Mont Blanc Study (MBS) (Bruttini et al 2020) to estimate the effects of altitude on retinal hemodynamics.

Methods: IOP, mean arterial pressure (MAP) and heart rate (HR) were measured in 33 healthy volunteers at 77m (Pavia, PV, Italy) and at 3,466m (Pointe Helbronner, PH, Mont Blanc Mountain, Italy) above sea level. A validated mathematical model for retinal hemodynamics (Guidoboni et al 2014) is utilized to analyze the MBS data. Pressures, flow rates and resistances in the central retinal artery and vein (CRA and CRV) and in the retinal microvasculature are predicted by the model, based on individually measured values of IOP, MAP and HR. The model accounts for IOP and MAP induced variables resistances in the retrobulbar segments of the CRA, CRV and in retinal venules (RV). Results between PV and PH are analyzed using t-test with $p < 0.05$ statistically significant.

Results: With altitude, the results predict a statistically significant increase in all retinal pressures ($p < 0.001$, which follows the increasing MAP with altitude observed in the MBS) and in the retinal blood flow across the full retinal circulation ($p < 0.001$, from the CRA inflow to the CRV outflow via the retinal microvasculature), Figure 1. With altitude, the results predict a significant decrease in CRA ($p < 0.001$) and RV (and $p = 0.003$) resistances, and a non-significant increase in the CRV resistance ($p = 0.253$), Figure 2. The resistance in the RV is markedly higher than in the CRA and CRV, suggesting that the venules are withstanding most of the IOP load on the vasculature.

Conclusions: Mathematical modeling can be used to enhance measured datasets with hemodynamic variables that cannot be measured directly, such as the venous resistance. This analysis suggests that venules bear the significant portion of IOP pressure load within the ocular vasculature. Advancement of this approach may include the study of the effect of altitude on oxygen saturation via autoregulation.

CONTROL ID: 3546955

SUBMITTER (NAME ONLY): Preston Girardot

TITLE: Long-term Systemic Pentosan Polysulfate Administration Causes Retinal Function Decrease with Changes in Cell Markers

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Girardot, M.A. Chrenek, J.T. Sellers, N. Zhang, N. Jain, J.M. Nickerson, J.H. Boatright, Department of Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|P. Girardot, J.H. Boatright, Atlanta VA Center for Visual & Neurocognitive Rehabilitation, Decatur, Georgia, UNITED STATES|X. Zhang, N. Zhang, Department of Ophthalmology, Second Xiangya Hospital, Changsha, Hunan, CHINA|X. Zhang, Emory University School of Medicine, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Pentosan Polysulfate Sodium (PPS) is prescribed to treat bladder pain or discomfort. Pearce et al. [2018] reported a maculopathy in adults taking this medication. We then showed that systemic treatment with PPS causes retinal function diminution in a common laboratory mouse [Girardot et al. 2019]. Here we report further ex-vivo features of this toxicity.

Methods: 10 male and 10 female 129S2/SvPasCrl mice were given intraperitoneal injections of 0.1X Hanks' Balanced Salt Solution (vehicle) or PPS (12 PPS, 8 vehicle mice). Injections were given several days weekly for 31 weeks. Concentration of drug was 10 mg/kg. Mice regularly had retinal function assessed by electroretinography (ERG). After sacrifice, one eye was fixed using freeze substitution for sagittal paraffin sectioning and histology. The contralateral globe was fixed in z-fix for RPE-flatmounts. Flatmounts were dissected within 1 week of sacrifice and stained for ZO-1 and α -catenin.

Results: At 2.5 months we reproduced findings of decreased ERG a- and b-wave amplitudes in the PPS-treated animals, ($p=0.0195$ for b-waves, 0.0084 for a-waves beginning at 3.5 months, two-way ANOVA). We observed several discrepancies in post-mortem immunostaining. In transverse sections, arrestin and rhodopsin staining was increased. Staining was also increased for synaptic markers PSD95 and synaptophysin, and PKC α , a marker of bipolar and retinal ganglion cells. En-face RPE flatmounts showed trends of decreased cytosolic and nuclear α -catenin, which has been associated with DNA damage responses [Serebryanny et al. 2017]. Gender differences were observed and are the subject of ongoing experiments.

Conclusions: PPS treatment has nuanced effects on the retina. Functional decline is accompanied by increases in a variety of cell markers, as well as a trend of differential α -catenin protein translocation. Maybe this is all indicative of damage-induced remodeling (Marc et al. 2003). We are still optimizing our model to simulate a phenomenon that is the result of years, and sometimes decades, of drug treatment. Perhaps cell death and more apparent morphological disruption comes with longer durations of treatment. The link between our work and the clinical observations may become clearer as we continue to improve our model and investigate the underlying biochemical mechanisms.

CONTROL ID: 3546958

SUBMITTER (NAME ONLY): Mitra Farnoodian-Tedrick

TITLE: Loss of ABCA4 Function And Altered Lipidomic of Retinal Pigment Epithelium: A New Link To Stargardt Pathogenesis

SESSION TITLE: Metabolism of the RPE and retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Farnoodian-Tedrick, F. BARONE, D. Bose, K. Bharti, Ocular Stem Cell & Translational Research Section, National Institutes of Health, Bethesda, Maryland, UNITED STATES|B. Jun, K. Do, W.C. Gordon, M. Kautzmann Guerin, N.G. Bazan, Neuroscience Center of Excellence, School of Medicine, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|M. Boyle, OGVFB, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Stargardt disease is inherited as an autosomal recessive trait caused by mutations in the ABCA4 gene, which lead to accelerated accumulation of lipofuscin in the retinal pigment epithelium (RPE) leading to RPE atrophy and photoreceptor cell death. There is currently inadequate information on the complexity of changes in lipid composition, homeostasis, metabolism, and lipid-mediated signaling of the RPE, leading to ABCA4 retinopathy. ABCA4^{-/-} mouse model has shown similar phenotypes of human ABCA4 retinopathy, particularly lipofuscin deposits in the RPE. To understand the role of ABCA4 in RPE lipid profile and its contribution to Stargardt disease pathogenesis, we used the ABCA4^{-/-} mouse model and developed Stargardt iPSC-derived RPE with complete loss of ABCA4 function as an in vitro disease model.

Methods: Lipid extraction was performed from collected RPE/choroid samples of 12-month-old wild type and ABCA4^{-/-} (C57BL/6J) mice. To validate the observed alterations in RPE/choroid's lipid profile obtained from ABCA4^{-/-} mice, fully characterized Stargardt iPSC (patient and two ABCA4^{-/-} iPSC lines) were differentiated into functionally validated RPE using a developmentally guided protocol. Stargardt- iRPE was cultured on semi-permeable membranes for six weeks to obtain a functionally mature and polarized monolayer tissue. For lipid extraction, cell medium and lysate from Stargardt- iRPE cells were collected after exposure to photoreceptor outer segment regimen (8 days). Lipid extracts were subjected to liquid chromatography–mass spectrometry (LC-MS/MS) for lipidomic analysis.

Results: LC-MS/MS analysis revealed altered RPE/choroid and Stargardt- iRPE lipid profile, including changes in phosphatidylcholine (PC), phosphatidylethanolamine (PE), and phosphatidylserine (PS) molecular species and fatty acids and their derivatives with complete loss of ABCA4 function. RPE/choroid samples collected from ABCA4^{-/-} mice showed general trends of having less amounts of stable metabolites leading to elovanoic pathways and less abundance of VLC-PUFAs (FA32:6 n3 and FA34:6 n3) compared with the wild type.

Conclusions: Our results indicate that ABCA4 plays an essential role in RPE lipid profile, and mutations in the ABCA4 result in the changed RPE lipidomic contributing to Stargardt disease pathogenesis. This work provides an improved understanding of Stargardt disease mechanism.

CONTROL ID: 3546959

SUBMITTER (NAME ONLY): David Mathew

TITLE: An Improved Circumlimbal Suture Model That Exhibits Gradual Increase in Intraocular Pressure

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Mathew, I. Livne-Bar, J. Sivak, Ophthalmology and Vision Sciences, Krembil Research Institute, Toronto, Ontario, CANADA|D. Mathew, I. Livne-Bar, J. Sivak, Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: We aimed to characterize a rodent model of gradual chronic ocular hypertension, without an initial intraocular pressure (IOP) spike common to many current inducible models.

Methods: Adult Long Evans rats were anesthetized and a Nylon 8-0 suture was passed around subconjunctivally 5-6 times 1.5 mm posterior to the limbus, and tied off using a slipknot anchored with 3-5 simple throws. Care was taken to make sutures snug, but not tight, without inducing an IOP spike. This generated gradual ocular hypertension (gOHT) as the sutures tightened over time. Control eyes (CON) were loosely sutured. Follow-up included weekly IOP measurements, monthly OCT scans of the angle and circumpapillary retinal nerve fiber layer (cpRNFL), and vision assessment using OptoMotry. Eyes were collected after 12 weeks of elevated IOP for cryosectioning and confocal microscopy. Anti-RBPMS was used to stain retinal ganglion cells for quantification of cell survival on 250 μ m from both sides of the optic nerve insertion.

Results: Baseline IOP (mean \pm SE) for CON and gOHT were 10.2 \pm 0.2 and 10.5 \pm 0.3 mmHg, respectively ($p=0.33$). IOP immediately after suturing were 9.2 \pm 0.2 and 9.6 \pm 0.2, respectively ($p=0.12$). IOP in gOHT increased above 20 mmHg 3-5 weeks post-suturing. After 12 weeks, the measurements were 15.2 \pm 0.8 and 27.8 \pm 0.8 mmHg in CON and gOHT groups, respectively ($p<0.001$). The number of RBPMS positive cells per 100 μ m was 4.22 \pm 0.06 for CON and 3.43 \pm 0.06 for gOHT ($p<0.001$). Optokinetic vision at baseline was 0.708 \pm 0.009 and 0.683 \pm 0.009 cycles/deg ($p=0.09$), respectively, and after 12 weeks of elevated IOP, 0.647 \pm 0.010 and 0.489 \pm 0.008 cycles/deg ($p<0.001$), respectively, representing a 28.4% decrease in gOHT. The average cpRNFL thickness was 42.7 \pm 0.4 and 43.6 \pm 0.8 at baseline ($p=0.31$), 41.7 \pm 0.2 and 39.3 \pm 1.1 at 8 weeks of elevated IOP ($p=0.05$) and 41.2 \pm 0.5 and 35.0 \pm 1.1 at 12 weeks of elevated IOP ($p<0.001$). Angles remained open throughout, and all sections were negative for CD68 (microglia), F4/80 (macrophages) and SOD2 (oxidative stress marker).

Conclusions: The gOHT model produces chronic mildly elevated IOP in rats, accompanied by loss of retinal ganglion cells and visual function, and no evidence of inflammatory cell infiltration. The advantages with this model include the absence of a pathological initial spike in IOP, no intraocular entry or inflammation, and induction of a gradual increase in IOP, similar to clinical glaucoma.

CONTROL ID: 3546960

SUBMITTER (NAME ONLY): Rebecca Zeng

TITLE: A Novel Active Learning Contrast Sensitivity Test to Assess Visual Function in Central Serous Chorioretinopathy

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Zeng, E. Kim, F. Vingopoulos, I. Garg, E. Choi, I. Lains, L.A. Kim, J.B. Miller, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|R. Zeng, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|M. Thomas, D.N. Zacks, University of Michigan, Ann Arbor, Michigan, UNITED STATES|L.A. Lesmes, Adaptive Sensory Technology, San Diego, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To characterize the contrast sensitivity function (CSF) in patients with central serous chorioretinopathy (CSCR) compared to healthy controls using novel computerized contrast sensitivity (CS) testing with active learning algorithms.

Methods: CSF was prospectively measured in CSCR eyes and healthy controls between December 2016 and November 2017 at W. K. Kellogg Eye Center and Massachusetts Eye and Ear Infirmary using the novel active learning Sentio Platform (Adaptive Sensory Technology, San Diego, CA). A mixed effects multivariate regression model was employed and outcomes included Area under the Log CSF (AULCSF), CS thresholds at 1, 1.5, 3, 12, and 18 cycles per degree (cpd) and best corrected visual acuity (BCVA). Associations of contrast outcomes with structural findings and subjective symptomatology were investigated.

Results: A total of 40 eyes of 36 CSCR patients and 84 healthy control eyes were included. Median BCVA in CSCR eyes was logMAR 0.10 (0.23) versus 0.00 (0.04) in controls ($P = 0.01$). The median AULCSF in CSCR eyes was 1.11(0.70) versus 1.24 (0.31) in controls. When accounting for age, the presence of CSR was associated with significantly reduced median AULCSF ($P = .02$, $\beta = -0.14$) and reduced mean CS thresholds at spatial frequencies of 6cpd ($P = .009$, $\beta = -0.18$), 12cpd ($P < .001$, $\beta = -0.23$) and 18cpd ($P = .04$, $\beta = -0.09$), compared to controls. Within the CSCR group, subjectively perceived visual impairment ($N=22$) was associated with decreased contrast thresholds at all spatial frequencies and in AULCSF, when compared to asymptomatic CSCR eyes ($N=18$). Ellipsoid zone attenuation was associated with decreased AULCSF ($P = 0.002$, $\beta = -0.473$) and decreased contrast thresholds specifically at 3,6 and 12 cpd, whereas presence of extrafoveal fluid was associated with decreased thresholds at 1, 1.5, 3 and 6 cpd.

Conclusions: Contrast sensitivity is significantly reduced in CSCR, and seems to strongly correlate with subjective visual impairment. Different structural biomarkers correlate with contrast thresholds reductions at different spatial frequencies. The novel qCSF method may serve as a valuable adjunct visual function metric for CSCR patients in the routine clinical practice.

CONTROL ID: 3546964

SUBMITTER (NAME ONLY): Elizabeth Zuniga-Sanchez

TITLE: Elucidating the Role of Neurofascin in the Outer Retina

SESSION TITLE: Inner retinal function

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Zuniga-Sanchez, S. Pourhoseini, D. Goswami-Sewell, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|E. Zuniga-Sanchez, Neuroscience, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Proper transmission of visual information relies on neurons forming appropriate synaptic connections to their respective targets during development. In the outer retina, photoreceptors are the main detectors of lights that synapse selectively to distinct partners. Cone photoreceptors synapse to the dendrites of horizontal cells and to the dendrites of cone bipolars, whereas rod photoreceptors synapse to the axon of horizontal cells and to the dendrites of rod bipolars. The molecular mechanisms that guide selective wiring of photoreceptors to their distinct targets remains poorly understood.

Methods: Our initial data identified the L1 cell adhesion molecule Neurofascin (Nfasc) to be localized in the developing synaptic layer and exclusively expressed in rods, horizontal cells, and rod bipolars. Moreover, other cell adhesion molecules (i.e. Cntn1, Caspr, Nrcam) that are known to work alongside Nfasc are expressed in the complementary cone pathway. Based on these data, we hypothesize that restricted expression of cell adhesion molecules mediates selective wiring of photoreceptors to their respective targets. To test our hypothesis, we perform loss- and gain-of-function experiments using mouse transgenics, in vivo genetic manipulations, and single neuron labeling approaches.

Results: We found that disruption of Nfasc leads to synaptic defects affecting rod connectivity but not cone connectivity. These include loss of pre- and post-synaptic protein expression among rods and rod bipolars as well as a decrease in rod-driven visual responses. However, synaptic connections among cones and cone bipolars do not appear to be affected. Moreover, ectopic expression of the cone-restricted cell adhesion molecule, Nrcam in rods results in rod terminals projecting deeper and making aberrant contacts to cone bipolars. These data suggest that Nfasc may be required for rod connectivity and Nrcam for cone connectivity.

Conclusions: Our findings support a novel role for Nfasc and Nrcam in photoreceptor connectivity. Future work will further disseminate these molecular interactions to reveal new molecular pathways that guide selective wiring of photoreceptors. Through these experiments, we will uncover the molecular mechanisms involved in complex wiring of neural circuits during development.

CONTROL ID: 3546965

SUBMITTER (NAME ONLY): John Hong

TITLE: Retinylation of Opsins by Retinyl Formate

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Hong, Ophthalmology, University of California Irvine School of Medicine, Irvine, California, UNITED STATES|Á. Placeres, G.P. Tochtrop, Chemistry, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Defects in visual cycle enzymes or retinoid carrier proteins may deplete 11-cis retinal (11cRAL) and are implicated in multiple blinding diseases. Therefore, retinal analogues that aid in vision independent of chromophore recycling have invaluable translational implications in addressing visual cycle impairments and controlling visual cycle kinetics. Conversely, intense light exposure causing overstimulation of photoreceptors can overwhelm the outer segment with atRAL that form toxic bisretinoid lipofuscin species that contribute to Age-Related Macular Degeneration. Therefore, retinal analogues also have an important role in either attenuating opsin activity or serving as transient molecular brakes of the visual cycle.

Methods: The chemistry of retinyl formate (RF) in forming a covalent interaction with primary amines of lysine was tested in solution with different solvent, and the resultant reaction mixture was analyzed by high performane liquid chromatography. The covalent binding efficiency of RF was assessed by UV-Vis spectrophotometry. The site of retinyl modification by RF was determined by protein digest of RF treated opsin, followed by peptide liquid chromatography mass spectrometry (LC-MS).

Results: RF interacts with primary amines to form a covalent interaction, producing a retinyl secondary amine. The UV-Vis spectrum of the RF treated opsin that was thoroughly washed shows a spectrum resembling opsin modified by a retinyl group. Over time, the spectrum gradually shifted to that of the Schiff base, demonstrating that the modification is transient and reverts to normal opsin physiology. Protein digest of our positive control in borohydride reduced native bovine rhodopsin and subsequent peptide LC-MS showed presence of retinyl peptides. The same will be done on RF treated rhodopsin.

Conclusions: RF can serve as retinylating agent of amines and therefore likely retinylates the amine side chain of lysine within the chromophore binding pocket of opsin. RF treated opsin shows spectrum indicative of such a reaction occuring within opsin. Retinylated opsin gradually oxidized to the Schiff base, suggesting that the modification can be a way to restore visual pigment. Protein digest and peptide LC-MS on borohydride reduce native bovine rhodopsin demonstrated efficacy in detecting retinyl peptides; therefore, the same can be done on retinylated opsin to confirm the retinylation modification and the preference site of modification within opsin.

CONTROL ID: 3546966

SUBMITTER (NAME ONLY): Shruti Patil

TITLE: A novel mouse model of TGFβ2-induced ocular hypertension using lentiviral gene delivery

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.V. Patil, R.B. Kasetti, C. Kiehlbauch, J. Millar, G. Zode, Department of Pharmacology and Neuroscience and the North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glaucoma is a multifactorial disease leading to irreversible blindness. Glaucoma is associated with elevation of intraocular pressure (IOP) due to damage to the trabecular meshwork (TM). Transforming growth factor (TGF)β2 is known to cause TM damage and elevate IOP. Mouse models of TGFβ2-induced IOP elevation help understand the underlying molecular mechanism of the disease progression. The goal of this study was to develop a mouse model of IOP elevation using lentiviral gene transfer of active TGFβ2.

Methods: Lentiviral vector constructs encoding active hTGFβ2(C226,228S) with CMV or CBh promoter were purchased from VectorBuilder. Empty lentivirus vector (LV-CMV-Null-Puro) obtained from SignaGen Labs was used as control. C57BL/6J and BALB/cJ mouse strains, age group of >4 months old, were used for the study. The ultra-pure lentiviral particles expressing TGFβ2 or null were intravitreally injected (2×10^6 TU/eyes) into contralateral eyes of each anesthetized mice. IOP was weekly monitored followed by assessment of aqueous outflow facility. TGFβ2 expression was assessed in aqueous humor (AH) and anterior segments of injected eyes. Hematoxylin and eosin staining was performed to examine the morphology of mouse eyes. Effect on RGC function and cell count was determined via pattern ERG (pERG) and RBPMS staining, respectively.

Results: Eyes injected with lenti-CMV-TGFβ2 viral particles significantly increased IOP post 3-weeks of injection compared to the control eyes. The average IOP elevation observed was 3.3 mmHg and stayed consistent up to 7-week post injection. Individual mice assessment revealed 50% response rate to lenti-TGFβ2-induced IOP elevation with average delta change of 6.19 mmHg among the responders. Likewise, the responder mice showed 64.05% drop in AH outflow facility. Nevertheless, no cellular or functional loss of RGC was observed even among the responders. Increased expression of active TGFβ2 was observed in both AH and anterior segment samples of injected mice compared to null injected mice. Mild development of lenticular opacity was detected in some TGFβ2-injected eyes, however, there were no visible signs of inflammation noticed in any of the injected eyes.

Conclusions: Sustained increase in IOP with consequent decrease in outflow facility was effectively demonstrated via lentiviral gene delivery of active TGFβ2 under control of CMV promoter.

CONTROL ID: 3546967

SUBMITTER (NAME ONLY): Marco Ruggeri

TITLE: Measurement of the average group refractive index of the human crystalline lens in vivo using OCT images acquired before and after IOL implantation

SESSION TITLE: IOL and Crystalline Lens Optics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Ruggeri, Y. Chang, B. Maceo Heilman, F. Cabot, S.H. yoo, J.A. Parel, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|M. Ruggeri, Y. Chang, B. Maceo Heilman, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|F. Cabot, S.H. yoo, Anne Bates Leach Eye Center, Bascom Palmer Eye Institute, University of Miami School of Medicine, Miami, Florida, UNITED STATES|J.A. Parel, BHVI, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Knowledge of the average refractive index of the human crystalline lens along its optical axis is useful to obtain accurate estimates of the lens thickness and posterior lens shape with OCT (Borja et al, Biomed Opt Express 2010). We present a method for measuring the average group refractive index of the lens by acquiring OCT images in patients before and after cataract surgery.

Methods: Eighteen eyes from 13 patients (age 73.5 ± 5.3 years) who underwent cataract surgery and IOL implantation at Bascom Palmer Eye Institute were imaged with an extended depth SD-OCT system at 840 nm (Ruggeri et al, Biomed Opt Express 2012) before and one to six months after surgery. All surgeries were performed by one of two surgeons using standard monofocal IOLs (Acrysof, Alcon). Optical path lengths of the anterior chamber, crystalline lens, IOL and vitreous were measured in the pre- and post-operative images of all eyes using custom-made software (MATLAB). Except for the crystalline lens, all intraocular optical lengths were converted to geometrical distances using the group refractive indices at 840 nm of the aqueous and vitreous ($n_{AQ} = n_V = 1.341$; Ruggeri et al Biomed Opt Express 2012) and of the IOL ($n_{IOL} = 1.601$), which was measured on a non-sterile IOL sample using the method of Uhlhorn et al (Vis. Res. 2008). For each eye, the geometrical thickness of the lens was calculated from the pre- and post-operative geometrical distances assuming that axial eye length does not change after surgery. The average group refractive index of the lens was then calculated as the ratio between the optical and geometrical lens thickness.

Results: The average group refractive indices of all crystalline lenses are summarized in the table, giving an overall average of 1.425 ± 0.009 mm (range: 1.413 – 1.439), which is comparable to the group refractive index measured with OCT in vitro (1.416 ± 0.004 ; Uhlhorn et al Vis. Res. 2008).

Conclusions: The study demonstrates the feasibility of measuring the average axial group refractive index of the crystalline lens in vivo by quantifying ocular distances before and after IOL implantation.

CONTROL ID: 3546969

SUBMITTER (NAME ONLY): Sara Toulouie

TITLE: Relationship of Retinal Vessel Diameters with Age-Related Macular Degeneration

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Toulouie, California Northstate University College of Medicine, Elk Grove, California, UNITED STATES|G. Yiu, J. Pan, S. Chang, K. Snyder, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A hemodynamic role in the pathogenesis of age-related macular degeneration (AMD) has been proposed, but the relationship of retinal vascular parameters and AMD severity has not been evaluated. Here, we explored if retinal arterial or venous diameters, or arteriole-to-venule ratio (AVR) may be associated with AMD severity by analyzing fundus photographs from the Age-Related Eye Disease Study (AREDS).

Methods: We evaluated field 1 color fundus photographs from 1172 eyes to measure retinal vascular parameters including central retinal artery equivalent (CRAE), central retinal vein equivalent (CRVE), and AVR. Images were graded by two masked graders using a semi-automated software to determine the diameters of the 6 largest venules and arterioles surrounding the optic disc and using the Parr-Hubbard formula to standardize vessel calibers. Univariate and multivariate regressions were used to determine the association of CRAE, CRVE, and AVR with age, sex, smoking status, and AMD severity based on the 9-step AMD severity score.

Results: Both CRAE and CRVE were higher in men than women ($P=0.001$), and in current smokers vs. former or never-smokers ($P<0.001$), consistent with prior studies. In eyes without late AMD, the AMD severity score was associated with older age ($P = 0.001$), current smokers ($P = 0.011$), and higher AVR ($P = 0.001$), but not with CRAE or CRVE. The prevalence of choroidal neovascularization (CNV) was associated with older age ($P = 0.003$), but not with retinal vascular parameters ($P=0.258-0.681$). The prevalence of central geographic atrophy (CGA) showed a significant association with lower CRAE ($P = 0.002$) and possible association with lower CRVE ($P = 0.045$) or AVR ($P = 0.080$). None of these retinal vascular measurements were predictive of change in AMD severity score, CNV, or CGA at 5 years.

Conclusions: Retinal vascular caliber parameters such as AVR may be associated with AMD severity, supporting a retinal hemodynamic contribution to the pathogenesis of this condition.

CONTROL ID: 3546970

SUBMITTER (NAME ONLY): Meera Ramakrishnan

TITLE: Balloon Dacryoplasty and Monocanalicular Stenting Outcomes in Congenital Nasolacrimal Duct Obstruction

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Ramakrishnan, S. Bautista, W. Katowitz, K. Revere, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|S. Bautista, D. Prat, W. Katowitz, K. Revere, J.A. Katowitz, The Children's Hospital of Philadelphia Division of Ophthalmology, Philadelphia, Pennsylvania, UNITED STATES|G. Luna, Queen's University, Kingston, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Congenital nasolacrimal duct obstruction (CNLDO) in children can be treated surgically with probing and irrigation, canalicular stenting, or balloon dacryoplasty. Success rates for both stenting and dacryoplasty have ranged from 73-90%. This study aims to determine the success rate of balloon dacryoplasty with concurrent monocanalicular stenting (BD+S) as a primary or secondary procedure in congenital nasolacrimal duct obstruction (CNLDO).

Methods: Single-center retrospective cohort study of all children with CNLDO who underwent BD+S from 2009-2019. Patients who had previous probing and stent placement or probing alone were also included. All BD+S procedures were performed at the Children's Hospital of Philadelphia by one of three surgeons (JK, WK, KR). Primary outcome was failure rate, defined as recurrence of tearing symptoms after stent removal.

Results: 98 children (143 NLD) were included in the study; 16 patients (16%) with 22 nasolacrimal ducts (15%) were under the age of 2 years. Mean follow up was 3.3 months (range 3 days – 9.3 months). On follow up, 46/143 (32%) eyes were still symptomatic. Recurrent tearing was seen in 5/22 (23%) NLD below age 2 years and 41/121 (34%) above age 2 years. Chi square analysis did not show any significant difference between the two groups ($p=0.36$). Failure rates were similar for primary (25/79, 32%) vs secondary (18/55, 33%) BD+S. Stenosis of the NLD was seen in 47% of the failures.

Conclusions: Balloon dacryoplasty with concurrent monocanalicular stenting either as a primary or secondary procedure had a success rate of 68% for reducing tearing in CNLDO, lower than previously reported rates of 73-87% for BD. Failures were frequently associated with NLD stenosis.

CONTROL ID: 3546972

SUBMITTER (NAME ONLY): Jade Harkin

TITLE: Towards a more efficient and reproducible method for retinal organoid specification from human pluripotent stem cells

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Harkin, Pharmacology and Toxicology, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|K. Lentsch, Department of Biology, Indiana University Purdue University at Indianapolis, Indianapolis, Indiana, UNITED STATES|J.S. Meyer, Medical and Molecular Genetics, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|J. Harkin, J.S. Meyer, Stark Neurosciences Research Institute, Indiana University School of Medicine, Indianapolis, Indiana, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jade Harkin: Commercial Relationship: Code N (No Commercial Relationship) | Kelly Lentsch: Commercial Relationship: Code N (No Commercial Relationship) | Jason Meyer: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal organoids are three-dimensional aggregates of cells that self-organize into retinal-like tissues. Current protocols utilize human pluripotent stem cells (hPSCs) to generate retinal organoids in vitro, however few protocols have explored the factors that regulate the earliest stages of retinal organoid specification. As such, a more reproducible and efficient method for differentiating early-stage retinal organoids would provide a reliable and reproducible platform for studying human retinogenesis and disease.

Methods: In the current study, 3D aggregates of hPSCs were generated using quick reaggregation methods in 96-well U-bottom plates to ensure reproducibility among culture conditions. Various cell densities were tested for the most efficient generation of retinal organoids. Additionally, a role for BMP signaling in retinal organoid differentiation was tested by treatment with either BMP4 or Noggin, and efficiency was assessed at different time points based on morphological analysis and expression of retinal progenitor markers. Ongoing experiments are assessing transcriptional changes that are associated with the specification of a retinal organoid fate.

Results: Results indicate that cell aggregates generated using the quick reaggregation differentiation method are highly reproducible in both their size and shape at early time points compared to traditional methods. Early-stage retinal organoid differentiation using the quick reaggregation method was also significantly improved after BMP4 activation. Ongoing experiments will continue to focus on optimizing current retinal organoid differentiation protocols, as well as identifying the transcriptional alterations that are associated with the development of retinal organoids.

Conclusions: The precise regulation of multiple parameters within this study provides a novel highly reproducible retinal organoid model that can improve our understanding of human retinogenesis as well as retinal degenerative diseases. The efficient generation of reproducible retinal organoids will also accelerate the development of translational approaches for debilitating blinding disorders.

CONTROL ID: 3546973

SUBMITTER (NAME ONLY): Finny Monickaraj

TITLE: The Chemokine CXCL1 Contributes to Vascular Inflammation and Disruption of Tight-Junctions Associated with Diabetic Retinopathy

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Monickaraj, G. Acosta, A. Cabrera, A. Das, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|F. Monickaraj, A. Das, NMVA Health Care System, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inflammation plays an important role in the pathogenesis of diabetic retinopathy. By examining the transcriptome profile and molecular signaling pathway analysis of human retinal endothelial cells (HREC) treated with advanced glycation end products, we have previously shown that the chemokine CXCL1 gene was significantly up-regulated. The purpose of the present study is to determine the effect of CXCL1 and its contribution to the increased vascular permeability and disruption of tight-junctions in retinal vessels in DR.

Methods: Recombinant CXCL1 (100 ng/eye) or sterile water (vehicle) was injected intravitreally into the eyes of C57bl/6 mice (n=5) followed by FACS analysis of immune cell infiltration in the retinas. Next, qPCR analysis was used to determine mRNA expression of key proteases and chemokines. Western Blot analysis was used to evaluate the expression of albumin and VE-cadherin. CXCL1 levels in retinas of streptozotocin induced diabetic mice b(two months duration) was measured by qPCR. ELISA was used to measure CXCL1 levels in serum samples of human diabetic retinopathy patients.

Results: Recombinant CXCL1 injected intravitreally caused significant increase in the infiltration of immune cells: two fold increase of neutrophils and 3-fold increase in monocytes. Importantly, qPCR analysis of retinas revealed increased mRNA expression of CCL2 (4-fold), MMP12 (3-fold) and Cathepsin L (2-fold). Western Blot analysis confirmed that CXCL1 caused a significant increase in retinal vessel permeability, which correlates with increased albumin and decreased VE-cadherin expression. CXCL1 expression was significantly increased in the retinas from diabetic mice. Also, CXCL1 level was significantly increased in the serum samples of diabetic retinopathy patients compared to non-diabetic subjects (p=0.001).

Conclusions: In this study we have shown the role of the chemokine CXCL1 in alteration of blood retinal barrier in diabetic retinopathy, and thus as a potential novel therapeutic target.

CONTROL ID: 3546975

SUBMITTER (NAME ONLY): JANE Gilmore

TITLE: Combined Dual Blade Goniotomy and Direct Viscodilation of the Collector Channels with Cataract Surgery: 4 Year Results

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Gilmore, L. Burk, UT Southwestern, The University of Texas Southwestern Medical Center, Dallas, TX, US, academic/hospital, Dallas, Texas, UNITED STATES|L.L. Gilmore, Dallas Eye and Ear, Dallas, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose is to evaluate a hybrid MIGS procedure using Goniotomy and Direct Viscodilation of the collector channels with cataract surgery in all levels of glaucoma. This unique technique called "clean the gutter and power wash the downspouts", not only removes the trabecular meshwork but also directly viscodilates the collector channels.

Methods: After cataract surgery, the Dual Blade removed 180° of trabecular meshwork. Viscoelastic was injected into the exposed ostium of the Collector Channels as the perpendicular viscoelastic cannula was held firmly against the outer wall and dragged through the gutted canal. Moderate to severe glaucoma comprised 64% of the 177 eyes followed at least 2 years. 32% had previous glaucoma surgery. 71% were African American. 44% were diabetics. 50% were on an anticoagulant.

Results: Initial IOP was 18.5mmHg(SD+/-7.2)on 1.6 medications. At 3 months the IOP was 15.6mmHg(SD+/-5.1). Throughout the first year the IOP hovered around 16.5mmHg. IOP then settled to 15.5mmHg (SD+/-4.4) in 74 of the 177 eyes that were seen for 3 years. Although the IOP was reduced by 15%, 85-90% of the eyes had all drops stopped. All eyes had ≤ 15 mmHg AND no meds in 71% (1yr), 59% (2 and 3yr), and 78% (4yr). The moderate to severe group had ≤ 15 mmHg AND no meds 70% (1yr), 50% (2yr), 55% (3yr), and 75% (4yr). Medications were reduced by 1.5 to 1.0 drops per eye over the course of 4 years.

Conclusions: The synergy of Goniotomy and Viscodilation markedly reduces drops even in advanced glaucoma with at least 50% of eyes achieving IOP ≤ 15 mmHg,thus improving compliance and reducing the associated financial burden. The Goniotomy-Viscodilation-Cataract technique addresses both trabecular outflow resistance and salvages the collapsed collector channels.

CONTROL ID: 3546977

SUBMITTER (NAME ONLY): Ricardo Lamy

TITLE: Pulsed Low Frequency Ultrasound for Corneal Phonophoresis

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lamy, M. Sahasrabudhe, J.M. Stewart, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|P.D. Jones, C.J. Diederich, Radiation Oncology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Purpose : To determine the effect of pulsed low frequency ultrasound (PLFU) at 250 kHz and 500 kHz on the delivery of topical compounds into the corneal stroma.

Methods: Fresh cadaveric rabbit eyes with intact corneal epithelium were placed in a solution of 0.1% riboflavin. Treated eyes received PLFU (60% duty cycle) with a Spatial Average Temporal Average Intensity (I_{sata}) of 1.0 W/cm² for 6 minutes at either 250 kHz or 500 kHz, and the eyes were then left in riboflavin solution for a total immersion time of 20 minutes. Control eyes without ultrasound treatment received the same exposure to riboflavin solution. Corneas were then excised, and confocal microscopy was performed to measure the penetration and distribution of riboflavin in the corneal stroma.

Results: At a corneal depth of 300 microns, the average fluorescence intensity of riboflavin in the groups treated with PLFU 250 kHz and 500 kHz was respectively 9232 ± 2595 A.U. (n = 6) and 7454 ± 2184 A.U. (n=6). When compared to controls (1449 ± 690 A.U.; n=6) the difference was statistically significant for both treated groups (p-value < 0.05), demonstrating 5 - 6 fold therapeutic gain. The difference between corneas treated at 250 KHz and 500 KHz was not statistically significant.

Conclusions: PLFU was very effective in delivering riboflavin into the corneal stroma despite the presence of a previously intact epithelial barrier. This approach may offer a means of achieving clinically useful concentrations and penetration of topically applied drugs in the corneal stroma without removing the corneal epithelium.

CONTROL ID: 3546978

SUBMITTER (NAME ONLY): Marta Grannonico

TITLE: In vivo quantification of mouse retinal nerve fiber layer changes using visible-light optical coherence tomography fibergraphy (Vis-OCTF)

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Grannonico, M. Liu, X. Liu, Biology, University of Virginia, Charlottesville, Virginia, UNITED STATES|D.A. Miller, H. Zhang, Biomedical Engineering, Northwestern University, Evanston, Illinois, UNITED STATES|P. Netland, X. Liu, Ophthalmology, University of Virginia, Charlottesville, Virginia, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have established vis-OCT fibergraphy (vis-OCTF) for visualizing and quantifying retinal ganglion cell (RGC) axon bundles in vivo. Here we further investigate whether we could track and quantify changes in the retinal nerve fiber layer (RNFL) in mice with optic nerve crush (ONC) injury.

Methods: Optic nerve crush procedure was performed on C57BL/6 mice. Mice were imaged using vis-OCT before and 12-days after ONC. For each mouse, we acquired four vis-OCT volumes (512 A-lines × 512 B-scans) from the same eye with the optic nerve head (ONH) aligned in the four corners of the field of view. After fibergram processing, the images from each mouse were montaged to generate the final vis-OCT fibergram. The four rectangular OCT image volumes were resampled from each retina to generate a 400 µm radius circumpapillary scan centered on the ONH. After acquiring vis-OCT data at 12-days post ONC, the same retinas were immunostained for RGC axons and imaged by confocal microscopy.

Results: We quantified the thickness of the retina and RGC axon bundle layer before and after ONC using the resampled circumpapillary B-scans. We found a significant reduction in overall retinal thickness as well as in RGC axon bundle layer thickness after ONC. We compared the vis-OCT fibergrams with their corresponding confocal images of flat-mounted retinas at 12-days post ONC. The Sholl regression coefficient (k) value, a measure for RGC axon bundle density, was consistent in vis-OCTF compared with confocal microscopy. Following ONC injury, the vis-OCTF k values increased for three mice that we have monitored, which corresponded to a higher slope in the Sholl regression plot. Our results indicate a faster change in RGC axon bundle density moving away from the ONH. We further quantified the axon bundle width for all five mice, and a 25% reduction in RGC axon bundle width was observed at 12 days after ONC.

Conclusions: Our results show that vis-OCTF can be used to evaluate RNFL damage in vivo in mice with optic neuropathy. The quantifications of lateral RGC axon bundle thickness and density could provide more detailed information for better diagnosis at the earlier stages of optic neuropathies.

CONTROL ID: 3546979

SUBMITTER (NAME ONLY): Kimberly Drenser

TITLE: Retrospective study of ellipsoid zone integrity following treatment with intravitreal ocriplasmin (OZONE study)

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.A. Drenser, Associated Retinal Consultants, Michigan, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kimberly Drenser: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess generalized- (GD) and focal-disruption (FD) of the ellipsoid zone (EZ) in patients with symptomatic vitreomacular adhesion (sVMA) using spectral domain optical coherence tomography (SD-OCT) following a single intravitreal injection of ocriplasmin (0.125 mg).

Methods: OZONE was a Phase 4, retrospective study of patients with sVMA treated with intravitreal ocriplasmin. Data from patients 18 years or older with a diagnosis of sVMA with at least 6 months of follow-up after ocriplasmin were included. A baseline visit within 30 days prior to ocriplasmin was required. SD-OCT was performed at baseline, and before Day 21 post-injection. Early observation (EO) data were obtained from the last SD-OCT scan available prior to Day 21. Last observation (LO) data were obtained from the last SD-OCT scan performed up to a maximum of 6 months post-injection or prior to vitrectomy. The main outcome measure was the development of new and the evolution of existing or new FD/GD by EO and LO. Fisher exact tests were used to assess if baseline characteristics were associated with persistent FD/GD at LO.

Results: The study enrolled 134 eyes of 134 patients from 22 retina centers across the USA. At baseline, 87 eyes (64.9%) had FD, 21 eyes (15.7%) had GD and 26 eyes (19.4%) were without EZ disruption. Among eyes without FD or GD at baseline, 13 (50%) developed FD and 8 (30.8%) developed GD following ocriplasmin. By LO, improvement or resolution of FD/GD was seen in over 80% of these eyes. Presence of FD/GD at baseline was associated with persistent FD/GD at LO ($P < 0.001$) and less than 40% of these eyes had improving or resolving EZ integrity at LO. Presence of MH at baseline was associated with persistent FD ($P = 0.027$), but not GD ($P = 0.281$) at LO.

Conclusions: The finding that a large majority of eyes had FD or GD prior to treatment with ocriplasmin indicates that EZ disruptions are common in sVMA and suggest that FD/GD are likely part of the natural history of this disorder. Presence of EZ disruptions at baseline were associated with persistent disruptions at LO. Given the high prevalence of FD/GD prior to treatment with ocriplasmin, it is likely that EZ disruptions arising after ocriplasmin treatment are at least in part due to the natural history of sVMA. Prospective analyses which include a sham control group would be required to test this hypothesis.

CONTROL ID: 3546981

SUBMITTER (NAME ONLY): Yvonne Adu-Agyeiwaah

TITLE: Intravitreal AAV2-SIRT1 administration reverses diabetic retinopathy in db/db mice

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Adu-Agyeiwaah, B. Asare-Bediako, Department of Optometry, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|C.P. Vieira, S. Li Calzi, M.B. Grant, Department of Ophthalmology, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|S.S. Hammer, J.V. Busik, Department of Physiology, Michigan State University, East Lansing, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy, a common complication of diabetes has been associated with the downregulation of the Sirtuin 1(SIRT1) gene. SIRT1 is a nutrient-sensing deacetylase whose dysfunction can result in chronic metabolic abnormalities. Previously we showed that activation of SIRT1 signaling in vivo reduced diabetes-induced inflammation, neural and vascular degeneration, and impairment in visual function. In this study, we examined the effect of intravitreal SIRT1-AAV therapy on reversal of diabetic retinopathy.

Methods: db/db mice were given either control virus (GFP-AAV2) or SIRT1-AAV2 via intravitreal injection at 9 months. Mice were euthanized at 12 months. Retina, peripheral blood cells and bone marrow cells were collected. Vascular changes were assessed by enumeration of acellular capillaries and retinal immune cells were assessed using flow cytometry. Immunohistochemistry was performed for SIRT1 to confirm upregulation, caspase 3 for apoptosis and IBA-1 for microglial activation. Neural function was assessed using electroretinogram responses and optomotor responses.

Results: SIRT1-AAV2 treated db/db mice showed increased retinal SIRT1 mRNA compared to control virus treated db/db mice (3 ± 0.9 vs 0.5 ± 0.1 respectively) and the number of SIRT1 positive cells in the retina was higher in SIRT1-AAV2 db/db mice (28.4 ± 6) compared to control virus treated db/db mice (13.9 ± 2). The number of acellular capillaries were reduced in SIRT1-AAV2 treated db/db mice (8.8 ± 3) compared to db/db mice (11.1 ± 4). Retinal Iba1⁺ cells were increased in db/db mice injected with control virus (9 ± 2) and reduced in SIRT1-AAV2-treated db/db mice (4 ± 1). Caspase-3 expression was reduced in SIRT1-AAV2-treated db/db mice (15 ± 5) compared to db/db mice (8 ± 3). There was a significant improvement in the b-wave in the ERG scotopic response in SIRT1-AAV2 db/db mice (326 ± 43) compared to db/db (188 ± 39). The retinal visual function as determined by optokinetic responses was improved in SIRT1-AAV2 treated db/db mice (0.39 ± 0.01) compared to the db/db mice (0.28 ± 0.02).

Conclusions: We demonstrate that diabetic retinopathy can be prevented using a SIRT1-AAV2 intravitreal administration. We show that in addition to reduction in retinal inflammation and apoptosis, SIRT1 treatment preserved retinal bipolar cells and retinal visual function and response can be restored using this therapy.

CONTROL ID: 3546982

SUBMITTER (NAME ONLY): Cynthia McClard

TITLE: Utility of Genetic Testing for Inherited Retinal Diseases in a Real-world Clinical Setting

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. McClard, F. Jamshidi, D. Pollalis, S. Lee, Ophthalmology, Dean McGee Eye Institute, Oklahoma City, Oklahoma, UNITED STATES|S. Lee, Physiology, The University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, UNITED STATES|

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ABSTRACT BODY:

Purpose: Attention to genetic testing for patients with inherited retinal diseases (IRD) has increased among patients and clinicians due to significant advances in genomics and gene therapy. However, routine genetic testing for clinically diagnosed IRD is not currently common practice for reasons including extra cost and clinicians' limited familiarity with its utility. In the current study, we share our experience in genetic testing of clinically diagnosed IRD patients using no-charge panel genetic testing.

Methods: Retrospective case analysis was performed of patients clinically diagnosed with IRD, who elected to undergo molecular genetic testing from 2019 to 2020 at a single academic center. Testing was performed with a saliva kit, in which 248 genes were assayed from a kit provided by Invitae (San Francisco, CA, USA) and sponsored by Spark Therapeutics (Philadelphia, PA, USA).

Results: Forty-seven patients (M 21: F 26) were included. The following diagnoses were represented:

1) photoreceptor disease (30/47, 63.8%), including retinitis pigmentosa (RP) (21/47, 44.7%), cone and cone-rod dystrophy (4/47, 8.5%), and syndromic RP (5/47, 10.6%); 2) macular diseases (11/47, 23.4%), including Stargardt's (5/47, 10.6%); and 3) other diseases (6/47, 12.8%), including choroideremia (3/47, 6.4%) and X-linked retinoschisis (2/47, 4.3%). Disease-causing genotypes were identified in 46.8% of patients (22/47), 42.3% in RP (11/26), 80% in Stargardt's (4/5), and 100% in choroideremia (3/3). Undetermined genotypes in 53.2% (25/47) patients were due to identifying either one recessive pathogenic mutation or multiple variants of unknown significance (VUS). Common VUS identified in our cohort were USHA2A(7), TUBGCP6 (6), CDH23(6), FSCN2(6), PCDH15(6), WHRN(6), ABCA4(5), and EYS(5).

Conclusions: Here, we report the results of currently available no-charge panel genetic testing to explore its utility in an established IRD clinic setting. We further plan to examine how testing utility may change depending on demographics or in phenotypic subdivisions in our cohort. Further studies interpreting the frequency of VUS and whether and how VUS are related to disease in our cohort will be pursued. In doing so, we aim to provide early guidance for retina specialists on the value of genetic testing in the practical management of IRDs.

CONTROL ID: 3546985

SUBMITTER (NAME ONLY): Nazanin Mirzaei

TITLE: Retinal tauopathy colocalizes in sites of synaptic loss in patients with mild cognitive impairment and Alzheimer's disease

SESSION TITLE: Retinal Degenerations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Mirzaei, J. Sheyn, A. Rentsendorj, D. Fuchs, M.R. Davis, K.L. Black, Y. Koronyo, M. Koronyo-Hamaoui, Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|D. lee, M. Selenica, Medicine, University of Kentucky, Lexington, Kentucky, UNITED STATES|R. Kayed, Neurology, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|P. Davies, Medicine, Northwell Health Feinstein Institutes for Medical Research, Manhasset, New York, UNITED STATES|C.A. Miller, Pathology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M. Koronyo-Hamaoui, Biomedical Sciences, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mounting evidence suggests that Alzheimer's disease (AD) neuropathological changes are also present in the retinae of patients. These include the proteinaceous accumulation of amyloid- β (A β) and hyperphosphorylated tau (pTau) assemblies, gliosis, vascular abnormalities, pericyte loss, and neurodegeneration. Electroretinogram and visual deficits, likely driven by these retinal pathologies, are also documented. Among the main neuropathological hallmarks of AD, tauopathy remains considerably understudied in the retina. Given that cerebral tauopathy is closely linked to neuronal loss and the severity of cognitive deficits in AD patients, it is possible that similar relations exist in the retina between pathologic tau burden, synaptic loss, and neurodegeneration. These may serve as biomarkers of not only retino-visual irregularities but also brain disease and cognitive status.

Methods: Here, using immunohistochemical approaches we visualized and quantified the spatial burden of various AD-related tau species, including pTau, oligomeric and citrullinated tau, and neurofibrillary tangles (NFTs) in the central and peripheral regions of post-mortem retinae from mild cognitive impairment (MCI) and AD patients, relative to cognitively normal controls (NC). Levels of synaptic biomarkers in the retina, as well as the thickness of retinal layers, were also measured in the same cohort of human donors.

Results: Elevated levels of various pTau sites were found in a geometric-dependent manner in the retinae of MCI and AD patients compared to NC. Increased burden of NFTs and citrullinated tau were also identified in retinal layers that were associated with higher retinal synaptic loss and neuronal atrophy. Investigations of retinal cell type susceptibility to tauopathy, including oligomeric tau accumulation in early and late disease stages, reveals the vulnerability of certain retinal neurons in MCI and AD patients.

Conclusions: To date, our results provide new evidence for the presence of AD-specific tauopathy and related synaptic loss as well as neuronal-specific susceptibility in the AD retina, similar to those observed in the brain.

CONTROL ID: 3546986

SUBMITTER (NAME ONLY): Natalia Mussi

TITLE: Mitochondrial and metabolic alterations in diabetic corneal epithelial cells

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Diabetic keratopathy affects up to 70% of patients with diabetes. Mitochondrial dysfunction is considered a central feature underlying diabetic complications. The purpose of this study was to characterize mitochondrial and metabolic alterations in primary cultured diabetic human corneal epithelial cells (HCECs) and in telomerase-immortalized human corneal epithelial (hTCEpi) cells exposed to hyperglycemic and hyperosmotic stress.

Methods: To determine the effects of diabetes on mitochondria and metabolism, donor human corneas from diabetics were obtained from Tissue Transplant Services at UT Southwestern Medical Center. Primary cultures were generated using an established lab protocol. HCECs and hTCEpi cells were cultured in a defined serum-free keratinocyte growth media containing 6 mM glucose. To determine the effects of hyperglycemia on hTCEpi cells, cells were cultured for 24 hours, 7 or 14 days in media containing an additional 19 mM glucose. Cells supplemented with 19 mM mannitol were used as an osmotic control. Mitochondrial morphology and polarization were assessed using MitoTracker and TMRE, respectively. Metabolic changes were quantified in real time using a Seahorse metabolic flux analyzer. Cell cycle was determined by staining with Propidium Iodide and analyzed using a Celigo imaging cytometer. Reactive oxygen species were measured using Amplex red. Expression of the mechanistic target of rapamycin (mTOR) and downstream effectors were assessed by western blot.

Results: Diabetic HCECs demonstrated variable growth rates in culture. Similarly, mitochondrial morphology varied greatly among diabetic HCECs ranging from mild to severe with robust fragmentation and depolarization. Exposure of hTCEpi cells to high glucose shifted cells towards a respiratory phenotype. Cell cycle was unaltered at 24 hours and at day 7. After 14 days of culture, hTCEpi cells in mannitol arrested in G2/M and this was associated with a decrease in mTOR expression.

Conclusions: These findings confirm the presence of mitochondrial and metabolic abnormalities in the diabetic corneal epithelium. Further studies are needed to determine the molecular mechanisms that underly these changes.

CONTROL ID: 3546987

SUBMITTER (NAME ONLY): Miruna Ghinia-Tegla

TITLE: SALL1 acts downstream of ONECUT1 to repress the rod photoreceptor generation

SESSION TITLE: Regulating Photoreceptor Development and Disease

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: The proper development of cone and rod photoreceptors (PRs) requires the timed activation of different genetic programs. Alterations in these specific programs trigger developmental defects of cell fate specification, that are likely to yield visual impairments.

Methods: Previous reports show that ONECUT1 (OC1) is involved in the repression of gene regulatory networks that trigger rod genesis (Emerson et al., 2013). To explore its contribution in the early decision of photoreceptor (PR) specification, we electroporated CrxEnh1::GFP (active in both cone and rods) and CAG::OC1Enr (a repressor form of OC1), at E5 in the chick retina (Jean-Charles et al., 2018). Transcriptomes of these cells were generated after culturing whole retinas for 2 day in vitro. Several rod-related genes were upregulated, while most cone-related genes were downregulated. We next screened candidate genes to test their involvement in the repression of rod programs, taking the following approach: retinas were electroporated at E5 with a reporter plasmid that drives GFP expression after the activation of the Rhodopsin promoter (Rho::GFP) (Jean-Charles et al., 2018), with either CAG::Enr or CAG::OC1Enr, in addition to an overexpression plasmid, that allowed the forced expression of each candidate genes.

Results: We identified that overexpression of SALL1 was able to reduce the early induction of Rhodopsin triggered by OC1 repression. We confirmed the expression of SALL1 in the cones of the chick retina as well as in the developing human retina, using retinal organoids. In addition, overexpression of SALL1 showed an increase number of RXRG-positive PRs.

We also analyzed SALL1 loss-of-function in the developing chick retina using CRISPR/Cas9. We determined that upon SALL1 gene editing, the Rhodopsin promoter was activated and the rod pathway was turned on.

Conclusions: We report for the first time that a cone-enriched gene, SALL1, that acts downstream of OC1 to repress the rod genesis pathway.

CONTROL ID: 3546989

SUBMITTER (NAME ONLY): Niranchana Manivannan

TITLE: Weighted feature point matching for registration of widefield fundus images

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As most features in the retina are found in the posterior pole, including the optical nerve head (ONH), the performance of registration algorithms when applied to widefield fundus images is generally sub-optimal in the periphery. In this research, we propose a weighted feature matching (WFM) to improve registration over the entire field of view of the widefield image.

Methods: Figure 1 shows the steps of the proposed algorithm. Both fixed and moving image pairs for registration are channel separated. Green channel is used for ONH detection [1]. Cornerness map from multi-scale Harris corner detection is multiplied with w_i before thresholding. If the fixed image is of size $m \times n$ and d_i is pixel distance from either the ONH (if detected) or from the center of the image (if ONH is not detected), the weighting factor is $w_i = d_i / (m \times n)$. Weighted vector distances between histogram of oriented gradients (HOG) descriptors (16×16 patches) are used for the feature point matching. Two registered images with and without WFM are generated for comparison.

Baseline and follow up images from 44 subjects (22 healthy and 22 with choroidal tumors, therapy-induced retinopathy, diabetic retinopathy and glaucoma) are acquired using CLARUSTM 500 (ZEISS, Dublin, CA). For each pair of images, cselect function in MATLAB is used to label 10 landmarks/points per image (5 in the center and 5 in the periphery). The angular distance between the points in the registered images should be zero degrees for perfect registration. The mean angular distance with and without WFM are calculated for the quantitative evaluation.

Results: The mean angular distance between the points in the registered images with and without WFM are $0.60 \pm 0.31^\circ$, $0.73 \pm 0.38^\circ$ (all points), $0.56 \pm 0.25^\circ$, $0.54 \pm 0.28^\circ$ (central points) and $0.63 \pm 0.35^\circ$, $0.92 \pm 0.38^\circ$ (peripheral points). With WFM, the overall performance of the registration is improved by 17.8% while the performance in the center of the image is decreased by 2.2%. Figure 2 shows the registered image with and without WFM.

Conclusions: The proposed registration with WFM improves the overall registration of the widefield fundus image by improving the performance in the periphery with minimum reduction to the performance in the center of the image.

Reference:

[1] Meng et al. IOVS 2020; 61(9): Abstract PB0060.

CONTROL ID: 3546992

SUBMITTER (NAME ONLY): Michael Sun

TITLE: Custom Ampliseq Targeted Sequencing Panel For Orphan Pediatric Retinal Diseases: Norrie Disease, FEVR, and Retinoschisis

SESSION TITLE: Genetics, (gen)omics, systems and computational biology in ocular health and disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sun, W.A. Dailey, A. Petrelli Cicerone, J. Felisky, K. Moyer, N. Haque, A. Guzman, K.P. Mitton, Eye Research Institute, Rochester, Michigan, UNITED STATES|M. Sun, Oakland University William Beaumont School of Medicine, Rochester, Michigan, UNITED STATES|K. Mellert, K.A. Drenser, Associated Retinal Consultants LLC, Royal Oak, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: DNA-sequencing is not readily available in countries with little research resources or where health insurance does not cover the costs even for those who have it. This is especially true for very rare (orphan) inheritable retinal diseases. We wanted to develop a rapid targeted-sequencing protocol for eight genes involved in Familial Exudative Vitreo-Retinopathy (FEVR), Norrie Disease, and Retinoschisis, at greatly reduced cost. Furthermore, we desired a workflow which could be deployed locally and support training in human genomics for science and medical students

Methods: DNA is extracted from 100 uL samples of whole frozen blood. An Ampliseq targeted-panel (180 amplicons) for 8 genes was designed with illumina's DesignStudio Sequencing Assay Designer, distributed into three pools (PCR reactions) per patient sample for complete coverage of 83 exons with 25 bp adjacent intron sequence. Target Genes were: NDP (ChrX), RS1 (Chr10); CTNNB1 (Chr3); TSPAN12 (Chr7); KIF11 (Chr10), FZD4 (Chr11), LRP5 (Chr11), ZNF408 (Chr11). Ampliseq libraries were quality controlled by capillary electrophoresis (Agilent Bioanalyzer) and several sample pool sizes were tested for capacity and coverage using sequencing and variant calling on the Illumina iSeq-100 platform.

Results: An average 2500-times read coverage was obtained for a pool of 16 patient libraries and 800-times for a pool of 48 patient libraries. Numerous potential disease-associated variants were detected in targeted libraries from patients diagnosed with Norrie Disease, FEVR, and Retinoschisis. Average numbers of variants per patient for the 48 patient pool were: 19.5 ± 1.6 SNVs, 0.6 ± 0.2 Inserts, and 0.6 ± 0.2 Deletions.

Conclusions: We developed a targeted exome-sequencing protocol using Illumina Ampliseq reagents and the iSeq-100 platform for three rare pediatric retinal diseases. Coverage validated the ability to pool 40-50 patients per run for eight genes and provides for excellent base call accuracy ($>Q30$). Over 90 patient samples were successfully sequenced during validation. Potential mono and digenic variant contributions in FEVR patients are detectable by testing multiple genes. Research analysis costs were reduced to \$250 per patient and now involve an academic eye research institute / retinal clinic research partnership.

CONTROL ID: 3546993

SUBMITTER (NAME ONLY): Bharani Krishna Mynampati Arunadithya

TITLE: Evaluation of Cytotoxicity of Anti-VEGF Molecules on Vascular Endothelial Growth Factor Enriched Choroidal Vascular Endothelial Cells

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Mynampati Arunadithya, S. grover, Ophthalmology, University of Florida Health, Jacksonville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Anti-VEGF therapy is currently an effective standard treatment for AMD; exploring the other possible pathways may provide an alternative strategy in the treatment of AMD. This includes combination of various anti-VEGF molecules such as Pazopanib, Palomid 529 and Bevacizumab (avastin) for targeting vascular endothelial growth factor (VEGF). However, the dose, time and combination effects of these molecules on VEGF-enriched choroidal vascular endothelial cells (CVECs) has not been well established in invitro. We evaluated the cytotoxicity of combination doses of Pazopanib, Palomid 529 and bevacizumab on CVECs.

Methods: Choroidal vascular endothelial cells (CVECs) were treated with VEGF (50ng/ml) and were treated with Bevacizumab, Palomid529, Pazopanib, Bevacizumab +Palomid 529, Bevacizumab +Pazopanib, Pazopanib+Palomid 529. Cell proliferation changes analyzed with water-soluble tetrazolium salts (WST-1) assay. Cytotoxicity was evaluated by trypan blue exclusion assay at different time intervals i.e 48h, 72h, 1 week. Simultaneously reactive oxygen species levels were also measured using dihydrorhodamine 123 at similar intervals. Apoptotic marker such as caspase 3 was also measured at 72h interval.

Results: VEGF-enriched CVECs treated with Bevacizumab, Palomid 529, Pazopanib, Bevacizumab+Palomid 529, Bevacizumab+Pazopanib, Pazopanib+Palomid 529 inhibited the proliferation of CVECs. CVECs showed a significant decrease in the cell proliferation rates when treated with combination of anti-VEGF molecules in comparison to single anti-VEGF molecules and to controls ($p < 0.0001$). Similarly, cell viability numbers also significantly reduced in combination of anti-VEGF molecules in comparison to single anti-VEGF molecule and to controls ($p < 0.0001$). Further, ROS levels were found to be significant in combination of anti-VEGF groups compared to drugs alone and controls ($p < 0.01$). Similarly, apoptotic marker caspase 3 levels were found to be increased by 10 folds in (Palomid 529+ Pazopanib) group compared to any other groups and control.

Conclusions: Although anti-VEGF molecules are effective in controlling the proliferation and cell viability rates of VEGF-enriched CVECs, a combination of these anti-VEGF molecules are more effective in inhibiting the cell proliferation rates than any one anti-VEGF molecule alone in comparison to control.

CONTROL ID: 3546995

SUBMITTER (NAME ONLY): Rebecca Schmidt

TITLE: E-cadherin and Par 3 expression in conjunctival melanoma and squamous cell carcinoma

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Cell-cell adhesion and cell-polarity protein complexes coordinate crucial processes that ensure epithelial integrity. Among these, the cell-cell adhesion molecule E-cadherin and the polarity protein PAR3 serve important functions in epithelial tissues and its loss is associated with dermal melanoma progression and elevated metastasis. The role of PAR3 or E-cadherin in conjunctival melanoma (CM) and in conjunctival squamous cell carcinoma (SCC) remains open. This study aims to analyze the expression of these central markers for cell-cell adhesion and cyto-architecture to gain insight into molecular changes during ocular surface tumor progression.

Methods: The expression of epithelial PAR3 and E-cadherin in 32 patients with human SCC, CM and the corresponding precancerous lesions have been analyzed immunohistochemically in formalin-fixed paraffin-embedded tissues.

Results: In SCC and its precancerous lesions conjunctival intraepithelial neoplasia (CIN) I-III, E-cadherin expression was significantly decreased compared to controls. Melanocytes and keratinocytes in healthy conjunctiva were E-cadherin positive. In CM E-cadherin expression was reduced. Conjunctival carcinomas switch their E-cadherin expression from extra- to intracellular. PAR3 was statistically significantly decreased expressed in the epithelium of CIN I-III, SCC, CM, and the melanoma in situ probes compared to controls.

Conclusions: In CIN, SCC, and CM a reduction of the cell-cell adhesion molecule E-cadherin and the polarity protein PAR3 is seen. This indicates that during carcinogenesis even the premalignant lesions lose expression of these markers. Loss of PAR3 and extracellular E-cadherin expression might be used as additional diagnostic tools to separate premalignant from benign lesions in the future and as a potential therapeutic target.

CONTROL ID: 3546997

SUBMITTER (NAME ONLY): Eleni Gatzios

TITLE: The Impact of the COVID-19 Pandemic on Adults with Visual Impairments in Canada

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Gatzios, Public Health Sciences, Queen's University, Kingston, Ontario, CANADA|E. Gatzios, M. Sukhai, C. Robbins, K. Forestell, CNIB, Toronto, Ontario, CANADA|M. Sukhai, Ophthalmology, Faculty of Health Sciences, Queen's University, Kingston, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The COVID-19 pandemic has had a substantial impact on society but has disproportionately affected the disability population. The CNIB COVID-19 Impact Survey was distributed throughout Canada in May 2020 to gather information on the experiences of adults with visual impairments during the pandemic. This cross-sectional study identified key aspects in which those with vision loss have been impacted by the pandemic and associated policies and procedures.

Methods: Analyses were conducted using IBM SPSS version 22 statistical software. Conventional descriptive statistics were used to describe the sample. Data were cross-tabulated by age, age of sight loss onset, severity of sight loss, other disability or health condition, employment status, and education.

Results: Approximately half (51%) of the sample had concerns about their healthcare, and just over half (58%) said they did not know where to get tested for SARS-CoV2.

Key concerns reported by respondents included:

1. Touching things in public such as elevator panels, self-serve kiosks, or restroom doors to check signage (68% agreed).
2. Due to social distancing, they feel more depressed, sad, and lonely (64% agreed).
3. Because the individual does not drive, they will not be able to get themselves or a family member to a COVID-19 test centre or to a hospital or healthcare facility if they present with severe COVID-19 symptoms (61% agreed).
4. Getting access to accurate and current information about those who may be infected in their area (59% agreed).
5. Concern about accessing emergency medical services (50% agreed).
6. Unsure how to maintain appropriate social distance in public (48% agreed).

Conclusions: The COVID-19 pandemic has impacted those with sight loss in many ways and in many different aspects of their lives. This study gave key insights into barriers affecting the societal participation of those with sight loss. While the findings of this study may have evolved over the course of the pandemic, these concerns are important for all levels of policy and advocacy leads to take into account while developing and revising existing policies. This study has provided evidence for the development of new policies and procedures, and the evaluation of existing policies and public health procedures to ensure those with sight loss are not put at an even greater disadvantage during these times and are able to receive the necessary supports.

CONTROL ID: 3546998

SUBMITTER (NAME ONLY): Prashanth Iyer

TITLE: Analysis of Choriocapillaris Flow Deficits Before and After Tears of the Retinal Pigment Epithelium using Swept Source OCT Angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Iyer, Y. Shi, O. Trivizki, M. Shen, W.J. Feuer, G. Gregori, P.J. Rosenfeld, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|Z. Chu, R.K. Wang, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tears of the retinal pigment epithelium (RPE) occur in age-related macular degeneration (AMD) as part of normal disease progression or after injections with anti-VEGF. This provides opportunity to investigate two questions: does the presence of an intact pigmented RPE interfere with our ability to measure choriocapillaris (CC) flow deficits (FDs) and is the survival of the CC dependent on an intact overlying RPE. To answer these questions, we compared our CC FD measurements before and after a RPE tear and followed the change in CC FDs over time once the overlying RPE was removed.

Methods: Patients with AMD who developed RPE tears were enrolled in a prospective, swept source OCT (SS-OCT) imaging study and 6x6 mm scans centered on the fovea were acquired (PLEX^o Elite 9000, Carl Zeiss Meditec, Dublin, CA). Scans were obtained before and after the RPE tear formation, and during follow-up visits. CC FDs were measured at the site of the tear and within a control region symmetrically positioned to the fovea.

Results: Three AMD patients were followed before and after the RPE tear developed for 18 months. Two patients had a history of type 1 macular neovascularization and anti-VEGF therapy, and one patient had non-neovascular AMD. All three had macular CC FD that were previously determined to be within the 95% normal limits for age-adjusted eyes. When CC FD before the RPE tear were compared with those at the first post-tear visit, the average CC FD percentage decreased -0.7% in region of tear and -1.0% in control region ($p=0.92$, paired t-test). When CC FD from the first post-RPE tear visit were compared to 18-month follow-up visit, the average CC FD percentage decreased -1.9% in region of tear and increased +2.0% in control region ($p=0.31$, paired t-test).

Conclusions: SS-OCTA imaging of eyes with RPE tears indicate that there were no significant changes in CC FD before and after the RPE tears. Although the sample size was small, it appears that our CC algorithm for measuring FDs is reliable demonstrated by consistent measurements before and after the RPE was removed. Furthermore, removal of the RPE did not lead to significant changes in the CC over 18 months. This differs from animal studies demonstrating that RPE removal resulted in rapid loss of CC. The relationship between CC and RPE may not be absolute as previously believed.

CONTROL ID: 3547000

SUBMITTER (NAME ONLY): Morgan Basta

TITLE: UTX demethylase function is required to decondense chromatin to create a “window of opportunity” for reprogramming to a fibrotic fate

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Basta, H. Paulson, S. Petruk, A. Mazo, J.L. Walker, Thomas Jefferson University, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of this study is to determine how a cell becomes epigenetically reprogrammed to a myofibroblast fate associated with lens fibrotic disease. For cell reprogramming to occur, transcription factors (TF) must overcome a condensed chromatin barrier typically marked by H3K27me3. Here, we investigated how chromatin structure becomes re-established shortly after DNA replication in myofibroblast progenitor cells to identify the “window of opportunity” for the adoption of a new pro-fibrotic transcription program.

Methods: Studies were performed in an ex-vivo mock cataract surgery wound healing/fibrosis chick embryo model to examine cell reprogramming to a myofibroblast fate, which occurs by 72hr post-injury. The chromatin assembly assay (CAA) was used to study how chromatin structure becomes re-established at the time of replication during cell reprogramming. To determine if TF binding occurs during replication, S phase entry was blocked by thymidine treatment. We examined how blocking ubiquitously transcribed tetratricopeptide repeat, X chromosome (UTX) demethylase function impacts both wound healing and reprogramming to a fibrotic phenotype.

Results: CAA revealed a delay in the accumulation of H3K27me3 on nascent DNA at 28hr post-injury, while at 48hr post-injury H3K27me3 accumulation was rapid. Thus, revealing a “window of opportunity” when chromatin is decondensed and amenable to new TF binding for cell reprogramming. The status of H3K27 is controlled by H3K27 modifying enzymes, the demethylase UTX and the methyltransferase enhancer of zeste homolog 2 (EZH2). By CAA, both UTX and EZH2 were recruited to nascent DNA at 28hr post-injury. However, blocking UTX function led to an accumulation of H3K27me3 to nascent DNA. This suggests that UTX masks EZH2 function to maintain a decondensed chromatin state for cell reprogramming. Recruitment of the pro-fibrotic TF, myocardin related transcription factor A (MRTF-A) to nascent DNA occurred during the “window of opportunity” and specifically at the time of replication. Lastly, we found that UTX demethylase function was required for MRTF-A binding to nascent DNA and transition to a fibrotic phenotype without preventing wound healing.

Conclusions: UTX demethylase activity is required to decondense post-replicative chromatin structure to make it amenable to the adoption of a new fibrotic transcription program.

CONTROL ID: 3547001

SUBMITTER (NAME ONLY): Delaram Mirzania

TITLE: Factors Associated with Ophthalmology Referral from a Teleretinal Screening Program in a Federally Qualified Health Center

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Mirzania, A. Song, N. Johnson, A. Ayala, K. Muir, A.C. Thompson, Duke Eye Center, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|K. Muir, Ophthalmology, Durham VA Medical Center, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Early detection of diabetic retinopathy (DR) and glaucoma is crucial to preventing vision loss. Previous studies have evaluated teleretinal screening programs for DR in well-insured populations. The purpose of this retrospective, observational study was to evaluate a teleretinal screening program in a population of uninsured and underinsured patients.

Methods: We conducted a retrospective chart review of patients (age \geq 18) who underwent teleretinal imaging (TRI) at a federally qualified health center between January 1, 2015 and September 4, 2019. TRI gradings, patient demographic information, relevant medical history, laboratory data, and information from subsequent ophthalmology visits were abstracted. Generalized estimating equations were used to identify factors associated with ophthalmology referral and adherence to ophthalmology referral.

Results: 3130 TRI were graded in 2216 eyes from 1108 patients. Only 47.4% (N=184) of the 388 patients referred for a dilated fundus examination based on TRI followed up with ophthalmology as recommended. Adherence to the recommended ophthalmology exam was not associated with any of the baseline clinical or demographic characteristics ($p>0.10$). Referral to ophthalmology based on TRI gradings was associated with a greater likelihood of also having diabetic nephropathy, diabetic neuropathy, hypertension, proteinuria, $GFR<60$, older age, and higher hemoglobin A1c (all $p<0.05$). Female (odds ratio [OR], 0.75; $p=0.001$) and Hispanic patients (OR, 0.79; $p=0.009$) were less likely to receive an ophthalmology referral compared with male and non-Hispanic patients respectively. In a multivariable model, older age, male sex, proteinuria, and A1c remained significantly associated with a greater likelihood of ophthalmology referral (all $p<0.05$). There was high agreement between TRI gradings for glaucoma or DR and final diagnoses for patients who underwent subsequent ophthalmology examination (88.9% and 92.1% respectively).

Conclusions: In this study of uninsured/underinsured patients, those referred to ophthalmology based on TRI were more likely to have other complications of diabetes. However, fewer than 50% of patients attended the recommended follow-up examination. Improved care coordination is critical to ensure patients adhere to follow-up recommendation for a dilated fundus examination following teleretinal screening.

CONTROL ID: 3547002

SUBMITTER (NAME ONLY): Nicholas Johnson

TITLE: Temporal relationship between ERG waveforms and the firing patterns of rat retinal ganglion cells

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Johnson, Molecular Physiology and Pharmacology, USF Health Morsani College of Medicine, Tampa, Florida, UNITED STATES|Y. Mohamed, C.L. Passaglia, Medical Engineering, University of South Florida College of Engineering, Tampa, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The contribution of retinal ganglion cell (RGC) activity to noninvasive measures of retinal health such as the electroretinogram (ERG) is a topic of clinical interest. We simultaneously recorded RGC spike trains and the full-field ERG for various stimulus paradigms to directly determine how ERG waveforms relate to the timing and pattern of activity in different RGC types.

Methods: Adult Brown Norway rats were kept at an anesthetic plane under a mixture of ketamine and xylazine. A craniotomy was performed at Bregma and a tungsten-in-glass electrode was advanced into the optic nerve to record the RGC spike trains. A gold ring electrode was placed on the limbus of the eye to record the ERG. Visual stimuli consisted of full-field flashes (10 – 500ms duration) of light ($0.018 - 1800 \text{ cd/m}^2/\text{s}$) or darkness ($1.8 \text{ cd/m}^2/\text{s}$ background) and full-field flicker (4 – 64 Hz) of 0.5 – 2 s duration presented via an LED-illuminated Ganzfeld dome. Tetrodotoxin (TTX; $6\mu\text{M}$) was used to block spiking activity.

Results: Spike trains from ON RGCs cluster into 'spike volleys' that correspond to oscillatory potentials in the ERG to bright flashes ($n=15$; $R^2>0.95$, $p<0.05$). Under these conditions, spike trains from OFF cells do not cluster into volleys but fire during the descending phase of the b-wave. Dark flashes produce a weak negative ERG wave analogous to the b-wave ($n=6$). Spike trains from OFF RGCs occur near the peak of the negative wave. The first harmonic amplitude of ON-transient ($n=1$) and OFF transient ($n=9$) RGC responses differed for short-duration flicker ($p<0.05$) but not for long-duration flicker. It did not differ for either short- or long-duration flicker for ON sustained ($n=14$) and OFF sustained ($n=3$) RGCs. TTX altered the ERG but did not eliminate OPs. Furthermore, cross correlation between the spontaneous activity of RGCs and the ERG did not reveal significant correlation ($n=9$).

Conclusions: OP generators in the retina drive oscillatory spike patterns in RGCs. Contrary to prior studies, there were no significant differences in the flicker responses of ON- and OFF-pathways.

CONTROL ID: 3547003

SUBMITTER (NAME ONLY): Lyna Azzouz

TITLE: Remote monitoring device for tracking the progression of Age-Related Macular Degeneration: Device and hardware validation

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Azzouz, A. Yim, A. Yu, University of Michigan Medical School, Ann Arbor, Michigan, UNITED STATES|Y.M. Paulus, Ophthalmology and Visual Sciences, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: COVID-19 has created a strong need for telemedicine and remote monitoring. Remote monitoring is especially important for diseases such as age-related macular degeneration (AMD), because prompt detection of subtle changes indicating neovascularization is critical to prevent blindness. This describes a novel, digital, handheld standalone device that delivers at-home AMD monitoring for patients and a hardware validation of that new device.

Methods: A prototype device (KalEYEdoscope) was developed consisting of an injection-molded 3D printed shell with a graduated focusing mechanism with a 10x magnifying 22mm biconcave lens, two tactile buttons, a battery, a processing unit, and a small OLED screen (Figure 1). The electronics include a battery powered small single-board computer (Raspberry Pi 3) connected to a 1.5-inch RGB OLED screen and two pushbuttons. The device is inherently monocular. The software uses the concept of shape discrimination hyperacuity to identify the patient's minimum distortion-detection threshold (MDDT). Upon use, the screen displays a series of circle-like images and, after each image, asks the user whether the image previously displayed appeared to be a perfect circle. The software then converges to the user's MDDT based on user input. Data is collected longitudinally and analyzed to determine a change in patient condition, which is then communicated as a message on the screen.

Results: Hardware validation was performed. The device had a weight of 0.211 kg and diameter of 61 mm. There was an appropriate push button resistance of 1.52 N, meeting the required engineering specifications of 1.4 to 5.6 N. The screen transition time was 0.7 seconds, and it took 1.834 seconds for the circle to appear on the screen. The total boot time of the software was 20.21 seconds, which was below the target of 30 seconds.

Conclusions: A digital, hand-held standalone device can be created that is compact, lightweight, and meets targeted engineering and design specifications for hardware and software. This device could have potential in performing home monitoring of AMD progression using shape discrimination hyperacuity to identify the patient's minimum distortion-detection threshold.

CONTROL ID: 3547004

SUBMITTER (NAME ONLY): Corey Lacher

TITLE: Retinal Vessel Diameter Reductions in Pre-perimetric Glaucoma correlate with Pattern Electroretinogram and Foveal Avascular Zone Area Parameters

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Lacher, A. Tirsi, J. Tsai, V. Gliaglias, S. Park, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|A. Tirsi, S. Park, S.A. Obstbaum, C. Tello, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|D. Orshan, New York Institute of Technology, Old Westbury, New York, UNITED STATES|P.H. Derr, Diopsys Inc., New York, UNITED STATES|S. Tello, Rye High School, Rye, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent literature suggests that average retinal vessel diameter is decreased in patients with open-angle glaucoma. We performed a prospective, observational cross-sectional study to determine whether changes in retinal vessel diameters were associated with steady state pattern electroretinogram (ssPERG) and Foveal Avascular Zone (FAZ) area parameters in patients with pre-perimetric glaucoma (PPG).

Methods: Five patients (8 eyes) with normal Humphrey 24-2 visual field tests, suspicious optic nerve head findings and with refractive errors $< \pm 5.0$ Diopters were enrolled in the study conducted at Manhattan Eye Ear and Throat Hospital. Participants underwent comprehensive ophthalmological examination and tests on Humphrey Field Analyzer (HFA) , Diopsys NOVA PERG and the Cirrus HD OCT-A Angioplex devices. Average vessel diameter of retinal arteries and veins was calculated using the vessel analysis plug-in on ImageJ. FAZ area was determined using ImageJ. Correlation analyses among vessel diameters, FAZ area and ssPERG parameters [Magnitude (Mag), MagnitudeD (MagD) and MagD/Mag ratio], were assessed to characterize these associations (Pearson's). P values < 0.05 considered statistically significant.

Results: Results were gathered from 8 eyes of 5 patients aged 59.90 ± 14.20 years of age, with mean IOP 18.30 ± 4.50 and HFA 24-2 mean deviation 0.21 ± 0.94 . Average vessel diameter was negatively correlated with FAZ area ($r = -0.955$, $p < 0.01$) and positively correlated with both ssPERG parameters MagD ($r = 0.733$, $p < 0.05$) and MagD/Mag ratio ($r = 0.819$, $p < 0.05$). No associations were observed between vessel diameter and Mag. FAZ area was negatively associated with MagD, however, this relationship was not significant ($r = -0.347$, $p = 0.055$).

Conclusions: To best of our knowledge, this is the first study to confirm the relationship between reductions in average vessel diameter measurements with abnormal ssPERG and enlarged FAZ area parameters in patients with PPG. These results suggest that retinal vascular abnormalities and retinal ganglion cell dysfunction may be present before changes in visual field tests. Future investigations are needed to better understand the relationships between arteriolar and venular diameters, as well as the effects of systemic diseases on vessel diameters.

CONTROL ID: 3547005

SUBMITTER (NAME ONLY): Dejuan Kong

TITLE: Inactivation of Mechanistic Target of Rapamycin Complex 1 Results in Loss of Retinal Ganglion cells

SESSION TITLE: Ganglion cells and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Kong, L. Elghazi, H. Hager, M. Losiewicz, S. Shanmugam, P.E. Fort, T.W. Gardner, S.F. Abcouwer, Department of Ophthalmology and Visual Science, University of Michigan, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mechanistic target of rapamycin (mTOR) signaling is central to trophic factor responses and nutrient sensing pathways. mTOR complex 1 (mTORC1) containing the regulatory-associated protein of mTOR (Raptor) regulates cell metabolism, growth and survival. Recently, we found that expression of mTORC1 components are relatively high in retinal ganglion cells (RGC, PMID:32622801). Here we examined the necessity of mTORC1 on RGC survival by conditional knockout (cKO) of mTOR and Raptor in the adult mouse retina.

Methods: mT/mG Cre-reporter mice were used to test the effectiveness of intravitreal (ivt) injection of AAV2Cre and a novel control virus encoding inactive Cre (AAV2CreΔC) on recombination in retinal cells. Adult *mtor*^{f/f} and *rptor*^{f/f} mice were ivt injected with these vectors to cause cKO of mTOR and Raptor, respectively, in cells within the ganglion cell layer (GCL). Activity of the mTORC1 pathway was evaluated by immunofluorescence (IF) analysis of phosphorylation of S6 ribosomal protein (p-S6, Ser240/244) and eukaryotic translation initiation factor 4E-binding protein 1 (p-4EBP1, Thr37/46) in retinal sections. RGC populations were examined using IF of the RGC marker RNA binding protein multiple splicing (RBPMS) and Hoechst staining in retinal sections.

Results: IvT injection of AAV2Cre caused effective recombination in cells within the GCL, whereas AAV2CreΔC did not. AAV2Cre-mediated cKO of mTOR or Raptor decreased mTORC1 activity in the GCL, as indicated by significant reductions of p-S6 and p-4EBP1 positive cells. At 12 wk after AAV2Cre injection, cKO of mTOR or Raptor did not change RGC or total GCL cell densities. However, at 24 wk after AAV2Cre injection, cKO of mTOR or Raptor caused 47% (p<0.01) and 43% (p<0.01) reductions in RBPMS-positive cells, respectively, relative to the contralateral eye injected with AAV2CreΔC vector. RBPMS IF intensities in RGC were also generally decreased. Densities of nuclei in the GCL decreased by 12% (p=0.2) and 26% (p<0.5), respectively, confirming cell loss.

Conclusions: Although some of the total decrease in RBPMS-positive cells may be attributed to down-regulation of RBPMS expression in mTORC1-deficient RGC, the results suggest that cKO of mTOR or Raptor caused an eventual loss of RGC in adult mice. mTORC1 function may thus be necessary for maintaining both RGC differentiation and long-term viability.

CONTROL ID: 3547006

SUBMITTER (NAME ONLY): Vuong Nguyen

TITLE: Variation in visual outcomes for neovascular age-related macular degeneration within and between practitioners

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Nguyen, M.C. Gillies, The University of Sydney Save Sight Institute, Sydney, New South Wales, AUSTRALIA|D. Barthelmes, UniversitätsSpital Zurich, Zurich, SWITZERLAND|

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ABSTRACT BODY:

Purpose: Clustering of visual outcomes for neovascular age-related macular degeneration (nAMD) within practitioners is likely to occur due to a combination of shared patient demographics and adherence, practitioner treatment strategy including choice of treatment and re-treatment intervals, and access to resources. Such clustering would subsequently result in variation in outcomes between practitioners. We report both the intraclass correlation and variation in 12-month outcomes within and between practitioners in a large cohort of patients from routine clinical practice.

Methods: Treatment-naïve patients in the Fight Retinal Blindness! registry initiating treatment with anti-vascular endothelial growth factor (anti-VEGF) injections from 2012 onwards with at least 12 months of follow-up were identified. Only practitioners with at least 10 eligible eyes were included. Data from Australia, France, Italy, Netherlands, New Zealand, and Spain were included.

The primary outcome was the practitioner intraclass correlation (ICC) for the change in visual acuity (VA) at 12 months. Other outcomes included the standard deviation of the 12-month VA change within and between practitioners. Mixed-effects modelling with the practitioner specified as a nested random-effect and baseline age and vision as fixed effects was used to estimate these outcomes.

Results: There were 7191 eyes from 6023 patients treated by 94 practitioners that met the inclusion criteria. The mean 12-month VA change and 95% confidence interval for each practitioner is shown in Figure 1. The ICC for the 12-month VA change was 0.016, which is negligible, and the between practitioner standard deviation was 2.25. In contrast, the within practitioner standard deviation was much higher at 14.8. This result was consistent across countries. The between practitioner standard deviation ranged from 0.73 in France to 4.14 in New Zealand.

Conclusions: We found a negligible practitioner ICC in VA change due to the substantial variation in outcomes within practitioner relative to the variation between practitioners. This indicates that the patient-level response is contributing far more to the variation in outcomes than the practitioner. It is possible that most practitioners these days are treating nAMD patients fairly similarly, at least in the short-term.

CONTROL ID: 3547008

SUBMITTER (NAME ONLY): Filippos Vingopoulos

TITLE: Contrast Sensitivity Function in Non-Neovascular Age-related Macular Degeneration Measured with Active Learning

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Vingopoulos, N. Patel, R. Katz, I. Garg, E.S. Lu, I. Lains, M. Kasetty, R. Silverman, A. Nigalye, I.K. Kim, L.A. Kim, D. Husain, J.W. Miller, D.G. Vavvas, J.B. Miller, Ophthalmology, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|L.A. Lesmes, Adaptive Sensory Technology, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Compared to visual acuity, contrast sensitivity function (CSF) better correlates with vision-related quality of life and subjectively perceived visual impairment, and may be affected earlier in the course of age-related macular degeneration (AMD). Inherent imperfections of the existing contrast tests have prevented its adoption in the clinical practice. Our aim is to characterize CSF in different stages of non-neovascular AMD (nnAMD) compared to healthy controls employing a novel active learning quick CSF (qCSF) method.

Methods: This prospective cross-sectional study included nnAMD patients graded by consensus grading (clinical exam, color fundus photos, and OCT) and healthy controls. Contrast was measured using the Manifold Contrast Vision Meter (Adaptive Sensory Technology, San Diego, CA). Outcomes included Area under the Log CSF (AULCSF), contrast sensitivity (CS) thresholds at 1, 1.5, 3, 6, 12, and 18 cycles per degree (cpd). Mixed-model multiple linear regression analyses were performed to evaluate the association between presence and stage of nnAMD (vs controls) and the CSF outcome measures.

Results: A total of 363 eyes were included, 249 nnAMD eyes (68 Early, 154 Intermediate, 27 Advanced) and 114 control eyes. Mean BCVA for controls was 0.020 versus 0.040 in early ($P > 0.05$), 0.140 in intermediate ($P = 0.002$) and 0.550 in advanced nnAMD eyes ($P < 0.001$). When controlling for age and lens status, early nnAMD was significantly

associated with reduced CSF thresholds at low spatial frequencies (1, 1.5, 3 cpd) ($\beta = -0.09$, $\beta = -0.09$, and $\beta = -0.11$, respectively, all $P < 0.01$) compared to controls, despite no difference in BCVA. Intermediate and advanced nnAMD were significantly associated with reduced CSF at 1, 1.5, 3, 6 and 12 cpd and reduced AULCSF (all $P < 0.01$). On trend analysis, nnAMD progression was associated with corresponding significant progressive decline in AULCSF (Early $\beta = -0.06$, Intermediate $\beta = -0.18$, Advanced $\beta = -0.64$ vs controls)(Figure 1).

Conclusions: Early nnAMD was associated with reduced CSF compared to controls as measured by the novel qCSF method, despite no difference in BCVA. Worsening nnAMD stages were associated with a progressive decline in AULCSF. The qCSF may emerge as a promising visual function endpoint in the routine clinical practice and future nnAMD clinical trials.

CONTROL ID: 3547009

SUBMITTER (NAME ONLY): Bhavana Sharma

TITLE: Microbiological spectrum and risk of transmission of infection from donor tissues of enucleated eyes harvested from septicemic patients

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the microbiological spectrum of corneas from septicemic donors and whether these corneas can be utilised for corneal transplantation. Study tested the hypothesis that cornea being an avascular tissue carries minimum risk of transmission of systemic infection from donor to recipient

Methods: In this prospective study, corneas donated to the eye bank of a tertiary eye care centre of Central India over a period of 2 years were included. During the corneal retrieval procedure based on the reports of blood culture, septicemic donors were defined as those whose blood culture tested positive. Donor corneas were allocated to either group I (septicemic donors) or group II (non-septicemic donors) based on blood culture reports and death certificate summary. Donor tissue in group I was subjected to a culture of the corneal tissue, scleral rim, aqueous and vitreous samples after retrieval, while in group II was subjected within 72 hours of retrieval. A microbial work-up flow chart was prepared and used for the sterility check of all the donor tissues. Variables were analysed using Fisher's exact test for probability and statistical significance

Results: A total of 264 corneas from 136 donors were analysed, 42 corneas of which were from septicemic donors. The microbial growth rates of the corneal tissue from group I and group II donors were close (7.142% vs 9.010%, $p=0.30$). Most common isolated organism was gram positive cocci. Only one corneal tissue showed similar bacterial growth as those from the blood culture. The rest of the contaminated corneas did not grow the same bacterial strains as those from their blood cultures. Results of the culture analysis of scleral (9.52% in Group I vs 10.81% in Group II), aqueous (4.76% in Group I and 2.25% in Group II), and vitreous (2.38% in Group I vs 1.35% in Group II) samples were statistically insignificant between both the groups

Conclusions: The study showed that corneas from septicemic donors have equally low infection rates as compared to non-septicemic donors hence can be utilised for corneal transplantation.

CONTROL ID: 3547011

SUBMITTER (NAME ONLY): Vishal Jhanji

TITLE: Photoacoustic determination of methicillin resistance in Staphylococcus aureus in ocular infections

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Antibiotic resistance is an ever growing problem in clinical management of infections of the eye, including keratitis. We used photoacoustic flow cytometry to detect and classify keratitis as methicillin sensitive or resistant by testing clinical samples from patients.

Methods: We developed photoacoustic flow cytometry to detect light absorbing particles under flow. This method induces acoustic waves in pigmented particles using laser irradiation, allowing for detection, enumeration, and capture. We acquired samples of Staphylococcus aureus from keratitis in 13 patients in the clinic. These Staphylococcus aureus samples were grown in the presence and absence of Oxacillin and were tested using photoacoustic flow cytometry. In order to create optical absorption in the S. aureus bacteria, purified bacteriophage SP1 virions were modified to incorporate Direct Red 81 dye. Bacteriophage SP1 has a broad host range and has been shown to infect approximately 98% of clinical S. aureus strains. We split each patient sample into two groups, those treated with oxacillin and those not treated. Modified bacteriophage SP1 were added to each group in equal amounts. Using photoacoustics, we then counted the number of bacteria with the expectation that methicillin sensitive samples treated with oxacillin would have greatly reduced numbers of bacteria.

Results: We counted the photoacoustic events in all 13 treated and untreated samples. Detections ranged from 2 to 818 counts. We took the ratio of treated over untreated detections and performed k-means clustering into two groups. The two groups corresponded exactly to the methicillin sensitive and resistant groups determined by PCR for the MecA gene in all 13 strains.

Conclusions: Photoacoustic flow cytometry has the ability to detect Staphylococcus aureus bacteria. By treating samples with antibiotic, it is possible to classify infections as sensitive or resistant, thus allowing for improved management of keratitis.

CONTROL ID: 3547012

SUBMITTER (NAME ONLY): Janice Walker

TITLE: The effect of exogenous TGF β on regulating the fibrotic response of resident immune cells in distinct wound environments

SESSION TITLE: Posterior Capsular Opacification and Fibrosis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.L. Walker, M. Basta, H. Paulson, Pathology, Anatomy and Cell Biology, Thomas Jefferson University Sidney Kimmel Medical College, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vimentin/CD44-rich leader cells, which we now identify as resident immune cells, are immediate responders to cataract surgery wounding and can mediate either a wound healing or a fibrotic response to injury depending upon the wound environment they encounter. The purpose of this study is to investigate the impact of two distinct wound environments on the transforming growth factor-beta (TGF β)-mediated fibrotic response of leader cells with properties of resident immune cells.

Methods: An ex vivo mock cataract surgery wound healing chick embryo model was used to follow the injury response within two distinct wound environments: 1) cell-denuded posterior lens capsule basement membrane and 2) the rigid tissue culture substrate surrounding the explant (extracapsular zone (ECZ)). To determine the effect of the distinct wound microenvironments on the TGF β -mediated fibrotic response of leader cells, ex vivo cataract surgery explant cultures were incubated +/- 10ng/ml TGF β , fixed, and labeled for the leader cell protein CD44 and/or markers of fibrosis. Proliferation was assessed by EdU labeling. Immunolabeling was analyzed by confocal microscopy imaging.

Results: In contrast to untreated ex vivo cataract surgery explants, the addition of TGF β induced leader cells located on the lens capsule to produce and deposit a fibrotic matrix that included tenascin-C and was rich in fibronectin EDA (FN-EDA). On day 3 post-injury, when wound healing on the lens capsule has completed, TGF β induced the appearance of pro-collagen I producing cells without an increased presence of alpha-smooth muscle actin (α SMA) stress-fiber+ myofibroblasts. Lens epithelial cells retained their cuboidal epithelial phenotype. In the environment of the ECZ, exogenous TGF β induced an accelerated and exacerbated fibrotic response by leader cells compared to controls. Exogenous TGF β also promoted CD44+ leader cell proliferation and the earlier transition of leader cells to α SMA+ myofibroblasts. Furthermore, TGF β treatment in the ECZ wound environment accelerated the appearance and the amount of pro-collagen I-producing cells as well as led to the increased accumulation of a FN fibrillar matrix network.

Conclusions: The wound microenvironment that resident immune cells encounter shapes their TGF β -mediated fibrotic response to injury.

CONTROL ID: 3547014

SUBMITTER (NAME ONLY): Lee Goldstein

TITLE: A PRE-Pivotal Study: β -Amyloid Detection in the Lens in Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) - Correlation with Amyloid-PET Brain Scanning

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L.E. Goldstein, Boston University Alzheimer's Disease Research Center, Boston, Massachusetts, UNITED STATES|L.E. Goldstein, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|S. Wilke, D. Nilan, Cognoptix Inc, Marlborough, Massachusetts, UNITED STATES|I. Goodman, Bioclinica Research, Orlando, Florida, UNITED STATES|C. Sadowsky, Premiere Research Institute, West Palm Beach, Florida, UNITED STATES|C. Sadowsky, Nova Southeastern University, Fort Lauderdale, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a great need for non-invasive diagnostic tools to screen, diagnose, and track patients with Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD). In AD, the brain accumulates β -amyloid ($A\beta$) as plaque detectable by amyloid-PET brain scans. $A\beta$ accumulates in lenses from AD patients but not patients with other neurodegenerative diseases (Goldstein et al., 2003). Identical $A\beta$ lens pathology has been identified in patients with Down syndrome (Moncaster et al., 2010), a chromosomal disorder in which $A\beta$ brain pathology is an invariant feature. We developed an non-invasive drug-device eye scanner to evaluate lens $A\beta$. The Sapphire II platform (Cognoptix) combines a topically-applied $A\beta$ -binding fluorescent ligand with a molecular spectroscopy ophthalmoscope that distinguishes normal subjects from those with probable AD (Kerbage et al., 2014). Sapphire II scan shows greater sensitivity and specificity than amyloid-PET scans vs clinical diagnosis for AD. This study evaluated Sapphire II screening vs amyloid-PET scans in earlier MCI and mild AD subjects.

Methods: 48 participants: 28 MCI, 16 Mild AD patients, 4 Normal Control subjects were studied. All MCI and AD subjects underwent cognitive testing and amyloid-PET scans. The Sapphire II system couples a medical imaging ointment that contains the $A\beta$ -binding fluorescent ligand, Aftobetin, and a Fluorescent Laser Eye Scanning (FLES) device that detects a spectral shifted fluorescent signature signal of bound Aftobetin- $A\beta$ complexes in the lens. Each scan takes <1 sec and multiple readings can be obtained in a single sitting.

Results: 43 subjects have been evaluated to date. No serious adverse events were reported. There was no instance where Sapphire II was negative and amyloid-PET scans were positive, indicating of a high degree of diagnostic specificity. Of the 39 Sapphire II positive subjects, positive amyloid-PET scans were noted in 26. Evaluation of individual PET scans and cognitive testing suggests that Sapphire II is more sensitive than amyloid-PET scans compared to clinical criteria.

Conclusions: Sapphire II is a convenient, inexpensive, rapid non-invasive screening tool that detects AD-related $A\beta$ accumulation in the lens of subjects with MCI and mild AD. We are exploring the utility of Sapphire II in patients with early prodromal asymptomatic AD ("preclinical AD").

CONTROL ID: 3547016

SUBMITTER (NAME ONLY): Christina Sabin

TITLE: Investigating the role of ocular shape changes in fovea development in chameleons along with wild-type and albino anole lizards

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.E. Sabin, J.D. Lauderdale, Neuroscience, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|A. Rasys, J.D. Lauderdale, Cell Biology, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|R. Osman, D. Menke, Genetics, University of Georgia Franklin College of Arts and Sciences, Athens, Georgia, UNITED STATES|P. Trainor, Stowers Institute for Medical Research, Kansas City, Missouri, UNITED STATES|P. Trainor, Anatomy and Cell Biology, The University of Kansas School of Medicine, Kansas City, Kansas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Dynamic changes in ocular shape during embryonic development have been observed in foveated vertebrates including humans, other primates and recently lizards. Areas that develop a fovea elongate shortly after retinal differentiation and then undergo ocular retraction or a return to ocular symmetry, during which time retinal remodeling occurs (pit formation, photoreceptor cell packing). We propose that fovea development is a protracted process that begins early in embryonic development and that ocular elongation followed by retraction are necessary steps for fovea formation. To better understand this, we investigated the role of morphological changes in eye shape in the foveated chameleon, *Chamaeleo calytratus*, and the bifoveated brown anole lizard, *Anolis sagrei*, before examining albino anoles with tyrosinase mutations. Wildtype chameleons have a central fovea while anoles have both a central and temporal fovea. Albino lizards with tyrosinase mutations fail to develop their temporal fovea.

Methods: Embryonic eyes were dissected and then measured along 3 different anatomical planes in chameleons as well as wildtype and albino anoles. Albino (*tyr*^{-/-}) lizards were created using a CRISPR gene editing approach.

Results: Between early and mid-embryonic development, the central and temporal regions of the wildtype anole eye elongate. Later, both regions retract, returning the eye to its' spherical shape, at which point the fovea develops. A similar process occurs in chameleons but only the central region undergoes ocular elongation, retraction, and fovea formation. Preliminary results of the albino anoles, which exhibit temporal fovea hypoplasia, suggest embryonic albino eyes exhibit a reduction in temporal ocular elongation but not in central elongation during development.

Conclusions: These results support the premise that ocular elongation and retraction are necessary steps in fovea formation and the idea that the onset of fovea development may occur much earlier than previously believed. Together these findings indicate that the anole lizard is a promising model system for studies investigating human ocular developmental disorders.

CONTROL ID: 3547020

SUBMITTER (NAME ONLY): Justis Ehlers

TITLE: Association of Ellipsoid Zone Integrity and Treatment Response in Subjects with Non-neovascular AMD Treated with Subcutaneous Elamipretide: Post Hoc Analysis of the Phase 1 ReCLAIM Study

SESSION TITLE: Imaging: posterior segment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.P. Ehlers, H. Cetin, A. Hanumanthu, T.K. Le, P. Kaiser, J. Reese, S. Srivastava, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the association between quantitatively assessed, higher-order optical coherence tomography (OCT) features, such as ellipsoid zone (EZ) integrity and sub-RPE compartment features, evaluated at baseline with visual outcomes in subjects with non-neovascular age-related macular degeneration (AMD) treated with subcutaneous elamipretide.

Methods: ReCLAIM was an open-label, phase 1 clinical trial of daily subcutaneous elamipretide (40 mg) in NNVAMD, stratified into pre-defined nonfoveal geographic atrophy (GA) and high-risk drusen (HRD) subgroups. The primary endpoint was change in low-luminance best corrected visual acuity (LLBCVA). Higher-order OCT features were evaluated via automated machine-learning augmented multilayer retinal segmentation with expert reader manual verification to quantify outer retinal integrity [e.g., EZ-RPE thickness, percent EZ attenuation, outer retinal parameters (i.e., outer nuclear layer (ONL) to RPE thickness)] and sub-RPE anatomical metrics. Post hoc analysis assessed correlation of baseline higher order OCT Features with change in LLBCVA from baseline to end of treatment (week 24).

Results: A total of 40 patients were evaluated (19 in the nonfoveal GA subgroup and 21 in the HRD subgroup). In the nonfoveal GA subgroup, the baseline macular percentage of total EZ attenuation ($r=-0.72$; $p=0.002$) and baseline panmacular EZ-RPE volume ($r=0.62$; $p=0.01$) were significantly correlated to change in LLBCVA from baseline to week 24. Eyes gaining 2 lines or more had significantly less macular total EZ attenuation at baseline (9.0% vs 27%; $p=0.03$) and significantly less percentage area of macular GA (4.7% vs 15.6%; $p=0.004$).

In the HRD subgroup, mean central macular (e.g., central 2 mm) retinal thickness positively correlated with improvement in LLBCVA ($r=0.58$; $p=0.009$). Eyes gaining 2 lines or more had significantly greater baseline preservation of the central macular outer retina (ONL-RPE thickness, 137 μ m vs 117 μ m, $p=0.006$) trended towards

less baseline macular partial EZ attenuation (1.1% vs 5.0%; $p=0.06$).

Conclusions: Baseline higher order OCT parameters, such as EZ integrity, were correlated with functional response and improved LLBCVA in eyes treated with subcutaneous elamipretide. Further research is needed to better characterize these potential imaging biomarkers.

CONTROL ID: 3547022

SUBMITTER (NAME ONLY): Javad Paknahad

TITLE: The sensitivity of Retinal Bipolar Cells Response to Long Stimulus Pulse Durations in Epiretinal Prostheses

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Epiretinal prosthetic systems have been developed to restore sight to the blind; however, the spatial resolution of current devices is still limited. Previous studies have demonstrated that long stimulus pulses (~ 25 ms) or low sinusoidal frequencies (5-25 Hz) can selectively target retinal bipolar cells (BCs) and, therefore, improve the spatial resolution of epiretinal implants by avoiding axonal activation of retinal ganglion cells (RGCs). In this study, we present a computational modeling framework that captures the biophysical factors that influence the stimulus threshold of BCs to long stimulus pulse durations.

Methods: Using the Admittance Method (AM)/NEURON computational platform, we implemented a model of spiking BCs, diffuse bipolar cell subtypes (DB4), that was verified with experimental and modeling data from the literature. We analyzed the response of BCs over a range of stimulus pulses, including cathodic monophasic and anodic-first biphasic pulses. We investigated the role of the hyperpolarization-activated, cyclic nucleotide-gated (HCN) channels at the presynaptic terminals in the high sensitivity of BCs to long stimulus pulse durations.

Results: We tested a range of pulse durations from 0.1 ms to 25 ms and compared the response of BCs to cathodic monophasic and anodic-first biphasic pulses. Our data show that long anodic-first biphasic pulse durations (> 8 ms) significantly reduce the stimulus threshold of BCs relative to long cathodic-first pulses from 98 μ A to 57 μ A. We further explored that the absence of HCN channels at the presynaptic terminals of BCs increases the stimulus threshold of BCs and, therefore, HCN channels contribute to the higher sensitivity of BCs to long anodic-first stimulus pulse widths.

Conclusions: Our computational findings suggest that the presence of long anodic pulses prior to cathodic pulses likely contributes to selective activation of BCs and the reported rounder shape of phosphene with epiretinal implants using long stimulus pulse widths. The reduced threshold and high sensitivity of BCs to low-frequency stimulation and long pulse durations are likely mediated by the high concentration of HCN channels at the terminals of BCs.

CONTROL ID: 3547027

SUBMITTER (NAME ONLY): Paula Sakemi Fukuhara

TITLE: Effects of melatonin on human Retinal Pigment Epithelial cells (ARPE-19) and Müller cells (MIO-M1) exposed to cobalt chloride (CoCl₂) in vitro

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Sakemi Fukuhara, N. Shekoh, B.D. Kuppermann, M. Kenney, Ophthalmology, University of California Irvine, Irvine, California, UNITED STATES|M. Chwa, University of California Irvine, Irvine, California, UNITED STATES|D.H. Lee, Mayo Clinic Arizona, Scottsdale, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Melatonin is synthesized mainly in the pineal gland and is important for circadian function. It is also produced in retina, lens, gastrointestinal tract and skin. It displays strong anti-oxidative properties and plays a protective role in human pathologies associated with oxidative stress, including retinal diseases. Cobalt chloride (CoCl₂) mimics hypoxic conditions and can affect cell viability. The present study evaluates and compares the protective effects of melatonin on ARPE-19 and MIO-M1 cells stressed with CoCl₂ in vitro to determine if the drug can modulate the inflammatory/oxidative stress systems and reduce the damage caused by retinal diseases.

Methods: Human ARPE-19 and MIO-M1 cells were cultured separately for 24 hours in 96-well plates. Cells were pretreated for 6 hours with melatonin (200µM, 400µM and 800µM) and then stressed with CoCl₂ in different concentrations: 350 µM for ARPE-19 cells and 500 µM for MIO-M1 cells for 48 hours. Cultures were analyzed for cell viability (MTT assay), reactive oxygen species (ROS/H₂DCFDA assay), and mitochondrial membrane potential (MMP, JC-1 assay). The conditions were: untreated, solution-control, and the melatonin in different concentrations.

Results: CoCl₂-treated ARPE-19 cells incubated with 400µM and 800µM melatonin had (a) increased cell viability with p=0.0352 and p=0.0016, respectively; and (b) increased MMP with p=0.0131 and p=0.0096, respectively. The cell viability and MMP were not altered after treatment with 200µM melatonin.

MIO-M1 cells stressed with CoCl₂ and rescued with melatonin 200µM and 400µM showed increased cell viability with p=0.0341 and p=0.0009, respectively. The MMP increased when treated with 800µM melatonin (p=0.0082), while the melatonin 200µM and 400µM cultures were not altered. No significant changes were seen in ROS levels for either cell line.

Conclusions: Each CoCl₂-stressed cell line had distinct responses with the melatonin at different concentrations. Our results suggest that melatonin improves cell viability and mitochondrial membrane potential but does not affect ROS production in CoCl₂-stressed cells. Our approach may be helpful to identify novel pathways to protect against retinal diseases and show differential responses by different cell lines to one drug.

CONTROL ID: 3547028

SUBMITTER (NAME ONLY): Zeynep Bas

TITLE: Eyelid Cancer Prevalence and Associated Factors in the AAO IRIS® Registry

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Bas, A. Yaghy, C. Shields, Ocular Oncology, Wills Eye Hospital Ocular Oncology Service, Philadelphia, Pennsylvania, UNITED STATES|J. Sharpe, Q. Zhang, L. Hyman, Vickie and Jack Farber Vision Research Center, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To estimate prevalence of eyelid cancers in the AAO IRIS® Registry and evaluate associated factors.

Methods: All patients with ICD-9/10 codes for eyelid cancers(basal cell carcinoma [BCC],squamous cell carcinoma[SCC],malignant melanoma[MM],melanoma in-situ[MIS], sebaceous cell carcinoma/other specified malignant neoplasm[SBCC] and unspecified malignant neoplasm[UMN]),in the IRIS® registry between 12/1/2010-12/1/2018, were included. Prevalence was estimated overall, by age (categorical),race(White[W],Hispanic[H],African-American[A-A], Asian[A],Other[O],Unknown[UK]), sex (Male[M], Female[F]), and smoking status. Prevalences were compared using χ^2 tests or Fisher's exact tests. Odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using multivariable logistic regression.

Results: 81,802 eyelid cancer patients were identified. Prevalence of Any Eyelid Cancer (AEC) was 0.14%. Tumor-specific prevalences ranged from: 0.088% (BCC), to 0.026% (UMN), 0.011% (SCC), 0.005% (SBCC), 0.004% (MM), and 0.0004% (MIS). Prevalence increased with increasing age for AEC and each tumor type (all $p < 0.0005$), was higher in M than F for any eyelid cancer and BCC, SCC, MM (all: $p < 0.0001$) and MIS ($p = 0.03$), but not UMN or SBCC. Prevalence was highest in W's compared with any other race for BCC, SCC, and SBCC (all $p < 0.0001$). Prevalence was also higher in current/former smokers vs. non-smokers for AEC and all tumor types (all $p < 0.01$). In the model, having AEC was associated with older ages [< 20 yrs (ref.); OR (CI): 20-39 yrs: 3.6 (3.2-4.0); 40-65 yrs: 16.0 (14.7-17.6); > 65 yrs: 25.6 (23.4-28.0)], M sex [F (ref.); 1.2 (1.2-1.2)], former/current smoking [never (ref.); former: 1.1 (1.1, 1.1), current: 1.2 (1.2-1.2)] and W race (inverse associations with A-A (0.1 (0.1-0.1), A (0.3 (0.3-0.3)) H (0.6 (0.5-0.6)) and O (0.6 (0.5-0.7)). Older age was associated with all tumor types, while other factors varied by type.

Conclusions: This is the first study to report on overall and tumor-specific prevalence of eyelid cancers from a large national clinical population. Associations with older age, male sex and white race are consistent with prior studies. The association with smoking for eyelid tumors offers guidance for disease prevention. This epidemiologic "real-world" data on eyelid cancers is valuable for risk factor assessment, planning treatment strategies, allocating medical resources, and improvements in cancer care.

CONTROL ID: 3547029

SUBMITTER (NAME ONLY): Judith Zavala

TITLE: Restoration of corneal clarity after transplantation of an engineered corneal endothelium: preliminary in vivo model

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zavala, M. Montalvo Parra, D. Loya, A. Bustamante Arias, M. Hernández, S. Guevara-Quintanilla, S. Garza, M. Salan-Gomez, J.E. Valdez, Escuela de Medicina, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO|

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ABSTRACT BODY:

Purpose: To determine the ability of an engineered corneal endothelium to restore corneal clarity in an animal model.

Methods: Corneal endothelial cells were isolated from three 3 months old New Zealand rabbits and harvested with a two-step approach. Collagen membranes were elaborated using bovine collagen type I ($5.6 \mu\text{L}/\text{mm}^2$ of the culture plate surface or 2X) dissolved in DMEM-F12 medium, 22 mM HEPES solution, 8% FBS, and 1 % antibiotics. The mixture was incubated 2h at 37 °C for gelation then placed in a 40 °C and 40% RH for 37 days. The corneal endothelial cells were seeded at a density of 1250 cells/ mm^2 overnight over 8 mm^2 membranes. Five male New Zealand rabbits 20 months old were used as models. Corneal endothelium was removed under local and general anesthesia and the membrane/cells constructs were transplanted into the anterior chamber of the right eye of 4 rabbits. One rabbit was transplanted using a collagen membrane elaborated with $8.4 \mu\text{L}/\text{mm}^2$ collagen (3X). The transplanted eyes were photo-documented for 30 days.

Results: The five eyes developed opacity after 5 min of corneal endothelium removal. The eyes transplanted with 2X membrane constructs (rabbits 1, 2, 3, and 4) recovered partially the peripheral clarity after 3 weeks. After 5 weeks, rabbits 1, 2, and 4 showed central corneal clarity. Central opacity remained in rabbit 3. The eye transplanted with 3X membrane construct remained with mild opacity after 5 weeks of transplantation.

Conclusions: Engineered corneal endothelium produced with corneal endothelial cells cultivated with a two-step approach and 2X collagen membranes restores the corneal clarity in old White New Zealand rabbits. The concentration of collagen in the fabrication of the membrane could affect the recovery of corneal clarity.

CONTROL ID: 3547030

SUBMITTER (NAME ONLY): Andrew Freedman

TITLE: Effect of enhanced lighting on detection of targets with artificially reduced acuity

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Freedman, G.E. Legge, Psychology, University of Minnesota Twin Cities, Minneapolis, Minnesota, UNITED STATES|

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ABSTRACT BODY:

Purpose: To design visually accessible spaces, it is important to understand how illumination and target-background luminance contrast affect detection of key features in the environment. Simply increasing overall room illumination ignores the crucial role of contrast in determining visibility, and directional lighting may reduce the contrast between an object and its background. This study examined the effects of illumination and luminance contrast on the detectability of objects in the environment for those with reduced acuity.

Methods: 13 normally sighted subjects, wearing blur goggles that reduced their acuity to approximately 20/900, completed a visual search task. Under typical ambient indoor lighting, subjects walked along a path, following a guideline, and visually searched for targets adjacent to the path. Subjects verbally identified the shape of targets as they walked. Performance was quantified with detection rate, the percent of targets subjects attempted to identify. Targets were white or grey Styrofoam objects on the floor, in a room with walls painted white or black. Spotlights were used to increase the illumination of targets placed against the walls to three fold their ambient illumination, creating two lighting conditions: ambient and enhanced. This served to either increase contrast (e.g. grey targets against black walls), or decrease contrast (grey targets against white walls). This created targets with high or low contrast with their background under both lighting conditions, for independent manipulation of both lighting and contrast. A multiple binomial logistic regression was performed to analyze the probability that a target would be detected.

Results: The model was statistically significant ($\chi^2(3)=92.89$, $p<.001$), and showed that detection odds were significantly increased by 3.41 fold for high vs low contrast targets (CI =1.80-6.44; $p<.001$). While increased illumination significantly increased detection rate by 29.2% for grey targets against a black background (CI=10.4-48.1%; $p=.006$), it did not significantly improve performance under other conditions, and was not statistically significant in the model.

Conclusions: Under low-acuity conditions in the environment tested here, luminance contrast was more predictive of object detectability than illumination. Notably, in some cases, increased illumination from directional lighting enhanced detectability by increasing target-background contrast.

CONTROL ID: 3547032

SUBMITTER (NAME ONLY): Peter Le

TITLE: A corneal tissue opacity model for the evaluation of corneal wound healing technologies

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Le, D. Myung, Ophthalmology, Stanford University School of Medicine, Palo Alto, California, UNITED STATES|P. Le, D. Myung, VA Palo Alto Health Care System, Palo Alto, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Peter Le: Commercial Relationship: Code N (No Commercial Relationship) | David Myung: Commercial Relationship(s);Stanford University:Code P (Patent)

ABSTRACT BODY:

Purpose: Corneal scarring is a major clinical problem worldwide that results in reduced vision and blindness. The development of new regenerative therapies to address corneal scarring and blindness requires a reliable, reproducible, and clinically relevant pre-clinical model of corneal scarring.

Methods: We have developed a method of creating a corneal scar of controlled diameter and depth on rabbit eyes through a transient microdose (TMD) of sodium hydroxide (NaOH). TMDs of varying time intervals and volumes were applied up to 30 seconds and 5 microliters, respectively. The eyes were then rinsed thoroughly with phosphate buffered saline for 10 seconds. The pH of the surface is checked to make sure no residual alkalinity remains. Optical coherence tomography (OCT) was used to evaluate the resulting depth and diameter of epithelial and stromal opacity formed, along with slit lamp images. A circular trephine is then used to perform an anterior lamellar keratectomy to remove the scar tissue and fill it with an in situ-forming hydrogel material to occupy the space where the scar was removed.

Results: We found that 0.2 microliters of 1M sodium hydroxide (NaOH) added to the surface of an ex vivo rabbit cornea for 20 seconds results in an approximately 50% depth opacity that is 3 mm in diameter. This size scar presents a visually significant corneal scar covering the visual axis that typically requires corneal transplantation. With OCT to aid in visualization, we found that the entirety of the scar with minimal surrounding transparent stroma can be removed via controlled-depth, trephine-assisted manual keratectomy and substituted with a transparent, in situ-forming gel matrix.

Conclusions: The technique described serves as a corneal opacity tissue model that can be utilized to evaluate regenerative therapies such as engineered, in situ-forming, pre-formed, and/or cell-based biomaterial therapies designed to avoid the need for penetrating keratoplasty. Future directions include translation of this technique into the in vivo setting and the testing of candidate therapies.

CONTROL ID: 3547033

SUBMITTER (NAME ONLY): Minchang Choi

TITLE: Changes in expression of regulators of protein phosphatase 2A are observed in lacrimal gland from a murine model of Sjögren's syndrome

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Choi, H. Guo, S.F. Hamm-Alvarez, Department of Pharmacology and Pharmaceutical Sciences, University of Southern California School of Pharmacy, Los Angeles, California, UNITED STATES|M. Edman, S.F. Hamm-Alvarez, Department of Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Minchang Choi: Commercial Relationship: Code N (No Commercial Relationship) | Hao Guo: Commercial Relationship: Code N (No Commercial Relationship) | Maria Edman: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Hamm-Alvarez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Sjögren's Syndrome (SS) is a systemic autoimmune disease associated with lymphocytic infiltration and loss of function of the lacrimal gland (LG). The cysteine protease, cathepsin S (CTSS), is increased in LG and tears in a murine model of SS; moreover, the protease's activity is elevated in SS patients' tears. Inhibition of CTSS activity in a murine model also suppressed ocular symptoms of SS. Protein phosphatase 2A (PP2A), through dephosphorylation of tristetraprolin (TTP), destabilizes CTSS mRNA; conversely, inhibition of PP2A leads to increased stability and expression of CTSS mRNA. To understand more about the mechanisms responsible for LG CTSS upregulation in SS, we have explored the expression of effectors of the PP2A-TTP pathway in LG from SS model and healthy control mice.

Methods: Age-matched (12-18 weeks) male NOD mice and male BALB/c mice LG were used to compare gene and protein expression of the PP2A-TTP axis components. Primers for PP2A catalytic subunit, TTP, SET (an endogenous PP2A inhibitor), and CIP2A (an endogenous PP2A inhibitor) were used for analysis by RT-qPCR of lysed LG cDNA. CIP2A protein expression in LG lysates from male NOD and BALB/c mouse LG were compared by Western Blotting. PP2A and CTSS activities were measured from male mouse BALB/c LG incubated ex vivo with either okadaic acid (OKA, 1uM), a commercially available PP2A inhibitor, or DMSO (vehicle) for 2 hr using commercially available kits PP2A (Milipore Cat # 17-313) and CTSS (Biovision Cat # K144).

Results: NOD mouse LG showed significantly less expression of PP2Ac mRNA compared to BALB/c mouse LG (n=4, p=0.0054). A comparable trend to increased expression of CIP2A, an endogenous PP2A inhibitor, was seen in NOD mouse LG (n=6, p=0.0663). This trend to increased expression was verified by Western blotting for CIP2A, showing an increase of 1.6 fold CIP2A (n=6, p=0.011) in NOD mouse LG lysates relative to BALB/c mouse. No significant changes in gene expression of SET or TTP were seen between strains. Lysates from BALB/c mouse LG ex vivo incubated with OKA showed a 2.2 fold increase in CTSS activity (n=5, p=0.0013) and a 0.6 fold decrease in PP2A activity (n=3, p=0.0395) compared to control.

Conclusions: Changes in expression of effectors of the PP2A-TTP pathway regulating CTSS mRNA stability suggest this as a possible mechanism governing increased expression of CTSS in SS.

CONTROL ID: 3547034

SUBMITTER (NAME ONLY): Anupam Mondal

TITLE: Impaired energy metabolism and mitochondrial damage precede rod photoreceptor cell death in retinal neurodegeneration caused by Pde6b^{rd1/rd1}

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Mondal, C. Jiang, Y. Adhlakha, J. Gumerson, J. Kim, M.R. Brooks, A. Boleda, L. Gieser, J. Nellissery, A. Swaroop, NNRL, National Eye Institute, Bethesda, Maryland, UNITED STATES|R. Balaban, R. Covian-Garcia, National Heart Lung and Blood Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited Retinal Degenerative diseases (IRDs) are a major cause of blindness mainly caused by premature death of rod photoreceptor cells in the retina. As a heterogeneous group of pathologies, IRDs can either be congenital or have early/mid-onset where progressive degeneration has severe impact in quality of life among patients. Although more than 270 different genes and loci have been implicated, disease mechanisms remain obscure resulting in little hope for therapy. In this study we use a multi-omics approach to elucidate gene network and pathways underlying disease pathogenesis in the rd1 mice model which mimics human pathology and has the most aggressive form of degeneration.

Methods: We designed this unique study to focus on the early stages of the rd1 retina - Postnatal day (P) 2 to P10 - to identify the molecular events in rod photoreceptors before cell death begins at P12. We performed time course RNAseq of purified rods and integrated it with mass-spectrometry based proteomics and metabolomics from rd1 and WT retina. Validations were performed with ultrastructural analysis and functional assays.

Results: Transcriptomic analysis revealed co-expression modules of oxidative phosphorylation (OXPHOS) genes to be significantly associated with rd1. Proteomic comparisons between WT and rd1 retina confirmed differential abundance of core subunits of OXPHOS complexes at P6, with further exacerbation by P10. Electron microscopy analysis of the rd1 retina between P6 and P10 highlighted loss of mitochondrial cristae, corroborating molecular findings of OXPHOS dysregulation as cells get close to disease onset. At the same time, metabolomics uncovered reduced flux in central carbon metabolism and additionally showed deregulation of essential biosynthetic pathways such as nucleic and amino acid metabolism. Furthermore, Seahorse assays validated lower mitochondrial reserve capacity and energy metabolism in ex vivo mutant retina.

Conclusions: This study for the first time describes molecular changes in rod photoreceptors before they succumb to apoptosis in IRDs. Through an omics driven approach we identify mitochondrial energy metabolism as a molecular converging point, leading us to hypothesize a critical role of metabolism and the mitochondria in IRDs. Identification of these disease related pathways will aid therapy development and disease management.

CONTROL ID: 3547035

SUBMITTER (NAME ONLY): Sana El Hajji

TITLE: Insulin for retinal ganglion cell dendrite regeneration: effect of intraocular pressure and identification of multiple downstream pathways

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. El Hajji, N. Belforte, H. Quintero, F. Dotigny, A. Di Polo, Neuroscience, Universite de Montreal, Montreal, Quebec, CANADA]

Commercial Relationships Disclosure (Abstract): Sana El Hajji: Commercial Relationship: Code N (No Commercial Relationship) | Nicolas Belforte: Commercial Relationship: Code N (No Commercial Relationship) | Heberto Quintero: Commercial Relationship: Code N (No Commercial Relationship) | Florence Dotigny: Commercial Relationship: Code N (No Commercial Relationship) | Adriana Di Polo: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The retraction of retinal ganglion cell (RGC) dendrites is one of the earliest pathological changes leading to functional deficits. We demonstrated that insulin, administered after arbor retraction, promotes RGC dendrite and synapse regeneration. Endogenous insulin and related molecules are naturally found in the retina. Thus, we asked the following questions: 1) is reduction of high intraocular pressure (IOP) sufficient to promote dendrite regeneration in the absence of exogenous insulin? 2) what are the signalling components downstream of insulin promoting RGC dendrite regeneration in glaucoma?

Methods: Thy1-YFP mice, which allow visualization of RGC dendritic arbors, received an intracameral injection of magnetic microbeads to induce ocular hypertension. Daily topical application of brinzolamide, a carbonic anhydrase inhibitor with negligible effects on neurons or vascular cells, was used to reduce IOP. RGC dendrites were imaged with confocal microscopy and 3D reconstructed using Imaris software. RGCs were isolated by Fluorescence Activated Cell Sorting (FACS) from insulin- or vehicle-treated glaucomatous retinas as well as non-injured controls, followed by RNA sequencing analysis.

Results: Brinzolamide effectively reduced IOP relative to vehicle treated controls (sham: 10.7 ± 0.3 mmHg, brinzolamide: 11.3 ± 0.4 mmHg, vehicle: 20.5 ± 0.8 mmHg, $n=12$ mice/group, Student's t-test, $p < 0.001$). Total RGC dendritic length and complexity increased in glaucomatous eyes treated with insulin ($4,515 \pm 149$ μ m) to values similar to those found in non-injured controls ($4,566 \pm 233$ μ m), but not in eyes treated with brinzolamide ($2,534 \pm 164$ μ m) or vehicle ($2,981 \pm 169$ μ m) ($n=6$ mice/group, ANOVA, $p < 0.001$). RNA-seq analysis of insulin- and vehicle-treated glaucomatous retinas identified key regulatory pathways that might be implicated in insulin-induced RGC dendrite regeneration including the mammalian target of rapamycin (mTOR), glycolysis, fatty acid metabolism, DNA repair, and myc-targets (FDR <0.05).

Conclusions: We conclude that: 1) IOP reduction alone is not sufficient to promote RGC dendrite regeneration, and 2) multiple downstream pathways are activated during insulin-mediated regeneration. These findings support a critical role for exogenous insulin administration, and identify differential gene expression of potential targets to restore RGC function in glaucoma.

CONTROL ID: 3547036

SUBMITTER (NAME ONLY): Arun Krishnan

TITLE: Macular rod function in retinitis pigmentosa (RP): Comparison of scotopic microperimeter to modified Humphrey field analyzer

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.K. Krishnan, A. Roman, M. Swider, S.G. Jacobson, A.V. Cideciyan, Perelman School of Medicine, Scheie Eye Institute, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate validity and reliability of macular rod photoreceptor function estimated with a retina-tracking microperimeter in dark-adapted eyes of patients with RP.

Methods: Twenty-two eyes of eleven patients (ages:7–66 yrs) with RP, and five eyes of five normal subjects (ages:22–55 yrs) were included. Dark-adapted chromatic perimetry (DACP) was performed with a modified Humphrey field analyzer (mHFA) in dilated eyes. Monochromatic mHFA stimuli were 500 nm blue and 650 nm red with 200 ms duration and 1.7 deg diameter. In addition, MP-1S microperimeter was used to obtain sensitivities to broad-band blue stimuli filtered through 0, 1, 2, 3 or 4 ND to expand the effective dynamic range from 20 dB to 60 dB. Test locations were along the two principal meridians at eccentricities of 6, 8, 10, 12, and 14 deg. Sensitivity loss (SL) was defined as the difference from the average normal value at each locus. mHFA results were used to censor those locations that showed cone mediation or greater than 30 dB of rod sensitivity loss. In addition, loci near transitions to deep scotomas (papillary boundary or retinal degeneration) were censored to allow a fair comparison between free-viewing mHFA and retina-tracking MP-1S results. All RP eyes were evaluated similarly with both methods during two visits separated by 6 months.

Results: Normal effective MP-1S sensitivities with blue stimuli were 43.5 ± 1.0 dB (mean \pm s.d.). In RP patients, after censoring, there were 241 evaluable loci. The range of SL was 2.2 to 30.2 dB for mHFA and 2.5 to 38.5 dB for MP-1S, respectively. SL estimates obtained with MP-1S were highly correlated ($r = 0.81$) with those obtained with mHFA; the relationship could be explained well by a line with an offset of 3.9 dB and a slope of 0.93. Assuming no disease progression during the 6-month interval, 95% coefficient of repeatability was 5.96 dB for mHFA and 7.34 dB for MP-1S, respectively. There was no evidence of a relationship of variability with mean sensitivity.

Conclusions: In a macular annulus extending from 6 to 14 degrees, rod sensitivity losses with the scotopic microperimeter MP-1S closely track those of the mHFA – long-standing gold-standard for DACP in RP patients. There is a tendency for MP-1S losses to be slightly larger and more variable than those of mHFA.

CONTROL ID: 3547038

SUBMITTER (NAME ONLY): Onelys Carrasquillo

TITLE: Abnormal Renal Profiles and Diabetic Eye Disease in Latino and African American Cohorts

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Carrasquillo, J. Levine, Ophthalmology, BronxCare Health System, Bronx, New York, UNITED STATES | J. Levine, Ophthalmology, Hadassah Academic College, Jerusalem, Jerusalem, ISRAEL |

Commercial Relationships Disclosure (Abstract): Onelys Carrasquillo: Commercial Relationship: Code N (No Commercial Relationship) | Jonathan Levine: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the association between abnormal renal profiles and presence of diabetic retinopathy (DR) and diabetic macular edema (DME) in Latino (LA) and African American (AA) patients of our South Bronx community. This will be an expanded version of our original pilot study of 100 patients to now include an n of over 1200.

Methods: This is a retrospective chart review of adult diabetic LA and AA patients seen in our hospital's eye clinic within the last 5 years. Demographic information and most recent renal profiles including serum creatinine levels, eGFR, and urinary microalbumin to creatinine ratios (ACR) will be recorded. In addition we will record hemoglobin A1C and cholesterol levels. Patients will be stratified based on presence or absence of Diabetic Macular Edema and/or Diabetic Retinopathy. Log values of ACR will be used for data analysis as the ACR values are not normally distributed. Lab values will be compared between groups and the unpaired Student's t-test will be used to calculate statistical significance.

Results: We have over 1200 diabetic patients included in our study, 439 AA and 809 in the LA cohort. We have reviewed nearly 200 charts thus far from the AA cohort, 55 with DR of some degree, and 142 with no DR. The DR group had a significantly higher mean ACR compared to the no DR group. (1.823 vs 1.269 p <.0005) The DME subgroup (n=14) also had a higher mean ACR than the no DR group but values did not reach statistical significance. (1.659 vs. 1.269 p > 0.05).

Conclusions: After reviewing 200 of the 1200 charts in our current study, we have already found significantly elevated ACR values among our African American patients with DR compared to non DR. We hope that a larger n will substantiate an association between ACR and DME as well. If so, then perhaps future studies could evaluate using abnormal ACR values as a prognostic indicator of future diabetic eye disease in these cohorts.

CONTROL ID: 3547041

SUBMITTER (NAME ONLY): Stephen Laswell

TITLE: Posterior Vitreous Detachment Assessment by Age Using Circumpapillary Optical Coherence Tomography

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Laswell, Research, Retina Consultants of Texas, Houston, Texas, UNITED STATES|C.C. Wykoff, D.M. Brown, Retina Consultants of Texas, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Stephen Laswell: Commercial Relationship: Code N (No Commercial Relationship) | Charles Wykoff: Commercial Relationship: Code N (No Commercial Relationship) | David Brown: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Consideration of posterior vitreous detachment (PVD) status is highly clinically relevant for managing a host of vitreoretinal disorders and in planning for vitreoretinal surgery. However, the translucent nature of vitreous humor makes definitive clinical assessment of PVD challenging. The goal of this study was to define patterns of posterior vitreous cortex (PVC) changes using circumpapillary spectral-domain optical coherence tomography (SD-OCT).

Methods: The vitreoretinal interface of 1685 eyes of 879 clinical retina patients were retrospectively analyzed using 100 ART HS circumpapillary OCT and 6mm² macular OCT (Heidelberg OCT2) by 3 masked graders. The primary outcome was the vitreoretinal interface status, graded using a modified staging system (initially described by Uchino et al, 2001); 0) no PVD: tight vitreoretinal adhesion with no discernible separation 1) insignificant separation: partial vitreoretinal separation, with no separation of the PVC within the papillo-macular bundle 2) Clinically relevant separation: separation of the PVC within the papillo-macular bundle with persistent vitreofoveal attachment 3) vitreofoveal separation with persistent vitreoretinal adhesion at the optic disc 4) Full PVD: Dark absence of signal anterior to the retina or with pinpoint translucence consistent with vitreous cells or hemorrhage.

Results: Complete separation between the circumpapillary retina and PVC was detected by circumpapillary OCT in 706 of 1678 eyes (41.90%). Of 1685 scans analyzed in this study, 4 (0.24%) were deemed to have an indeterminate PVD status. By age, PVD was detected in 0/42 eyes age 1-18 ($P < 0.001$), 2/72 eyes (2.78%) age 19-29 ($P < 0.001$), 11/127 eyes (8.66%) age 30-39 ($P < 0.001$), 17/203 eyes (8.37%) age 40-49 ($P < 0.001$), 106/307 eyes (34.53%) age 50-59 ($P < 0.05$), 229/461 eyes (49.67%) age 60-69 ($P < 0.01$), 211/324 eyes (65.12%) age 70-79 ($P < 0.001$), 110/128 eyes (85.94%) age 80-89 ($P < 0.001$), and 20/21 eyes (95.24%) age 90+ ($P < 0.001$).

Conclusions: Analysis of the PVC with routine circumpapillary OCT scans is shown to be an effective, readily available means of evaluating PVD status; circumpapillary OCT may be valuable in discerning the vitreoretinal interface status for cases in which it may be clinically ambiguous. Results corroborate well-established progression of PVD with age while showing evidence that PVD initiates at earlier ages than previously reported.

CONTROL ID: 3547043

SUBMITTER (NAME ONLY): Seerat Elahi

TITLE: Comprehensive study of immune landscape in aging retina

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Elahi, P. Mattar, Ottawa Hospital Research Institute, Ottawa, Ontario, CANADA|P. Mattar, Cellular and Molecular Medicine, University of Ottawa Faculty of Medicine, Ottawa, Ontario, CANADA|

Commercial Relationships Disclosure (Abstract): Seerat Elahi: Commercial Relationship: Code N (No Commercial Relationship) | Pierre Mattar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aging is the one of the major risk factors for degenerative retinal disorders. While a role for immune cells in the progression of the degenerative process has been implicated, studies on the retinal immune landscape, mostly due to sparsity and lack of markers to identify various cell populations, and how these cells are affected by aging are scattered. In this study, we aimed to comprehensively explore the dynamics of innate and adaptive immune cells of the murine retina from birth to death. To this end, we designed a multi-color flow cytometry panel and identified various populations of innate and adaptive immune system, including different types of microglia, dendritic cells (DCs), neutrophils, monocytes, T and B cells, and analyzed their changes over time.

Methods: In this study, we performed multi-color flow cytometry analysis on retinal cells of CD1 and C57/B6 mice at various time points from birth (P0) to up to 2 years.

Results: Our study revealed that CD45⁺ hematopoietic cells were surprisingly frequent within the retina. Interestingly, we found that the frequency of both myeloid (CD45⁺/CD11C⁺/MHCII⁺/CD11B⁺) and lymphoid (CD45⁺/CD11C⁺/MHCII⁺/CD11B⁻) DCs increased strikingly with age. The higher expression of MHCII complex on dendritic cells over time was echoed by an elevation in the frequency of CD11c⁺ microglia (CD45⁺/CD11C⁺/MHCII⁻/CD11B⁺), while CD11c⁻ microglia (CD45⁺/CD11C⁻/CD11B⁺/LY6G⁻/LY6C⁻) were not affected. This data suggests different roles for CD11C positive and negative microglia in homeostasis and sub-clinical inflammation. In contrast to previous studies that tried to capture the dynamics of lymphocytes over time by immunofluorescence staining, our flow cytometry approach revealed that CD4⁺ T cells (CD45⁺/CD19⁻/CD3⁺/CD4⁺/CD8⁻) are present within the retina immediately after birth while CD8⁺ T cells (CD45⁺/CD19⁻/CD3⁺/CD4⁻/CD8⁺) begin to present themselves after 6 months. Interestingly, the frequency of both of CD4⁺ and CD8⁺ T cells increased continuously as the mice aged, while B cells were not observed.

Conclusions: Here we introduce a flow cytometry strategy to capture a global image of various and rare populations of immune cells residing in retina effectively and simultaneously. Moreover, our data suggest that while para-inflammation state of aged retina is thought to arise via microglia/complement activation, activated DCs may also contribute to neuroimmune inflammatory processes.

CONTROL ID: 3547046

SUBMITTER (NAME ONLY): Austen Knapp

TITLE: Swept-Source Optical Coherence Tomography Angiography Findings in Adults with a History of Prematurity

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Knapp, C. Chen, K. Baynes, D. Burton, P.K. Kaiser, S. Srivastava, A. Rachitskaya, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Most babies born prematurely do not develop retinopathy requiring treatment. Complications in this specific population are known to occur in adults. To assess the vasculature in these adult patients with a history of premature birth, we analyzed swept source optical coherence tomography angiograms (SS-OCTA) to identify potential novel imaging biomarkers.

Methods: This is a retrospective IRB approved study. Seventeen eyes from ten adult patients with a history of prematurity (mean age 44 years; range 23-76) imaged with SS-OCTA (Zeiss Plex Elite) were compared to 19 age matched control eyes. SS-OCTA superficial capillary plexus en face 3x3 mm and 6x6 mm scans were analyzed. The border of the foveal avascular zone (FAZ) was traced manually, and FAZ metrics of total area, perimeter, and circularity index (given as a number between 0 and 1, 1 indicating a perfect uniform circle) were calculated with ImageJ software (NIH, Bethesda, MD). Spectral domain OCT (SD-OCT) metrics were also evaluated. Independent t tests were used to compare OCTA and OCT features.

Results: Adults born prematurely had significantly smaller FAZ area ($p=0.001$) of less uniform shape as indicated by circularity index ($p<0.001$) than controls. The mean FAZ area (mm^2), perimeter (mm), and circularity index (0-1) on SS-OCTA were 0.11 ± 0.084 , 1.7 ± 0.72 , and 0.46 ± 0.17 , respectively, in adults with premature birth and 0.21 ± 0.079 , 2.0 ± 0.41 , 0.67 ± 0.11 in controls. There was no significant difference in the mean central subfield thickness (CST, mm), central volume (CV, μm^3), and cube average thickness (CAT, mm) on SD-OCT in adults born prematurely (293 ± 32.5 , 9.92 ± 1.07 , and 276 ± 29.3) and in controls (277 ± 22.6 , 10.4 ± 0.370 , 290 ± 10.3).

Conclusions: SS-OCTA in adult patients with a history of premature birth without treated retinopathy demonstrated significantly smaller and less uniform FAZ than controls. This increased vascularity as seen within the fovea on SS-OCTA may be a useful imaging modality to identify these patients.

CONTROL ID: 3547047

SUBMITTER (NAME ONLY): Monica Del-Rio-Vellosillo

TITLE: Comparison of diagnosis accuracy of the ganglion cell complex thickness in the 7-degree inclined versus horizontalized 8x8 grid of the posterior pole algorithm to distinguish between healthy and glaucomatous eyes

SESSION TITLE: OCT - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Del-Rio-Vellosillo, Hospital Clinico Universitario Virgen de la Arrixaca, El Palmar, Murcia, SPAIN|A. Alvarez-Sarrion, Hospital General Universitario Reina Sofia, Murcia, Murcia, SPAIN|M. Lopez-Bernal, E. Rubio-Velazquez, J. Garcia-Medina, Hospital General Universitario Jose M Morales Meseguer, Murcia, Murcia, SPAIN|M.D. Pinazo-Duran, Universitat de Valencia Facultat de Medicina i Odontologia, Valencia, Comunitat Valenciana, SPAIN|

Commercial Relationships Disclosure (Abstract): Monica Del-Rio-Vellosillo: Commercial Relationship: Code N (No Commercial Relationship) | Aurora Alvarez-Sarrion: Commercial Relationship: Code N (No Commercial Relationship) | Maria Dolores Lopez-Bernal: Commercial Relationship: Code N (No Commercial Relationship) | Elena Rubio-Velazquez: Commercial Relationship: Code N (No Commercial Relationship) | Maria Pinazo-Duran: Commercial Relationship: Code N (No Commercial Relationship) | Jose Javier Garcia-Medina: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the diagnostic performance of the 8x8 grid of the posterior pole algorithm with two different fovea-to-disc inclinations to discriminate between healthy and primary open-angle glaucoma (POAG).

Methods: 85 eyes of 85 glaucomatous patients and 74 eyes of 74 early POAG patients were included. All underwent macular OCT scans (Spectralis, Heidelberg) using the 8x8 posterior pole algorithm with an automatic 7-degree inclination of the fovea-to-disc axis. Ganglion cell complex (GCC) thickness was obtained for the 64 superpixels of the grid. Then, horizontalization of the grid in each eye was performed and the results of GCC were also exported. The areas under the receiver operating characteristics curves (AUROC) values were obtained for the GCC thickness in the 64 cells for 7-degree inclined grid and for horizontalized grid. Heat maps were plotted to represent the AUROC values. The thickness of superpixels with AUROC values ≥ 0.75 were combined for each inclination obtaining a global index for the 7-degree inclined grid (7degINDEX) and the horizontalized grid (horINDEX).

Results: AUROC values were ≥ 0.75 in 25 superpixels in the 7-degree inclined grid (the highest was the superpixel 2.8, AUROC=0.821) and 24 superpixels in the horizontalized grid (the highest was also the superpixel 2.8, AUROC=0.807). We found no significant difference between 7degINDEX AUROC (0.827) and horINDEX AUROC (0.824) ($p > 0.05$, DeLong test).

Conclusions: The 7-degree inclination of the 8x8 grid of the posterior pole algorithm measuring GCC thickness does not seem to outperform the horizontalized grid when discriminating between POAG and healthy eyes.

CONTROL ID: 3547048

SUBMITTER (NAME ONLY): Mortada Najem

TITLE: Assessing clinical and anatomical outcomes for central serous chorioretinopathy treated with standard of care or experimental hyperoxia

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.S. Najem, C. Lemire, A. Ralph, B. Seto, K. Yamada, J.G. Arroyo, Ophthalmology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, UNITED STATES|M.S. Najem, A. Ralph, Boston University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The presence of subretinal fluid (SRF) in central serous chorioretinopathy (CSCR) separates the photoreceptors from the blood supply of the choroid, which could lead to disruptions of the cells in the outer retina especially when CSCR is chronic or recurrent. In this retrospective study, we sought to determine the functional and anatomical outcomes of CSCR based on standard treatment methods as well as experimental normobaric hyperoxia (NBH), which has been proposed to reduce macular edema and improve vision.

Methods: Clinical outcomes and ocular coherence tomography findings were compared for patients with CSCR undergoing observation, laser/photodynamic therapy (PDT), or NBH. A total of 47 patients with active CSCR, acute (≤ 6 months) or chronic (> 6 months), were included and underwent either observation ($n=23$), laser/PDT therapy ($n=7$), 3-hour NBH sessions ($n=13$), or nocturnal NBH ($n=4$). Best corrected visual acuity (BCVA), recurrence, and the thickness of the central macula (CMT), SRF, photoreceptor layer (PL), and outer nuclear layer (ONL) were assessed.

Results: A total of 49 eyes were classified as acute ($n=39$) or chronic ($n=16$) and non-recurrent ($n=26$) or recurrent ($n=15$). Time for complete resolution of SRF was 3.5 ± 1.5 months for acute patients and 11 ± 4.2 months for chronic patients. BCVA improved from baseline for all resolving patients regardless of treatment type. None of the patients in the laser therapy group experienced a recurrent episode after an average follow-up of 38.7 ± 19.7 months (range of 3.6 – 56.6 months) while 48% of observation-only patients experienced a recurrence within an average of 24.9 ± 23.7 months (range of 1.7 to 68.8 months). Patients in the 3hr NBH group showed no statistical difference in any of the parameters tested before and after treatment. When compared to observation patients, resolving nocturnal NBH patients demonstrated a decrease in the time for resolution of SRF (4.5 ± 3.1 and 3.8 months, respectively). In resolving patients, there were consistent decreases in CMT and PL thickness, and little to no change in the thickness of the ONL.

Conclusions: We show that patients with CSCR have a high probability of recurrence and that this may be reduced by laser/PDT therapy. Nocturnal NBH may facilitate earlier resolution of SRF and vision loss. Together, these treatment strategies may improve clinical outcomes for CSCR.

CONTROL ID: 3547050

SUBMITTER (NAME ONLY): Mark Pennesi

TITLE: Twelve-month Findings from Two Phase 1/2 Clinical Studies of Subretinal Gene Therapy Drugs for Achromatopsia

SESSION TITLE: Stem cells/gene therapy/transplantation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M.E. Pennesi, P. Yang, A. Lauer, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|C. Kay, VitreoRetinal Associates PA, Gainesville, Florida, UNITED STATES|R.A. Sisk, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, UNITED STATES|J.M. Comander, R.M. Huckfeldt, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|E. Averbuhk, E. Banin, Hadassah Medical Center, Jerusalem, Israel|B.L. Lam, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|N. Gregori, J.L. Davis, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|E. Leone, D. Halliman, N. Ihekoromadu, M. Feinsod, AGTC, Alachua, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Achromatopsia (ACHM) is an autosomal recessive retinal disease characterized by absence of cone photoreceptor function. Clinical manifestations include reduced visual acuity, complete loss of color discrimination, and photophobia under daylight conditions. Gene therapy drugs, AGTC-401 and AGTC-402, are being developed to compensate for the mutated genes responsible for over 80% of the ACHM cases, CNGA3 and CNGB3. This is an initial report on the twelve-month safety and efficacy findings from two ongoing, Phase 1/2, open-label, dose-escalation trials using recombinant adeno-associated virus (rAAV) viral vectors.

Methods: A single subretinal injection of either AGTC-401 (rAAV2tYF-PR1.7-hCNGB3) or AGTC-402 (rAAV2tYF-PR1.7-hCNGA3) was administered to participants (n=24), age ≥14, into the macula region of the study eye. Participants were sequentially assigned to one of four dose groups in both studies. The safety and efficacy outcomes were measured by best-corrected visual acuity (BCVA) using ETDRS, light discomfort testing (LDT) by ocular photosensitivity analyzer (OPA), ERG/mfERG, retinal sensitivity by static perimetry and microperimetry, color vision testing by Farnsworth D15 and CAD, and patient-reported outcomes (PROs) using a QoL questionnaire (VLSQ-8).

Results: Both drugs were well-tolerated across all dose ranges. Most AEs were mild-moderate. No SAE was drug-related, and 2 participants had SAEs related to raised IOP due to concomitant steroids. AEs due to ocular inflammation were controlled after modification of the steroid regimen. Immunological response to AAV and genes CNGA3 or CNGB3 were not indicative of a safety concern. Among the 24 treated participants, 4 had a 5-letter improvement on BCVA at month 12. Five participants had a 1-log₁₀ lux or more improvement for light sensitivity threshold on OPA analysis. PROs showed patient improvement in outdoor light sensitivity, severity of worst light

sensitivity, and headache. There were small changes for most assessments at month 12 compared to baseline.

Conclusions: Safety results suggest AGTC-401 and AGTC-402 are safe and well tolerated in ACHM patients. There were no indications of significant immunological responses to the vector or capsid. Data across both studies show encouraging signs of biologic activity. Additional patients will be enrolled in both studies and followed through 5 years.

CONTROL ID: 3547055

SUBMITTER (NAME ONLY): Bridget Peterson

TITLE: Revisiting genotype-phenotype correlations in ABCA4-related Stargardt's disease

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Peterson, K. Huang, S. Chan, N. Mergia, V. Selian, J. Szczygiel, H. De Bruyn, A.B. Fulton, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|T. Glavan, J. Bratko, I. Mihalek, Department of Molecular Medicine and Biotechnology, School of Medicine, University of Rijeka, CROATIA|

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ABSTRACT BODY:

Purpose: The phenotypic information surrounding ABCA4-related Stargardt's disease most commonly available in the literature is the age of onset. Based on that information only, we note that the genotypes where neither ABCA4 allele produces a functional protein result in the early onset of the disease (Fig 1A and 1B). However, to begin to understand the disease progression, the longitudinal data are of particular value, Fig. 1C.

Methods: We have collected the disease progression data from 38 patients diagnosed with ABCA4-related Stargardt's disease. The medical literature search resulted in further 600 genotype-phenotype pairs. Therein the longitudinal data, we note, remains scarce.

Results: Based on our dataset, we propose the model in which the rapid decline in the visual acuity is a consequence of the feedback interplay between the photoreceptors (PRs) and the retinal pigment epithelium (RPE). In a nutshell, we argue that if the RPE declined over time in a simple proportion to the number of its cells under the toxic attack by A2E, the byproduct of dysfunctional ABCA4 in the PRs, the decline would be exponential. However, because the PRs themselves depend on the RPE for their viability, the decline must be faster, leading to super-exponential decline in the RPE and, consequently, in visual acuity (VA). This corresponds well with the clinical observation, Fig 1D.

Conclusions: Our hope is that the model will serve as the starting point for discussion of the Stargardt's disease phenotype as a function of ABCA4 genotype (rather than individual alleles). The hope is also that it will motivate systematic collection and publication of Stargardt's disease progression data, and further experimental characterization of the disease-related variants needed for the development of detailed models applicable in the clinical setting.

CONTROL ID: 3547056

SUBMITTER (NAME ONLY): Abdul-Hadi Kaakour

TITLE: Performance of an Artificial Intelligence model in retinal fluid quantification for patients with diabetic macular edema and retinal vein occlusions.

SESSION TITLE: AI in the retina: Clinical Applications

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Kaakour, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|W. Song, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, UNITED STATES|A. Kalur, A. Iyer, J. Muste, R.P. Singh, Center for Ophthalmic Bioinformatics, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|R.P. Singh, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Computational image recognition and machine learning techniques have been used to develop algorithms that distinguish normal retinal morphological features from distorted contours occurring due to the presence of fluid between and within tissue layers. A deep neural network has previously demonstrated efficacy for the detection and quantification of exudative fluid in age-related macular degeneration. However, it lacks validation in diabetic macular edema (DME) or retinal vein occlusion (RVO). This study aims to externally evaluate the performance of NOA against expert graders for the classification and quantification of fluid in DME and RVO.

Methods: Retrospective, non-randomized cohort study performed at Cole Eye Institute, Cleveland, OH. Scans were graded by the Notal OCT Analyzer (NOA, Notal Vision Ltd, Tel Aviv, Israel) machine learning and image recognition algorithm and manually measured by two expert graders who assessed the quantification of fluid using OCTExplorer (Iowa Institute for Biomedical Imaging, Iowa City, IA). The results from manual and NOA reading were compared to determine interclass correlation and Pearson's correlation coefficient. Categorical variables were described using frequencies and percentages, and continuous variables using medians, interquartile ranges, means, and standard deviations.

Results: Twenty DME and 20 RVO Cirrus SD-OCT B-scan macular cubes with retinal fluid were analyzed. In the DME cohort, the overall fluid grader-grader agreement (GGA) was 91.9%, while the NOA-grader agreement (NGA) was 76.5%. This further stratified into 92.2%, 98.9% GGA and 82.3%, 80.8% NGA for intraretinal and subretinal fluid (IRF, SRF) respectively. RVO overall fluid GGA was 96.6% and 68% NGA, differentiating into 96.4%, 99.8% GGA and 42.2%, 42.9% NGA in the IRF and SRF categories.

Conclusions: Manual expert graders exhibited high levels of agreement in both the DME and RVO cohorts, generally higher in evaluating SRF. Between the manual graders and the NOA algorithm a satisfactory level of agreement was found, albeit relatively lower in comparison to human graders. Additionally, there was higher machine-human agreement in the DME cohort than the RVO group. The NOA algorithm is helpful in the classification and quantification of retinal fluid may be a useful clinical diagnostic and management tool to augment decision making.

CONTROL ID: 3547057

SUBMITTER (NAME ONLY): Christian Hyacinthe

TITLE: Characteristics of patients receiving intravitreal injections during COVID-19

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.F. Hyacinthe, S.A. Sadiq, A. Clingerman, R. Desai, A.T. Lyon, R. Mirza, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: After the Illinois shelter-in-place COVID-19 mandate was instituted on March 16, 2020, outpatient ophthalmology care was limited to patients with vision-threatening conditions. In order to better understand the impact of the mandate on patients receiving intravitreal injections (IVIs), we compared key demographic and clinical features of patients seen before and after quarantine measures.

Methods: Retina patients receiving IVIs at Northwestern Medicine sites between 12/1/19 and 6/30/20 were identified and divided into “pre-COVID” (PC) and “Strict-Quarantine” (SQ) groups (12/1/19-3/15/20 and 3/16/20-6/30/20, respectively). A subset of patients lost to follow-up (LTFU), defined as having been seen at least once in the PC period but not at all during the SQ period, were also identified. Comparison of primary diagnoses and self-reported demographic data was performed between these three sub-groups. Primary diagnoses necessitating IVIs were identified as age-related macular degeneration (AMD), diabetic retinopathy (DR), retinal vein occlusion (RVO), and other causes of neovascularization (other).

Results: 1426 injections were administered to 716 patients during the PC period compared to 1121 injections to 637 patients during the SQ period. More injections per patient were performed in the PC period compared to the SQ period (1.99 ± 1.00 vs 1.76 ± 0.87 , $p = 5.87E-06$). There were no significant differences in primary diagnosis or demographic characteristics between these two groups ($p = 0.852$, 0.974 , respectively). 24.2% of PC patients (173 patients) were identified as LTFU. Of the LTFU patients, a lower percentage identified as White and higher percentages identified as Black, Asian and Other in comparison to the PC ($p = 0.0413$) and SQ ($p = 0.00853$) groups. LTFU patients proportionally had a higher percentage of DR (35.88%) and RVO (20.59%) primary diagnoses and a lower proportion of AMD (33.53%) primary diagnoses than patients in the PC ($p=0.0011$) and SQ ($p=0.0014$) groups.

Conclusions: The COVID-19 pandemic resulted in disruption of normal ophthalmic clinic operations. Because Black and other non-white patients and patients with diabetic retinopathy made up higher percentages of the LTFU group, efforts should be made to understand and address any barriers to medically necessary follow-up during this unprecedented public health crisis.

CONTROL ID: 3547059

SUBMITTER (NAME ONLY): Cadmus Rich

TITLE: Development of AU-011 for Choroidal Metastasis

SESSION TITLE: Advances in intra and extra ocular pathologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.C. Rich, A. Savinainen, R. Kines, Aura Biosciences, Inc, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: AU-011 is an investigational virus-like drug conjugate composed of a virus-like particle conjugated to a photosensitizer. AU-011 binds to tumor cells by selectively targeting specifically modified heparan sulphate proteoglycans (HSPGs) on the tumor cell surface. Upon light activation, AU-011 is designed to cause membrane disruption leading to acute cellular necrosis and tumor regression in vivo. The HPV derived VLPs have a tumor tropic nature and have been previously described to have the ability to target a large panel of tumor types. As such, AU-011 has the potential to treat choroidal metastasis using the same treatment paradigm. The most common primary tumors known to metastasize to the choroid are breast and lung. The purpose of this study was to evaluate the potential to treat choroidal metastasis by evaluating the effect of AU-011 in these cancer types both in vitro and in vivo.

Methods: In vitro efficacy was evaluated in a panel of human breast and lung cancer cell lines. Cells were treated with AU-011, and cell binding and cell killing were evaluated by flow cytometry. HSPG targeting and tumor specificity were assessed by inhibiting binding to HSPGs with exogenous heparin. In vivo efficacy was evaluated by utilizing 4T1 and EMT6 syngeneic mouse models for breast cancer. Tumor cells were implanted subcutaneously. AU-011 treatment was initiated when tumors reached approximately 50 mm³. Treatment consisted of a single intravenous administration of AU-011 followed 12 hours later by external exposure to near-IR light. Tumor volumes were measured over time.

Results: In both panels of cancer cell lines, the in vitro cell binding and cell killing potency were in the picomolar range (EC₅₀: 17-250pM). Cell binding and subsequent AU-011 mediated cell death was inhibited by heparin, demonstrating that AU-011 can bind to these tumor cell types in an HSPG dependent manner. In vivo AU-011 treatment demonstrated activity and reduction of growth in 4T1 and EMT6 murine breast tumor models, further corroborating data previously obtained in other murine cancer models.

Conclusions: These data demonstrated that AU-011 can bind to, and kill, cells derived from the most common cancer types known to metastasize to the choroid. Furthermore, AU-011 showed activity in vivo using cognate tumor models. The studies herein support further development of AU-011 for choroidal metastasis.

CONTROL ID: 3547063

SUBMITTER (NAME ONLY): Sarah Zhang

TITLE: Activation of NADPH oxidase 4 Promotes Angiogenic Progenitor Dysfunction in Diabetic Retinopathy

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.X. Zhang, C. Liao, J.J. Wang, Department of Ophthalmology and Ross Eye Institute, University at Buffalo, Buffalo, New York, UNITED STATES|S.X. Zhang, Department of Biochemistry, University at Buffalo, Buffalo, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Oxidative stress resulting from excessive reactive oxygen species (ROS) generation is a major cause of angiogenic progenitor dysfunction that contributes to the development of persistent vascular damage in diabetic retinopathy (DR). Main sources of ROS in blood vessels include mitochondria and NADPH oxidases. However, the expression and role of NADPH oxidases in diabetic angiogenic progenitors and their implication in DR remain poorly understood. Herein, we investigate the role of NADPH oxidase 4 (Nox4) in diabetic angiogenic progenitor dysfunction and DR.

Methods: Diabetes was induced in Tie2-cre mediated Nox4 conditional KO (cKO) mice and wild type (WT) mice. Expression of Nox isoforms (Nox1, Nox2, and Nox4) was examined in bone marrow-derived endothelial outgrowth cells (EOCs) at 1, 3, 6, or 9 months after the induction of diabetes. Cell proliferation, colony formation, apoptosis, senescence, migration, and ROS generation were examined in EOCs from 6-month diabetic Nox4 cKO and WT mice. Signaling pathways of oxidative stress, ER stress, and expression of integrins were investigated.

Results: At 6 and 9 months after diabetes, Nox4 expression in EOCs was significantly increased, while Nox2 expression in EOCs was increased only after 9 months diabetes and no change was observed in Nox1 expression at any time points. In addition, ROS levels were significantly increased in 6 month-diabetic EOCs and the increase was largely abolished in Nox4 cKO cells. Compared to non-diabetic controls, EOCs derived from 6-month diabetic WT mice demonstrated reduced proliferation and colony formation, enhanced apoptosis, increased senescence, and impaired migration in response to VEGF, all of which were significantly improved in EOCs from diabetic Nox4 cKO mice. Mechanically, Nox4 deletion remarkably reduced endoplasmic reticulum (ER) stress and alleviated CHOP and caspase-3 activation in diabetic EOCs. Furthermore, downregulation of Nox4 or inhibition of ER stress significantly alleviated diabetes-induced reduction of integrin b1 improving mobilization of EOCs.

Conclusions: Our results suggest that the aberrant upregulation of Nox4 in diabetic EOCs resulting in increased ROS, enhanced ER stress and disrupted integrin expression may play an important role in angiogenic progenitor dysfunction and DR development.

CONTROL ID: 3547065

SUBMITTER (NAME ONLY): Nejmi Dilmac

TITLE: CRISPR gene editing rescues deficits in human USH2A mutant retinal organoids

SESSION TITLE: Gene therapy in ocular diseases

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: N. Dilmac, N. Haider, B. Desrosiers, R. Pattali, S. Jin, C. Albright, Editas Medicine, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Usher Syndrome type II (USH2A) is a retinal degenerative disease leading to hearing and vision loss that is most commonly caused by recessive mutations in exon 13. USH2A protein is localized in the connecting cilium between inner and outer segments, supporting inner/outer segment formation in photoreceptors. A human iPSC-derived retinal organoid model was developed to test the hypothesis that deleting or inverting USH2A exon 13 (redundant protein domain) could restore deficits caused by USH2A mutation.

Methods: Human iPSC lines were generated from a USH2A patient containing homozygous c.2299delG mutation in exon 13 and healthy control individuals. In patient iPSC clones, exon 13 was deleted (or inverted) by high fidelity CRISPR gene editing. iPSCs from control (n=2), patient (n=5), exon 13-deleted (n=3) and exon 13-inverted (n=3) clones were differentiated at least for 250 days to form high-quality retinal organoids. These organoids were characterized at various time points during organogenesis by gene expression (RT-qPCR), immunohistochemistry (IHC), and morphology.

Results: Control and exon 13-deleted and inverted iPSC clones showed similar gene and protein expression patterns and overall retinal organoid morphologies that are consistent with normal development and published results. In contrast, USH2A mutant iPSC-derived organoids showed irregularity in photoreceptor morphology and deficits in cilia and inner/outer segment organization. Moreover, USH2A, Whirlin and Vldlr proteins were stably expressed in WT but not in mutant retinal organoids. These USH2A mutant abnormalities were rescued by exon 13 deletion (and inversion) using precision gene editing.

Conclusions: USH2A-c.2299delG homozygous mutation caused deficits in photoreceptor morphology, cilia and inner/outer segment formation and destabilization of Usher protein complex (Whirlin/Vldlr/USH2A) during retinal organogenesis. These abnormalities were rescued by precision CRISPR-mediated deletion (and inversion) of exon 13, providing strong support for our exon 13-deletion therapeutic strategy for the treatment of USH2A-associated retinal degenerative diseases.

CONTROL ID: 3547066

SUBMITTER (NAME ONLY): Zakariya Jarrar

TITLE: Heritability, concordance and prevalence of epiretinal membrane (ERM) in a twin population

SESSION TITLE: Vitreoretinal interface diseases / PVR

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O.A. Mahroo, NIHR Biomedical Research Centre at Moorfields and the UCL Institute of Ophthalmology, UNITED KINGDOM|Z. Jarrar, K. Williams, O.A. Mahroo, C.J. Hammond, King's College London Section of Ophthalmology, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To explore the heritability, concordance and prevalence of ERM in a twin population.

Methods: Macular OCT scans (Optovue iVue 100, Optovue, Freemont, CA) taken between 2014-2019 from participants of the TwinsUK cohort were graded for signs of ERM. Zygosity was ascertained using the “peas in a pod” questionnaire. Casewise concordance was calculated for mono- (MZ) and dizygotic (DZ) twin pairs using $2C/(2C + D)$, where C=number of twin pairs concordant and D=number of twin pairs discordant for ERM. The covariance of ERM within MZ and DZ twin pairs was compared, and genetic modelling techniques were used to determine the relative contributions of genes and environment to the variation in ERM and adjusted for age using OpenMx (<http://openmx.psyc.virginia.edu/>) package in R.

Results: OCT scans from 1098 twin pairs (704 monozygotic [MZ] and 394 dizygotic [DZ]) aged 18-89 (mean 54 SD ± 17) were analysed. ERMs were present in 250 individuals, prevalence 11.4%. 35 MZ and 13 DZ twin pairs were concordant for ERM. 80 MZ and 74 DZ twin pairs were discordant for ERM. Concordance was 0.47 and 0.26 for MZ and DZ twins, respectively, suggesting a role for genes. A model combining additive genetic and unique environmental effects provided the best fit and resulted in an ERM heritability estimate of 0.49 (95% CI, 0.38–0.64).

Conclusions: This is the first classic twin study describing the concordance and heritability of ERM. The findings suggest that ERM has significant underlying genetic influences. Further research to better understand these genetics influences is needed.

CONTROL ID: 3547067

SUBMITTER (NAME ONLY): Natalina Martiniello

TITLE: The influence of reading medium on braille reading speed

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Martiniello, W. Wittich, School of Optometry, Universite de Montreal, Montreal, Quebec, CANADA|N. Martiniello, W. Wittich, Centre de recherche interdisciplinaire en readaptation du Montreal metropolitain, Montreal, Quebec, CANADA|

Commercial Relationships Disclosure (Abstract): Natalina Martiniello: Commercial Relationship: Code N (No Commercial Relationship) | Walter Wittich: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The use of braille is associated with higher levels of education and more positive employment outcomes. Braille is read by individuals with visual impairments either in hard copy (paper) or through the use of electronic refreshable braille displays, which provide instant access to information. Braille displays have dots of greater height than traditional paper based formats and may thus provide benefits for older adults with reduced tactile sensitivity. As the cost of braille technologies decline, there is a need to understand how such devices may influence braille reading outcomes. The goal of this study was to explore the influence of reading medium on braille reading speed among a sample of experienced working-age and older adult braille users.

Methods: Forty-six participants (age 23-88, M=52.3, SD=14.9, 15 male) who began learning braille between the ages of 4 and 63 (M=11.75, SD=9.46) read two braille passages from the International Reading Speed Test (IReST) on paper and two passages on display. Demographic information including age and frequency of braille use was collected. Descriptive statistics, Pearson correlations, paired two-sample t-tests and Kruskal-Wallis analyses were conducted.

Results: Reading speeds of 34 to 600 characters/min (M=245.31, SD=157.85) were achieved, with reading on an electronic display being marginally slower (M=241.19, SD=157.71) than reading on paper (M=249.43, SD=164.31). Frequency of braille use led to significant differences in braille reading performance on both paper, $H(4) = 14.317$, $p = .006$, and display, $H(4) = 16.207$, $p = .003$. The age at which braille was first learned was significantly negatively correlated with reading speed on both a display, $r(84) = -0.59$, $p < .001$, and paper, $r(84) = -.63$, $p < .001$.

Conclusions: This study is one of the first to report on differences in reading performance between electronic and paper braille. Results suggest that among experienced readers, there are no significant differences in reading speed when reading on paper versus a refreshable display. Future research should examine differences based on the nature of reading task and whether the benefit of refreshable braille displays may be more pronounced for older adults with reduced tactile sensitivity.

CONTROL ID: 3547068

SUBMITTER (NAME ONLY): Ethan Buhr

TITLE: Opsin 5 (OPN5) photoreceptors are induced in the mouse cornea following epithelial debridement.

SESSION TITLE: Corneal Biology: Epithelial Repair, Neuropathy, Stroma, and Development

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Buhr, N.M. Diaz, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ethan Buhr: Commercial Relationship: Code N (No Commercial Relationship) | Nicolas Diaz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The cornea is typically transparent to most wavelengths of light. Following dissection and organotypic culture, the cornea begins to express the photoreceptor, Opsin 5 (Opn5) which absorbs short-wavelength light. This confers a light sensitivity to the cornea, particularly to wavelengths in the UVA to violet range. These cells are found primarily in the epithelial layer and co-stain with known epithelial cell markers. We wished to replicate ex vivo observations of photoreceptor induction in vivo using a cornea wounding model.

Methods: Mice which express a fluorescent reporter for Opn5 expression (Opn5^{Cre}; Ai14) were anesthetized and given cornea epithelial debridement using an algerbrush. Cells of these mice will produce red fluorescent protein (RFP) when Opn5 is transcriptionally active. Mice were between 1 and 6 months of age and were of both sexes. Three mice were euthanized and corneas collected at 0, 6, 12, 24, and 48 hours post-surgery. Observed fluorescent cells were used as a representation of OPN5 positive cells. The untreated eyes were used as a control group.

Results: OPN5 cells were observed in the epithelial layer of debrided corneas in a manner consistent to what we previously observed ex vivo. Opn5-positive cells were induced by 6 hours after debridement and were no longer present by 48 hours. The peak number of cells was observed at 12 hours post-surgery. This is a much faster induction than we had measured ex vivo, in which the OPN5 cells begin to appear approximately 18 to 24 hours post-dissection. The induced cells were found close to the healing perimeter, but also throughout the epithelium. No induction of Opn5-positive cells was observed in the untreated corneas.

Conclusions: A photoreceptive system is induced in the mouse cornea after epithelial debridement. These photoreceptive cells express the opsin OPN5 and confer direct light sensitivity to the cornea both in vivo and ex vivo. In the future we hope to assess any role these cells play in the healing process.

CONTROL ID: 3547069

SUBMITTER (NAME ONLY): Cynthia McAnally

TITLE:

Evaluation of Antiviral Efficacy for Contact Lens Care Products with Herpes Simplex Virus

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. McAnally, R. Walters, M.M. Gabriel, P. Shannon, R&D Microbiology, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES]

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ABSTRACT BODY:

Purpose: Contact lens care (CLC) products require robust activity against microorganisms in order to clean and disinfect contact lenses (CL). CLC products are required to meet criteria for disinfection of CLs against bacteria, yeast and mold. However, contamination of CLs is not limited to microorganisms, as viruses can also cause keratitis in patients. Herpes simplex virus type 1 (HSV-1) is the leading infectious cause of keratitis and reoccurrences are common. This study assesses multipurpose and hydrogen peroxide CLC products for antiviral efficacy against HSV-1 in the presence and absence of contact lenses.

Methods: A modified version of ISO 14729 was utilized to assess the antiviral activity of CLC products against Human herpes virus 1 ATCC VR 260 with stand-alone and/or regimen testing. Three multipurpose solutions containing polyquaternium-1 and myristamidopropyl dimethylamine (MPS-1,-2,-3), and two hydrogen peroxide products containing 3% hydrogen peroxide (HP-1,-2) were utilized. For stand-alone tests, all three MPS were inoculated with 10^{5-10^8} TCID₅₀/mL of HSV-1 and allowed to disinfect for six hours prior to recovery of viable virus particles. For regimen tests with MPS-1, HP-1 and HP-2, soft contact lenses (Groups 1 and 4) were inoculated with 10^5-10^7 TCID₅₀/lens, cleaned and/or rinsed, and soaked in lens cases according to label instructions. Following disinfection time, samples were serially diluted and plated on VERO cells in order to determine the titer of viable virus. Log and percent (%) reductions were determined based differences between starting counts and survivors at DT. There are no criteria for the antiviral efficacy of CLC products tested with Herpes simplex virus.

Results: For MPS-1, MPS-2 and MPS-3, the log and percent reduction in the stand-alone test (without lenses) at disinfection time was 3.2 (99.9%), 1.7 (90%) and 1.5 (90%) respectively. For the regimen test (with lenses in lens cases), no viable virus particles were recovered from the lenses or from MPS-1, HP-1 or HP-2 solutions after completing the cleaning, and/or rinsing, and disinfection steps resulting in an avg. log reduction of 5.0 (99.999%).

Conclusions: Contact lens care products tested with and without contact lenses showed antiviral activity in tests for Human herpesvirus 1. This information could be useful when counseling contact lens patients with a history of HSV-1 keratitis.

CONTROL ID: 3547073

SUBMITTER (NAME ONLY): Thanasis Panorgias

TITLE: Retinal and perceptual responses to peripheral optical blur in children

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Panorgias, A. Jnawali, F.A. Vera-Diaz, New England College of Optometry, Boston, Massachusetts, UNITED STATES|P. Bex, Psychology, Northeastern University, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Thanasis Panorgias: Commercial Relationship: Code N (No Commercial Relationship) | Peter Bex: Commercial Relationship: Code N (No Commercial Relationship) | Ashutosh Jnawali: Commercial Relationship: Code N (No Commercial Relationship) | Fuensanta Vera-Diaz: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Blur signals play an important role in emmetropization. The purpose of this study was to measure retinal responses and perceptual sensitivity to different types and levels of simulated optical blur across the visual field in young children with normal vision.

Methods: Children ($n=27$, 7.83 ± 0.96 yrs) with functional emmetropia ($SE\ OD +0.91 \pm 0.41D$) participated in 2 tests. (1) Pattern ERGs (pERGs) were recorded using a dead leaves stimulus, previously used in adults. The stimulus was computationally blurred with defocus (DEF) or primary spherical aberration (SA) at three retinal eccentricities (beyond 0° , 6° , and 12°). The stimulus was viewed from a distance of 40 cm and subtended 30° of visual angle. (2) Blur discrimination thresholds were measured with an adaptive 4AFC task previously used in adults. Dead leaves stimuli were blurred with different pedestal levels and increments of DEF or SA beyond 0° , 6° , or 12° eccentricity at a viewing distance of 40 cm. Participants chose which quadrant appeared blurriest. Blur discrimination thresholds were fit with a 2-parameter (Intrinsic Blur, Blur Criterion) dipper function. The data were analyzed using a parametric 2-way ANOVA (pERGs) and nonparametric Friedman's 2-way ANOVA (Blur perception) with Bonferroni corrections for post hoc analyses.

Results: (1) Generally, there was an effect of blur eccentricity on the pERG amplitude, with higher amplitude for the 12° condition compared to the 0° (DEF: $p < 0.0001$, SA: $p = 0.011$) and 6° condition (DEF: $p < 0.0001$, SA: $p = 0.544$), but no differences between the 6° and 0° deg conditions (DEF: $p = 1.0$, SA: $p = 0.827$). (2) The psychophysical data show the same trend as the ERG data, i.e., a significant increase in the intrinsic blur between the 0° and 12° conditions (DEF: $p < 0.0001$, SA: $p = 0.001$) and between the 6° and 12° conditions (DEF: $p = 0.004$, SA: $p = 0.021$). There was also a significant increase in Blur Criterion between the 0° and 12° conditions for DEF ($p = 0.01$), but not for SA ($p = 0.134$) and not between the 6° and 12° conditions for both DEF and SA (DEF: $p = 0.089$, SA: $p = 0.088$).

Conclusions: Blur discrimination data and pERGs using simulated optical blur show similar trends, i.e. higher retinal responses correspond to lower perceptual blur discrimination. Generally, the perceptual blur discrimination data and retinal responses independently indicate that an area between 6° and 12° plays a significant role in blur encoding.

CONTROL ID: 3547074

SUBMITTER (NAME ONLY): Raphaëlle Denis

TITLE: Unintended Placement of Intraocular Lens Haptics in the Sulcus and Association with Posterior Capsular Opacification

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Denis, G. Nassrallah, A.B. Dias, H. Ito, C. Mastromonaco, N. Saheb, M.N. Burnier, McGill University, Montreal, Quebec, CANADA]

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ABSTRACT BODY:

Purpose: Unintended sulcus placement of intraocular lens (IOL) haptics following cataract surgery can lead to severe glaucoma secondary to hemorrhage or inflammation from iris chafing. The occurrence of posterior capsular opacification (PCO), which is the most common complication of cataract surgery, is less well studied in these cases. This study aims to assess the prevalence of sulcus haptics and their potential association with PCO.

Methods: A total of 429 post-mortem human eyes with IOLs, obtained from the Minnesota Eye Bank, were used in this cross-sectional cohort study at the MUHC-McGill University Ocular Pathology & Translational Research Laboratory. Each eye was assessed for sulcus placed IOL haptics using digital images, and PCO, as well as Soemmering's Ring (SR) density, were quantified using Automated Detector Opacification Software (ADOS) as a factor of intensity and area. Two-tailed T-test was used to assess the mean difference in PCO and SR between eyes with sulcus haptics and controls. SR distribution pattern was also assessed and qualified as either focal, diffuse or absent. Odds ratios were calculated to determine if some patterns were more prevalent in each group.

Results: Nineteen (4.4%) eyes contained IOLs with sulcus haptics. PCO was significantly more present in eyes with sulcus haptics (0.910 vs 0.680; mean difference 0.229, 95% CI 0.069-0.390, $p = 0.019$). Similarly, SR was also more present (13.751 vs 8.287; mean difference 5.464, 95% CI 2.336-8.592, $p < 0.001$). When compared to eyes with both haptics in the capsule, eyes with sulcus haptics were more likely to have focal SR opacity (OR 11.98, 95% CI 4.09-35.06) and far less likely to have diffuse opacity (OR 0.049, 95% CI 0.006-0.371).

Conclusions: The prevalence of IOLs with haptics placed in the sulcus was significant in this study. Moreover, the occurrence of PCO and SR is more common in these eyes, with a more distinct pattern of opacification when compared with in bag haptics IOL. Given the significant ocular morbidity associated with sulcus haptics, this study offers signs suggesting their occurrence which may prompt earlier appropriate intervention.

CONTROL ID: 3547075

SUBMITTER (NAME ONLY): Roxanne Noronha

TITLE: Development of a Pediatric Ophthalmology Biobank

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Noronha, K. Flegg, H. Dimaras, The Hospital for Sick Children, Toronto, Ontario, CANADA|H. Dimaras, University of Toronto, Toronto, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: To establish a biobank at the Hospital for Sick Children (SickKids) that catalyzes innovative research in pediatric ophthalmology, and document its first 6 months of operations.

Methods: The biobank leveraged the structural and technological foundation of the SickKids central biobank, which includes state-of-the-art liquid nitrogen facilities, CentraXX data management software, and technical experts trained in biobank operations. Eligible participants, identified in the electronic medical record, included any SickKids patient scheduled to have a tissue removed as part of standard of care that would otherwise be discarded. A broad informed consent model was adopted, allowing storage of tissues for future use in unspecified research; patients were provided with the option to opt-out of specific research components and contact preferences, as per standard SickKids broad consent practice. With patient informed consent, tissues were collected by the patient's circle of care, then processed and stored according to international standards. Clinical annotated data associated with the tissues were collected from the patient's electronic medical record and stored in CentraXX.

A governance structure to oversee sharing of specimens with scientists was developed. The biobank was approved by the SickKids Research Ethics Board.

Results: From June to December 2020, 16 eligible patients were identified; 14 were approached and 13 provided written informed consent (13/14=93% consent rate). Of consented patients, 13 agreed to whole genome sequencing research, 10 to sharing genomic sequencing data with industry, 13 to development of cell lines, 10 to sharing cell lines with industry, and 12 to other research by industry partners; 12 wished to be informed of carrier status and 10 agreed to future research contact. Patients covered 3 diagnoses (retinoblastoma, Coat's disease, von-Hippel Lindau syndrome) and contributed 10 specimens (including tumor, retinal tissue, vitreous humor, aqueous humor and subretinal fluid), resulting in 18 aliquots for use in future research.

Conclusions: This is the first pediatric ophthalmology biobank of its kind. Future steps include registration with relevant biobank databases, and collaboration with additional clinical sites to increase tissue collection, patient partners to enhance recruitment, and scientists to promote use of the tissues.

CONTROL ID: 3547076

SUBMITTER (NAME ONLY): Binapani Mahaling

TITLE: A non-invasive sustained dual-drug delivery system as eye drop for endophthalmitis

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Mahaling, N. Maisha, E. Lavik, Department of Chemical, Biochemical and Environmental Engineering, University of Maryland Baltimore County, Baltimore, Maryland, UNITED STATES|N. Baruah, N. Ahamad, D. Katti, Department of Biological Sciences and Bioengineering, Indian Institute of Technology Kanpur, Kanpur, Uttar Pradesh, INDIA|

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ABSTRACT BODY:

Purpose: Endophthalmitis is a sight threatening condition due to inflammation after microbial infections affecting posterior parts of the eye. Treatments including repeated intravitreal injections of antimicrobial agents may exacerbate complications. However, eye drop/gel system or systemic administration is unable to cross the ocular barriers resulting in reduced bioavailability of drugs in the eye. There is a need for non-invasive drug delivery system (DDS) that can maintain therapeutically relevant intraocular concentration of drugs for a sufficient period of time. Thus, we hypothesized that a slow degrading DDS formulated as eye drop possessing high permeability across the ocular barriers could be an effective non-invasive method of drug (antimicrobial and anti-inflammatory) administration for endophthalmitis.

Methods: Nanoparticles (NPs) with hydrophobic core of slow degrading poly-L-lactide (PLA) loaded with macrolide-antibiotic, azithromycin (AZM) and a corticosteroid, triamcinolone acetonide (TCA) anti-inflammatory drugs were coated with a hydrophilic shell of chitosan (CHI) having mucoadhesive and penetration enhancing properties. The NPs were characterized for size, zeta potential, surface morphology, hydrophilicity, cytocompatibility, hemocompatibility, plasma recalcification, whole blood clotting, antibacterial and anti-inflammatory activity. Additionally, we investigated localization of the coumarin loaded NPs as eye drops in C57BL/6 mice.

Results: The NPs were spherical, ~250nm, moderately hydrophilic, mucoadhesive and cyto-/hemo-compatible. When the NPs were administered as eye drops in C57BL/6 mice, PLA-CHI NPs showed higher bioavailability in retina when compared to PLA NPs. Surprisingly, PLA-CHI itself showed antibacterial properties in both gram positive and gram-negative bacteria and both PLA-CHI-TCA and PLA-CHI-AZM showed higher antibacterial and anti-inflammatory properties than the drug or NPs alone. It showed anti-inflammatory effect against LPS activated BV-2 microglia cells.

Conclusions: The dual drug delivery system showed cyto-/hemo-compatibility, antibacterial and anti-inflammatory properties, adequate bioavailability and provided sustained drug release making it suitable for retinal drug delivery. It also showed synergistic effect than either of the drugs or NPs alone making it more applicable for endophthalmitis, though further evaluation of in vivo diseases model is needed.

CONTROL ID: 3547077

SUBMITTER (NAME ONLY): Joseph Grieco

TITLE: Topline Results From a Multicenter, Open-label, Phase 4 Study of Repository Corticotropin Injection in Patients With Treatment-resistant Severe Non-infectious Keratitis

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.B. McLaurin, Total Eye Care, Memphis, Tennessee, UNITED STATES|G.W. Ousler, Ora, Inc, Andover, Massachusetts, UNITED STATES|D. Wirta, Eye Research Foundation, Newport Beach, California, UNITED STATES|J. Grieco, J. Liu, O. Kacmaz, Mallinckrodt Pharmaceuticals, Bedminster, New Jersey, UNITED STATES|

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ABSTRACT BODY:

Purpose: Keratitis is a painful inflammation of the cornea commonly treated with immunosuppressive drugs. However, additional treatments are needed for patients in whom keratitis is not responsive to standard therapies. Repository corticotropin injection (RCI, Acthar[®] Gel) has anti-inflammatory and immunomodulatory effects through interaction with melanocortin receptors. The goal of this multicenter, open-label, phase 4 study was to evaluate the efficacy and safety of RCI in patients with refractory severe non-infectious keratitis (Clinicaltrials.gov, NCT04169061).

Methods: Patients ≥18 years of age with severe keratitis that is refractory to standard of care received 80 U RCI subcutaneously twice weekly for 12 weeks. Initial assessments included Impact of Dry Eye on Everyday Life (IDEEL) score, Visual Analogue Scale (VAS) for burning/stinging and eye discomfort, corneal fluorescein staining, and conjunctival lissamine green staining as measured by Ora Calibra[™] scales. One-sample binomial tests (null hypothesis: 5%) or one-sample t tests (null hypothesis: no change) were used to perform statistical analyses, as appropriate; significance vs baseline was determined as p<0.05. Adverse events (AEs) were also evaluated.

Results: Topline results in 35 patients showed that a significant proportion (41%-65%) of patients improved ≥20% at weeks 2, 4, 6, and 12 (all measured time points) on the symptom bother score module of the IDEEL questionnaire. A clinically meaningful ≥12-point improvement on the symptom bother score module was achieved in a significant proportion (50%-56%) of patients at all measured time points. VAS score for burning/stinging significantly improved at weeks 2, 6, and 12, as did the VAS score for eye discomfort at all measured time points. Inferior, superior, and central corneal fluorescein staining detecting corneal damage significantly decreased at weeks 4, 6, and 12. Both temporal and nasal conjunctival lissamine green staining for dry eyes were significantly reduced at week 6. Most AEs were rare, with hypertension being the most common, occurring in 2 patients. No serious AEs were related to the study drug.

Conclusions: Topline results of this open-label study showed that RCI significantly reduced the signs and symptoms of refractory severe non-infectious keratitis, in alignment with patient perceptions.

CONTROL ID: 3547078

SUBMITTER (NAME ONLY): Reddikumar Maddipatla

TITLE: High-speed, high-resolution optical coherence microscopy combined with dual-channel fluorescence microscopy for small animal models imaging

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Maddipatla, S. Murugan, C. Liu, P. Tankam, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Usage of small animal models has become a common practice in understanding pathological conditions. The purpose of this work is to develop a non-invasive, high-speed, and high-resolution optical coherence microscopy (OCM) combined with a dual-channel scanning fluorescence microscopy (FM) to enable longitudinal studies of the cornea in mouse models.

Methods: A high-resolution OCM was developed using a source (central wavelength at 850 nm and FWHM of 165 nm) that offers a theoretical axial resolution of $\sim 1.5 \mu\text{m}$ (in tissue). A dual-detection channel FM system with two excitation peaks at 488 nm and 594 nm for green and red fluorophore variants was integrated with OCM. Beams from both systems were combined and focused onto the sample using a 10X objective, which yields a lateral resolution of $\sim 2 \mu\text{m}$. To evaluate this system, a conditional knockout mouse model to express tdTomato transgene that converts into green fluorescent proteins (GFP) on exposure to Cre recombinase was developed using the tet-O-Cre system. Rosa mT/mG reporter mice were crossed with the Keratocan rtTA/ tet-O-Cre transgenic mice to express the tdTomato gene in the corneal stroma. On treatment with doxycycline, part of the tdTomato transgene in the stroma gets converted to GFP over time. Both red and green fluorescence, as well as structural information of the stroma, were simultaneously imaged on a sacrificed mouse using the combined system.

Results: OCM achieved an axial resolution of $\sim 2.4 \mu\text{m}$ in the cornea, which was slightly lower than the theoretical value due to dispersion. A $2.2 \mu\text{m}$ lateral resolution was demonstrated with the combined system. Reflectance and fluorescence were registered simultaneously with the speed of 250 kHz. Fig.1 shows a $1.3 \times 1.3 \text{ mm}^2$ image of the mouse cornea. A $0.3 \times 0.3 \text{ mm}^2$ field of view of the different layers of the cornea is shown in Fig.2, highlighting the epithelial cells, the keratocytes, and endothelial cells.

Conclusions: A combined system integrating a high-resolution OCM and a dual-channel FM was developed and evaluated in imaging mouse cornea. Future work will focus on improving the depth sectioning of FM to enable 3D reflectance and fluorescence in vivo imaging of the mouse cornea.

CONTROL ID: 3547083

SUBMITTER (NAME ONLY): Travis Redd

TITLE: Automated Differentiation of Bacterial from Fungal Keratitis Using Deep Learning

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Infectious keratitis is a leading cause of blindness worldwide. Efforts to address this burden are limited by clinically significant gaps in our ability to rapidly diagnose the causative pathogen. Culture results are delayed and have poor sensitivity, and prior studies demonstrate that human experts are only accurate 66% of the time when differentiating bacterial from fungal keratitis based on clinical appearance. This results in delayed initiation of appropriate antimicrobial therapy and worsened visual outcomes. Herein we address this gap by developing and evaluating a deep learning artificial intelligence system to distinguish culture-proven bacterial and fungal keratitis using corneal photographs.

Methods: We established an image database by collating 1,010 external photographs from handheld digital cameras obtained as part of several randomized clinical trials conducted by the Aravind Eye Care System in India and the Proctor Foundation in San Francisco since 2006. 940 images were used to train the deep learning system, and 70 were reserved as an independent testing set. 50% of the training image set consisted of images from bacterial ulcers, and 50% were from fungal ulcers. We used a transfer learning approach adapting a pre-trained deep learning system (EyeMeter) built on the ResNet-50 convolutional neural network architecture.

Results: This deep learning system demonstrated 76% overall accuracy for differentiating bacterial and fungal corneal ulcers from photographs alone. For detecting bacterial keratitis, the system had 70% sensitivity and 80% specificity. For detecting fungal keratitis, the system had 80% sensitivity and 70% specificity.

Conclusions: A deep learning system trained using photographs from inexpensive handheld cameras was able to distinguish bacterial from fungal keratitis with greater accuracy than the published performance of expert human cornea specialists. Future incorporation of similar technology into mobile telemedicine platforms may reduce blindness from infectious keratitis, particularly in low- and middle-income countries where disease burden is highest but clinical and microbiologic expertise are scarce. Future directions include collection of additional images from geographically diverse sources to optimize and validate this technology.

CONTROL ID: 3547085

SUBMITTER (NAME ONLY): Claire Bell

TITLE: Simultaneous single-cell lineage tracing and transcriptomics of the developing mammalian retina

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Bell, S. Cole, C. Berlinicke, D.J. Zack, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|W. Fang, H. Ji, Johns Hopkins University Bloomberg School of Public Health, Baltimore, Maryland, UNITED STATES|K. Leeper, P. Zhang, T. Wang, R. Kalhor, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retina provides a valuable system for studying neuronal lineages and differentiation through development. Using a novel method we have designed for combining single-cell transcriptomics and lineage tracing, we aim to improve the resolution of developmental mapping of retinal cells as well as to provide comparative analysis of retinal lineages between mice and human iPSC-derived retinal organoids. With this technology, we hope to provide new insights into the transcriptional changes that accompany individual retinal cell-fate decisions and yield a deeper understanding of the mechanisms of retinal development and disease.

Methods: We have developed DREAM-seq (DNA/RNA extraction, amplification, and multiplexing), a high-throughput, multi-omic method for reading transcriptomic and targeted genomic output from single cells. Human iPS cells and mice have been barcoded using the homing guide RNA (hgRNA) system (Kalhor et al. Science 2018), thereby making possible continuous lineage tracing of individual cells throughout development. We are using DREAM-seq to read out single-cell transcriptomes and lineage barcodes at timepoints throughout development from both murine retinas and hPSC-derived retinal organoids. Novel bioinformatic strategies are being implemented in order to generate high-resolution single-cell lineage maps of retinal development.

Results: The methodology and model systems have been developed and validated for performing these lineage tracing studies. We are collecting data from organoids and murine retinas at a range of developmental timepoints, while concurrently developing and testing the necessary bioinformatic tools using in silico modeling and simulation of the data to reconstruct single-cell lineage relationships.

Conclusions: Using DREAM-seq for the parallel analysis of single-cell transcriptomes and lineages will provide us with a deeper understanding of developing retinal cell fates. This will allow us to identify the timing of cell fate decisions, detect rare or intermediate cell types that occur during retinal development, understand the mechanisms of developing cellular subtypes, and potentially identify targets for trans-differentiation. This level of detail will add to our current understanding of retinal development and have implications for treating retinal disease.

CONTROL ID: 3547087

SUBMITTER (NAME ONLY): Cécile Vullings

TITLE: Detailed binocular scotoma mapping reveals adaptive saccades in macular degeneration

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Vullings, Z. Lively, P. Verghese, Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: When the scotoma is binocular in macular degeneration (MD), objects can be obscured and individuals are often unaware that they are missing information. Current methods of detailed scotoma mapping are mainly monocular; very few methods offer the same level of precision for binocular scotoma. We propose a new method to map precisely the binocular scotoma and use this detailed map to investigate adaptive saccade strategies in visual search.

Methods: Six individuals with MD and 4 age-matched controls participated in our study. First, we measured the peripheral fixation locus, the location of the foveal pit and the extent of the monocular scotoma in each eye using an OCT/SLO. Then, we extensively mapped the monocular and binocular scotomata with an eyetracker while fixation was carefully monitored. Participants fixated a cross and responded whenever they detected a briefly flashed dot. The flashes were first presented on a coarse grid, and then at manually selected points to examine the edges of the scotoma in finer detail (Fig 1A). Finally, participants completed a visual search task where they had to report the number of Gaussian blobs randomly distributed across a natural scene.

Results: Monocular scotomata measured in the SLO and eyetracker were highly similar (mean d' value = 2.54), validating the eyetracking method to map scotoma. Moreover, all participants used clustered fixation loci corresponding to their dominant preferred fixation locus. Importantly, the binocular map from the eyetracker was consistent with the overlap of the monocular scotoma profiles from the SLO. In the visual-search task, all participants made mostly horizontal saccades, but individuals with MD made significantly more saccades toward their scotoma than controls for the same directions (Fig 1B). However, their median amplitude was smaller, and therefore a single saccade was not sufficient to fully uncover the region hidden by a large scotoma (Fig 1C). Instead of making sequential saccades toward the scotoma, participants frequently made backward saccades directed to newly uncovered regions.

Conclusions: Our eyetracker method offers a reliable and sensitive tool for measuring the functional binocular scotomata. Determining the location and extent of the binocular scotoma with respect to the fixation locus reveals oculomotor adaptations in daily life such as backward saccades to explore newly uncovered regions during visual search.

CONTROL ID: 3547089

SUBMITTER (NAME ONLY): Zujaja Tauqeer

TITLE: Glucagon-like peptide-1 receptor agonists are associated with decreased risk of progression from non-proliferative diabetic retinopathy to vision threatening diabetic retinopathy

SESSION TITLE: Diabetic retinopathy - risk factors and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Z. Tauqeer, P. Bracha, Q.N. Cui, B.L. VanderBeek, Department of Ophthalmology, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|P. Bracha, Gundersen Eye Institute, Gundersen Health System, La Crosse, Wisconsin, UNITED STATES|B.L. VanderBeek, Center for Pharmacoepidemiology Research and Training, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|P. Hua, Center for Preventative Ophthalmology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Glucagon-like peptide-1 receptor (GLP1R) agonists are a class of incretin mimetics used to treat type 2 diabetes by augmenting insulin release and sensitivity. Despite improved glycemic control, clinical trials have shown a transient worsening of diabetic retinopathy in some patients treated with GLP1R agonists. We examined this paradoxical worsening and assessed risk for progression of nonproliferative diabetic retinopathy (NPDR) to vision-threatening diabetic retinopathy (VTDR), and in particular, proliferative diabetic retinopathy (PDR) and diabetic macular edema (DME).

Methods: A retrospective cohort of patients with NPDR newly started on a GLP1R agonist from a national insurance claims database was compared to a cohort of patients treated with other oral agents and matched for age, sex, race, index year, and number of active diabetic medications. Exclusion occurred for <2 years in database before diagnosis; prior diagnosis of PDR, DME, vitreous hemorrhage, other retinal vascular diseases; or prior VTDR treatment. Primary outcomes were incidence of VTDR, PDR, and DME. Inverse probability of treatment weight (IPTW) was used within a multivariable Cox proportional hazard regression model to test the association between GLP1R agonist exposure and progression to VTDR, PDR and DME. IPTW was derived from a propensity score model based on Diabetic Complications Severity index, hemoglobin A1c (HbA1c), demographic factors and systemic health conditions. HbA1c was modeled in a time-updating fashion.

Results: 3,668 GLP1R users meeting inclusion criteria were matched to 4,821 unexposed controls. In the GLP1R cohort, 132 (3.6%), 22 (0.6%) and 118 (3.2%) patients progressed to VTDR, PDR and DME, respectively. This compared to 353 (7.3%) VTDR, 156 (3.2%) PDR, and 242 (5.0%) DME patients in the control group. Accounting for underlying DM severity with IPTW, GLP1R agonist use conferred a reduced hazard of developing VTDR (hazard ratio [HR] = 0.44, 95% CI: 0.38-0.50, p<0.001), PDR (HR = 0.16, 95% CI: 0.12-0.22, p<0.001), and DME (HR = 0.57, 95% CI: 0.49-0.66, p<0.001).

Conclusions: GLP1R agonist use was associated with statistically significant and clinically meaningful reductions in progression from NPDR to VTDR, PDR, and DME. These results may have implications in treatment choice for patients with diabetic retinopathy.

CONTROL ID: 3547092

SUBMITTER (NAME ONLY): Anelise Dias

TITLE: Diagnosis and histopathological evaluation of soft drusen in patients that underwent evisceration and enucleation

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.S. Dias, H. Ito, S. Bergeron, J. Coblentz, A.A. Goyeneche, M.N. Burnier, MUHC – McGill University Ocular Pathology & Translational Research Laboratory, McGill University Faculty of Medicine, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Soft drusen is large dome-shaped, hyaline granular deposits with poorly demarcated boundaries beneath the (Retinal Pigment Epithelium) RPE. This drusen increases the risk for advanced Age Macular Degeneration (AMD), which can result in vision loss. Soft drusen lifecycle includes growth, anterior migration of RPE atop drusen, followed by collapse, and atrophy. The aim of this study is to correlate the prevalence of soft drusen in histopathological sections of macular region, obtained from enucleated and eviscerated eyes.

Methods: A total of 158 eyes from 158 patients were examined, from the MUHC – McGill University Ocular Pathology & Translational Research Laboratory, Montreal, Canada (2013-2019). Of the 158 eyes, 79 (50%) were enucleated and 79 (50%) were eviscerated. The specimens were considered for the study based on the following inclusion criteria: 1. patients over 50 years of age; 2. histopathologically preserved macular area; 3. presence of sufficient residual tissue for additional cuts; 4. identification by histological criteria of macular area; 5. concrete data of patients, such as age and diagnosis that led to enucleation or evisceration. Histopathological review was performed in digitalized H&E slides (Zeiss AxioScan.Z1) in all patients. Each case was assessed based on the presence of soft drusen and divided by age in decades in both eviscerated and enucleated eyes.

Results: Histopathological analysis of soft drusen was possible in both groups. There was no difference in the frequency of soft drusen between enucleated and eviscerated eyes in patients aged 50 to 59 years [$\chi^2(1)=0,046$, $p = 0,829$], 60 to 69 years [$\chi^2(1)=0,130$, $p = 0,719$], 70 to 79 years [$\chi^2(1)=0,142$, $p = 0,706$] and ≥ 80 years [$\chi^2(1)=0,027$, $p = 0,870$]. The presence of soft drusen increased with age in eviscerated or enucleated patients that were submitted.

Conclusions: The presence and characteristics of soft drusen could be analyzed in both enucleated and eviscerated eyes with similar results. It was possible to find soft drusen using the same histopathological criteria, both in enucleation and evisceration eyes. Prevalence of macular drusen from enucleated and eviscerated ocular specimens in patients over 50 years of age is comparable to the incidence of age-related macular degeneration in this population.

CONTROL ID: 3547093

SUBMITTER (NAME ONLY): Darlene Miller

TITLE: Functional Diversity and Carbon Substrate Metabolic Profiles of Fusarium-Associated Microbiota.

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Miller, J. Maestre-Mesa, J.A. Parel, H.W. Flynn, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Information on the metabolic and functional diversity of the ocular surface fungal-associated microbiota and their role in fungal keratitis is just beginning to be explored Fungal associated microbiomes may help modulate carbon substrate utilization, signaling pathways and mycotoxins production at the ocular surface.

Purpose: To compare and document the impact on the functional diversity, carbon utilization profile (n=31) and mycotoxin production of Fusarium keratitis isolates with unique microbiomes after growth on chocolate agar (choc), potato dextrose agar (pda) and sabouraud agar (sab) with antibiotics (gentamicin and chloramphenicol).

Methods: We used a combination of Whole Genome Sequencing (CosmosID) and Biolog EcoPlates to identify and compare a) Fusarium associated microbiomes; b) percent functional diversity and c) carbon substrate utilization profiles of three Fusarium isolates- Fusarium solani (n=2, FS1, FS2), and Fusarium oxysporum (n=1, FO) recovered from patients with Fusarium keratitis.

Results: The three fungal microbiomes, FS1, FS2 and FO were unique but dominated by 3 phyla, Actinobacteria (57.3% vs 86% v 46.5%), Firmicutes (41.3% vs 9.4% vs 23%) and Proteobacteria (1.2% vs 4.5% and 23%) respectively. Phylum Bacteroidetes was more commonly associated with the FO community (6.8%) than FS1 or FS2 (both <1%). Modulating species for each community (>1%) included Bacillus species and Cellulosimicrobium cellulans for F1, Staphylococcus epidermidis and Brevundimonas diminuta, FS2, Cutibacterium acnes, Citrobacter koseri, Cellulosimicrobium cellulans, Corynebacterium species and Streptomyces species for FO. Functional diversity and carbon utilization profiles differed by isolates and growth environment. In general, functional diversity was highest for the FS1 and FS2 isolates recovered on sabouraud agar (54.8%, 70.7% vs 25.8%) for FO. Community functional diversity was highest for the FO community when recovered on chocolate (45.6% vs 19.5% vs 38.7%) respectively. Complex polymers and carbohydrates were the preferred carbon substrates for all three communities. Genes for fumonisin and trichothecene expression were more likely to be associated with the two fungal microbiomes harboring minimal numbers of Brevundimonas diminuta

Conclusions: Fusarium associated microbiota may impact functional diversity, carbon metabolic profiles and fungal-bacterial interactions at the ocular surface.

CONTROL ID: 3547094

SUBMITTER (NAME ONLY): Fernando Correa

TITLE: Biophysical Characterization of Antibody Biopolymer Conjugate (ABC) Platform for Improved Therapy of Retinal Vascular Diseases

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Correa, C. Su, L. Pham, N. Prasad, C. Chakraborty, J. Lu, R. Jacobson, B. Jandeleit, D. Benoit, X. Huang, A. Jayagopal, H. Liang, V. Perlroth, Kodiak Sciences Inc., California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intravitreally-administered therapies for retinal vascular diseases impose a significant treatment burden due to injection frequency. To address this, we have developed an antibody biopolymer conjugate (ABC) platform, in which a high molecular weight (800 kDa), hydrophilic, zwitterionic, and branched phosphorylcholine based biopolymer is site-specifically conjugated to a full length, humanized, and highly potent anti-VEGF antibody. We investigated the biophysical properties of an ABC in advanced clinical trials, KSI-301, using a series of spectroscopic and biochemical characterization assays.

Methods: Intermolecular interactions of KSI-301 or its payload antibody alone were assessed by size exclusion chromatography, dynamic and static light scattering, and zeta potential, under a range of pH and ionic conditions. Protein secondary and tertiary structure and stability were evaluated by circular dichroism (CD). The relative structural orientations of the antibody and biopolymer portions of KSI-301 were visualized by electron microscopy (EM). KSI-301 and protein FcRn binding and recycling properties were characterized using bioluminescence and endothelial cell-based assays.

Results: Light scattering measurements indicated polymer modifies antibody colloidal properties by reducing nonspecific interactions between protein molecules. These data coupled with CD analysis supported high thermal and steric stabilization of the ABC with preserved antibody secondary and tertiary structure. The 1:1 antibody:biopolymer conjugation ratio was supported by SEC-MALS, SDS-PAGE and EM. FcRn assays indicated that biopolymer conjugation to the antibody prevents FcRn recycling, contributing toward fast plasma clearance of ABCs.

Conclusions: The ABC platform stabilizes antibody structure and imparts favorable clinical properties, such as low nonspecific interactions and reduced antibody recycling through FcRn. These underlying biophysical properties may also contribute to the observed enhanced tissue penetration and improved treatment durability seen for ABC-based therapeutics such as KSI-301. In addition to KSI-301, various ABC platform based biologic or biologic + small molecule therapeutics are in earlier stages of development. Altogether, our continuing studies support the potential of the ABC platform to meaningfully improve or enable the treatment of a myriad of retinal diseases.

CONTROL ID: 3547099

SUBMITTER (NAME ONLY): Tais Estrela

TITLE: Longitudinal Changes in the Central Visual Field and Risk of Visual Acuity Loss in Glaucoma

SESSION TITLE: Clinical Studies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T. Estrela, A.A. Jammal, E.B. Mariottoni, L. Shigueoka, F.A. Medeiros, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess whether longitudinal changes in central visual field increase the risk of visual acuity (VA) loss in patients with Primary Open Angle Glaucoma (POAG).

Methods: VA loss was defined as a loss of 0.2 logarithm of the minimum angle of resolution (logMAR) or more in 2 consecutive exams. The mean value of the 4 innermost paracentral point locations from the total deviation (TD) plot of a 24-2 standard automated perimetry (SAP) test, threat to fixation area (TTF), was calculated and a joint longitudinal survival models were used to evaluate the rates of changes in the TTF area for predicting VA loss over time, adjusting for confounding variables, such SAP mean deviation (MD), age and central corneal thickness (CCT) at baseline, and intraocular pressure (IOP) measurement during follow-up. A separated analysis was performed in a subgroup that included only pseudophakic eyes.

Results: This study included 4,131 SAP tests and 17,704 clinical visits of 1,207 eyes of 900 POAG patients followed for an average of 4.0 ± 3.2 years. The rates of change of paracentral points in TD plot were significantly predictive of VA loss with an increase of 2.6-times the risk of developing VA loss for each 1 dB/year decrease in the slope (HR 2.56, CI, 1.73, 3.82; $P < 0.001$), after adjusting for age, SAP MD and CCT at baseline, and for IOP measurements during follow-up. The risk for VA loss was also higher for the pseudophakic eyes. For this group, rates of change on mean TD of the 4 central points were associated with VA loss with a HR of 4.63 (95% CI:2.38, 8.93; $P < 0.001$) the multivariable analysis.

Conclusions: In our study longitudinal changes on the mean of 4 central points from SAP TD was predictive of development of VA loss in glaucoma patients and should be included in the assessment of risk for visual impairment.

CONTROL ID: 3547100

SUBMITTER (NAME ONLY): Grant Carlisle

TITLE: Impact of Corneal Culture Results on Management of Suspected Microbial Keratitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Carlisle, O. Waldron, I.U. Scott, S. Pantanelli, G. Vora, M.C. Chen, Ophthalmology, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|I.U. Scott, Public Health Sciences, Penn State Health Milton S Hershey Medical Center, Hershey, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the impact of corneal culture results on the management of patients treated for suspected microbial keratitis at a tertiary-care academic institution.

Methods: The Penn State College of Medicine Institutional Review Board reviewed the study protocol and determined the study was exempt from further review. Medical records were reviewed of patients who underwent corneal culture (CPT code 65430) at Penn State Eye Center between 01/01/2015 and 09/01/2020.

Results: A total of 59 corneal cultures from 54 patients were reviewed. The overall culture positivity rate was 46%. Forty-four percent of the positive cultures and 69% of the negative cultures were obtained from eyes treated with topical antibiotics prior to the culture being taken. Bacteria were isolated most commonly (82%), followed by fungi (11%), and Acanthamoeba (7%). The most common bacteria isolated were Staphylococcus aureus (33%), Staphylococcus epidermidis (25%), coagulase negative Staphylococcus (12%), and Pseudomonas aeruginosa (8%). Fungal species isolated included Candida albicans, Candida parapsilosis, Gorodonia species and Fusarium species with equal prevalence. Of the Staphylococcus species isolated, one was resistant to moxifloxacin (S. aureus) and seven were resistant to oxacillin (S. aureus and S. epidermidis). Initial therapy included fortified vancomycin and tobramycin in 61% of eyes and moxifloxacin in 22 % of eyes. Culture results resulted in a management change in 38% of eyes: In 10% of eyes, treatment was escalated, defined as adding or changing to fortified antibiotics, antifungal or anti-acanthamoeba agents, and in 28% of eyes, treatment was de-escalated, defined as discontinuing either vancomycin or tobramycin or changing from fortified antibiotics to commercially available fluoroquinolones.

Conclusions: Culturing corneas with suspected microbial keratitis can impact management in a significant proportion of cases.

CONTROL ID: 3547101

SUBMITTER (NAME ONLY): Arathy Kartha

TITLE: Object Rankings and Notification Preferences for an Object Finder System among People with Ultra-Low Vision

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kartha, S. Lee, G. Dagnelie, Ophthalmology, Johns Hopkins Medicine, Baltimore, Maryland, UNITED STATES|R. Sadeghi, Biomedical Engineering, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|R. Chamberlain, K. Kramer, Minnesota Health Solutions, Minnesota, UNITED STATES|P. Gibson, Advanced Medical Electronics, Minnesota, UNITED STATES|N. Singh, S. Ju, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop a list of everyday items based on the Common Objects in Context (COCO) dataset, that are highly useful among people with native and artificial ultra-low vision (ULV) so that successful computer vision algorithms can be developed for object identification.

Methods: 10 participants with ULV (VA 20/1600) and 5 Argus II users were given 150 items from the COCO dataset and asked to rate the objects as very useful, useful, neutral, not useful, definitely not useful and the scores were 2, 1, 0, -1, -2 respectively. They were also asked about their preferences for system notifications (visual, speech, sound and haptic) for passive (general scanning) and active modes (scanning for a specific object).

Results: Participants with native ULV and Argus II users rated more than 50% of the items on the dataset as useful and very useful. The objects that were reported to be most useful were similar in both groups, the top 5 useful objects reported that would benefit from using an object finder device were phone, empty seat, remote control, person and toilet. The category that was rated the highest was person and the category with the lowest rating was animal (Fig 1). All participants preferred speech and sound notifications compared to visual or haptic notifications for both passive and active modes irrespective of their level of residual vision (between 1.4 and 3.5 log MAR).

Conclusions: We developed a priority list of useful objects from everyday life based on the COCO dataset among people with native ULV and Argus II users. This list of objects will be used to develop an object finder system using machine learning algorithms for people with ULV. Using the subjective ratings from this study, performance measures will be developed to determine the effect of an object finder system on functional performance and accessibility in people with ULV and visual prosthesis. Future studies will compare the effect of different modalities of notifications on functional performance in people with ULV and visual prosthesis.

CONTROL ID: 3547105

SUBMITTER (NAME ONLY): Jay Wang

TITLE: The impact of image processing algorithms on quantitative optical coherence tomography angiography metrics in diabetic retinopathy

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.C. Wang, I. Freedman, L. Hui, E. Li, K.H. Nwanyanwu, Ophthalmology & Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|E. Li, Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|L. Hui, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of using different image processing algorithms to calculate commonly reported quantitative metrics in optical coherence tomography angiography (OCTA) images in patients with various stages of diabetic retinopathy.

Methods: Single center, retrospective, observational study. Patients with diabetes from September 2017 to December 2018 were included. Complete ophthalmological exams and OCTA imaging with the Cirrus HD-OCT 5000 AngioPlex (Carl Zeiss Meditec, Inc., Oberkochen, Germany) were performed at each visit. Patients with coexisting chorioretinal disease were excluded. Scans with poor signal strength or significant motion or segmentation artifact were excluded. Demographic and clinical variables including age, gender, visual acuity, stage of diabetic retinopathy (DR), and presence of diabetic macular edema (DME) were recorded. 8 x 8 mm superficial slab images were thresholded using the Huang, Otsu, or Niblack algorithms in ImageJ (NIH, Bethesda, MD). The vessel density (VD) and skeletonized VD (SVD) were calculated for each image. Mixed-effect uni- and multivariate linear regressions were performed using the Stata statistical package (StataCorp LLC, College Station, TX). P-values < 0.05 were considered statistically significant.

Results: 144 scans from 48 patients were included. 54 were excluded for poor signal strength or significant artifact. Of the remaining 90, 26 had no DR, 47 had nonproliferative diabetic retinopathy (NPDR), and 17 had proliferative diabetic retinopathy (PDR). 24 of 90 scans had DME. The thresholding algorithm used significantly impacted VD and SVD even when controlling for age, DME, and DR stage (p-values < 0.001). The Otsu and Niblack algorithms gave significantly lower measurements of VD and SVD than the Huang algorithm (p-values < 0.001). DME was significantly associated with lower VD and SVD across all algorithms (p-values < 0.015). PDR was borderline significant for lower VD (p = 0.056) and significant for lower SVD using the Huang algorithm (p = 0.010) but not significant using Otsu and Niblack.

Conclusions: Caution must be taken when quantitatively analyzing OCTA images, as the specific thresholding algorithm used may impact the results of any given study. There is a need for standardization of image processing algorithms to ensure robust and consistent analysis of OCTA imaging.

CONTROL ID: 3547106

SUBMITTER (NAME ONLY): Ines Zamoun

TITLE: Automated analysis of large vessel blood flow using AOSLO

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Zamoun, S. Ongun, S. Houston, J. Greenwood, A. Dubis, Department of Ophthalmology, University College London, London, London, UNITED KINGDOM|A. Dubis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Several studies have shown ocular blood flow anomalies in vascular disorders (diabetes, multiple sclerosis, and dementia) disorders using adaptive optics scanning ophthalmoscopy (AOSLO). One AOSLO method for studying vascular change been XT, where spatial data is acquired for part of the scan, then freezing the fast scanner to measure cells coming past the scanner (Figure 1). The challenge is that while data is becoming easier to acquire, analysis routines that stabilize eye motion, extract vessel features, and flow data are still manual and time-consuming.

Methods: Blood flow video sequences were acquired using a bespoke multimodal AOSLO (Boston Micromachines Corp, Boston, MA). The AOSLO simultaneously acquires up to four video sequences at 26Hz. Image motion stabilization and removal of bad frames is the first step, accomplished through a novel template matching algorithm. Next, line and edge detectors were employed to detect the vessel to scan direction angle. Cell speed was extracted by line detection techniques that detected the slope of the cell tracks in the Time portion (Figure 1). Lastly, to assess the validity of our extraction automated measures were compared to frames quantified manually by two graders.

Results: The comparison of manual and automated methods was made over 100 images. For this image set, 98% were manually measurable compared to 80% using automated methods. For this shared dataset, the most experienced grader had a slight bias (-2.61; limits: -12.5 to 7.3 mm/s, with greater variability at higher velocities) between trials, with poorer repeatability to the less experienced grader (bias: - 13.07; limits -33.8 to 7.7 mm/s). In comparison, automated methods showed results with 70% accuracy (bias: 2.42; limits -15 to 13 mm/s). The greatest benefit was in time-saving where manual processing took 43 ± 5 min to complete, automated methods took 2.83 sec to extract up to 96 cell profiles per frame.

Conclusions: The method presented here simplifies the processing pipeline from three steps to a single workflow. In addition, there is a drastic reduction in time consumption for data extraction, while providing comparable results. These processing improvements will allow this technology to proliferate and potentially. We aim at developing tools to quantitatively model the changes in blood velocity profiles in the human eye, non-invasively.

CONTROL ID: 3547107

SUBMITTER (NAME ONLY): Joseph Anaya

TITLE: Synchronous Audio-Visual Telemedicine at Wills Eye Hospital During Covid-19

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Anaya, J. Anhalt, Z. Bas, J.R. Bilyk, M. Fuska, S. Lally, P.L. Mellen, A. Murchison, M. Schoen, C. Shields, A. Yaghy, J. Haller, Wills Eye Hospital, Wills Eye Hospital, Philadelphia, PA, US, hospital, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the use of synchronous audio-visual telemedicine at Wills Eye Hospital (WEH) during the COVID-19 pandemic.

Methods: A retrospective chart review was performed on visits coded as synchronous, audio-visual telemedicine, covering March 15th to May 15th, 2020. Telemedicine software reported the length of synchronous patient and physician time in the visit. Patient satisfaction surveys were completed at the conclusion of each visit. Results are analyzed with descriptive statistics.

Results: During the study period, WEH performed synchronous, audio-visual telemedicine for 495 patients. Patients averaged 51 years of age, with a range from 1 to 98 years. 61% of patients were female and 44% identified as white. The Primary Eyecare Service performed the plurality of evaluations (40%), with the remainder performed by the departments of Ocular Oncology (20%), Cornea (12%), Neuro-Ophthalmology (11%), Oculoplastics (6%), Pediatric Ophthalmology (6%), Glaucoma (5%), and Retina (1%). The most common diagnosis categories were blepharitis or dry eye (10%); stye, chalazion or other eyelid pathology (8%); glaucoma (6%); anterior uveitis (4%); choroidal melanoma (4%); corneal abrasion (3%); allergic conjunctivitis (3%); herpetic dermatitis (3%); viral conjunctivitis (2%); and strabismus (2%). Median synchronous patient-physician time in the visit was 9 minutes. Patients, on average, answered 9.2 out of 10 as their likelihood of recommending the service to a friend.

Conclusions: During the initial phase of the COVID-19 pandemic, WEH employed synchronous audio-visual telemedicine across a wide range of clinical indications with acceptable operational efficiency and high patient satisfaction.

CONTROL ID: 3547108

SUBMITTER (NAME ONLY): Sushil Dubey

TITLE: Histone deacetylases 1 and 2 regulate chromatin modifying enzymes in mouse retinal pigment epithelium

SESSION TITLE: Retinal diseases: molecular and biochemical disease mechanisms

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.K. Dubey, K. Mohan, K. Jung, M.E. Kleinman, Department of Surgery, East Tennessee State University, Johnson City, Tennessee, UNITED STATES|J. Liu, Department of Biostatistics, Virginia Commonwealth University, Richmond, Virginia, UNITED STATES|Q.J. Wang, Department of Ophthalmology and Visual Sciences, University of Kentucky, Lexington, Kentucky, UNITED STATES|

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ABSTRACT BODY:

Purpose: Histone deacetylases (HDACs) 1 and 2 are highly conserved nuclear enzymes that are the core components of the corepressor complexes. HDAC1 and 2 regulate the chromatin structure and function and play a key role in critical biological processes like aging, oxidative stress, autophagy, and proteinopathy. Although these cellular processes are risk factors for several age-related eye diseases, the role of HDAC 1 and 2 are not well defined in the context of the eye and eye-related disorders. The current study explores a previously unrecognized role for HDAC1 and HDAC2 in regulating chromatin modifying enzymes in mouse RPE.

Methods: We used CRISPR/Cas9 genome editing system to generate single or combinatorial depletion of HDAC 1 and 2 in ARPE19 cells. Also, in vivo effects of HDAC 1 and 2 on chromatin modifying enzymes were determined using a transgenic mouse that expresses Cre recombinase in the RPE with floxed HDAC 1 and 2. RNA was isolated from both the ARPE19 and mouse RPE cells (at 4 and 8 weeks). qPCR was conducted to transcriptionally profile a panel of 84 epigenetic chromatin modifying genes that included DNA and histone methyltransferases, DNA and histone demethylases, histone acetyltransferases, deacetylases, phosphorylases, and set domain proteins.

Results: Ablation of HDAC 1 or 2 leads to compensatory upregulation of other HDACs. Simultaneous deletion of HDAC 1 and 2 leads to repression of several chromatin modifying enzymes. The mouse RPE showed differential expression of approximately 16 % genes at 4-week, and this drastically increases to 50 % genes at 8-week. This is concordant with the qPCR data as 8-week old mouse RPE had lower levels of HDAC1 and 2 transcripts than 4-week old RPE. Interestingly, except class II MHC transactivator (Ciita) gene, all the other genes were downregulated. Some of the genes which display altered expression as early as 4 weeks and continue the trend in 8-week mouse RPE include Atf2, Kat2b, Ncoa1, Ube2b, Usp21, and Hsp90ab1. Interestingly, HDAC 1 and 2 depleted RPE cells show downregulation of many HDACs with the maximum depletion of HDAC11 amounting to nearly 50 % of control. Thus the data shows that combined depletion of HDAC1 and HDAC2 can alter the transcript levels of many chromatin modifying enzymes.

Conclusions: In conclusion, these data show that HDAC1 and HDAC2 play an essential role in the transcriptional regulation of chromatin modifiers.

CONTROL ID: 3547110

SUBMITTER (NAME ONLY): Robert Zawadzki

TITLE: Progress on measurements and interpretation of Optoretinograms (ORG) in mice.

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.J. Zawadzki, P. Zhang, G. Peinado, R. Meleppat, E.N. Pugh, Cell Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|R.J. Zawadzki, Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|E. Pijewska, M. Meina, M. Szkulmowski, Institute of Physics, Uniwersytet Mikolaja Kopernika w Toruniu, Torun, Kujawsko-Pomorskie, POLAND|

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ABSTRACT BODY:

Purpose: To present recent advancements in measurements, interpretation, and modeling of the light-evoked functional retinal imaging with Optical Coherence Tomography. To endorse use of the term Optoretinogram (ORG).

Methods: Albino (Balb/c) mice were imaged in vivo with a custom Scanning Light Ophthalmoscopy / Optical Coherence Tomography (SLO/OCT) retinal imaging system. Before the ORG experiments, mice were dark-adapted for over 6 hours. In addition to our standard OCT intensity-based ORG analysis (time-dependent changes of the depth scattering profiles of retinal layers), we have also extracted phase-based ORG signals (time-dependent changes of the phase difference (path length) between retinal layers) from the same data sets. To test the impact of retinal water homeostasis on the light-evoked retinal response, we have induced a mild, diffuse central retinal edema by intraperitoneal (IP) injection of distilled water.

Results: The depth scattering ORG profiles extracted from the OCT data reveal correlations between depth positions and intensity of different outer retina bands. The phase-based ORG signals extracted from the same data sets, although more sensitive to retina motion and more computationally demanding, provided an order of magnitude higher sensitivity of detecting changes in retina layer positions. The comparison between ORG responses during mild, diffuse central retinal edema and the normal retina without water injection shows several differences in the kinetics of the retina layers swelling and OCT scattering, suggesting that water movements play an important role in standard light-evoked PRC-NVU functional response. These results also indicate that ORG could be used to assess alterations in retinal water homeostasis

Conclusions: Successful implementation of phase-based ORG signal analysis in mice provided higher sensitivity for detecting changes in retina layer positions, what should potentially allow separation of Cone and Rod based ORGs in mice. Changes in the ORG signals caused by a mild, diffuse central retinal edema further confirmed the water movement between different compartments of the outer retina as the origin of measured ORGs. The use of "ORG" term draws an instructive parallel to the ERG (electroretinogram), which has long been used to assess retinal function in vivo. Specifically, the ORG, like the ERG, comprises multiple components arising from distinct cells and mechanisms.

CONTROL ID: 3547112

SUBMITTER (NAME ONLY): Simone Tzaridis

TITLE: Functional relevance of hyper-reflectivity in macular telangiectasia type 2 (MacTel)

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Tzaridis, M. Friedlander, The Lowy Medical Research Institute, La Jolla, California, UNITED STATES|S. Tzaridis, M. Friedlander, Molecular Medicine, The Scripps Research Institute, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A common finding associated with disease progression in macular telangiectasia type 2 (MacTel) is the presence of hyper-reflective changes on optical coherence tomography (OCT). However, an association between hyper-reflectivity and any functional impairment has not yet been evaluated. In a retrospective, cross-sectional cohort study, we quantify hyper-reflectivity on en face-OCT and study its functional relevance to MacTel.

Methods: Baseline image and functional data from participants of a phase 2 clinical trial (NCT01949324) that studied the effect of Ciliary Neurotrophic Factor in patients with MacTel were analyzed. The projection of hyper-reflectivity within different layers on OCT was used to generate an en face view and measure the en face size of hyper-reflectivity. Ellipsoid zone (EZ)-loss was additionally evaluated, and en face images were superimposed onto microperimetry sensitivity maps permitting an estimate of mean retinal sensitivity within areas displaying hyper-reflectivity and EZ-loss, respectively. Best-corrected visual acuity (BCVA) and reading speed were also analyzed.

Results: 52 eyes from 52 patients were analyzed. Hyper-reflectivity was present in 32 (62%), and EZ-loss in 50 (96%) eyes. Mean lesion size was 0.11mm² (range 0.01-0.26) for hyper-reflectivity and 0.51mm² (range 0.02-1.34) for EZ-loss, and lesion sizes correlated strongly (Spearman $r=0.79$, $p<0.001$). While both lesions were associated with a significant decrease in retinal sensitivity, comparison of mean sensitivity thresholds in hyper-reflective and EZ-loss lesions differed significantly (0.9 ± 2.6 dB vs 16.3 ± 5.8 dB [mean \pm SD]; $p<0.001$), demonstrating an almost complete loss of sensitivity in hyper-reflective areas.

No correlations were found between the size of hyper-reflectivity and BCVA ($r=0.09$) or reading speed ($r=-0.17$).

Conclusions: We present a method to quantify hyper-reflectivity on en face OCT in MacTel. The en face projection of hyper-reflectivity enables a direct correlation with retinal function as evaluated by microperimetry. We demonstrate that hyper-reflectivity in MacTel is associated with severe functional impairment, resulting in an almost complete loss of retinal sensitivity within those lesions.

CONTROL ID: 3547115

SUBMITTER (NAME ONLY): Debresha Shelton

TITLE: The effects of light-induced retinal damage (LIRD) in C57BL6/J mouse is mediated by RPE-65 activity

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Shelton, S. Ferdous, V. Summers, I. Gefke, M.A. Chrenek, P. Girardot, J.H. Boatright, J.M. Nickerson, Department of Ophthalmology, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Controversy exists in the field regarding the extent of heterogeneity in microglial responses in a damage dependent context in the eye. We investigated the hypothesis that mutations in genes involved in the visual cycle, namely rpe65, can be used to study changes in damage kinetics and immune cell recruitment by modulating the extent of phototoxicity

Methods: Using mice containing the wildtype Rpe-65(Leucine at aa450) and the low activity variant (L450M), we used light-induced retinal damage (LIRD) to study how changes in Rpe-65 affects damage kinetics in the C57BL6/J line. Mice were aged to P60+. We used both L450 and L450M animals that were exposed to LIRD at 50,000 lux for 5 hours during the dark phase of their circadian rhythm (ZT12-ZT17). Animals were then grouped into day 3, 5, 7, and 10 post LIRD groups, at which time retinal thickness and morphology were measured via SD-OCT and cSLO. Animals were sacrificed immediately after terminal in vivo data collection and ocular tissue was collected for RPE flat mounts. RPE flat mounts were stained with markers for microglia (IBA-1), zonula occludins (ZO-1), and cell nuclei (Hoescht). The IBA-1 positive cells that were deposited into the RPE sheet were then counted and examined for morphology.

Results: Preliminary data suggest that post LIRD mice expressing the L450 wildtype version of Rpe65 exhibit early signs of morphological changes in fundus images and SD-OCT images compared to animals expressing the L450M variant. The L450 animals have an increased presence of autofluorescent dots (postulated to be microglia) in cSLO images that are detectable at ~ 3 days within the RPE layer. Additionally, quantification of IBA-1- positive cells in the RPE layer by immunohistochemistry show that there is a significant difference between IBA+ cell deposition between L450 and L450M mice at days 3, 5, and 7 (p-value <0.05). The most significant differences in IBA+ cell counts at the RPE were on day 7 (p-value < 0.001) post LIRD (n=3/group).

Conclusions: The L450M Rpe65 variant has 60% of the wildtype Rpe65 (L450) activity level. Here we show that the L450 are more susceptible to LIRD damage as characterized by SD-OCT, cSLO, and IHC images. This data suggests that changes in RPE function via reduction of Rpe65 can change both the extent of damage and the kinetics of damage resolution.

CONTROL ID: 3547116

SUBMITTER (NAME ONLY): Tatyana Appelbaum

TITLE: Reactive changes of retinal microglia, astrocytes, and Müller glial cells in canine model of retinal atrophy caused by the mutation in RPE65 gene.

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Appelbaum, E. Santana, K.L. Gardiner, G.D. Aguirre, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Leber congenital amaurosis (LCA) is a group of retinal diseases characterized by severe visual impairment. One form of LCA is caused by mutations in the RPE65 gene, which encodes the retinal pigment epithelium (RPE) isomerase. The aim of this study is to evaluate an impact of RPE65 deficiency on retinal glial cells response.

Methods: Retinas of middle-aged normal and RPE65 mutant dogs were processed for morphologic evaluation and immunohistochemistry using cell-specific markers.

Results: In RPE65 mutant dogs, active migration of IBA1⁺/CD18⁺ microglia and GFAP⁺/VIM⁻ astrocytes toward the outer retinal layers was found in peripheral, mid-peripheral and to a lesser extent in central part of superior retina. We further observed disease associated changes in expression pattern of glutamine synthetase (GS) and excitatory amino acid transporter 1 (EAAT1), the key proteins in glial-neuronal transmitter recycling. In normal retina GS and EAAT1 are expressed in Müller cell bodies and processes. In RPE65 deficient retinas expression of GS and EAAT1 was significantly reduced in Müller cell processes in the ONL that extended toward the OLM. Furthermore, we observed in Müller glia induction of axon guidance receptor ROBO1 expression and upregulation of type III intermediate filament protein VIM, indicating an activation of gliotic responses. Interestingly, the disease associated changes in ROBO1 expression were accompanied by upregulation of its ligand SLIT2 in PAX6⁺ amacrine cells.

Conclusions: The study data provides new insight into RPE65 disease pathology and can be applied to the interpretation of outcomes of retinal gene therapy in animal models and humans.

CONTROL ID: 3547121

SUBMITTER (NAME ONLY): Rupak Dhoot

TITLE: Emergency Department Utilization of Ophthalmology Services

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Yearly rising emergency department (ED) visits, especially for nonemergent conditions, create significant strain on hospital systems. This study aims to determine the percentage of nonemergent ophthalmology ED consults at a Level 1 trauma center and identify associated risk factors.

Methods: All ED encounters at Memorial Hermann Hospital (Houston, TX) from 1/2015-1/2020 with ophthalmology consultation were reviewed to determine the principal ophthalmic ICD10 diagnosis code. Ophthalmic ICD10 codes were categorized as emergent, nonemergent, or unspecified based on whether it represented an immediate threat to vision or could be managed outpatient. Procedures performed, patient demographics including home zip code, and insurance type were recorded. The zip code was used to calculate distance to the hospital and obtain published median income data for that area. Risk factors that affect the incidence of nonemergent visits were identified using stepwise logistic regression analysis.

Results: There were 6789 encounters of which 5075(75%) were emergent, 1275(19%) were nonemergent, and 437(6%) were unspecified. The mean age was 41.6 years (± 21.2) and 3942(58%) were males. The most frequent diagnosis was a fracture related diagnosis such as orbital floor or medial wall fracture 1170(17%), followed by eyelid laceration 507(7%) and corneal abrasion 373(5%). 1293 procedures were performed with the most frequent procedures being repair of open globe 284(22%), margin laceration 232(18%), and simple eyelid laceration 205(16%). Risk factors for nonemergent encounters were: females (Odds ratio (OR)=1.9 vs males, $P<0.001$), seniors 65+ (OR=1.5 vs adult 18–34 years, $P<0.001$), median income $>100k$ (OR=1.4 compared to \$40–\$60k, $P=0.021$), patients who live <10 miles from the hospital (OR=1.5 vs >30 miles, $P<0.001$) and patients who had commercial insurance (OR=1.6 vs self pay, $P<0.001$).

Conclusions: Most encounters resulted in an emergent diagnosis underscoring the importance of ophthalmic emergency triage. The most frequent diagnosis (fracture) however did not correspond to most frequently performed ophthalmic interventions illustrating that a large portion of ED ophthalmic care does not result in surgical intervention. This data and the demonstrated risk factors for non-emergent use may help identify areas for intervention to optimize ED efficiency.

CONTROL ID: 3547122

SUBMITTER (NAME ONLY): Alfred Yu

TITLE: Activated microglia target specific ganglion cell types in experimental glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A.K. Yu, L. Della Santina, M. Soliño, Y. Ou, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: While it is well known that pathological consequences of glaucoma involve degeneration of retinal ganglion cells (RGCs) and their axons, increasing evidence has pointed to selective vulnerability of specific RGC types. We have previously shown that microglia activation increases following glaucomatous injury, but their role in synapse disassembly in the inner plexiform layer (IPL) and specific RGC type vulnerability is unknown. Here we determined whether microglia are positioned to play a role in the selective vulnerability of alpha OFF-transient RGCs.

Methods: Laser-induced ocular hypertension (LIOH) was performed unilaterally on adult CD-1 mice expressing Cx3cr1-GFP, in which microglia are fluorescently labeled. Mice were sacrificed 7 days-post LIOH and individual RGCs were labeled by ballistic delivery of dextran dye. Immunolabeling was used to detect expression of postsynaptic protein, PSD95. Z-stacks were acquired using confocal microscopy. Microglia contact with individual RGCs was analyzed with VolumeCut (<https://lucadellasantina.github.io/VolumeCut/>) and colocalization of PSD95 with RGCs and microglia were evaluated throughout the IPL using ObjectFinder (<https://lucadellasantina.github.io/ObjectFinder/>). Statistics were performed using the Wilcoxon rank-sum test and one-way ANOVA.

Results: After IOP elevation, contact points made between microglia and individual alpha RGCs increased for OFF-sustained (OFF-S), OFF-transient (OFF-T), ON-sustained (ON-S), and ON-transient (ON-T) RGCs (42.5%, $p=0.34$; 189%, $p=0.03$; 264%, $p=0.02$; 215%, $p=0.003$, respectively). The percent change was significantly greater in OFF-T compared to OFF-S RGCs ($p=0.04$). This increase in contact points also resulted in greater colocalization of microglia with PSD95 sites on individual RGCs: for OFF-S (75.4%, $p=0.02$), OFF-T (298%, $p=0.02$), ON-S (155%, $p=0.06$), and ON-T (282%, $p=0.007$). The percent change was significantly greater in OFF-T compared to OFF-S ($p=0.03$), and in ON-T compared to ON-S ($p=0.04$).

Conclusions: Following IOP elevation, microglia in the IPL increase their contact with individual RGCs. Microglia contact favored OFF-T over OFF-S RGCs and targeted PSD95 sites to a greater degree in the transient vs. sustained RGC types, suggesting that microglia may play a role in the selective vulnerabilities of specific RGC types.

CONTROL ID: 3547123

SUBMITTER (NAME ONLY): Sylvia Groth

TITLE: Novel Virtual-Reality Perimetry in normal children compared to Humphrey Field Analyzer

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.L. Groth, E. Linton, E. Brown, S. Donahue, Ophthalmology, Vanderbilt University, Nashville, Tennessee, UNITED STATES|F. makadia, Ophthalmology, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Perimetry in children is an invaluable modality for assessing afferent function. Current threshold perimeters demonstrate relatively poor reliability and satisfaction. The Olleyes VisuALL (OV) is a commercially available video-game based automated static threshold perimeter that uses a Virtual Reality headset, and a wireless remote.

Methods: Fifty normal subjects ages 9-17 (mean=13 years, 50% female) performed Humphrey Visual Field (HVF) 24-2 and Olleyes VisuALL pediatric threshold perimetry. Test time, reliability parameters, and effects of age, gender, and ethnicity were evaluated. Normative threshold sensitivities were established by percentile. Patient satisfaction surveys were administered.

Results: Median time to completion for OV and HVF was 7.06 and 5.25 min/eye respectively. Age-adjusted thresholds were similarly distributed between OV and HVF (Mean sensitivity 31.8 ± 1.11 dB OV, 31.0 ± 1.53 dB HVF), mean inter-subject variability was no different as measured by Gini's Mean Difference (2.7 ± 0.4 OV and 2.7 ± 0.6 HVF, $p > 0.25$). Mild age-effects on threshold sensitivity in OV were similar to HVF ($R^2 = 0.10$ $p < 0.01$ OV; $R^2 = 0.08$ $p < 0.01$ HVF). Mean threshold sensitivities in the same eye were compared by linear regression ($R^2 = 0.11$ $p < 0.001$), and 5th percentile values were derived empirically at each location. Geographic effects on sensitivity and variability were concentric in the HVF as expected, and more sporadic for the OV. Patient satisfaction scores favored the OV device experience (1-5 scale, Wilcoxon matched-pairs signed rank test $p < 0.01$).

Conclusions: Attention to the task has long been a challenge in pediatric visual field testing. This game-based perimeter has higher patient satisfaction as well as tight correlation to the standard of care perimeter. Direct comparison of the two demonstrates less variability and tighter thresholds with the portable instrument which should translate into better ability to detect defects. The portability of the test allows it to be done in myriad environments lending to flexibility that can benefit children.

CONTROL ID: 3547124

SUBMITTER (NAME ONLY): Margarete Karg

TITLE: In vivo epigenetic reprogramming reverses the age-induced morphological decline of retinal pigment epithelial cells

SESSION TITLE: RPE pathology in AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Lu, D. Sinclair, Department of Genetics, Harvard Medical School, Blavatnik Institute, Paul F. Glenn Center for Biology of Aging Research, Boston, Massachusetts, UNITED STATES|D. Sinclair, Department of Pharmacology, School of Medical Sciences, Laboratory for Ageing Research, Sydney, New South Wales, AUSTRALIA|M. Karg, E. Hoffmann, H. Philipose, B. Ksander, M. Saint-Geniez, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M. Karg, B. Ksander, M. Saint-Geniez, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Aging of the retina results in a gradual visual loss due to the dysfunction and ultimately death of cells within the neural retina and retinal pigment epithelium (RPE). Importantly, aging is the highest risk factor for severe eye diseases, such as glaucoma and AMD. As the increased susceptibility of aging cells to pathological insults is a major root-cause for disease development, cell rejuvenation may prevent disease onset and/or progression. We recently reported that partial epigenetic reprogramming in vivo using AAV2-OSK (Oct4, Sox2, Klf4) reversed the biological age of retinal ganglion cells (RGCs) in 12-month-old mice as determined by their epigenetic clock, increased visual function, and “youthful” methylome and transcriptome profiles. In the current study we examined whether in vivo epigenetic reprogramming can be applied to RPE and reverse aging of the outer-retina complex.

Methods: 24-month-old mice received subretinal injections of AAV2-OSK. Negative controls included mice that received AAV2-GFP, or no injections. Young mice (4-6 months) were used as positive controls. Visual acuity was measured via optomotor reflex (OMR), and phototransduction assessed by scotopic ERG. Morphological examinations were conducted on retinal sections via TEM and by immunostaining of RPE whole mounts.

Results: Compared to young mice, aged mice showed reduced visual acuity ($p < 0.05$, $n = 12$) with marked loss of photoreceptor, bipolar and RPE ERG responses (a and b wave $p < 0.0001$, c wave $p < 0.001$, $n = 10$). Subretinal injection of AAV2-OSK transduced approximately 50% of the RPE and did not alter cell number, area and nuclei/cells at two weeks. Histological analysis showed improved retinal morphology in the OSK+ regions of experimental aged mice compared to the controls (AAV2-GFP, or uninjected). Ultrastructural imaging confirmed reduced phenotypic markers of RPE dysfunction and aging in OKS-treated eyes characterized by decreased dysmorphic RPE, reduced lipofuscin and undigested outer-segment accumulation, increased choriocapillaris fenestrations and reduced basal laminar deposits.

Conclusions: In vivo epigenetic reprogramming with OSK reversed these age-induce morphological changes, restoring RPE to a youthful morphology. These data imply epigenetic reprogramming can reverse the effects of aging and restore function to aging RPE, which may lead to a new approach to therapeutically treat AMD.

CONTROL ID: 3547125

SUBMITTER (NAME ONLY): Belén Montabes de la Cruz

TITLE: Investigating sound content in the early visual cortex of aphantasia participants

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Sound content can be decoded from brain activity patterns in the early visual cortex of blindfolded (Vetter et al. 2014) and congenitally blind (Vetter et al., 2020) participants, especially in the periphery. What is the role of visual imagery in this effect? We explored this question by replicating Vetter et al.'s (2014) experimental design on a sample of aphantasic individuals who experience no visual imagery.

Methods: We controlled 5 self-reported aphantasics (4 females, Mage=34, SD=15.65) with the voluntary visual imagery questionnaire (VVIQ; Marks, 1973) and for involuntary imagery with the spontaneous use of imagery scale (SUIS; Kosslyn et al., 1998). We also used a behavioural test assessing the degree to which imagery can prime a binocular rivalry display (Bergmann et al., preprint).

In a 3T fMRI experiment we presented our blindfolded participants with 3 natural sounds in a block design. We functionally localised auditory (positive control) and motor areas (negative control), early visual areas (V1, V2 and V3) and their respective eccentricities (fovea, periphery, far periphery). We fed each area's Z-normalised beta weights signal into a linear support vector machine classification algorithm (LIBSVM) contrasting auditory scenes. We assessed the statistical significance of our classification with a permutation test.

Results: Our participants scored low on the VVIQ (Mean=19.8, SD=1.92), SUIS (Mean=19.4; SD=3.85) and had close to chance priming scores (Mean=0.54, SD=0.07).

Our positive ($p < 0.001$) and negative ($p > 0.05$) controls performed as expected. Two participants had significant classification accuracies in visual areas. However, at the group level our permutation analysis rendered non-significant accuracies in all retinotopic areas (whole early visual cortex: 43%, V1: 42%, V2: 40% and V3: 42%; all $p > 0.05$) and in their respective eccentricities (all $p > 0.05$).

Conclusions: Since our participants scored low for spontaneous visual imagery, and because Vetter et al.'s (2014) reported deactivation patterns and eccentricity differences do not fit a voluntary visual imagery account, we suggest that our lack of findings arose from our participants' inability to engage in involuntary imagery. Moreover, we propose that auditory feedback to the early visual cortex may stand as a form of involuntary imagery which does not necessitate awareness, being elicited through previously integrated multisensory associations.

CONTROL ID: 3547127

SUBMITTER (NAME ONLY): Joey Tran

TITLE: Effect of Lumen Diameter on Intraocular Pressure in the Early Postoperative Period Following Tube-Shunt Implantation

SESSION TITLE: Blood flow/ Ischemia/reperfusion/Aqueous humor dynamics/IOP

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tran, W.N. Deane, Research & Development Engineering, New World Medical Inc, Rancho Cucamonga, California, UNITED STATES|L.E. Vazquez, Clinical Ophthalmology, University of Miami Mary and Edward Norton Library of Ophthalmology, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joey Tran: Commercial Relationship(s);New World Medical:Code E (Employment) | Luis Vazquez: Commercial Relationship: Code N (No Commercial Relationship) | Wyatt Deane: Commercial Relationship(s);New World Medical:Code E (Employment)

ABSTRACT BODY:

Purpose: To determine if the inner diameter of a tube-shunt device for IOP lowering in glaucoma has a significant impact on outflow, and thus IOP.

Methods: A series of benchtop experiments were conducted using tubes with same dimensions as commercial tube-shunt products: Ahmed Clear Path (305µm); Ahmed Glaucoma Valve (305µm); Baerveldt Glaucoma Implant (305µm); PAUL (127µm). For the valved device (Ahmed Glaucoma Valve), the flow regulator was removed to isolate the effect of tube inner diameter on IOP. All tubes were tested at the commercially available length of 16mm.

Theoretical (expected) IOP was calculated using the Hagen Poiseuille Equation based on each tube's dimensions: 305µm tube (0.02mmHg); 127µm tube (0.6mmHg). Water was then run through each tube at a fixed flow rate of 2.75 µL/min to determine the steady-state IOP. This mimics the early postoperative period before a capsule has formed to provide flow resistance.

Results: The observed benchtop IOPs were as follows: 0.03mmHg for the 305µm tubes and 0.6mmHg for the 127µm tube. A small rise in IOP (from 0.02mmHg to 0.6mmHg) was derived by reducing the tube's inner diameter from 305µm to 127µm.

Conclusions: Hypotony occurs when IOP falls to 5-6mmHg or below, which means that a theoretical IOP of at least 5mm Hg is required for a tube to be considered restrictive to prevent hypotony. None of the tubes tested in these experiments maintained IOP above this threshold. Thus, none of these devices would be expected to prevent early postoperative hypotony based on tube diameter alone.

These laboratory findings are published clinical studies: Ahmed Clear Path 7.1%; Ahmed Glaucoma Valve 5.7%; Baerveldt Glaucoma Implant 8.3%; PAUL Glaucoma Implant 9.5%.

All 4 tube-shunt devices are associated with some incidences of early postoperative hypotony (~6-10%). These rates appear independent of tube inner diameter, although the Ahmed Glaucoma Valve shows the lowest rate of hypotony likely due to a benefit from the presence of a flow-restriction valve.

Both benchtop testing and clinical data, show that none of the devices evaluated show flow restrictive properties that would prevent hypotony, including the device with the smallest diameter tube (PAUL Glaucoma Implant). Instead, early postoperative hypotony is likely attributable to other factors than device selection.

CONTROL ID: 3547128

SUBMITTER (NAME ONLY): Mingzhe Hu

TITLE: Deep learning approach for automated detection of retinal pathology from ultra-widefield retinal images

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: This study aims to develop a deep learning approach that can automatically detect retinopathy in ultra-widefield (UWF) retinal images with limited training data. It can serve as the steppingstone for large scale deployment of real-time automated retinopathy detection tools using UWF images where no similar approach has been developed.

Methods: The dataset used to train and validate the approach includes 324 3-channel images obtained using the ultra-widefield fundus camera (UWF Primary, Optos) on 162 diabetic patients at Duke Endocrinology. An image preprocessing method that did affine transformation and added noise to raw images was developed to increase data amount. A Residual Neural Network (ResNet) was trained to detect retinal pathology. Specifically, 75% of ultra-widefield retinal images were used to train the ResNet, and the rest 25% of the images were used for the test. Figure 1 shows an overview of our approach.

Results: Our approach achieved 87.97% (95% CI [85.88%, 90.05%]) accuracy in detecting referable retinopathy, along with the False Negative Rate of 13.23% (95% CI [11.06%, 15.41%]), Recall of 86.77% (95% CI [84.59%, 88.94%]), Precision of 86.82%(95% CI [84.65%, 88.99%]), F1 Score of 86.79% (95% CI [84.62, 88.96]), and AUC-ROC of 86.77% (95% CI [84.59%, 88.94%]). The confusion matrix is shown in Figure 2.

Conclusions: Our model, trained with limited data, can successfully detect retinopathy in ultra-widefield retinal images. It could be used as a useful real-time automated tool in clinical practice. Future studies will improve detection performance by collecting more UWF images and combining demographics information as model input.

CONTROL ID: 3547129

SUBMITTER (NAME ONLY): Xuwei Wang

TITLE: The polycomb group protein Ezh2 promotes optic nerve regeneration

SESSION TITLE: Retinal ganglion cells and central visual areas in disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: X. Wang, S. Yang, C. Zhang, M. Hu, R. Wang, A. Kosanam, J. Jiang, J. Qian, C. Liu, F. Zhou, Johns Hopkins University School of Medicine, Baltimore, Maryland, UNITED STATES|C. Liu, Institute of Zoology, Chinese Academy of Sciences, Beijing, CHINA|

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ABSTRACT BODY:

Purpose: In mammals, neurons in the central nervous system (CNS) lose their axon growth abilities as they mature. On the contrary, mature neurons in the peripheral nervous system (PNS) still possess such an ability and can spontaneously regenerate axons upon axonal injury by initiating a regenerative response. Emerging evidence suggests that such a response largely involves epigenetic regulation of chromatin accessibility. Here we first characterized the role of Ezh2, a H3K27 methyltransferase, in PNS axon regeneration, and then tested if its modulation could induce CNS axon regeneration.

Methods: Western blot and immunostaining were used to compare protein levels. Dorsal root ganglion (DRG) neuronal culture and sciatic nerve regeneration were used as in vitro and in vivo PNS regeneration models, respectively. Optic nerve regeneration was used as an in vivo CNS axon regeneration model. Fluorescence-activated cell sorting was used to enrich RGCs from dissociated retinal cells. RNA-seq of RGCs was conducted to explore molecular mechanisms by which Ezh2 supports axon regeneration.

Results: Ezh2 was significantly upregulated in mouse lumbar 4 and 5 (L4/5) DRGs 3 days after sciatic nerve transection. Functionally, Ezh2 knockdown (KD) or knockout (KO) in cultured DRG neurons impaired axon growth in vitro. In consistence, KD or KO of Ezh2 in L4/5 DRGs or conditional KO of Ezh2 in sensory neurons impaired sensory axon regeneration after sciatic nerve crush. More importantly, we found that Ezh2 overexpression in RGCs significantly promoted optic nerve regeneration and RGC survival after optic nerve crush. Interestingly, the axon regeneration promoting effect of Ezh2 was not solely dependent on its methyltransferase function, as overexpression of a mutant form of Ezh2 lacking the methyltransferase function also produced RGC axon regeneration, although to a lesser extent. RNA-seq revealed that mRNA levels of a large number of genes involved in synaptic transmission were downregulated by Ezh2 overexpression. Overexpression of Slc6a13 (encoding Gat2), a gene suppressed by Ezh2, partially blocked RGC axon regeneration induced by Ezh2 overexpression.

Conclusions: Our study demonstrated that Ezh2 was necessary for the successful spontaneous axon regeneration in the PNS, and that Ezh2 gain-of-function in RGCs could promote optic nerve regeneration by silencing synaptic transmission-associated genes.

CONTROL ID: 3547130

SUBMITTER (NAME ONLY): James Cole

TITLE: In vivo and in vitro assessment of neural damage in Aniridia

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Aniridia is a devastating panocular eye disease that affects 1 in every 50,000 to 100,000 newborns, typically caused by heterozygous mutations in the PAX6 gene. Patients with aniridia exhibit a diverse range of ocular abnormalities, each to differing extents, including corneal opacification, cataract, optic nerve hypoplasia, and foveal hypoplasia. Little is known about how the disease impacts retinal health during early development. We performed a series of in vivo assessments of retinal health and visual function and tracked their changes in aniridia mice.

Methods: We used the Pax6^{Sey+/-} mouse model of aniridia, as it possesses a nonsense mutation identical to those in most cases of human aniridia. We whole mounted 15 retinas in 4 key age groups (P10, P60, P100, P200) and immunostained them with markers such as SMI-32 for subtype RGCs and DAPI for nuclei of retinal cells. 6 retinal sagittal sections were also examined to assess changes in retinal layer structures. Intraocular pressure (IOP) was measured regularly using rebound tonometry to monitor glaucomatous damage which is a common symptom of aniridia. Visual behavior was monitored using the qOMR system which projects a virtual cylinder with moving black and white bars. The subject's innate ability to perceive the movement of these bars at varying frequencies measure their visual acuity. Finally, we used visible-light optical coherence tomography (Vis-OCT), an imaging technique with post imaging data analysis established by our laboratories, to examine cross-sectional and en face retinal scans in vivo.

Results: IOP was found to increase with age in Pax6^{Sey+/-} mice, averaging ~25mmHg as opposed to ~15mmHg in WT mice. Visual acuity measurements confirm that this visual deficit continues to worsen with age. The mean acuity for WT mice was 0.41 ±0.02cyc/deg, while the mean acuity for Pax6^{Sey+/-} was 0.21 ±0.05 cyc/deg. Confocal imaging of flat-mount retinas and retinal sections confirmed that the retina continues to degrade with age in Pax6^{Sey+/-} mice. Our initial vis-OCT imaging data also confirms that retinal structure is impaired in Pax6^{Sey+/-}, particularly in the optic nerve head.

Conclusions: Our data shows that neural damage and vision deteriorates with age in Pax6^{Sey+/-} mice. The combination of in vivo assessments makes it possible to track changes in individuals, which enables a better understanding of retinal developmental defects in aniridia.

CONTROL ID: 3547131

SUBMITTER (NAME ONLY): Amal Al-Lozi

TITLE: Characteristics of Tele-ophthalmology visits at a Large Academic Medical Center during the COVID-19 Pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Al-Lozi, H. Gabr, K. Jackson, X. Zhang, G. Andrew, D.S. Grewal, D. Gupta, Ophthalmology, Duke Eye Center, Duke University Department of Ophthalmology, Durham, NC, US, academic/meddep, Durham, North Carolina, UNITED STATES|H. Gabr, Ain Shams University, Cairo, EGYPT|

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ABSTRACT BODY:

Purpose: To describe the experience of tele-ophthalmology at a large academic medical center during the COVID-19 pandemic.

Methods: This is a retrospective review of tele-ophthalmology encounters conducted at the Duke Eye Center between March 13th and July 15th, 2020. Collected data includes patient demographics, mode of communication (video or telephone), visit type (new, routine return, or urgent), diagnoses, prescribed medications, management plan, and follow-up care.

Results: Five hundred and ninety-two routine return visits, 75 urgent visits, and 75 new patient visits were conducted over 742 tele-ophthalmology encounters spanning nine ophthalmology sub-specialty services: pediatric ophthalmology (224), oculoplastics (118), glaucoma (115), vitreoretina (69), cornea (67), inherited retinal disease (45), comprehensive ophthalmology (37), neuro-ophthalmology (34), and ocular oncology (24). The average patient age was 44.2 years (range, 1 month - 100 years). Figure 1 shows the most common diagnoses addressed. Video was the preferred mode of communication over telephone (439 versus 276 encounters). The show rate was 97.4%. The average time spent with patients was 18.0 minutes. The longest average visits occurred during inherited retinal disease (38.2 minutes) and neuro-ophthalmology (23.2 minutes) encounters. An active management decision was made in 36 of the new patient encounters (47.3%), 51 urgent encounters (70.8%), and 116 routine return encounters (20.2%). Figure 2 shows the top prescribed medication classes by subspecialty. In-person follow-up within 4 weeks was required for 28.0% urgent visits, 12.0% new patients, and 4.2% routine return visits.

Conclusions: Tele-ophthalmology was utilized during the COVID-19 pandemic across a wide range of patient ages and ophthalmology sub-specialties. A substantial percentage of virtual encounters led to an active management decision, and the majority of encounters did not require a sooner than scheduled in-person follow-up. More research and follow-up are needed to determine if the accuracy of tele-ophthalmology diagnosis and management matches that of in-person encounters.

CONTROL ID: 3547132

SUBMITTER (NAME ONLY): Wade Rich

TITLE: Effects of ascorbic acid on mechanical and optical properties of cultured porcine lenses

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Rich, Z. Chen, D. Mackessy, T. Brandt, D. Valenzuela, B. Kumar, K.E. Swindle-Reilly, M.A. Reilly, Biomedical Engineering, The Ohio State University, Columbus, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mechanical and optical properties of patient's lenses are known to change after vitrectomy, potentially contributing to diseases such as cataract and posterior capsule opacification. Ascorbic acid (AA) is highly concentrated in the vitreous. This study evaluated whether AA protected cultured lenses against changes in mechanical and optical properties.

Methods: Pairs of fresh porcine eyes were acquired then intact, encapsulated lenses removed. Lenses were cultured in one of four environments consisting of (1) M199 cell culture media alone (control), as well as M199 supplemented with (2) vitreous humor, (3) 365 mg/mL ascorbic acid (AA), or (4) AA and vitreous humor. Media was changed every 24 hours. Paired lenses were cultured in similar conditions except one lens was cultured with supplementary AA while the other was not. Whole lenses were removed from culture after incubation periods of 12 hours to 8 days. Optical transmission and elastic modulus were estimated using photography and a spinning test, respectively. The nucleus of each lens was also analyzed with Raman spectroscopy and shear rheometry.

Results: Rheologic data from some lens pairs showed decreased lens stiffening over time in the presence of vitreous when compared to control lenses. Optical transmittance from shorter incubation times were improved with vitreous , AA, and vitreous with added AA. Lenses cultured for longer times were always stiffer in rheologic analysis.

Conclusions: We previously found that inclusion of vitreous in lens tissue culture experiments improved lens viability over time. These findings suggest that AA may be the active ingredient in the vitreous preserving the lens' viability and material properties during culture.

CONTROL ID: 3547133

SUBMITTER (NAME ONLY): Arman Athwal

TITLE: Measurement of spatial and temporal retinal perfusion heterogeneity using OCTA

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Athwal, M.V. Sarunic, M. Ju, Simon Fraser University, Burnaby, British Columbia, CANADA|A. Athwal, D. Yu, P. Yu, C. Balaratnasingham, A. Mehnert, S. Cringle, Lions Eye Institute, Nedlands, Western Australia, AUSTRALIA|D. Yu, P. Yu, C. Balaratnasingham, A. Mehnert, S. Cringle, University of Western Australia Centre for Ophthalmology and Visual Science, Perth, Western Australia, AUSTRALIA|Z. Mammo, The University of British Columbia Faculty of Medicine, Vancouver, British Columbia, CANADA|Z. Mammo, M. Ju, The University of British Columbia Department of Ophthalmology & Visual Sciences, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Capillary perfusion is spatially and temporally heterogeneous in the retina, and likely plays a role in the pathogenesis of human retinal vascular diseases, for example Diabetic Retinopathy. We propose that variation in sequentially acquired OCT angiography (OCTA) volumes can be measured to estimate retinal perfusion heterogeneity, and investigate the sensitivity of the measurement to the OCTA acquisition parameters and OCTA processing methods used.

Methods: Ten porcine eyes were perfused with red blood cells for OCTA image acquisition by cannulation of the central retinal artery. For each eye, 20 OCTA volumes were sequentially acquired under two imaging protocols with a custom developed 200 kHz SS OCT: 2BM and 4BM, where 'BM' denotes the number of repeated B-scans acquired at each location. Each OCT data set was processed independently using four different methods for generating the angiography signal: subtraction, decorrelation, speckle-variance, and complex-variance. OCTA volumes were then layer-wise segmented to generate 2D superficial vascular complex (SVC) and deep vascular complex (DVC) en face images. The coefficient of variation (CoV; defined as the standard deviation of a signal divided by its mean value) was calculated for each pixel in the temporally stacked SVC and DVC images. The mean CoV for each BM acquisition and OCTA processing method combination was then calculated.

Results: The mean CoV differed significantly ($P < .05$) between each BM acquisition/OCTA processing method combination, as well as between each vascular complex. Mean CoV was, on average: higher for 2BM acquisition than 4BM; higher for complex- and speckle-variance OCTA than either of decorrelation or subtraction OCTA methods; and lower in the SVC than in the DVC. Quantitative CoV results are summarized in Figure 1, and these results are presented qualitatively in Figure 2 as CoV-based heat maps.

Conclusions: Retinal perfusion heterogeneity may be measured with OCTA, but measurements differ based on the OCTA acquisition and processing methods used. These differences should be further investigated to determine the optimal OCTA image acquisition and processing method for detecting retinal perfusion heterogeneity. Future work will combine this method with 3D motion correction to perform perfusion heterogeneity analysis on human OCTA data.

CONTROL ID: 3547136

SUBMITTER (NAME ONLY): Ariel Chen

TITLE: Incidence of post-operative endophthalmitis for cataract surgery combined with other intraocular surgery in the United States

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chen, S. Zafar, D. Srikumaran, F. Woreta, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|C. Dun, M. Makary, Department of Surgery, Johns Hopkins University, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endophthalmitis is a devastating complication of intraocular surgery; however, there is limited data on the rates of endophthalmitis in cataract surgeries combined with additional intraocular surgery. We performed a retrospective analysis to determine the incidence and characteristics of endophthalmitis for cataract surgery with a combined procedure in the United States.

Methods: This was a retrospective analysis using 100% Medicare fee-for-service claims data for endophthalmitis after cataract surgery from 2011 to 2019. Retina surgeries included retinal detachment repair and posterior vitreous procedures; glaucoma surgeries included trabeculectomy, tube shunt implant and minimally invasive glaucoma surgery; cornea surgeries included penetrating keratoplasty, endothelial keratoplasty, and keratoprosthesis; other surgeries included anterior chamber washout, ruptured globe repair, and iridotomy. Patients with prior intraocular surgery or intravitreal injection within 3 months and diagnosis of endophthalmitis within 12 months were excluded.

Results: 19,552 cases of endophthalmitis occurred following 14,396,438 cataract surgeries from 2011 to 2019. 289,778 (2.01%) of cataract surgeries were performed with glaucoma surgery, 51,131 (0.35%) with retina surgery, 20,918 (0.15%) with cornea surgery, and 57,752 (0.40%) with other intraocular surgery. The overall rate of endophthalmitis per 1000 cataract surgeries was 1.36. Cataract surgery endophthalmitis rates per 1000 surgeries was 1.30 for cataract surgery alone, 7.33 for combined retina surgery, 2.72 for combined cornea surgery, 2.20 for combined glaucoma surgery, and 7.12 for other combined surgery. In a multivariate model, the adjusted odds ratio of endophthalmitis with combined surgery versus cataract surgery alone was 2.51 (95% CI, 2.03, 3.10) for retina surgery, 1.08 (95% CI, 0.78, 1.51) for cornea surgery, 0.78 (95% CI, 0.63, 0.97) for glaucoma surgery and 2.13 (95% CI, 1.76, 2.58) for other intraocular surgery.

Conclusions: Rates of endophthalmitis were higher in patients who had cataract surgery with a combined procedure of cataract and retina or other intraocular surgery. These findings can improve patient counseling and future research should focus on endophthalmitis prevention in these higher risk cases.

CONTROL ID: 3547138

SUBMITTER (NAME ONLY): Megan Straiko

TITLE: Modification of an eye bank pre-loaded DMEK graft preparation protocol to accommodate “flat” grafts

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Straiko, T. Hikes, P.K. Dye, K.D. Tran, Lions VisionGift, Portland, Oregon, UNITED STATES|M.A. Terry, Cornea, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: During DMEK graft processing, eye bank technicians occasionally encounter “flat” grafts that do not spontaneously scroll easily and are difficult to load without causing damage to the graft. In this eye bank laboratory-based study, we sought to determine if modification to the standard pre-loaded DMEK preparation technique resulted in additional damage or a characteristic pattern of damage to the graft after short-term storage.

Methods: Six pairs of human donor corneas (age 65-80, with comparable cell counts and pre-processing damage) were prestripped, punched and loaded as a single scrolled graft by two experienced processing technicians. The OD graft was drawn into a Straiko modified Jones tube filled with Life4C using suction (standard loading procedure for our eye bank). The OS graft was picked up with forceps and dropped into a Life4C filled Straiko modified Jones tube. Grafts were stored in a Life4C filled Krolman viewing chamber for 24 hours at 4°C and then ejected onto a bed of calcein AM-supplemented viscoelastic, imaged with a fluorescent light microscope and analyzed for endothelial cell loss by FIJI segmentation. Mean endothelial cell loss was determined for standard loading and drop-in loading grafts and statistical significance determined using an unpaired Student’s t-test.

Results: There was no difference in endothelial cell counts as determined by specular microscopy prior to graft processing (standard loading grafts, 2728.4 ± 333.8 cells/mm²; drop-in loading grafts, 2635.6 ± 369.2 cells/mm², $P = 0.6877$). Mean ECL for standard loading protocol grafts was $21.4\% \pm 4.8\%$; mean ECL for drop-in loading grafts was $18.9\% \pm 4.6\%$, $P = 0.4310$. There was no consistent pattern of damage noted in DMEK grafts that underwent either standard loading or drop-in loading.

Conclusions: Modification to the standard technique of preloading DMEK grafts by grasping the stripped, punched graft and dropping it into a storage media filled Straiko modified Jones tube does not result in additional damage to a DMEK graft as measured by vital dye staining, nor does it result in a characteristic pattern of cell death. This technique may be useful with flat DMEK grafts that are difficult to load without excessive contact with the edge of the Straiko modified Jones tube.

CONTROL ID: 3547140

SUBMITTER (NAME ONLY): Alp Atik

TITLE: Comparison of glaucoma diagnosis by ophthalmologist, optometrist, and telemedicine with OCT

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Atik, T.A. Swain, G. McGwin, C. Owsley, C.A. Girkin, L.A. Rhodes, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|A. Atik, T.A. Swain, G. McGwin, C. Owsley, C.A. Girkin, L.A. Rhodes, Department of Ophthalmology and Visual Sciences, UAB Callahan Eye Hospital, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Telemedicine is a novel, emerging medium addressing the challenges of accessing in-person glaucoma care by utilizing objective tools such as optical coherence tomography (OCT) for remote diagnosis. This study assessed the agreement of the diagnosis of glaucoma performed by an in-person ophthalmologist (MD), in-person optometrist (OD) and 2 telemedicine ophthalmologists (TMD1 and TMD2) with that of OCT alone.

Methods: This was a cross-sectional study of patients presenting to an academic tertiary referral glaucoma clinic who were independently examined for glaucoma with a dilated exam and optic nerve testing (visual field, optical coherence tomography, and photos) by both an MD and OD. Optic nerve testing was then reviewed by TMD1 and TMD2 with blinding to the MD and OD diagnoses. The OCT software labelled each scan as within normal limits, borderline or outside normal limits. "Borderline" was considered as both outside normal limits (OCT1) and within normal limits (OCT2). Agreement between each method of diagnosis (MD, OD, and TMD1 and TMD2) of normal vs. glaucoma (open angle glaucoma, normal tension glaucoma, other type of glaucoma, ocular hypertension, glaucoma suspect) compared to OCT1 and OCT2 for each eye was calculated using Cohen's unweighted Kappa statistic and 95% confidence intervals. The predictive ability of OCT alone compared to TM2 was assessed by the area under the curve (AUC) of the receiver operating characteristics curve.

Results: 100 study participants (200 eyes) with a mean age of 66.7 years (IQR 59-72) were 40% male and 62% white. There was moderate agreement between OCT1 and telemedicine (TMD1: $K=0.45$ [95% CI 0.32-0.57], TMD2: $K=0.46$ [0.34-0.58]) in determining a diagnosis of normal from glaucoma. There was only fair agreement between OCT1 and in-person review by an MD ($K=0.32$ [0.19-0.45]) and OD ($K=0.35$ [0.22-0.48]). These results were similar for OCT2 agreement with telemedicine (TMD1, $K=0.39$ [0.28-0.51], TMD2, $K=0.40$ [0.28-0.51]), MD ($K=0.34$ [0.22-0.46]), and OD ($K=0.29$ [0.17-0.41]). When assessing the ability of OCT1 to diagnose glaucoma as compared to TMD2, the AUC was 0.73 (95% CI: 0.67-0.79) (Figure 1).

Conclusions: Although OCT is an important tool, it is not sufficient for the diagnosis of glaucoma in a telemedicine model as other parameters such as visual fields and optic nerve photos provide key information.

CONTROL ID: 3547141

SUBMITTER (NAME ONLY): Ryo Kubota

TITLE: Effect of short-term peripheral myopic defocus on ocular biometrics using Fresnel “press-on” lenses in human subjects

SESSION TITLE: Peripheral optics and vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: R. Kubota, A. Gupta, Kubota Vision Inc., Seattle, Washington, UNITED STATES|N.R. Joshi, I. Samandarova, M. Oliva, A. Selenow, S.R. Ali, Manhattan Vision Associates/Institute for Vision Research, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: This study aimed to assess axial length and choroidal thickness changes following short-term peripheral myopic defocus sessions.

Methods: 20 visually-normal subjects (13 females and 7 males) of mean age 25.5 years (range 19-31) with mean spherical equivalent refractive error of -2.02 D (range 0 to -4.13 D, cyl < 0.75 D) were enrolled. 14 subjects were Asian and 6 were Caucasian. Subjects underwent defocus sessions by watching projected (ViewSonix PX706 projector) color movies (screen dimensions: 8 ft H X 12 ft W) 4 meters away under controlled conditions (room illumination of approximately 80 lux) while wearing standard spectacle lenses corrected for distance refraction (both eyes) for 4 hours between 8:00 am to 12:00 pm. The right (test) eye was peripherally defocused using a Fresnel lens overlay of +3.50D with a central clear aperture of 15 degree diameter, which was centered for the subject’s pupillary axis on primary gaze, while the fully-corrected left eye served as the control. A subset of 10 subjects from the same cohort also further underwent similar defocus sessions with +5.00D of peripheral defocus supplied through the Fresnel lenses on a different day following a wash-out of at least 1 day. Axial length was measured with a Lenstar APS 900 from Haag-Streit Holding, and radial choroidal scans were obtained from Heidelberg SD-OCT with EDI, before and after the defocus sessions.

Results: The test eye was approximately 11 µm shorter than the control eye when measured after 4 hours of defocus for both +3.50D and +5.00 D peripheral myopic defocus conditions (corrected p<0.05). The thickening of choroidal thickness after defocus was more robust for the +5.00D condition compared to the +3.50 condition (p>0.05 for both conditions).

Conclusions: We have shown, for the first time, that short-term peripheral myopic defocus is capable of inhibiting eye-elongation, which gives additional insight towards the physiological effect of peripheral myopic defocus.

CONTROL ID: 3547142

SUBMITTER (NAME ONLY): Jonathan Yi

TITLE: Evaluation of Sleep, Activity, and Burnout after Implementation of Night-Float and Post-Call Relief in PGY-2 Ophthalmology Residents

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Yi, J. Huang, S. Feng, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Lack of sleep and activity are commonly associated with resident burnout. Proposed strategies to address resident burnout include restructuring traditional call schedules to provide time for sleep recovery post call. This study examines the effects of implementing night-float and post-call relief on sleep, activity, and burnout in post-graduate year (PGY)-2 ophthalmology residents at the University of Washington (UW) between 2017-2021 using wrist actigraphy and standardized burnout surveys.

Methods: Data from 20 PGY-2 ophthalmology residents at UW were collected with Fitbit Alta HR wrist actigraphers between 2017-2020. Three residents were excluded due to insufficient sleep or activity data. From 2017-2019, residents took home call every 5 nights and returned to full clinical duties on their post-call workday. From 2019-2021, a night-float resident without daytime clinical duties took call for 3 nights a week while remaining residents rotated call duties for the remaining 4 nights of the week with no clinical duties assigned past noon on their post-call day. Burnout was evaluated by Maslach Burnout Inventory surveys and Depression Anxiety Stress scales. T-tests were used to compare average sleep, activity, and sedentary time between residents before and after implementing night-float and post-call relief. Pearson correlation was used to associate sleep and activity metrics with averaged median burnout scores.

Results: PGY-2 residents with night-float and post-call relief (N=8) had greater average daily activity (17.1 ± 10 min vs 5.60 ± 3.5 min, $p=0.02$) and lower average sedentary time (14.1 ± 2.5 hours vs 17.5 ± 2.7 hours, $p=0.02$) compared to residents without night-float and post-call relief (N=9). No statistically significant differences in sleep or burnout were found in the two cohorts, though residents with night-float and post-call relief trended toward lower emotional exhaustion ($p=0.10$) and stress ($p=0.10$). For all PGY-2 residents, there was a negative correlation between activity and stress, and a positive correlation between sedentary time and emotional exhaustion, anxiety, and stress.

Conclusions: Night-float and post-call relief led to greater average physical activity and lower average sedentary time in PGY-2 ophthalmology residents. Increased physical activity and decreased sedentary time correlates to decreased emotional exhaustion, anxiety, and stress.

CONTROL ID: 3547143

SUBMITTER (NAME ONLY): Angela Nguyen

TITLE: Gonioscopy Findings in a Childhood Variant Angle Closure Glaucoma after Laser Peripheral Iridotomy

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.V. Nguyen, School of Osteopathic Medicine, University of the Incarnate Word, San Antonio, Texas, UNITED STATES|W.E. Sponsel, Director, WESMDPA, San Antonio, Texas, UNITED STATES|G. Slagle, Clinical Research, Sponsel Foundation, San Antonio, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Angela Nguyen: Commercial Relationship: Code N (No Commercial Relationship) | Grant Slagle: Commercial Relationship: Code N (No Commercial Relationship) | William Sponsel: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Pediatric Eversional Angle Closure with Headache (PEACH) is a childhood variant intermittent angle closure glaucoma characterized by 1) recurrent frontal headache, 2) iris laxity on dynamic gonioscopy, and 3) concentric visual field loss on Frequency Doubling Technology perimetry. Prior reports demonstrate nearly universal symptom improvement with laser peripheral iridotomy (LPI), but gonioscopy findings in these patients have not been reported. This retrospective observational study evaluates gonioscopy findings in PEACH eyes pre- and post- LPI.

Methods: We retrospectively analyzed 166 eyes of 91 subjects (5 to 18 years) with PEACH who had LPI (VISULAS YAG III, Zeiss, Jena, Germany) between March 2011 and September 2020. Dynamic gonioscopy was performed using a 4-mirror gonio lens and graded using the Spaeth system before (n=166) and after (n=98) LPI. Frequency percentages were calculated for all variables. Iris insertion, angle width, and pigment were evaluated with Wilcoxon's signed-rank test and iris configuration with chi-square.

Results: Iris configuration of Q was the most sensitive index (92%) for PEACH diagnosis, most commonly presenting as (R)Q (82.7%). Other common findings: 75.95% of eyes had iris insertion deep to the ciliary body (Spaeth D, range A-E), 50.6% had iris angle width of 40 degrees (range 0-55°), and 54.2% of subjects had concentric iris folds. Significant portions of eyes had pigment dust anterior to Schwalbe's line (42.8%) with only a minority showing synechiae (15.7%). Iris insertion became less deep after LPI ($p<0.001$), mean angle width decreased from 40 ± 7 to 34 ± 6 degrees ($p<0.001$), and mean pigment increased from 1 ± 1 to 2 ± 1 ($p=0.03$). Significantly, in eyes in perpetual Q pre-LPI, 87.5% reverted to Spaeth R post-LPI. In baseline (R)Q eyes, 93.7% reverted to R [$\chi^2(20, N=96)=33.6, p<0.001$]. Thus LPI may impart resistance to reverse pupillary block in PEACH.

Conclusions: Gonioscopy is a sensitive tool essential to the diagnosis and monitoring of PEACH patients, and must be considered alongside historical and perimetric factors to arrive at an accurate diagnosis and verify effective therapy. The iridocorneal angle structures change in response to LPI and may be mechanistically related to improvements in PEACH symptomatology.

CONTROL ID: 3547146

SUBMITTER (NAME ONLY): Jennifer Phillips

TITLE: Zebrafish PCDH15 (USH1F) mutants display visual and audiovestibular defects

SESSION TITLE: Models to study retinal degeneration and remodeling

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J.B. Phillips, S. Buchner, M. Westerfield, Institute of Neuroscience, University of Oregon, Eugene, Oregon, UNITED STATES|M. Ivanchenko, D.P. Corey, Department of Neurobiology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in PCDH15 cause severe early onset visual dysfunction, along with profound congenital deafness and loss of vestibular function. *pcdh15b*, previously shown by morpholino knock-down to be critical for photoreceptor function and survival with no observed effect on hearing or balance, but no zebrafish mutant studies have been published to date.

Methods: Mutations induced by CRISPR/Cas9 injection into zygotes were verified by Sanger sequencing and propagated. We assayed hearing, balance, mechanosensory hair cells, photoreceptor morphology, and cell death with behavioral and histological methods. Light exposure experiments were performed using broad-spectrum light and petri dishes treated with tinted window film. Western blot analysis was performed on extracts from enucleated larval retinas.

Results: Optokinetic response was detected at reduced levels in 5 day postfertilization (dpf) mutant larvae, and immunohistochemical, SEM and TEM analysis of mutant photoreceptors revealed morphologically abnormal calyceal processes and outer segments. An antibody recognizing zebrafish *pcdh15* labeled the region of the calyceal processes in wild-type photoreceptors with no specific labeling in mutants. We observed elevated cell death, assayed by Caspase-3, in the outer nuclear layer. We examined levels of *e1fa* and CHOP by Western blot to determine whether ER stress was induced by *Pcdh15b* dysfunction and found no elevation in either. We observed enhanced photoreceptor death by rearing larvae in bright light, and that filtering out short wavelength while keeping Lux values constant resulted in lower rates of cell death. Although mutants exhibited normal startle responses, indicative of acoustic function, they had impaired balance. Consistent with this finding, stereocilia of the inner ear were perturbed more in the utricle than the saccule, and expression of the orthologous gene *pcdh15a* was enriched only in the saccule of 5dpf mutants compared to wild-type levels.

Conclusions: The zebrafish model of visual and vestibular defects in USH1F exhibits severe, early defects consistent with human symptoms. Our data indicate that both *pcdh15a* and *pcdh15b* are required for hearing and balance, and that genetic compensation by *pcdh15a* is evident in the acoustic hair cells of *pcdh15b* mutants. These characterizations provide numerous measures of disease progression and an advantageous system to test potential pharmacological interventions.

CONTROL ID: 3547148

SUBMITTER (NAME ONLY): Bayasgalan Surenkhuu

TITLE: Recombinant Deoxyribonuclease I (DNase) Eye Drops for Ocular Graft vs Hosts Disease (oGVHD): Results of a Randomized Clinical Trial

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Surenkhuu, C. Mun, N. Atassi, N. Dhall, J. Mun, C. Berek, C. Kim, M.A. Sarwar, A. Pradeep, S. Jain, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have previously shown that Neutrophil Extracellular Traps (NETs) are present on the ocular surface of oGVHD patients and they contribute to inflammation and surface disease. Therefore, we performed a clinical trial using DNase eye drops to test the hypothesis that reducing the abundance of NETs from the ocular surface will reduce signs, and symptoms of oGVHD.

Methods: A prospective, phase I/II, randomized, placebo-controlled, double-masked clinical trial was performed to compare the safety and preliminary efficacy of DNase (0.1%) eye drops four times a day for 8 weeks in patients with oGVHD (n=51). Available data and intent-to-treat analyses were performed to determine the change in safety outcome measures (drug tolerability and proportion of adverse events) and efficacy outcome measures (OSDI score and corneal staining) between baseline and week 8. The clinical trial was performed under a IND assigned by the FDA and a protocol approved by UIC IRB.

Results: Tolerability and adverse events were similar in Vehicle group and DNase group. Within the DNase group (but not Vehicle group), corneal staining showed a statistically significant and clinically meaningful reduction at week 8 (3.50 [2.75; 5.00]) compared to baseline (5.00 [3.00; 7.00]). The OSDI score also showed a significant median reduction of 18.4 [9.16; 33.1, p<0.001] at week 8 compared to baseline (45.5 [31.8; 50.0]) within the DNase group. Proportion of eyes that had improvement in Subjective global assessment (SGA) and mucous discharge were significantly greater in the DNase group (55.6% and 57.7% at weeks 4 and 8, respectively; p < 0.0001 at both time points) as compared to the Vehicle group (35.7% and 34.0% at weeks 4 and 8, respectively). Proportion of eyes that had improvement on CGI at week 8 were significantly greater in the DNase group (94.2%; p < 0.0001) as compared to the Vehicle group (22.0%).

Conclusions: Treatment of patients with oGVHD using DNase eye drops is safe and demonstrates a preliminary efficacy. DNase eye drops have the potential to reduce the severity of signs and symptoms of ocular surface disease in oGVHD patients.

CONTROL ID: 3547149

SUBMITTER (NAME ONLY): Sarkis Sislyan

TITLE: Effects of Dexamethasone on Wnt Signalling Expression in Human Trabecular Meshwork

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Sislyan, C. Han, L.U. Sanchez, C. Zhang, J.J. Zheng, University of California Los Angeles, Los Angeles, California, UNITED STATES|E. Cohen, Weill Cornell Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Damage to the trabecular meshwork (TM) is commonly thought to lead to elevated intraocular pressure (IOP) and glaucoma development, but the exact mechanisms that increase IOP remain unresolved. Prior studies indicate Dexamethasone(Dex)-induced glaucoma may involve increased Wnt signaling activity. This study employs RNA sequencing to investigate the specific changes in gene expression that can result from Dex treatment of human TM cells.

Methods: The TM from 3 human corneal tissue (TM 3, TM 4, and TM 5) were isolated and plated with 20% fetal bovine serum (FBS) media. After reaching confluency, each TM cell line was treated with dexamethasone (D) or ethanol vehicle (V). RNA was isolated from each group, and the data was sequenced using Illumina HiSeq 3000. The data was demultiplexed using Illumina Bcl2fastq2 v. 2.17. Using Bowtie2 v. 2.1.0, the reads were mapped, and gene expression was determined using RSEM v. 1.2.15. The data was normalized using the trimmed mean of M-values. Data analysis was performed using Rstudio. Heatmaps were generated using the pheatmap R package and were scaled by row.

Results: RNA sequencing data was converted into heatmaps on Rstudio. Both figures displayed similar relationships across genes and treatment groups. DKK1 had lower expression in Dex treated groups, particularly TM 5 cells. SFRP1 and SFRP 4 expression was lower in Dex treated groups. FZD4 showed a stark increased expression in Dex treated groups, especially TM 5 cells.

Conclusions: Overall, Dex treatment caused wide-ranging changes in the expression of Wnt signaling genes, consistent with the idea that Wnt signaling plays a key role in the human TM's function of regulating IOP. This is supported by a decreased expression of DKK1, SFRP1 and SFRP4, which are Wnt signaling inhibitors, in Dex-treated groups. Similarly, FZD4 is a receptor in the canonical Wnt pathway, where increased expression leads to greater Wnt signaling. Together, these results indicate a potential mechanism which involves the reduction of Wnt inhibition in glaucomatous TM cells.

CONTROL ID: 3547152

SUBMITTER (NAME ONLY): yingying shi

TITLE: Hyper-Transmission Defects Detected on En Face OCT Images are a Risk Factor for Nascent Geographic Atrophy in Eyes with Intermediate AMD

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. shi, J. Yang, W.J. Feuer, G. Gregori, P.J. Rosenfeld, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine if the detection of choroidal hyper-transmission defects (hyperTDs) on en face OCT images serve as a risk factor for the formation of nascent geographic atrophy (nGA) or GA in eyes with intermediate AMD (iAMD), we compared the onset and persistence of hyperTDs with the gold-standard detection of nGA using averaged OCT B-scans

Methods: Patients with bilateral large drusen were enrolled in a natural history study and imaged with both Spectralis SD-OCT (Heidelberg Engineering, Heidelberg, Germany) and Cirrus SD-OCT (Carl Zeiss Meditec, Dublin, CA) instruments at 6-month interval over 36 months. The Spectralis SD-OCT B-scans were used to grade for nGA at the Centre for Eye Research Australia. En face Cirrus SD-OCT images were graded for the presence of hyperTDs in a masked fashion at the Bascom Palmer Eye Institute. HyperTDs with greatest linear dimensions (GLDs) $\geq 125\mu\text{m}$ were measured and tracked throughout all available visits. The size cut-off for persistent and non-persistent hyperTDs was determined based on baseline GLD measurements. Over 36 months, the association between these HTDs and the presence of nGA was assessed.

Results: A total of 157 eyes from 81 patients were available to be graded. At baseline, Cirrus SD-OCT scans were available on 133 eyes, and 39 hyperTDs from 27 eyes of 22 subjects were classified as either persistent (26 lesions) or non-persistent (13 lesions) over 36 months. Receiver Operating Characteristic curve analysis suggested hyperTDs with baseline GLDs above a threshold of $250\mu\text{m}$ to $300\mu\text{m}$ fulfilled the definition of persistent lesions. After grading the entire population of 157 eyes, a significant association ($p < 0.001$) was found between nGA gradings and the masked gradings of hyperTDs with $\text{GLD} \geq 250\mu\text{m}$ (OR, 14.5, 95% CI: 4.8, 54.0) or $300\mu\text{m}$ (OR, 15.2, 95% CI: 5.0, 56.7). HyperTDs with $\text{GLD} \geq 250$ or $300\mu\text{m}$ had an excellent negative predictive value of $\geq 94\%$, but a poor positive predictive value (PPV) of $\leq 40\%$ for detecting nGA. The poor PPV appeared to be due to the earlier detection of lesions that would become nGA.

Conclusions: Choroidal hyperTDs detected on en face SD-OCT images with a $\text{GLD} \geq 250\mu\text{m}$ or $300\mu\text{m}$ were strongly associated with the presence of nGA and may serve as a useful risk factor for the early detection of disease progression of iAMD to GA.

CONTROL ID: 3547154

SUBMITTER (NAME ONLY): Betul Bayraktutar

TITLE: Dysimmune Neuropathy: An Underinvestigated Cause of Dry Eye Disease?

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Bayraktutar, L. Yavuz-Saricay, V. Atocha, P. Hamrah, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|B. Bayraktutar, L. Yavuz-Saricay, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The role of inflammation and neurosensory abnormalities in dry eye disease (DED) has been defined by dry eye workshop II report. The etiologic role of autoimmune diseases, such as Sjögren's syndrome, mixed connective tissue diseases, sarcoidosis, and related nerve loss has been established in DED. However, dysimmune neuropathies, which are caused by specific autoantibodies (Abs) against peripheral nerve axons and myelin have not been investigated. Therefore, our purpose was to evaluate the potential systemic etiologies in DED, by assessing serological Abs used for dysimmune neuropathies as well as autoimmune diseases.

Methods: Patients with moderate to severe DED (n=37) underwent serological testing for inflammatory (ESR, CRP), autoimmune, and dysimmune neuropathy Abs (anti-TSHDS, anti-FGFR3, anti-sulfatide IgM, anti-Histone H3, Anti-GD1a).

Results: At least one abnormal result was detected in 24 patients (64.8%) with 54.0% showing at least one positive dysimmune neuropathy Ab. Anti-TS-HDS and anti-FGFR3 were positive in 48.6% and 21.6% of patients, respectively. Acute inflammation markers ESR and CRP were positive in 24.3% and 16.2%, respectively. ANA was positive in 32.4% of patients. SS-A (13.5%) and SS-B (13.5%) were the most common disease specific autoimmune Abs followed by RF (5.4%). At least one positive Celiac Ab (anti-gliadin IgA, IgG, tissue transglutaminase IgA, IgG) was detected in 2.7% of patients.

Conclusions: Our findings suggest that dysimmune neuropathy may play a crucial role in DED etiology. Detailed serological evaluation detects higher positivity rates for dysimmune neuropathy Abs compared to well-known systemic etiologies, such as Sjögren's syndrome and rheumatoid arthritis Abs, suggesting that neurosensorial abnormalities need further investigation in the course of DED.

CONTROL ID: 3547155

SUBMITTER (NAME ONLY): Jessica Wong

TITLE: Trends in emergent and inpatient encounters before and after clinic shutdowns related to COVID-19

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Wong, N. Tran, J. Katuri, The University of Texas Health Science Center at San Antonio Joe R and Teresa Lozano Long School of Medicine, San Antonio, Texas, UNITED STATES|H. Nguyen, The University of Texas Health Science Center at San Antonio, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Delay in outpatient chronic care management can lead to a rise in acute complications. COVID-19 related clinic and ambulatory shutdowns came into effect in South Texas by the end of 3/2020. Recent studies have shown delays in care and more severe disease presentations during the COVID-19 shutdown. We evaluate trends in ophthalmic pathologies in relation to patient follow-up behaviors after ED and inpatient encounters in South Texas.

Methods: A retrospective study used electronic medical records to collect consultation logistics, patient clinical data, and clinical follow up for ophthalmic inpatient and emergent encounters from 7/2019 - 7/2020. Proliferative disease-associated vitreous hemorrhage (VH) and neovascular glaucoma (NVG) were used as markers for acute on chronic complications. Patient follow-up rate and time were compared to recommended follow-up during the two eras to analyze trends in patient behavior.

Results: 501 records were evaluated. Pre- and post-shutdown weekday (14 hour) volume of encounters were 5.7 ± 3.2 and 3.7 ± 2 , respectively. Weekend (24 hour) encounters changed from 12.7 ± 4.6 to 9.9 ± 5.5 . Pre-shutdown average weekday time of encounter was $21:36 \pm 4.6$ hrs compared to $20:59 \pm 4.0$ hrs post-shutdown, and for weekend time of encounter was $19:49 \pm 6.2$ hrs compared to $19:23 \pm 5.6$ hrs. Pre-shutdown recommended follow-up was 6.9 ± 8.7 days compared to 9.9 ± 10.5 days post-shutdown, with patients delaying the originally recommended appointment by 11.3 ± 50.9 days pre-shutdown and 7.1 ± 25.3 days post-shutdown. Missed appointment rate was 35% pre-shutdown and 47% post-shutdown. Of the 216 pre-shutdown encounters, 9% needed urgent surgery and 5% needed a bedside procedure. Post-shutdown, 8% needed surgery and 6% needed a bedside procedure. Pre- and post-shutdown incidence respectively was 4% and 4% for NVG, and 5% and 7% for VH.

Conclusions: During the COVID-19 shutdown, the volume of ophthalmic ED evaluations decreased, but not significantly. Patient encounter time and procedural intervention rate were also not significantly altered, suggesting that the urgency profile of pathologies did not change significantly. More patients missed clinic follow-up but appointment delays were comparable to the pre-shutdown era. There was a slightly higher incidence of acute on chronic proliferative pathologies.

CONTROL ID: 3547156

SUBMITTER (NAME ONLY): Nicolaas DeRuyter

TITLE: Using a handheld facial vibration device is associated with reduction in pain associated with onabotulinumtoxinA injections for Benign Essential Blepharospasm

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.P. DeRuyter, B. Barahimi, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|Y. Liu, Q. Chen, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Nicolaas DeRuyter: Commercial Relationship: Code N (No Commercial Relationship) | Yuhan Liu: Commercial Relationship: Code N (No Commercial Relationship) | Qingxia Chen: Commercial Relationship: Code N (No Commercial Relationship) | Behin Barahimi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Strategies to mitigate pain associated with periorbital onabotulinumtoxinA (BOTOX) injections for Benign Essential Blepharospasm (BEB) are insufficient in the current era. We conducted a randomly controlled trial to test the hypothesis that using a handheld facial vibration device would improve BOTOX injection associated pain for patients with BEB.

Methods: Adults 18 or older with a clinical diagnosis of BEB were randomized to receive facial vibration with the handheld Yeamon vibration device (frequency = 100Hz) to only one side of their face (right vs. left) during periorbital BOTOX injections. Following treatment, subjects completed a pain rating survey scaled 1-10 (1 = no pain, 10 = worst pain) for each side of the face. Baseline demographic data was collected. Pain rating between treatment and control was compared using linear mixed effect model regression.

Results: 21 patients participated in the trial. Median age and years since diagnosis was 65 and four years, respectively. For treatment pain rating, the median score was 4.0; for no treatment, the median score was 5.0. Mean score and standard deviation between treatment and control was 4.4 ± 2.1 vs. 5.7 ± 2.1 . Vibration stimulation was associated with a statistically significant lower score when controlling for age of patient and number of injected units during treatment ($p=0.0198$).

Conclusions: Using a handheld facial vibration device is associated with reduction in patient pain during periorbital BOTOX injections for BEB. This can be considered for use in the injection specialist's armamentarium to improve patient comfort.

CONTROL ID: 3547157

SUBMITTER (NAME ONLY): Aparna Raghuram

TITLE: Vergence and accommodation deficits subacutely and chronically in concussion recovery

SESSION TITLE: Refractive error, refraction, accommodation and presbyopia

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Raghuram, E.K. Wiecek, A.S. Shah, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Raghuram, R.N. Chinn, E.K. Wiecek, C. Marshall, A.S. Shah, Ophthalmology, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|T.L. Roberts, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|R. Stevens, K.K. Hawash, Neurology, Boston Children's Hospital Department of Neurology, Boston, Massachusetts, UNITED STATES|M. O'Brien, Sports Medicine, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|M. O'Brien, Orthopedics, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Deficits in vergence and accommodation are commonly reported following concussion. We explored if the frequency and subtypes of vergence deficits (VD) and accommodation deficits (AD) vary between subacute (>15 days to 12 weeks) and chronic (> 12 weeks to < 1 year) phases of concussion recovery along with sex-based differences.

Methods: Retrospective cross-sectional study. Chart review of patients with concussion evaluated at Boston Children's Hospital between August 2012 and March 2020. Inclusion criteria: 7-18 years; 20/30 vision or better in each eye; complete assessment of vergence and accommodation; no strabismus, amblyopia, or other ocular pathology. Results were compared to a non-concussed control group (n= 30; median age: 9.2, IQR: 8.1 -10.6 years) recruited and evaluated from April to October 2016. VD and AD were characterized based on clinical findings falling outside of the 95th percentile of the control group. Chi-square and Fischer's exact test (FET) were used to assess diagnosis and subtype differences.

Results: A total of 256/423 (61%) patients fit inclusion criteria with 115 evaluated in the subacute (median age: 15 IQR: 13.6 - 16 years; 60% females) and 141 in the chronic (median age: 15.4; IQR: 13.7 -16.8 years; 67% female) phases of concussion recovery. Frequency and subtype of VD and AD were not significantly different between subacute and chronic cohorts (45% vs 52% and 84% vs 83%, respectively). In the subacute phase, the frequency of AD was lower in females compared to males (65.3% vs 82.6%, $\chi^2 = 4.15$, $p=0.04$). In the chronic phase, frequency of AD was similar in both sexes (67% vs 75%), but there was a difference in subtype of AD (FET, $p<0.001$) with accommodative insufficiency in 56% vs. 23% ($\chi^2 = 14.48$, $p<0.001$), accommodative excess in 7.4% vs 15% ($\chi^2 = 2.1$, $p=0.15$) and accommodative dysfunction in 10.5% vs. 26.1% ($\chi^2 = 5.69$, $p=0.017$) females vs males, respectively. This difference is likely due to a trend towards higher failure rate with accommodation amplitude in females (64% vs 50%, FET $p=0.07$) and higher failure rate of accommodative facility in males (52% vs 25%; FET, $p=0.002$).

Conclusions: We found no difference in the frequency of VD or AD in the subacute and chronic phases of concussion recovery. In the chronic phase sex-based differences were noted in subtype of AD. Low accommodative amplitude drove AD in females but poor accommodative facility drove AD in males.

CONTROL ID: 3547159

SUBMITTER (NAME ONLY): Tahreem Mir

TITLE: The Impact of the Affordable Care Act on Eye-Related Emergency Department Utilization in the United States

SESSION TITLE: Public Health

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: T.A. Mir, S. Mehta, K. Qiang, I. Freedman, J. Chow, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the impact of the affordable care act (ACA) on nationwide eye-related emergency department (ED) utilization

Methods: Nationally representative data from the US Nationwide Emergency Department Sample (NEDS) were used to analyze eye-related ED visits before (2010-2013) and after (2014-2017) the ACA was mandated. The primary outcome was to compare the nationwide and regional incidence of eye-related ED visits per 100,000 US population before and after the ACA was mandated. Secondary outcomes measures included change in payor status, relative proportion of urgent versus non-urgent eye-related ED visits and charges per ED visit.

Results: A total of 16,808,343 eye-related ED visits occurred in the United States during the study period from 2010-2017. Of these, 8,088,203 ED visits occurred before the ACA was mandated (2010-2013) and 8,720,766 ED visits occurred after the ACA was mandated (2014-2017). The median age of individuals presenting to the ED with eye-related problems was 30 years and 53.4% of them were male. After the ACA was mandated in 2014, there was an initial decline in incidence of eye-related ED visits from 652.4 per 100,000 in 2013 to 593.0 per 100,000 in 2014, followed by a rapid increase in incidence to 658.5 per 100,000 population in 2015, with a further increase to 746.6 per 100,000 population in 2016. The percentage of uninsured patients decreased from 19% to 14.3% and those with Medicaid coverage increased from 29.4% to 36.0%. The increase in ED utilization was greatest for individuals belonging to the lowest income quartile (895.1 per 100,000 population in 2013 to 964.0 per 100,000 in 2017). Overall, only 38.3% of the ED visits during the study period were due to emergent eye conditions. The inflation adjusted median charge per ED visit increased from \$718.4 to \$999.5 after the ACA was mandated.

Conclusions: Although the ACA increased insurance coverage for Americans belonging to low socioeconomic status and minorities, it did not translate into improved and more equitable access to outpatient ophthalmic care. Emergency department utilization for non-emergent ophthalmic conditions continues to increase, resulting in more costly and less specialized care. Additional measures beyond expanding insurance coverage may be necessary to provide high quality, efficient and equitable healthcare to all Americans.

CONTROL ID: 3547160

SUBMITTER (NAME ONLY): Nicholas Pfahler

TITLE: Platelet complement activity reveals a new target for AMD treatment

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Pfahler, I. Bielskus, A. Kakouri, P.A. Knepper, Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|N.J. Volpe, P.A. Knepper, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|M. Giovino, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age-related macular degeneration (AMD) is linked in part to genetic defects in complement system proteins as well as inflammatory markers of the innate immune system. Previously, our laboratory reported that AMD platelets have increased surface levels of complement component C3b at baseline and after platelet activation. In this study, we measured platelet levels of proteins from all three complement pathways as well as several innate immune proteins with associations to AMD.

Methods: Whole blood was obtained from 13 pre-advanced AMD and 6 age-matched control subjects after receiving IRB approval and informed consent. Platelet-rich plasma was isolated by centrifugation and samples were prepared in buffer containing fibrin inhibitor Gly-Pro-Arg-Pro. Fluorescently-conjugated antibodies against complement proteins C1R, C3b, CFH, MASP-1/3, and Ficolin-2, as well as innate immune proteins Toll-like receptor 4 (TLR4) and TIMP-3, were measured at baseline and after activation with dual platelet agonists thrombin and convulxin (T/C) using a Beckman Coulter CytoFLEX S flow cytometer. Inhibitors of the TLR4 pathway resveratrol, quercetin, and curcumin were evaluated in combination (RQC) for their potential to reduce systemic vascular complement activation.

Results: In AMD platelets, C1R ($P=0.003$), C3b ($P=0.02$), and innate immune receptor TLR4 ($P=0.01$) were significantly increased at baseline compared with controls. CFH, a negative regulator of complement activity, was decreased at baseline ($P=0.04$). Platelet activation with T/C increased surface levels of all measured proteins. Pre-treatment with RQC significantly inhibited the activation-induced increase in C1R ($P=0.001$), C3b ($P=0.001$), CFH ($p=0.0001$), MASP-1/3 ($P=0.008$), Ficolin-2 ($P=0.0004$), TLR4 ($P=0.01$), and TIMP-3 ($P=0.0008$).

Conclusions: Systemic levels of complement and TLR4-associated innate immune system proteins are increased in AMD. Platelet complement and innate immune pathways may be a new target for AMD treatment.

CONTROL ID: 3547163

SUBMITTER (NAME ONLY): Daniel Wang

TITLE: Assessment of the Readability, Accessibility and Quality of Online Source Material for Myopia and Myopic Degeneration

SESSION TITLE: Myopia epidemiology and refractive error

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Wang, J. Fallon, D. Harris, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Myopia is a common cause of visual impairment globally with its prevalence set to rise over the next several decades, particularly in Asian nations. Patients increasingly rely upon Google searches on the internet to provide supplemental information regarding their ophthalmic and medical conditions. This study seeks to compare the quality, readability, and accessibility of online content available to the public regarding myopia and myopic degeneration.

Methods: A cross-sectional analysis of the top 15 google sites using a general search strategy (terms: Myopia and Myopic Degeneration) was performed between November 2020 and December 2020. Identified sites were stratified into either private or academic sources. Website quality was assessed using the internationally recognized DISCERN and the Health on the Net (HONcode) criteria. Readability was graded using an online readability tool. Website accessibility features available to patients were also evaluated.

Results: Eight academic and seven private websites were included in the analysis. Academic websites had a significantly higher quality index (43.4 ± 9.2) compared to the private sites (29.3 ± 7.6 ; $P < 0.007$) determined by the DISCERN criteria. Similarly, the average quality score based on the HONcode criteria for academic websites (8.1 ± 2.6) was statistically significantly higher compared to the private websites (3.6 ± 1.4 ; $P < 0.001$). The mean consensus reading grade level was similar between the academic (11.4 ± 1.8) and private websites (11.6 ± 1.5 ; $P = 0.82$). Language translation and accessibility features for visual impairment was offered by only 7 of the 15 identified websites.

Conclusions: The quality of freely available online information regarding myopia and myopic degeneration is variable by source, but in general is of poor quality according to the specified criteria. Online content provided by academic sites was of significantly higher quality compared to private websites. Improving the readability of online source content and implementing universal accessibility features is needed to aid patients in their understanding of ophthalmic conditions.

CONTROL ID: 3547164

SUBMITTER (NAME ONLY): R Glenn Hepfer

TITLE: A multifactorial blast injury model induces consistent and controllable damage in ex vivo and in vivo animal studies

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Hepfer, H. Yao, Oral Health Sciences, Medical University of South Carolina, Charleston, South Carolina, UNITED STATES|P. Chen, H. Yao, Bioengineering, Clemson University, Clemson, South Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Ocular blast injuries result from a variety of damage mechanisms. Primary blast waves can cause damage with local increases in pressure. Secondary injuries from projectiles can cause penetrating and blunt trauma. Current injury models study a single mechanism and do not consider possible additive effects of multifactorial damage. The goal of this study is to produce and test a repeatable and controllable combined injury model in ex vivo porcine eyes and in in vivo rabbits.

Methods: A custom injury model device was fabricated that produces a primary blast wave, secondary corneal puncture injury, and blunt trauma in a simultaneous event. The physical effects of pressure, blade length, and blunt force were measured or calculated with a pressure transducer, microscopy, and projectile velocity, respectively. Immediate pathological effects were measured on fresh, intact porcine eyes, which were obtained from a local slaughterhouse. Blade lengths of 200, 400, and 600 μm were tested. Porcine corneas were analyzed with cornea strip extensometry and histology. The injury model was further tested in New Zealand white rabbits. Wound healing was observed with ophthalmic exams at regular intervals and with histology at days 3 and 14 following injury.

Results: The injury device produced consistent and controllable peak pressure, blade length, and blunt force. In porcine eyes, corneal strip extensometry showed a decrease in elastic modulus ($p < 0.01$, ANOVA) and ultimate stress ($p < 0.0001$, ANOVA) with increased blade length ($n = 6$). Histology showed that the wound depth correlated with blade length. In the in vivo study, fluorescein staining in ophthalmic exams and collagen imaging in histological analysis revealed a consistent location and depth of injury. By day 3, epithelial cells migrated and proliferated in the wound, and by day 14, scar tissue was observed through alpha-smooth muscle actin staining.

Conclusions: Our results demonstrate a novel model that combines damage mechanisms underlying blast injury. The model produces consistent and controllable damage in ex vivo porcine eyes and in in vivo rabbits. The model could be used to assess compounding effects of blast injury mechanisms and to test multipronged therapies for these injuries.

CONTROL ID: 3547165

SUBMITTER (NAME ONLY): Dusanka Deretic

TITLE: Rab11, the TRAPP II complex, and phosphorylation regulate Rabin8 during ciliary trafficking of rhodopsin

SESSION TITLE: Biochemistry and molecular biology of the retina

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Deretic, T. Fresquez, Ophthalmology and Visual Sciences, University of New Mexico Health Sciences Center, Albuquerque, New Mexico, UNITED STATES|B.M. Tam, O.L. Moritz, Ophthalmology, The University of British Columbia, Vancouver, British Columbia, CANADA|

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ABSTRACT BODY:

Purpose: Sorting into rhodopsin transport carriers (RTCs) is regulated by the Rab8 GEF Rabin8, the backbone of the Rab11-Rabin8-Rab8 ciliogenesis complex. Rabin8 phosphorylation by NDR2 (aka STK38L), a canine early retinal degeneration (erd) gene, regulates its membrane association and function. The role of Rabin8 is not clear, however its interactions with multiple ciliary complexes suggest a central role in ciliary pathways of rhodopsin and other sensory receptors.

Methods: A GFP-Rabin8 WT and C (AA 251-460) fragment of human Rabin8 were constructed by site-directed mutagenesis and cloned into the XOP0.8 eGFP-N1 expression vector for the generation of transgenic *X. laevis*. The following mutants were generated: GFP-Rabin8 S272E and GFP-Rabin8 S272A; GFP-Rabin8 E192A and F201A GEF domain mutants and GFP-Rabin8 Δ 300-305 Rab11 binding mutant. The resulting phenotypes were analyzed by confocal microscopy.

Results: GFP-Rabin8 WT co-localized with rhodopsin in the Golgi and on RTCs, similar to the known localization of endogenous Rabin8 in photoreceptors cells. GFP-Rabin8 WT concentrated at the Golgi exit sites (GES), and at the RTC fusion sites. GFP-Rabin8 C was completely cytosolic, indicating that the binding of its N-terminal domain to the TRAPP II complex is essential for localization. GFP-Rabin8 S272E mutant, a phosphomimetic that decreases Rabin8 binding affinity for phosphatidyl serine (PS) but increases affinity for the Sec15 component of the exocyst ciliary complex, was predominantly localized at the base of the cilium, indicating that NDR2 phosphorylation directs Rabin8 to this location. The GFP-Rabin8 S272A mutant accumulated at the GES, where Rabin8 phosphorylation likely occurs. The phenotype of GFP-Rabin8 E192A and F201A mutants, which cannot activate Rab8, was similar to that of the S272E mutant, suggesting that Rabin8 phosphorylation and Rab8 activation occur at the similar site. The GFP-Rabin8 Δ 300-305 mutant was completely cytosolic, indicating that Rabin8 binding to Rab11 is also essential for its localization.

Conclusions: Our results implicate Rab11, the TRAPP II complex and the NDR2 kinase in the control of Rabin8 localization and function during the targeting of rhodopsin from the Golgi to the cilium and ROS. Ongoing experiments will establish the linkages between Rabin8 regulatory interactions and the discrete steps in rhodopsin ciliary trafficking.

CONTROL ID: 3547167

SUBMITTER (NAME ONLY): Bright Asare-Bediako

TITLE: Physiological Recruitment of Hematopoietic Cells and Innervation in the Developing Retina

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Asare-Bediako, C. Huang, C.P. Vieira, Y. Adu-Agyeiwaah, M.B. Grant, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham Department of Ophthalmology and Visual Sciences, Birmingham, Alabama, UNITED STATES|B. Asare-Bediako, Y. Adu-Agyeiwaah, School of Optometry Vision Science Graduate Program, University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|

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ABSTRACT BODY:

Purpose: Hematopoietic stem/progenitor cells (HS/PCs) play a vital role in retinal injury and repair. Studies have shown that the egress of HS/PCs from the bone marrow via circulation to target tissues is influenced by both sympathetic and sensory nerves whose neurotransmitters activate adrenergic and sensory receptors expressed on HS/PCs and regulate HS/PC migration and proliferation (Gao et al, 2020). However, the role HS/PCs play in retinal development and the role of the sympathetic and sensory neurons in physiological recruitment during retinal development remains unclear. We sought to investigate the earliest time point at which HS/PCs are recruited into the neonatal retina in mice and to characterize the phenotype of the recruited cells. We also investigated whether HS/PC recruitment is associated with the sympathetic or sensory innervation of the neonatal retina.

Methods: Wild-type C57BL/6J mice at postnatal days 0, 3, 5 and 7 were euthanized and their eyes enucleated. The retinas were isolated and processed for immunohistochemistry. Bone marrow-derived cells in the retina were identified with the hematopoietic-specific marker VAV1. Vascular endothelial cells, sympathetic and sensory neurons were labelled with CD 31, tyrosine hydroxylase and calcitonin gene-related peptide, respectively. The number and phenotype of hematopoietic cells was quantified and the density of sympathetic and sensory neurons assessed at each time point.

Results: HS/PCs (VAV1-positive) were observed in the retina less than 24 hours after birth (P0) and did not increase significantly between P0 and P3 ($p=0.114$), P5 ($p=0.114$) and P7 ($p=0.057$). Between P0 (67.16%) and P7 (68.09%, $p=0.601$), the majority of hematopoietic cells in the developing retina were F4/80-positive, indicating a macrophage/microglial phenotype. Sympathetic neurons were not observed until at P3 in the inner nuclear layer and increased rapidly at P5 ($p=0.028$) and P7 ($p=0.029$). However, cells expressing CGRP were observed from P0 to P7 in the nuclear layers of the retina, and only reduced significantly at P7 ($p=0.008$).

Conclusions: Our data suggests that HS/PCs may be recruited into the developing healthy retina prenatally as predominantly phagocytic cells, and their recruitment may be facilitated by sensory innervation to the retina.

CONTROL ID: 3547169

SUBMITTER (NAME ONLY): Norma Morales

TITLE: Ten Year Experience of Optical Keratoplasty in Mexican Children

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Morales, A. Navas, L. Pedro Aguilar, A. Ramirez Miranda, E.O. Graue-Hernandez, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To describe the indications and outcomes associated to keratoplasty in children.

Methods: This is a retrospective descriptive study performed at the Instituto de Oftalmologia Conde de Valenciana.

The medical records of all patients under 18 years of age that underwent keratoplasty from 2009 to 2019 were reviewed. The data reviewed was: patients demographics, indication for keratoplasty, visual acuity at presentation and at last visit, surgeries previous, during or after keratoplasty, glaucoma incidence and time to graft failure

Results: A total of 46 patients (53 eyes) under the age of 18 were included in this review. The mean age was 13.75 ± 3.89 years. The most common indication was keratoconus in 26 eyes (49%). The most common procedure was penetrating keratoplasty in 47 eyes (89%). Mean logMAR vision acuity at presentation was 2.05 ± 0.99 and at last visit 0.82 ± 1.33 ($p < 0.05$). The mean follow up time was 56.98 ± 42.83 months while the mean survival time was 130.34 months. The survival rate was 86.79% per year. The survival time of the eyes with previous surgery and the eyes that had concomitant surgery was different compared to the eyes without previous surgeries ($p = 0.02$). The survival time of the 15 eyes that had surgery after the keratoplasty was not different ($p = 0.601$). A total of 17 eyes (32.1%) had ocular hypertension of which 8 (15.1%) had confirmed diagnosis of glaucoma. Mean survival time of patients without glaucoma was 116.

Conclusions: The most common indication for keratoplasty was keratoconus and the survival rate of the grafts over a mean follow up time of 56.98 ± 42.83 months was 86.79% per year. This survival rate was worse in patients who had had previous surgeries or concomitant surgeries at time of keratoplasty. The most common complication was ocular hypertension. Interestingly, even though many studies have reported that glaucoma affects the survival rate in adults and children, in this study, there was no difference in survival time between eyes that had glaucoma and the ones without glaucoma.

CONTROL ID: 3547172

SUBMITTER (NAME ONLY): Diana Kim

TITLE: Associations Between Patient and Eye Care Provider-Related Factors and Endophthalmitis Following Intravitreal Injections

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Kim, B.L. VanderBeek, Scheie Eye Institute, Philadelphia, Pennsylvania, UNITED STATES|G. Emerson, Phillips Eye Institute, Minneapolis, Minnesota, UNITED STATES|J.D. Stein, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|J.D. Stein, University of Michigan School of Public Health, Ann Arbor, Michigan, UNITED STATES|M. Rahman, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Diana Kim: Commercial Relationship: Code N (No Commercial Relationship) | Geoffrey Emerson: Commercial Relationship(s);Novartis:Code I (Personal Financial Interest);Regeneron:Code I (Personal Financial Interest) | Moshur Rahman: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Stein: Commercial Relationship: Code N (No Commercial Relationship) | Brian VanderBeek: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate associations between patient-related factors, provider-related factors, and the risk of postinjection endophthalmitis.

Methods: Retrospective nationally-representative sample of Medicare beneficiaries undergoing ≥ 1 intravitreal injection between January 1, 2013 and December 31, 2017. Logistic regression analysis was performed to assess whether patient-related factors (age at injection, race, sex, agent injected, injection-associated diagnosis, year of injection), and provider-related factors (retina subspecialist versus non-subspecialist, board certification status) were associated with an increased or decreased risk of postinjection endophthalmitis. Main outcomes were measured with odds ratio (OR) with 95% confidence intervals of receiving a diagnosis of endophthalmitis in the 14 days after intravitreal injection.

Results: 2,907,324 intravitreal injections were performed on 219,640 patients by 4,315 ophthalmologists, 3,196 (74%) who were retina specialists and 4,021 (92%) who were certified by the American Board of Ophthalmology (ABO). The mean (SD) age of the patients was 78.2 (10.2), there were 131,284 females (59.8%), and 192,544 whites (87.7%), and 13,220 blacks (6.0%). Overall, there were 1,088 (0.037%) cases of postinjection endophthalmitis, 1,024 (0.037%) among patients receiving injections by ABO certified ophthalmologists and 64 (0.050%) by non-ABO-certified ophthalmologists ($p=0.01$). Patients receiving injections by ABO-certified ophthalmologist had a 28% reduced odds of endophthalmitis (OR=0.72; 95% CI: 0.523-0.996, $P = 0.047$). Subspecialty training in retina was not associated with the rate of endophthalmitis (OR=1.00; 95% CI: 0.734-1.362 $P = 1.00$).

Conclusions: ABO board certification was associated with decreased odds of endophthalmitis after intravitreal injection. While some risk factors are not modifiable, restricting intravitreal injection to board certified ophthalmologists may reduce the risk of sight-threatening postinjection endophthalmitis.

CONTROL ID: 3547173

SUBMITTER (NAME ONLY): Bhavatharini Ramakrishnan

TITLE: Effect of Alternating and In phase flicker occlusion on vergence eye movements

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Ramakrishnan, S.B. Stevenson, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Bhavatharini Ramakrishnan: Commercial Relationship: Code N (No Commercial Relationship) | Scott Stevenson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Rapid alternate occlusion of the eyes has been shown to improve stereoacuity and visual acuity in some amblyopic subjects¹. Previously we looked at the effect of alternate occlusion on vergence eye movements in subjects with normal ocular health. In this current study, we want to compare the effect of alternate vs. in phase occlusion of different frequency on vergence eye movements and to see if it is the presence of flicker per se or alternate occlusion of the eyes that has an effect on vergence.

Reference:

¹ A flicker therapy for the treatment of Amblyopia, Fuensanta. A. Vera-Diaz, Bruce Moore, Eric Hussey, Gayathri Srinivasan, Catherine Johnson, Vision development and Rehabilitation, Volume 2 Issue 2, June 2016.

Methods: Vergence eye movements were measured using a dual Purkinje image eye tracker. The stimulus used for the testing was a filtered noise pattern of spatial frequency 0.25 or 2 c/deg with a bandwidth of 1 octave and variable contrast. Trials were 2 seconds long, with a near or far 1 deg disparity step at either 250 or 350 msec into the trial. Both alternating and in-phase flickers of different frequencies (2, 4, 8, 16, 32 Hz) were used. Data were collected in blocks of 240 trials (6 contrast x 5 flickers x 2 directions x 2 onset times x 2 phases) in shuffled order. Data were collected in 2 subjects and for two spatial frequencies (2 and 0.25 cycles per degree) in separate sessions. Three variables were analyzed and compared between the two phases of flickers: Latency to reach half the amplitude, Peak velocity, and the final amplitude.

Results: At higher flicker rates of 16 and 32 Hz, Vergence responses were robust, with peak velocities of 4 to 6 degrees per second and reaching the 1-degree demand within one second. At lower flicker rates, 2 and 4 Hz, and to a lesser extent at 8Hz, alternating flicker reduced vergence amplitude and increased latency dramatically while in phase flicker had only a small effect.

Conclusions: The results of this study show that vergence responses are disrupted by alternate flicker more than in phase flicker, particularly at lower frequencies. With alternate occlusion at 8 Hz, which has been used in Amblyopia treatment, vergence is intact but somewhat impaired. Results of this study will be helpful in refining Flicker glasses as a therapy for Amblyopia.

CONTROL ID: 3547176

SUBMITTER (NAME ONLY): Kiran Vupparaboina

TITLE: Automated choroid layer segmentation based on wide-field SS-OCT images using deep residual encoder-decoder architecture

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K.K. Vupparaboina, A. Selvam, J. Sahel, K.K. Dansingani, J. Chhablani, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|M.N. Ibrahim, S. Jana, Electrical Engineering, Indian Institute of Technology Hyderabad, Hyderabad, Telangana, INDIA|S. Suthaharan, Computer Science, University of North Carolina at Greensboro, Greensboro, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The choroid is a vascular structure of the ocular posterior segment which serves a number of crucial metabolic and homeostatic functions. Choroidal dysfunction is implicated causally in several macular diseases, so there is considerable interest in characterizing choroidal structure in terms of specific biomarkers, using in vivo imaging. However, clinical studies have so far been based on optical coherence tomography (OCT) images corresponding to 6mm × 6mm macular scanning area. A wide-field swept-source OCT (SS-OCT) imaging system provides denser raster scans over a larger, 12mm × 12mm scanning area that includes the optic nerve. The aim of this study was to achieve automated segmentation of the choroid in wide-field SS-OCT scans. A deep learning architecture based on residual encoder-decoder modules proved efficacious for this purpose.

Methods: A retrospective dataset of 613 wide-field SS-OCT B-scans with a resolution of 12mm × 3mm (1024×1536 in pixels) taken from healthy eyes was used in this experiment. Images were captured using a wide-field SS-OCT device (Carl Zeiss Plex Elite 9000). Inspired by the ability of deep residual networks to propagate the information without loss and the success of encoder-decoder architecture in image segmentation, we adopted residual U-Net (ResUnet) for choroidal segmentation (Fig. 1). A random 70:30 data split was considered for training and testing (unseen). Ground truth annotations (masks) required for training the model were obtained by a previously validated segmentation tool and all annotations were verified by clinicians. Images were resized to 256x256. Further, the model was trained for 80 epochs, with a batch size of 8, to minimize Dice coefficient (DC) loss. The DC criterion was also used for performance evaluation.

Results: Training and Testing DC values were found to be 99.42% and 97.81%, respectively, which were desirably high. Segmentation results on representative test images, depicted in Fig.1, visually demonstrate the efficacy of the ResUnet architecture.

Conclusions: The proposed ResUnet approach demonstrated performance close to the ground truth. We next plan to extend the methodology to diseased datasets. Further, we envisage extending the 2D approach to train directly on 3D volumes.

CONTROL ID: 3547177

SUBMITTER (NAME ONLY): Mariacarmela Allocca

TITLE: Advances towards a dual AAV CRISPR-Cas9-based 'Knockout and Replace' strategy to treat rhodopsin-associated autosomal dominant Retinitis Pigmentosa

SESSION TITLE: Gene editing and ocular therapies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Allocca, D. Reyon, Editas Medicine, Cambridge, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mariacarmela Allocca: Commercial Relationship(s);Editas Medicine:Code E (Employment) | Deepak Reyon: Commercial Relationship(s);Editas Medicine:Code E (Employment)

ABSTRACT BODY:

Purpose: Mutations in the rhodopsin (RHO) gene are the most common cause of autosomal dominant Retinitis Pigmentosa (adRP), a retinal disease that results in blindness due to photoreceptor degeneration. Over 150 autosomal dominant mutations have been identified in the RHO gene. Therefore, we are developing a CRISPR-Cas9-based mutation-independent therapeutic strategy that simultaneously 'knocks out' endogenous RHO, and 'replaces' it with exogenous functional RHO using a dual AAV system.

Potent, highly specific guide RNAs and an optimized RHO expression vector have been identified and used in studies to address the following questions:

- 1.Could the novel alleles generated as a consequence of on-target editing be dominant negative?
- 2.What is the optimal ratio of the two AAV vectors?

Methods: An in vitro overexpression system was developed to quantify the effect of novel, editing-induced, alleles on cell viability. Three novel alleles were tested, one in each open-reading-frame as an indicator of potential novel alleles generated by on-target editing. The system was benchmarked using RHO-P23H as the dominant negative allele and WT RHO as the normal allele. To confirm in vitro results, and to identify the optimal ratio of the two AAVs, the dual AAV system was tested at multiple ratios in humanized RHO mice. The optimal ratio of vectors and percentage of potential novel deleterious alleles was determined by quantifying on-target editing by NGS at 6 and 13-weeks post subretinal injection.

Results: Examination of the on-target editing site in humanized mice by NGS revealed low percentage of potential deleterious allele and a consistent INDEL profile at 6 and 13-weeks post injection, demonstrating that the risk of generating novel dominant negative alleles is minimal. Different ratios of dual AAV vectors showed corresponding change in the level of RHO KO and replacement. The configuration that provides the highest level of RHO replacement and sufficient on-target editing has been identified as the 'optimal ratio' for future studies.

Conclusions: We have demonstrated minimal risk of generating novel dominant negative alleles and the feasibility of achieving therapeutically relevant levels of editing and replacement using an optimized ratio of the two AAV vectors. We are moving forward to preclinical studies for further characterization of dual AAV system in vivo.

CONTROL ID: 3547178

SUBMITTER (NAME ONLY): Mason Posner

TITLE: Characterizing zebrafish lens abnormalities following CRISPR gene knockout

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Posner, A. Butterbaugh, T. Kaye, A. Hussen, Biology and Toxicology, Ashland University, Ashland, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Mason Posner: Commercial Relationship: Code N (No Commercial Relationship) | Alexis Butterbaugh: Commercial Relationship: Code N (No Commercial Relationship) | Taylor Kaye: Commercial Relationship: Code N (No Commercial Relationship) | Adil Hussen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The usefulness of zebrafish for examining molecular mechanisms of lens development could be enhanced by producing consistent terminology for abnormal lens phenotypes. Here we characterize a variety of lens abnormalities stemming from knockout of crystallin, transcription factor and RNA-binding protein genes after CRISPR/Cas9 editing.

Methods: We used two approaches to disable individual genes with CRISPR/Cas9 editing. First, we produced two gRNAs designed to delete a region spanning a gene's promoter and first exon to prevent translation of any resulting mRNA. Second, we designed a mix of four gRNAs to produce multiple gene mutations in the coding region of a targeted gene. In each case, we co-injected one nanoliter into one-cell stage zebrafish zygotes containing a total of 500 picograms of gRNA and 250 picograms of recombinant Cas9 protein. For the first method, we raised the injected embryos to adulthood, outcrossed them to wildtype individuals, and genotyped offspring to identify null mutants, which were then used to produce lines of homozygous mutant fish. In the case of the four guide mix, we examined phenotypes directly in injected embryos.

Results: We generated zebrafish missing ~800 basepairs of the cryaa gene and confirmed by western analysis a decrease in α A-crystallin protein levels. Seventy-eight embryos from a cross of injected fish with this large cryaa deletion showed a decreased proportion of normal lenses compared to wildtype embryos at four dpf (46.2% versus 94.3%; p-value<0.0001). Lenses in these cryaa mutant embryos showed a mix of three different abnormalities (prevalence shown in parentheses): a central roughness (43.6%), disorganization of the concentric fiber cell rings (20.5%), and excessive pitting (6.4%). Mixes of four guides targeting several genes resulted in observable lens phenotypes directly in injected embryos. Targeting of both zebrafish γ N-crystallin genes (crygn1 or crygn2) produced lenses with excessive gaps between fiber cells. Similar gaps were seen after targeting the transcription factor gene prox2. A unique lens abnormality affecting the central lens was seen after targeting the ribonuclease endou2.

Conclusions: These data demonstrate that gene disruption can produce diverse phenotypes in the lens. We suggest that future studies using zebrafish as a model for lens development carefully characterize these abnormalities so that they can be compared between studies.

CONTROL ID: 3547180

SUBMITTER (NAME ONLY): Abeir Baltmr

TITLE: Delaying Anti-VEGF treatment for diabetic macular oedema during the pandemic- effect on vision and anatomical outcomes

SESSION TITLE: Diabetic retinopathy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Baltmr, P. Vouzounis, S. Alkhalilil, M. Farag, R. Krishnan, C. Rennie, University Hospital Southampton NHS Foundation Trust, Southampton, Southampton, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Diabetic macular oedema (DMO) is the commonest cause of vision loss in patients with diabetes. As per the Royal College of ophthalmologists of the UK guidelines during the 2020 COVID-19 pandemic, in an effort to reduce injection and clinic visit frequency, and to minimize the risk of exposure of patients and healthcare staff many patients attending the eye unit had their appointments and treatment postponed. Patients with diabetic retinopathy were offered clinic review and treatment during this time but many of these patients chose not to attend their appointments because they were at high risk from the virus.

To evaluate the impact of delays in anti-VEGF treatment during the pandemic at a single university hospital clinic. Specifically, to identify the gap in treatment, and to examine the impact of this on visual acuity and anatomical outcomes.

Methods: Retrospective data collection from the electronic medical record system (medisoft ophthalmology), and OCT scans of patients with DMO. Patients were included if they have active diagnosis of DMO with Anti-VEGF treatment in the 12 weeks prior to national lockdown and restriction of services. Exclusion criteria included patients with no follow up visits.

Results: Average gap in treatment is 16.5 (range) weeks and Average reduction of the best corrected visual acuity from last recorded before treatment gap to visual acuity when patient was reviewed, or treatment restarted was -0.15. ($P > 0.05$). One patient showed progression of his diabetic retinopathy to proliferative stage.

Conclusions: Information was gathered for 328 patients (125 F, 203 M), who were treated with Anti-VEGF between 01/01/2020 & 01/09/2020

Preliminary data analysis of 134 eyes of 105 consecutive patients showed average gap in treatment of 13.2 (10-31) weeks. The average reduction of the best corrected visual acuity from last recorded before treatment gap to visual acuity when patient was reviewed, or treatment restarted was -0.05 LogMar. ($P > 0.05$) with mean VA 0.4 (range 0-1.6 LogMar) pre break and mean VA post treatment of 0.45 LogMar (range 0.06-1.6). 27/134 lost 5 letters or more of vision, 6 eyes lost 15 letters, 63 were within ± 5 letters of baseline vision.

One patient showed progression of his diabetic retinopathy to proliferative stage, and two patients showed improvement in their DMO after their treatment gap, and their Anti-VEGF treatment was stopped.

CONTROL ID: 3547185

SUBMITTER (NAME ONLY): Arsia Jamali

TITLE: EFFICACY of CELL-BASED PLASMACYTOID DENDRITIC CELL THERAPY FOR CORNEAL WOUND HEALING

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Jamali, B. Bayraktutar, D.L. Harris, V.G. Sendra, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|A. Jamali, B. Bayraktutar, P. Hamrah, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have recently shown that plasmacytoid dendritic cells (pDCs) play a significant role in corneal homeostasis. The current study aims to determine the efficacy and safety of local adoptive transfer of pDCs for the treatment of corneal epithelial wounds.

Methods: Splenic pDCs from 6-8-week-old wild-type (WT) C57BL/6 or DPE-GFP \times RAG1^{-/-} mice, receiving FLT3L-secreting B16 melanoma cells to enhance pDC density, were isolated by flow cytometric sorting. Central corneal epithelial debridement using a 2 mm trephine was performed on WT mice to assess the density of labelled pDCs. Epithelial debridement of central corneas was performed on PSGL-1 KO mice using a 1.5 mm trephine in order to assess the effect of pDC therapy on corneal wounds, ruling out the effect of infiltrating cells. Mice received topical fibrin sealant (sham-transfer) or 10,000 splenic pDCs. Corneal fluorescein staining was conducted 24, 48, and 72 hours after the procedure to assess wound healing. Wound areas were measured using ImageJ. Corneal wound-mounts were imaged on day 2, 5, 7, and 14 after the adoptive transfer to measure the density of transferred cells. T test was used to determine differences and $p < 0.05$ was considered significant.

Results: Adoptive transfer did not result in corneal opacity or neovascularization. Adoptively-transferred GFP⁺ pDCs were observed in the central cornea on day 2 and remained in the cornea 14 days following adoptive transfer, although in reduced numbers compared to day 2 ($p < 0.05$). We observed that one-time adoptive transfer of pDCs significantly decreased epithelial defect size by 1.7-, 3.0- and 6.1-fold, at 24, 48, and 72 hour following corneal epithelial wounding, as compared to sham-transfer ($p < 0.05$).

Conclusions: Local adoptive transfer of pDCs is a safe procedure, which significantly improves corneal wound healing.

CONTROL ID: 3547189

SUBMITTER (NAME ONLY): Emma Stenz

TITLE: Outcomes of Eyes with Multiple Retinal Detachments Following Primary Rhegmatogenous Retinal Detachment Repair

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Stenz, The University of Texas Health Science Center at Houston John P and Katherine G McGovern Medical School, Houston, Texas, UNITED STATES|E. Stenz, H. Yu, T. Wong, A.S. Shah, J. Major, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|C.C. Wykoff, Blanton Eye Institute, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Failure of primary rhegmatogenous retinal detachment (RRD) repair is an unwanted clinical outcome associated with decreased final visual outcomes compared to successful primary RRD repair. The current study characterized surgical approaches and rates of recurrent RRD (re-RRD) repair.

Methods: Data was retrospectively collected from electronic health records from a large, urban retina practice with 14 physicians. Inclusion criteria were failed primary RRD repair with ≥ 2 RRD repairs from 2016 through 2020. Exclusion criteria were non-rhegmatogenous etiologies of RD, previous vitreoretinal surgery in the study eye, and proliferative diabetic retinopathy. Analyzed parameters included epidemiological data, surgical information, and post-operative outcomes. Statistical analysis was performed using Pearson's chi-squared test and one-way ANOVA analysis with Tukey's HSD to assess the relationship of surgical procedure with re-RRD rates and recurrence time. Statistical significance was defined as $P < 0.05$.

Results: 195 among 2,187 eyes undergoing primary RRD repair developed re-RRD (8.9%). Among this population, the mean number of RRD repairs performed was 2.4 ± 0.7 (range 2-5). During initial RRD repair, 9.2% of eyes received an encircling scleral buckle (SB) without pars plana vitrectomy (PPV) while 90.8% of eyes underwent PPV \pm SB. The likelihood of repair success following the second RRD repair was 72.3% while 27.7% of eyes required ≥ 3 RRD surgeries (Table 1), and the risk of subsequent RRD repair with respect to the number of pre-existing RRD repairs is summarized in Table 2. Eyes undergoing one RRD repair were less likely to undergo further procedures (8.9%) than eyes undergoing ≥ 2 RRD repairs; after the second RRD repair, the risk for further RRD repairs appeared to remain constant (20.4-27.7%) (Table 2). Moreover, repair of the presenting RRD with an encircling SB alone was associated with a lower rate of need for additional repairs than initial repair by PPV \pm SB ($P < 0.05$).

Conclusions: This study, limited by its retrospective design and inherent biases, describes the rates of re-RRD repair among all patients presenting with RRD. An association was observed between the primary surgery type and need for re-RRD repair which may be valuable for patient counseling. Additional work regarding risk factors for undergoing re-RRD repair may allow for mitigating strategies to be considered.

CONTROL ID: 3547191

SUBMITTER (NAME ONLY): EMELINE MAILLET

TITLE: Anti-Inflammatory and Protective Effects of Topical Ophthalmic (R)-DOI 0.01% in Allergic Conjunctivitis and Recurrent Intermediate Uveitis Disease Models in Rabbits.

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. MAILLET, D. Skutnik, J.A. Jamison, D. Bailey, M. Bacellar-Galdino, D. Garlick, Eleusis Therapeutics Inc., NEW YORK, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): EMELINE MAILLET: Commercial Relationship(s);Eleusis Therapeutics:Code E (Employment) | Daniel Skutnik: Commercial Relationship(s);Eleusis Therapeutics:Code F (Financial Support) | Jeffrey Jamison: Commercial Relationship(s);Eleusis Therapeutics:Code F (Financial Support) | David Bailey: Commercial Relationship(s);Eleusis Therapeutics:Code F (Financial Support) | Marianna Bacellar-Galdino: Commercial Relationship(s);Eleusis Therapeutics:Code F (Financial Support) | David Garlick: Commercial Relationship(s);Eleusis Therapeutics:Code F (Financial Support)

ABSTRACT BODY:

Purpose: Recent evidences indicate that (R)-DOI, a 5-HT_{2R} agonist, can modulate inflammatory processes and prevent allergic asthma in mice. In addition, (R)-DOI reduced complications from Herpes Simplex Virus-associated ocular disease. Given the foreseen applications in ophthalmology for a new immuno-modulatory drug class, we set out to investigate the therapeutic viability of topical eye drops (R)-DOI for ocular inflammatory diseases.

Methods: 1/ Ocular and plasma pharmacokinetics of a single topical administration of (R)-DOI 0.1% were determined using LC-MS/MS (LLOQ of 0.1ng/g) in DB rabbits.

2/ Compound 48/80 was used to induce an anaphylactic response, pruritis, and inflammation modeling allergic conjunctivitis in NZW rabbits. Animal groups were pretreated with topical (R)-DOI 0.05%, 0.01% or 0.001%.

3/ Topical (R)-DOI 0.01% was applied TID subsequent to disease induction in the antigen TB-induced recurrent intermediate uveitis model in NZW rabbits.

Results: 1/ The observed C (ng/mL-ng) values were: cornea-10900, iris-ciliary body-7810, conjunctiva-5680, choroid-1240, aqueous humor-297, retina-195, vitreous humor-3.47 and plasma-1.82. The terminal half-life ranged from 35 to 11 hrs in ocular tissues and was 1.9 in plasma. A follow up study established the ability of R-DOI to interact with melanin pigments.

2/ (R)-DOI 0.01% demonstrated the most significant inhibition of the allergic response (64% mean inhibition of total clinical score).

3/ R)-DOI treatment prevented worsening of vitreous haze (VH) in eyes presenting a mild uveitis disease at treatment initiation. Treatment improved time to resolution (VH) in moderate to severely graded eyes by 35% on the primary induction and by ~50% following re-induction. Histopathology assessments at Day 35 revealed decreased intensity of inflammatory cell infiltrates involving the choroid and retina in treated animals as well as a reduced frequency of retinal degeneration.

Conclusions: Topical ophthalmic (R)-DOI is readily absorbed into the rabbit eye and effectively reaches both anterior and posterior segments at therapeutically relevant concentrations.(R)-DOI demonstrated antiinflammatory efficacy and protection in both anterior and posterior ocular tissues against acute and chronic disease states in allergic conjunctivitis and intermediate uveitis models in rabbits.

CONTROL ID: 3547192

SUBMITTER (NAME ONLY): Marvarakumari Jhala

TITLE:

Characterization of inflammatory cytokine effects on retinal cell NF-kB P65 nuclear translocation and cytokine and cell adhesion molecule expression

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Jhala, S. Palmer, A. Galloway, C. Ramos, D.A. Padovani-Claudio, Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|J.S. Penn, Ophthalmology and Visual Sciences, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic Retinopathy (DR) is characterized by inflammation and microvascular abnormalities leading to vision loss. Muller cells (MC) are a major source of cytokines whose vitreous elevation correlates with DR progression. We previously showed that, after direct stimulation of human retinal microvascular endothelial cells (hRMEC) with IL1 β , TNF α , IL8, and IL6, only TNF α and IL1 β significantly affected cytokine auto-amplification and cell adhesion molecule expression in hRMEC. Now, we explore paracrine effects of inflammatory cytokine-stimulated human MC (hMC) on NF-kB translocation, and expression of inflammatory cytokines and cell adhesion molecules in hRMEC.

Methods: Primary hMC were stimulated with IL1 β , TNF α , IL8, and IL6 vs vehicle for 2 hours and the media replaced. 6 hrs after replacement, hMC-conditioned media was collected. hRMEC were stimulated directly with 1ng/mL of IL1 β , TNF α , IL8, and IL6 vs vehicle, or with conditioned media from stimulated hMC. hRMEC were fixed after 30 min stimulation and assayed by immunocytochemistry for NF-KB P65 nuclear translocation. hRMEC were lysed 4hr after stimulation with hMC-conditioned media, mRNA isolated, and cDNA generated and subjected to qRT-PCR with IL1 β , TNF α , CXCL8/IL8, IL6, ICAM, VCAM, SELE versus TBP (housekeeping control) TaqMan probes.

Results:

NFkB nuclear translocation was observed after direct hRMEC stimulation with either TNF α or IL1 β (P<0.0001) but only after hRMEC treatment with conditioned media from IL1 β - (and not TNF α , IL8 or IL6-) stimulated hMC (P<0.0001). Likewise, only conditioned media from IL1 β -stimulated hMC significantly increased hRMEC expression of IL1 β , TNF α , CXCL8/IL8, and IL6 by 31.2, 17.9, 10.4 and 8.8 fold, respectively (P<0.0001) and of ICAM, VCAM, SELE by 8, 200, and 70 fold, respectively (P< 0.001). IL6 and IL8 stimulation did not significantly affect any outcomes measured.

Conclusions: We observed NFkB nuclear translocation and increased expression of IL1 β , TNF α , IL8/CXCL8, IL6, ICAM, VCAM, and E-SELECTIN in hRMEC only after direct TNF α and IL1 β stimulation or after stimulation with conditioned media from IL1 β -stimulated hMC. This data suggests that NFkB activation may be involved in hRMEC pro-inflammatory transcriptome alterations and that IL1 β may be a key regulator of inflammatory amplification and a valuable target for early DR therapies.

CONTROL ID: 3547197

SUBMITTER (NAME ONLY): Sabeeh Kamil

TITLE: Long term tolerability of AAV5-Decorin gene therapy for the cornea

SESSION TITLE: Corneal stromal wound repair and healing

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Kamil, S. Gupta, R. Tripathi, P. Balne, P.R. Sinha, N.R. Sinha, L.M. Martin, N. Hesemann, R.R. Mohan, Departments of VMTH and Biomedical Sciences, College of Veterinary Medicine, University of Missouri System, Columbia, Missouri, UNITED STATES|S. Kamil, S. Gupta, R. Tripathi, P. Balne, P.R. Sinha, N.R. Sinha, L.M. Martin, R.R. Mohan, Harry S. Truman Memorial Veterans' Hospital, Missouri, UNITED STATES|N. Hesemann, Mason Eye Institute, School of Medicine, University of Missouri System, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: Gene therapy is an emerging treatment modality. The cornea is an ideal tissue for gene therapy approaches owing to its easy accessibility and immune-privileged status. Earlier, we have shown that AAV5-Decorin gene therapy treats corneal haze (Invest Ophthalmol Vis Sci., 2011;52:4833-41) and retards corneal neovascularization (PLoS One 2011; 6:e26432) in established preclinical rabbit disease models. This study investigated the long-term tolerability of AAV5-Decorin gene therapy in vivo. Tolerability studies documenting safety are essential for drug development.

Methods: New Zealand White rabbits were used in three groups (naïve, naked vector, and AAV5-Decorin gene delivered) as per ARVO guidelines. Six eyes of rabbits were topically administered AAV5-Decorin gene therapy and followed for six months. Six eyes each for naïve and naked vector groups were used as controls. Eyes were periodically (3 days-6 month) examined clinically with the slit lamp, stereo-microscope, pachymetry, fluorescein eye staining, tonometry, and in vivo confocal microscopy with HRT3-RCM. Modified Hackett-McDonald scale was used to record the findings of clinical examinations. At the end of six months, rabbits were humanely euthanized and corneal tissues were collected for histological, immunofluorescence, and qPCR analyses.

Results: AAV5 decorin gene delivered eyes did not show any significant change in corneal thickness and intraocular pressures until six months when compared to that in the naïve and naked vector group ($p>0.05$). AAV5-Decorin gene delivered eyes revealed normal pupillary reflex, no conjunctival congestion, swelling, and discharge, no signs of corneal opacity, and neovascularization. HRT3-RCM biomicroscopy showed normal corneal architecture at the surface epithelium, stromal and endothelial levels in naïve and AAV5-decorin gene delivered eyes at the sixth month. Histological, immunofluorescence, and qPCR analyses are underway.

Conclusions: Topical AAV5 decorin gene therapy appears tolerable to the cornea in the long term and has potential for bench-to-bedside translation.

CONTROL ID: 3547200

SUBMITTER (NAME ONLY): Jacquelyn Laplant

TITLE: Intravitreal Chemotherapy Eligibility and Ocular Survival for Advanced Retinoblastoma

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Laplant, M.W. Wilson, Ocular Oncology, St Jude Children's Research Hospital Department of Oncology, Memphis, Tennessee, UNITED STATES|M.W. Wilson, B.A. King, Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|F. Wang, H. Pan, Biostatistics, St Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES|R. Brennan, St Jude Children's Research Hospital Department of Oncology, Memphis, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vitreous seeding is a common cause of tumor relapse and poor ocular survival in patients with intraocular retinoblastoma. Intravitreal chemotherapy (IVC) is predominantly employed as salvage treatment for persistent or recurrent vitreous seeding. The purpose of this study was to determine the feasibility of primary IVC for the treatment of intraocular retinoblastoma with vitreous seeding.

Methods: We identified patients treated on a single institution phase II clinical trial for the treatment of retinoblastoma (NCT00186888). RET CAM images of each patient were retrospectively reviewed to identify eyes amenable to IVC at diagnosis and at subsequent examinations. Event-free survival (EFS) was defined as length of time to external-beam radiotherapy (EBRT) or enucleation. A log-rank test with p-values based on marginal computation was used for statistical analysis.

Results: 27 patients (54 eyes) were reviewed. Eyes were classified as Reese-Ellsworth group I-III (n=12) and IV-V (n=42) and International Classification of Retinoblastoma group A-B (n=17) and C-E (n=37). 27 eyes (50%) were deemed eligible for IVC at diagnosis. Of these 27 eyes, 6 (22%) had vitreous seeding. Of the 27 eyes deemed not eligible for IVC at diagnosis, 1 was excluded due to diffuse vitreous seeding, 1 due to phthisis bulbi, and 25 due to extensive subretinal detachment. Of these 27 eyes, 7 (26%) had vitreous seeding. After the completion of two courses of systemic vincristine and topotecan, 21 of these 27 eyes became eligible for IVC prior to the 3rd cycle of systemic chemotherapy.

Two additional eyes were deemed eligible prior to the 6th cycle of chemotherapy. 4 eyes (7%) did not reach eligibility due to either a persistent retinal detachment (n=1) or progressive disease (n=3). The EFS rate was 100% in eyes that were eligible for injection at time of diagnosis compared to 81% of those who reached eligibility at course 3 (p=0.019) and 0% of those who became eligible at course 6 or did not reach eligibility (p<0.0001).

Conclusions: Our retrospective study suggests that IVC can be incorporated early in the treatment of intraocular retinoblastoma to mitigate risk of recalcitrant vitreous disease. 89% were eligible for IVC prior to the 3rd course of chemotherapy. As expected, clearing of vitreous seeding correlated to improved EFS.

CONTROL ID: 3547204

SUBMITTER (NAME ONLY): Joseph Mootz

TITLE: Retinal Ganglion Cell Functional recovery after topical Intraocular Pressure Lowering Therapy in Preperimetric Glaucoma and Its Long-term Benefits Assessed by Pattern Electroretinogram.

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Mootz, A. Tirsi, V. Gliaglias, J. Tsai, S. Park, S.A. Obstbaum, C. Tello, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, UNITED STATES|D. Orshan, New York Institute of Technology College of Osteopathic Medicine, Old Westbury, New York, UNITED STATES|P.H. Derr, DIOPSYS INC, New Jersey, UNITED STATES|A. Tirsi, S. Park, S.A. Obstbaum, C. Tello, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Recent literature has shown that retinal ganglion cell (RGC) dysfunction is reversible in early glaucoma after 3 months of topical intraocular pressure (IOP) lowering treatment, but no studies reported those effects beyond that period in pre-perimetric glaucoma (PPG). The purpose of this cross-sectional study was to evaluate the utility of Pattern Electroretinogram (PERG) for quantifying RGC functional improvement in PPG after IOP lowering treatment over a period of over a year.

Methods: Six subjects (8 eyes) underwent topical IOP lowering treatment based on their clinical examination were observed at Manhattan Ear, Eye, and Throat Hospital over an average of 16.1 months. During this time, participants underwent full ophthalmological exam and were evaluated with Diopsys NOVA PERG [Magnitude (Mag), MagnitudeD (MagD), and MagnitudeD/Magnitude ratio (MagD/Mag ratio)] at three different timepoints: pre-treatment, 4 months (4.2 ± 0.82 months) and 16 months (16.1 ± 3.0) after treatment was started. Goldman applanation tonometry was used to measure IOP at each visit. One-way repeated measures ANOVA were conducted to determine statistical significance.

Results: One-way repeated measures ANOVA was conducted to determine whether there were statistically significant differences in PERG parameters at 4 months and 16 months. Both timepoints demonstrated significantly improved MagD and MagD/Mag ratios ($F(1, 7) = 6.351$, $p = 0.04$, partial $\eta^2 = 0.476$) and ($F(1, 7) = 7.843$, $p = 0.027$, partial $\eta^2 = 0.528$). Additionally, MagD and MagD/Mag ratio showed significant increases from pretreatment at both 4 months ($47.32\% \pm 52.91\%$ and $22.46\% \pm 46.53\%$) and 16 months ($20.02\% \pm 20.72\%$ and $8.43\% \pm 21.25\%$). As expected, the IOP lowering treatments resulted in significant decreases in IOP at both 4 months ($-18.10\% \pm 12.08\%$) and 16 months ($-16.43\% \pm 8.98\%$).

Conclusions: PERG is an effective method of measuring RGC functional recovery following administration of topical IOP lowering treatments. Reduction in IOP at both the 4-month and 16-month timepoint correlated with an improvement in MagD and MagD/Mag ratio, with a more pronounced effect during early stages of treatment.

CONTROL ID: 3547205

SUBMITTER (NAME ONLY): Mahadeo Sukhai

TITLE: Access to healthcare, medication and daily help for Canadians with vision loss.

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sukhai, C. Robbins, Research, CNIB, Kingston, Ontario, CANADA|M. Sukhai, Ophthalmology, Queen's University, Kingston, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: The Canadian Survey on Disability (CSD) 2017 is a nationwide assessment of the lived experience of persons with disabilities, across a variety of social determinants of health. Here, we examined the impact of demographic characteristics (age, severity of vision loss, other disabilities) on access to healthcare services, prescription drugs, and help with daily living tasks for Canadians living with vision loss.

Methods: The population sample for the CSD was derived from individuals who indicated they had difficulty with activities of daily living in the 2016 Canadian Census. Respondents were 15 years of age and above, and identified with a functional limitation, and represented more than 6 million (n = 6,246,640) Canadians. A subset of the larger dataset was created with individuals with seeing disability (n = 1,519,840) and weighted descriptive analyses were performed using SPSS.

Results: Access to allied healthcare services. Respondents with vision loss were most likely to receive physiotherapy, massage or chiropractic services (27.9%), compared to 17.2% accessing psychology or social work services, 6.8% accessing support group services, 4.5% accessing nursing care at home, and 2.9% accessing occupational therapy services. Adults under 65 were more likely to access physiotherapy, massage, chiropractic, psychology or social work services; conversely, adults over 65 were more likely to access support group services or nursing care at home. 54.5% of those with sight loss did not access healthcare services.

Prescription medication. 72.8% of the Canadian vision loss population take prescription drugs at least once per week; 66% of respondents under 65 compared to 85.2% for those over 65. 13.1% of Canadians with vision loss were unable to purchase prescription medications because of cost. 13.3% of Canadians with vision loss took prescription medications less often because of cost.

Help with daily living tasks. 54.9% of respondents received help with daily activities (average of 3.5 activities). Age, age of onset and number of disabilities were positively correlated with receiving help with daily activities.

Conclusions: Age, age of onset and number of disabilities correlated significantly with access to allied healthcare services, prescription medication, and help with daily living tasks for Canadians with vision loss.

CONTROL ID: 3547206

SUBMITTER (NAME ONLY): Dan-Ning Hu

TITLE: Cultured human uveal melanocytes express/secrete CXCL1 and CXCL2 constitutively and are increased by lipopolysaccharide via activation of Toll-like receptor 4

SESSION TITLE: Cornea, cytokines, anti-inflammatory

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Hu, R. Zhang, R.B. Rosen, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|W. Yang, Chung Shan Medical University, TAIWAN|S. Yang, Chung Shan Medical University, TAIWAN|

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ABSTRACT BODY:

Purpose: CXCL1 and CXCL2 are potent chemoattractants of neutrophils. Their levels are significantly increased in intraocular fluids or serum specimens from patients suffering from infectious endophthalmitis and non-granulomatous uveitis. We tested the hypothesis that lipopolysaccharide (LPS, agonist of TLR4) can stimulate the expression/secretion of CXCL1 and CXCL2 by cultured human uveal melanocytes via the activation of TLR4.

Methods: Effects of LPS on the expression of TLR4 were tested by using real time PCR, flow cytometry and fluorescence immunostaining. Effects of LPS-induced expression/secretion of CXCL1, -2 were studied by using real time PCR in cell lysates and ELISA in conditioned media of cultured uveal melanocytes. NF- κ B in nuclear extracts and phosphorylated MAPK signals were tested in cells with and without LPS treatment. Effects of various signal inhibitors on p38, ERK1/2, JNK1/2 and NF- κ B on the secretion of CXCL1 and CXCL2 were tested by using ELISA analysis.

Results: LPS stimulation increased the expression of TLR4 mRNA (3.34 ± 0.93 fold, mean \pm SD, $P < 0.05$) and protein ($36.9 \pm 4.5\%$, $P < 0.05$) in culture uveal melanocytes. LPS (100 ng/ml, 24 hr) stimulated the secretion of CXCL1 and CXCL2 proteins by 15.1 ± 2.0 fold and 7.51 ± 0.6 fold (mean \pm SD), respectively ($P < 0.05$); and increased the expression of CXCL1 and CXCL2 mRNA by 22.7 ± 3.5 fold and 15.7 ± 1.3 fold, respectively ($P < 0.05$). LPS mainly increased the activated NF- κ B (3.68 ± 0.14 fold) and phosphorylated JNK1/2 (3.43 ± 0.2 fold) (both $P < 0.05$). NF- κ B and JNK1/2 inhibitors significantly blocked LPS-induced expression of CXCL1 and CXCL2 in uveal melanocytes.

Conclusions: The present study validates our hypothesis that LPS can stimulate the expression/secretion of CXCL1 and CXCL2 by cultured human uveal melanocytes via the activation of TLR4. This result indicated that uveal melanocytes may play a role in the immune reaction to eliminate invading pathogens and also in the pathogenesis of non-granulomatous uveitis.

CONTROL ID: 3547207

SUBMITTER (NAME ONLY): Jerome Abdel-Maseih

TITLE: Correlation of Corneal & Retinal Thickness Ratio At Annular Points Aligned to Astigmatic Axis

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Abdel-Maseih, Rutgers The State University of New Jersey, New Brunswick, New Jersey, UNITED STATES|F. Shafik, New York Medical College, Valhalla, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop algorithms and protocols for Ophthalmic Evaluations as they pertain to different disease states and pre-operative evaluations.

Methods: Corneal tomographic & retinal OCT thicknesses in millimeters were directly correlated along rings at 5 and 7 mm from the central axis in correspondence from the cornea and the retina along the astigmatic steep axis; N=120. The steep axis was chosen as a peak point and hypothesized as aspect of vector summation of internal forces acting in a fashion to tissue planes: anterior & posterior. Analysis and comparison by Student T-Test

Results: There appears to be a direct correlation between the corneal and retinal thicknesses as a ratio in regard to the isolated rings segments (Sup & Inf) as highlighted in the table.

Conclusions: It is believed that the forces as they relate to pressing aspects to the anterior portion of the eye, ie, the cornea carry a proportional and effecting aspect to the posterior portion of the eye, ie, the retina. Physiologically there may be other factors, but on a relative basis of comparison this holds for the given statement of proportionality and a promise for quick clinical correlates for decision making.

CONTROL ID: 3547210

SUBMITTER (NAME ONLY): Waseem Ahamed Shihabuddeen

TITLE: Detailed phenotypic investigation of HtrA1 transgenic mice model

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Shihabuddeen, Y. Yanagi, R.Y. Chuan, V.A. Barathi, X. Wang, G.C. Cheung, Retina, Singapore Eye Research Institute, Singapore, SINGAPORE]

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ABSTRACT BODY:

Purpose: High-temperature requirement 1 (HtrA1) is linked with age-related macular degeneration(AMD)/polypoidal choroidal vasculopathy (PCV). Reportedly, polypoidal lesions, choroidal neovascularization(CNV) and lipid deposition are some of the common phenotypes of HtrA1 transgenic mice model. Moreover, overexpressed HtrA1 in mice RPE cells is associated with change in Bruch membrane composition. This study aims to clarify the phenotype of HtrA1 Tg mice in detail and to investigate the underlying pathophysiological mechanism of AMD and PCV.

Methods: In-vivo imaging was performed using funduscopy and optical coherence tomography (Micron,Phoenix), fluorescein angiography (FA: Micron), indocyanine green angiography (ICGA: HRA2, Heidelberg),and optical coherence tomography angiography (OCT-A: Plex Elite, Carl Zeiss). Eyes were sectioned or flat-mounted for Hematoxylin and eosin (H&E) and Immunofluorescence staining using CD31 (endothelial marker), APOE (drusen component), F4/80 (macrophage marker) and vitronectin antibodies to investigate the neovascularization, drusen formation, and infiltration of macrophage. Laser-induced CNV model was used to evaluate the role of HtrA1 on CNV activity.

Results: We examined 60 Tg and 15 wild type aged mice (23 – 30 months). Abnormal subretinal lesions [(Tg -33% (20/60) and WT – 7% (1/15)] were detected on color fundus photography and OCT. ICGA images represent from middle to late phase hyperfluorescent nodules corresponding to the areas of white material deposition [Tg - 40% (4/10)], whereas no leakage was observed in FA. En-face OCT-A and cross-sectional OCT-A failed to confirm vascular flow signals. In addition, IHC stains showed no difference in APOE and CD31 between HtrA1 Tg and wild type mice groups which is supported by the mRNA sequencing data. From H&E stains, we confirmed that lesions are in fact RPE cell migrations. Retina and RPE flatmount demonstrated increase macrophage infiltration and activation in HtrA1 Tg mice. Laser induced CNV in young HtrA1 Tg mice(n=12 for HtrA1 and WT) showed increased leakage from CNV compared to wild type mice (P<0.05).

Conclusions: The subretinal lesions from mice have different composition compared to that of humans observed in PCV. Hence, these drusen-like deposits might be the representation of immune cells which have been migrated into the subretinal space. Such subclinical inflammation may have resulted in the increased activity of laser-induced CNV.

CONTROL ID: 3547214

SUBMITTER (NAME ONLY): Steven Abcouwer

TITLE: High fat diets, but not high sucrose diets, cause a loss of retinal protein malonylation

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.F. Abcouwer, S. Shanmugam, W. Kardasis, P. Kish, P.E. Fort, T.W. Gardner, Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, UNITED STATES|A.E. Rumora, E. Feldman, Neurology, University of Michigan Michigan Medicine, Ann Arbor, Michigan, UNITED STATES|J. Baek, S. Pennathur, Medicine, University of Michigan, University of Michigan, Ann Arbor, MI, US, academic, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Loss of retinal metabolic homeostasis can lead to the development of diabetic retinopathy (DR). Post-translational modification (PTM) of proteins by the addition of a malonyl groups to lysine residues (MalK) fine tune the activities of metabolic enzymes to match nutritional conditions. To understand how the retina adapts to over-nutrition, as in metabolic syndrome and diabetes, we examined how high fat diets (HFD) and a high sucrose diet (HSD) affects retinal MalK content.

Methods: C57BL6/J mice were divided into seven groups (n=6/group). Groups were fed continuously for 24 wk HFDs with 60% of calories coming from either lard or sunflower oil (SFO), a HSD (10% calories from fat, 35% calories from sucrose), or a standard chow diet (SD, 10% calories from fat, low sucrose) Additional groups were fed the lard-based HFD for 16 wk and then switched to one of the other three diets for the final 8 wk. An antibody that specifically binds to MalK residues was used to probe retinal sections; fluorescence microscopy and image analysis was used to quantify retinal MalK content.

Results: Feeding mice HFDs containing lard or SFO for 24 wk significantly decreased the amount of MalK PTM in retinal tissue, when compared to low fat diets with either high or low sucrose. Feeding HSD had no significant effect on retinal MalK content compared SD fed controls. The decreases in malonylation caused by HFD feeding occurred in both the ganglion cell layer and the entire retina, and ranged from 30% to 41% relative to the SD fed group. Mice fed the lard-HFD for 16 weeks and then switched to any other diet (SD, HSD, oleate-HFD) for the final 8 weeks, exhibited normal MalK PTM.

Conclusions: The studies suggest that the retina alters its protein malonylation to adapt to nutrient conditions imposed by HFDs containing either highly saturated fat (lard) or monounsaturated fat (SFO). Future studies will examine how removal of saturated fat from the diet led to normal MalK levels and determine if loss of MalK represents a beneficial adaptation or a maladaptation that could contribute to the risk of developing DR.

CONTROL ID: 3547216

SUBMITTER (NAME ONLY): Joseph Park

TITLE: Individualized finite element (FE) models demonstrate stress concentration in optic disc and peripapillary tissue caused by variations in globe and orbital size during adduction tethering.

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Park, S. Jafari, J.L. Demer, Ophthalmology, Stein Eye Institute, UCLA, Los Angeles, California, UNITED STATES|J. Park, Bioengineering, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Primary open-angle glaucoma (POAG) with normal intraocular pressure (IOP) has been proposed to be caused by repetitive stress on the optic nerve (ON) when it becomes tethered during adduction, and is more common in East Asians than Caucasians. We hypothesized that variations in globe and orbital dimensions may influence stress concentration on the globe-optic nerve (ON) junction during adduction.

Methods: Surface coil magnetic resonance imaging was employed to collect axial images of the orbits of 22 normal controls (Male: 8, Female:14, 59.2 ± 13.4 yrs) and 23 POAG patients (Male: 7, Female:16, 63.7 ± 10.4 yrs) with IOP never exceeding 21mmHg. Globe equatorial diameter, axial length (AL), and orbital length (OL) from globe center to orbital apex were measured to specify individualized mesh models of the globe and ON. FE simulations were repeated performed in each of 45 individual cases using 6° additional adduction from an initial 26° adducted configuration employing identical average human tissue material properties and boundary conditions.

Results: The ratio of OL to AL ratio in subjects with POAG was 1.46 ± 0.20 (\pm SD) was significantly less than in controls at 1.59 ± 0.20 ($P=0.005$). FE simulations showed that stresses caused by adduction tethering were mostly concentrated at the temporal globe-ON junction near the retro-lamina region and peripapillary sclera encircling the optic disc. Subjects with POAG had 44.2 ± 6.0 kPa mean stress in the entire finite element model, significantly higher at 40.7 ± 5.2 kPa than normal subjects ($P=0.022$). Mean stress on the peripapillary ring was 34.0 ± 4.9 kPa for POAG, significantly greater than 30.6 ± 4.2 kPa for normal subjects ($P=0.008$). However, the mean stress on the optic disc was similar ($P=0.4$) for both POAG (15.3 ± 1.4 kPa) and controls (15.3 ± 1.7 kPa).

Conclusions: Subjects with POAG at normal IOP tend to have shorter orbits relative to globe axial lengths than healthy subjects. These morphological characteristics are predicted to cause higher stress on the globe-ON junction when ON tethers during adduction.

CONTROL ID: 3547221

SUBMITTER (NAME ONLY): Roxana Radu

TITLE: Membrane attack complex induces RPE cell death in Stargardt Disease

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Radu, N. Kady, M.B. Gorin, A. Matynia, J.G. Hu, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|R.A. Radu, N. Kady, M.B. Gorin, A. Matynia, J.G. Hu, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in the ABCA4 gene are responsible for recessive Stargardt (STGD1), a central blinding disease similar to AMD. STGD1 patients and Abca4^{-/-} mouse model exhibit deposition of bisretinoids in the retinal pigment epithelium (RPE) and photoreceptor degeneration. Bisretinoid-mediated complement activation was reported in cultured RPE cells and detected in the RPE of Abca4^{-/-} mice and STGD1 donor eye. Here, we used induced pluripotent stem cell (iPSC) derived RPE from a STGD1 patient to investigate the role of complement in disease pathogenesis.

Methods: STGD1 patient, with two ABCA4 mutations on different alleles: (1) c.3386G>T; p.Arg1129Leu and (2) c.[5461-10T>C;5603A>T]; p.[Thr1821Aspfs*6,Thr1821Vals*13;(Asn1868Ile)], and control (no ABCA4 mutations) fibroblasts were reprogrammed into iPSCs and differentiated to RPE cells using standard protocols. iPSC-RPE cells were grown on filters and analyzed at 3- and 12-mo by confocal and electron microscopy. Cell count and height were determined by morphometric analysis. Transepithelial resistance (TER) was measured to evaluate the RPE monolayer integrity. Immunohistochemistry was performed on the flatmount of iPSC-RPE cells with antibodies against ZO1, 4-hydroxynonenal (4HNE), complement negative regulators (CD46 and CD59), C3/C3b/iC3b, C3aR, and membrane attack complex (MAC).

Results: At 3-mo, control and STGD1 iPSC-RPE cells displayed normal morphology with silimar ZO1 staining, TER measurements, and cell count. Over time, STGD1 iPSC-RPE cells accumulated autofluorescence at ~1.2- and ~1.6-fold higher levels vs control at 3- and 12-mo respectively. 4HNE immunostaining was also enhanced in STGD1 RPE cells. While levels of C3aR and CD59 were similar, CD46 levels were reduced by half in the RPE of STGD1 vs control. In contrast, C3/C3b/iC3b and MAC levels were ~1.5-fold higher in the RPE of STGD1 vs control. At 12-mo, STGD1 RPE cells height and number were reduced by ~30% vs control. Changes in morphology correlated with ~80% reduction of TER in STGD1 vs control RPE, consistent with cell membranes disruption.

Conclusions: Using STGD1 patient iPSC-derived RPE cells, we provide evidence of complement dysregulation triggered by the buildup of autofluorescence material. Additionally, ongoing complement activation led to MAC-mediated cellular death in 12-mo cultured STGD1 iPSC-RPE cells. These findings strongly support a common inflammatory etiology of AMD and STGD1 maculopathy.

CONTROL ID: 3547224

SUBMITTER (NAME ONLY): Paul Knepper

TITLE: Microvascular permeability in geographic atrophy; on the role of PLVAP

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.A. Knepper, I. Bielskus, N. Pfahler, A. Kakouri, Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|P.A. Knepper, N.J. Volpe, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|A. Kakouri, M. Giovino, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Microvascular permeability is a fundamental property of blood vessels. The protein plasmalemma vesicle-associated protein (PLVAP) is a key structural protein in fenestrated capillaries, stomatal diaphragms in caveolae, and transendothelial channels. PLVAP assembles as heterodimers to form radial fibers in a spoke-like endothelial barrier. One theory for age-related macular degeneration (AMD) is the vascular theory in which fenestrated vessels in the choriocapillaris form ghost vessels leading to underperfusion of the overlying macula. The protein (PLVAP) is critical for the normal functioning of vascular fenestrations and plays a role in angiogenesis and vessel integrity. In this study, we measured platelet PLVAP protein content by western blot in AMD and healthy control subjects.

Methods: Whole blood was obtained from 12 AMD and 5 age-matched control subjects after IRB approval and informed consent. Platelet-rich plasma was isolated by centrifugation and lysed in lysis buffer. PLVAP protein content was analyzed under reducing conditions using standard western blot protocols and non-reducing conditions using blue-native gel electrophoresis. PLVAP was detected using a monoclonal antibody against PLVAP (Abcam, 1:1000) and a secondary polyclonal antibody (Cell Signaling, 1:1000) labeled with horseradish peroxidase using a GE ECL system and Coomassie blue staining. Relative quantification of PLVAP was performed by densitometry. Pre-advanced AMD, nascent GA, and advanced GA were defined as the presence of drusen $\geq 63 \mu\text{m}$ in width, hypofluorescent regions of macular atrophy greater than 0.015 mm^2 , and hypofluorescent regions of atrophy no greater than 0.015 mm^2 , respectively.

Results: Three PLVAP-positive bands were observed at apparent molecular weights of 70, 60, and 12 kDa. AMD subjects with both nascent and advanced GA had significantly higher levels of the 60 kDa band ($p=0.03$) and 12 kDa ($p=0.04$) compared with controls. Notably, under non-reducing conditions, subjects with GA had minimal heterodimer formation, indicating a possible defect in PLVAP assembly.

Conclusions: Platelet PLVAP expression is altered in GA under reducing and non-reducing conditions. Consequently, the function of fenestrated capillaries in the choriocapillaris in GA may be impaired, leading to defective microvascular permeability. Therefore, PLVAP may be a viable therapeutic target in GA.

CONTROL ID: 3547226

SUBMITTER (NAME ONLY): Jae Eun Lee

TITLE: Macular Thickness Fluctuation as Biomarker: Impact on Visual Acuity Following Anti-VEGF Therapy for Diabetic Macular Edema

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Lee, Baylor College of Medicine, Houston, Texas, UNITED STATES|H. Yu, S. Laswell, D.M. Brown, C.C. Wykoff, Retina Consultants of Texas, Houston, Texas, UNITED STATES|D.M. Brown, C.C. Wykoff, Blanton Eye Institute, Houston Methodist Hospital & Weill Cornell Medical College, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: While intravitreal anti-vascular endothelial growth factor (VEGF) therapy revolutionized the treatment of diabetic macular edema (DME), there remains a proportion of afflicted eyes that do not achieve optimal visual acuity (VA) outcomes. Previous studies have shown that the amount of fluctuation in macular thickness may be associated with worse VA outcomes in multiple exudative retinal diseases. The current study assessed this relationship among patients with DME undergoing prolonged anti-VEGF therapy.

Methods: Medical records were retrospectively reviewed for patients diagnosed with treatment naïve DME between January 2016 and August 2017. Eyes were included if they had an anti-VEGF injection ≤ 31 days of initial diagnosis, a follow up period ≥ 44 weeks, and ≥ 3 central subfield thickness (CST) measurements. Fluctuations in CST were determined by standard deviation (SD) of CST measurements across visits. Statistical analysis included Chi-squared test and one-way analysis of variance (ANOVA).

Results: 242 eyes from 170 subjects were included in the current study. Mean CST at baseline and final visit was 353.1 μm (95% CI, 341.3-364.8) and 285.6 μm (95% CI, 276-296), respectively; mean SD was 46.2 μm (95% CI, 39.9-52.4). Mean number of visits was 21.8 (range, 4-67) and mean length of follow up was 149 weeks (range, 51-230.3). 41.7% of eyes received laser treatment with a mean 17.2 anti-VEGF injections (95% CI, 15.9-18.5). Eyes were stratified into quartiles based on CST SD. From the first (lowest SD) to fourth (highest SD) quartile, final VA was 0.32 (20/40 Snellen equivalent), 0.34 (20/40), 0.43 (20/50), and 0.62 (20/80) logMAR ($p=0.0004$), respectively, with a mean 13.8, 17.1, 18.4, and 19.5 anti-VEGF injections ($p=0.01$). Pairwise comparisons showed quartile 1 received significantly fewer injections and quartile 4 demonstrated significantly worse final VA compared to other quartiles ($p<0.05$). There were no significant differences between quartiles in length of follow up, number of visits, or laser treatment status ($p>0.05$).

Conclusions: The current study demonstrated increased CST fluctuations resulted in worse VA outcomes, consistent with other studies involving exudative retinal diseases. Also, decreased CST fluctuations was associated with fewer anti-VEGF injections, while length of follow up, number of visits, and laser treatment status were not similarly associated.

CONTROL ID: 3547228

SUBMITTER (NAME ONLY): Isaac Freedman

TITLE: Perioperative outcomes of carotid endarterectomy for retinal artery occlusion versus cerebrovascular accident

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I.G. Freedman, J.C. Wang, Ophthalmology & Visual Sciences, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Isaac Freedman: Commercial Relationship: Code N (No Commercial Relationship) | Jay Wang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To compare perioperative outcomes in patients who undergo carotid endarterectomy (CEA) for retinal artery occlusion (RAO) versus for cerebrovascular accident (CVA) in the United States and to determine comparative predictors of 30-day perioperative outcomes.

Methods: A retrospective, multicenter nationwide study of the American College of Surgeons National Surgical Quality Improvement Program database in the eight-year period 2010-2017 of all patients with a diagnosis of RAO or CVA who underwent CEA. Patients were selected based on primary international classification of diseases-9 (2010-2015) or 10 (2015 or later) codes corresponding to RAO or CVA and had a primary procedural current procedural terminology code of CEA. Ideal caliper width 1:1 propensity score (PS) matching was performed on age and sex to yield balanced cohorts. Demographic characteristics, preoperative and intraoperative variables, length of stay (LOS), and 30-day adverse events (AEs) were recorded. Nonparametric hypothesis tests and uni- and multivariate linear and logistic regressions were constructed to determine independent predictors of prolonged LOS or AE.

Results: 52 (1.9%) underwent primary CEA for RAO and 2,757 (98.1%) for CVA. After PS-matching the cohorts were balanced on age ($p=1.0$) and sex ($p=1.0$). The median age in both groups was 72.5 years (IQR: 63-78.5 years) and both were 38.5% female. RAO patients were more likely to have a history of COPD (26.8% vs. 4.0%, $p=0.015$) but there was no significant difference between the two groups in any other demographic characteristics, preoperative, or intraoperative variables. The median hospital LOS was significantly longer in the CVA group (3 [IQR 1-6] vs. 6 [3-8], $p=0.005$). The most common AEs were pulmonary, myocardial infarction, bleed, and stroke. There was no significant difference in AEs between the two groups, though subsequent stroke was more common in the CVA group (3.8% vs 1.9%). When controlling for other variables, CVA (RR 3.0, 95% CI 1.4-4.7 days, $p<0.001$) and history of COPD (RR 2.8, 0.3-5.3, $p=0.030$) significantly predicted prolonged LOS.

Conclusions: In this comparative analysis of patients who received CEA for RAO vs. CVA, CVA and history of COPD were associated with significantly prolonged LOS. As other perioperative measures were similar between the groups, the prolonged LOS in the CVA group may reflect lengthier recovery from the CVA itself.

CONTROL ID: 3547230

SUBMITTER (NAME ONLY): Elliot Kirstein

TITLE: Early Feasibility Study for Substantial Equivalence Testing and Design Evaluation of the OcuFLOW-Composite Ocular Circulatory Analyzer (COCA) for Measuring and Monitoring Ocular Circulation to Guide Therapeutic Intervention and Prevent Glaucoma Blindness

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.M. Kirstein, Harper's Point Eye Associates, Cincinnati, Ohio, UNITED STATES|T. Kramer, R. DuBois, R. Grebe, M. Brink, OcuFLOW, Inc., Glen Arm, Maryland, UNITED STATES|R. Xian, Political Science, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|R. Xian, Annenberg School for Communication, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: In addition to intraocular pressure (IOP), measurement of vascular risk factors is now key in the management of glaucoma. The OcuFLOW-composite ocular circulatory analyzer (COCA) is a reinvented pneumatonometer that measures IOP, pulse amplitude (PA), pulsatile ocular blood flow (POBF), ocular perfusion pressure (OPP) and an autoregulation index (AI). It is the only device that measures global choroidal blood flow, equivalent to 90% of ocular blood flow. The purpose of this study is to assess the safety of measuring IOP, pulse amplitude (PA), pulsatile ocular blood flow (POBF), and ocular perfusion pressure (OPP). A secondary purpose is completion of early feasibility clinical studies comparing the investigational OcuFLOW-COCATM (OcuFLOW) to the Goldmann applanation tonometer (GAT), the CATSTM tonometer prism (CATS), and the Dynamic Contour TonometerTM (DCT) for the measurement of IOP, devices that have prior FDA 510(k) clearance.

Methods: This study was a prospective, open-label study. Human IRB approval was completed by Sterling IRB, Inc. Eight healthy subjects underwent informed consent and review of inclusion and exclusion criteria. Brachial blood pressure was measured and recorded in the software. After instillation of topical proparacaine anesthesia, multiple ocular circulation parameters were measured in each subject, as defined by the known device applications.

Results: The OcuFLOW-COCATM was successfully able to measure the IOP, PA, POBF and calculate the OPP. The range of IOP paired differences for all four devices was between -5 and 4. The IOP paired difference range for the OcuFLOW was smallest of the four test devices at 5.2, compared to 7 (GAT), 8 (CATS), and 6.4 (DCT).

Conclusions: The OcuFLOW-COCATM was successfully able to safely and efficaciously measure the IOP, PA, POBF and OPP. For IOP measurement, the OcuFLOW is substantially equivalent to the GAT, the CATS, and the DCT, and appears to be more accurate for measuring IOP, especially. The early feasibility study design limits the data set. Further study is needed.

CONTROL ID: 3547234

SUBMITTER (NAME ONLY): Chi Zhang

TITLE: Dexamethasone mediates MYOC expression in primary human trabecular meshwork cells modulated by small-molecules Wnt inhibitors

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Zhang, J.J. Zheng, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|C. Zhang, J.J. Zheng, Ophthalmology, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Steroid treatments including the use of dexamethasone (Dex) has been shown to increase the intraocular pressure (IOP) and the risk of ocular hypertension, which can cause the steroid-induced glaucoma. It has been reported that Dex treatment can lead to irregular TM structure and potentially reduce outward flow of intraocular fluid through altering Wnt signaling. To further elucidate the role of Wnt signaling in the Dex-induced glaucomatous phenotype, we studied the mRNA expression patterns across MYOC, AXIN2, and extracellular matrix (ECM) genes. Furthermore, we used novel Wnt small molecule regulators to investigate whether these modulators would affect Dex-mediated phenotype on primary human TM cells.

Methods: Primary human TM cells cultured from corneal-scleral rims were treated every day for 5-days or 7-days, with 100 nM Dex, DMSO vehicle, or Dex in combination with Wnt signaling regulators. RNA was isolated and followed by quantitative PCR analysis to measure MYOC, AXIN2, and ECM genes expression.

Results: Dex-treated TM cells showed increased levels of MYOC, AXIN2 and ECM gene expression compared to their vehicle counterparts. Combination of the Wnt inhibitors with Dex abolished the effects of Dex on the TM cells, whereas Wnt activators maintained the Dex-induced phenotype. Furthermore, Wnt modulators has distinct effects on different passages of the primary TM cells.

Conclusions: Dex-induced phenotypic changes in primary human TM cells are consistent with previously reported phenotypes contributing to ocular hypertension, therefore leading to glaucoma progression. Regulating the activity of Wnt alleviates these Dex-mediated effects indicates that Dex-induced glaucomatous TM cell activities is associated with aberrant Wnt signaling. The different effects among Wnt modulators exhibited on the TM cells suggests that proper balanced Wnt signaling is required to maintain the homeostasis of the TM tissue.

CONTROL ID: 3547235

SUBMITTER (NAME ONLY): Bilal Haj Najeeb

TITLE: The RAP study, Report 4: Discoloration of the macular region in patients with macular neovascularization type 3

SESSION TITLE: AMD: clinical research - biomarkers and outcomes

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Haj Najeeb, G. Deak, U. Schmidt-Erfurth, B. Gerendas, Eye Department, Medical University of Vienna, Vienna, Vienna, AUSTRIA]

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ABSTRACT BODY:

Purpose: To explore the prevalence and pattern of distribution of macular hemorrhage and exudate in macular neovascularization type 3 (MNV3), previously known as retinal angiomatous proliferation, and to find out whether they can be valuable diagnostic markers for MNV3 in patients with neovascular age-related macular degeneration.

Methods: 83 eyes of 83 consecutive treatment naïve patients with stage 3 MNV3 were enrolled. The diagnosis was based on fluorescein angiography (FA) and optical coherence tomography (OCT). Sub- and intraretinal hemorrhage and dense exudates were evaluated on color fundus photography. FA images and OCT scans were used to identify the axial location of the hemorrhage. 83 patients with MNV1 and 83 with MNV2 were included as two control groups.

Results: In the MNV3 group 62 (75%) eyes had intraretinal hemorrhage and 52 (63%) had dense exudates. 73 (88%) eyes had intraretinal hemorrhage and/or dense exudates. 41 (49%) had both pathologies. The intraretinal hemorrhage was flame shaped over the lesion and punctate or semi-punctate further away from it and directed to the fovea. No subretinal hemorrhage was noticed. In the MNV1 and MNV2 groups 11 (13%) and 24 (29%) eyes had subretinal hemorrhage or dense exudates, respectively. No intraretinal hemorrhage was seen in the two control groups. The incidence of exudates and hemorrhage (irrespective of its location) was greater in MNV3 than in MNV1 or 2 ($p < 0.0001$).

Conclusions: The existence and pattern of distribution of intraretinal hemorrhage is pathognomonic of MNV3. It makes (alone or with dense exudates) the diagnose MNV3 possible using fundoscopy or color fundus photo and without further diagnostic expenditure.

CONTROL ID: 3547241

SUBMITTER (NAME ONLY): Zizhu Tan

TITLE: Depletion of optic nerve microglia does not improve visual function in experimental glaucoma

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Tan, Y. Guo, M. Shrestha, M.S. Gregory-Ksander, T.C. Jakobs, Ophthalmology, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Z. Tan, Ophthalmology, Xi'an Jiaotong University, Xi'an, Shaanxi, CHINA|

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ABSTRACT BODY:

Purpose: Microglia become reactive in response to pathological stimuli, such as an increase in IOP. It has been reported that depending on the nature and the duration of the insult activated microglia in the brain can instruct neighboring astrocytes to assume a predominantly neuroprotective or a predominantly neurotoxic phenotype (Liddelow et al, 2017). We tested whether depletion of microglia with the CSF1R inhibitor PLX5622 has an effect on the visual function or ganglion cell loss during experimental glaucoma. We also compared the gene expression profile of isolated astrocytes from microglia-depleted and control nerves over a 4-weeks course of IOP elevation.

Methods: Two groups of C57BL/6 mice were placed on microglia depletion diet (n=32) or control diet (n=26) for 3 weeks. Magnetic microbeads were injected into the anterior chamber of the right eye. Visual function was measured by pattern ERG and observation of the optomotor reflex. Retinal ganglion cells and axons were counted. In addition, a cohort of mice received either depletion or control diet and microbead injection. At 7 days, 14 days, 21 days, and 28 days after injection the optic nerve heads were dissociated and individual astrocytes from were collected under microscopic control. The gene expression profile was assayed by quantitative PCR.

Results: Treatment with PLX5622 led to complete depletion of microglia from the retina over the time course of the study. However, there was a small population of cells with microglial morphology that remained in the myelinated portion of the optic nerve even after 7 weeks total on the PLX5622 diet. IOP elevation led to a significant decrease of visual acuity (0.296 ± 0.072 versus 0.42 ± 0.017 cycles/degree in the control group, $p < 0.001$), whereas saline injection had no effect on the IOP or the visual acuity. Pattern ERG amplitude was decreased from 21.46 ± 4.9 uV at baseline to 14.33 ± 4.6 uV after microbead injection ($p < 0.001$). However, there was no significant difference between the microglia depleted and the control groups. Genes associated with the putative neuroprotective astrocyte phenotype were up-regulated under control conditions. In astrocytes from microglia-depleted nerves this up-regulation was attenuated.

Conclusions: Our preliminary results suggest that microglia depletion does not appear to be a promising strategy to improve visual function in experimental glaucoma.

CONTROL ID: 3547244

SUBMITTER (NAME ONLY): Ann Murchison

TITLE: Feasibility of Ophthalmic telemedicine Consultation in Urgent Settings (FOCUS)

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Murchison, Emergency Medicine, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|J.R. Bilyk, Oculoplastic and Orbital Surgery, Wills Eye Hospital, Philadelphia, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ann Murchison: Commercial Relationship: Code N (No Commercial Relationship) | Jurij Bilyk: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Ophthalmologist are not always available for on-site consultation in emergency departments. We performed a prospective, double-masked pilot study to determine the feasibility for an ophthalmologist to provide triage consultation virtually.

Methods: This study used a convenience sample of adult patients from an eye emergency department. Ophthalmic telemedicine consultation was provided by an ophthalmology attending physician (OAP) using a synchronous telehealth interface and in-person consultation was provided by second OAP. The remainder of the visit followed usual care. The primary outcomes were feasibility and urgency of recommended in-person ophthalmic examination. Feasibility was measured as the ability to enroll patients and transmit the necessary audiovisual information. Urgency of recommended full ophthalmic examination was collected from both the in-person and virtual ophthalmic triage providers. The secondary outcome was time to perform ophthalmic consultation. An exploratory outcome was concordance of triage-based diagnoses between the in-person and telehealth OAPs. Descriptive statistics were used for evaluation.

Results: This pilot study enrolled 31 of 33 (93.9%) patients. The majority (74.2%) were female and the median age was 57 years (range 24-86; mean 54.2). The majority of patients identified as African American (48.4%) followed by Caucasian (45.2%). There were no dropped calls or audiovisual problems reported with the telemedicine interface. The recommended urgency of in-person full examination between the in-person and telemedicine consultation was concordant 90.3% of the time. The duration range of the consultation was 1.5-6 minutes via telemedicine and 2-7 minutes in person with a mean of 2.5 and 2.7 minutes, respectively. The exploratory outcome of diagnostic concordance was 93.5%.

Conclusions: Telemedicine emergency ophthalmic consultation appear to be feasible, with good patient acceptance and ability to obtain necessary audio and visual data. The duration of the visits was similar for in person and telemedicine consultations, supporting the potential feasibility. The diagnostic concordance was high between both the telemedicine and in person ophthalmic consultation compared to the full ophthalmic evaluation. More data on this approach in general emergency room settings would be useful to aid in expediting urgent ophthalmic care and make ophthalmic consultation more widely available.

CONTROL ID: 3547246

SUBMITTER (NAME ONLY): Scott Walter

TITLE: Real-world efficacy and safety of brolucizumab

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.D. Walter, Retina Consultants, P.C., Hartford, Connecticut, UNITED STATES|S.D. Walter, N.J. Saba, Surgery, University of Connecticut School of Medicine, Farmington, Connecticut, UNITED STATES|N.J. Saba, Medicine, Eastern Connecticut Health Network, Manchester, Connecticut, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Scott Walter: Commercial Relationship(s);Novartis:Code C (Consultant);Genentech:Code C (Consultant);Castle Biosciences:Code C (Consultant);Spark Therapeutics:Code C (Consultant);Allergan:Code C (Consultant) | Nicholas Saba: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Brolucizumab (Beovu) is a novel anti-vascular endothelial growth factor (VEGF) drug approved for the treatment of neovascular age-related macular degeneration (NVAMD). In this post-marketing surveillance study, we evaluated the efficacy and safety of brolucizumab in our practice during the initial 7.5 months following its commercial release.

Methods: Retrospective consecutive case series of 544 patients with NVAMD who were treated with intravitreal injections (IVI) of brolucizumab in a private retina practice between 10/1/2019 and 5/15/2020. The study population included NVAMD patients who were treatment-naïve and others who were switched from an alternate anti-VEGF therapy. Visual acuity (VA) was compared before initiation of brolucizumab therapy and at the end of the study period. Anatomic outcomes were assessed with spectral-domain optical coherence tomography and included central subfield thickness (CST), macular volume (MV), presence of intraretinal fluid (IRF), presence of subretinal fluid (SRF), and presence of serous pigment epithelial detachment (sPED) on foveal line scans. The cumulative incidence of drug-related adverse effects during the study period was also reported.

Results: 544 patients received a total of 1438 brolucizumab IVIs during the study period. A statistically significant improvement in VA was observed in treatment-naïve eyes (+3.7 letters, $p=0.038$) but not in eyes switched from another anti-VEGF agent (-0.5 letters, $p=0.41$). For both groups of patients, there were significant reductions in CST (-47.8 μ m), MV (-0.40mm³), presence of IRF (-18.5%), presence of SRF (-28.6%), and presence of sPED (-7.3%; all $p<0.001$). Drug-related adverse events occurred in 26 patients (4.8%), including intraocular inflammation (25), retinal vasculitis (3), retinal artery occlusion (1), and urticarial rash (1) after an average of 2.0 IVIs.

Conclusions: Brolucizumab proved to be a potent drying agent in both treatment-naïve and previously anti-VEGF treated eyes. However, no VA improvement was observed when eyes were switched to brolucizumab from an alternate anti-VEGF agent. The incidence of brolucizumab-related inflammatory events observed in this post-marketing surveillance study corroborates a recent reanalysis of clinical trial data by the Safety Review Committee.

CONTROL ID: 3547248

SUBMITTER (NAME ONLY): Luis Rodríguez

TITLE: Accelerated corneal cross-linking in pediatric patients with keratoconus from the northeast of Mexico: A 3-year follow-up

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Rodríguez, V. Holguin, D. Loya, Ophthalmology, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO]

Commercial Relationships Disclosure (Abstract): Luis Rodríguez: Commercial Relationship: Code N (No Commercial Relationship) | Victoria Holguin: Commercial Relationship: Code N (No Commercial Relationship) | Denise Loya: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the 3 year follow-up clinical characteristics, visual and topographic outcomes of pulsed-light accelerated crosslinking (A-CXL) protocol in a northeastern Mexican pediatric population with progressive keratoconus

Methods: Retrospective case series study of pediatric patients with keratoconus in whom crosslinking was performed between January 2016 and December 2020. Inclusion criteria comprised patients aged 18 or under with progressive keratoconus treated with epi-off pulsed-light A-CXL protocol (30mW/cm² x 8 min, total energy dose of 7.2J/cm²). Medical history, BCVA, slit lamp examination, endothelial cell count (ECC), spherical equivalent (SE) and Scheimpflug corneal tomography previous and after crosslinking were analyzed. Statistical analysis was performed using the paired t-test with the STATA software

Results: A total of 28 eyes of 17 patients, 15 (88.2%) males and 2 (11.8%) females were included. Mean follow-up time was 646±411 days since the diagnosis of keratoconus. Mean Body Mass Index was 25.7± 9.5 (overweight). Allergic conjunctivitis was present in 65% of patients, and 47% of patients reported rubbing their eyes. Mean age at surgery was 13.8±2.72 years (range, 9-18). Mean BCVA was 0.64±0.59 logMAR at baseline and 0.34±0.32 logMAR at the last follow up (p=0.0019). Baseline SE was -3.88 and -4.12 at the last follow up, refractive cylinder values were -3.72 at baseline and -4.38 at the last follow up. Mean baseline K1, K2, and Km values were 47.54 D, 54.97 D, and 50.71 D, respectively; at the last time follow up these values decreased to 47.37 D (p=0.62), 54.56 D (p=0.42) and 50.65 D (p=0.58) respectively. Preoperative central and thinnest pachymetry by Pentacam were 475.48 um and 460.77 um respectively, compared to post-operative values of 470.00 um (p=0.90) and 456.63 um (p=0.80). The most common topographic pattern was inferotemporal steepening 32.1%, ECC decreased from a mean preoperative value of 2903 cells to 2886 cells (p=0.81). Two eyes developed infectious keratitis after the procedure, and 1 eye had hydrops after crosslinking

Conclusions: There seems to be an association between allergic conjunctivitis, overweight patients and keratoconus progression in these patients. A-CXL seems to be safe and effective to halt progression in this population with improvement of BCVA. Further follow up is necessary to measure long-term effects

CONTROL ID: 3547250

SUBMITTER (NAME ONLY): Ujjaldeep Jaggi

TITLE: Effect of further shifting the M2-like macrophage responses by cellular adjuvant on primary and latent HSV-1 infection

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Jaggi, H. Matundan, J. Yu, H. Ghiasi, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ujjaldeep Jaggi: Commercial Relationship: Code N (No Commercial Relationship) | Harry Matundan: Commercial Relationship: Code N (No Commercial Relationship) | Jack Yu: Commercial Relationship: Code N (No Commercial Relationship) | Homayon Ghiasi: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Macrophages are one of the dominant infiltrates in the corneas of ocularly infected mice. Previously, we demonstrated that M2 macrophages have a protective effect on ocular virus, eye disease, latency, and reactivation than M1 macrophages using HSV-1 infected WT mice. To further explore the role of M1 and M2 macrophages on the HSV-1 responses, we used M2^{-/-} (GATA3 deleted) and M2-OE (GATA3 overexpressed) mice and infected them with HSV-IL4 (to further push toward M2) or HSV-IFNg (to further push toward M1).

Methods: M2^{-/-} and M2-OE mice were ocularly infected with 2×10^5 pfu/eye of HSV-1 recombinant viruses expressing IL4 or IFNg or parental control virus. Following ocular infection with each virus, primary virus replication in the eye, viral and cellular expressions in the cornea and trigeminal ganglia (TG) on various times post-infection (PI) and survival, corneal scarring (CS) and latency-reactivation on day 28 PI were determined.

Results: Primary infection in the eye was significantly reduced in HSV-IL4 infected mice on day 3 PI compared to mice infected with either HSV-IFNg or control viruses. CS was higher in HSV-IFNg infected mice compared with HSV-IL4 or control viruses. Latent infection in TG was reduced in both HSV-IL4 and HSV-IFNg groups compared with the parental virus, while the level of latency in HSV-IL4 infected mice was significantly lower than HSV-IFNg infected mice. In addition, reactivation was also lower in HSV-IL4 infected mice as compared with HSV-IFNg and control infected mice.

Conclusions: Our findings demonstrate that: 1) Both HSV-IL4 and HSV-IFNg viruses shifted macrophage polarization toward M2 and M1, respectively; and 2) HSV-IL4 was more effective in providing protection against both primary and latent infection and reactivation compared to HSV-IFNg or parental virus. Our results suggest that inclusion of cellular factor(s) as part of a vaccination regiment to coax responses of macrophages toward M2 polarization, as compared to the M1 polarization, may further improve vaccine efficacy against ocular HSV-1 replication and latency-reactivation in the ocularly infected mice.

CONTROL ID: 3547253

SUBMITTER (NAME ONLY): Jesus Guerrero

TITLE: Infectious keratitis following penetrating keratoplasty: clinical and visual outcomes

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Guerrero, F. Anaya Barragán, A. Ramirez Miranda, A. Navas, E.O. Graue-Hernandez, Cornea, external diseases and refractive surgery, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|H. Kim, Retina and vitreous, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|A. Jiménez Corona, Ocular epidemiology, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

Commercial Relationships Disclosure (Abstract): Jesus Guerrero: Commercial Relationship: Code N (No Commercial Relationship) | Hae Jin Kim: Commercial Relationship: Code N (No Commercial Relationship) | Fabiola Anaya Barragán: Commercial Relationship: Code N (No Commercial Relationship) | Aida Jiménez Corona: Commercial Relationship: Code N (No Commercial Relationship) | Arturo Ramirez Miranda: Commercial Relationship: Code N (No Commercial Relationship) | Alejandro Navas: Commercial Relationship: Code N (No Commercial Relationship) | Enrique Graue-Hernandez: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe clinical features of infectious keratitis following keratoplasty

Methods: A 17-year (2001-2018) retrospective review of clinical records. Analyzed variables included: microbiology, previous ocular surgeries and medications, history of contact lens use, ocular surface disease, and lid abnormalities. Also treatment characteristics, indications for surgery and clinical outcomes were noted. Descriptive statistics, means, and SD were used for continuous variables; percentages were used to describe categorical variables. P, 0.05 was regarded as evidence of significance. All analyses were done with STATA v.10 software.

Results: A total of 105 eyes of 105 patients were included in this study. Mean age was 52.64 years, 48% were female. Mean time to infection after PKP was 20.11 (range 0.5 - 114 months). The mean number of previous grafts was 1.24 (range 1-7). Of the 105 cases 16 patients (15.24%) had 2 or more PKPs, and 89 patients (84.76%) had just one graft. 23 patients (21.90%) had clinical signs of blepharitis and 3 (2.83%) had palpebral alterations. 13 patients (12.50%) had glaucoma drainage device and just 10 patients (9.52%) were contact lens users.

Indications for corneal transplantation were bacterial keratitis in the 20% (n = 21) and trauma in 15.23% (n = 16). The corneal graft had failed in: 52 patients (49.52%), clear graft in 37 patients (35.23%) and 14 patients (14.7%) had rejection episode at the time of infection. Of those grafts that were clear only 19 cases remained clear (51.35%). 76 patients (72.38%) had sutures at the time of the episode, and of these, 25% the infection was judged to be related to sutures. Gram positive organism were responsible for 42% of the cases, gram negatives 30% , Herpetic 20% and fungi 8%. The most common gram+ bacteria was Staphylococcus epidermidis in 17 cases (16.19%) and the most common gram- was pseudomonas aeruginosa in 11 cases (10.47%).

Conclusions: Infectious keratitis following PKP is an important cause of graft failure, specifically bacterial. Patients with PKP require close monitoring to identify risk factors for developing infectious keratitis and posterior failure of the graft.

CONTROL ID: 3547254

SUBMITTER (NAME ONLY): Nagozim Mathieson

TITLE: The role of Corneal Nerves in Bacterial Keratitis

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.O. Mathieson, School of Medicine, University of Nottingham Faculty of Medicine and Health Sciences, Nottingham, Nottingham, UNITED KINGDOM|A. Elsahn, University of Nottingham, Nottingham, Nottinghamshire, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Infectious bacterial keratitis and infectious crystalline keratopathy (ICK) are both serious and visually threatening ocular infections. We hypothesise corneal nerves, and their derivatives, are important in the pathogenesis of both bacterial keratitis and ICK. We performed a systematic review into the role of corneal nerves during infectious bacterial keratitis and ICK to highlight areas of interest, or possible future research, for the development of new and improved treatment regimens for infectious bacterial keratitis and ICK.

Methods: A systematic literature search of the PubMed database was performed, identifying 64 articles relating to the role of corneal nerves in bacterial keratitis or ICK. Articles were screened and selected, leaving a total of 23 papers included for review.

Results: The results of our study detail the alterations of nerve structure during infection, demonstrate the influence of corneal nerves on bacterial keratitis, and suggest the consequences of the lack of nerves in ICK. Neurochemistry was shown to have a distinctive influence on inflammation, chemotaxis of inflammatory cells, and resolution of infection. In addition to this, MicroRNA and tear cytokines were associated with corneal nerves, their structural changes, and disease response. Corneal nerves and their neurochemistry also altered the corneal healing response during infection.

Conclusions: Corneal nerves are imperative in the immune response towards infectious bacterial keratitis. Corneal nerves influence and coordinate a spectrum of host responses to infection, including cytokine production, immunomodulation, and corneal healing. Therapeutic agents targeting corneal nerves and ocular neurochemistry should be studied and considered as possible treatments for the infection and recovery of infectious bacterial keratitis. More research into physiological mechanisms is also needed to improve our understanding of corneal nerves during infection.

CONTROL ID: 3547255

SUBMITTER (NAME ONLY): Yuzuru Sasamoto

TITLE: Regulation of SARS-CoV2 viral entry-related proteins in human ocular surface epithelium

SESSION TITLE: Corneal Stromal Repair and Corneal Biology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Sasamoto, C. Lee, G. Martin, N. Frank, Division of Genetics, Brigham and Women's Hospital, Boston, Massachusetts, UNITED STATES|Y. Sasamoto, C. Lee, G. Martin, M.H. Frank, Transplant Research Program, Boston Children's Hospital, Boston, Massachusetts, UNITED STATES|M. Yoshihara, Biosciences and Nutrition, Karolinska Institutet, Stockholm, Stockholm, SWEDEN|B. Ksander, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|M.H. Frank, N. Frank, Harvard Stem Cell Institute, Harvard University, Cambridge, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coronavirus disease 2019 (COVID-19) is caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). While the ocular surface is considered one of the major SARS-CoV2 transmission routes, SARS-CoV2 specific tropism in ocular epithelial cells is not fully understood. In the current study, we evaluated the expression of two SARS-CoV2 viral entry proteins, ACE2 and TMPRSS2, in human ocular epithelial cells. Additionally, we investigated the role of an eye-specific transcription factor PAX6 in regulating the expression of ACE2 and TMPRSS2.

Methods: Human donor corneas were obtained from the Saving Sight eye bank, Kansas City, MO. Flow cytometry was performed to detect ACE2 and TMPRSS2 in ABCB5-positive LSCs and ABCB5-negative limbal epithelial cells. RNAseq data of conjunctival swab samples were obtained from GSE135455 Gene Expression Omnibus datasets, and Spearman's rank correlation coefficients between PAX6, ACE2 and TMPRSS2 were calculated using R version 4.0.3. RNAseq analyses of PAX6 overexpressing oral mucosal epithelial cells were obtained from the DNA Data Bank of Japan Sequence Read Archive (DRA002960). PAX6 knockdown (KD) was performed in cultured immortalized conjunctival epithelial cells using five distinct siRNAs. PAX6, ACE2, and TMPRSS2 expression was analyzed by qRT-PCR and Western blotting.

Results: Flow cytometry analyses revealed enhanced expression of ACE2 and TMPRSS2 in PAX6 low-expressing ABCB5-positive LSCs compared to PAX6 high-expressing ABCB5-negative limbal epithelial cells. Intriguingly, TMPRSS2 mRNA expression negatively correlated with PAX6 in conjunctival swab samples ($R=-0.48$, $p<0.0001$). Mechanistically, PAX6 overexpression in oral mucosal epithelial cells decreased TMPRSS2 mRNA levels by 76.8%, while PAX6 KD in immortalized conjunctival epithelial cells resulted in induction of TMPRSS2 RNA and protein expression suggesting a possible functional role of PAX6 in regulating TMPRSS2.

Conclusions: High expression of ACE2 and TMPRSS2 in LSCs raises the possibility of specific COVID-19 cellular tropism to this cell population. Based on the here reported novel role of PAX6 as a negative regulator of TMPRSS2 expression, lower levels of PAX6 might contribute to the induction of TMPRSS2 in LSCs. Our study points to the importance of COVID-19 testing of donor corneas before clinical transplantation to patients with limbal stem cell deficiency.

CONTROL ID: 3547258

SUBMITTER (NAME ONLY): Marie Elise Torm

TITLE: Selective transparency of perifoveolar white ring in Niemann-Pick disease on adaptive optics fundus photography

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.W. Torm, C. Eckmann-Hansen, M. Larsen, Department of Ophthalmology, Rigshospitalet, Copenhagen, DENMARK|M.W. Torm, C. Eckmann-Hansen, F. Skovby, M. Larsen, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, DENMARK|F. Skovby, Section for Clinical Genetics, Department of Pediatrics, Zealand University Hospital, Roskilde, DENMARK|

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ABSTRACT BODY:

Purpose: To describe fundus optical imaging and vision characteristics in a patient with Niemann-Pick disease.

Methods: Retrospective chart review of the case of a young adult male who was incidentally found, in relation to a spectacle prescription consultation, to have a bilateral white perifoveolar ring in both eyes. He was subsequently found to have homozygosity for a pathogenic missense variant in SMPD1 and diagnosed with Niemann-Pick disease, a sphingomyelin lysosomal neural storage disease.

Results: Visual acuity was 1.0/1.0 in both eyes with correction for myopia -1.0/-0.25 diopters. The patient had no subjective pericentral scotoma. Intraocular pressure was 12 mmHg, and photopic microperimetry was normal in both eyes. Color fundus photography was normal except for the presence of a white ring of inner retinal hyperreflectivity encircling the foveola in both eyes. Optical coherence tomography showed a slight signal reduction of the retina behind the ring, but otherwise the retina and choroid were normal. On infrared scanning laser ophthalmoscopy, the white material was invisible and entirely transparent. The ring was also transparent on adaptive optics fundus photography in 850 nm illumination (rtx1, Imagine Eyes, Orsay, France), but when the cone photoreceptors on either side of the ring were in focus, the photoreceptors behind the ring were out of focus, and vice versa.

Conclusions: The sphingomyelin in the perifoveolar inner layers of the retina that obstructs the imaging of the deeper layers of the retina in visible light is transparent in infrared, but it shifts the focal plane of the rtx1 adaptive optics camera sufficiently to require an adjustment of its focal plane, possibly because the material increases the refractive index of the nerve fiber layer in the inner retina.

CONTROL ID: 3547262

SUBMITTER (NAME ONLY): Saidas Nair

TITLE: Retinal compensatory mechanism involved in ocular axial growth and refractive development

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Nair, S. Koli, P. Roy, C. Labelle-Dumais, Ophthalmology, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in retinal secreted serine protease PRSS56 and transmembrane glycoprotein MFRP, a factor predominantly expressed in the retinal pigment epithelium (RPE) constitute major causes of nanophthalmos, a condition characterized by severe reduction in ocular axial length/extreme hyperopia. Interestingly, common variants of these genes have been implicated in myopia, a condition associated with ocular axial elongation. In fact, mice with loss of function mutation in PRSS56 or MFRP exhibit a reduction in ocular axial length. We found that Adamts19 expression is significantly upregulated in the retina of mice lacking either Prss56 or Mfrp. Here, we test the hypothesis that retinal Adamts19 upregulation compensates for lack of PRSS56 or MFRP in supporting ocular axial growth. Additionally, we test the requirement of Prss56 or Mfrp in supporting excessive ocular elongation caused by a null mutation in the gene coding for Interphotoreceptor retinoid-binding protein (IRBP).

Methods: We crossed Prss56 or Mfrp mutant mice with mice deficient in Adamts19 to determine the effect of Adamts19 inactivation on ocular size reduction caused by loss of Prss56 or Mfrp function. In parallel, Prss56 and Mfrp mutant mice were crossed to Irbp deficient mice. A detailed ocular biometric ocular assessment was conducted on the progeny of various genotypes using the SD-OCT.

Results: Ocular axial length and vitreous chamber depth (VCD) exhibited a significantly greater reduction in double mutants (Prss56^{-/-};Adamts19^{-/-} or Mfrp^{-/-};Adamts19^{-/-}) as compared to respective Prss56 or Mfrp single mutants. Overall, we demonstrate that while ADAMTS19 is not required for ocular growth during normal development, its inactivation exacerbates ocular axial length reduction in Prss56 and Mfrp mutant mice. Furthermore, we demonstrate that inactivation of either Prss56 or Mfrp prevented ocular axial elongation in Irbp mutant mice (Irbp^{-/-};Prss56^{-/-} and Irbp^{-/-};Mfrp^{-/-}, respectively). Thus, both PRSS56 and MFRP are necessary for supporting excessive ocular elongation due to a null mutation in Irbp.

Conclusions: We identified ADAMTS19 as a novel factor involved in ocular size regulation and demonstrate that the retinal Adamts19 upregulation is part of an adaptive response to overcome impaired ocular growth. Furthermore, our findings support a role for molecular crosstalk between the retina and RPE involved in refractive development.

CONTROL ID: 3547263

SUBMITTER (NAME ONLY): Jacqueline Coblentz

TITLE: Ocular findings in patients undergoing cancer treatment

SESSION TITLE: Advances in intra and extra ocular pathologies

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Coblentz, C. Mastromonaco, S. Bergeron, G. Nassrallah, A.B. Dias, A.S. Dias, M.N. Burnier, McGill University Health Centre, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Cancer is a major public health problem in North America and many other parts of the world. Cancer care has greatly improved in the last few decades, as evidenced by a 22% decline in the overall cancer-related death rate in the United States since 1991, translating to more than 1.7 million deaths averted through 2012. Our goal is to perform complete clinical ophthalmologic exam in patients receiving treatment (radiation, chemotherapy, or combinations) in order to assess adverse ocular events.

Methods: This study was conducted at the McGill University Health Centre. Necessary approval by the hospital ethics regulatory board was obtained prior to recruitment of patients and commencement of the study. The details of the study were explained to patients prior to securing informed consent. Inclusion criteria: all patients receiving any modality of treatment for any type of cancer, with or without ocular complaints. Exclusion criteria: inability to or difficulty in visiting the eye clinic for subsequent follow-ups. A thorough ophthalmologic examination, including measure of visual acuity, slit lamp biomicroscopy, intraocular pressure measurement, dilated fundus examination, and OCT of both anterior and posterior segments were performed. Data gathered from the initial visit served as baseline for the patient's symptoms and health status of the patient's eye, as well as type of cancer and treatment modality.

Results: We analyzed data for 118 patients with cancer diagnosis. Median age was 67 years old (29-93 years old). Regarding gender, 73 (61.86%) were female and 45 (38.14%) were male. Among all patients, 51 (43.22%) had breast cancer, 29 (24.58%) had lung cancer, 21 (17.80%) had hematological cancer and 17 (14.41%) had gastrointestinal cancer. Eighty-two patients (69.49%) received chemotherapy as main treatment, whereas 36 (30.51%) received radiation therapy. We identified 69 patients (58.47%) with alterations in the ocular examination, which consisted of dry eyes in 41 patients (34.75%) and cataracts in 28 patients (23.73%).

Conclusions: Cancer treatment may lead to ocular signs and symptoms including affecting visual acuity. Early recognition of these side effects is important to minimize ocular manifestations and to improve quality of life throughout the treatment. Specific associations between ocular findings and a particular cancer treatment need yet to be determined.

CONTROL ID: 3547264

SUBMITTER (NAME ONLY): Borna Sarker

TITLE: Fibrinogen in Microglia-Mediated Inflammation in Diabetic Retinopathy

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Sarker, S.M. Cardona, D. Vanegas, K. Church, A. Cardona, Biology, The University of Texas at San Antonio College of Sciences, San Antonio, Texas, UNITED STATES|A.S. Mendiola, Gladstone Institute of Neurological Disease, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Microglia-mediated inflammation plays a significant role in neuronal and vascular damage in diabetic retinopathy (DR), but the mechanism linking inflammation, neurodegeneration, and impaired vascular integrity is still unclear. Our previous studies from diabetic mouse models exhibiting systemic inflammation showed that fractalkine (FKN), a neuronal-derived chemokine, and its microglial receptor, CX3CR1, exert neuroprotective roles in the retina. Our main goal is to elucidate the role of fibrinogen in CX3CR1-mediated inflammation during DR. We hypothesize that aberrant CX3CR1 signaling and fibrinogen-mediated microglial activation leads to inflammation and neuronal loss, followed by blood-retinal barrier damage, which can be ameliorated by reducing fibrinogen levels. We also hypothesize that DR pathology in human retinas mirrors observations from mouse models.

Methods: To analyze DR pathology hallmarks, we used a murine model of diabetes and obtained post-mortem human retinas from nondiabetic and diabetic patients. To characterize retinal pathology, microglial number and morphology, vascular damage, and fibrinogen extravasation were evaluated by immunohistochemistry. To determine effects of reducing fibrinogen in diabetic mice, the defibrinogenating agent ancrod was administered, after which retinal pathology and visual acuity were assessed.

Results: Histopathological analyses revealed increased microglial activation, vascular aberrations, and fibrinogen deposition in both diabetic patients and mouse retinas. After ancrod treatment, diabetic mice appeared to improve visual acuity, with reduced retinal inflammation and extravasated fibrinogen.

Conclusions: Our results show that pathological hallmarks observed in diabetic human retinas are corroborated in retinas from experimental diabetic models and that CX3CR1 signaling plays a key role in mediating neuroprotection in DR. Furthermore, ancrod administration to diabetic mice appears to dampen inflammation and vascular damage, with improvement in visual acuity. Together, these findings suggest that fibrinogen can be uniquely targeted as a novel therapeutic strategy for diabetic patients.

CONTROL ID: 3547265

SUBMITTER (NAME ONLY): Xiaoyun Jiang

TITLE: Reflective mirror-based line-scan adaptive optics optical coherence tomography

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Jiang, V. Pandiyan, J. Kuchenbecker, R. Sabesan, Ophthalmology, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics line-scan OCT offers high speed, resolution and sensitivity for imaging retinal structure and function. Here we report its implementation with reflective mirror based telescopes, optimized for improved resolution of fast light-induced retinal activity and weak retinal reflections.

Methods: Two wavelength bands from a supercontinuum light source were used for illumination - OCT (λ : 820 ± 40 nm) and line-scan ophthalmoscope (λ : 750 ± 6 nm), while a superluminescent diode (λ : 980 ± 10 nm) was used for wavefront sensing. A cylindrical lens created a linear illumination at the entrance pupil. In the sample arm, the entrance pupil was optically conjugated to a 1D galvo scanner, deformable mirror and the eye's pupil via three spherical-mirror telescopes. In the reference arm, the OCT beam was propagated via three spherical-mirror telescope relays to minimize the diffraction resulting from the 8.5 meter long travel, intended to match the sample arm optical path length. Non-planar telescope folding was followed and Zemax optimization was performed for the entire optical design, including the sample, reference and detection arms. In detection, band-pass filters separated OCT, LSO and wavefront sensing channels. An anamorphic telescope composed of two positive cylindrical lenses enabled efficient optimization of spatial and spectral resolution simultaneously in detection. The system's performance was assessed by imaging the structure of foveal cones, retinal ganglion cells and the functional response of parafoveal cones to a 660 nm flash stimulus.

Results: Over a 2.2 deg field-of-view and 3.2 D vergence range, the system's optical performance was optimized to remain under the diffraction-limit. The anamorphic configuration significantly improved signal collection efficiency and roll-off. Cones at ~ 0.2 deg from the foveal center, and retinal ganglion cells at 10 deg eccentricity were resolved in the OCT en face images. The temporal evolution of phase difference between individual cone inner/outer segment junction and outer segment tips provided a measure of light-induced activity in cones and was resolvable at ~ 0.2 deg. eccentricity from the foveal center.

Conclusions: We implemented the first reflective mirror-based line-scan OCT and demonstrated its feasibility for foveal cone optoretinography and visualizing retinal ganglion cell structure.

CONTROL ID: 3547266

SUBMITTER (NAME ONLY): Young Seol

TITLE: Papillomas and Primary Malignancy of the Lacrimal Sac: A Case Series and Review of the Literature

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Seol, C. Iacob, H. Reddy, New York Eye and Ear Infirmary of Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: It is exceedingly rare for sinonasal papillomas, which typically originate from nasal mucosa, to develop from the lacrimal sac. We performed a retrospective chart and literature review to categorize the demographic, clinical, and histopathological findings associated with this unusual pathogenesis with potential for malignant transformation.

Methods: A literature search in PubMed was performed to include all articles published in English between 1980 and June 2020. A series of 12 case reports of lacrimal sac papillomas were identified for review. The authors contribute 3 novel cases, including one illustrative case of a contiguous papilloma arising from the lacrimal sac and protruding through both upper and lower lacrimal puncta (Figure 1). We also review 5 patients with primary malignancies of the lacrimal sac in the setting of papilloma, including 1 novel case. (Table 1)

Results: All patients with benign lacrimal sac papillomas presented with epiphora (86%), swelling (76%), or both (71%). Their ages ranged from 24 to 73 with a median of 45. Seven (47%) were male, and eight (53%) were female, including one transgender woman.

Diagnosis was made with histologic analysis in all cases. The majority of papillomas were of the inverted subtype (60%), with three cases of exophytic (20%) papillomas. Three patients (20%) also presented with features of both. Treatment was with surgical excision in all cases, almost always via dacryocystorhinostomy (DCR, 92%) though additional surgery was required in 46% of cases.

All five cases of malignant transformation were inverted subtype. A majority (60%) were squamous cell carcinomas. Patients' ages ranged from 35 to 58 with four males and one female. All patients underwent DCR, and three required concurrent maxillectomy or ethmoidectomy for adequate removal. Radiotherapy and exenteration were further utilized in two cases of recurrence.

Conclusions: We present 15 cases of lacrimal sac papillomas and 5 cases of malignancy, including 4 of our own. These tumors may masquerade as chronic dacryocystitis. Inverted subtype papillomas are at greatest risk of malignant transformation. Surgeons and pathologists should be aware of this rare entity, and consideration should be given towards routine histopathologic examination of DCR specimens. Recurrence is rare but can be devastating, and prognosis following excision is generally good.

CONTROL ID: 3547267

SUBMITTER (NAME ONLY): Jeffrey Tapley

TITLE: Keratoconus-like Changes After Descemet Membrane Endothelial Keratoplasty in Patients with Fuchs' Dystrophy

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Tapley, A. Bauer, M. Straiko, M.A. Terry, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Descemet membrane endothelial keratoplasty (DMEK) rapidly deturgescence a cornea that is edematous due to endothelial dysfunction. In some cases, the central cornea deturgescence reveals localized posterior corneal steepening similar to that of keratoconus. Our aim was to describe changes in corneal thickness and identify the incidence of posterior corneal changes characteristic of keratoconus after DMEK surgery.

Methods: A retrospective chart review was conducted for 50 eyes that received cataract surgery and 50 eyes that received DMEK for Fuchs' Dystrophy. 6 month and 1 year follow-up images were reviewed for the DMEK group using an Oculus Pentacam. The central corneal thickness (CCT) of the preoperative cataract surgery eyes served as normal controls and was compared to the CCT of the postoperative DMEK eyes at 6 months and 1 year. Pentacam images in the DMEK group were also reviewed for characteristics resembling keratoconus. Statistical significance comparing CCT was determined using the Student's T-test.

Results: The normal CCT from 50 eyes at our center was $543\mu\text{m} \pm 35\mu\text{m}$. The 6 month postoperative CCT in the DMEK group was $534\mu\text{m} \pm 35\mu\text{m}$ ($P=0.23$) and the 1 year CCT was $536\mu\text{m} \pm 35\mu\text{m}$ ($P=0.33$). 19 out of 50 DMEK eyes (38%) had posterior steepening resembling keratoconus at the 6 month visit. A subgroup analysis of the preoperative CCT from those 19 eyes vs 31 eyes without keratoconus-like changes was not statistically different ($611\mu\text{m} \pm 51\mu\text{m}$ vs $615\mu\text{m} \pm 56\mu\text{m}$, $P=0.80$). All 19 of those eyes had the same posterior corneal changes at the 1 year visit.

Conclusions: CCT after DMEK was not statistically different compared to normal corneas at 6 months and 1 year postoperative. The posterior corneal steepening seen in 38% of DMEK corneas may be a consequence of stromal keratocyte apoptosis due to chronic edema. The localized steepening persists out to 1 year postoperative, suggesting that there may be structural loss in the stroma.

CONTROL ID: 3547268

SUBMITTER (NAME ONLY): Paul Varghese

TITLE: Tyrosinase Immobilized to Ni-NTA Magnetic Beads Shows Improved Protein Thermostability

SESSION TITLE: Retina/RPE: Biochemistry and molecular biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Varghese, M. Abu-Asab, E. Dimitriadis, M.B. Dolinska, G. Morcos, Y.V. Sergeev, Biochemistry, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Tyrosinase (Tyr) initiates the melanogenesis pathway by producing dopachrome (DC). The isolation of DC is essential to having a quantitative characterization of Tyr function with regard to mutations linked to oculocutaneous albinism 1 (OCA1). Previously we offered a method of DC isolation to allow current research to obtain this quantitative analysis by immobilizing Tyr to magnetic beads (Tyr-MB). Here we show increased thermostability of Tyr bound to Ni-NTA magnetic beads (MB) and have characterized and performed experiments on Tyr-MB to further our understanding of the role of wildtype and OCA1-related mutant Tyr within the melanogenesis pathway.

Methods: Whole T. ni larvae expressing recombinant truncated human Tyr (residues 19-469) was purified using Immobilized Metal Affinity and Size Exclusion Chromatography. 100 μ L of MB were incubated with Tyr for 30 minutes at room temperature to allow Tyr to bind. L-DOPA substrate (12, 6, 3, 1.5, 0.75, 0.38, 0.19, or 0.09 mM) was then incubated (1:1) with Tyr-MB complexes for 30 min. at different temperatures (25, 31, 37, 43, or 50 $^{\circ}$ C) to produce DC. After isolating DC with a magnetic separator, Tyr activity for DC formation was tracked by colorimetric activity (475 nm). Bare MB and Tyr-MB were imaged and analyzed using Atomic Force Microscopy (AFM) and Transmission Electron Microscopy (TEM).

Results: A dose-dependent hill plot ($R^2 = 0.99$) using different L-DOPA concentrations confirmed similar behavior between Tyr-MB and native Tyr (positive cooperativity; hill coefficient: 1.65 and 1.71 respectively; L-DOPA concentration that produces 50% of maximal DC production: 3.18 and 3.01 mM respectively.) A temperature dependence curve revealed a direct correlation ($R^2 = 0.97$) of Tyr-MB DC production with temperature. Under 50 $^{\circ}$ C, Tyr-MB remained functional and produced significantly more orange-brown DC than native Tyr (clear solution) as the MB increased Tyr thermostability. AFM and TEM showed the "texture and roughness" of bare MB and Tyr-MB and the relative diameter of Tyr-MB (168.2 ± 24.4 nm).

Conclusions: The analysis suggests using MB for DC isolation to obtain a quantitative characterization of Tyr function is an efficient approach as it increases the thermostability of Tyr. This approach will further illuminate the role of OCA1 mutant Tyr with regard to melanogenesis and open doors for treating albinism-related disorders.

CONTROL ID: 3547271

SUBMITTER (NAME ONLY): Christina Douglas

TITLE: Investigating the role of circulating microRNAs as potential biomarkers for Thyroid Eye Disease

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.E. Douglas, E. Roztocil, C. Hammond, M. Gonzalez, S.E. Feldon, C. Woeller, Ophthalmology, University of Rochester Medical Center, Rochester, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Thyroid Eye Disease (TED), also referred to as Graves' orbitopathy, is a disfiguring and sight threatening autoimmune disease that involves inflammation and remodeling of the orbit. TED can present with mostly orbital fat (Type 1), connective tissue (Type 2) or a combination of both. Patients with thyroid autoimmune diseases are at risk for developing TED; however, only 50-60% of Graves' disease patients will also show symptoms of TED. Currently, it is unclear why certain patients develop TED and whether the disease will manifest into either Type 1 or Type 2 phenotypes. New biomarkers may help identify patients who are at risk for TED. MicroRNAs (miRNAs) are a class of small, non-coding RNAs that play a role in the development of autoimmune diseases and are readily detectable in blood samples making them ideal candidate biomarkers.

Methods: Blood samples from control, non-TED patients and patients with Type 1 or Type 2 disease were collected in heparinized tubes and processed. Small RNAs, including miRNAs, were isolated from 0.25 mL of plasma. MiRNA samples were treated with heparinase and cDNA was generated. The levels of specific miRNAs were measured using TaqMan based real-time quantitative PCR. MiRNA expression was normalized using NormFinder software and then compared between non-TED and TED patients (both Type 1 and Type 2).

Results: The expression of several miRNAs including: miR-155-5p, miR-146a-5a, miR-130a-3p, miR-130b-3p were readily detected in control and TED patient plasma. Several of the miRNAs identified have been reported to be differentially expressed in TED orbital tissue compared to non-TED orbital tissue. MiR-130a, which was recently found to contribute to Type 1 disease phenotype, was upregulated in TED patient plasma.

Conclusions: MiRNAs associated with TED are readily detected in patient plasma samples. The expression of miR-130a is elevated in TED patient samples and may be indicative of Type 1 disease. The identification of novel miRNA biomarkers could be important for patients at risk for TED, and could lead to additional strategies that may mitigate disease before severe symptoms appear.

CONTROL ID: 3547273

SUBMITTER (NAME ONLY): Daniel Brock

TITLE: Characterization of the novel mitochondrial deglycase GATD3A in the retina

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.C. Brock, J. Nellissery, J. Advani, A. Swaroop, Neurobiology Neurodegeneration & Repair Laboratory, National Eye Institute, Bethesda, Maryland, UNITED STATES|A.J. Smith, Washington University in St Louis, St Louis, Missouri, UNITED STATES|J. Gumerson, Retinal Cell Biology & Degeneration Section, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Reactive dicarbonyls, glyoxal (GO) and methylglyoxal (MGO), react with proteins and nucleotides, eventually leading to the formation of advanced glycation end products (AGEs). AGEs are associated with aging-related diseases, including age-related macular degeneration and cataracts. We recently identified GATD3A as a novel mitochondrial specific deglycase, with similar activity to the Parkinsonism associated deglycase DJ-1/Park7. Notably, loss of DJ-1 results in retinal associated phenotypes. This project aimed to validate GATD3A's biochemical activity and elucidate its necessity for retinal function.

Methods: Subcellular fractionation was utilized to determine organelle compartmentalization. Enzyme activity assays using recombinant GATD3A were used to confirm deglycation of amino species. A novel CRISPR-mediated Gat3da knockout mouse was generated, and complete loss of mature protein was confirmed via retinal and heart immunoblot. Retinal function was assessed via scotopic and photopic ERG. Histological and electron microscopy imaging were used to examine both retinal and heart structure. Using mouse embryonic fibroblasts (MEFs) from the Gatd3a knockout mice, mitochondrial biogenesis was quantified with qPCR and mitochondrial morphology was examined using confocal image-based morphometric analysis.

Results: GATD3A has glyoxalase activity primarily against GO and localized to the mitochondrial matrix. Gatd3a knockout resulted in disrupted mitochondrial dynamics in the heart and MEFs, with mitochondria displaying more rounded morphology and electron lucent cristae. Gatd3a knockout mice displayed a 3-4-fold increase in dicarbonyl and AGE immunoreactivity in the heart. Knockout mice exhibited left ventricular heart fibrosis. Surprisingly, 4-month-old and 18-month-old retinas did not display any reduced functionality in either scotopic or photopic ERG. The retina did not display changes in morphology or levels of fibrosis.

Conclusions: GATD3A exhibits glyoxalase activity which functions in the prevention of AGE accumulation and fibrosis in the heart. However, Gatd3a knockout displayed no detectable changes in the retina under normal physiological conditions. Future directions include stress induction via provision of a high-glycemic diet in order to increase the prevalence of AGEs and exacerbate previously identified phenotypes in Gatd3a knockout mice. We will further quantify AGE species using LC-MS/MS based methods.

CONTROL ID: 3547275

SUBMITTER (NAME ONLY): Lbachir BenMohamed

TITLE: Up-Regulation of Multiple CD8⁺ T Cell Exhaustion Pathways is Associated to Recurrent Ocular Herpes Simplex Virus Type 1 Infection

SESSION TITLE: Corneal immunology and neovascularization I

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. BenMohamed, S. Prakash, R. Srivastava, N. Dhanushkodi, P.A. Coulon, Gavin Herbert Eye Institute, University of California Irvine Health Affairs, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: A large proportion of the world's population harbors latent herpes simplex virus type 1 (HSV-1). Crosstalk between antiviral CD8⁺ T cells and HSV-1 appear to control latency/reactivation cycles.

Methods: In the present study, we compared the transcriptome, phenotype, and function of memory CD8⁺ T cells, sharing the same HLA-A*0201-restricted HSV-1 epitope-specificities freshly isolated from peripheral blood and trigeminal ganglia (TG) of HSV-1 infected ASYMP and SYMP patients and HLA transgenic (Tg) mice, respectively.

Results: We report that HSV-specific CD8⁺ T cells from SYMP patients are phenotypically and functionally exhausted, highly co-expressing LAG-3 with three others inhibitory receptors while being defective in expression of functional markers. Moreover, the blocking of LAG-3 and PD-1 synergistically restored anti-viral CD8⁺ T cell responses, reduced HSV-1 reactivation from latently-infected TG, and reduced UV-B induced recurrent ocular herpetic infection and disease in latently-infected HLA-A*0201 transgenic mice.

Conclusions: These findings confirm antiviral CD8⁺ T cell exhaustion during symptomatic herpes infection and pave the way to targeting immune checkpoints to combat recurrent ocular herpes.

CONTROL ID: 3547277

SUBMITTER (NAME ONLY): Shashvat Purohit

TITLE: Relative Retinal Blood Flow in Patients with Central Retinal Artery Occlusions

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Central Retinal Artery Occlusions (CRAOs) are occlusions of the central retinal artery, which often presents clinically as sudden, painless loss of vision in one eye. The central retinal artery is the primary blood supply to the inner retinal layers of the macula, and therefore CRAOs result in irreversible loss of vision in the affected eyes. Currently, there is no established treatment that can alter the course progression of the disease other than to prevent subsequent neovascularization. The purpose of this study is to use the imaging instrument Laser Speckle Flowgraphy (LSFG), a relatively novel diagnostic tool to help quantify the degree of loss of blood flow in CRAO patients, using the metric relative blood flow (RBF). RBF allows for a unitless ratio comparison of blood flow from the patients' healthy eye to the affected eye and establish the degree of ischemia.

Methods: Three separate LSFG scans were performed on seven patients with clinical history of CRAOs and twenty control patients to measure the mean blur rate (MBR) in the optic nerve head (ONH) of both healthy and affected eyes. MBR is a measurement of laser scatter directly correlated with the flow of red blood cells through tissue and vasculature. RBF, a unitless ratio of respective MBRs was then calculated to measure the average loss of blood flow through the ONH due to the CRAO.

Results: A Welch two sample t-test was used to calculate statistical significance, resulting in indicating strong significant difference in RBF between healthy control patients and CRAO patients. In control patient's RBF was calculated to be 1.021332 ($p = 0.6843$) indicating no significant difference in RBF between healthy eyes. In CRAO patients, RBF was calculated to be 0.503304 ± 0.1433871 ($p = 1.06 \times 10^{-5}$), indicating on average a 50 percent loss in blood flow to the ONH in eyes with CRAOs.

Conclusions: These results support our current understanding of the pathophysiology of CRAOs, and provides researchers and clinicians with a diagnostic tool capable of truly quantifying loss of blood flow. RBF measurements of CRAO patients confirm a dramatic loss in blood flow in affected eyes due to occlusive injury. Prospective studies could utilize LSFG measurements to longitudinally analyze blood flow in affected eyes throughout disease progression and determine the possibility of a correlation between the return of blood flow and a return of visual acuity.

CONTROL ID: 3547283

SUBMITTER (NAME ONLY): yoshimichi hirota

TITLE: Prognostic Optical Coherence Tomography Marker for the Recurrence of Vogt-Koyanagi-Harada Disease

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. hirota, Y. Muraoka, M. Ishikura, A. Uji, S. Kadomoto, S. morooka, A. Tsujikawa, Kyoto Daigaku, Kyoto, JAPAN|

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ABSTRACT BODY:

Purpose: Vogt-Koyanagi-Harada (VKH) disease is bilateral and granulomatous uveitis. At the acute phase, the VKH-patients often suffer from decrease in the visual acuity (VA), and metamorphopsia because of serous retinal detachment (SRD), undulations of the retinal pigment epithelium (RPE), or choroidal fold at the fovea. Systemic steroid therapy for the inflammation is often effective, however, it is problematic that the inflammation can be recurrent generally when the dose of the steroid agent is reduced. Optical coherence tomography (OCT) is clinically useful for diagnosing and quantitatively evaluating the chorioretinal pathologies, however, there have been no valid OCT markers for predicting the recurrence. In this study, we focused to examine the OCT-reflectivity of the RPE at the acute phase, and the association with the future recurrence of the VKH-disease.

Methods: We included 40 eyes (both eyes of 9 men and 11 women) with treatment naïve acute VKH-disease whom we can observe for more than 12 months. We excluded patients with uveitis other than VKH disease, and patients who had received steroid therapy for other pathologies. Using OCT B scans at the fovea, we measured the RPE-reflectivity by calculating the ratio of the difference in the reflectivities between the RPE and the vitreous body to that in the reflectivities between the retinal nerve fibers and the vitreous body. We defined the recurrence as the reappearance of inflammations in the anterior segment, or those in the posterior segment including SRD, undulation of the RPE, and thickening of the choroid on OCT during the observational period.

Results: During the mean observational period of 37.2 months, 22 eyes of the 11 patients (55 %) had the recurrence. Logistic analysis using factors of age, retinal and thicknesses at the fovea, and RPE-reflectivity showed that the only RPE reflectivity was significantly associated with the recurrence (adjusted odds ratio: 40.560, 95% confidence interval: 1.20-1372.40, $p = 0.039$). Compared to eyes without the recurrence, the logMAR VA was poorer (0.08 ± 0.17 vs. 0.63 ± 0.70 , $p = 0.002$), and the RPE reflectivity was greater at the initial visit in eyes with the recurrence (1.25 ± 0.19 vs. 1.54 ± 0.43 , $p = 0.010$).

Conclusions: In addition to the initial poor VA, the greater RPE-reflectivity on OCT may be a prognostic marker for the future recurrence of the VKH-disease.

CONTROL ID: 3547285

SUBMITTER (NAME ONLY): Lara Asroui

TITLE: Treatment Decentration in Small Incision Lenticule Extraction (SMILE)

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Asroui, W.J. Dupps, J. Randleman, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine the percentage of visually significant decentered treatments in SMILE, and the impact of treatment decentration on patient-reported visual outcomes.

Methods: A retrospective evaluation of 31 eyes that underwent SMILE over the past year was conducted. Treatment decentration was determined on both pachymetry difference maps and Scheimpflug anterior tangential curvature difference maps, derived from preoperative and 3-month postoperative maps. Decentration was determined as the vector magnitude from the center of the visual axis, or center of the respective difference map, to the center of treatment. The center of treatment was determined by means of superimposing a schematic of concentric circles with a grid at the center, on the difference maps. The schematic was overlaid such that the treatment zone was best-fit into one of the circles. The center of the grid was taken as the center of treatment.

Results: Average treatment decentration in all eyes was 0.45 ± 0.24 mm based on the pachymetry difference maps, and 0.36 ± 0.16 mm based on the anterior tangential curvature difference maps ($p=0.005$). 22 (70.97%) eyes demonstrated good patient-reported visual outcome, while 9 (29.03%) eyes had suboptimal results, some of which requiring an enhancement surgery. Based on the pachymetry maps, average decentration was 0.45 ± 0.25 mm in the group with good visual outcome, and 0.46 ± 0.21 mm in the group with suboptimal visual outcome ($p=0.8$). Based on the anterior tangential curvature maps, average decentration was 0.32 ± 0.16 mm in the group with good visual outcome, and 0.43 ± 0.14 mm in the group with suboptimal visual outcome ($p=0.09$).

Conclusions: The magnitude of treatment decentration in SMILE differs depending on whether decentration is determined using pachymetry maps or anterior tangential curvature maps. The magnitude of decentration, as determined by use of either anterior tangential curvature maps or pachymetry maps, does not differ between eyes with good patient-reported visual outcomes and those with suboptimal outcomes.

CONTROL ID: 3547286

SUBMITTER (NAME ONLY): Clayton Kirk

TITLE: The neuroprotective effect of propranolol against retinal degeneration in a mouse model of light injury.

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Kirk, J.F. McDonnell, J. Perlman, P. Bu, Ophthalmology, Loyola University Chicago, Maywood, Illinois, UNITED STATES|Z. TAN, University of California Irvine, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Age related macular degeneration (AMD) is the leading cause of vision loss in developed countries. Propranolol is a commonly used, nonspecific β_1/β_2 adrenergic receptor antagonist (BARA) that has been shown to have a neuroprotective effect on various mouse retinal injury models. We hypothesize that systemic propranolol will exhibit a protective effect against retinal degeneration in the mouse model and has potential to protect from vision loss related to AMD in the future.

Methods: BALB/c albino mice were divided into 2 groups: vehicle-treated mice and propranolol treated. Light injury mice were exposed to 8,000 lux-cool, white, fluorescent light for 2 hours to induce light injury. Vehicle (4% v/v citrate buffer in normal saline) or propranolol (20 mg/kg/dose freshly prepared in normal saline solution before injection, stock solution at 50mg/ml in citrate buffer) was injected subcutaneously following light injury for 4 days. Scotopic electroretinography (ERG) was recorded before light injury and 5 days following light injury.

Results: Following retinal light injury, ERG a- and b-wave amplitudes were significantly reduced in the control mice. Propranolol treatment significantly attenuated light-induced loss of retinal function as compared to control treated mice. Before treatment, scotopic ERG a- and b-wave amplitudes were an average of 347.9 μ V and 616.4 μ V, respectively, in the control group and 368.6 μ V and 618.9 μ V, respectively, in the propranolol treatment group. Following retinal light injury, ERG a-wave amplitudes were 71.75 μ V in the control group and 161.2 μ V in the propranolol treatment group ($p < 0.01$). Following retinal light injury, ERG b-wave amplitudes were 142.4 μ V in the control group and 360.2 μ V in the propranolol treatment group ($p < 0.01$).

Conclusions: Propranolol treatment of mice demonstrated a substantial effect on preserving ERG a- and b-wave amplitudes following retinal light injury as compared to a control group. These initial findings suggest that propranolol may represent a novel therapy for retinal degenerative conditions.

CONTROL ID: 3547287

SUBMITTER (NAME ONLY): Samaneh Davoudi

TITLE: Low vitamin D is associated with infectious and non-infectious ocular diseases in Florida.

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Davoudi, R. Roohipour, S.S. Iyer, G.S. Khurshid, C. Beal, W. Martinez, E. Grieser, R. Blake, J. LiVecchi, Y. Islam, S. Duff, S. Tuli, Ophthalmology, University of Florida, Gainesville, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vitamin D has an important role in immune systems. Association of hypovitaminosis D and non-infectious inflammatory ocular diseases have been showed previously but this association was not studied in inflammatory infectious ocular diseases and area with high sun exposure. Our aim is to determine whether there is any association between vitamin D levels and infectious and non-infectious ocular diseases in Florida.

Methods: In this retrospective study, 1468 patients (28.9% male) and 490 controls (27% male) were recruited. Cases were diagnosed by an ophthalmologist with infectious (endophthalmitis, cellulitis, keratitis, infectious uveitis) and non-infectious ocular inflammation (uveitis and scleritis) after exclusion of neoplastic causes. Controls had no history of eye inflammation. They had recorded 25 hydroxy (OH) vitamin D levels. Clinical and demographic data were collected from patients 's record. Logistic regression models were created to examine the association between ocular inflammation and hypovitaminosis D using Stata (college Station, TX). Age, gender, race, smoking, and history of systemic diseases were included in multivariate model.

Results: Vitamin D levels means and standard deviations were 33 ± 12.7 and 28 ± 13.9 nanograms per milliliter in controls and cases. The odds of having infectious and non-infectious ocular inflammation was 2.2 higher in patients with hypovitaminosis D compared to normal vitamin D level [(odds ratio (OR) =2.2, 95% Confidence Interval (CI) = 1.76-2.67, $P= 1.8 \times 10^{-13}$). The association remained significant in multivariate regression, after adjusting for age, gender, race and smoking (OR =2.7, 95%, CI = 2.19-3.44, $P= 8.17 \times 10^{-19}$). The odds of developing infectious and non-infectious inflammation was 3% lower for every unit increase in vitamin D level (OR =0.97, 95%, CI = 0.97-0.98, $P= 6.35 \times 10^{-9}$).

Conclusions: Low vitamin D is associated with increased risk of infectious and non-infectious ocular inflammation in a large population in Florida in a retrospective study.

CONTROL ID: 3547288

SUBMITTER (NAME ONLY): Stephanie Llop Santiago

TITLE: The Impact of Polymerase Chain Reaction (PCR) on Management in Infectious Uveitis

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.M. Llop Santiago, Ophthalmology, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|J. Fallon, Ophthalmology, New York Eye and Ear Infirmary of Mount Sinai Ophthalmology, New York, New York, UNITED STATES|J. Lin, Ophthalmology, Icahn School of Medicine at Mount Sinai, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the impact of PCR sampling on diagnosis and treatment of infectious uveitides at a large tertiary care facility

Methods: This is a retrospective chart review of patients with at least one PCR sample performed from 2014-2019 at New York Eye and Ear Infirmary of Mount Sinai. At least one follow up visit following results of PCR testing was required for inclusion. If a patient had multiple PCR samples taken, only the first sample was included. The samples were divided into three categories based on pre-PCR diagnosis: those where pre-sampling diagnosis was presumed not infectious (group 1), those where pre-sampling diagnosis was presumed infectious (group 2) and those where pre-sampling diagnosis was concerning for infection but still unknown (group 3).

Results: 108 cases were available for analysis in the study. 25 of the 108 samples yielded a positive PCR result (23%). Majority of patients fell into group 3 where diagnosis was unknown (56%). Presumed infectious and noninfectious cases made up 22% of the population each. Table 1 summarizes treatment and diagnostic changes made in response to PCR sampling results. A chi square analysis was performed. The results of PCR testing had a more significant impact on diagnosis in those cases where pre-sampling diagnosis was unknown versus those where it was presumed infectious or presumed noninfectious (77% vs. 21%; 77% vs. 13%, $p<0.0001$). In cases where the presumed diagnosis was infectious, the rate of diagnosis change was similar to those where the diagnosis was presumed noninfectious (21% vs. 13%, $p>0.05$). Similarly, treatment changes were made based on PCR results more frequently in cases where the diagnosis was unknown compared to when an infectious entity is presumed (38% vs. 25%, $p<0.0001$). There were no cases where treatment was changed in relation to PCR when a noninfectious entity was the pre-sampling diagnosis.

Conclusions: In our experience, PCR sampling is undertaken in various clinical scenarios, including when an infectious entity is not suspected, when an infectious entity is suspected, and when diagnosis is unknown. As expected, it has the greatest impact on diagnosis and treatment when the clinical diagnosis is unknown. When PCR sampling is confirmatory in nature, it has a minimal impact on diagnosis and treatment, especially when compared to unknown cases.

CONTROL ID: 3547290

SUBMITTER (NAME ONLY): Jessica Shantha

TITLE: COVID-19 Associated Retinopathy

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Shantha, S. Auld, C. Anthony, L. Ward, K. Price, M. Adelman, T. Fashina, N. McNair, N. Rouphael, J. Jacob, D. Murphy, S. Yeh, Emory University, Atlanta, Georgia, UNITED STATES|

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ABSTRACT BODY:

Purpose: Coronavirus disease (COVID-19) has escalated to a global pandemic with increasing reports of ophthalmic disease. We report ophthalmic observations of hospitalized COVID-19 patients and correlate retinal disease findings with clinical and laboratory data.

Methods: Retrospective review of COVID-19 patients who underwent ophthalmic exam during hospitalization within Emory Healthcare between April-July 2020.

Results: Thirty-seven patients were examined with 23 (62%) females and a mean age of 54 years. 35 patients were admitted to the ICU. Ophthalmic manifestations included conjunctival injection in 12 eyes (17%), chemosis in 8 (11%) and retinopathy in 20 eyes (27%) with bilateral retinopathy in 6 patients (16%). No difference in baseline comorbidities or COVID-19 complication development was observed between patients with and without retinopathy. However, patients with retinopathy required ICU care for 1 week longer than those without retinopathy (27.6 vs 19.9 days $p=0.19$). The mean sequential organ failure assessment score at ICU admission was 6.18. All patients with retinopathy required both mechanical ventilation and vasopressors, while in patients without retinopathy, 15 (65%) and 12 (52%) required mechanical ventilation and vasopressors respectively ($p=0.015$, $p=0.002$). 6 patients with retinopathy required extracorporeal membrane oxygenation compared to 1 without retinopathy ($p=0.0070$). While the mean peak D-Dimer was elevated at 18477, in the entire cohort, the peak D-Dimer was higher in patients with retinopathy (28,971 vs 12,575, $p=0.0298$). The fibrinogen nadir during hospitalization was on average 338 for the entire cohort, and reduced in patients with retinopathy (262 vs 381, $p=0.029$). Peak D-dimer analyses with a threshold of 16,508 showed an odds ratio of 16.7 (95% CI 3.11-89.3) for retinopathy. Fibrinogen nadir with a threshold of 367 showed odds ratio of 0.06 (95% CI 0.01-0.53) with 0.75 concordance.

Conclusions: Retinopathy was the most common ophthalmic manifestation in a critically ill COVID-19 population, exceeding 25% of patients. Elevated D-dimers and a lower fibrinogen nadir in patients with retinopathy suggest a pathogenic relationship between coagulation pathways and retinal microangiopathy.

CONTROL ID: 3547291

SUBMITTER (NAME ONLY): Kirsten Lampi

TITLE: Upon oxidation, deamidated gammaS-crystallin has increased aggregation compared to wild type gammaS-crystallin

SESSION TITLE: Lens Mechanics, Crystallins and Pathology

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K.J. Lampi, S. Wheeler, IBDS, Oregon Health & Science University, Portland, Oregon, UNITED STATES|K. Zientek, L.L. David, Oregon Health & Science University School of Medicine, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: We have recently reported that deamidations associated with cataracts increase aggregation. The purpose of this study was to quantify the disulfides in wild type and deamidated gammaS-crystallin upon oxidation and correlate levels to aggregation.

Methods: Wild type gammaS and deamidated gammaS (N14D, N76D, N143D) crystallins were reduced and then rapidly exchanged into phosphate buffer containing amounts of GSH:GSSH ranging from 5 mM:0 mM to 0 mM:2.5 mM. This approximated the loss of both reduced and total glutathione in normal vs cataractous lenses and mimicked the oxidative environment found during cataract formation. Proteins were then incubated for 2-24 hours at 37 or 60 degrees C before whole mass measurement using an Orbitrap Fusion mass spectrometer (Thermo Scientific). The overall numbers of disulfide bonds and glutathione adducts were determined and correlated to changes in aggregation. Aggregation was measured by dynamic light scattering using a DynaPro NanoStar Reader (Wyatt Tech. Co.).

Results: We identified an increase in non-native disulfide bonds in oxidized, deamidated gammaS-crystallin. The intermolecular C24-C24 crosslink was increased in deamidated gammaS during oxidation in vitro, as was the C144-C114 crosslink. After 2 h incubation at 1:1 ratio of GSH:GSSH, the deamidated gammaS had increased radii of the main monomer peak and increased aggregates at radii > 10 nm compared to wild type. The monomer peak was 3.2 nm compared to 2.5 nm of the wild type and the higher radii species contributed 3% of the mass compared to none detected in the wild type. The overall shape of the light scattering autocorrelation curves suggested multimodal distribution for both proteins, but the curves were distinctly different with the curve for the deamidated gammaS not reaching baseline as fast suggesting larger species.

Conclusions: Our findings support that deamidation predisposes crystallins to further modifications that then lead to higher-ordered oligomers and eventually large light scattering aggregates associated with cataracts.

CONTROL ID: 3547292

SUBMITTER (NAME ONLY): Paul Yang

TITLE: Six Month Findings from a Phase 1/2 Clinical Study of Subretinal Gene Therapy Drug AGTC-501 for X-Linked Retinitis Pigmentosa Show Clinically Meaningful Improvement in Macular Sensitivity

SESSION TITLE: Gene Therapy

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: X-linked retinitis pigmentosa (XLRP) is an inherited retinal disease (IRD) characterized by night blindness beginning in adolescence, and progressive loss of peripheral vision that eventually leads to central vision loss. Gene therapy approaches for treating XLRP have explored the use of recombinant adeno-associated viral (rAAV) vectors to deliver a normal copy of the mutated gene responsible for retina cell loss. This is an initial report from an ongoing, Phase 1/2, open label, dose escalation clinical trial using an rAAV2 viral vector to deliver a functioning gene copy of

retinitis pigmentosa GTPase regulator (RPGR) via subretinal injection.

Methods: Male participants (n=29), age ≥ 6 , received subretinal injection of AGTC-501 (rAAV2tYF-GRK1-RPGR) into the central or peripheral macula region of the study eye. Participants were sequentially assigned to one of five dose groups to assess safety (primary outcome) and changes in visual function (secondary outcome), measured by MAIA microperimetry and best-corrected visual acuity (BCVA) as assessed by ETDRS. Patient data was analyzed 6 months post-treatment.

Results: Subretinal administration of AGTC-501 was well-tolerated across a wide dose range. The majority of adverse events were mild-moderate in severity, consistent with the subretinal injection and vitrectomy procedures, and/or concomitant prophylactic steroid regimen used to mitigate inflammation. Among the 21 centrally dosed participants, 18 had evaluable microperimetry data of which there were 8 responders, classified as a ≥ 7 decibel improvement in at least 5 loci within the central 36 loci macular area ($p \leq 0.05$). Eleven of the 20 participants with evaluable BCVA data demonstrated improvement of ≥ 5 letters in the treated eyes compared to the fellow eyes ($p = 0.001$). Among peripherally treated patients, BCVA remained stable.

Conclusions: Robust safety and efficacy signals in the study eyes of participants who underwent subretinal administration of AGTC-501 were observed through month 6. There was clinically meaningful improvement in macular sensitivity and statistically significant improvement in BCVA for the study eyes vs. untreated fellow eyes. Follow-up is ongoing through 5 years to assess long-term safety and durability of response.

CONTROL ID: 3547293

SUBMITTER (NAME ONLY): Shilpa Kodati

TITLE: Ocular Symptoms in COVID-19 infection: A Survey Study

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ocular findings have been reported in association with the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Despite these reports, less is known on the frequency, spectrum and duration of associated ocular symptoms and their onset in the disease course. The purpose of this study is to systematically characterize ocular symptoms in participants with COVID-19 infection.

Methods: An online Research Electronic Data Capture (REDCap) survey designed to characterize ocular symptoms was developed and the study information distributed to NIH employees who had tested positive for SARS-CoV-19. The survey was also advertised to the public through social media and patient recruitment mailing lists. All responses were anonymous, and participants were asked to consent to completing the survey, confirm a positive SARS-CoV PCR test and that they were 18 years of age or older. This study was approved as exempt by the National Institutes of Health (NIH) Office of IRB Operations.

Results: Following exclusion of ineligible participants and incomplete responses, 181 (20.4% male and 79.0% female) complete survey responses were included for analysis including from hospitalized (9.9%) and non-hospitalized (90.1%) respondents as well NIH employees (27.1%). Ocular symptoms were reported by 77.9% of participants (mean number of ocular symptoms per participant: 2.19+/- 2.36). The most commonly reported ocular symptoms were light sensitivity 28.1%, itchy eyes (26.0%), tearing (25.4%), eye redness (24.9%), mucous discharge (20.1%), foreign body sensation (17.1%), and new onset floaters (15.4%). With the exception of itchy eyes, no significant differences in eye symptoms were found between age groups. The onset of ocular symptoms occurred mostly frequently at the same time as systemic symptoms (53.8%) compared to before (18.9%) and after systemic symptoms (27.3%). Notably, 10.6% of respondents with ocular symptoms sought medical attention by an eye care professional and 21.2% reported eye symptoms lasting ≥ 14 days.

Conclusions: Our results show that the majority of survey respondents experienced ocular symptoms though only a minority required ophthalmic examination and our study is likely biased towards respondents with eye symptoms. Consistent with other reports, ocular surface related symptoms were more common and vision affecting symptoms were rare. Further work is needed to identify the sequelae of ocular symptoms associated with SARS-COV-2.

CONTROL ID: 3547295

SUBMITTER (NAME ONLY): Indre Bielskus

TITLE: Can drusen growth in age-related macular degeneration be slowed by oral curcumin?

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: I. Bielskus, N. Pfahler, A. Kakouri, P.A. Knepper, Ophthalmology and Visual Sciences, University of Illinois at Chicago College of Medicine, Chicago, Illinois, UNITED STATES|A. Kakouri, Ophthalmology, John H Stroger Hospital of Cook County, Chicago, Illinois, UNITED STATES|S. Aman, Z. Zaporackas, P.A. Knepper, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Drusen size is a hallmark of AMD progression to geographic atrophy (GA) or choroidal neovascularization (CNV) leading to loss of vision. Drusen formation accompanies retinal pigment epithelium atrophy and is a risk factor for disease progression. Although the cause remains unclear, drusen size predicts the likelihood of progression to advanced AMD. In this study, we evaluated the effect of oral curcumin, an inhibitor of the innate immune receptor TLR4, on drusen size and disease progression over the course of one year in a cohort of pre-advanced AMD subjects.

Methods: Participants with pre-advanced AMD (n=18) were recruited from the office of Zaporackas and Knepper, Ltd. in Chicago, IL after IRB approval and informed consent. Pre-advanced AMD was defined as the presence drusen ≥ 63 μm in width without GA or CNV. Participants were provided oral curcumin at a dose of 2660 mg/day and imaged using ocular coherence tomography (OCT) at baseline and every 3 months for 1 year. The primary outcome was macular drusen volume. As an internal control, drusen size was measured up to 6 months prior to beginning oral administration of curcumin. Drusen volume was measured manually using ImageJ software. Macular regions were defined using the 1, 3, and 6 mm grid. The cohort was classified as responder or non-responder using an arbitrary cutoff of $\pm 10\%$ change.

Results: After one year, total macular drusen volume decreased from 0.0204 to 0.0184 mm^3 (-9.8%, $P=0.009$), foveal drusen volume decreased from 0.0092 to 0.0079 mm^3 (-13.9%, $P=0.03$), parafoveal volume decreased from 0.0086 to 0.0078 mm^3 (-9.1%, $P=0.10$), and perifoveal volume increased (30.9%, $P=0.08$). In the 6 months prior to beginning the study, the growth rate of total macular drusen volume was 0.0035 mm^3/year , consistent with natural history studies in the literature (Folgar, 2016) and significantly higher than the rate after beginning curcumin of -0.0020 mm^3/year ($P=0.002$). The percent of responders and non-responders was 56% and 19%, respectively, which was significantly different from the expected percentages of 12% and 48%, respectively, found in the literature ($P=0.0005$; Yehoshua, 2011). Importantly, no subjects developed GA or CNV after 1 year.

Conclusions: These preliminary results, though limited, may demonstrate the efficacy of RQC in slowing the growth of drusen in AMD – a finding that would be very promising as it may reduce the risk of disease progression.

CONTROL ID: 3547298

SUBMITTER (NAME ONLY): Brendon Lee

TITLE:

Use of thalidomide and doxycycline in the management of junctional epidermolysis bullosa laryngo-onycho-cutaneous syndrome (JEB-LOC).

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose:

Junctional epidermolysis bullosa laryngo-onycho-cutaneous (JEB-LOC) is an overlap multisystem disorder characterised by extensive granulation tissue formation in the dermis, submucosa, larynx, and eyes. Ocular complications in JEB-LOC remain devastating and recalcitrant to many available treatment modalities.

Methods: We report the results of an interventional clinical study on the novel use of oral thalidomide and doxycycline in a case of an 18-year-old male JEB-LOC. Ocular and cutaneous tissue samples were collected pre- and post-treatment and underwent histopathological and immunofluorescence analysis.

Results:

Ocular involvement was observed to begin in this male at 15 months of age with eyelid ulcerations and granulation tissue formation in the conjunctiva bilaterally. By 13 years of age, this had progressed to recurrent, painful corneal erosions with associated cicatrising conjunctivitis leading to symblepharon, epiphora, severe photophobia, and visual loss (Right: 1/60, Left: 2/36). This occurred despite multidisciplinary management with numerous ocular surgical excisions and maximal medical therapy of antibiotics, anti-inflammatory medications, ocular lubricants, and steroids. He was commenced on thalidomide (50mg/day) and doxycycline (100mg/day) at 15 years of age. Within 3 months, he experienced significant improvement of his photophobia, epiphora, and pain. There was also significant improvement of his vision (Right: 6/12, Left: 6/18), accelerated physical growth, and no new cutaneous lesions formed. However, wary of long-term safety, treatment was ceased temporarily which resulted in a resurgence of symptoms. This was controlled by reintroduction of the therapy every second day, which was well tolerated and monitored by nerve conduction studies. Immunofluorescent and histopathological analysis demonstrated significant decrease in inflammatory marker (tumour necrosis factor) and laminin V expression in both ocular and cutaneous tissues after treatment initiation.

Conclusions:

Oral thalidomide and doxycycline therapy may have potential in managing the cutaneous and ocular complications of JEB-LOC. Its use may be warranted in patients with other forms of epidermolysis bullosa refractory to treatment.

CONTROL ID: 3547300

SUBMITTER (NAME ONLY): Gabrielle Monterano Mesquita

TITLE: Inter-Individual Variability of the Scleral and Ciliary Muscle Optical Attenuation and its Implication for Transscleral Laser Therapy

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Monterano Mesquita, D. Patel, Y. Chang, F. Cabot, M. Ruggeri, S.H. yoo, J.A. Parel, A. Ho, F. Manns, Ophthalmic Biophysics Center, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|G. Monterano Mesquita, D. Patel, Y. Chang, M. Ruggeri, F. Manns, Department of Biomedical Engineering, University of Miami College of Engineering, Coral Gables, Florida, UNITED STATES|F. Cabot, S.H. yoo, Anne Bates Leach Eye Hospital, Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, Miami, Florida, UNITED STATES|J.A. Parel, A. Ho, Brien Holden Vision Institute Limited, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: Inter-individual variations in the optical properties of the sclera and ciliary body may be a factor in the variability of treatment outcomes of transscleral and transpupillary laser therapies, such as cyclophotocoagulation. The goal of this study is to quantify inter-individual variations of the attenuation of the sclera and ciliary muscle with OCT.

Methods: The sclera and ciliary body of the left eye of 41 healthy subjects (age range: 16 to 60 years) were imaged using a commercial spectral domain OCT system following an IRB-approved protocol ($\lambda_c = 1325$ nm, Telesto I, Thorlabs, NJ). Rectangular regions of interest (ROI) consisting of 100 A-lines (width = 0.35 mm) were identified in the sclera from the episcleral - sclera to the sclera - ciliary muscle boundary (depth: 0.43 ± 0.06 mm) and in the ciliary muscle from the sclera - ciliary muscle boundary to the muscle inner boundary (depth: 0.29 ± 0.07 mm). The attenuation coefficient (AC) along each A-line of the ROI was calculated from an exponential fit of the axial intensity profile (Fig 1). A-lines with ACs that were outside 2 standard deviations from the mean were discarded. This step was repeated and the truncated mean and standard deviation of the AC within the ROI, with outliers removed was calculated.

Results: The ACs of the sclera and ciliary muscle ranged from 1.38 to 4.55 mm^{-1} and 1.88 to 5.00 mm^{-1} (mean: $3.26 \pm 0.95 \text{ mm}^{-1}$ and $3.74 \pm 0.76 \text{ mm}^{-1}$), respectively (Fig 2).

Conclusions: There is a large inter-individual variation of the scleral and ciliary muscle attenuation which produces significant variations in the energy reaching the ciliary body. The results suggest that a personalized laser treatment that takes into account scleral attenuation might improve treatment outcomes across individuals.

CONTROL ID: 3547302

SUBMITTER (NAME ONLY): Colin Lemire

TITLE: Longitudinal Retinal Blood Flow Changes Associated with Unilateral Central Retinal Vein Occlusions

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C.A. Lemire, N. Hazra, R. Koch, B. Seto, K. Yamada, J.G. Arroyo, Ophthalmology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal blood flow is reduced in patients with vascular occlusions and can be quantified by comparing blood flow between the affected eye and the fellow eye. In this prospective study, we describe short- and long-term changes in retinal blood flow in patients with unilateral central retinal vein occlusions (CRVOs).

Methods: The eyes of patients with acute, less than 1 month old ($n = 8$), and chronic, greater than 2 years old ($n = 18$), unilateral CRVOs were imaged using laser-speckle flowgraphy at the optic nerve head. For each patient, the relative blood flow (RBF) was calculated by dividing the mean blur rate of the occluded eye by the mean blur rate of the unaffected fellow eye. Patients with follow-up measurements ($n = 11$) were used to compare the change in RBF within 6 months in acute and chronic CRVOs. Additionally, the RBF in CRVO patients was compared to control subjects without any ocular disease ($n = 18$). RBF measurements were also compared to visual acuity and central macular thickness obtained at the time of measurement as well as to the number of injections each patient required after measurement. Data was analyzed using the Wilcoxon Rank Sum Test.

Results: Eyes with acute CRVO showed a reduction in relative blood flow of 33% (SE: 15%, $p < 0.001$), compared to 27% (SE: 11%, $p < 0.001$) in eyes with chronic CRVO. There was a significant difference in the average 6-month change in RBF between acute and chronic CRVOs, with acute eyes increasing by 9.7% and chronic eyes decreasing by 1.2% (SE: 5%, $p < 0.01$).

Conclusions: CRVOs can cause a marked reduction in blood flow that persists for years. Eyes with acute CRVOs are more likely than chronic CRVOs to experience increased perfusion over time, which may be correlated with improved functional and anatomical outcomes. These results also highlight the need for animal models of CRVOs to consider the long-term complications that can arise from chronic reductions in retinal blood flow.

CONTROL ID: 3547303

SUBMITTER (NAME ONLY): Enrique Graue-Hernandez

TITLE: 3 year outcomes of corneal wavefront guided PRK and simultaneous accelerated crosslinking in keratoconus

SESSION TITLE: Corneal transplantation and surgeries

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.O. Graue-Hernandez, E. Gonzalez Lubcke, J. Cabral-Macías, D. Pinkus, A. Ramirez Miranda, A. Lichtinger-Dondish, A. Navas, Cornea, Instituto de Oftalmologia Fundacion Conde de Valenciana IAP, Mexico City, Mexico City, MEXICO|

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ABSTRACT BODY:

Purpose: To report long term outcomes of corneal wavefront guided PRK followed by same day accelerated crosslinking in keratoconus patients.

Methods: Retrospective review of clinical records. Grade I and II keratoconus (Amsler-Krumeich classification) with evidence of clinical progression were included. In all cases, corneal wavefront guided PRK (Sirius corneal tomographer and Amaris 750 Hz Schwind) combined with accelerated. corneal crosslinking 0.1% riboflavin (Vibex RapidTM) for 10 minutes.UVA pulsed radiation (365 nm) for 8 minutes at 30mW/cm2 with an interval of one second (Avedro). Measured variables included UCVA, CDVA, Sphere, Cylinder, pachymetry, and spherical aberration, coma, trefoil and MTF and RMS. Follow-up was performed at 1 day, 1 week, month 1, 3, 6, 12, 48 and 72. Results are presented using waring standard graphs and statistical analysis with STATA v.12.

Results: 30 eyes of 16 patients were treated. Mean age was 29.53. Mean follow-up 32 ± 9.7 months (range 9-44) Mean central ablation was 37.63 microns. Preoperative values and postoperative values at the last follow-up were: LogMAR UDVA $0.86 \pm .34$ vs $0.18 \pm .19$; LogMAR CDVA 0.5 ± 0.8 vs 0.04 ± 0.08 ; sphere (D) 1.09 ± 1.45 vs 0.25 ± 0.8 ; Cylinder -2.76 ± 1.45 vs 1.5 ± 1.1 ; MRSE -2.46 ± 1.17 vs 1.19 ± 1.4 ; corneal thinnest point(μ) 501.7 ± 25.95 vs 459 ± 31.4 ; K1 42.9 ± 1.15 vs 41.74 ± 1.30 ; K2 45.95 ± 1.19 vs 43.9 ± 2.2 ; WFE RMS (μ) 2.01 ± 0.1 vs 1.44 ± 0.8 ;HOA(μ) 0.64 ± 0.4 vs 0.54 ± 0.2 ; Spherical Aberration(μ) 0.09 ± 0.6 vs 0.9 ± 0.1 ; Trefoil 0.4 ± 0.3 vs 0.33 ± 0.2 and Coma (μ) 0.33 ± 0.26 vs 0.27 ± 0.18 . All comparisons of pre and post op values were statistically significant with $p < 0.05$ with the exception of CDVA $p 0.68$, Spherical aberration 0.9, and Coma 0.31. Only 1 eye (3.3%) lost 2 lines of CDVA and 16 eyes (53%) gained at least 1 line of CVDVA. Refraction remained stable over the followup period. Complications: 6 eyes had irregular conreal surface that resolved in the first month and mild corneal haze (Grade I) was observed in all eyes and resolved spontaneously by 3 months.

Conclusions: Combination of photorefractive keratectomy and corneal cross linking is a safe and effective treatment that produces corneal and refractive changes that remain stable 3 years after the procedure. No signs of progression were observed in patients keratoconus grade I and II.,

CONTROL ID: 3547304

SUBMITTER (NAME ONLY): Arpita Dave

TITLE: MeCP2-mediated mitochondrial impairment evidenced in Stargardt disease

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.R. Dave, E. Ng, Z. Jiang, J.G. Hu, M.B. Gorin, A. Matynia, R.A. Radu, UCLA Stein Eye Institute, Los Angeles, California, UNITED STATES|A.R. Dave, E. Ng, Z. Jiang, J.G. Hu, M.B. Gorin, A. Matynia, R.A. Radu, Ophthalmology, University of California Los Angeles David Geffen School of Medicine, Los Angeles, California, UNITED STATES|L. Stiles, Mitochondria and Metabolism Core, Department of Medicine: Endocrinology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Clinical and basic studies implicate the retinal pigment epithelium (RPE) as the primary site of two related central blinding maculopathies such as AMD and Stargardt disease (STGD1). Links of epigenetics to aging have been proposed but a specific epigenetic-mediated mechanism responsible for the RPE cellular death is yet to be identified. Preliminary data suggest a role of Methyl-CpG-binding protein 2 (MeCP2), an epigenetic factor, in mitochondria dynamics of aged and diseased RPE cells. Using *Abca4*^{-/-} mice and human STGD1 iPSC-derived RPE cells, we correlated the MeCP2 protein profile and mitochondrial functions. We employed proteomics analysis to identify MeCP2-regulated molecular targets responsible for age-dependent mitochondrial changes.

Methods: 1-, 3-, and 6-mo old background-matched wild-type (WT) and *Abca4*^{-/-} mice and human normal and STGD1 iPSC-derived RPE cells homogenates were used to measure the levels of MeCP2 by quantitative immunoblotting (normalized to beta-actin; n=3). By LC-MS proteomics analysis, we determined oxidative phosphorylation (OXPHOS) and glycolysis proteins using 4 mouse RPE sheets (n=3). Mouse and human primary RPE cultures (n=4) were used to evaluate mitochondria functions by Seahorse respirometry. Statistical analysis was done using t-test or One-way ANOVA.

Results: By immunoblotting, we found a ~2- and ~4-fold increased MeCP2 level in 3-mo- and in 6-mo-old respectively when compared to 1-mo-old *Abca4*^{-/-} RPE cells. Importantly, RPE cell homogenate from 6-mo-old *Abca4*^{-/-} mice showed ~2-fold higher MeCP2 level vs age-matched WT mice. Analysis of human iPSC-derived RPE grown for 2-mo in culture indicated increased MeCP2 level in STGD1 vs normal cells. Proteomics analysis revealed significantly (p<0.05 to p<0.001) reduced levels of the OXPHOS complexes (I, II, III, and V) and elevated levels of the glycolysis proteins. Consistently, Seahorse respirometry analysis indicated increased glycolytic activity in *Abca4*^{-/-} vs WT RPE cells.

Conclusions: Our data evidenced an age-dependent MeCP2 protein changes that correlated with altered mitochondrial functions in the RPE cells of the STGD1 models. These studies inform on a specific regulatory role of MeCP2 and its targeted molecular players in the RPE cells that are involved in disease progression. Importantly, modulation of MeCP2 in the RPE cells may potentially rescue the mitochondria deficiency to mitigate RPE functions and prevent blindness.

CONTROL ID: 3547307

SUBMITTER (NAME ONLY): Alaina Softing Hataye

TITLE: Abstract: Glaucoma provider practice patterns for low vision referrals

SESSION TITLE: Visual Impairment - Services and Visual Function

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Purpose: Glaucoma patients experience irreversible vision loss that affects activities of daily living including reading, driving and mobility. Published literature has shown that a quarter of glaucoma providers follow the American Academy of Ophthalmology practice guidelines of referring patients to low vision service when visual acuity in the better seeing eye drops to 20/40 or worse. Data on referral rates and completion of low vision services in this patient group is lacking. A retrospective chart review in a tertiary care center was completed to identify the number of low vision referrals from the glaucoma service and the number of those patients who attended their low vision exams.

Methods: Methods: A retrospective record review of patients seen in the glaucoma service of an academic medical center from 7/2 - 7/18/18 was conducted. Patients with visual acuity of 20/40 or worse in the better eye were identified. The following data were gathered: age, gender, visual acuities of both eyes, completed low vision exams, documented discussion of low vision services, how long the patient had 20/40 or worse in the better eye prior to receiving services and referral source (OD vs MD). Descriptive statistics were used.

Results: Results: 509 charts were reviewed, 29 patients with 20/40 or worse in the better eye were identified. Mean age was 78 [16.9] years of age, with a range of 24-96 years of age. Male/female distribution was 13/16 (45% male and 55% female). Average visual acuity in the better seeing eye was 0.639logmar, in the worse eye 0.929logmar. Low vision consultation was completed for 15/29 (52%) patients, all of which had documentation of low vision service discussion and referrals. Of the patients who did not receive low vision services 14/29 (48%) only two had documented discussions about low vision care. 11/15 (73%) of the patients who received low vision services, had vision worse than 20/40 for > 2 years before being seen by a low vision specialist. Of the 15 completed examinations, 6 were referred by ophthalmologists and 9 were referred by optometrists.

Conclusions: Conclusion: 52% of low vision patients seen by glaucoma providers were referred and received low vision care. This is higher than referral rates reported in the literature, in addition to self-reported rates by glaucoma providers. However, the majority of low vision patients had their vision loss for > 2 years before seeing a low vision specialist

CONTROL ID: 3547308

SUBMITTER (NAME ONLY): Sunil Srivastava

TITLE: Predictive Relationship of OCT Characteristics for Efficacy in an Intravitreal Injection of Allogeneic Human Retinal Progenitor Cells (hRPC) for the Treatment of Retinitis Pigmentosa

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Srivastava, P.K. Kaiser, Cole Eye Institute, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|R. Kammer, B.D. Kuppermann, M.C. Mehta, J. Yang, H. Klassen, University of California Irvine, Irvine, California, UNITED STATES|D.S. Boyer, D. Liao, Retina Vitreous Associates, Los Angeles, California, UNITED STATES|J. Heier, A. Joseph, OCB, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sunil Srivastava: Commercial Relationship(s);Regeneron:Code C (Consultant);Abbvie:Code C (Consultant);Santen:Code F (Financial Support);Novartis:Code C (Consultant);Eyepoint:Code F (Financial Support);Allergan:Code F (Financial Support);Bausch:Code F (Financial Support) | Peter Kaiser: Commercial Relationship(s);J Cyte:Code F (Financial Support);J Cyte:Code C (Consultant) | Rebecca Kammer: Commercial Relationship(s);J Cyte:Code C (Consultant) | David Boyer: Commercial Relationship(s);J Cyte:Code F (Financial Support);J Cyte:Code C (Consultant) | Jeffrey Heier: Commercial Relationship(s);J Cyte:Code F (Financial Support);J Cyte:Code C (Consultant) | Baruch Kuppermann: Commercial Relationship(s);J Cyte:Code F (Financial Support);J Cyte:Code C (Consultant) | David Liao: Commercial Relationship(s);J Cyte:Code F (Financial Support) | Mitul Mehta: Commercial Relationship(s);J Cyte:Code F (Financial Support) | Anthony Joseph: Commercial Relationship(s);J Cyte:Code F (Financial Support) | Jing Yang: Commercial Relationship(s);J Cyte:Code F (Financial Support);J Cyte:Code I (Personal Financial Interest);J Cyte:Code C (Consultant);J Cyte:Code P (Patent);J Cyte:Code S (Non-remunerative) | Henry Klassen: Commercial Relationship(s);J Cyte:Code F (Financial Support);J Cyte:Code I (Personal Financial Interest);J Cyte:Code S (Non-remunerative);J Cyte:Code P (Patent)

ABSTRACT BODY:

Purpose: The recession of the ellipsoid zone (EZ) and more generally the thinning of the outer zone have become potential structural surrogates for disease severity in retinitis pigmentosa (RP). During a Phase 2b trial conducted to evaluate the intravitreal injection of allogeneic hRPC for treatment of RP, spectral-domain optical coherence tomography (SD-OCT) baseline characteristics of subjects were explored to identify predictors of efficacy in a more responsive target population.

Methods: In a post hoc analysis, a target subgroup of patients with less measurement variability was identified (n=37). From this subgroup, readable SD-OCT volumetric data (n=29; sham, n=10, low dose, n=9, high dose, n=10) was analyzed. Frame by frame macular cube scans were processed using automated segmentation followed by EZ mapping with manual correction for segmentation errors by masked graders. A three-dimensional volume map of the EZ-RPE for the entire macular cube generated measures of mean foveal thickness within the subfield or mid-subfield, mean central foveal thickness (CFT), EZ-RPE subfield or mid-subfield volume and thickness (with or without fluid). Correlational analysis was performed between each OCT parameter and change in each of the phase 2b trial endpoints from baseline to 12 months (Best Corrected Visual Acuity, Contrast Sensitivity, Kinetic Visual Fields, Low Luminance Mobility Test, and a VFQ).

Results: Two parameters from the OCT analysis demonstrated moderate to strong correlations in all trial endpoints in the high dose (single injection of 6×10^6 cells) target group with most relationships being statistically significant despite the small sample size. The parameters were mean CFT ($p < 0.05$ for BCVA, VF, CS, LLMT, VFQ) and mid-subfield mean EZ thickness ($p < 0.05$ for VF, CS, VFQ) with greater values in each parameter corresponding to greater improvement in endpoints. The low dose (3×10^6 cells) did not demonstrate a significant relationship.

Conclusions: Given the small number of subjects in the target population subset and the post hoc nature of the analyses, these results should be viewed cautiously. However, we believe that having a certain minimum EZ or mean CFT thickness will facilitate selection of a population with the greatest chance for response in a phase 3 study from the neutrophic effects of hRPCs

CONTROL ID: 3547309

SUBMITTER (NAME ONLY): Zihan Sun

TITLE: Longitudinal Changes of Macular Vessel Density in Preclinical Diabetic Retinopathy: An Optical Coherence Tomography Angiography (OCTA) Study

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Sun, F. Tang, Z. Tang, D. Yang, D. Ng, C. Cheung, Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, HONG KONG

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ABSTRACT BODY:

Purpose: To prospectively characterize the longitudinal changes of macular vessel density (VD) imaged by optical coherence tomography angiography (OCTA) in diabetic subjects without clinically detectable retinopathy.

Methods: We recruited diabetic subjects without diabetic retinopathy (DR) from an ongoing prospective, observational study conducted at a tertiary center in Hong Kong. DR progression was defined as a 2-step increase in severity level according to the modified Airlie House classification system. All subjects underwent OCTA with a swept-source OCT platform (DRI-OCT Triton, Topcon, Inc, Tokyo, Japan) with a 3mm*3mm volumetric scan centered at the macula. OCTA images of the superficial capillary plexus (SCP) and deep capillary plexus (DCP) were generated by IMAGENet6. After image quality control, we calculated VD by using a customized MATLAB program. In statistical analysis, we used the linear mixed-effect model to estimate the rates of VD changes over time in the SCP and DCP with adjustment of confounding factors.

Results: Over a median follow-up duration of 2.97 years, 16 eyes showed DR progression. After excluding these eyes with DR progression, a total 180 eyes of 111 subjects were included in the final analysis. In the longitudinal analysis, VD of the DCP significantly decreased ($P<0.0001$) over time after adjusting for age, duration of diabetes, axial length, mean arterial blood pressure, intraocular pressure, HbA1c, and image quality score. On the contrary, there was no detectable VD reduction in the SCP ($P=0.3$). The estimated rate of VD reduction at the DCP was $-0.41\%/year$ (standard error: 0.09; $P<0.0001$).

Conclusions: Macular vessel density of the DCP progressively decreased over time among eyes without DR, whereas that of the SCP did not show significant change. This longitudinal study adds to current cross-sectional evidence and suggests that OCTA can detect microvascular changes before clinically detectable signs occur, and hence may challenge the existing paradigms of disease monitoring of DR.

CONTROL ID: 3547310

SUBMITTER (NAME ONLY): Mohssen Kassir

TITLE: Improving Image Resolution of Ophthalmoscopy using Artificial Neural Networks

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Kassir, J. Guo, Department of Bioengineering, University of California Riverside, Riverside, California, UNITED STATES|X. Wang, Y. Zhang, Doheny Eye Institute, Los Angeles, California, UNITED STATES|X. Wang, Y. Zhang, Department of Ophthalmology, University of California Los Angeles, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adaptive optics has enabled in vivo imaging of the living human retina with diffraction limited spatial resolution and thereby can image the retinal structure at the cellular level. However, adaptive optics may not readily be available for all imaging modalities, and in some cases its performance may be compromised by incomplete compensation of ocular wave aberrations. We investigate a deep learning based method to enhance the spatial resolution of retinal images without or with adaptive optics.

Methods: Twelve high resolution retinal images were obtained using an adaptive optics near-confocal ophthalmoscope (AONCO) as the ground truth. To model the image blur induced by ocular optical defects, we introduced various wave aberrations (with varying Zernike coefficients up to the 7th order). To expand the dataset, the AONCO images were split into small patches (2820 patches/image on average). With 8 different blurring kernels applied, there were 270,736 image patches in total for training and testing. In application of the trained networks, the corrected patches were combined to form images of their original sizes.

The artificial neural network was based on a U-net architecture. We performed a 4-fold cross validation study with a quarter of the images reserved for testing per cross validation.

The normalized mean squared error (NMSE) and structural similarity index measure (SSIM) were calculated for the images before and after correcting for the blurring effects, using the ground truth images as the reference.

Results: After correction with the neural networks, the NMSE was reduced by 36% on average, from 0.063 ± 0.026 to 0.040 ± 0.013 . The SSIM was improved by 89% on average, from 0.22 ± 0.10 to 0.40 ± 0.14 . The improvements were significant (by paired t-tests, $p < 0.001$ for both the NMSE and the SSIM). Image examples are shown in Figures 1 and 2.

Conclusions: Our preliminary results showed that deep learning may be useful in correcting the retinal image blur caused by ocular wave aberrations. Further optimization with larger datasets and more types of blurring effects are underway to improve its performance and the generalizability of the network.

CONTROL ID: 3547311

SUBMITTER (NAME ONLY): Tiffany DeVine

TITLE: Development and characterization of an iPSC-derived RPE cell model of LCHAD-associated retinopathy

SESSION TITLE: Metabolism and protein processing: retina, photoreceptors and RPE

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. DeVine, G. Gaston, C. Harding, M. Gillingham, Molecular and Medical Genetics, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: A progressive chorioretinopathy is associated with Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHADD). The pathophysiology of LCHADD retinopathy is incompletely understood. We have established a cell model of LCHADD to explore disease mechanisms.

Methods: Four LCHADD fibroblast lines (HADHA c.1528G>C) were reprogrammed into iPSCs. Two wild type iPSC lines were purchased as controls. iPSCs were differentiated into RPE and assayed for several RPE markers, transepithelial electrical resistance (TEER), and ability to phagocytose labeled outer segments. RPE were fed palmitate (C16) and FAO was measured with the Seahorse bioanalyzer. Acylcarnitines were measured with tandem mass spectrometry. Beta-hydroxybutyrate (BOH) was assayed from transwells. Neutral lipids were detected using LipidTOX and triglycerides were measured. RPE were treated with H₂O₂ and C16, viability monitored by alamarBlue.

Results: All RPE lines showed similar expression of RPE markers. Wild type and LCHADD RPE were able to phagocytose outer segments. TEER in wild type ($288 \pm 13 \Omega/\text{cm}^2$) and LCHADD ($277 \pm 14 \Omega/\text{cm}^2$) RPE was similar. The basal oxygen consumption rate (OCR) for wild type RPE increased after C16 compared to BSA alone (41 ± 6.7 BSA to 68 ± 8.5 BSA-C16, $p < 0.0001$). In contrast, no change was observed in LCHADD (45 ± 7.7 BSA, 51 ± 4.7 BSA-C16). Apical levels of BOH increased in wild type RPE when treated with BSA-C16 ($p < 0.002$) with no significant change in LCHADD RPE. Increased triglycerides and neutral lipid staining were observed only in LCHADD RPE after C16 exposure. Media from LCHADD RPE accumulated palmitoyl (C16) and 3-hydroxypalmitoyl-carnitine (C16-OH). When treated with H₂O₂ in the presence of C16, LCHAD RPE showed a decrease in viability compared to wild type RPE ($p < 0.0001$).

Conclusions: LCHADD RPE have impaired FAO and ketone body production. Acylcarnitine profiles from LCHADD RPE are similar to those of LCHADD patients. The viability of LCHADD RPE decreased when treated with H₂O₂ in the presence of long-chain fats. LCHADD RPE may be more susceptible to oxidative stress due to the accumulation of toxic metabolic intermediates such as C16-OH.

CONTROL ID: 3547312

SUBMITTER (NAME ONLY): Mikaela Louie

TITLE: Direct comparison of in vitro retinal organoids with in vivo eye development using Rax-Cre;tdTomato mice and iPSC-derived retinal organoids

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Louie, A. Miltner, S.K. Cheema, A. La Torre, N.L. Brown, Cellular Biology and Human Anatomy, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our understanding of the molecular steps of mammalian eye development remains incomplete. This holds especially true for early eye development where in vivo experiments are difficult due to the small size of the tissue. Here, we directly compared in vitro differentiation of stem cells into retinal tissue or, retinal organoids (ROs), to in vivo eye development, using BAC transgenic Rax-Cre and flox-stop tdTomato (Ai9) lineage reporter mice. Embryos of the same genotype were used to make the stem cell lines for RO differentiation. The Rax/Rx transcription factor is one of the earliest genes to demarcate the eye field. The time-course and characteristics of ROs arising from these lines were directly compared to in vivo eye formation.

Methods: Embryos containing both Rax-Cre and Ai9 transgenes were previously reported to recapitulate Rax spatiotemporal expression during early eye formation eye (Bosze et al., 2020). We extended the time course of Ai9 expression during embryogenesis using live imaging and immunofluorescence. The morphologic and molecular progression of ROs, derived from double-transgenic iPSC lines, using established protocols (Sasai et al 2011, La Torre et al. 2016), was analyzed by the same methods, plus RT-qPCR.

Results: Rax-Cre;Ai9 (Rc;Ai9) embryos show Ai9 expression from the embryonic day 7.5 (E7.5). At E9.5 and E11.5, the developing ventral diencephalon -including the optic vesicle- and telencephalon express high levels of Ai9. Rc;Ai9 undifferentiated stem cell colonies are indistinguishable from mouse embryonic stem cells (mESCs). When differentiated into ROs, retinal markers increase in expression while markers of pluripotency are down-regulated, comparable to differentiated mESCs. Ai9 expression began on day 4 and, by day 6, all ROs expressed Ai9. Interestingly, these cells respond to well-known morphogens such as Sonic Hedgehog (Shh). Hence, the addition of Shh changes proliferation rates compared to control ROs.

Conclusions: The Rc;Ai9 mice have been shown a to be a powerful tool for retinal lineage tracing. Similarly, Rc;Ai9 ROs mimic normal developing retinas in gene expression, cell morphology, and Ai9 expression. Importantly, these ROs can be used to study molecular mechanism early development, and also to inform strategies to advance the current protocols to generate ROs.

CONTROL ID: 3547313

SUBMITTER (NAME ONLY): Emily Watson

TITLE: The relationship in binocular summation between high and low contrast letter acuities

SESSION TITLE: Eye Movements and Binocular Vision

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Watson, D. Yu, The Ohio State University, The Ohio State University, Columbus, OH, US, academic, Ohio, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Emily Watson: Commercial Relationship: Code N (No Commercial Relationship) | Deyue Yu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Binocular summation is a well-known phenomenon in letter acuity measurement. This study is to examine the relationship in binocular summation between high and low contrast letter acuities using common commercially available visual acuity charts and investigate whether people who exhibit stronger binocular summation at high contrast tend to have greater summation at low contrast.

Methods: Corrected high and low contrast letter acuities were assessed monocularly and binocularly in 325 normal vision observers aged 18 to 40 years using Bailey-Lovie charts. All observers had high contrast acuities of 0.1 LogMAR or better and no known eye disease. Binocular summation was calculated as the difference in LogMAR between the better eye acuity and binocular acuity.

Results: At high contrast, letter acuities for right, left and both eyes were -0.066 ± 0.004 (SE), -0.065 ± 0.004 , and -0.130 ± 0.003 , respectively. The corresponding acuities at low contrast were 0.087 ± 0.006 , 0.087 ± 0.006 and -0.007 ± 0.005 . Consistent with previous studies, we found binocular summation at both contrast levels with higher magnitude of summation at low contrast (0.045 ± 0.002 for high and 0.068 ± 0.003 for low contrast). Binocular summation at high contrast had a weak correlation with summation at low contrast ($r = 0.116$, $p = 0.036$), whereas it had a strong inverse relationship with the change in binocular summation between the two contrast levels ($r = -0.614$, $p < 0.001$).

Conclusions: Using common commercially available letter acuity charts, we replicated the findings on binocular summation for acuity in normal vision for both high and low contrast letters. While overall binocular summation is greater for low contrast acuity, people who exhibit stronger binocular summation at high contrast tend to have less enhanced (or even reduced) summation for low contrast acuity.

CONTROL ID: 3547319

SUBMITTER (NAME ONLY): Marcel Bernucci

TITLE: Measuring S, M, and L cone sensitivities in the living human eye using phase-sensitive AO-OCT

SESSION TITLE: Advances in Retinal Imaging

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Bernucci, K. Kurokawa, Y. Liu, J.A. Crowell, D.T. Miller, School of Optometry, Indiana University Bloomington, Bloomington, Indiana, UNITED STATES|F. Zhang, Center for Devices and Radiological Health, US Food and Drug Administration, Silver Spring, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Human color vision is based on the spectral sensitivities of S, M, and L cone photoreceptors, yet methods to objectively measure cone sensitivity as a function of wavelength over the entire visible light spectrum in the living human eye still do not exist. Here, we demonstrate a new, high resolution method based on phase-sensitive adaptive optics optical coherence tomography (AO-OCT) for measuring spectral sensitivities of the three different cone types.

Methods: AO-OCT volumes of $1^\circ \times 0.8^\circ$ at 3.8° temporal retina were acquired over 5 s for two color normal subjects. At 2.5 s, a 5 ms flash of 450 nm, 520 nm or 635 nm light with variable strength was delivered to the retina. The resulting temporal changes in the cone outer segment optical path length (ΔOPL) were extracted from the volume images and used to determine the spectral type [1] and sensitivity of each cone. Sensitivity was determined by fitting the cones' average peak response at each wavelength to a power function of stimulus photon strength after compensating for lenticular and macular absorption. We then separately scaled the measured sensitivity function for each cone type to best align with widely accepted psychophysical measurements [2]. In both subjects, spectral sensitivity 95% confidence intervals (CI) were calculated for S, M, and L cone types at the three stimulus wavelengths by computing the average and standard deviation values of S, M and L cone average peak response per stimulus flash strength and using the resulting probability distributions to estimate the CIs via a Monte Carlo simulation.

Results: For both subjects, CI were $<6.0\text{e-}3$ at all wavelengths and for all cone types (except we had insufficient response to calculate a CI for S cones at 635 nm). After aligning our data to the psychophysical results, the least-squares error across 450 nm, 520 nm, and 635 nm wavelengths for S, M, and L cones, respectively, was $[5.50\text{e-}4, 2.62\text{e-}4, 2.4\text{e-}3]$ for Subject 1, and $[1.04\text{e-}4, 3.4\text{e-}2, 1.23\text{e-}4]$ for Subject 2.

Conclusions: We demonstrate the first objective measurements of cone spectral sensitivities using phase-sensitive AO-OCT. Excellent agreement is obtained with Stockman & Sharpe's psychophysical measurements.

[1] Zhang, et al. PNAS 116.16 (2019): 7951-6.

[2] Stockman, A., & Sharpe, L. T. (2000). Vision Res. 40, 1711-1737.

CONTROL ID: 3547322

SUBMITTER (NAME ONLY): Timothy Maley

TITLE: The Use of Optogenetics to Study Inhibition in the Ex Vivo Mouse Electroretinogram

SESSION TITLE: Retinal Circuitry

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T.D. Maley, E. Eggers, Physiological sciences GIDP, University of Arizona, Tucson, Arizona, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Timothy Maley: Commercial Relationship: Code N (No Commercial Relationship) | Erika Eggers: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The mouse Electroretinogram is a well characterized tool used to measure hyperpolarization of photoreceptors followed by excitatory activation of bipolar cells and ganglion cells across the entire retina. While the interaction of inner retinal neurons can be measured, we are not able to measure inhibition in isolation across the entire retina. Previous data has shown that inhibition likely plays an important role in light adaptation. Finding a way to measure inhibition across the entire retina could be an important tool to understanding the mechanisms of light adaptation and the role inhibition plays.

Methods: Retinas were isolated from 7-10 week old B6.Cg-Tg(Slc32a1-COP4*H134R/EYFP) male and female mice and placed in a custom ERG chamber. Retinas were perfused with Ringers solution and bubbled with 95% O₂-5% CO₂. These mice contain ChR2 in the inhibitory amacrine and horizontal cells under the VGAT promoter and were optogenetically activated with 5ms, (20 hz frequency) light stimulations (λ 470 nm) at 3.19×10^9 photons/ μm^2 . ERGs were recorded under ambient room light. Photoreceptor inputs were pharmacologically blocked with CNQX (25 μM), APV (50 μM), ACET (1 μM), and L-AP4 (50 μM). Inhibitory responses were blocked with TPMPA (50 μM), Gabazine (20 μM), and Strychnine (5 μM). D1 receptors were agonized with SKF-38393 (20 μM). Normalized peak amplitudes of the 1st (fast) and 2nd (slow) responses were calculated for each response before and after antagonizing the GABA_C, GABA_A and Glycine receptors.

Results: Treatment with GABA_C, GABA_A and Glycine receptor antagonists (n=5) did not cause significant changes to the fast response. This suggests the response is a measurement of the depolarization of amacrine and horizontal cells. However, the inhibitory block did cause a significant decrease in the normalized peak amplitude of the slow response. This suggest the slow response is likely a measure of inhibition generated by the activation of amacrine cells in the INL. Furthermore, the application of a D1 agonist (n=4) did not cause a change in the normalized peak amplitude of the slow response.

Conclusions: Optogenetic activation of ChR2 in the inhibitory amacrine and horizontal cells may be a novel way to measure inhibition across the entire retina. It is also possible to isolate the amacrine cell mediated inhibitory circuits in the mouse retina by blocking upstream photoreceptors and recording from bipolar cells.

CONTROL ID: 3547326

SUBMITTER (NAME ONLY): Ali Salehi

TITLE: Dense Optic Nerve Head Deformation Estimated using CNN as a Structural Biomarker of Glaucoma Progression

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Salehi, M. Balasubramanian, Electrical and Computer Engineering, The University of Memphis Herff College of Engineering, Memphis, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ali Salehi: Commercial Relationship: Code N (No Commercial Relationship) | Madhusudhanan Balasubramanian: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucomatous structural changes are observable non-invasively using optical imaging techniques. The aim of this study is to test the hypothesis that our newly designed convolutional neural networks (CNN) trained for estimating transformations in generic image sequences can be useful for estimating glaucomatous progression from confocal image sequences of the optic nerve head (ONH).

Methods: Optical flow provides a dense pixel-wise estimate of a scene transformation from an image sequence. We propose the average magnitude of flow velocities within the ONH region as a structural biomarker of glaucoma progression. Dense ONH structural transformation between a baseline scan and the most recent follow-up scan was estimated using various pre-trained CNNs namely FlowNet Correlation and FlowNet2¹, Teney², and our newly designed compact deep-dilated CNN (DDCNet) framework³. Diagnostic accuracy of the proposed flow-based structural biomarker was evaluated using longitudinal HRT-II exams of study participants in the UCSD Diagnostic Innovations in Glaucoma Study. 36 eyes progressed by stereophotos or visual field guided progression analysis, and 21 eyes were longitudinal normal eyes. Diagnostic sensitivity and specificity were estimated using a maximum likelihood classifier.

Results: The area under the ROC curve, sensitivity, and specificity of our deep-learning methods for estimating ONH structural transformations and other legacy computational methods (POD framework and TCA⁴) are presented in Table 1.

Conclusions: CNNs trained to estimate dense transformations in generic scenes were able to detect glaucomatous progression from HRT scans of the ONH with higher diagnostic accuracy. We anticipate that fine-tuning these networks using ONH sequences may further improve their diagnostic performance. Further, we conclude that the average magnitude of ONH structural changes estimated using the CNNs is a robust candidate biomarker for detecting glaucoma progression.

CONTROL ID: 3547327

SUBMITTER (NAME ONLY): Bruce Burkemper

TITLE: Risk Factors for lens opacities in African Americans: The African American Eye Disease Study (AFEDS)

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Burkemper, R. McKean-Cowdin, X. Jiang, Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M. Torres, R. Varma, Ophthalmology, Southern California Eye Institute, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine independent risk factors (RFs) for lens opacities (LOP) in a population-based study of African Americans (AAs) ages 40 and older.

Methods: AFEDS participants, residents of Inglewood, Los Angeles County, California, completed a detailed questionnaire and comprehensive ophthalmic examination. Clinical ophthalmologists performed slit lamp exams and diagnosed LOP according to the Lens Opacities Classification System II (LOCS II). Cases were subdivided into 4 mutually exclusive categories based on opacity type present in either eye: nuclear only (NUC), cortical only (COR), post-subcapsular only (PSC) and mixed (MIX: >1 LOP type present). Multivariable logistic regression models identified factors independently associated with each LOP category (except PSC, due to too few cases).

Results: After excluding those with bilateral cataract surgery and missing LOCS II grades, LOP among the remaining 5867 AFEDS participants were distributed as follows—NUC: 602 (10.3%), COR: 622 (10.6%), PSC: 21 (0.4%), MIX: 1386 (23.6%); 3200 subjects with no LOP in either eye were the reference group for each model. Higher waist-hip ratio (WHR) was an RF for each LOP category: after controlling for all covariates, 4th vs 1st WHR quartile subjects were 47% more likely to have NUC (OR 1.47, 95% CI 1.09-2.00), 46% more likely to have COR (OR 1.46, 95% CI 1.12-1.92), and 59% more likely to have MIX (OR 1.59, 95% CI 1.23-2.04). Older age and being unemployed were additional RFs shared among all LOP categories. Protective factors included taller height (COR) and alcohol use (NUC). Greater comorbidities and smoking were additional RFs for NUC. Additional RFs for MIX included female sex, low education, diabetes, glaucoma, shorter axial length and high systolic blood pressure (alcohol use was protective, as with NUC).

Conclusions: AFEDS is the largest population-based study exclusively of AAs and provides a unique opportunity to identify RFs for ocular diseases such as LOP. Three RFs are common to each category of LOP examined, one of which (WHR) represents a modifiable risk factor. Factors leading to greater WHR, such as a sedentary lifestyle and poor diet, likely increase LOP risk in AAs. RFs for the most prevalent LOP category (mixed) also include high systolic blood pressure and diabetes, providing additional evidence for a link between obesity and increased LOP risk in AAs.

CONTROL ID: 3547329

SUBMITTER (NAME ONLY): Rose Tan

TITLE: Evaluation of chorioretinal vascular changes in diabetic kidney disease using optical coherence tomography angiography

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To evaluate the retinal and choroidal vasculature changes in type 2 diabetic patients with and without chronic kidney disease using optical coherence tomography angiography (OCTA).

Methods: Cross-sectional study. One hundred and two diabetic patients without diabetic kidney disease (DKD) and 28 with DKD recruited from a tertiary eye clinic in Singapore, were included in this study. All subjects aged 40 years old and above. DKD was defined as an estimated glomerular filtration rate (eGFR) below 60mL/min/1.73m^2 . All subjects underwent $3\times 3\text{mm}^2$ scans using a swept-source optical coherence tomography angiography (PlexElite 9000, Zeiss Meditec). Vessel density (VD) and perfusion density (PD) were evaluated separately for large vessels and capillaries in the superficial vascular plexus (SCP). For the choroidal vasculature, flow void density was evaluated on the choriocapillaris slab. All OCTA metrics were compared between the two groups using a t-test.

Results: The VD was significantly higher in the DKD group compared with the non-DKD group only for large vessels (4.0 ± 0.7 vs 3.6 ± 0.6 , $p = 0.005$). There was no significant change in VD for capillaries between the two groups (14.7 ± 3.6 vs 15.1 ± 2.8 , $p = 0.58$). The PD of large vessels and capillaries was not significantly different between the two groups (all $p > 0.1$). Choriocapillaris flow void density was significantly higher in the DKD group compared with the non-DKD group (18.2 ± 1.8 vs 17.2 ± 1.3 , $p = 0.01$).

Conclusions: Type 2 diabetic subjects with chronic kidney disease have increased vessel density in the large retinal vessels and increased choriocapillaris flow void density compared with subjects without DKD. Larger sample size is required to understand if these chorioretinal vasculature changes are independent of diabetic retinopathy.

CONTROL ID: 3547330

SUBMITTER (NAME ONLY): Brittini Scruggs

TITLE: Transient vision loss associated with aflibercept pre-filled syringes

SESSION TITLE: Anti-VEGF therapy for AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Scruggs, D.J. Lee, M. Thomas, A. Faridi, Department of Ophthalmology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|A. Faridi, Department of Ophthalmology, Veterans Affairs Portland Health Care System, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe cases of significant vision loss following intravitreal aflibercept (Eylea™; Regeneron) injections using pre-filled syringes (PFS), which were approved by the Food and Drug Administration (FDA) in 2019.

Methods: All retina specialists (N=13) at Oregon Health & Science University and the Veterans Affairs Portland Medical Center were queried in December 2020 to determine their experience with aflibercept PFS. The specialists were asked to report any episodes of post-injection severe vision loss with or without the need for an anterior chamber paracentesis after administering aflibercept PFS. Medical records of all patients who had this complication were reviewed for demographics and pertinent ocular history.

Results: All specialists reported using aflibercept PFS starting in February 2020 when the PFS was made available at our institutions. Three specialists had no cases of vision loss with PFS use, whereas 10 specialists (76.9%) reported a perceived increase in post-injection vision loss with aflibercept PFS. There were 16 reported events of no light perception (NLP) or light perception (LP) vision immediately after aflibercept PFS. Seven physicians reported one case each; another specialist described two cases; one reported three events; and one reported four events. Chart review was performed for 12 of these events. The indication for aflibercept was exudative age-related macular degeneration (N=8), diabetic macular edema (N=3), or central serous retinopathy (N=1). The median age of the affected patients was 71 years (range 49-94). Two patients were being treated for glaucoma (N=1) or ocular hypertension (N=1); one patient was a glaucoma suspect. Three patients required anterior chamber paracentesis, and the remaining patients had improved vision without procedural intervention.

Conclusions: Pre-filled syringes have several advantages over traditional vial packaging (e.g., reduced total injection time, decreased endophthalmitis rates). However, retina specialists in our institution have noted numerous cases of transient central retinal artery occlusions with the recent adoption of aflibercept PFS. As a result, the majority of affected patients have reported increased injection-related anxiety. Further studies by our team include comparing PFS and traditional 1mL syringes as well as developing a national survey for query of retinal specialists performing aflibercept injections using pre-filled syringes.

CONTROL ID: 3547331

SUBMITTER (NAME ONLY): Patrick Donegan

TITLE: Patient Knowledge of Potential Ocular Toxicity from Systemic Medications in a Veterans Administration Eye Clinic

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P.J. Donegan, Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|P.J. Donegan, Vanderbilt University School of Medicine, Nashville, Tennessee, UNITED STATES|A. Chomsky, VA Tennessee Valley Healthcare System, Nashville, Tennessee, UNITED STATES|A. Chomsky, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: The purpose of the study is to determine the patient knowledge rate of potential ocular toxicity from systemic medications, specifically hydroxychloroquine, amiodarone and ethambutol. Secondly, the study aims to determine if there are certain patient characteristics or prescribing provider types that may impact that knowledge rate.

Methods: A cross-sectional survey was carried out among 37 patients presenting to the Nashville Veterans Affairs Medical Center Eye Clinic between November 2020 and January 2021 using a questionnaire. Patients taking amiodarone, ethambutol, or hydroxychloroquine were asked if they could identify what medication they were taking, if they knew it could cause eye toxicity, and if they recall receiving education from the prescriber. Data were summarized with descriptive statistics while Fisher's exact test was used for categorical variables at $p < 0.05$.

Results: Among 37 patients surveyed to date, 73% knew why they were having an eye exam that day, 78% correctly identified the medication they were taking, and 46% were aware of the medication's potential ocular toxicity. Age over 70 years was significantly associated with not knowing their medication could cause ocular toxicity ($p=0.007$), while correctly identifying which medication they were on failed to show a statistical significance ($p=0.44$). Greater knowledge of medication toxicity among patients with trainee prescribers (defined as resident physicians or fellows) was found to be statistically significant compared to nurse practitioners ($p=0.01$) and non-trainee physicians ($p=0.04$). Among all groups, no comparisons showed statistical significance in correctly identifying the medication they were taking.

Conclusions: Our results suggest that there are significant differences in knowledge of medication ocular toxicity in a Veterans Affairs patient population depending on patient age and prescribing provider. Non-elderly patients and those prescribed their medication by a trainee were more likely to know that their medication could cause ocular toxicity. This study is limited by its small sample size.

CONTROL ID: 3547332

SUBMITTER (NAME ONLY): Ashley Sohn

TITLE: Age as a prognostic factor for the visual or surgical outcome after scleral buckle (SB) or pneumatic retinopexy (PR) for primary macula-off rhegmatogenous retinal detachment (RRD)

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.H. Sohn, G. Sanchez, J. McGinnis, D. Mantopoulos, Ophthalmology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, UNITED STATES]

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ABSTRACT BODY:

Purpose: To determine whether a patient's age changes the visual or surgical outcome following SB or PR for repair of a primary macula-off RRD.

Methods: Retrospective, consecutive case series. The charts of patients who presented to our institution with a primary macula-off RRD between January 2012 and October 2020 were reviewed. Those who underwent treatment with SB or PR were included. These patients were divided into the following two age groups: (A) ≤ 60 years-old and (B) ≥ 61 years-old. The primary outcome was postoperative BCVA. The secondary outcome was single-surgery anatomic success (SSAS) rate.

Results: Of the 193 patients who underwent PR or SB, 45 met inclusion criteria. Twenty-seven of them were male. The mean age \pm SD was 57.1 ± 15.1 years-old. The mean follow-up period was 9.4 ± 14.2 months. From these, 21 (47%) were in age group A and 24 (53%) were in age group B. In the SB group, the final mean logMAR (Snellen) BCVA was 0.72 (20/100) for group A and 0.51 (20/63) for group B ($p = 0.36$). In the PR group, the final mean logMAR (Snellen) BCVA was 0.14 (20/25) in group A and 0.33 (20/40) in group B ($p = 0.09$). From those who underwent PR, the SSAS rate was 80% in group A compared to 57% in group B ($p = 0.24$). The SSAS rate of SB was 91% in group A compared to 80% in group B ($p = 0.47$).

Conclusions: Despite the strong trend for different outcomes between the different subgroups, the patient's age was not found to have a prognostic significance for the final surgical or visual outcome after RRD repair with SB or PR. More studies with a larger sample size are needed to confirm or reject this hypothesis.

CONTROL ID: 3547333

SUBMITTER (NAME ONLY): Sangwan Park

TITLE: Evaluation of function-related corneal endothelial markers in TAZ deficient mice over time

SESSION TITLE: Corneal endothelium

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Mice deficient in *Wwtr1*, the gene that encodes transcriptional co-activator with PDZ-binding motif (TAZ), show softer Descemet's membrane and decreased corneal endothelial cell (CEnC) density reminiscent of late-onset Fuchs' endothelial dystrophy in humans. The purpose of this study was to evaluate the expression of proteins critical to barrier and pump functions of CEnC in wildtype (WT) and homozygous TAZ (*Wwtr1*^{-/-}) and heterozygous TAZ deficient (*Wwtr1*^{+/-}) mice over time.

Methods: At least 3 corneas from different animals were collected for each genotype from various age groups (2, 6, 12, and 16 months old). After fixation, corneas were dissected from enucleated globes. Corneal flatmounts were sectioned into several pieces and incubated with primary antibodies against zonula occludens-1 (ZO-1) and Na/K-ATPase separately for evaluation of barrier and pump function of corneal endothelium, respectively. Subsequently, tissues were incubated with fluorophore conjugated secondary antibodies and nuclei were counterstained with DAPI. Whole-mount corneal tissues were mounted endothelial side up on a slide and were imaged using a fluorescent microscope with 20X and 40X objectives.

Results: In WT mice, ZO-1 staining demonstrated a typical hexagonal pattern with a zig-zag distribution along the cell border while Na/K-ATPase demonstrated expected finger-like projections along the basolateral membrane. The *Wwtr1*^{+/-} mice showed an expression pattern similar to WT for both markers over time. However, the *Wwtr1*^{-/-} exhibited different patterns of expression although high variability existed between animals and regions of the cornea. Specifically, ZO-1 staining was disrupted or absent resulting in partial loss of hexagonal appearance from 2 months old and Na/K-ATPase staining had a more diffuse and lobulated staining pattern lining the cell membrane from 6 months old in *Wwtr1*^{-/-} mice when compared with WT controls.

Conclusions: Data demonstrated that homozygous TAZ deficiency caused partial loss of ZO-1 expression and altered immunolabeling of Na/K-ATPase in the corneal endothelium of mice. These findings could potentially affect the barrier and pump function and further study is needed to explain the pathophysiologic mechanism and clinical significance for these findings.

CONTROL ID: 3547334

SUBMITTER (NAME ONLY): Debra Goldstein

TITLE: Uveitic Macular Edema: OCT Anatomic and Temporal Biomarkers

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Kapik, T.A. Ciulla, Clearside Biomedical Inc, Alpharetta, Georgia, UNITED STATES | D.A. Goldstein, Ophthalmology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, UNITED STATES |

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ABSTRACT BODY:

Purpose: To evaluate a potential correlation between best corrected visual acuity (BCVA) and optical coherence tomography (OCT) anatomic and temporal features in macular edema (ME) due to noninfectious uveitis (NIU). This analysis builds on a prior analysis which showed moderate correlation between BCVA and central subfield thickness (CST).

Methods: This post hoc analysis of uveitic eyes evaluated the relationship between BCVA and the presence of cystoid spaces, presence of subretinal fluid (SRF), and ellipsoid zone (EZ) integrity collected during two Phase 3, 24-week clinical trials. Correlation analyses evaluating baseline and change from baseline relationships were conducted. A longitudinal treatment-response analysis was created to model the temporal relationship between change in BCVA and CST. Early CST anatomic response, defined as a reduction in CST of 50 μ m or greater at 4 weeks, was assessed for relationship to BCVA prognosis.

Results: The analyzed data set included a total of 198 uveitic eyes. For EZ at baseline, mean BCVA progressively worsened with each EZ grade, trends which were not evident for cystoid space or SRF gradations. Eyes with normal EZ experienced greater 24-week change in BCVA than those with abnormal baseline EZ (11.9 vs 9.4 letters, $p=0.006$). In contrast, eyes without cystoid spaces and/or SRF with center-involvement at baseline showed less improvement (5.5 letters or 9.5 letters, respectively) improvement at 24 weeks, compared to those eyes with center-involvement (13.7 letters, $P=0.012$ or 17.2 letter, $P<0.001$, respectively). Longitudinal modeling in uveitic eyes showed a more rapid effect for CST than BCVA, with CST requiring approximately 3 weeks to reach over 90% of full response and BCVA requiring approximately 9 weeks to reach the same magnitude of response. Eyes that showed an early anatomical response, experienced a greater 24-week improvement in BCVA, compared to those without an early response (12.6 vs 4.9 letters, $P=0.007$ for difference).

Conclusions: Important and clinically meaningful relationships exist between BCVA and OCT anatomic and temporal features in eyes with uveitic macular edema, with anatomic improvement preceding BCVA improvement.

CONTROL ID: 3547335

SUBMITTER (NAME ONLY): Fred Nugen

TITLE: Effects of high myopia on in vivo compliance of anterior scleral canal opening and lamina cribrosa depth in juvenile tree shrews

SESSION TITLE: Environmental and genetics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. Nugen, M. El Hamdaoui, M.T. KhalafAllah, P. Fuchs, A. Levy, B.C. Samuels, R. Grytz, Ophthalmology and Visual Sciences, The University of Alabama at Birmingham, Birmingham, Alabama, UNITED STATES|M.J. Girard, Duke-NUS Medical School, Singapore, SINGAPORE|M.J. Girard, Ophthalmic Engineering & Innovation Laboratory, Singapore, SINGAPORE|A. Thiéry, Statistics and Applied Probability, National University of Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To investigate in vivo effects of high myopia on the deformation response of the anterior scleral canal opening (ASCO) area and lamina cribrosa (LC) depth with acute changes in IOP.

Methods: Juvenile tree shrews were randomly assigned to two groups: normal visual experience (n = 6) and monocular -10D lens treatment to induce high myopia (n = 6). Lens treatment started at 24 days of visual experience (DVE). At 59 DVE, eyes were cannulated and the optic nerve head was imaged via optical coherence tomography (Spectralis OCT2, Heidelberg Engineering) at four IOP levels (5, 15, 30, 45mmHg) with at least 5 minutes rest after IOP changes. A deep learning algorithm (Reflectivity, Abyss Processing) was trained with 489 manually segmented OCT scans and used for auto-segmentation of the anterior LC surface. ASCO points were manually segmented. ASCO area and central LC depth were computed in 3D and analyzed after nonlinear distortion correction (Grytz R, et al. IOVS 2020; 61: ARVO E-Abstract 4778) from 48 radial B-Scans per OCT scan. Mixed design analysis of variance split-plot ANOVA and Wilcoxon analysis were used to test for significant IOP-group interactions and group differences at each IOP level, respectively.

Results: ASCO deformations were small across all groups with significant changes in IOP-group interactions between treated and control eyes. For IOPs 30 and 45 mmHg, ASCO area changes were significantly higher in treated vs control eyes ($p < 0.05$). In a large number of eyes, ASCO area was decreasing with IOP (9/12 normal, 5/6 control, 3/7 treated). No significant differences were found for central LC depth changes.

Conclusions: Our results suggest that high myopia has a small but measurable effect on ASCO area changes with IOP in juvenile tree shrews. This increase in optic nerve head compliance during juvenile myopia may contribute to subsequent ONH remodeling and increased risk of glaucoma later in life.

CONTROL ID: 3547336

SUBMITTER (NAME ONLY): Ala Moshiri

TITLE: Retinal Nerve Fiber Layer Thickness in Normal Rhesus Macaques and in Animals with a Polymorphism in OPA1

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We measured the thickness of the circumpapillary retinal nerve fiber layer (RNFL) in normal rhesus macaques (*Macaca mulatta*) and also in animals with a single nucleotide polymorphism (SNP) in the OPA1 gene predicted to be pathologic. We hypothesized a decreased RNFL thickness in OPA1 mutants compared to normal counterparts. There is no treatment for Dominant Optic Atrophy (DOA) associated with mutations in OPA1 and a large animal disease model could accelerate clinical trials.

Methods: Seven primates with a SNP in the OPA1 gene and 51 wild type animals underwent ophthalmic exams that included a circumpapillary OCT scan of the RNFL. Electroretinography (ERG) was performed, including photopic negative response (PhNR) to assess retinal ganglion cell (RGC) function. Results of the RNFL scans were analyzed using a two-way ANOVA and Sidak's multiple comparison test. The PhNR results were analyzed with a Mann-Whitney non-parametric test.

Results: Female NHPs have thicker RNFL than males in the inferotemporal region at location 270 Degrees ($P=0.039$). There was no significant difference in the RNFL thickness between the OPA1 and wildtype groups at any location. However, when OPA1 animals were compared to age- and sex-matched individuals (Fig 1), two of the oldest OPA1 animals had RNFL thinning in the temporal and nasal regions. OPA1 animals as a group had reduced RGC function (Fig 2) as measured by PhNR at 72 ms ($P=0.0121$) and at the PhNR minimum ($P=0.0098$).

Conclusions: The RNFL of rhesus monkeys shows significant regional differences between sexes, as seen in humans. There were no RNFL differences between OPA1 animals and controls. However, when comparing the individual OPA1 mutants to age- and sex-matched wildtype counterparts, there was RNFL thinning in older OPA1 individuals. OPA1 animals had reduced RGC function when compared to wild type controls suggesting reduced function at all ages. Since DOA can have a relatively late onset of disease, it is possible animals with this OPA1 polymorphism represent an NHP model of hereditary optic neuropathy.

CONTROL ID: 3547337

SUBMITTER (NAME ONLY): Denise Loya

TITLE: Scleral lenses for the management of corneal irregularities. Visual and aberrometric outcomes in Mexico.

SESSION TITLE: Contact Lens

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Loya, G. Ortiz-Morales, M. Herrera-Rodriguez, J. Hernandez-Camarena, G. Garcia de la Rosa, J. Valdez-Garcia, Ophthalmology and Visual Sciences, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MEXICO]

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ABSTRACT BODY:

Purpose: To describe the performance of scleral lenses (SL) for visual rehabilitation in patients with corneal irregularities.

Methods: Retrospective review of clinical records of patients with corneal irregularities fitted with SL for visual rehabilitation. Data analyzed included demographics, medical history, spherical equivalent, keratometry measurements and SL parameters. Visual outcomes in logMAR and aberrometric parameters were assessed using paired t-tests before and after SL fitting. The level of statistical significance was taken as $p < 0.05$.

Results: Thirty-Three eyes of nineteen participants are included in this study. Mean age was 33.39 ± 13.44 years. 64.71% were male. The most frequent diagnosis was keratoconus (66.67%), followed by irregular astigmatism either by corneal grafts or scarring and post-LASIK ectasia. History of corneal crosslinking and keratoplasty was present in 41.18% and 5.88% of the patients respectively. Mean spherical equivalent was -9.70 D, Mean K1 46.10 ± 3.82 and K2 50.62 ± 6.33 D. Mean SL base curve was 7.43 and a mean power of -7.51D, all SL had a 15 mm diameter. Mean logMAR VA significantly improved from 1.03 ± 0.66 to 0.067 ± 0.14 ($p=0.0001$). Total Root Mean Square (RMS) values reduced from $10.065 \mu\text{m}$ to $0.710 \mu\text{m}$ ($p=0.03$) measured after SL fitting. No complications associated with SL use were reported.

Conclusions: Scleral lenses are effective in improving quantitative and qualitative optimal visual function in patients with irregular corneas by improving visual acuity and reducing ocular aberrations.

CONTROL ID: 3547338

SUBMITTER (NAME ONLY): Jayanth Kandukuri

TITLE: Correlation between ocular blood flow metrics and clinical metrics used for glaucoma assessment

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Kandukuri, K. Cho, A. Sinha, A. Rege, Vasoptic Medical, Inc., Baltimore, Maryland, UNITED STATES|A. Vinnett, S. Asanad, J. Pottenburgh, O. Saeedi, Ophthalmology, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: To assess the correlation between traditional metrics used for glaucoma assessment and ocular blood flow (OBF) metrics obtained with high temporal resolution using the XyCAM RI (Vasoptic Medical, MD, USA).

Methods: Unilateral imaging of duration six seconds using the XyCAM RI was done in a total of twenty healthy subjects, seventeen glaucoma suspect subjects, and ten subjects with moderate to severe glaucoma, as determined by the Hodapp-Andersen-Parrish criteria. As illustrated in Fig. 1, pulsatile OBF waveforms were obtained by averaging blood flow velocity index (BFVi) values in retinal vessels within the optic disc ("Disc Vessels"), and region of the optic disc with retinal vessels masked out ("Disc Perfusion"). From these waveforms, each cardiac cycle (from Dip to Dip) was isolated and three measurements were considered – Dip BFVi, Peak BFVi, and the mean BFVi over the cardiac cycle ("Cycle Mean"), and an average of each across all cardiac cycles from each subject. Pearson correlation coefficients were computed between these BFVi measurements and clinical data, including age, intraocular pressure (IOP), cup-to-disc ratio (CDR), OCT metrics such as minimum rim width (MRW) and retinal nerve fiber layer (RNFL) thickness, and visual field (VF) metrics including mean deviation and pattern standard deviation.

Results: As shown in Fig. 2, significant negative correlations were observed between all BFVi measurements and CDR, while correlations were inconclusive between BFVi measurements and IOP. BFVi in the Disc Vessels was significantly correlated with all considered OCT and VF metrics, whereas BFVi in the Disc Perfusion was significantly correlated only with MRW. Correlation between each of OCT and VF metrics and Dip BFVi is greater than their correlation with Peak BFVi.

Conclusions: OBF metrics obtained using the XyCAM RI may hold insights that are useful for glaucoma assessment and their clinical value should be investigated in greater detail in a prospective clinical trial.

CONTROL ID: 3547344

SUBMITTER (NAME ONLY): Wesley Brundridge

TITLE: Repair of the Lower Eyelid with the Versatile Bucket Handle Flap

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Brundridge, D. Holck, C. DeBacker, Eyeplastx, San Antonio, Texas, UNITED STATES|D. Berry, Paul L. Foster School of Medicine, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Many techniques have been described for the repair of lower eyelid cicatricial ectropion and large lower eyelid defects following Mohs surgical repair. A significant obstacle can be the incidence of post-operative cicatricial ectropion when repairing this area. The bi-pedicle Tripiier flap or “bucket handle” provides bulk, excellent vascularization, and support from the upper eyelid. We describe our surgical experience to previously described techniques.

Methods: A retrospective chart review was performed of two surgeon’s charts over a two year period. All patients’ charts that underwent a bucket handle flap were selected. Outcomes measured included underlying pathology, Mohs defect area, and total number of procedures performed on the individual patient. All patients were followed through postoperative month three.

Results: A total of 11 bucket handle flaps were performed. Five patients had a diagnosis of basal cell carcinoma, three patients had a diagnosis of squamous cell carcinoma, and the remaining three had cicatricial ectropion from previous lower eyelid surgery following Mohs surgery. The average defect area was 12.72 cm². One patient required a lateral tarsorrhaphy for neurotrophic keratopathy. Otherwise, no patients developed post op cicatricial ectropion, and no patients required further procedures.

Conclusions: The bucket handle flap is a useful technique for repair of cicatricial ectropion and large lower eyelid defects following Mohs repair. This technique allows for reconstruction of a challenging area with a low complication rate.

CONTROL ID: 3547345

SUBMITTER (NAME ONLY): Sumarth Mehta

TITLE: Characteristics of Nationwide ED Presentations of Acute Angle-Closure Glaucoma from 2008-2017

SESSION TITLE: Imaging in Glaucoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.K. Mehta, T. Mir, I.G. Freedman, A. Sheth, S. Sarrafpour, J. Liu, C. Teng, Ophthalmology and Visual Sciences, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|

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ABSTRACT BODY:

Purpose: Acute angle closure glaucoma (AACG) is an ophthalmologic emergency with a rising incidence in the United States. Nationwide data on the epidemiology and clinical characteristics of AACG are lacking despite the significant morbidity and costs associated with the condition. We performed a nationally-representative, retrospective cross-sectional study using the Nationwide Emergency Department Sample (NEDS).

Methods: NEDS was queried by ICD-9/10 code for cases of AACG in a ten-year study period from 2008 to 2017. Cases with AACG as primary ED diagnosis were included. Weights specified in NEDS were used to compute nationally representative estimates. Linear regression analysis and seasonality (Edwards and Hewitt's) tests were used to identify significant trends. Reported outcomes include trends in the incidence, demographics, seasonality, and economic impact of AACG.

Results: A total of 29,645 AACG related ED visits were identified nationally over the study period. AACG was found to occur most frequently among female patients in the seventh decade of life. Incidence increased significantly over the study period (average increase of 0.044 cases per 100,000 individuals per year, $p=0.01$). The most common systemic comorbidity was hypertension, and the most common procedures were iridotomy and iridectomy. The Northeast U.S. geographic region had the highest average incidence of AACG (1.18 per 100,000), followed by the West (0.96 per 100,000), South (0.93 per 100,000), and Midwest (0.73 per 100,000). Significant seasonal variation was seen nationally and in each region ($p<0.01$), with increased national incidence from July to December ($p=0.048$). Inflation adjusted charges associated with AACG related ED visits over the study period totaled \$152.8 million.

Conclusions: The rising incidence of AACG poses an increasing burden on the U.S. healthcare system. High-risk groups that may benefit most from preventative strategies include women, individuals of low socioeconomic status, and those between ages 50 and 70. Ophthalmologists should be aware of significant regional and seasonal trends in the presentation of AACG.

CONTROL ID: 3547346

SUBMITTER (NAME ONLY): Samarendra Mohanty

TITLE: An OCT guided laser microirradiation system for development of animal model of retinal degeneration

SESSION TITLE: Pathology and Pathobiology of AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mohanty, S. Kim, M. Carlson, S. Batabyal, W. Wright, Nanoscope Technologies LLC, Bedford, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Vision degradation caused by damage to the phototransduction circuitry of retina in dry-age-related macular degeneration (dry-AMD) represents the most common cause of irreversible vision loss in the ageing society. To date, no single mouse strain developing all the features of AMD exist. Also, there often is a need to target specific or multiple retinal cell types to emulate the disease model such as RGC associated damage in Glaucoma. In order to generate spatiotemporal rodent model for dry-AMD and other layer specific injury model, we integrated an irradiation laser with the optical coherence tomography (OCT) where temperature rise at micro-focused spots is significant enough to allow site and layer-specific injury.

Methods: We utilized real-time depth-resolved imaging by OCT for guidance of the microirradiation laser. OCT allows live imaging guidance to target specific area and enables live monitoring of the injury. Therefore, we improved the spatiotemporal aspect of the laser irradiation ablation model. With scanning control of the irradiation beam, arbitrarily shaped injury to selected retinal layer could be achieved. For selective damage of different cell types, the wavelength of irradiation laser was varied from visible to near infrared. In addition, to target specific layer and cell type, we tuned the focal plane of the microirradiation spot. The laser can be focused on specific layer by tuning the variable focal lens in the integrated system.

Results: Instantaneous swelling of the targeted layer occurred in response to the laser microirradiation, followed by change in OCT image contrast. Longitudinal OCT measurements of laser-injured retina exhibited progressive degeneration of targeted layer: photoreceptors or RPE without damaging other layers. Thinning of retina of laser-injured site correlated with focal ERG measurements.

Conclusions: Our results demonstrate successful development of OCT guided laser microirradiation system and its implementation for spatially targeted injury to specific retina layers and cell types. OCT guided laser based targeted microirradiation will enable development of animal models of retinal degenerative diseases while characterizing the disease progression and therapeutic intervention.

CONTROL ID: 3547348

SUBMITTER (NAME ONLY): Jesse Sengillo

TITLE: Long-term Outcomes of Fellow Eyes in Patients with Non-traumatic Rhegmatogenous Retinal Detachments due to Giant Retinal Tears

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Sengillo, A.L. Kunkler, H. Al-khersan, N.A. Yannuzzi, W.E. Smiddy, H.W. Flynn, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine clinical characteristics and long-term outcomes for fellow eyes of patients with a prior rhegmatogenous retinal detachment (RRD) due to a giant retinal tear (GRT)

Methods: Retrospective, observational analysis of patients evaluated at the Bascom Palmer Eye Institute for RRD secondary to GRTs. Patients with one or more years of follow-up were included. Patients with retinal detachments occurring in the setting of trauma were excluded.

Results: Of 44 patients who underwent retinal detachment repair for a non-traumatic GRT-associated RRD, 39 met inclusion criteria. The majority of patients were men in this cohort (n = 25, 64%). Average age at the time of initial retinal detachment repair was 67 (range 10-81). Mean follow-up time was 7 years (range 1-16 years). Risk factors for retinal detachment included lattice degeneration in 6 patients (15%) and myopia in 8 patients (21%). Eleven fellow eyes (28% of patients) in this cohort were pseudophakic. During follow-up of the fellow eye, 3 patients (8%) received prophylactic laser retinopexy for retinal tears (n=2) and a progressing schisis cavity (n=1). Six patients (15%) were diagnosed with retinal detachments that required surgery in the fellow eye during follow-up. One patient already had a prior history of retinal detachment in the fellow eye at presentation. Visual acuity of the fellow eye at the most recent visit was 20/40 or better in 33 patients (85%) and in just 2 of 6 (33%) patients who developed an RRD in the fellow eye.

Conclusions: In the current series we identify retinal tears and/or detachments to be relatively common in the fellow eyes of patients with a history of GRT associated RRD during follow-up. Regular dilated fundus exams are warranted for patients with a history of giant retinal tears.

CONTROL ID: 3547349

SUBMITTER (NAME ONLY): Erica Smith

TITLE: An evaluation of the use of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors (statins) and progression of age-related macular degeneration

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Smith, C. Kirk, S. Kirk, P. Bu, E.B. Stubbs, F. de Alba, Ophthalmology, Loyola University Health System, Maywood, Illinois, UNITED STATES|

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ABSTRACT BODY:

Purpose: Although age-related macular degeneration (AMD) is the leading cause of irreversible vision loss in the U.S. adult population, only vitamin supplementation and risk factor modulation are used to prevent progression of this disease from non-neovascular to neovascular. Prior studies have demonstrated a beneficial effect of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors (statins) on retinal physiology (Barathi 2014, Tian 2017, Zheng 2015). We performed a retrospective, observational clinical study to evaluate if statins protect against the progression of AMD from the non-neovascular to the neovascular form.

Methods: A retrospective chart review was performed for patient encounters with the ICD-9 and ICD-10 codes for non-neovascular or neovascular AMD from 2009 to 2019. Patients were included if they initially presented with non-neovascular AMD and if they were followed for at least two clinic visits. The resulting 1,631 patients were then divided into two groups based on whether or not they were on statin therapy—935 (57.3%) were on statin therapy and 696 (42.7%) were not. Patients were then evaluated for progression to neovascular AMD in at least one eye based on ICD-9 and ICD-10 codes for follow up encounters. A chi-square and odds ratio statistical analysis was used to evaluate if a difference exists between the patients on statin therapy and patients not on statin therapy with respect to progression from non-neovascular to neovascular AMD.

Results: Preliminary data analysis demonstrated that 57.3% of patients with non-neovascular AMD were taking a statin. Of these patients, 12.6% developed neovascular AMD. For patients who were not taking a statin, 11.2% progressed to neovascular AMD. This analysis did not demonstrate a protective effect of statins against progression from non-neovascular to neovascular AMD: χ^2 (2, N=1,631) = 0.75, p=0.39. The odds ratio for this analysis was 1.14 with a 95% confidence interval of 0.84-1.54.

Conclusions: Approximately half of our patients with non-neovascular AMD were on statin therapy. In this analysis, use of statins did not provide a protective benefit against progression from non-neovascular to neovascular AMD. Further studies regarding the relationship between statins and AMD as well as other treatment options for AMD are important due to the prevalence of this sight-threatening disease.

CONTROL ID: 3547352

SUBMITTER (NAME ONLY): Anthony Cruz

TITLE: Deconvolution of tumor immune microenvironment in uveal melanoma

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Cruz, Ophthalmology, University of Miami School of Medicine, Miami, Florida, UNITED STATES|S. Kurtenbach, J.W. Harbour, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|S. Kurtenbach, J.W. Harbour, Sylvester Comprehensive Cancer Center, Miami, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Anthony Cruz: Commercial Relationship: Code N (No Commercial Relationship) | Stefan Kurtenbach: Commercial Relationship: Code N (No Commercial Relationship) | J. Harbour: Commercial Relationship(s);Castle Biosciences:Code C (Consultant)

ABSTRACT BODY:

Purpose: Uveal melanoma (UM) is the most common primary eye cancer and remains uniformly fatal. In contrast to cutaneous melanoma, UM is an immunologically “cold” tumor that is poorly responsive to immunotherapy. The purpose of this study was to bioinformatically deconvolute the tumor immune microenvironment (TIM) after stratification for key molecular biomarkers associated.

Methods: RNA-seq data were downloaded from The Cancer Genome Atlas Uveal Melanoma (TCGA-UVM) dataset (n=80). Samples were stratified by gene expression profile (GEP) class 1 versus class 2, PRAME expression (negative versus positive), and LAG3 expression (low versus high). TIM deconvolution was performed using Quantiseq from the Immunedecconv R package.

Results: Class 2 UM were inferred to comprise 2.64-fold fewer CD4+ T cells ($p=0.0013$), 2.3-fold fewer myeloid dendritic cells ($p=0.026$), 1.74-fold more M2 macrophages ($p=4.37E-9$), 2.02-fold more NK cells ($p=1.2E-6$), and 53-fold more CD8+ T cells ($p=0.0007$) compared to class 1 UM. PRAME-positive UM contained 1.26-fold more M2 macrophages ($p=0.022$), 1.39-fold more NK cells ($p=0.005$), and 2.29-fold fewer CD4+ T cells ($p=0.0054$) than PRAME-negative UM. LAG3 expression was strongly associated with class 2 UM ($p=0.0026$), increased M1 ($p=0.00057$) and M2 macrophages ($p=5.6E-6$), NK cells ($p=0.016$), CD8+ T cells ($p=1.77E-11$), Tregs ($p=2.27E-5$), and decreased CD4+ T cells ($p=0.0045$).

Conclusions: The two strongest predictors of metastasis in UM – class 2 GEP and PRAME expression – are strongly associated with an inhibitory TIM. LAG3, which we recently showed by single cell RNA sequencing to be the predominant T cell exhaustion marker in UM, was associated with an increased global inflammatory signature. The data suggest that a subset of Class 2 Tumors are prime candidates for LAG3 Immune Checkpoint Inhibition. Correlation between key molecular biomarkers and TIM will facilitate the development of targeted immune therapy for patients with UM.

CONTROL ID: 3547353

SUBMITTER (NAME ONLY): Xuejuan Jiang

TITLE: Relationship between Retinal Nerve Fiber Layer Thickness and Visual Field Loss in a Multiethnic Glaucomatous Population

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Jiang, G. Richter, Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|D. Noursome, R. McKean-Cowdin, B. Burkemper, Preventive Medicine, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|M. Torres, R. Varma, Southern California Eye Institute, CHA Hollywood Presbyterian Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We investigated the relationship between retinal nerve fiber layer (RNFL) thickness and visual field loss among Latino, African, and Chinese American eyes with a clinical diagnosis of glaucoma.

Methods: We obtained data from 50+-year-old participants with a clinical diagnosis of glaucoma from three multiethnic population-based studies of eye diseases in the Los Angeles area: the Los Angeles Latino Eye Study (LALES), Chinese American Eye Study (CHES), and the African American Eye Disease Study (AFEDS). Imaging was completed using the Cirrus HD-OCT with the Optic Disc Cube 200x200 protocol. Scans with low signal strength (<6) were excluded. Associations between RNFL thickness and visual field loss (mean deviation) and potential covariates were assessed using multivariable linear mixed regression.

Results: There were 1742 OCT scans available from 966 individuals with glaucoma, including 263 Latinos, 348 Chinese Americans, and 355 African Americans. 58% were female. The average RNFL thickness was 86 μm (95% CI: 76-95 μm) among all glaucoma eyes. Average RNFL was lower in African American eyes than Chinese and Latino eyes, even after accounting for age, waist-hip ratio, axial length, and visual field mean deviation. Also, a significant interaction was observed between race/ethnicity and visual field defect on the average RNFL thickness and the inferior quadrant RNFL thickness ($P < 0.05$). With each decibel of loss in visual field mean deviation among glaucoma eyes, Chinese eyes and Latino eyes had more reduction in RNFL thickness (-1.03 and -1.00 μm , respectively) than African American eyes (-0.77 μm). This pattern was observed in the inferior quadrant as well.

Conclusions: This multiethnic population-based study suggests that the relationship between visual field loss and RNFL thickness in glaucoma varies by ethnicity/race. It indicates that race/ethnicity should be considered for the use of OCT in diagnosing glaucoma.

CONTROL ID: 3547354

SUBMITTER (NAME ONLY): Lan Yue

TITLE: Spatial pattern of the retinal activation by frequency modulated electrical stimuli

SESSION TITLE: Retinal prostheses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: L. Yue, P. Lo, M. Humayun, Ophthalmology, University of Southern California, Los Angeles, California, UNITED STATES|L. Yue, J. Castillo, P. Lo, M. Humayun, Ginsburg Institute for Biomedical Therapeutics, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: In the investigation of the electrically-elicited color perception in the blind Argus II patients, we found that increase of the stimulation frequency led to not only blue-shifted color percepts but also elongated shapes of the phosphene sensation in some patients. Here we studied the spatial characteristics of the retinal activation under frequency modulation (FM), seeking to decode the changes in the phosphene shape observed clinically.

Methods: We used Ca^{2+} imaging to visualize spatial responses in wholemount mouse retina (wildtype C57BL/6 mice). AAV2-CAG-GCaMP6f was used to impart Ca^{2+} -dependent fluorescence on mouse retinal ganglion cells (RGCs). The retina was acutely dissected 3-4 weeks after intravitreal injection of the viral vectors and the wholemount was placed in an electrode array embedded chamber for simultaneous electrical stimulation and optical recording. Biphasic stimuli of 1-ms pulse width were delivered repetitively for 1-s at the frequency ranging between 5 and 120 Hz, similar to those tested in humans. A cocktail of synaptic blockers was applied to pharmacologically isolate the ganglion cell. Changes in the fluorescence ($\Delta F/F$) of the pixels in the cells were analyzed.

Results: The resulting $\Delta F/F$ maps show that increased stimulation frequency led to marked enhancement in the RGC activation in the direction along the axons of passage opposite to the optic disc. In comparison, increased amplitude resulted in a uniform expansion of a focal activation in all directions. Increasing the stimulation frequency from 5 Hz to 120 Hz reduced the standard deviation of the activation angle ($\Delta\theta$) by an average of 60%, whereas increasing the stimulation amplitude while keeping a 5Hz stimulation rate did not result in a significant change in $\Delta\theta$. When the synaptic input to the RGCs was blocked, the directional activation resulting from FM was largely maintained whereas the focal activation resulting from amplitude modulation (AM) was substantially eliminated.

Conclusions: Increased stimulation frequency resulted in increasingly directional activation map of the RGCs, consistent with the elongated phosphene sensation reported by some Argus II patients. The insensitivity of the directional activation to synaptic blockers and the alignment between the activation direction and the axon orientation strongly suggest an antidromic mechanism that may involve enhanced activation by axonal multi-pulse integration.

CONTROL ID: 3547355

SUBMITTER (NAME ONLY): Jawad Khan

TITLE: Incidence of Second Primary Malignancy in Primary Optic Nerve Glioma: A US National Database Analysis

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Khan, Z. Hussain, F. Dihowm, Texas Tech University Health Sciences Center El Paso Paul L Foster School of Medicine, El Paso, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jawad Khan: Commercial Relationship: Code N (No Commercial Relationship) | Zain Hussain: Commercial Relationship: Code N (No Commercial Relationship) | Fatma Dihowm: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Advanced understanding of screening and therapeutic modalities acts as provision for increased survival in patients diagnosed with optic nerve gliomas. Second primary malignancies (SPM) and latency periods is currently an uncharacterized frontier. This US national database analysis showcases incidences of SPMs and latency periods in patients with optic nerve gliomas.

Methods: The Surveillance, Epidemiology, and End Results (SEER) database was executed for procurement of nationally de-identified cases of first primary optic nerve glioma. Standardized incidence ratios (SIR) and excess absolute risk (EAR) were calculated using the SEER-specific multiple outcome analysis. 95% SIR confidence intervals are demonstrated with statistical significance achieved at $p < 0.05$.

Results: 622 patients with primary optic nerve glioma were selected. Mean age was 14.6 ± 19 years (range 00–80). 315 (50.6%) patients and 307 (49.4%) patients were female and male, respectively. Relative to the US national population, patients afflicted with primary optic nerve gliomas demonstrated significantly increased risk for multiple SPMs. Primary malignancies originating from soft tissues (including the heart) (SIR 33.2, CI 6.9–97.1, EAR 5.1), breast (SIR 4.99, CI 1.4–12.8, EAR 5.6), female breast (SIR 5.0, CI 1.4–12.9, EAR 5.6), brain (SIR 105.4, CI 65.2–161.1, EAR 36.2), cranial nerves (SIR 103.3, CI 12.5–373.1, EAR 3.5), non-lymphocytic leukemia (SIR 15.6, CI 1.9–54.4, EAR 3.3), myeloid and monocytic leukemia (SIR 16.3, CI 1.97–58.8, EAR 3.3), and Kaposi sarcoma (SIR 79.9, CI 2.0–445.1, EAR 1.7) demonstrated significantly increased SIR as SPMs as showcased in Table 1. In totality, cumulative SPM (SIR 6.04, CI 4.3–8.2, EAR 59.6) showcases overall significance in incidence rates of SPM in patients diagnosed with optic nerve gliomas.

Conclusions: As compared to the US national population, diagnosis of first primary optic nerve gliomas prognosticates increased chances for formation of second primary malignancies, including tumors of all sites, soft-tissue, brain, cranial nerve, non-lymphocytic leukemia, myeloid and monocytic leukemia and Kaposi's sarcoma. Advancements related to diagnosis and treatment modalities may sustain survival. Yet, some treatments may increase incidence of malignancies. Clinical decision-making should reconcile enhanced propensities for development of second primary malignancies.

CONTROL ID: 3547356

SUBMITTER (NAME ONLY): Yukun Guo

TITLE: Nonperfusion area segmentation in three retinal plexuses on wide-field OCT angiography using a deep convolutional neural network

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Guo, T.T. Hormel, M. Gao, Q. You, J. Wang, C.J. Flaxel, S. Bailey, T.S. Hwang, Y. Jia, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: To train and validate a convolutional neural network (CNN) to segment nonperfusion areas (NPA) in three retinal plexuses on wide-field OCTA.

Methods: We obtained consecutive 6×6-mm OCTA scans at central macular, optic disc, and temporal regions on one eye from 202 participants in a clinical diabetic retinopathy (DR) study with a 70-kHz OCT commercial system (RTVue-XR; Optovue, Inc). Projection-resolved OCTA algorithm was applied to remove projection artifacts in voxel. We designed a deep convolutional neural network [Fig. 1 D] to detect NPA [blue in Fig. 1 E] and distinguish from signal reduction artifacts [yellow in Fig. 1 E] from superficial vascular complexes (SVC), intermediate capillary plexuses (ICP) and deep capillary plexuses (DCP). The input to the network contains the inner retinal thickness map [Fig. 1 A], reflectance mean projection [Fig. 1 B] and en face angiograms of montaged scans at three regions [Fig. 1 C]. In the temporal region where the ICP merges with the DCP, we treated the ICP and the DCP as a single slab for segmentation and NPA measurement. Expert graders manually determined the ground truth for NPA and signal reduction artifacts. Six-fold cross-validation was used to evaluate our algorithm on the entire dataset.

Results: This study had 202 participants, including 39 healthy controls, 25 participants with diabetes without retinopathy, 59 participants with mild to moderate nonproliferative DR (NPDR) and 79 participants with severe NPDR or proliferative DR (PDR). The signal strength index (SSI) ranged from 55 to 87. On the test set, the proposed algorithm had high agreement with ground truth on NPA detection in three retinal plexuses on montaged wide-field OCTA (F-score (mean±standard deviation): SVC 0.83±0.08, ICP 0.81±0.10, and DCP 0.78±0.12). The algorithm showed high performance on both healthy controls and eyes with varying severities of DR [Fig. 2]. Shown by all scans from healthy controls, the proposed method was independent of SSI (Pearson correlation, p-value = 0.146).

Conclusions: A deep learning network can accurately segment NPA in individual retinal capillary plexuses and distinguish from signal reduction artifacts prevalent on wide-field OCTA.

CONTROL ID: 3547358

SUBMITTER (NAME ONLY): Yesenia Dorantes Diez

TITLE: Is There a Benefit of Systemic Citicoline Administration in End-Stage Glaucoma Patients?

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y.Y. Dorantes Diez, Centro de Diagnóstico y Control del Glaucoma, Puebla, Puebla, MEXICO|Y.Y. Dorantes Diez, M.A. Ibañez Sandoval, L.A. Giorgi-Sandoval, Research and Development, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Research Department, Unidad de Diagnóstico Temprano de Glaucoma, Guadalajara, Jalisco, MEXICO|M.A. Ibañez Sandoval, M.Y. Guzmán Ornelas, School of Medicine, Universidad Guadalajara LAMAR, Guadalajara, Jalisco, MEXICO|M.A. Dorantes Diez, School of Medicine, Universidad Popular Autonoma del Estado de Puebla, Puebla, Puebla, MEXICO|

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ABSTRACT BODY:

Purpose: Glaucoma is the leading cause of irreversible blindness in the general population. End-stage glaucoma carries a relevant challenge in its clinical management. Some scientific evidence has suggested that citicoline can be used as a supplement to preserve vision in glaucoma patients. The aim of this study is to investigate the effect of systemically administered citicoline in the visual function in patients with end-stage glaucoma in a real-world setting.

Methods: A retrospective assessment of 134 electronic medical records of consecutive patients with end-stage glaucoma under treatment with citicoline (orally, 500 mg BID) for at least three months was performed. Clinical data including best-corrected visual acuity (BCVA), IOP, number of glaucoma medications, visual field indexes (VFI) evaluated by applanation tonometry, cup-to-disc (CD) ratio, peripapillary retinal nerve fiber layer (RNFL) and perimacular ganglion cell complex (GCC) thickness by OCT. Tolerability and safety issues were also recorded.

Results: From 134 patients under oral citicoline treatment, 27 were excluded; therefore, 206 eyes from 107 patients were analyzed in this study (58 females, 49 males). This population had a mean age of 68.0 ± 17.6 years and a greater proportion of primary open-angle glaucoma (60.7%), as well as at least two glaucoma medications (70.8%) for topical administration. Mean time of citicoline administration was 5.1 ± 0.7 months. Baseline measurements of IOP of both eyes (RE, 13.6 ± 6.3 mmHg; LE, 13.4 ± 5.8 mmHg; $P=0.80$) was not significantly different as compared to the last follow-up quantification (RE, 13.4 ± 6.1 mmHg; LE, 13.3 ± 6.0 mmHg; $P=0.86$). BCVA, VFI (with exception of LE mean deviation), CD ratio, CFNR and GCC were not statistically different when baseline mean values were compared to the ones measured in the last visit ($p>0.05$). Only mean deviation for the left eyes was different after comparison (-21.53 ± 10.36 mmHg; LE, -24.32 ± 8.4 mmHg; $P=0.005$). Minor headache (12.1%) and intermittent diarrhea (2.8%) were the only tolerability issues recorded. Twenty three patients (21.5%) claimed to have a subjective improvement in their vision.

Conclusions: In this retrospective "real world" study of end-stage glaucoma patients, no significant improvement was observed when citicoline was orally administered during a short-term period. Safety and tolerability were acceptable. A subjective improvement perception was uncommon.

CONTROL ID: 3547361

SUBMITTER (NAME ONLY): Charles Ludowici

TITLE: Development of preferred retinal loci for fixation in response to binocular asymmetric simulated central scotomas

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Ludowici, S.T. Chung, Optometry, University of California Berkeley, Berkeley, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Charles Ludowici: Commercial Relationship: Code N (No Commercial Relationship) | Susana Chung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The loss of the central visual field in macular disease means that patients must use peripheral vision to conduct most visual tasks. With time, most patients develop a preferred retinal locus (PRL) outside of their scotoma for visual tasks. To date, it is unclear how the PRL develops, especially in response to asymmetric progression of the disease in the two eyes. This study investigated how participants with normal vision develop a "PRL" in response to simulated bilateral central field loss; in particular, when the field loss is asymmetric in the two eyes.

Methods: We simulated central field loss with a gaze-contingent paradigm by tracking participants' gaze position as they performed a training task viewed through a stereoscope, and occluding a 2 degree circle around their gaze positions (the artificial scotoma) on the computer screens. Training consisted of repeated trials of identifying the orientation of a Tumbling-E. Participants performed multiple days of training. Oculomotor responses, including fixation stability, saccade latency and accuracy, were continuously monitored. To simulate the asymmetric progression of macular disease, we increased the size of the scotoma to 4 degrees in one eye after participants' oculomotor responses to the bilateral artificial scotoma reached a plateau.

Results: Participants' gaze positions were analyzed using a kernel density estimator to determine the location of the "PRL", defined as the most probable stimulus location relative to central gaze position. Each participant's "PRL" was initially within the scotoma, but over time shifted outside the artificial scotoma (regression coefficients for time and distance were positive, $p < .03$). When the size of the scotoma was increased in one eye, the distance between the PRL and central gaze did not increase with time like in the first phase of training, indicating that participants did not change the location of the PRL in response to binocular asymmetry.

Conclusions: Participants with normal vision are able to shift their "PRL" from central vision to outside a scotoma in response to bilateral simulated central field loss. Subsequent changes in the size of a scotoma, causing a binocular asymmetry, have little effect on the distance of the "PRL" from central vision. This finding suggests that the location of a PRL for patients with bilateral macular disease is likely governed by the better eye.

CONTROL ID: 3547365

SUBMITTER (NAME ONLY): Sarah Webster

TITLE: Regeneration of retinal neurons using an $\alpha 7$ nAChR agonist in adult murine disease models

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Webster, C. Linn, Biological Sciences, Western Michigan University, Kalamazoo, Michigan, UNITED STATES|N. Sklar, Western Michigan University Homer Stryker MD School of Medicine, Kalamazoo, Michigan, UNITED STATES|D. Linn, Biomedical Sciences, Grand Valley State University, Allendale, Michigan, UNITED STATES|D.C. Otteson, Optometry, University of Houston, Houston, Texas, UNITED STATES|
Commercial Relationships Disclosure (Abstract): Sarah Webster: Commercial Relationship: Code N (No Commercial Relationship) | Nathan Sklar: Commercial Relationship: Code N (No Commercial Relationship) | David Linn: Commercial Relationship: Code N (No Commercial Relationship) | Deborah Otteson: Commercial Relationship: Code N (No Commercial Relationship) | Cindy Linn: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The purpose of this research was to test the hypothesis that PNU-282987 (PNU) causes regeneration of neurons lost to damage in adult mice.

Methods: Male and female 129/SvJ wild-type and Rbp1-CreERT2;Rosa26-tdTomato transgenic mice (3 to 6 months) were used. Glaucoma-like damage was elicited using episcleral vein injections of hypertonic saline. Retinitis pigmentosa (RP)-like damage was induced with single intraperitoneal injection of 60mg/kg N-methyl-N-nitrosourea (MNU). Animals were treated bilaterally, once daily, with eye drops containing 1mg/mL BrdU with 1mM PNU added in experimental groups. MNU-injected mice were treated with PNU for 7 days, starting 3 days after MNU injection (Group M1) or treated with PNU for 3 days, starting 10 days post MNU injection (Group M2). After 3-14 days treatment, retinas were immunostained for BrdU incorporation, expression of differentiated cell markers, and lineage tracing. Statistical analysis between control and experimental cell counts was performed using ANOVA.

Results: Hypertonic saline injections significantly increased intraocular pressure, from 8.86 ± 0.8 mmHg to 14.38 ± 1.9 mmHg (SEM; $p < 0.05$; $n = 11$) and significantly decreased Thy1.2+ RGCs ($28.31 \pm 1.5\%$ (SEM; $p < 0.001$, $n = 8$) at 28 days post injection. Glaucomatous eyes treated with PNU and BrdU for 72 hours had an average of $8.29 \pm 1.05\%$ (SEM; $p < 0.05$; $n = 4$) RGCs double labeled for BrdU and Thy1.2, whereas glaucomatous eyes treated with BrdU only contained no BrdU+ cells. In glaucomatous eyes treated for 14 days with PNU, $22.06 \pm 2.28\%$ (SEM; $p < 0.001$; $n = 4$) of Thy1.2+ RGCs were tdTomato positive. At 10 days following MNU injection, the ONL was significantly thinner, decreasing from $65.041 \pm 3.69 \mu\text{m}$ in control retinas to $52.089 \pm 1.27 \mu\text{m}$ (SEM; $p < 0.01$; $n = 4$) at 10-days post injection. The ONL in Groups M1 and M2 was thicker in PNU treated eyes vs. control MNU-injected eyes but was still thinner than uninjured control retinas. In Group M2, new cells were detected following PNU treatment, and $12.43 \pm 2.1\%$ (SEM; $p < 0.01$; $n = 4$) of cells in the ONL BrdU+, of which 88.25% were ($10.97 \pm 1.1\%$ SEM; $n = 4$) double labeled for BrdU and a differentiated photoreceptor marker.

Conclusions: Induction of glaucoma and RP-like damage caused a significant loss of RGCs and photoreceptors in this study. With PNU-282987 treatment, regeneration of disease-specific damaged cells was demonstrated.

CONTROL ID: 3547366

SUBMITTER (NAME ONLY): Youssef Mohamed

TITLE: Micropump Device Capable of Measuring Outflow Facility in Awake Freely Moving Rats

SESSION TITLE: Aqueous humor, trabecular meshwork, and ciliary body

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. Mohamed, C.L. Passaglia, Medical Engineering, University of South Florida, Tampa, Florida, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Youssef Mohamed: Commercial Relationship: Code N (No Commercial Relationship) | Christopher Passaglia: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Most animal models of hypertensive glaucoma elevate pressure by experimentally disrupting aqueous drainage pathways, which alters the outflow facility and intraocular pressure (IOP) of the eye in an imprecise and unpredictable manner. This study presents the continued development of a micropump system capable of continuously measuring and controlling IOP through a cannula implanted in the anterior chamber. Furthermore, the device allows for repeated outflow facility measurement in conscious free-moving rats.

Methods: The system is comprised of an implantable cannula and tether system, a pressure sensor, a micropump, and a flow restrictor. MATLAB was used to create a model of the eye and simulate the device to verify theory and optimize the feedback algorithm. The device pressure calibration and resistance were measured daily over a month to check for drift. Bench testing was conducted with an inline flow meter to verify flow rates produced by the device. The device was then tested on rats anesthetized with ketamine and xylazine using one of two paradigms (constant flow or feedback-controlled flow) to measure outflow facility. Finally, the system was deployed in an awake rat to demonstrate proof of concept.

Results: The device showed no drift in flow-restrictor resistance, pressure generation, or pressure sensor readings over 30+ days when subjected to flow rates between 0 and 2 ul/min. It was bench tested with a small-diameter cannula and reported an outflow facility of 1.109 ± 0.041 ul/min/mmHg, which was not significantly different from the value of 1.134 ± 0.094 ul/min/mmHg measured using a commercial pump. MATLAB simulations indicated a feedback control algorithm would allow for over 5X faster measurements and later confirmed during testing in anesthetized animals. When tested on anesthetized rats utilizing the feedback algorithm, mean outflow facility was 0.0228 ± 0.003 ul/min/mmHg as measured by the device and 0.0233 ± 0.0032 ul/min/mmHg as measured with an inline flowmeter (N=14, p=0.29). In the awake animal (n=2) a diurnal rhythm was recorded, with outflow facility lowest at night (~ 0.01 ul/min/mmHg) and highest during the day (~ 0.025 ul/min/mmHg).

Conclusions: The system displayed reliability in outflow facility measurements over multiple weeks and can be used to study outflow facility in conscious freely-moving rats. The feedback algorithm provides an increased temporal resolution.

CONTROL ID: 3547367

SUBMITTER (NAME ONLY): Majda Hadziahmetovic

TITLE: Remote diagnosis of referable retinal pathology in diabetic patients visiting primary care clinic

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hadziahmetovic, J. Amason, S. Cousins, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|T. Lee, Duke Medicine, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Majda Hadziahmetovic: Commercial Relationship: Code N (No Commercial Relationship) | Joshua Amason: Commercial Relationship: Code N (No Commercial Relationship) | Terry Lee: Commercial Relationship: Code N (No Commercial Relationship) | Scott Cousins: Commercial Relationship(s);NotalVision:Code I (Personal Financial Interest);Stealth:Code C (Consultant);PanOptica:Code C (Consultant);Merc Pharm.:Code C (Consultant);Clearside:Code C (Consultant)

ABSTRACT BODY:

Purpose: To test the feasibility of remote ophthalmic imaging technology for early identification of referable retinal pathology in the setting with relatively low disease prevalence.

Methods: Prospective, non-randomized study on 635 patients (1270 eyes) conducted on diabetic patients in Duke primary care clinic. Adult patients with type 1 and 2 diabetes underwent retinal screening using color fundus (CFP) and optical coherence tomography (OCT) camera (MaestroCare, Topcon) on un-dilated pupils. Obtained images were graded by masked readers for interpretability and the presence of predetermined retinal pathology, with each eye graded independently. Retinal pathology was defined as referable to a retina specialist, requiring further intervention or follow-up, and incidental findings referable to the retina or comprehensive ophthalmology.

Results: The mean age of screened patients was 66.1 (SD±13.5), the mean A1c 7.6 (SD±1.7), with an average disease duration of 5.9 years (demographics presented in Table 1). Remote image interpretability was significantly better by the OCT relative to CFP (97.9% vs. 83.5%, $p<0.0001$). We have identified 58 patients with different stages of Diabetic Retinopathy (Table 1 and Table 2 A), 114 patients with other retinal pathologies that required further retina evaluation, and 50 patients with incidental retinal findings that needed comprehensive ophthalmology follow-up (Table 1 and the most common incidental findings are presented in Table 2 B). Considerable agreement in the final diagnosis was found between the gold standard (dilated exam by the Duke ophthalmology) and the screening outcome for a limited number of patients assessed at Duke. The screening significantly improved providers' HealthCare Effectiveness Data and Information Set (HEDIS, from 4 to 5 star; 74% to 84%).

Conclusions: Ophthalmic imaging technologies at the point of service may harbor sufficient diagnostic information to enable accurate referral and timely treatment of retinal pathology. In return, this might lead to improved clinical and cost-effectiveness. Additionally, this approach might be attractive to primary care and endocrinology clinics, as it might significantly improve their quality performance (HEDIS) measures and bonus insurance reimbursements.

CONTROL ID: 3547373

SUBMITTER (NAME ONLY): Yinjie Guo

TITLE: Caspase-8-mediated inflammation but not apoptosis drives the development of glaucoma

SESSION TITLE: Neurodegeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: Y. Guo, M. Shrestha, M.S. Gregory-Ksander, Schepens Eye Research Institute of Massachusetts Eye and Ear, Boston, Massachusetts, UNITED STATES|Y. Guo, M. Shrestha, M.S. Gregory-Ksander, Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|A. Marshak-Rothstein, Medicine, University of Massachusetts Medical School, Worcester, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Yinjie Guo: Commercial Relationship: Code N (No Commercial Relationship) | Maleeka Shrestha: Commercial Relationship: Code N (No Commercial Relationship) | Ann Marshak-Rothstein: Commercial Relationship: Code N (No Commercial Relationship) | Meredith Gregory-Ksander: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Glaucoma is a complex multifactorial disease where apoptosis and inflammation represent two key pathogenic mechanisms. However, the relative contribution of apoptosis versus inflammation in axon degeneration and death of retinal ganglion cells (RGCs) is unknown. We previously demonstrated that Fas-FasL signaling is required for the development of glaucoma. While triggering of the Fas receptor is best known for inducing apoptosis through the activation of caspase-8, activated caspase-8 can also induce the production of pro-inflammatory mediators and caspase-8-mediated inflammation has been linked to the death of RGCs in glaucoma. The recent development of a caspase-8 mutant mouse (Casp8^{DA/DA}) in which a point mutation in the auto-cleavage site blocks caspase-8-mediated apoptosis but does not block caspase-8-mediated inflammation, will allow us for the first time to uncouple the two pathways and definitively determine the extent to which caspase-8-mediated inflammation and/or apoptosis contributes to the death of RGCs in glaucoma.

Methods: Intracameral injection of magnetic microbeads (control: saline) was used to elevate the intraocular pressure (IOP) in Casp8^{DA/DA} mutant mice and WT littermates. IOP was monitored by rebound tonometry twice a week and RGC function was monitored by pattern ERG (pERG). At 4 weeks post microbead injection, RGC density was measured in retinal whole mounts stained with a RGC-specific anti-Brn3a antibody.

Results: Rebound tonometry showed equivalent elevation of IOP in microbead-injected Casp8^{DA/DA} mutant mice and WT littermates. At 2 weeks post microbead injection, pERG amplitude was significantly decreased in both Casp8^{DA/DA} mutant mice (22.60 ± 1.2 uV at baseline to 16.27 ± 1.0 uV, $p < 0.05$) and WT mice from (21.99 ± 3.1 uV at baseline to 15.27 ± 1.2 uV, $p < 0.05$). At 4 weeks post microbead injection, quantification of RGCs revealed a significant decrease in RGC density in both microbead-injected Casp8^{DA/DA} mutant mice (3359.4 ± 95.1 RGCs/mm²) and WT littermates (3768.4 ± 212.4 RGCs/mm²) when compared to saline-injected WT controls (4428.6 ± 114.0 RGCs/mm², $p < 0.05$).

Conclusions: Our preliminary results indicate that caspase-8-mediated apoptosis is not required for the death of RGCs in a microbead-induced mouse model of glaucoma, indicating that caspase-8-mediated inflammation, but not apoptosis is the driving force in the development of glaucoma.

CONTROL ID: 3547381

SUBMITTER (NAME ONLY): Farid Shafik

TITLE: Arterial Length as a predictor for Glaucoma Status

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F.F. Shafik, J. Abdel-Maseih, Ophthalmology, New York Medical College School of Medicine, Valhalla, New York, UNITED STATES|F.F. Shafik, Ophthalmology, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Farid Shafik: Commercial Relationship: Code N (No Commercial Relationship) | Jerome Abdel-Maseih: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Using primary arterial lengths as an indicator of overall macular fibers. We hypothesize that the arterial lengths delineate the macular area. With decrease in macular fibers there would be less binding and expected expansion of the major arterioles of the superotemporal (ST) and inferotemporal (IT).

Methods: Arteriolar lengths were measured in a standardized system from first branching at the optic nerve to the first bifurcation. Comparison was made between Normal (N=25) vs the given open angle glaucoma states of: mild (N=47), moderate (N=49), severe (N=43). A ratio was carried out between Normal to given disease state, Student T-Test carried out for comparison.

Results: Glaucoma Categories show a difference from normal arterial lengths. There is a lengthening of the arterial segment.

Conclusions: With the lengthening of the arterial segment relative to glaucomatous status, it is sensed that this purports to widening of the macular arcades due to decreased anchoring from the nerve fiber layer as it relates to glaucoma, ie, with more glaucomatous change there is a resultant decrease in NFL. More development and testing will be needed to develop such algorithms.

CONTROL ID: 3547382

SUBMITTER (NAME ONLY): Shervonne Poleon

TITLE: Group-based trajectory modeling in electronically monitored adherence data in patients with glaucoma

SESSION TITLE: GL - diet, environment and prevention

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Poleon, Optometry and Vision Science, The University of Alabama at Birmingham School of Optometry, Birmingham, Alabama, UNITED STATES|S. Abu, T. Thomas, L. Racette, Department of Ophthalmology and Visual Sciences, The University of Alabama at Birmingham School of Medicine, Birmingham, Alabama, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Shervonne Poleon: Commercial Relationship: Code N (No Commercial Relationship) | Sampson Abu: Commercial Relationship: Code N (No Commercial Relationship) | Tracy Thomas: Commercial Relationship: Code N (No Commercial Relationship) | Lyne Racette: Commercial Relationship(s);Olleyes Inc:Code C (Consultant)

ABSTRACT BODY:

Purpose: Group-Based Trajectory Modeling (GBTM) is a statistical approach that clusters persons with similar behavioral and developmental trajectories. When applied to administrative claims data which document the frequency of ocular hypotensive prescription refills, GBTM has revealed distinct patterns of medication adherence. In this study, we applied GBTM to electronically monitored data which document daily eye drop use in order to identify distinct patterns of medication adherence in glaucoma patients.

Methods: We performed GBTM with ancillary adherence data from 100 participants enrolled in an NIH-funded glaucoma progression study at the University of Alabama at Birmingham. Participants were included if they were above age 18, used hypotensive eye drops, had 2 or more reliable visual field tests, and had visual acuity better than 20/40 at baseline. Adherence was monitored for 6 months using Medication Event Monitoring Systems (Aardex, Switzerland) which record the date and time at which the devices are opened to use the eye drops stored inside. Using the Proc Traj macro (SAS Institute, Cary NC), quadratic functions [RL(1) [sp2] were fitted to weekly mean adherence data to estimate trajectory models with 2, 3, 4, 5, and 6 groups. The trajectory model that included 5% or more of participants in each group and had the highest Bayesian Information Criterion (BIC) was identified as optimal.

Results: Mean age was 68.6 ± 8.3 years, and mean baseline intraocular pressure was 25 ± 4.8 mmHg (right eye) and 23.9 ± 6.5 mmHg (left eye). Mean adherence was $80 \pm .21\%$ and the BIC for the final model was -437.5. Five trajectory groups were estimated: Near-perfect adherence (30.7% of participants), Good adherence (32.7%), Initially Good but Declining adherence (6% of participants), Consistently Poor adherence (18.7% of participants), and Poor and Declining adherence (11.9% of participants).

Conclusions: We identified "Near-perfect" adherence and "Initially Good but Declining" adherence as two patterns that had not been previously captured in administrative data. Utilizing different metrics to quantify adherence may provide additional insight into the dynamic nature of medication adherence, which may help to predict adherence to prescribed hypotensive therapy.

CONTROL ID: 3547384

SUBMITTER (NAME ONLY): Samer Habeel

TITLE: Eyelid Blinking Dynamics in Adults with Facial Paralysis Using High Speed Video Photography

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Habeel, M. Chen, P. MacIntosh, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Samer Habeel: Commercial Relationship: Code N (No Commercial Relationship) | Michael Chen: Commercial Relationship: Code N (No Commercial Relationship) | Peter MacIntosh: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Eyelid blinking serves to protect against drying through continuous tear distribution. Facial paralysis can lead to paralytic lagophthalmos, resulting in exposure of the ocular surface that can lead to corneal dryness, infection and ulceration. There are few studies of eyelid blinking dynamics. We are studying subjects with facial paralysis to better understand and treat it.

Methods: We studied five adult subjects with facial paralysis but without adnexal, ocular or other, neurologic pathology that may affect blinking. One minute of spontaneous, bilateral blinking was recorded at 240 frames per second in upright and supine positions. Eyelid closure velocity, amplitude, and closure percentage (relative to the palpebral fissure) were calculated in horizontal (x) and vertical (y) axes for each eye using the Tracker® Video Analysis and Modeling Tool program.

Results: Average age amongst patients was 57.2 years, with an average duration of facial paralysis of 56.2 months (SD 53.88 months). Compared to non-paralyzed eyes, paralyzed eyes moved vertically with 62.7mm/s slower velocity and 4.28mm less amplitude in upright and 50.27mm/s slower velocity and 3.97mm less amplitude in supine position. In the horizontal plane, the eyes moved with 34.57mm/s slower velocity and 2.40mm less amplitude in upright and 20.72mm/s slower velocity and 1.90mm less amplitude in supine position. Mean percent closure for paralyzed eyes was 44% less in upright and 45% less in supine position compared to non-paralyzed eyes.

Conclusions: Facial paralysis led to decreases in all vertical and horizontal measurements, except percent closure, by greater than 50% relative to non-paralyzed eyes, in both upright and supine positions. The decrease in percent closure was almost the same in both positions, suggesting that gravity did not have as much of an effect on the closure percentage as paralysis did. Furthermore, paralyzed eyes often displayed a horizontal wobbling motion during closure rather than the medial movement seen in normal eyes, which could have implications in tear film spread and tear drainage. Future studies should include analysis of larger numbers of subjects as well as subjects with surgical interventions for paralytic lagophthalmos to better understand approaches to reanimating the eyelid.

CONTROL ID: 3547385

SUBMITTER (NAME ONLY): Charlotte Joslin

TITLE: Prevalence of Visual Disability among Hispanic/Latino Individuals of Diverse Backgrounds in the US: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

SESSION TITLE: Visual Impairment

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C.E. Joslin, H. Pauls, L. Ulanski, T.S. Vajaranant, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|C.E. Joslin, Epidemiology and Biostatistics, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|D. Wu, M. Daviglus, Institute for Minority Health Research, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|B.L. Lam, C. Mendoza, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|D. Lee, L. McClure, D.D. Zheng, University of Miami Department of Public Health Sciences, Miami, Florida, UNITED STATES|N. Schneiderman, Department of Psychology, Sylvester Comprehensive Cancer Center, University of Miami, Coral Gables, Florida, UNITED STATES|L. Ulanski, Ophthalmology, Surgery, Captain James A Lovell Federal Health Care Center, North Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Charlotte Joslin: Commercial Relationship: Code N (No Commercial Relationship) | Dongong Wu: Commercial Relationship: Code N (No Commercial Relationship) | Martha Daviglus: Commercial Relationship: Code N (No Commercial Relationship) | Byron Lam: Commercial Relationship: Code N (No Commercial Relationship) | David Lee: Commercial Relationship: Code N (No Commercial Relationship) | Laura McClure: Commercial Relationship: Code N (No Commercial Relationship) | Carlos Mendoza: Commercial Relationship: Code N (No Commercial Relationship) | Heather Pauls: Commercial Relationship: Code N (No Commercial Relationship) | Neil Schneiderman: Commercial Relationship: Code N (No Commercial Relationship) | Lawrence Ulanski: Commercial Relationship: Code N (No Commercial Relationship) | Thasarat Vajaranant: Commercial Relationship: Code N (No Commercial Relationship) | Diane Zheng: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Context: The US Census Bureau's American Community Survey (ACS) estimates a national prevalence of visual disability, defined as "being blind or having serious difficulty seeing even when wearing glasses" of 2.6% in adults ≥ 40 years (y). The prevalence of visual disability has not been assessed specifically across diverse Hispanic/Latino groups. Objective: To characterize the prevalence of visual disability in Hispanic/Latinos of diverse backgrounds by age.

Methods: Design, Setting and Participants: Multicenter, prospective, population-based Hispanic Community Health Study/Study of Latinos (HCHS/SOL) including 9663 participants aged ≥ 40 y who completed Visit #2 (2014-2017). Age-adjusted, sex-specific prevalence of visual disability was calculated weighting for study design and non-response. Analyses included those with Cuban (n=1455), Dominican (n=804), Mexican (n=3746), Puerto Rican (n=1485), Central American (n=965), South American (n=669) and Other (n=199) backgrounds. Main outcome measure: Prevalence and 95% confidence interval (95%CI) of self-reported visual disability defined using national ACS definitions assessed at Visit #2.

Results: Analysis included 9324 with complete data (35.9% men), with a mean age of 55.4y in men and 56.5y in women. Prevalence (%) was associated with increasing age in both men [estimate and 95%CI; 40-49y: 6.1(3.7-8.5); 50-59y: 10.5(8.3-12.6); 60-69y: 12.0(9.3-14.6); 70+y: 19.5(13.8-25.2] and women [40-49y: 10.5(7.9-13.1); 50-59y: 12.1(10.1-14.2); 60-69y: 16.5(13.9-19.1); 70+y: 18.8(15.0-22.7)]. Age-adjusted prevalence varied significantly by Hispanic/Latino background. In men, prevalence was highest in Puerto Ricans 14.6(10.7-18.5) and lowest in Mexicans 6.6(4.7-8.6); in women, prevalence was highest in Dominicans 24.5(19.8-29.2) and lowest in Cubans 8.8(6.4-11.2).

Conclusions: Sex-specific results demonstrate significant variability in the prevalence of visual disability by age and across diverse Hispanic/Latino backgrounds. Results support objectives of SOL Ojos, an ancillary HCHS/SOL study that will examine 3000 participants to systematically assess associations of lifestyle exposures (e.g., CVD risk factors, acculturation, sociocultural variables, healthcare access, physical activity, diet) with objectively measured chronic eye disease in a diverse cohort of Hispanics/Latinos.

CONTROL ID: 3547387

SUBMITTER (NAME ONLY): Linda Musil

TITLE: Tonic ErbB signaling underlies TGF β -induced activation of ERK and is required for lens cell EMyT

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Musil, Chemical Physiology & Biochemistry, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Linda Musil: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In primary lens cell cultures, inhibitors of either ErbBs (EGF receptor family members) or ERK kinases prevent TGF β from inducing epithelial-to-myofibroblast transition (EMyT). Despite its relevance for fibrotic PCO, we do not understand why ErbB activity is essential for TGF β -induced EMyT of lens cells.

Methods: Western blotting and immunofluorescent microscopy were used to assess the expression of markers of lens cell differentiation in serum-free primary cultures of embryonic chick lens epithelial cells grown on laminin (DCDMLs). Activation of ErbBs, Smad3, ERK, and p38 was assessed using phospho-specific antibodies.

Results: Inhibitors of either ERK or ErbB signaling block TGF β from upregulating both early (fibronectin) and late (α SMA) markers of myofibroblast differentiation. TGF β stimulates ERK in DCDMLs within 1.5 h. Kinase inhibitors of ErbBs, but not of other growth factor receptors active in lens cells, reduce the phosphoERK signal to below basal levels in either the absence or presence of TGF β . This effect is attributable to constitutive ErbB activity playing a major role in regulating the basal levels pERK. Additional studies support a model in which TGF β -generated reactive oxygen species serve to indirectly amplify ERK signaling downstream of tonically active ErbBs to mediate EMyT.

Conclusions: By mechanistically linking TGF β , ErbB, and ERK signaling to myofibroblast differentiation, our data elucidate a new role for ErbB in the lens and reveal a novel mode by which ERK directs lens cell fate.

CONTROL ID: 3547388

SUBMITTER (NAME ONLY): Oleg Alekseev

TITLE: Inflammatory Findings in Autosomal Recessive Retinitis Pigmentosa (ARRP) Associated with EYS Gene Mutations

SESSION TITLE: Retinitis pigmentosa/ retinal prostheses

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: O. Alekseev, A. Iannaccone, Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|G. Adamus, Ophthalmology, Oregon Health & Science University Casey Eye Institute, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Oleg Alekseev: Commercial Relationship: Code N (No Commercial Relationship) | Grazyna Adamus: Commercial Relationship: Code N (No Commercial Relationship) | Alessandro Iannaccone: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To report the characteristics of inflammatory features seen in EYS-associated ARRP.

Methods: We retrospectively identified 20 subjects (M=8/F=12, age 23-80), all of whom had undergone a complete eye examination, inclusive of visual fields (VFs) and flash ERGs, macular (n=20) and optic nerve (n=13) spectral domain optical coherence tomography (SD-OCT) and, in 12 of them, fluorescein angiography (FA) and CLIA-certified testing for circulating auto-antibodies (AABs) against retinal and/or retrobulbar optic nerve antigens by either immunoblot or Western blot, as well as retinal immunohistochemistry (IHC).

Results: All 12 patients who underwent FA showed optic nerve head leakage, involving also the vascular arcades in 4 cases. RNFL was thickened, most often sectorally, in 12 of 13 patients assessed, and correlated well with FA leakage, helping explain disproportionate visual acuity losses compared to foveal findings or disproportionate VF loss compared to retinal imaging or functional findings. Cystoid macular edema (CME) was seen by SD-OCT in only 3 patients. AABs were identified in all tested subjects. Anti-retinal AABs were found in 11 of the 12 tested patients [most common: anti enolase (8/12) and TULP1 (4/12)]. AABs recognizing anti-optic nerve antigens were found in 8 out of 9 tested patients. AABs against both tissues were seen in 6 patients. Retinal IHC showed positive staining in 9 of 12 cases, predominantly labeling photoreceptors (8/12) and less frequently ganglion cells and RNFL. Altogether, 70% (14/20) of patients exhibited signs of overt inflammation and, in 12 of them, they were associated with an autoimmune component that correlated closely with imaging and functional findings. These patients received intravitreal and/or sub-Tenon steroid injections, with both subjective and measurable increase in vision (acuity, visual field, or both), associated with improved OCT and IVFA characteristics achieved in most.

Conclusions: Inflammation involving both retina and/or optic nerve (disc, RNFL, RGC) appears to be a common yet underdiagnosed feature of EYS-associated ARRP, affecting the majority of patients. These changes can be readily detected with OCT and FA, and can be further confirmed by AAB/IHC testing. Identification of these complications is clinically and prognostically important, as meaningful vision improvement can be achieved with peri/intraocular steroid injections.

CONTROL ID: 3547389

SUBMITTER (NAME ONLY): Sonny Caplash

TITLE: Choroidal thickness distribution among different types of CSCR based on multimodal-imaging based classification

SESSION TITLE: CNV

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: We recently reported a multimodal, imaging-based classification classifying Central Serous Chorioretinopathy (CSCR) into simple and complex types depending upon the extent of the disease. In this retrospective, multi-center, observational clinical study, we aimed to investigate subfoveal choroidal thickness (SFCT) among different types of CSCR and its predictive role for treatment outcomes for each subgroup.

Methods: 104 patients with CSCR underwent retrospective chart review focusing on date of initial presentation followed by 3, 6 and 12 month follow-up. Patients were classified into simple or complex CSCR based on a priori clinical criteria and then further classified into primary, recurrent or resolved depending on their clinical course. Various OCT parameters including SFCT, outer retinal atrophy, and central macular thickness (CMT) were evaluated at each visit by masked observers.

Results: Of all studied patients, average age was 52.7 ± 10.6 years with 66.7% being male. The odds ratio of developing recurrent CSCR versus primary CSCR between simple and complex initial presentations was 0.115 (95% CI 0.040-0.350). The mean initial CMT in simple primary was 446.19 ± 136.51 versus 360 ± 48.56 ($p < 0.05$). The mean initial SFCT between simple CSCR and complex CSCR was 384.95 ± 97.48 and 419.05 ± 106.64 ($p < 0.10$).

Conclusions: Preliminary data suggests that there is prognostic and diagnostic value in SFCT and CMT on initial presentation. The future implication for this project is to use clinically objective data to guide treatment as per a new multimodal classification. Further retrospective chart review is underway to increase statistical power and there is ongoing analysis to investigate the relationship between SFCT and CMT to treatment response.

CONTROL ID: 3547391

SUBMITTER (NAME ONLY): Eric Williams

TITLE: Emergency Department Ophthalmology Consultation Trends at Two Level-One Trauma Centers

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Williams, A. Marin, H. Neves da Silva, J. Patnaik, R. Pieterick, N. Fischer, J. Smith, Ophthalmology, University of Colorado, Denver, Colorado, UNITED STATES|

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ABSTRACT BODY:

Purpose: Limited outcome and descriptive data exist regarding ocular complaints that presents to Emergency Departments (ED) within the United States. We performed a retrospective review of ophthalmology consults at two level-one trauma centers in Colorado to identify trends for ophthalmic consultation and factors associated with urgent and emergent pathology.

Methods: This study consisted of a retrospective chart review of ED consults to the ophthalmology service that occurred between Feb 25th, 2016 and Feb 25th, 2018. Characteristics such as patient age, sex, race/ethnicity, illicit drug use, and medical insurance status were recorded. Encounter measures included chief complaint, diagnostic steps, diagnosis at the ED, timeframe to follow-up, final ophthalmologic diagnosis as well as intervention and disposition. We categorized consultations into three groups depending on the final ophthalmic diagnosis: emergent, urgent, and non-emergent. Emergent diagnoses were defined as those requiring a procedure or surgery during the encounter. Urgent diagnoses were pre-defined conditions that required prompt treatment such as uveitis, orbital fracture, and corneal ulcer among others. Non-urgent diagnoses did not require further treatment or intervention.

Results: A total of 695 charts were identified, 288 at the University of Colorado Hospital and 407 at Denver Health Medical Center. Females comprised 247 (35.5%) of the encounters. The average age at presentation to the ED was 42 years old. Most ED visits were emergent, 53.7%, followed by non-urgent, 29.8%, and 15.8% were urgent. Only 465 (67.5%) of all visits had a visual acuity checked. Males were significantly more likely to present with trauma (33.9% vs 15.4%, $p < 0.0001$) and more likely to have emergent or urgent diagnoses (67.0% and 75.4% male, $p = 0.0001$) compared to females. Of the 473 patients that were discharged from the ED with ophthalmology follow-up, only 283 (59.8%) were seen within 30 days of their initial presentation.

Conclusions: Ophthalmology consultation analyses in the emergency room allow us to identify areas for improvement in care of our patients related to urgent complaints. Inconsistency of initial ED exams may account for high numbers of unnecessary ophthalmology consultations. More information is needed to understand why there is poor ophthalmology follow-up after ED consultations.

CONTROL ID: 3547394

SUBMITTER (NAME ONLY): Noor-UI-Ain Shekoh

TITLE: Endpoint management in central serous chorioretinopathy

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Central serous chorioretinopathy (CSCR) is a disorder characterized by hyperpermeability of choroid and accumulation of serous fluid between retinal pigment epithelial (RPE) and outer photoreceptors, with RPE focal defects and detachments. It is mostly a self-limiting disease but sometimes results in chronic accumulation of fluid and consequent visual dysfunction.

Several treatment modalities are available including focal Argon photocoagulation, micropulse therapy, endpoint management with thermal laser, and reduced fluence photodynamic therapy (PDT). The purpose of our study was to see the effect of endpoint management (EPM) with thermal laser on the resolution of subretinal in CSCR. We chose this modality because it is efficient in stimulating RPE to pump fluid out of the retina and safe because it does not damage RPE as evident on retinal imaging.

Methods: Seventeen patients diagnosed with CSCR on clinical exam and multimodal imaging- Fluorescein angiography (FA), fundus autofluorescence (FAF), and optical coherence tomography (OCT), with center involving subretinal fluid (SRF), were selected. Patients with any other central retinal problems were excluded from the study. After obtaining informed consent, a light intensity burn was applied outside the vascular arcades then the laser power was titrated to 30%. The affected area was treated. Patients were followed up on post-op week 1, month 1, and month 3 for the clinical exam. OCT testing with Heidelberg Spectralis was done to evaluate treatment results.

Results: Patients were followed up to see the effect of laser on the resolution of fluid. In the case of partial resolution/recurrent SRF, retreatment was done on month 3.

SRF resolved in 52.9%, improved in 23.5%, and remained stable in 23.5% of patients.

Visual Acuity improved in 52.9%, deteriorated in 17.6%, and remained stable in 29.4% of patients.

The absence of RPE scarring or atrophy attributable to laser was confirmed on OCT in all patients.

Conclusions: Endpoint management is an effective and efficient method of treating center involving CSR with vision loss. It speeds up sub-retinal fluid absorption and improves visual rehabilitation without damaging retinal pigment epithelium.

CONTROL ID: 3547395

SUBMITTER (NAME ONLY): Harry Matundan

TITLE: The suppressive effect of ICP22 on CD80 promoter is altered by a recombinant virus lacking CD80 binding site

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Matundan, S. Wang, U. Jaggi, J. Yu, H. Ghiasi, Surgery, Cedars-Sinai Medical Center, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: We recently reported that ICP22 plays a major role in downregulating the host CD80 expression upon HSV-1 ocular infection in mice. Our previous report demonstrated that using D22 virus which has a complete deletion of full length ICP22, maintained CD80 expression and still remained virulent despite lower viral replication and ex vivo reactivation. To further study the effect of ICP22 on viral replication and disease severity, we mapped the ICP22 binding site to CD80 and constructed a mutant HSV-1 which is not binding to CD80. We now have characterized the effect of the absence of ICP22 binding to host CD80 in vitro and in vivo. expression.

Methods: To identify the binding region of ICP22 to CD80 promoter, ICP22 gene was fragmented to shorter regions and the effect of these fragments on suppression of CD80 promoter were analyzed with luciferase assay. Based on these assays, we have constructed a recombinant HSV-1 which is not binding to CD80 (KOS-ICP22Δ40). We compared KOS-ICP22Δ40 virus replication in vitro with parental control virus. Following corneal scarification, BALB/c mice were ocularly infected with 2×10^5 pfu/eye of KOS-ICP22Δ40 and parental viruses and primary virus replication in the eye, corneal scarring and latency-reactivation in the infected mice were determined.

Results: Western blot analysis of 293 HEK cells infected with KOS-ICP22Δ40 virus expressed a smaller fragment of ICP22 as compared to parental virus infected cells. CD80 expression was restored in the mice infected with KOS-ICP22Δ40 virus as compared with the parental control virus. Interestingly, primary viral replication in the eye and corneal scarring was slightly reduced in KOS-ICP22Δ40 virus infected mice as compared to the parental KOS infected mice. The level of latency and reactivation remained the same in both the infected mice groups.

Conclusions: We have identified HSV-1 ICP22 binding site to cellular CD80 and shown that blocking this interaction using a recombinant HSV-1 lacking CD80 binding site reduced primary virus replication in the eye and eye disease but had no effect on latency-reactivation. As there is currently no effective treatment for HSV-1 recurrences, interfering with ICP22-CD80 interaction may represent a clinically effective and expedient target in developing HSV-1 therapeutics.

CONTROL ID: 3547396

SUBMITTER (NAME ONLY): Agni Kakouri

TITLE: Slowing the progression of geographic atrophy with oral resveratrol, quercetin, and curcumin

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Geographic atrophy (GA) is a progressive form of AMD characterized by sharply defined oval-to-round areas of retinal atrophy which increase in size and coalesce to cause loss of vision affecting more than 5 million people worldwide. Currently, there is no effective treatment for GA. In this study, we evaluated the effects of oral supplementation with resveratrol, quercetin, and curcumin (RQC) on the size and annual GA growth rate in subjects with advanced dry AMD over one year.

Methods: AMD patients with nascent (n=3) or advanced (n=7) GA were recruited from Zaparackas and Knepper, Ltd after IRB approval and written consent. A total of 12 eyes were included in the study consisting of 3 with nascent GA and 9 with advanced GA. Each patient received 200 mg resveratrol, 240 mg quercetin, and 2000 mg curcumin per day for twelve months and had fundus autofluorescence (FAF) images recorded with the Heidelberg Spectralis OCT at three-month intervals. Advanced GA was defined as hypofluorescent regions of macular atrophy greater than 0.15 mm² and was confirmed on OCT images using hyperreflectivity in the choroid region. Nascent GA was defined as regions of atrophy no greater than 0.015 mm². GA area was quantified using a precise and reproducible post-processing procedure with ImageJ software. GA growth rate was reported in mm²/year and square root transformed mm/year.

Results: The annual growth rate for advanced GA was 0.35 ± 0.66 mm²/year (square root transformed 0.10 ± 0.11 mm/year). The growth rate for nascent GA was 0.01 ± 0.02 mm²/year (square root transformed 0.02 ± 0.03 mm/year). Compared with the natural GA growth rate reported by Yehoshua, et al. (2011) of 1.20 ± 0.90 mm²/year (square root transformed 0.18 mm/year), the GA growth rate of subjects taking oral RQC was significantly lower (P=0.003).

Conclusions: The annual rate of GA growth was significantly decreased in subjects taking oral RQC. Our results indicate that RQC may be the first safe and efficacious therapy for the slowing or prevention of GA progression.

CONTROL ID: 3547400

SUBMITTER (NAME ONLY): Jose Paczka

TITLE: Six-Month Results on Efficacy and Safety in Eyes with Good Vision after Treatment with Micropulse Transscleral Cyclophotocoagulation

SESSION TITLE: Ocular Blood Flow, Laser Therapy, and IOP Measurements

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. Paczka, A. Tornero-Jimenez, Instituto de Oftalmologia y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|J.A. Paczka, S. Garcia y Otero Sánchez, A. Tornero-Jimenez, Research, Global Glaucoma Institute, Guadalajara, Jalisco, MEXICO|M.A. Ibañez Sandoval, Escuela de Medicina, Universidad Guadalajara LAMAR, Guadalajara, Jalisco, MEXICO|M.A. Ibañez Sandoval, Research & Development, Asistencia e Investigación en Glaucoma, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: The micropulse transscleral cyclophotocoagulation (MP-TSCPC) has been proven to treat refractory glaucomas, mainly with very limited vision. Very scarce information is present regarding results with this relatively new treatment on patients with good vision. The aim of this study is to investigate the short-term efficacy and safety of MP-TSCPC on a consecutive case series of refractory glaucoma cases in eyes with good vision.

Methods: A retrospective review of consecutive case series of adult patients with refractory glaucoma and BCVA \geq 20/40 which underwent MP TSCPC in a specialized center in Western Mexico. All consecutive cases with complete clinical information during at least 6 months of follow up were included. A surgical procedure success was defined if the following standard criteria were met: (1) the postoperative OP remained in a range of 5-21 mm Hg and was reduced at least 30% compared to the baseline IOP with or without medication (complete or qualified success), (2) there was no loss of light perception or vision threatening severe complications, and (3) no additional glaucoma surgery was required. Minor and major complications as well as their outcomes were also registered. A p value \leq 0.05 was considered statistically significant.

Results: Fourteen eyes of 14 patients (mean age, 58.5 ± 21.6 years; 8 female, 6 male) were included in the study. All eyes had a logMAR BCVA above 0.4. Mean power and time of MP TSCPC were $2,550 \pm 208.4$ mW and 146.3 ± 45.6 seconds, respectively. Preoperatively, the mean intraocular pressure (IOP) was 36.42 ± 9.81 mm Hg. Postoperatively, the mean IOP significantly decreased at all follow up points: 24.6 ± 7.9 mm Hg at 1 day ($P=0.0004$), 14.12 ± 5.9 mm Hg at 7 days ($P<0.0001$), 13.2 ± 6.5 mm Hg at 1 month ($P<0.0001$), 14.9 ± 6.2 mm Hg at 3 months ($P<0.0001$), and 16.3 ± 5.4 mm Hg ($P<0.0001$) at 6 months. The success rate was 85.7% at 6 months. Two cases required reoperation during the 6 months of follow up. Two cases with prior macular edema had a self-limited recurrence.

Conclusions: This study provides short-term evidence that MTS-CPC when used in eyes with good vision is a clinically useful procedure that effectively reduces IOP maintaining a very good safety profile.

CONTROL ID: 3547402

SUBMITTER (NAME ONLY): Anthony Salles

TITLE: Optical coherence tomography offers a new window into newt lens regeneration

SESSION TITLE: Lens Development and Differentiation

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Salles, G. Tsissios, W. Chen, H. Wang, K. Del Rio-Tsonis, Miami University, Oxford, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: In adult newts lens regeneration is especially fascinating as the regenerated lens originates from a completely different tissue through reprogramming of the iris pigmented epithelium. However, this process has never been visualized in real time or 3D. Our goal was to establish optical coherence tomography (OCT) as an in vivo imaging platform to characterize the process of lens regeneration.

Methods: Two separate studies were performed in adult red spotted newts, *Notophthalmus viridescens*. In the first study, the lens was surgically removed from 39 newts. Over the course of 80 days 3 newts were taken per time point, imaged by OCT, then immediately sacrificed and the eyes processed for histology. The second study consisted of acquiring OCT images over 60 days from a single newt. At the 60th day, the newt eye was collected and processed for histology. OCT images were acquired at 800nm with ~8µm lateral resolution and ~3µm axial resolution.

Results: OCT captured key morphological changes associated with lens regeneration in live newts such as corneal wound healing, accumulation of ECM, migratory cells, lens vesicle formation and its differentiation into a lens with clear lens epithelium and lens fibers as well as dilation of blood vessels. These OCT images were validated with corresponding histological images collected from the same newt eye. The 3D view provided by OCT demonstrated the regenerating lens vesicle adopts an elliptical form extending along the dorsal iris tip. The lens vesicle became spherical in shape around 4 weeks post lentiectomy. From the 3D reconstructions, we calculated the changes in volume size enabling a quantitative measure to monitor the progression of the lens regeneration process with time.

Conclusions: This is the 1st report describing both in vivo and 3D imaging of the newt lens regeneration process using OCT. As verified by histological analysis, OCT is a reliable imaging tool to monitor the regenerating lens and the dynamic changes that occur in the eye during this process. Detecting the lens vesicle in as little as two weeks after lentiectomy highlights the power of OCT. Future work includes characterizing the identity and function of the migrating cells detected by OCT, and to establish OCT as a semi-high throughput quantitative platform to screen inhibitors and activators of lens regenerative potential in the newt eye.

CONTROL ID: 3547406

SUBMITTER (NAME ONLY): Karen Revere

TITLE: Timing of Orbital Fracture Repair in Children

SESSION TITLE: Neuro-Ophthalmology and Oculoplastics

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Revere, E. Meer, Y. Schein, A. Spiller, G. Binenbaum, Ophthalmology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|K. Revere, Y. Yu, G. Ying, Ophthalmology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: Delaying repair of orbital fractures without muscle entrapment has recently been advocated in adults. Observation may result in recovery without a need for surgery, and outcomes following later surgery appear similar to earlier surgery. However, studies addressing this issue in children are limited. We sought to determine the preferred timing for orbital fracture repair in children.

Methods: Retrospective cohort study of children with orbital fracture, classified into groups based on presence of entrapment and timing of repair. Early repair was defined as surgery within 3 weeks of injury. A successful clinical outcome was defined as absence of both enophthalmos and strabismus at latest follow-up. Presenting findings, including muscle entrapment, enophthalmos, motility restriction, and fracture size, were considered as potential confounding factors or indications for surgery.

Results: We studied 147 children with orbital fracture (median age 12 years, range 0.2-18; median follow up 3.1 months, range 0.3-103). 11(7.5%) had entrapment and had surgery at median 1 day post-injury (range 0-15). Among 136 without entrapment, 30 had early repair (median 12.6 days, range 1-18) and 106 did not, of which 5 eventually had surgery (median 57 days, range 47-157) and 101 had no surgery. Successful outcomes were seen in 91% of children with entrapment, 93% of early repair, and 95% late/no repair ($p=0.65$). Success did not differ between early and late surgery (93% vs. 80%, $p=0.38$). Among 31 children with fracture size $>50\%$ and no entrapment, successful outcomes occurred in 19/21 (90.5%) with early surgery, 2/2 (100%) with late surgery, and 10/11 (91%) of children with no surgery. Among patients without entrapment, enophthalmos and motility limitation at baseline resolved without surgery in 6/8 (75%) and 9/10 (90%) cases, respectively.

Conclusions: Muscle entrapment is an indication for urgent orbital fracture repair. Otherwise, pediatric orbital fractures without entrapment should be observed for 3 months or more, as many patients will eventually not require surgery, and early surgery does not appear to improve outcomes. Contrary to long-held belief, extraocular motility limitation without entrapment, enophthalmos, or fracture size $>50\%$ are not indications for early surgery, as motility limitation and enophthalmos may resolve without surgery in a majority of cases, even when fracture size is large.

CONTROL ID: 3547411

SUBMITTER (NAME ONLY): Judy Chen

TITLE: High-Frequency Ultrasound Biomicroscopy Imaging of the Ciliary Body in Patients with Intraocular Inflammation

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.L. Chen, E. Tsui, G.N. Holland, Jules Stein Eye Institute, Los Angeles, California, UNITED STATES|N.J. Jackson, University of California Los Angeles Division of General Internal Medicine and Health Services Research, Los Angeles, California, UNITED STATES|M. Marchand-Gareau, T. Gallant, M. Lim, University of California Davis, Sacramento, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To determine whether hypotony in patients with histories of intraocular inflammation is associated with anatomic changes in the ciliary body (CB) on high-frequency ultrasound biomicroscopy (UBM).

Methods: In this pilot study, we performed a retrospective chart review of patients with histories of intraocular inflammation, seen by 3 uveitis providers (2016-20), who underwent UBM, performed with the VuMAX HD (SonomedEscalon) using immersion technique (an exception was a child intolerant of the immersion shell, who underwent direct contact technique). Using ImageJ (National Institutes of Health), we measured CB thickness, and ciliary process (CP) length, thickness, density, and area for available high-quality scans of each quadrant. Patients were categorized into 2 groups based on UBM indication: hypotony (IOP \leq 5mmHg) or other. Linear regression with clustered robust standard errors at the patient-eye level were used to assess group differences in CB measurements.

Results: A total of 159 scans (35 eyes, 28 patients) were included. Each patient underwent a median of 4 scans (range 3–12). Mean age at time of UBM was 48.1 \pm 24.5 years (range 10–78 years), and 20 patients (71.4%) were female. Seventeen patients (60.7%) underwent UBM for hypotony and 11 (39.3%) for evaluation of intraocular lens position or preoperative planning. Categories of disease were: anterior (n=19, 67.9%), intermediate (n=2, 7.1%), posterior (n=2, 7.1%), and pan- (n=4, 14.3%) uveitis, and chronic post-operative endophthalmitis (n=1, 3.6%). Median disease duration at time of UBM was 2.7 years (range 14 days–23.0 years); the hypotony group had longer median duration of disease (5.0 vs. 1.3 years). Mean CB thickness was increased in the hypotony group versus the non-hypotony group (0.660 \pm 0.041 vs. 0.559 \pm 0.024 mm, p=.038). Means of all CP measures were decreased in the hypotony group versus the non-hypotony group, including length (0.502 \pm 0.066 vs. 0.738 \pm 0.039 mm, p=.004), thickness (0.254 \pm 0.031 vs. 0.370 \pm 0.014 mm, p=.001), density (2.9 \pm 0.3 vs. 3.8 \pm 0.1 processes/2 mm, p=.011), and area (0.920 \pm 0.12 vs. 1.44 \pm 0.08 mm², p=.001).

Conclusions: Hypotony as a late complication of intraocular inflammation appears to be related to anatomic changes in the ciliary body, which may result in decreased aqueous humor production. This hypothesis should be tested in a longitudinal study of uveitis patients who do and do not develop hypotony.

CONTROL ID: 3547412

SUBMITTER (NAME ONLY): Justine Chee

TITLE: Formation of glycine through serine-glycine biosynthesis is essential for transfer of single-carbon units to folate metabolism for early eye formation

SESSION TITLE: Molecular and Structural

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chee, Oakland University, Rochester, Michigan, UNITED STATES|L. Lanoue, D. Clary, K. Lloyd, A. Moshiri, University of California Davis, Davis, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The genes and pathways that contribute to early eye development are not well known. We hypothesize that screening of the International Mouse Phenotyping Consortium (IMPC) database for unique knockout mouse lines with embryonic eye defects will yield novel genes and pathways important for eye embryogenesis.

Methods: The IMPC web portal (impc.org) was interrogated for mouse embryos with ocular defects. Most of the eye abnormalities in knockout mouse embryos were small or absent eyes, findings most relevant to microphthalmia, anophthalmia, and coloboma (MAC) spectrum disease in humans. A literature search was performed to determine which of these mouse knockouts have been reported previously and if there were eye abnormalities associated with them. In addition, a "gold standard" list was created based on clinical literature of established genes associated with congenital MAC spectrum disease in humans. Gene ontology, protein-protein interaction networks, and functional annotation bioinformatics microarray analysis were used to analyze the predicted relationship between 1. human orthologs of the IMPC mouse genes and 2. the gold-standard MAC spectrum human disease genes to identify biochemical pathways involved in eye embryogenesis.

Results: Screening of the IMPC database of over 7,000 knockout lines resulted in 63 unique genes associated with embryonic eye defects. The literature search showed that 41 of the 63 had previously published knockout mouse models, and 22 did not. Out of the 41 published knockout mouse models, only 13 of them noted ocular defects in the original publication, and 28 of them did not. Therefore, the 28 published knockouts which did not previously detect ocular abnormalities and the 22 unpublished knockouts together represent 50 novel genes that contribute to early eye development in mice. The literature search also resulted in 114 gold standard human MAC disease genes, which were vetted against the 63 IMPC genes to show that several of the IMPC genes reveal a critical role for serine-glycine biosynthesis in early eye formation.

Conclusions: The genetic underpinnings of MAC spectrum disease are incompletely understood, however, serine-glycine biosynthesis may be a novel pathway associated with early eye development. Analysis of this pathway may hasten the diagnosis and treatment of this congenital blinding disease.

CONTROL ID: 3547414

SUBMITTER (NAME ONLY): Tomas Meijome

TITLE: Evaluation of in vivo murine modeling of Staphylococcus aureus bacterial keratitis

SESSION TITLE: Corneal immunology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Staphylococcus aureus, a predominant pathogen in bacterial keratitis (BK), is a significant contributor to worldwide disease burden of corneal vision loss and blindness. Validated animal models have historically played a critical role in the study of BK; however, a direct correlation to human disease has yet to be thoroughly established. We propose to advance our understanding of an established murine model of BK by correlating advanced image analysis, disease severity, and bacterial burden.

Methods: Twenty BALB/c strain mice underwent three parallel scratches of the left corneal epithelium and anterior stroma with subsequent inoculation of 5×10^6 S. aureus cells (50ml of 10^8 S. aureus cells/ml). At 48 hours post-infection, subjective clinical disease severity was graded based on an established scale from 0 (no clinically evident disease) to 4 (corneal perforation). Slit-lamp photography and image annotation with ImageJ were used to measure stromal infiltrate area (mm^2). Eyes were homogenized, and the bacterial load (colony forming units or CFU) was determined. Pearson and Spearman correlations were used to estimate the linear association between severity grade, ulcer size and CFUs.

Results: The average ulcer size was 1.3 mm^2 (SD = 0.9) and 50% were identified as grade 2 clinical severity (0: 5%, 1: 10%, 2: 50%, 3: 25%, 4: 10%). Bacterial burden was evaluated in twenty mice with mean of 8×10^5 CFU/ml (SD = 1.4×10^5 CFU/ml). A strong linear association was found between bacterial burden (CFUs) and stromal infiltrate measurements (Pearson correlation = 0.72, p = 0.0026,) and between CFUs and severity grade (Spearman correlation = 0.79, p = 0.0005). No significant correlation was found between severity grade and stromal infiltrate measurements (p = 0.17).

Conclusions: Clinical severity and corneal infiltrate size were both strongly correlated with the bacterial corneal load, suggesting that both clinical grading and image annotation approaches have potential to estimate disease severity in this murine model of BK. Further research in animal models will be important in developing risk stratification models and standardized treatment methods for human disease.

CONTROL ID: 3547415

SUBMITTER (NAME ONLY): Su Bin Yoon

TITLE: Using protein-protein interactions to identify novel genes and demonstrate the interconnected network formation of genes in Retinitis Pigmentosa pathogenesis

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Retinitis Pigmentosa (RP) is a rare monogenic retinal disease that causes the atrophy of photoreceptor, cone and rod cells. Based on the defect of even a single causal gene converging at the same disease, we hypothesized that all of the genes that cause RP must be connected to each other through protein-protein interactions (PPIs) in this computational correlation study.

Methods: A final list of 161 genes that are known to cause RP was compiled using RetNet (<https://sph.uth.edu/RetNet/>) on Feb. 15, 2019. Of 161 genes, 159 were recognized and mapped by Search Tool for the Retrieval of Interacting Genes/Proteins (STRING), which uses PPIs as the measure of association. On the basis of the hypothesized interconnectedness among RP genes, we defined novel genes as the genes that may cause RP by interacting with the genes already attributed to the disease. The novel genes, which connect the ten previously disconnected genes, were then identified based on the PPI confidence levels to complete the network of RP genes. Further reorganization based on subcellular localization and previous literature of the 169 genes was conducted for analysis.

Results: Ten novel genes were discovered through PPIs at a minimum of 40% confidence for the initial 161 genes (Figure 2a). The categorization of cells based on subcellular localization showed that the genes with protein products localized in the rod outer segment (ROS) have the greatest number of PPIs. With the inclusion of these novel genes, all known causal genes of RP were connected to each other as hypothesized.

Conclusions: The successful establishment of PPIs among all documented genes and the discovery of novel genes for Retinitis Pigmentosa strongly support the global interconnectedness of the genes that cause the disease on the molecular level as hypothesized. Furthermore, the additional findings such as the greatest number of PPIs with respect to ROS and previous literature on the association of novel genes to RP support the hypothesis that all genes that cause Retinitis Pigmentosa must be interconnected.

CONTROL ID: 3547416

SUBMITTER (NAME ONLY): Lawrence Ulanski

TITLE: Prevalence of Visual Disability and Cardiovascular Disease Risk Factors in Hispanic/Latinos of Diverse Backgrounds: Results from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

SESSION TITLE: Visual Function, Vision QoL and visual impairment

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Chronic eye diseases (CED) share risk factors (RF) with cardiovascular disease (CVD). HCHS/SOL showed marked variation in 5 major CVD RFs (diabetes mellitus-DM, hypertension-HTN, smoking-SM, obesity-OB, hypercholesterolemia-HChl) by Hispanic/Latino group. Estimates of CED in Hispanics/Latinos without considering RF heterogeneity (e.g., only Mexican-Americans) yield inaccurate estimates of disease prevalence. We characterize the prevalence of visual disability and associated CVD RFs in HCHS/SOL.

Methods: Design, Setting and Participants: Multicenter, prospective, population-based HCHS/SOL subjects (n=9663), ≥40y age, completing Visit #2 (2014-2017). Age-adjusted prevalence of visual disability and CVD RFs were calculated weighting for study design. Adverse CVD RFs were defined using national guidelines. Main outcome measure: Age-adjusted prevalence of self-reported visual disability defined by the US Census Bureau's American Community Survey definition, "being blind or having serious difficulty seeing even when wearing glasses."

Results: 9324 subjects with complete data were analyzed. Sex-specific prevalence of CVD RFs and adverse CVD RF profile varied significantly by Hispanic/Latino group. Visual disability prevalence (%) was higher in men with DM (estimate and 95%CI) 13.4% (10.4-16.4), HTN 11.3% (9.5-13.1), HChl 11.7% (9.8-13.7), OB 11.8% (9.5-14.1) and SM 12.5% (9.1-15.9) versus the overall estimate 10.6% (9.2-12.1). In women, visual disability prevalence was higher with DM 16.1% (13.5-18.8), HTN 15.5% (13.5-17.6), HChl 14.6% (12.3-16.9), OB 13.9% (12.0-15.7) and SM 16.8% (12.6-21.0) versus the overall estimate 13.5% (12.0-14.9). In men, visual disability prevalence was similar with 0-1 adverse CVD RFs [8.0% (3.9-12.1); 7.1% (5.1-9.1)] but increased with 2-3 adverse CVD RFs [10.9% (8.3-13.5); 13.5% (10.8-16.2)]. In women, visual disability prevalence increased with increasing adverse CVD RFs [0 RF, 9.5% (6.5-12.5); 1 RF 11.8% (9.4-14.2); 2 RFs 13.4% (10.8-16.0); 3 RFs 16.7% (14.0-19.5)].

Conclusions: A sizeable burden with marked variation exists for the prevalence of visual disability and adverse CVD RFs in Hispanic/Latinos. Results support SOL Ojos, an ancillary study that leverages HCHS/SOL heterogeneity, to assess CED-CVD risk factor associations in Hispanic/Latinos of diverse backgrounds.

CONTROL ID: 3547419

SUBMITTER (NAME ONLY): Omar Mahroo

TITLE: Visual impairment registrations in England and Wales between 2009 and 2019: focus on hereditary and diabetic eye disease

SESSION TITLE: Diabetic Retinopathy Epidemiology and Care Management

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Whilst diabetic eye disease (DED) has long been a leading cause of certifiable visual impairment in the working age, hereditary eye disease (HED) has also become a leading cause in some countries. We explored trends in these causes of visual impairment registration in England and Wales over 10 years.

Methods: Individuals who meet specific criteria are eligible for a Certificate of Visual Impairment (CVI), at one of two levels, sight-impaired (SI) or severely sight-impaired (SSI). A single main cause is listed, together with additional causes where applicable. We explored CVI registrations for the 10 years between 2009 and 2019, where DED or HED were listed as main cause, in the working age (16-64 years) in particular, and also proportions of males in HED CVIs.

Results: In 2009-10, similar numbers of CVIs had DED and HED as the main cause (1334 and 1338 respectively). In 2018-19, respective numbers were 904 and 1539. Since 2014-15, CVIs due to DED were consistently <1000 annually, whilst those due to HED were >1400. In the 16-64 age group, DED and HED were the main causes for 600 and 720 CVIs respectively in 2009-10, and for 499 and 963 CVIs in 2018-19. In this age group, slightly more SI registrations were due to DED (n=355) than HED (n=350) in 2009-10. From 2013-2014 onwards, HED SI registrations were consistently higher; in 2019-19, 278 and 407 SI registrations were due to DED and HED respectively. For SSI registrations, these were consistently higher for HED, but the numbers diverged over the period: 279 SSI registrations were due to DED in 2009-10, and 347 in 2018-19; for HED, the numbers were 387 and 602. Over the period, males accounted for 53% of working age HED CVI registrations (95% CI, 0.52-0.54), for 55% of HED SSI registrations (0.53-0.56) and 51% of HED SI registrations (0.49-0.52).

Conclusions: In England and Wales, annual CVI registrations due to DED have fallen whilst those due to HED have risen. HED was consistently the leading cause of SSI registration in the working age, and overtook DED as leading cause of SI registration from 2013-14 onwards. Males accounted for just over 50% of HED CVI and HED SSI registrations (confidence intervals did not cross 50%). This might relate in part to males more severely affected by X-linked disease. Our findings highlight the increasing burden of visual impairment due to HED and the need for developing therapies.

CONTROL ID: 3547420

SUBMITTER (NAME ONLY): Matthew Wilneff

TITLE: The Effect of Patient Facemask Usage on Post-Injection Endophthalmitis Among Intravitreally Injected Patients in Ohio from 2019-2020

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Wilneff, R. Paloka, Florida Atlantic University Charles E Schmidt College of Medicine, Boca Raton, Florida, UNITED STATES|A. Wuller, D. Wuller, C. Miller, D.G. Miller, Retina Associates of Cleveland Inc, Beachwood, Ohio, UNITED STATES|A. Wuller, University of Illinois at Urbana-Champaign, Urbana, Illinois, UNITED STATES|D. Wuller, C. Miller, University of Notre Dame, Notre Dame, Indiana, UNITED STATES|S. Wuller, Florida Department of Health in Palm Beach County, West Palm Beach, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the incidence of post-injection endophthalmitis in patients wearing facemasks. We hypothesize that the incidence of post-injection endophthalmitis in patients wearing facemasks would be significantly greater than patients who were not wearing facemasks.

Methods: A retrospective cohort study was performed at a private retinal practice in Ohio. The practice management database was searched using CPT codes for endophthalmitis over two, six-month periods. The first cohort from 6/01/2019-12/31/2019, and the second, following universal facemask usage due to COVID 19, from 6/01/2020-12/31/2020. Patients who developed endophthalmitis post-intravitreal injection during the study period had their charts reviewed. Data collected included: age, sex, visual acuity, medication injected, administering physician, date of diagnosis, length of follow up, intervention, and cultured organism. Means of variables and chi-squared analyses were performed to determine statistical difference between non-masked and masked cohorts.

Results: A total of 25029 intravitreal injections were performed in the first study period with 34019 injections in the second. Of those injections, endophthalmitis occurred in 8 and 12 patients respectively. Incidence of post-injection endophthalmitis in the 2019 was .00039 and .00041 in 2020 (p-value= 0.8289). The mean age of patients was 69 years in 2019 and in 68 years in 2020. Average length of follow up in 2019 was 472 days, and 74 days in 2020. Average change in visual acuity from diagnosis to last follow up was .707 in 2019 and .945 in 2020. In 2019 all six positive cultures grew coagulase negative staph, in 2020 the three positive cultures yielded Streptococcus mitis, gram positive cocci, and rare skin flora.

Conclusions: We reject our hypothesis of, if patients were wearing masks during intravitreal injections, then there would be a significantly greater incidence of post-injection endophthalmitis. There was no significant association between wearing facemasks and post-injection endophthalmitis within our six-month study periods in 2019 and 2020. However, cultures between the two cohorts yielded different organisms, with one culture in 2020 presenting an organism typically found in oral flora.

CONTROL ID: 3547422

SUBMITTER (NAME ONLY): Jonathan Vande Geest

TITLE: Effect of genipin on the metabolic activity of porcine lamina cribrosa cells

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.P. Vande Geest, J. Liou, Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|J.P. Vande Geest, Ophthalmology, University of Pittsburgh, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the effect of scleral stiffness on the susceptibility to glaucoma, Kimball et al. treated mouse eyes with glyceraldehyde alone via subconjunctival injections and found no effect on retinal structure or function. However, in mice with experimental glaucoma, glyceraldehyde significantly increases intraocular pressure and axon loss at 6 weeks. It therefore may be that de-stiffening of the sclera can rescue or halt glaucomatous damage. The effect that stiffening or de-stiffening agents have on the health of lamina cribrosa cells has not been fully quantified in the literature. In this preliminary study, we evaluated the effects of genipin on optic nerve head cells, specifically, lamina cribrosa cells.

Methods: Porcine lamina cribrosa (LC) cells were isolated from three fresh pig eyes purchased commercially. Cell characterization was performed using anti-alpha smooth muscle actin (α SMA) and anti-glial fibrillary acidic protein (GFAP) antibodies from Abcam. Cells at passage 3 were seeded onto a 24-well plate and cultured in DMEM medium with 10% Fetal Bovine Serum, 2.5% HEPES, 1% Amphotericin B and 1% Penicillin-Streptomycin. Genipin was reconstituted in medium at a final concentration of 10 mM. MTS assays were performed on day 3, day 7, and day 10 to quantify the metabolic activity of these cells.

Results: Porcine LC cells are characterized as α SMA positive and GFAP negative (Figure 1A). Genipin at 10 mM significantly reduces the metabolic activity of LC cells in monolayer cultures on day 3, day 7, and day 10 (Figure 1B). The metabolic activity of genipin group is no different than the negative control (Figure 1B).

Conclusions: Genipin at 10 mM reduces the metabolic activity of LC cells. Future investigations are needed to examine the effects of genipin at a lower concentration (1 mM or 5 mM) in order to conclude the cytotoxic effects of genipin. We are currently working on eye culture with genipin treatment and examine the stiffening effects via whole globe inflation tests.

CONTROL ID: 3547423

SUBMITTER (NAME ONLY): Krista Cosert

TITLE: Metal Oxide Nanoparticles Induce Stiffening of Rabbit Corneal Fibroblasts in vitro

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Metal oxide nanoparticles (NPs) zinc oxide (ZnO) and titanium dioxide (TiO₂) are routinely applied near the eye via cosmetics and sunscreens. Despite the high probability of exposure there remains a paucity of research as to the ocular consequences. The biomechanics of the corneal stroma are altered during wound repair, indicating a need to examine mechanics in ocular toxicity. We hypothesize that ZnO and TiO₂ NPs increase the mechanical stiffness of corneal fibroblast cells, and thus contribute to keratocyte-fibroblast-myofibroblast transformation.

Methods: Rabbit Corneal Fibroblasts (RCFs) at passage 6 were cultured with and without 10 ng/mL Transforming Growth Factor Beta 1 (TGFβ-1) for 48 h at which time phosphate buffered saline (PBS-control), 10 µg/mL ZnO or 250 µg/mL TiO₂ NPs were added, and cells incubated for an additional 24 hrs. After incubation cells were then gently washed 3x with PBS and live cell stiffness measured by Atomic Force Microscopy (AFM). For each experimental condition, 5 force curves per cell were collected from 10 individual cells. Force curves were taken with PNP-TR-50 silicon nitride cantilevers that were calibrated for the deflection inverse optical lever sensitivity by indentation in PBS on glass and the spring constant determined using the Asylum Research software at a scan velocity of 1.98 µm/s. Data were analyzed to determine elastic modulus and were obtained by mathematically fitting the indentation curves to the Hertz model for spherical geometry and then subjected to a one-way analysis of variance (ANOVA) followed by Tukey's test.

Results: RCFs exposed to ZnO and TiO₂ NPs had a significantly ($p < 0.001$) greater elastic modulus than control cells to a degree that approximated the effect seen with TGFβ-1 alone. For ZnO, the degree of stiffening was not augmented by the presence of TGFβ-1. RCFs treated with TiO₂ NPs were stiffer and in contrast to results obtained with ZnO NPs, the effect was significantly augmented by TGFβ-1.

Conclusions: ZnO as well as TiO₂ NPs increased stiffness of RCFs. The degree of stiffening induced by ZnO NPs was unaffected by the presence or absence of TGFβ-1. For TiO₂, TGFβ-1 further increased the stiffness of cells. These results suggest that ZnO and TiO₂ NPs alter cytoskeletal dynamics and further studies of the NPs on KFM transformation during stromal wound healing are warranted.

CONTROL ID: 3547426

SUBMITTER (NAME ONLY): Kaira Church

TITLE: Retinal Microglia Depletion as a Tool to Determine the role of Microglia-Mediated Inflammation in the Diabetic Retina

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Church, D. Vanegas, A. Cardona, Biology, The University of Texas at San Antonio, San Antonio, Texas, UNITED STATES|A.S. Mendiola, University of California San Francisco, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Diabetic retinopathy (DR), an incurable eye disease caused by prolonged high glucose levels in the retina, is a leading complication of diabetes mellitus and the leading cause of blindness amongst working age adults. Chronic hyperglycemia damages retinal blood vessels leading to hemorrhages, ischemia and ultimately vision loss. Microglia, the resident immune cells of the central nervous system, are believed to contribute to the development of DR. Microglial activation is largely regulated via the CX3CR1-fractalkine (FKN) signaling axis in which microglia express the CX3CR1 receptor, and neurons express it's only ligand, FKN. A polymorphic variant of the CX3CR1 gene, present in 25% of the population, causes the CX3CR1 receptor to be adhesive defective to FKN. Previous studies have shown that aberrantly activated microglia in the diabetic retina are responsible for increased vascular damage, microglial clustering around vascular lesions, fibrinogen leakage, microgliosis, and up-regulation of proinflammatory mediators in CX3CR1-KO and human CX3CR1^{I249V/M280} expressing mice. Microglia appear to play an important role in mediating neuroretinal inflammation and degradation in DR. To understand the role of microglia in DR progression we depleted microglia to determine if strategies to downregulate microglia mediated inflammation can prevent neuronal damage and hence vision loss.

Methods: Utilizing a genetic model using mice expressing an inducible Cre under the CX3CR1 promoter and the DTR gene under the Rosa 26 promoter (CX3CR1^{CreER}:R26^{iDTR}), expression of DTR by CX3CR1-expressing cells only occurs upon tamoxifen (TAM) treatment, rendering microglia susceptible to the effects of diphtheria toxin.

Results: Following acute microglia depletion in diabetic CX3CR1^{CreER}:R26^{iDTR} mice, we depleted ~90% of microglia in the retina without depleting CX3CR1-expressing cells in the periphery. We observed an increase in neuronal cell loss and astrogliosis, without significant axonal damage. These results reveal that we can successfully deplete microglia in the retina without effecting peripheral immune cells or eliciting neurotoxic effects in the murine diabetic retina.

Conclusions: Further studies looking at chronic depletion of activated microglia and aberrantly activated CX3CR1-M280 microglia in DR retinas are crucial to potentially to ameliorate inflammatory-mediated damage to neurons.

CONTROL ID: 3547427

SUBMITTER (NAME ONLY): Nundehui Diaz-Lezama

TITLE: PDGF Receptor Alpha is key for Müller cell homeostasis functions

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Müller cells, the major retinal macroglia, contribute to maintain vascular integrity as well as retinal fluid and ion homeostasis. Although PDGF receptor expression in Müller glia has been reported earlier, their actual role for Müller cell function and intimate interaction with cells of the retinal neurovascular unit remains unclear.

Methods: Müller cell-specific PDGF receptor alpha (PDGFR α) knockout (KO) were generated by crossbreeding a tamoxifen-inducible Glast-CreER^{T2} driver line with PDGFR α ^{fl/fl} mice. We isolated Müller cells (4 weeks post-tamoxifen injection) by MAC sorting and analyzed the efficiency of Müller cell-specific deletion of PDGFR α at mRNA and protein level by qPCR and immunofluorescence. To analyze the functional role of PDGF in Müller cell physiology, we performed volume regulation experiments in vital retinal slices. We also evaluated the retinal functional integrity by electroretinogram recordings (ERG). To investigate the role of PDGF signaling in Müller glia in retinal diseases, we subjected Müller cell-specific PDGFR α KO mice to a model of choroidal neovascularization (CNV) and analyze the retinal vasopermeability.

Results: We demonstrated the usability of double transgenic Glast-CreER^{T2};PDGFR α ^{fl/fl} (PDGFR α KO) mice to induce Müller cell-specific PDGFR α knockout. The vast majority of isolated Müller cells from those mice were lacking immunoreaction for PDGFR α and the mRNA levels of Pdgfra were also significantly downregulated in comparison to wild type controls. PDGFR α -deficient Müller cells could not counterbalance hypoosmotic stress as efficiently as their wildtype counterparts. In wildtypes, the PDGFR α ligand PDGF-BB prevented Müller cell swelling induced by administration of barium ions. This effect could be blocked by the PDGFR family inhibitor AC710. PDGF-BB could not restore the capability of an efficient volume regulation in PDGFR α KO Müller cells. Additionally, PDGFR α KO mice displayed reduced ERG response. Remarkably, Müller cell-specific PDGFR α KO resulted in less vascular leakage and smaller lesion area in the CNV model.

Conclusions: In sum, our data support the hypothesis that PDGF signaling is central for retinal functions under physiological conditions. These data imply that targeting PDGF to treat retinal neovascular diseases may have short term beneficial effects, but may elicit unwarranted side effects given the putative negative effects on Müller cell homeostatic functions.

CONTROL ID: 3547428

SUBMITTER (NAME ONLY): RENATO LECA

TITLE: Study of the corneal temperature variation during photo-refractive procedures

SESSION TITLE: Multidisciplinary imaging technologies and applications

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Refractive surgery, although it causes very few complications and a rapid recovery of the patient, very little attention has been given to the issue of corneal temperature during this type of surgical procedure. The temperature becomes something important to be evaluated because an ablation laser is used during the procedure, which can cause injuries to the tissue due to the thermal energy inserted locally in the ablation region. Thus, the idea of this study is to deepen this knowledge using a digital infrared thermal image to evaluate how invasive this procedure can be from a perspective of the thermal energy inserted in this process and its relationship with the physiology of cornea.

Methods: Thermal digital images were obtained at a distance of 40cm from the ocular surface and performed at a rate of 30 frames/s using infrared cameras, model: T540 (sensitivity <40mK/resolution 464 x 348 pixels) and A6753sc (sensitivity <30mK/640x512 pixels Flir System), the data were analyzed via software and we used infrared radiation intensity and temperature of regions of interest, ablation site, pre and post procedure eye temperature, and all areas of interest were analyzed the maximum, minimum and average temperature, and also calculated the dissipated energy in Watts. Surgery was performed in an environment with controlled temperature and humidity, ablation of the corneal surface was performed with Excimer laser, with a spherical profile of 6-7mm and maximum ablation time of 16s.

Results: Thirty uneventful surgical procedures were analyzed, with the patients acclimatized in a room at 23°C and 50% relative humidity. The average global ocular surface temperature was 30.33±0.45°C after flap-elevating in LASIK procedures or epithelial debridement in PRK procedures, before the ablation; energy input was 0.26 Watts/s exposure. The tissue returned to pre-exposure temperature 3.5s after the application of laser, on average. The peak temperature is closely linked to the laser exposure time, and the maximum peak observed was 36.11°C.

Conclusions:

In this research, in photo-refractive procedures, where peaks of almost 6 ° C on the corneal surface were observed, the 30 corneas studied were able to return to the temperature before the procedure very quickly, 3.5 seconds on average, showing a prepared physiology for these temperature variations, avoiding tissue damage. Larger diopters led to a longer recovery time.

CONTROL ID: 3547429

SUBMITTER (NAME ONLY): Ratheesh Kumar Meleppat

TITLE: Multicolor confocal fluorescence microscopy provides the enhanced visualization and fluorescent emission properties of intrinsic fluorophores in retinal pigment epithelium cells

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Meleppat, S.J. Karlen, E.N. Pugh, R.J. Zawadzki, Cell Biology & Human Anatomy, University of California Davis, Davis, California, UNITED STATES|R. Meleppat, K. Kothandath, R.J. Zawadzki, Dept. of Ophthalmology & Vision Science, University of California Davis, Sacramento, California, UNITED STATES|K. Ronning, M. Burns, Center for Neuroscience, University of California Davis, Davis, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ratheesh Kumar Meleppat: Commercial Relationship: Code N (No Commercial Relationship) | Kaitryn Ronning: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Karlen: Commercial Relationship: Code N (No Commercial Relationship) | Karuna Kesavan Kothandath: Commercial Relationship: Code N (No Commercial Relationship) | Marie Burns: Commercial Relationship: Code N (No Commercial Relationship) | Edward Pugh: Commercial Relationship: Code N (No Commercial Relationship) | Robert Zawadzki: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To investigate the intrinsic autofluorescent (AF) granules in the retinal epithelium (RPE) cells of mouse retina and their AF emission properties using multicolor confocal fluorescent microscopy (MCFM). Compare the in vivo recorded spectra with ex vivo measured spectra with MCFM for the mouse model of Stargardt's disease (*Abca4*^{-/-} [129S4]) and agouti WT control.

Methods: In situ imaging of RPE flat-mounts from agouti *Abca4*^{-/-} (129S4) and agouti WT (129S1/SvImJ) controls, was performed with a Nikon A1 confocal microscope. High-resolution confocal image z-stacks of the RPE cell mosaic were acquired with four different excitation wavelengths (405nm, 488nm, 561nm, and 640nm). In vivo AF spectra for same four excitation wavelengths are acquired with a spectrometer-integrated SLO system from both mice strains. The autofluorescence images of RPE, including voxel-by-voxel emission spectra, were acquired, and processed with Nikon NIS-AR Elements software.

Results: MCFM provided an enhanced visualization of the RPE cell mosaic, including melanosomes and lipofuscin granules, and their variations in *Abca4*^{-/-} and agouti WT control mice. MCFM allowed the extraction of AF emission spectrum from the individual granules. Acquired in vivo spectra are compared with the ex vivo measured spectra for both mice strains.

Conclusions: MCFM can delineate individual RPE autofluorescent granules and provide their characteristics AF emission spectra. Lipofuscin granules and melanosomes are the two major pigmented granules. Lipofuscin granules are identified as the major source of AF from RPE whereas, melanosomes completely lack fluorescence in visible excitation ranges. The in vivo acquired spectra are in good agreement with the ex vivo spectra. This comparison also revealed the source of FAF and their changes in disease model.

CONTROL ID: 3547430

SUBMITTER (NAME ONLY): Durga Borkar

TITLE: Utility of a postoperative hour one intraocular pressure evaluation to predict postoperative day one management changes after uncomplicated pars plana vitrectomy

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.S. Borkar, F. Brodie, A. Ponugoti, A. Song, A. Ayala, X. Zhang, Duke University Eye Center, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: The current COVID-19 pandemic has emphasized the need for streamlining in person office visits while maintaining clinical outcomes and patient safety. Prior studies have shown that an intraocular pressure (IOP) increase at postoperative day one (POD1) is the primary clinical finding necessitating an unexpected management change after uncomplicated pars plana vitrectomy in asymptomatic patients. The purpose of this study was to evaluate whether a postoperative hour one (POH1) IOP measurement in the postoperative recovery area can predict a POD1 IOP elevation.

Methods: Retrospective chart review was performed at an academic medical center of all cases of uncomplicated pars plana vitrectomy (with or without scleral buckle) for which POH1 IOP was measured between November 2019 and May 2020. The preoperative evaluation, operative report, and POD1 visit were reviewed. Relevant clinical characteristics were recorded including history of glaucoma or ocular hypertension, administration of intraoperative acetazolamide, POH1 IOP, POD1 IOP, and any additional unexpected management changes at the POD1 visit.

Results: During the study period, 63 cases of 62 eyes had POH1 IOP evaluated. The most common indications for surgery were rhegmatogenous retinal detachment (61.9%) and macular hole repair (25.4%) After excluding eyes with a history of glaucoma or ocular hypertension, 5 patients had a POD1 IOP measurements over 30mmHg. All of these eyes had a POH1 IOP measurement over 20 mm Hg. No other significant unexpected management changes were prescribed at the POD1 timepoint in asymptomatic eyes.

Conclusions: In non-glaucomatous eyes, POHR1 IOP measurements provide a promising tool to predict POD1 IOP elevations that would necessitate changes in management. As a result, POHR1 IOP data may help us streamline postoperative care for asymptomatic patients after uncomplicated vitreoretinal surgery during the COVID-19 pandemic.

CONTROL ID: 3547431

SUBMITTER (NAME ONLY): SO GOTO

TITLE: Ocular heterotopic bone formation in guinea pig: A case report with 7 months follow-up using advanced ophthalmic imaging technology

SESSION TITLE: Anterior segment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. GOTO, Q. Zhu, J. Torres, C.F. Wildsoet, University of California Berkeley School of Optometry, Berkeley, California, UNITED STATES|S. GOTO, Ophthalmology, Osaka University Graduate School of Medicine, JAPAN|K. Jensen, Office of Laboratory Animal Care, University of California Berkeley, Berkeley, California, UNITED STATES|Q. Zhu, Optometry and Visual Science, West China Hospital of Sichuan University, CHINA|

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ABSTRACT BODY:

Purpose: To establish reference ophthalmic findings, which include seven months follow-up data from one guinea pig diagnosed with heterotopic bone formation (HBF).

Methods: Slit lamp biomicroscopy, gonioscopy, optical biometry, rebound tonometry, anterior segment optical coherence tomography (AS-OCT), and posterior segment spectral domain optical coherence tomography (SD-OCT) were all performed on a 3.8-year-old male guinea pig suspected of having heterotopic bone formation. The eyes of this animal underwent further evaluation 7 months after the initial evaluation.

Results: Slit lamp biomicroscopy revealed vascularized, white masses in the anterior chamber, adjacent to the limbus, both nasally and temporally in the right eye, and both superiorly and temporally in the left eye. Their apparent locations, between the posterior corneal (endothelium) surface and anterior iris, were confirmed by gonioscopy and AS-OCT examinations. The right eye showed slightly elevated intraocular pressure compared to the left eye (18.3 vs. 13.3 mmHg) and recorded a slightly longer axial length (10.40 vs. 10.29 mm). However, SD-OCT showed no obvious differences in the shape or appearance of the optic nerve heads of the two eyes. Measurements made 7 months after the initial examination revealed significant progression in both eyes, in terms of the areal extent of the HBF lesions, as revealed by slit-lamp biomicroscopy and AS-OCT imaging. In the right eye, the lesions had extended into both superior and inferior limbal regions and in the left eye, into the nasal region. Recorded IOPs were only slightly higher than the earlier readings and still within a normal range, although a disparity between right and left eyes was again in evidence, with the right eye recording being 5.3 mmHg higher. Nonetheless, no changes in either nerve fiber layer thickness or total retinal thickness in the vicinity of the optic nerve heads were observed.

Conclusions: Advanced ophthalmic imaging techniques including OCT can provide important clinical insights into the pathophysiological changes in HBF. This case report provides reference time course data for ocular HBF in the guinea pig.

CONTROL ID: 3547433

SUBMITTER (NAME ONLY): Joshua Wang

TITLE: Redox Regulation of Endothelial Progenitor Function and Senescence in Aging Retina

SESSION TITLE: Retinal diseases: molecular and biochemical mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.J. Wang, C. Liao, S.X. Zhang, University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joshua Wang: Commercial Relationship: Code N (No Commercial Relationship) | Chunfen Liao: Commercial Relationship: Code N (No Commercial Relationship) | Sarah Zhang: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aging is a significant risk factor for neurovascular injury in diseases such as diabetic retinopathy. This is in part attributable to declined function of progenitor cells to repair and replenish damaged endothelium resulting in sustained damage and loss of blood vessels. Herein, we investigated the role of NADPH oxidase 4 (Nox4), a key regulator of redox homeostasis, in endothelial progenitor function and senescence associated with retinal changes during aging.

Methods: Bone marrow-derived endothelial outgrowth cells (EOCs) were isolated and cultured from Tie2-specific human Nox4 overexpression (Nox4-Tg) mice or Nox4 KO mice at ages 5, 8, 12, and 24 months. EOC cell proliferation, migration, senescence, apoptosis, ROS generation were determined. Gene expression of signaling pathways underlying the cellular events were examined.

Results: The mRNA and protein levels of Nox4 were markedly increased, accompanied by enhanced ROS levels, in EOCs from mice of age 12 months, and to a significantly greater extent in EOCs from 24 month-old mice, when compared to young adults. Substantial increase of Nox4 and ROS were confirmed in EOCs from Nox4 Tg mice and reduction in Nox4 KO EOCs. Age or overexpression of NOX4 showed no effect on cell proliferation, but led to a significant increase in apoptosis and senescence of EOCs. Nox4 deletion significantly attenuated apoptosis, reduced pro-apoptotic gene CHOP expression, and inhibited caspase-3 activation in aging EOCs. Nox4 deletion also significantly decreased p53 and p21 expression, and demonstrated a trend in reducing senescence of aging EOCs. In addition, knockout Nox4 markedly improved the basal level and stromal derived factor-1 (SDF-1)-stimulated EOC migration through upregulation of CXCR4. Consistent with the changes in EOCs, Nox4 Tg mice demonstrated significantly increased acellular capillary formation in the retina compared to age-matched wild type.

Conclusions: Our results suggest that Nox4-derived ROS is implicated in age-related endothelial progenitor cell apoptosis and senescence. Approaches that manipulate Nox4 and ROS production may improve the function of endothelial progenitor cells thus reducing the risk of vascular damage in retinal diseases.

CONTROL ID: 3547434

SUBMITTER (NAME ONLY): Lauren Malaya

TITLE: Histological Correlation of Basement Membrane Deposits in Age-Related Macular Degeneration and Renal Dense Deposit Disease

SESSION TITLE: AMD: Biochemical and molecular disease mechanisms

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Afrouzian, P. Gupta, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|L. Malaya, The University of Texas Medical Branch at Galveston School of Medicine, Galveston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Lauren Malaya: Commercial Relationship: Code N (No Commercial Relationship) | Marjan Afrouzian: Commercial Relationship: Code N (No Commercial Relationship) | Praveena Gupta: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The pathophysiology of drusen formation in dry age-related macular degeneration (AMD) is incompletely understood. Studies have found common molecular components of the complement system in drusen of dry AMD and dense deposit disease (DDD) of the kidney. To understand the pathophysiology of AMD we compared the morphological features of the two diseases by light (LM) and immunofluorescence (IF) microscopy.

Methods: Human donor eyes with dry AMD (n=3) and kidney biopsies from patients diagnosed with DDD (n=2) were studied in compliance with the institutional guidelines. Formalin-fixed and snap-frozen fresh samples from both eye and kidney specimens were cut at 2 and 5 microns, respectively, and stained with H&E, PAS, Masson's trichrome, Jones silver, Verhoeff's stains, and anti-C3 antibody. Unstained sections were used as controls for autofluorescence. Slides were analyzed under bright field and confocal fluorescence microscope.

Results: Morphological similarities were observed between drusen and DDD deposits: Significant thickening of the Bruch's membrane (BrM) and glomerular basement membrane (GBM) was found in both diseases by PAS stain, suggesting the presence of excess matrix formation composed of polysaccharides and mucins. While multiple large laminar deposits of drusen were diffusely dispersed alongside the BrM, by LM, the GBM in DDD did not reveal the deposits by LM. By PAS stain, the cleavage edge – splitting of BrM between the basement membrane of the RPE and the inner collagenous layer – was observed in AMD specimens, while the DDD specimens revealed double contouring of the GBM. Abundant notched inter-capillary pillars were seen in AMD, mirroring increases in mesangial matrix seen in DDD specimens. Jones silver staining revealed extracellular matrix (abundance of oxidized carbohydrates), particularly around capillaries in both specimens. By IF, linear deposits of C3 were found in dry AMD along the BrM compared to strong deposits of C3 seen along the GBM in DDD sections.

Conclusions: We show similarities in the structural defects in the membranes of dry AMD eye and the DDD kidney. Moreover, C3 deposition in the BrM and GBM in drusen and DDD have similarities in terms of pattern and intensity. As DDD has a complement-mediated pathogenesis, hypothetically, it is possible that the pathogenesis in AMD is also related to complement system dysfunction.

CONTROL ID: 3547437

SUBMITTER (NAME ONLY): Kai Seely

TITLE: Association between retinal microanatomy at 36 weeks postmenstrual age and grating acuity at 9 months in preterm infants.

SESSION TITLE: Retinopathy of prematurity/vein occlusion

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: K. Seely, N. Sarin, S. Mangalesh, S.F. Freedman, C.A. Toth, Department of Ophthalmology, Duke University, Durham, North Carolina, UNITED STATES|B. McGeehan, G. Ying, Center for Preventive Ophthalmology and Biostatistics, University of Pennsylvania, Philadelphia, Pennsylvania, UNITED STATES|C.A. Toth, Department of Biomedical Engineering, Duke University, Durham, North Carolina, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Kai Seely: Commercial Relationship: Code N (No Commercial Relationship) | Brendan McGeehan: Commercial Relationship: Code N (No Commercial Relationship) | Gui-Shuang Ying: Commercial Relationship: Code N (No Commercial Relationship) | Neeru Sarin: Commercial Relationship: Code N (No Commercial Relationship) | Shwetha Mangalesh: Commercial Relationship: Code N (No Commercial Relationship) | Sharon Freedman: Commercial Relationship: Code N (No Commercial Relationship) | Cynthia Toth: Commercial Relationship(s);Theia Imaging:Code I (Personal Financial Interest);Alcon:Code R (Recipient);EMMES:Code C (Consultant)

ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the association between retinal microanatomy at 36 weeks postmenstrual age and Teller card grating visual acuity (VA) at 9 months in preterm infants.

Methods: For each infant and for each eye, we analyzed optical coherence tomography (OCT) images from one bedside imaging session captured at 35-37 weeks postmenstrual age. We also analyzed retinopathy of prematurity (ROP) stage (the same day as OCT imaging), infant demographics, and Teller card grating VA at 9 months corrected age. We captured all measures prospectively from preterm infants enrolled in the Study of Eye imaging in Preterm infants (BabySTEPS; NCT02887157). Expert graders, masked to other study data except for age, extracted OCT microanatomy features (e.g., presence/severity of macular edema) and retinal thicknesses, including: inner layer complex (retinal nerve fiber layer [RNFL], ganglion cell, and inner plexiform layer) thickness at the foveal center; inner nuclear layer thickness at the foveal center; total retina thickness at the foveal center; choroid thickness averaged across the foveal 1mm; and RNFL thickness at the papillomacular bundle (PMB). We analyzed for associations of OCT retinal microanatomy features with categorized VA (normal vs. subnormal, using a threshold of 3.70 cycles/degree) using logistic regression models and with continuous logMAR VA using linear regression models. We accounted for inter-eye correlation by using generalized estimating equations.

Results: Of the 130 eyes of 65 infants with both OCT and VA data, 71 (55%) eyes of 40 infants had subnormal VA (<3.70 cycles/degree), and 12 (9%) eyes of 6 infants had prior ROP treatment. On univariable linear regression, low gestational age, low birthweight, prior ROP treatment, and RNFL thinning at the PMB were associated with higher logMAR. On multivariable linear regression, ROP treatment ($p=0.006$) and RNFL thinning at the PMB ($p=0.007$) were independently associated with higher logMAR. On logistic regression, only prior ROP treatment ($p=0.021$) was associated with subnormal VA, though RNFL thinning at the PMB ($p=0.097$) approached significance.

Conclusions: RNFL thinning at the PMB is associated with poorer 9-month VA in preterm infants, independent of ROP severity and demographic features.

CONTROL ID: 3547439

SUBMITTER (NAME ONLY): Salvatore Stella

TITLE: Activation of A₁ and A₃ adenosine receptors protect zebrafish photoreceptors from neurodegeneration in a light-induced retinal degeneration model

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S.L. Stella, T.D. Friemel, A.S. Khan, Neural and Behavioral Sciences, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|T.D. Friemel, Basic Biomedical Sciences, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota, UNITED STATES|A.S. Khan, Division of Anatomy, Albany Medical College, Albany, New York, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Salvatore Stella: Commercial Relationship: Code N (No Commercial Relationship) | Taylor Friemel: Commercial Relationship: Code N (No Commercial Relationship) | Amanda Khan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal diseases that damage photoreceptors, particularly those that affect cones such as the “dry” form of age-related macular degeneration (AMD), have dire consequences for vision. Models of light-induced retinal degeneration (LIRD) recapitulate some of the damage observed in dry AMD. One strategy for treating AMD is to utilize a “druggable” therapy targeted to neuroprotective mechanisms in photoreceptors. Adenosine has neuroprotective properties at neurons within the central nervous system and prevents neurodegeneration. The purpose of this study was to determine which adenosine receptors mediate neuroprotection of photoreceptors in a zebrafish LIRD model.

Methods: Adult wild-type and Tg(nrd:GFP) zebrafish were dark-adapted for 24 hours, followed by intravitreal injections of adenosine or adenosine receptor agonists (A₁R, A_{2A}R, A_{2B}R, A₃R). Controls were injected with saline in both eyes. All zebrafish were exposed to high-intensity light (28,000 lux) and collected at 0 and 96 hours post dark-adaptation. Immunohistochemical analysis with cell specific markers, TUNEL assays, and optomotor response measurements were performed on zebrafish in order to assess the impact of adenosine and adenosine receptor agonists on LIRD.

Results: Treatment of retinas with adenosine resulted in a dose-dependent survival of both rod and cone photoreceptors after LIRD that was mediated by both A₁R and A₃R in the retina. Any damage observed in adenosine-treated retinas was not enough to stimulate a regenerative response, arguing in favor of a neuroprotective mechanism. Moreover, higher concentrations of adenosine prevented structural damage and apoptosis of rods and cones while preserving both visual acuity and contrast sensitivity in zebrafish retinas, suggesting that adenosine has the capacity to preserve photoreceptor function.

Conclusions: These findings clearly demonstrate that adenosine acting on A₁R and A₃R has a significant capacity for neuroprotection and provides evidence of a potential novel therapeutic target for the treatment of the dry form of AMD.

CONTROL ID: 3547440

SUBMITTER (NAME ONLY): Daniel Rosenberg

TITLE: Long-term efficacy and treatment burden of treat-and-extend versus fixed or PRN regimens for nAMD: a systematic review and meta-analysis.

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Rosenberg, J. Gould, A. Sothivannan, Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, CANADA|D. Deonarain, McMaster University, Hamilton, Ontario, CANADA|M. Phillips, V. Chaudhary, McMaster University Department of Health Research Methods Evidence and Impact, Hamilton, Ontario, CANADA|V. Chaudhary, McMaster University Department of Surgery, Hamilton, Ontario, CANADA|

Commercial Relationships Disclosure (Abstract): Daniel Rosenberg: Commercial Relationship: Code N (No Commercial Relationship) | Deven Deonarain: Commercial Relationship: Code N (No Commercial Relationship) | Jonah Gould: Commercial Relationship: Code N (No Commercial Relationship) | Amirthan Sothivannan: Commercial Relationship: Code N (No Commercial Relationship) | Mark Phillips: Commercial Relationship: Code N (No Commercial Relationship) | Varun Chaudhary: Commercial Relationship(s);Novartis:Code C (Consultant);Bayer:Code C (Consultant);Novartis:Code F (Financial Support);Bayer:Code F (Financial Support);Allergan:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To compare efficacy and treatment burden of a treat-and-extend (T&E) anti-VEGF treatment of age-related macular degeneration (AMD) against fixed and pro re nata (PRN) schedules.

Methods: MEDLINE, CENTRAL, and EMBASE were searched from 2004 to August 2020. Randomized-controlled trials and observational studies comparing T&E to PRN or fixed dosing for treatment-naïve AMD patients were included. Mean difference (MD), and 95% confidence intervals (CI) for visual acuity (VA) and injection frequency are presented. Risk of bias was assessed according to Cochrane guidelines. Methodology was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Results: 6 RCTs and 5 observational studies were identified. VA improvement was similar for eyes receiving T&E and fixed dosing at one (743 eyes T&E, 725 eyes fixed; MD -0.08 letters, 95% CI -2.52-2.36, $p = 0.95$, $I^2 = 69\%$) and two years (260 eyes T&E, 249 eyes fixed; MD 0.58 letters, 95% CI -1.74-2.90, $p = 0.62$, $I^2 = 0\%$). In contrast, visual acuity improvements were significantly greater for T&E eyes when compared against a PRN regimen at one (525 eyes T&E, 748 eyes PRN; MD 3.95 letters, 95% CI 2.13-5.77, $p < 0.0001$, $I^2 = 40\%$) and two years (85 eyes T&E, 187 eyes PRN; MD 4.08 letters, 95% CI 1.67-6.49, $p < 0.001$, $I^2 = 0\%$). Significantly fewer ranibizumab injections were administered in the T&E arm at one (628 eyes T&E, 604 eyes fixed; MD -2.42 injections, 95% CI -2.71 to -2.14, $p < 0.0001$, $I^2 = 0\%$) and two years (267 eyes T&E, 249 eyes fixed; MD -6.06 injections, 95% CI -6.79 to -5.34, $p < 0.00001$, $I^2 = 17\%$) relative to fixed dosing. Fewer aflibercept injections were likewise administered to patients on a T&E regimen versus fixed dosing at one year (127 eyes T&E, 124 eyes fixed; MD -0.78 injections, 95% CI -1.14 to -0.42, $p < 0.0001$, $I^2 = 53\%$). No studies compared T&E to fixed aflibercept at two years. Significant heterogeneity precluded meta-analysis of injection frequency among studies comparing T&E to PRN dosing.

Conclusions: T&E preserves VA similar to fixed schedules with significantly fewer injections at one and two years. Patients on a PRN regimen receive fewer injections than those on T&E dosing, but with less favourable visual outcomes. Additional studies are required for more robust meta-analysis of anti-VEGF injection frequency at 1 year and beyond.

CONTROL ID: 3547441

SUBMITTER (NAME ONLY): Vishnu Adi

TITLE: Longitudinal age effects of optineurin E50K mutation and deficiency on visual function

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Adi, J. Sims, D. Forlenza, C. Liu, H. Song, G. Hamilton-Fletcher, N. Colwell, M.A. Faiq, H. Ishikawa, G. Wollstein, J.S. Schuman, K. Chan, Department of Ophthalmology, New York University School of Medicine, New York, New York, UNITED STATES|H. Ishikawa, G. Wollstein, J.S. Schuman, Department of Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|H. Tseng, Duke University Department of Ophthalmology, Durham, North Carolina, UNITED STATES|K. Chan, Department of Radiology, New York University School of Medicine, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Mutations in optineurin (OPTN) are associated with familial normal tension glaucoma and other neurodegenerative diseases. It remains unclear how OPTN loss or mutation alters visual function during aging. Here, we used transgenic mouse models and in vivo assessments to test the hypothesis that OPTN dysfunction contributes to progressive visual impairment through a toxic gain of function mechanism.

Methods: Mice with C57BL/6 background were used (Fig 1): wildtype (WT; n=19), homozygous OPTN knock-out (mOPTN-KO; n=13), hemizygous mouse E50K OPTN knock-in (mE50K-het; n=8), homozygous mouse E50K OPTN knock-in (mE50K homoz; n=10), and human E50K OPTN bacterial artificial chromosome overexpression (hE50K BAC; n=6) (PMID: 31076632, 25818176). Intraocular pressure (IOP), total retinal thickness (TRT), visual acuity (VA), and contrast sensitivity (CS) were measured at 6, 12, and 18 months of age in the same mice using the TonoLab rebound tonometer, Bioptigen spectral-domain optical coherence tomography imaging, and OptoMotry optokinetic virtual reality system, respectively. Left and right eye data were averaged and analyzed using ANOVAs followed by posthoc tests between genotype and age groups, as well as linear regressions for VA versus contrast threshold (CT).

Results: Our longitudinal study of the same mice during the aging process showed that IOP remained normal between 10-15 mmHg (Fig 2A). Small to no difference in TRT over time or compared to WT was observed (Fig 2B). mE50K-homoz, mE50K-het, and hE50K BAC mice exhibited greater age-dependent decline in VA and CT than WT or mOPTN-KO mice (Fig 2C, 2D, 2E). In contrast, mOPTN-KO mice showed preservation of VA and CT over time compared to WT. Consistently, mice with one copy of E50K OPTN (mE50K het) experienced less deterioration of VA and CT compared to mice with two copies (mE50K homoz) or mild overexpression (hE50K BAC).

Conclusions: Despite limited IOP and TRT changes between age and genotype groups, E50K OPTN was associated with differential age-dependent visual impairment (greater for CS than VA). Surprisingly, OPTN deficiency preserved visual function such that CS in knockout mice was better than WT mice. Our results suggest visual loss associated with E50K OPTN is due to a toxic gain of function mechanism, and that suppression of OPTN might constitute a therapeutic strategy for glaucomatous neurodegeneration.

CONTROL ID: 3547444

SUBMITTER (NAME ONLY): Caitlin Samson

TITLE: Etiologic Spectrum, Disease Severity, and Vision Outcomes in Pediatric Uveitis: A Single Referral Center Experience

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Samson, J.M. Samson, C.M. Samson, Ophthalmology, Manhattan Eye Ear and Throat Institute, New York, New York, UNITED STATES|J.M. Samson, University of California San Diego, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Caitlin Samson: Commercial Relationship: Code N (No Commercial Relationship) | James Samson: Commercial Relationship: Code N (No Commercial Relationship) | C Samson: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To describe the characteristics and outcomes of pediatric uveitis seen and managed at a tertiary care center in New York City.

Methods: Charts of pediatric patients (<18 years of age) with a diagnosis of uveitis seen on the Uveitis Service at the Manhattan Eye, Ear, and Throat Hospital between 2017 and 2020 were reviewed. Gender, anatomical location of uveitis, laterality, uveitis etiology, age of uveitis onset, visual outcome, need for immunomodulatory therapy, need for surgery, and drug free remission, were collected.

Results: A total of 78 patient charts were reviewed. Most patients were female (71.8%). Anterior uveitis was the most common type (78.2%). The most common etiologies were idiopathic (48.7%) and JIA (37.2%). 80.8% children had undergone treatment with immunomodulatory therapy (IMT) during their disease course. Of these, 46% have discontinued their IMT during the follow-up period: 89.7% remained in drug-free remission at 5 years. 24.4% of children required surgery. Most of the children (94.3%) had vision of 20/40 or better in at least one eye, and no patients were legally blind.

Conclusions: Pediatric uveitis patients managed at a tertiary care center often required immunomodulatory therapy, and 1/4 required surgery. Great visual outcomes were achievable, and many children remain inflammation free after discontinuation of IMT.

CONTROL ID: 3547448

SUBMITTER (NAME ONLY): Ala Morshedian

TITLE: The D167A mutation in PDEA greatly depresses PDE expression but produces sensitive (though slower) rod responses and remarkably slow degeneration

SESSION TITLE: Retinal neurodegeneration and protection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: A. Morshedian, G. Sendek, S.Y. Ng, R.A. Radu, G.L. Fain, Jules Stein Eye Institute, University of California Los Angeles, Los Angeles, California, UNITED STATES|K. Boyd, N. Artemyev, University of Iowa, Iowa City, Iowa, UNITED STATES|A. Abtout, J. Reingruber, Institut de Biologie de l'École Normale Supérieure, Paris, FRANCE|M. Liu, Institute of Life Science, East China Normal University, Shanghai, CHINA|

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ABSTRACT BODY:

Purpose: Mutations in the beta subunit of phosphodiesterase 6 expressed in rod photoreceptors have been shown to cause rapid retinal degeneration in mouse models such as rd1. In this study we demonstrate that the D167A mutation in PDEA leaves rods with less than 10% of normal PDE expression, but this is enough to protect the cells from precipitous degeneration.

Methods: The CRISPR-Cas system was used in mouse to convert the aspartic acid at position 167 of PDE6A to alanine. Protein content was measured by serial-dilution Western blots, and PDE activity was quantified with a biochemical assay. Retinal morphology was assessed and quantified with light microscopy. Single cell photocurrents were recorded from the outer-segment of mouse rods with suction-electrode recording, and a mathematical model was used to fit the collected data.

Results: The D167A mutation in the PDE6A results in a greater than 10-fold reduction in PDE6B, with PDE6A almost undetectable. A significant reduction in basal PDE6 catalytic activity as well as trypsin-activated PDE6 activity was observed in these retinas. Degeneration was slow, with 70% of rod nuclei still remaining at 6 months. No detectable changes were observed in the sensitivity of single cells, though activation and recovery of the photoresponse were both significantly slower. These changes could be mathematically modeled by a reduction in the dark rate of PDE (b_d), a reduced rate of PDE activation, and a small elevation in dark Ca^{2+} concentration, all of which are compatible with a reduction in PDE activity.

Conclusions: The changes observed in the temporal properties of rod photoreceptors in the D167A animal can be explained by the reduction in PDE concentration and activity. The small PDE6B expression seems to be forming sufficient functional phosphodiesterase enzyme to provide protection against rapid degeneration.

CONTROL ID: 3547449

SUBMITTER (NAME ONLY): FAN XIA

TITLE: Early alterations of neurovascular unit in the retina in mouse models of tauopathy

SESSION TITLE: Retinal Cell Biology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. XIA, Y. Ha, S. shi, Y. Li, S. li, J. Luisi, M. Motamedi, H. Liu, W. Zhang, The University of Texas Medical Branch at Galveston, Galveston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The retina, as the only visually accessible tissue in the central nervous system, has attracted significant attention for evaluating it as a biomarker for neurodegenerative diseases. Yet, most of studies focus on characterizing the loss of retinal ganglion cells (RGCs) and degeneration of their axons. There is no integrated analysis addressing temporal alterations of different retinal cells in the neurovascular unit (NVU) in particular retinal vessels. Here we assessed NVU changes in two mouse models of tauopathy and evaluated the therapeutic effects of a tau oligomer monoclonal antibody (TOMA).

Methods: Studies were performed in P301S and P301L transgenic mice which overexpress the human tau mutated gene. Optical coherence tomography, scanning laser ophthalmoscopy and electroretinography were applied to non-invasively analyze retinal structural and functional changes. Vascular leakage was determined by analyzing FITC-BSA extravasation into the retina. Leukocyte adhesion was assessed by Concanavalin A labeling. Alterations of adhesion junction, microglia, leukocytes and RGCs were assessed by immunostaining in retinal flatmounts. TOMA was utilized to treat tauopathy.

Results: Retinal edema and breakdown of blood-retina barrier were observed at the very early stage of tauopathy. Leukocyte adhesion/infiltration, and microglial recruitment/activation were constantly increased in the retinal ganglion cell layer of tau transgenic mice at different ages, while Müller cell gliosis was only detected in relatively older tau mice. Concomitantly, the number and function of RGCs progressively decreased during aging although they were not considerably altered in the very early stage of tauopathy. Moreover, intrinsically photosensitive RGCs appeared more sensitive to tauopathy. Remarkably, TOMA treatment in young tau transgenic mice significantly attenuated vascular leakage, inflammation and RGC loss.

Conclusions: Our data provide compelling evidence that abnormal tau accumulation can lead to pathology in the retinal neurovascular unit, and vascular alterations occur more manifest and earlier than neurodegeneration in the retina. Oligomeric tau-targeted immunotherapy has the potential to treat tau-induced retinopathies. Retinal NVU may serve as a potential biomarker for diagnosis and staging of tauopathy as well as a platform to study the molecular mechanisms of neurodegeneration.

CONTROL ID: 3547452

SUBMITTER (NAME ONLY): Hasan Cetin

TITLE: Impact of Varying Dataset Composition Ratios on the Machine Learning Model Segmentation Performance for Subretinal Hyperreflective Material: A Quantitative and Qualitative Evaluation

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: H. Cetin, J. Whitney, D. Sevgi, J. Hach, S. Srivastava, J. Reese, J.P. Ehlers, Cleveland Clinic Cole Eye Institute, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Detection of specific features of interest on OCT is strongly linked to training data composition. For many targeted features, large comprehensive ground-truth annotated datasets are not available. Smaller datasets may be more susceptible to class imbalance potentially affecting the machine learning (ML) performance. The purpose of this study was to evaluate the impact of the variable ratios of positive to negative training data on ML performance based on quantitative and qualitative parameters on segmentation of subretinal material (SRM).

Methods: : A U-Net architecture convolutional model was executed and evaluated on training datasets with varying ratios of annotated OCT images containing (positive) and not containing (negative) SRM in neovascular age-related macular degeneration. ML performance based on 5 different ratios of positive (P) and negative (N) data: 30P-70N, 40P-60N, 50P-50N, 60P-40N, 70P-30N was assessed. The quantitative performance evaluation was calculated using F-scores. Qualitative performance evaluation was based on multiple experts' reviews of the model outputs in a tiled configuration for assessment of optimal segmentation (Figure 1).

Results: The results demonstrated variable model performance related to the training dataset ratio. Based on quantitative model performance, the F-scores ranged from 0.59 to 0.72. The highest performing model based on F-score was the 70P-30N training set. However, qualitative model performance assessment demonstrated that the 30P-70N (F-score = 0.61) was the preferred training set. In qualitative review, the 70P-30N model demonstrated excellent detection of subretinal material with few false negatives, but with an excess of false positives that was clinically impactful (Figure 1). Conversely, the 30P-70N demonstrated a more conservative segmentation with dramatic reduction in false positives while maintaining minimal false negatives.

Conclusions: This study demonstrates the important of dataset composition and positive/negative sampling ratios in datasets of limited size. In addition, this analysis identifies the potential disconnect between qualitative/practical model performance and quantitative performance metrics.

CONTROL ID: 3547455

SUBMITTER (NAME ONLY): Veeral Sheth

TITLE: Avacincaptad Pegol, A Novel C5 Inhibitor, Demonstrates a Continued Reduction in the Mean Rate of Geographic Atrophy Growth: 18-Month Results from the GATHER1 Clinical Trial

SESSION TITLE: AMD: Clinical and translational research II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: V. Sheth, University Retina, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Veeral Sheth: Commercial Relationship(s);Iveric Bio:Code C (Consultant)

ABSTRACT BODY:

Purpose: Avacincaptad pegol, a polyethylene glycol-conjugated oligonucleotide, is a potent C5 inhibitor delivered via a 100 µl intravitreal injection. The 18-month results of GATHER1, a randomized, double-masked, multi-national, sham-controlled clinical trial evaluating avacincaptad pegol for treatment of geographic atrophy (GA) secondary to age-related macular degeneration, are reported here.

Methods: Patients were randomized to avacincaptad pegol 1 mg, avacincaptad pegol 2 mg, avacincaptad pegol 4 mg or sham injection. GA progression was evaluated as a change in GA lesion area over 18 months measured by fundus autofluorescence; square-root transformation was applied to mitigate the impact of baseline factors on GA growth. Other assessments included visual function (best-corrected visual acuity and low-luminance visual acuity) and safety analysis.

Results: The least-squares mean change from baseline to month 18 in square-root GA lesion area was 0.599 mm in sham-treated patients vs 0.430 mm in avacincaptad pegol 2 mg-treated patients (28% reduction; $p < 0.0014$). The least-squares mean change from baseline to month 18 in square-root GA lesion area was 0.559 mm in sham-treated patients vs 0.391 mm in avacincaptad pegol 4 mg-treated patients (30% reduction; $p < 0.0021$). There were no significant differences in best-corrected visual acuity or low-luminance visual acuity between avacincaptad and sham-treated patients. Avacincaptad pegol was generally well tolerated after 18 months of administration, with no drug-related adverse events or trial discontinuations.

Conclusions: Intravitreal avacincaptad pegol resulted in a decrease in the rate of GA lesion growth over 18 months of treatment versus sham injection. GATHER2, a second pivotal clinical trial comparing avacincaptad 2 mg vs sham, has been initiated and is currently enrolling patients.

CONTROL ID: 3547457

SUBMITTER (NAME ONLY): Zhaoxia Zhang

TITLE: The value of OCT angiography (OCTA) to discriminate neovascular central serous chorioretinopathy (nCSC)

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. Zhang, B. Sun, C. Yan, Shanxi Eye Hospital, Taiyuan, Shanxi, CHINA|

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ABSTRACT BODY:

Purpose: Central serous chorioretinopathy (CSC) mainly affects middle-aged men and is characterized by serous detachment of neurosensory retina and retinal pigment epithelium (RPE). Although choroidal neovascularization (CNV) is a well-known complication in eyes with chronic CSC, CNV can also be detected in acute CSC, named as neovascular central serous chorioretinopathy (nCSC). This study is aimed to evaluate neovascular CSC with OCTA.

Methods: Twenty-three eyes presenating with CSC (35~50 years, 18 male and 5 female) were included in this study. Macular angiograms (3×3 mm) were obtained using spectral-domain OCT (SD-OCT, RTVue XR; Optovue). CNV was defined as flow in the outer retinal slab between the outer plexiform layer and Bruch's membrane. Eyes with nCSC were treated with anti-VEGF therapy (aflibercept 2.0mg/0.05ml intravitreal injection, 3+PRN). Clinical characteristics and OCTA were performed at the time of no more than two months after diagnosis of CSC and follow-up.

Results: Of twenty-three eyes with CSC, three eyes (13.04%) with the flat, irregular RPE elevation or PED were determined as type 1 CNV in outer retina of OCTA, even though symptomatic macular detachments resolved spontaneously. All the patients with nCSC were female, who showed a significantly worse initial best corrected visual acuity (BCVA) (Snellen 20/40) compared to eyes with non-neovascular CSC (Snellen 20/25) ($p<0.05$). BCVA, central macular thickness, subretinal fluid significantly decreased, while the CNV area and vessel density did not change after treatment.

Conclusions: OCTA provides a promising CNV detection rate in CSC. Eyes with nCSC may have acute CSC, not chronic CSC, and should be carefully examined with OCTA to determine. Anti-VEGF therapy can stabilize the nCSC.

CONTROL ID: 3547459

SUBMITTER (NAME ONLY): George Asimellis

TITLE: Central and Peripheral Corneal Pachymetry, measured by Fourier-Domain Optical Coherence Tomography and Scheimpflug Topometry in Healthy, Keratoconic, and Post-LASIK eyes

SESSION TITLE: Keratoconus and biomechanics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Asimellis, M. Stergiou, College of Optometry, University of Pikeville, Pikeville, Kentucky, UNITED STATES|M. Stergiou, Medical School, Demokriteio Panepistemio Thrakes, Komotini, East Macedonia and Thrace, GREECE|

Commercial Relationships Disclosure (Abstract): George Asimellis: Commercial Relationship: Code N (No Commercial Relationship) | Marianthi Stergiou: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate corneal pachymetry accuracy and precision by two different devices, a Fourier Domain Optical Coherence Tomography (AS-SD OCT) and a Scheimpflug Topography (Pentacam), in healthy, keratoconic, and post-LASIK eyes.

Methods: 140 eyes were examined (76 female and 64 male). Group A 80 healthy, Group B 20 keratoconic, and Group C 40 post-LASIK eyes. We used Anterior Segment-Fourier Domain Optical Coherence Tomography (OCT) and Scheimplug imaging (Pentacam). Measurements were taken at center (2 mm), periphery (5 mm average of superior, inferior, nasal, and temporal) and the thinnest location. Statistical analysis evaluated mean, STDV, and interquartile range.

Results: There was a statistically significant difference between the OCT and the Pentacam, with the Pentacam results at an average of 5% higher than those obtained by OCT.

A) In Healthy eyes the mean central by OCT is 550.35 ± 21.84 and by Pentacam which is 572.30 ± 21.66 , the mean peripheral by OCT is 573.35 ± 21.93 and by Pentacam is 626.45 ± 24.79 and the mean thinnest by OCT is 545.40 ± 21.62 and by Pentacam is 568.4 ± 20.74 . T-test is less than zero (0) with ($p < 0.001$) so there is a statistical significant difference.

B) In Keratoconic eyes the mean central OCT is 442.5 ± 21.90 in contrast to Pentacam which is 458.4 ± 23.31 , the mean peripheral OCT is 489 ± 20.44 and by Pentacam is 558.1 ± 20.36 and the mean thinnest by OCT is 434.2 ± 22.17 and by Pentacam is 453.25 ± 25.72 . In all parts the T-test is less than zero (0) with ($p < 0.001$) so there is a statistical significant difference.

C) In post-LASIK eyes the mean central OCT is 455.6 ± 26.06 in contrast to Pentacam which is 458.15 ± 27.39 , the mean peripheral by OCT is 493.5 ± 18.64 and by Pentacam is 543.45 ± 18.56 and the mean thinnest location by OCT is 428 ± 29.37 and by Pentacam is 443.95 ± 27.25 . The T-test in central is 0.43 ($p > 0.05$), in contrast to peripheral and pachymetry in thinnest location which is less than zero (0) ($p < 0.001$). The data suggest a statistical significant difference between OCT and pentacam at the periphery and thinnest location.

Conclusions: The Pentacam shows thicker corneas than OCT, attributed to the different principles of imaging. While the clinical trend in corneal pachymetry is shifting towards optical imaging, there are considerable cross-device differences in pachymetry data that need to be evaluated.

CONTROL ID: 3547465

SUBMITTER (NAME ONLY): Sampathkumar Rangasamy

TITLE: Transcriptional Dynamics of Retinal Endothelial cells underlying Blood-Retinal Barrier (BRB) alteration in Diabetic Retinopathy

SESSION TITLE: Regulating endothelial cell homeostasis

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Rangasamy, C. Legendre, Neurogenomics Division, Translational Genomics Research Institute, Phoenix, Arizona, UNITED STATES|F. Monickaraj, A. Das, University of New Mexico School of Medicine, Albuquerque, New Mexico, UNITED STATES|A. Das, New Mexico VA Health Care System, Albuquerque, New Mexico, UNITED STATES|

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ABSTRACT BODY:

Purpose: Endothelial cell dysfunction and increased vascular permeability constituting the blood–retinal barrier (BRB) alteration is the hallmark of diabetic macular edema (DME). Using next generation sequencing (NGS), we investigated the gene expression and transcriptional regulatory network dynamics across human and mouse retinal endothelial cells to understand the molecular mechanisms of DME

Methods: Retinal Endothelial (ECs) from the non-diabetic and diabetic (n=12) mouse retina were obtained through fluorescent activated cell sorting (FACS) using endothelial cell specific marker (CD31-FITC) staining. RNA sequencing of isolated E retinal ECs was done using paired-end Illumina sequencing (NovaSeq 6000 System). Single-cell RNA sequencing (scRNA) of in vitro human retinal endothelial microvessel model was performed under low and high- glucose conditions. DESeq2 analysis was performed to identify the differentially expressed genes (DEGs) set, followed by gene set enrichment analysis (GSEA) analysis and the top genes were identified using custom functional analysis tools.

Results: Transcriptomic analysis of isolated retinal ECs from diabetic animals showed differential expression of genes linked to barrier maintenance and prosurvival. We also identified enrichment of divergent transcriptional clusters connected to cellular stress response pathway in the diabetic retinal EC. In vitro expression analysis of human retinal ECs revealed early upregulation of proinflammatory and angiogenic factors such as IL-6, ICAM-1, CCL2, ANG2, which are well documented to play a critical role in BRB alterations. Integrated analysis of human and mouse retinal endothelial cells revealed identification of novel upstream signaling mediators and transcription factors such as BRK1, PKIG, HEXIM1, AND DDIT4 involved in the regulation of proinflammatory and angiogenic factors involved in the retinal vascular permeability alterations. Further, using single-cell transcriptome analysis, we characterized retinal endothelial specific robust cell markers.

Conclusions: Our study highlights the importance of endothelial cell-specific transcriptomic analysis to understand the pathogenesis of diabetic retinopathy. A detailed understanding of the transcriptional landscape of endothelial cells in diabetes will help in the development of novel molecular targets and therapies for DME.

CONTROL ID: 3547466

SUBMITTER (NAME ONLY): Margaret Runner

TITLE: Concurrent Acute Retinal Necrosis and Ocular Syphilis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.M. Runner, B.C. Toy, A.A. Moshfeghi, H. Ameri, N.A. Rao, Ophthalmology, University of Southern California, University of Southern California, Los Angeles, CA, US, academic, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Independent from one another, both acute retinal necrosis (ARN) and ocular syphilis are rare ocular infections that can present in healthy individuals as well as immunocompromised patients. To our knowledge, ARN with concurrent ocular neurosyphilis has not been reported. Herein, we describe a case of a male with newly diagnosis human immunodeficiency virus (HIV) present with ARN from herpes simplex virus-1 (HSV1) with a second co-infection of ocular syphilis.

Methods: A detailed retrospective review was conducted of a case who presented in Los Angeles County, USA with ARN confirmed with positive ocular fluid HSV1 polymerase chain reaction (PCR) and co-infection of ocular syphilis confirmed with positive cerebrospinal fluid (CSF) venereal disease research laboratory (VDRL) antibody and serum fluorescent treponemal antibody absorption (FTA-ABS).

Results: A 54-year-old previously healthy male with a gradual three month decline in vision of the left eye, presented with acute painless vision loss of the right eye. On exam, the right eye had count fingers vision with active anterior chamber inflammation, dense vitritis, and a well-demarcated wedge-shaped peripheral chorioretinal lesion. Left eye was light perception vision with a quiet anterior chamber but with heterochromia of the iris and dense white uveitic cataract obscuring the view to posterior pole but ultrasound confirmed dense vitritis. Laboratory workup revealed a new diagnosis of HIV-1 and neurosyphilis confirmed with positive VDRL of the CSF. Anterior chamber fluid of the right eye was HSV1 positive, whereas anterior and vitreal samples of the left eye were HSV1 negative. The patient underwent a series of intravitreal foscarnet injections of the right eye and oral valacyclovir and two-week course of intravenous penicillin. The vitritis and vision improved in both eyes with the right eye recovering back to 20/40 vision.

Conclusions: Though a rare infection, the rate of ocular syphilis continues to rise especially in the Los Angeles County health network. Over the past five years the Los Angeles County ophthalmology service has treated roughly 55 patients with ocular syphilis, and as far as the authors are aware, this is the first case of ocular syphilis with a co-infection of viral acute retinal necrosis. Given the rise in these ocular infections, it is important to recognize and effectively treat the various clinical presentations of infectious panuveitis.

CONTROL ID: 3547472

SUBMITTER (NAME ONLY): Romell Gletten

TITLE: Histological comparison of cytoplasmic AQP5-containing structures in bovine and mouse ocular lens fiber cells

SESSION TITLE: Lens Biochemistry/Cataract

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.B. Gletten, K.L. Schey, Biochemistry, Vanderbilt University, Nashville, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Romell Gletten: Commercial Relationship: Code N (No Commercial Relationship) | Kevin Schey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Aquaporin-5 (AQP5) is the second most abundant aquaporin in ocular lens fiber cells. Previously we have shown that in bovine outer cortical lens fiber cells, cytoplasmic AQP5 localizes to spheroidal, tubular compartments. Transmission electron microscopy revealed morphologically similar autophagosomes with degrading mitochondria. The connection between, and conservation of, these structures in mammalian lenses is unclear. The purpose of this work is to histologically define AQP5-associated cytoplasmic structures in bovine and mouse lenses to better understand lens AQP5 function and regulation.

Methods: High resolution immunofluorescence (IF) confocal microscopy was conducted on bovine and mouse lens cryosections. Colocalization analyses of cytoplasmic AQP5 and biological markers of various organelles including TOMM20 (mitochondrial marker), calnexin (endoplasmic reticulum [ER] protein), and DiI_{C₁₈}(3) (DiI; marker dye of lipid membranes) were conducted. Colocalization analysis of LC3B (autophagosomal marker) and TOMM20 was also conducted.

Results: In the bovine lens outer cortex, AQP5-associated, TOMM-20 positive cytoplasmic compartments are juxtaposed to calnexin-positive compartments. In mouse outer cortical lens fiber cells, AQP5-positive cytoplasmic structures and TOMM20-positive cytoplasmic structures were detected in separate assays. Both of these mouse lens structures are spheroidal, tubular in morphology. In mouse lenses, calnexin-positive compartments are not juxtaposed to AQP5-associated cytoplasmic compartments. In mouse and bovine lenses, TOMM20-positive cytoplasmic structures become LC3B-positive late in fiber cell maturation.

Conclusions: Bovine lens outer cortical fiber cells contain spheroidal, tubular AQP5-associated, cytoplasmic structures comprised of mitochondrial membranes that associate with the ER. These structures likely undergo autophagic degradation with fiber cell maturation. Similar AQP5-associated cytoplasmic structures are present in the mouse lens but the association of these structures with ER compartments is unclear. Future experiments will focus on further defining the relationship between AQP5, mitochondria, autophagy, and fiber cell differentiation in the mammalian lens.

CONTROL ID: 3547475

SUBMITTER (NAME ONLY): Dimosthenis Mantopoulos

TITLE: Ganglion Cell Layer Thickness Change in Neovascular Age-Related Macular Degeneration Treated with Anti-VEGF Injections

SESSION TITLE: AI in the retina/ AMD imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Mantopoulos, G. Sanchez, Ophthalmology, Dartmouth College Geisel School of Medicine, Hanover, New Hampshire, UNITED STATES|H. Ray, D. Roth, Robert Wood Johnson University Hospital, New Brunswick, New Jersey, UNITED STATES|R. Pokroy, Barzilai Medical Centre Ashkelon, Ashkelon, Southern, ISRAEL|

Commercial Relationships Disclosure (Abstract): Dimosthenis Mantopoulos: Commercial Relationship: Code N (No Commercial Relationship) | Hetal Ray: Commercial Relationship: Code N (No Commercial Relationship) | George Sanchez: Commercial Relationship: Code N (No Commercial Relationship) | Russell Pokroy: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Roth: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To assess bilateral ganglion cell layer-inner plexiform layer (GCL-IPL) thickness changes in patients with unilateral neovascular age-related macular degeneration (nAMD) treated with anti-vascular endothelial growth factor (aVEGF)

Methods: Single center, retrospective, cohort study. The medical records of patients with unilateral nAMD treated with aVEGF were reviewed. The treatment group included eyes with newly diagnosed nAMD that subsequently underwent treatment with intravitreal aVEGF injections. The control group was the fellow eye with dry age-related macular degeneration (dAMD). Eyes that received at least 10 intravitreal injections were included. Measurement of the GCL-IPL thickness was performed at different timepoints using spectral domain-optical coherence tomography (SD-OCT).

Results: A total of 216 eyes/108 patients met the inclusion criteria. The mean age [\pm standard deviation] was 80.1 years [\pm 10.7 years]. Eyes in the treatment group underwent a mean of 20.2 ± 7.2 injections in 43.2 ± 13.9 months. The mean GCL-IPL thickness decreased from $74.8 \pm 6.6 \mu\text{m}$ to 69.6 ± 9.5 ($p < 0.001$) in the treatment group and from $74.4 \pm 6.2 \mu\text{m}$ to 72.8 ± 8.2 [DM1] μm in the control group ($p = 0.013$). Other variables such as age, duration of treatment, number of injections, IOP, and central retinal thickness did not correlate with GCL-IPL thickness change.

Conclusions: The GCL-IPL thickness decreased in the treatment group and the control group. The mechanism and the clinical significance of this observation warrant further study.

CONTROL ID: 3547476

SUBMITTER (NAME ONLY): Joy Li

TITLE: Factors Associated with Obtaining a Faculty Position at Well-Regarded U.S. Ophthalmology Programs

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Li, J. O'Fee, S. Kang, B.C. Toy, USC Roski Eye Institute, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Joy Li: Commercial Relationship: Code N (No Commercial Relationship) | John O'Fee: Commercial Relationship: Code N (No Commercial Relationship) | Sara Kang: Commercial Relationship: Code N (No Commercial Relationship) | Brian Toy: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Careers in academic ophthalmology are highly competitive. The purpose of our study was to identify factors that may be associated with obtaining a faculty position at a well-regarded program.

Methods: Full-time academic ophthalmology faculty from 123 institutions with Accreditation Council for Graduate Medical Education-approved ophthalmology residency programs were included. Ophthalmology residency programs were categorized into "Top" (top 25 programs) and "Other" (non-top 25 programs) using Doximity Residency Navigator 2020-2021. Medical school rankings were determined using U.S. News and World Report 2021 and similarly categorized into "Top" and "Other" programs. Preliminary data from 38 programs (8 Top programs and 30 Other program) are reported below.

Results: A total of 979 faculty from 38 programs were included (Table 1). Compared to Other programs, Top programs had a greater number of faculty ($P = 0.0002$), proportion of fellowship-trained faculty ($P < 0.0001$), and faculty with at least one or more non-medical graduate degrees ($P < 0.0001$). Compared to Top programs, Other programs had a greater proportion of pediatric ophthalmology fellowship-trained faculty ($P = 0.0494$). Compared to Other programs, Top programs had significantly higher proportions of faculty who trained at Top medical schools ($P < 0.0001$), Top residency programs ($P < 0.0001$), and who were fellowship-trained at their current institution (Fig. 1, $P < 0.0001$). There were no significant differences between Top and Other programs in the proportion of faculty who completed at least part of their training outside the United States ($P = 0.3944$), or who completed a research fellowship ($P = 0.3274$).

Conclusions: In this preliminary study, we found faculty at top-ranked programs were significantly more likely to be fellowship-trained, have completed a fellowship at their current institution, and have had prior training at their current institution or at other top-ranked programs.

CONTROL ID: 3547479

SUBMITTER (NAME ONLY): James David

TITLE: Outcomes of Cataract Extraction with Kahook Dual Blade Goniotomy Versus iStent Trabecular Micro-Bypass Device With Minimum Two Year Follow-Up

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.A. David, J.A. Tran, Z. Fang, L.J. Al-Dujaili, Ophthalmology, LSU Health New Orleans, New Orleans, Louisiana, UNITED STATES|C. Grenier, M. Morgan, Ophthalmology, Ochsner Health System, Baton Rouge, Louisiana, UNITED STATES|

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ABSTRACT BODY:

Purpose: Kahook Dual Blade (KDB) goniotomy and iStent trabecular micro-bypass device implantation are two minimally invasive glaucoma surgical (MIGS) procedures used at time of cataract extraction to reduce intraocular pressure (IOP), but there are limited head-to-head comparisons and limited long-term data regarding their efficacy. We performed a retrospective chart review to determine long-term success rates of both devices and identify variables predictive of surgical success as well as safety profiles.

Methods: A retrospective chart review of all mild-to-moderate open angle glaucoma patients whom had cataract extraction combined with KDB or iStent with a minimum two year follow up by two surgeons. 138 eyes were treated with iStent and 50 eyes were treated with KDB. Success was defined as intraocular pressure (IOP) reduction of at least 20% of baseline IOP or reduced use of at least one IOP-lowering medication. Secondary analyses included decrease in IOP from baseline, decrease in number of IOP medications, evaluation of variables predictive of surgical success, and complication rates. Statistical analyses included paired t-test, two-group t test, Wilcoxon signed rank test, Chi-square test, and Chi-square approximation.

Results: The groups were well balanced other than slightly larger cup-to-disc ratio in iStent group (0.55 vs 0.47, $p < 0.01$). Success rates for iStent and KDB at two years were 64% and 55% ($p = 0.28$) and at three years they were 63% and 76% ($p = 0.28$), respectively. At two years, IOP decreased from baseline in the iStent group (-2.8, $p < 0.01$) but not the KDB group (-0.9, $p = 0.78$), while number of medications decreased in both groups (-0.3 for iStent with $p < 0.01$ and -0.3 for KDB with $p = 0.02$). No variables were consistently predictive of success across multiple time points. KDB had a higher incidence of prolonged postoperative iritis (8% vs 0%, $p = 0.01$), while all other complications were similar between groups.

Conclusions: These data suggest that overall, iStent and KDB are similar in terms of success rates at two and three years for patients with mild-to-moderate open angle glaucoma, although iStent may lower IOP slightly more than KDB. There are no variables that consistently predicted surgical success. Both devices had low complication rates. Further data with larger sample sizes should confirm these results.

CONTROL ID: 3547481

SUBMITTER (NAME ONLY): Caoimhe Normile

TITLE: Investigating the role of Plasminogen Activator Inhibitor-1 (PAI-1) in lamina cribrosa fibrosis using single cell RNA sequencing.

SESSION TITLE: Glaucoma: biochemistry, molecular biology, biomechanics, genomics and proteomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Simpson, O. Cappa, Wellcome – Wolfson Institute for Experimental Medicine, School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, Belfast, UNITED KINGDOM|A.F. Clark, 4Dept. Cell Biology & Immunology and the North Texas Eye Research Institute, University of North Texas Health Science Center, Fort Worth, Texas, UNITED STATES|C.J. O'Brien, Institute of Ophthalmology, Mater Misericordiae University Hospital, Dublin, IRELAND|C. Normile, M. Irnaten, C.J. O'Brien, Clinical Research Centre, UCD School of Medicine, Mater Misericordiae Hospital, University College Dublin, Dublin, IRELAND|

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ABSTRACT BODY:

Purpose: PAI-1, through its inhibition of urokinase-type and tissue-type plasminogen activators (uPA, tPA), plays a key role in fibrosis, inhibiting cellular degradation of extracellular matrix proteins. Elevated levels of PAI-1 have previously been found in studies of liver, kidney, heart and lung fibrosis. The aim of this study was to analyse the difference in gene expression between normal and glaucoma lamina cribrosa (LC) cells, in particular focusing on genes involved in fibrosis.

Methods: We obtained LC cells from 2 normal and 2 confirmed glaucoma donors. Cells were cultured and dissociated using papain dissociation method. The suspension viability was >90%. Cells from all 4 individuals were pooled and the suspension was processed on the 10x Genomics platform at Queens University Belfast (QUB) Genomics Core Technology Unit to capture a total of ~5000 cells. Sequencing was performed on an Illumina Novaseq which generated ~800 million reads. Bioinformatic analysis was performed in QUB, with SNP data used to demultiplex the individuals using the Demuxlet package.

Results: We found that the expression levels of PAI-1 and related proteins such as Vitronectin (VTN), Thrombospondin 1 (THBS1) and Somatomedin B and Thrombospondin Type 1 Domain Containing (SBSPON) are significantly enhanced in glaucomatous LC cells. tPA was overexpressed in normal LC cells compared to glaucoma LC cells.

Conclusions: Single cell RNA sequencing has revealed glaucomatous LC cells show a differential expression of pro-fibrotic genes. Increased PAI-1 leads to excess collagen accumulation and reduced extracellular matrix proteolysis, thus contributing to LC fibrosis and optic disc cupping. The overexpression of tPA in normal LC cells and its relevance to the fibrinolysis pathway may represent a novel therapeutic path.

CONTROL ID: 3547482

SUBMITTER (NAME ONLY): Michael Sun

TITLE: Assessing the Effect of Intraocular Pressure on Elastic Wave Propagation Using Optical Coherence Elastography

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Sun, T. Son, Q. Zhou, G. Yazdanpanah, V.H. Guaiquil, A.R. Djalilian, X. Yao, M. Rosenblatt, Illinois Eye and Ear Infirmary, Department of Ophthalmology and Visual Sciences, University of Chicago, Chicago, Illinois, UNITED STATES | M. Sun, T. Son, L. Nammari, J. Crutison, H. Palnitkar, G. Yazdanpanah, D. Klatt, X. Yao, T. Royston, Bioengineering, University of Chicago, Chicago, Illinois, UNITED STATES |

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ABSTRACT BODY:

Purpose: Abnormalities in the mechanical stiffness of corneal tissue as in the cases of fibrosis, keratoconus, or excessive crosslinking can remodel the corneal architecture and significantly impair vision. Optical coherence elastography (OCE) is an emerging imaging technique that has shown potential for the acquisition of high-resolution spatial information of corneal stiffness directly in vivo. Accurate assessment of tissue stiffness, however, relies on a more comprehensive understanding of elastic wave propagation through corneal tissue. Here, we assess the effects of intraocular pressure on the elastic wave propagation and the accuracy of OCE-acquired stiffness measurements.

Methods: An OCE system was custom-built and consisted of a spectral domain-OCT (SD-OCT) coupled with a mechanical piezo actuator. OCT imaging was timed with the mechanical stimulation of the piezo so that elastic wave propagation could be tracked. The raw OCT phase data was processed in MATLAB software. System calibration was performed using phantoms made of gelatin-methacrylate prior to any corneal experiments. Once calibrated, whole porcine globes were used to study elastic wave propagation in ex vivo corneal tissue. The porcine globes were cannulated, and the intraocular pressure (IOP) was controlled using a custom-built apparatus and a pressure sensor. The elastic wave speed was measured at different IOPs. Computational models were constructed using COMSOL software to assess the effect of IOP and tensile prestress on wave propagation.

Results: Preliminary results suggest that IOP has a significant effect on the propagation speed of elastic waves traveling through porcine corneal tissue. Computational models demonstrate that the increase in tensile prestress from higher IOPs increases the wave speed and lowers the accuracy of OCE-based corneal stiffness measurements.

Conclusions: Significant changes in intraocular pressure create tensile prestress within the corneal tissue, resulting in inaccurate measurements of corneal mechanical properties. Our computational model helps to understand and correct the OCE measurements. The development of OCE for clinical application may allow for direct monitoring of corneal stiffness and other mechanical properties during disease progression or after clinical therapies.

CONTROL ID: 3547484

SUBMITTER (NAME ONLY): Bennett Hong

TITLE: Optic Nerve Head Cavernous Voids in Glaucoma Suspect and Glaucoma Patients

SESSION TITLE: Structure/Function, Visual Fields, Psychophysics, and Electrophysiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Hong, R. Kinast, B. Fortune, C.F. Burgoyne, S.L. Mansberger, Ophthalmology, Legacy Devers Eye Institute at Legacy Good Samaritan Medical Center, Portland, Oregon, UNITED STATES|B. Hong, Ophthalmology, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

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ABSTRACT BODY:

Purpose: Structural changes of the optic nerve head (ONH) such as lamina cribosa defects, prelaminar schisis, and peripapillary retinal schisis have been associated with glaucoma. We describe cases of previously undescribed ONH cavernous voids that were found on routine optic nerve head imaging (spectral domain optical coherence tomography [SD OCT], Spectralis, Heidelberg Engineering).

Methods: We include a case series (n=5 eyes, 4 patients) of ONH cavernous voids with demographic and clinical information. Visual field (SITA Standard 24-2 or 30-2) progression was defined by the clinician's analysis of the final scan and averaged 13 years of follow up. Visual acuity, recorded cup to disc ratios, and intraocular pressures (IOP) were noted.

Results: The SD OCT images (Figure 1) demonstrate cystic, hyporeflective spaces that are sharply delineated from surrounding tissue. They appear to be located anterior to the lamina cribosa. Cases 1,2, and 3 may be situated within Bruch's membrane opening (BMO), while case 4 is clearly situated lateral to BMO. They are all located inferonasally and can extend ~3 clock hours (cases 1 and 4) or ~6 clock hours (cases 2 and 3). In cases 1, 3, 4 this is found exclusively in the right eye. Case 2 had simultaneous nasal presentation of similar size in the left eye. In all cases there was no clinically significant global RNFL tissue loss over time. Vision remained stable in cases 1,3,4, except case 2 who developed macular degeneration requiring anti-VEGF injections. Visual field progression was observed in Case 1 and 4, while Case 2 and 3 had stable and/or full fields over 13 and 20 years of follow up, respectively. IOP averaged 15.9 +/- 4.7 mmHg across patients and all timepoints. Cup to disc ratio remained stable in all cases, except case 2.

Conclusions: Large optic nerve head cavernous voids can present in glaucoma suspects and glaucoma patients. Longitudinal volumetric analysis may shed light on whether the size of these voids change over time.

CONTROL ID: 3547485

SUBMITTER (NAME ONLY): William Sponsel

TITLE: Monocular Jigsaw: Time Averaged CNS Maximization of the Ipsilateral Field of Vision

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W.E. Sponsel, G. Slagle, Glaucoma Research, Sponsel Foundation, San Antonio, Texas, UNITED STATES|A.V. Nguyen, K. Welburn, School of Osteopathic Medicine, University of the Incarnate Word, San Antonio, Texas, UNITED STATES|T. Maddess, John Curtin School of Medical Research, Australian National University, Canberra, Australian Capital Territory, AUSTRALIA|M.A. Reilly, Biomedical Engineering, Ohio State University, Columbus, Ohio, UNITED STATES|A. Gonzalez, Ollyes, Inc., Summit, New Jersey, UNITED STATES|W.E. Sponsel, Visual Sciences, University of the Incarnate Word, San Antonio, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Visual field loss in glaucoma patients is optimized to maximize the binocular field of vision via reciprocally asymmetric scotomal patterns in fellow eyes. (Jigsaw Effect; TVST 3.3.1, 2014). We now observe similar maximization of monocular fields arising over a physiologic time-frame. Discrete scotomal regions appear to be switched on and off via CNS coordinated alternation over a period of minutes. With MD tending to remain stable, one set of scotomal zones become visually active while adjacent segments of the previously intact visual field are switched off. These findings were discovered during a post-hoc analysis of prospective test-retest (TR) reliability of a new virtual reality perimeter.

Methods: Prospectively enrolled glaucoma patients with ≥ 5 years of highly reliable (FL, FP, and FN < 20%) and stable ($\Delta MD < 5$ dB over 5yr) Humphrey SITA visual field testing history were tested with the VisuALL virtual reality perimeter (Ollyes Inc., Summit, New Jersey, USA) using its 24-2 normal threshold algorithm twice, back-to-back. Monte Carlo simulations were used to test the hypothesis that test-retest (TR) variability within ipsilateral visual field measurements could be contributing to improved function and visual field survival in these diseased eyes. Visual fields were randomized 1,000,000 times and compared using a published method respecting the hill of vision (see TVST 3.3.1, 4.2.8 and 4.3.7).

Results: 44 eyes of 22 patients were included in the analysis. The best composite uniocular TR measurements were significantly worse than the mean randomized composite for the same eye ($p < 0.05$). However, when combined, the resulting oscillating monocular fields were significantly better than the mean from 1,000,000 randomizations ($p < 0.0001$; +1.37 dB), better than the best randomly-generated field (+0.17 dB).

Conclusions: Composite visual field patterns were significantly better than random variation, indicating CNS-directed throttling of neuronal function to maximize time-averaged visual field function in glaucomatous eyes, optimizing metabolic activation and recovery and minimizing apoptosis. Short-term fluctuation in perimetrically reliable patients may thus be a positive finding reflecting the existence of this dynamic protective phenomenon.

CONTROL ID: 3547486

SUBMITTER (NAME ONLY): Anthony Nesburn

TITLE: High Frequency of IFN-g-Producing PLZF^{lo} RORgt^{lo} iNKT1 Cells Infiltrating HSV-1 Infected Cornea is Associated with Protection from Ocular Herpes Infection and Disease

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A.B. Nesburn, R. Srivastava, S. Prakash, P.A. Coulon, L. BenMohamed, N. Dhanushkodi, Ophthalmology, Gavin Herbert Eye Institute, Irvine, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The invariant natural killer (iNKT) cells are among the first innate immune cells to elicit early protective immunity that control invading viral pathogens. The role of iNKT cells and of their three major subsets, iNKT1, iNKT2, and iNKT17, in herpes immunity remains to be fully elucidated. In this study, we examined the protective role of corneal-resident iNKT cell subsets, using the mouse model of ocular herpes infection and disease.

Methods: Wild type (WT) C57BL/6 mice and CD1d knockout (KO) mice were infected ocularly with HSV-1 (strain McKrae). Cornea, spleen and liver were harvested at 2, 5, 8 and 14-days post-infection (p.i.) and the frequency and function of the three major iNKT cell subsets were analyzed by immunostaining and flow cytometry. The profiles of sixteen major cytokines were analyzed in corneal lysates using western blot and Luminex assays.

Results: Early during ocular herpes infection (i.e. day 2), the PLZF^{lo} RORgt^{lo} iNKT1 cell subset, was the predominate iNKT cell subset in the infected asymptomatic corneas. Asymptomatic mice (with reduced corneal herpetic disease) had more functional IFN-g-producing PLZF^{lo} RORgt^{lo} iNKT1 cells, compared to symptomatic mice. Moreover, compared to HSV-1 infected WT mice, the CD1d KO mice, with iNKT cell deficiency, are more susceptible to HSV-1 ocular infection and disease. This was associated with a decrease in: (i) IFN-γ production, and (ii) activation of MAPK (ERK1/2) and NFκB pathways in the cornea.

Conclusions: Our findings suggest that the IFN-γ-producing PLZF^{lo} RORgt^{lo} iNKT1 cells play a protective role against ocular herpes.

CONTROL ID: 3547488

SUBMITTER (NAME ONLY): Edwin Sarver

TITLE: Real-time Detection of Multilabel Image Artifacts In an Ophthalmic Instrument
Using a Convolutional Neural Network / Deep Neural Network Model

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E.J. Sarver, Sarver and Associates, Inc., Cookeville, Tennessee, UNITED STATES|M. Hall, Alcon Laboratories Inc, Fort Worth, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Edwin Sarver: Commercial Relationship(s);Alcon:Code C (Consultant) | Max Hall: Commercial Relationship(s);Alcon:Code E (Employment)

ABSTRACT BODY:

Purpose: Purpose: An intraoperative Talbot-Moire interferometer uses Fourier analysis of captured images to generate exam data. The quality of the processed data can be degraded by the presence of artifacts in the images. A two-stage software module combined a convolutional neural network (CNN) front end with a deep neural network (DNN) back end capable of detecting in real time the artifacts appearing singly or in combination.

Methods: Methods: The first stage of the detection module employed pre-trained weights for a VGG16 CNN model, and the second stage was a fully connected DNN. The CNN weights were fully specified. Only the DNN and weights needed to be determined. The CNN inputs the image to be analyzed and outputs a length-512 real-valued vector. This vector is a collection of image features suitable for classification tasks for a large range of image types. The DNN inputs the output vector from the CNN and produces a vector estimating the probability of the presence of each of the artifacts. The data set consisted of 287 hand-labeled interferometer images. Each image could contain one or more artifacts. These image artifact labels included: one or more bubbles present, one or more floaters present, and corneal glint present. The data set was randomly split into 229 images for training the model and 58 images for testing the model.

Results: Results: 99% of the training set images were classified correctly for the presence of glint and 97% were classified correctly for the presence of floaters and bubbles. 91% of the test set images were classified correctly for the presence of glint, 95% were classified correctly for floaters, and 97% were classified correctly for bubbles. 97% of training images were correctly identified as being free from artifacts or having one or more artifacts, compared to 91% of the test images being correctly identified as being free from artifacts or not.

Conclusions: Conclusion: The CNN/DNN module developed was reasonably successful at identifying the artifacts in the image test set. We believe further training with a much larger image data set will increase performance. In addition, optimizing the threshold for the output layer values would allow customization of likelihood of detecting a "bad" image at the expense of increasing the likelihood of rejecting an artifact-free image.

CONTROL ID: 3547491

SUBMITTER (NAME ONLY): Benjamin Young

TITLE: Neovascularization as Self-Organized Criticality in Ultra-widefield Fluorescein Angiography Imaging of Diabetic Retinopathy

SESSION TITLE: Image processing and interpretation

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Young, G. Yu, T. Patel, L. Azzouz, C. Powell, Y.M. Paulus, W K Kellogg Eye Center, Ann Arbor, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Describe the distribution of area of non-perfusion (NP) and neovascularization (NV) on ultra-widefield fluorescein angiography in patients with diabetic retinopathy (DR).

Methods: This retrospective, cross-sectional study included all ultra-widefield fluorescein angiograms taken for DR at the Kellogg Eye Center after approval from the UM IRB from January 2009 to May 2018 that included 651 eyes. Exclusion criteria included previous panretinal photocoagulation and images with significant media opacity (e.g. vitreous hemorrhage or significant cataract). These images were manually segmented for retinal surface areas of NP and NV. The total area per patient were organized by frequency in a histogram, and which were tested against power law and exponential distributions.

Results: Analysis of areas of NV across a population of 189 patients with proliferative DR demonstrates a power law distribution with an R2 fit of 0.9672 and shown by least squares method to be a superior fit to an exponential distribution with $p < 0.05$. Areas of NP over 794 patients with DR demonstrated a fit with an exponential distribution, with a superior fit compared to the power law distribution with $p < 0.05$. When the far periphery was excluded, the R2 fit for the exponential distribution was 0.9618.

Conclusions: NV in patients with diabetes follows a power law distribution, and NP follows an exponential distribution. The difference in event distribution suggests that though the two phenomena are related, they are of fundamentally different. While exponential distributions are seen in many gradual, progressive phenomena in nature, the power law distribution tends to occur in constructs which follow the principle of self-organized criticality, suggesting that NV may propagate as a catastrophic local event in an unpredictable manner.

CONTROL ID: 3547492

SUBMITTER (NAME ONLY): Wei Li

TITLE: Cone mitochondria act as microlenses to enhance light delivery and confer Stiles-Crawford-like direction sensitivity

SESSION TITLE: Photoreceptors

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: W. Li, J. Ball, S. Chen, NEI/RNS, National Institutes of Health, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Wei Li: Commercial Relationship: Code N (No Commercial Relationship) | John Ball: Commercial Relationship: Code N (No Commercial Relationship) | Shan Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The vertebrate retina features an inverted structure with multiple neural layers through which photons must pass—risking premature absorption or scattering—prior to detection by light-sensitive opsin molecules located in photoreceptor outer segments (OS). Intriguingly, mammalian photoceptors hold numerous mitochondria in their ellipsoid region immediately before light reaching the OS. These mitochondria, likely supporting the high metabolic needs of phototransduction, however, could potentially impair light delivery to the OS due to their high membrane contents that might cause excessive light scattering. Conversely, they might enhance the delivery of light to the OS, taking up a potential optic role, which is not unprecedented for retinal structures (e.g. rod nuclei, Müller glia, and cone oil droplets). We thus set out to investigate the potential optic role of mitochondria in photoreceptor ellipsoid region.

Methods: Here, using a horizontal slice preparation from the ground squirrel retina, in which plentiful cones contain mitochondria in a bundled arrangement closely resembling those in primate, we directly imaged light transmitted through the mitochondria bundle (MtB). In addition, we performed electromagnetic simulations of light transmission based on the MtB structures translated from reconstructions of Blockface Scanning EM images.

Results: We directly demonstrated that such MtB concentrates light several fold onto the OS for detection. In addition, this “microlens”-like feature of cone mitochondria produces an angular dependence of light intensity quantitatively consistent with the Stiles-Crawford effect, a psychophysical phenomenon believed to improve visual resolution.

Conclusions: Thus, in addition to their function as a necessary powerhouse, cone mitochondria play a critical optical role. These findings provide needed insights into their role in interpreting results from noninvasive optical tools in ophthalmology.

CONTROL ID: 3547494

SUBMITTER (NAME ONLY): Stephanie Cox

TITLE: Corneal in vivo confocal microscopy demonstrates correlations between morphological changes in dendritiform cells and corneal nerve alterations in patients with dry eye disease

SESSION TITLE: Dry eye and microbiome clinical

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Cox, B. Bayraktutar, G. Dieckmann, P. Hamrah, Center for Translational Ocular Immunology, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|P. Hamrah, Cornea Service, New England Eye Center, Department of Ophthalmology, Tufts Medical Center, Tufts University School of Medicine, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: Corneal neuro-immune crosstalk has been of interest given advances in in vivo confocal microscopy (IVCM) imaging, given that IVCM is able to capture the presence of both immune cells and nerves. However, correlations between nerve alterations and dendritiform immune cell (DC) parameters in dry eye disease (DED) have not been investigated to date, which is the aim of the current study.

Methods: This retrospective cross-sectional cohort study included 105 patients with DED. Patients were included in the study if they had symptoms of DED, a tear break-up time (TBUT) of less than 10 seconds and/or corneal fluorescein staining score of at least 1 on the Oxford scale. Three representative images were selected for the study eye for analysis using ImageJ. Morphological alterations of DCs per image was quantified by Image J. NeuronJ was used to quantify corneal nerve density for each image for main and total nerves.

Results: The average age of the patients was 58.8 ± 1.7 years, and 76.2% of them were female. The average DC size was $108.54 \pm 5.70 \mu\text{m}^2$, and the average number of dendrites was 0.59 ± 0.08 per immune cell. The mean immune cell density was $47.73 \pm 5.43/\text{mm}^2$. Main, total, and branch nerve densities were $8,011.58 \pm 269.74 \text{ mm}/\text{mm}^2$, $12,516.58 \pm 450.89$, and 4504.99 ± 264.20 , respectively. DC size was inversely correlated to total nerve density ($\rho = -0.339$, $p = 0.001$) and branch nerve density ($\rho = -0.386$, $p < 0.001$). In addition, number of dendrites had an inverse correlation to total nerve density ($\rho = -0.212$, $p = 0.035$) and branch nerve density ($\rho = -0.211$, $p = 0.036$). The inverse correlation of DC size and dendrite number and nerve density suggest that larger, more mature DCs are associated with nerve loss or vice versa.

Conclusions: IVCM reveals an increased density and morphologic changes of corneal DCs in DED. There is a strong and significant correlation between the increase in DC size and number of dendrites and the decreased subbasal corneal nerves, suggesting a potential interaction between the immune and nervous system in the cornea during DED.

CONTROL ID: 3547495

SUBMITTER (NAME ONLY): REBECCA KAMMER

TITLE: Validation of a Low Luminance Mobility Test for Retinitis Pigmentosa

SESSION TITLE: Visual Impairment - Reading and Selected Topics

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To rigorously assess the test-retest repeatability, content validity and construct validity of a novel Low Luminance Mobility Test (LLMT) and scoring algorithm to determine whether this new performance task is a suitable endpoint to include in clinical trials of retinitis pigmentosa (RP).

Methods: A prospective, observational study, included both subjects with RP (n=20), mean best corrected visual acuity (BCVA) of 1.05 logMAR (range 0.55-1.56 logMAR), and without RP (NoRP, n=16, normal BCVA <0.05 logMAR). The LLMT used 13 light levels from 0.12 lux in increasing steps of 0.3 log units up to 500 lux. A novel scoring algorithm utilized MNREAD principles and R programming to develop a Critical Illumination Level (CIL) and Maximum Step Speed (MSS) score. The CIL is the lowest light level prior to a significant drop in adjusted step speed. MSS is the mean speed for the fastest trials on the plateau of the curve. Subjects completed the LLMT monocularly twice over two weeks, and video recordings of the trials, which were masked to visit and light levels, were sent to trained raters for scoring. For inter-rater and intra-rater reliability, grading of video trials of the LLMT across two studies using three raters allowed for the largest sample. In addition, BCVA, contrast sensitivity (CS), kinetic visual fields (KVF), and the VA LV VFQ-48 were compared to CIL scores to establish content validity.

Results: The LLMT differentiated between NoRP and RP since NoRP subjects had a median CIL of 0.12 lux and mean MSS of 61.0 ± 11.01 steps per minute (spm), whereas RP subjects varied widely in performance with a median CIL of 32 lux (range 0.12-1000 lux) and mean MSS of 33.6 ± 14.93 spm. There was no change in the CIL between test sessions for 75% of RP subjects (n=15), and the five with variability all had constricted KVF diameter $<12^\circ$. All visual function measures were significantly related to the CIL in a multiple regression model, $R^2=0.75$ (p=0.004) but CS was the greatest contributor. Bland Altman plots for inter-rater and intra-rater video grading indicated biases close to zero, and there were no significant differences between graders (p>0.05).

Conclusions: The LLMT is a novel low luminance clinical trial endpoint validated for RP with strong test-retest reliability, good content and construct validity, and an objective scoring system. The LLMT is a useful and reliable endpoint for studying low luminance mobility function in RP.

CONTROL ID: 3547497

SUBMITTER (NAME ONLY): Sona Shah

TITLE: Uveal Lymphoma with Concurrent Endogenous Bacterial Endophthalmitis

SESSION TITLE: Endophthalmitis/ trauma

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Independent of one another, endogenous bacterial endophthalmitis (EBE) and uveal lymphoma are extremely rare. Herein, we describe two cases of EBE secondary to group B streptococcus (GBS) in eyes with secondary uveal lymphoma confirmed on histopathology. Understanding the characteristics of these presentations is critical to informing our approach to patients with EBE in the setting of underlying systemic leukemia / lymphoma.

Methods: A retrospective review was conducted of two cases who presented with endogenous bacterial endophthalmitis secondary to GBS who underwent enucleation and histopathology confirmed concurrent intraocular manifestation of systemic lymphoma.

Results: A 65-year-old male with a history of a lymphoproliferative disorder treated previously presented with a red, painful left eye and loss of vision. He was found to have endogenous endophthalmitis secondary to GBS bacteremia as determined by blood and vitreous cultures. Enucleation was performed. Histologically, the ocular specimen showed gram positive cocci in pairs in addition to atypical lymphocytic infiltrate in both the uvea and conjunctiva. Tumor cells were positive for CD20 and focally co-expressing CD43 on immunohistochemistry. A diagnosis of bacterial endophthalmitis and extranodal marginal zone B-cell lymphoma involving the uvea and conjunctiva was made. A 70-year-old male with a history of Hepatitis B, facial squamous cell carcinoma, and diabetes mellitus type II, similarly presented with acute, painless vision loss of the left eye, and was also found to have endogenous endophthalmitis secondary to GBS bacteremia as confirmed on blood, anterior chamber and vitreous cultures. Enucleation was performed, and immunohistochemistry of the uveal and retinal tissues was positive for CD20 and CD5, with co-expression of CD23, CD43, and BCL2. The patient was diagnosed with CD5+ small B-cell lymphoproliferative disorder with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) immunophenotype.

Conclusions: To our knowledge, no reports have discussed EBE with concurrent secondary intraocular malignancy. The clinical course of both patients' EBE was rapidly progressive. It may be that the presence of uveal lymphoma weakens the intraocular immune system and increases the eye's susceptibility to infection.

CONTROL ID: 3547500

SUBMITTER (NAME ONLY): Rogerio Garcia Nespolo

TITLE: Surgical Phase Identification and Pupil Tracking in Phacoemulsification Cataract Surgery as a Foundation for Surgical Guidance

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: As a foundation to develop tools for surgical guidance, we sought to develop an agent capable of autonomously identifying the various steps and phases of phacoemulsification cataract surgery in real-time together with pupil segmentation, such that the generated output is capable of informing surgical decision making.

Methods: Heterogeneous videos were annotated by ophthalmic surgeons in order to achieve robustness of pupil detection, phase identification and tissue segmentation by the algorithm.

The application acquires video frames, in real time, from a surgical microscope-based video capture device. Then, a Region Based Convolutional Neural Network (R-CNN) performs the following functions for each analyzed frame (figure 1):

i) pupil location and area

ii) surgical phase identification according to the instruments in use

Results: 1. We evaluated the performance of the R-CNN via comparison with annotation of surgical videos performed by ophthalmic surgeons (Table 1). We achieved high values in accuracy, precision, and sensitivity across each of the four phases (idle, capsulorhexis, phacoemulsification and cortex removal), leading to F1-scores above 90%.

2. There was also strong correlation among the graders' assessment of the size of the pupil with the pupil area detected by the algorithm, yielding precision, sensitivity, and intersection over union area (IoU) of 82.07%, 87.19%, and 95.14%, respectively.

3. The algorithm executed these tasks at an average processing speed of 82 ± 20 frames per second (FPS), well above the output of 60 FPS at which most contemporary surgical visualization systems display images.

Conclusions: It is important to state that no current machine learning solution combines phase identification with pupil tracking. We have developed a platform that provides the foundations for a real-time surgical guidance tool for phacoemulsification cataract surgery by using object detection and classification for surgical phase classification. Future machine learning-based tools can utilize these capabilities for the creation of novel surgical guidance tools and feedback mechanisms.

CONTROL ID: 3547501

SUBMITTER (NAME ONLY): Michael Carlson

TITLE: OCT guided micro-focal ERG system with multiple stimulation wavelengths for characterization of ocular health

SESSION TITLE: Electrophysiology: Advances, disease and injury

SESSION TYPE: Paper Session

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ABSTRACT BODY:

Purpose: Functional characterization at cellular resolution is key to the advancement and evaluation of new therapeutic interventions such as gene and cell replacement therapies. Here, we report development of optical coherence tomography (OCT) guided micro-focal multi-color light stimulated electroretinogram (ERG) platform for highly localized monitoring of retina function. Functional evaluation of wild type and animals with degenerated retina was carried out using OCT guided micro-focal ERG (μ fERG) with selected stimulation wavelengths for S, M and L cones as well as rod photoreceptors.

Methods: The stimulation light beam was fiber coupled and combined with the OCT imaging beam. Using Nanoscope Instrument's NS-Neel OCT guided μ fERG platform, μ fERG responses from different retinal locations were recorded. Light flashes were elicited by pre-selected wavelengths (Blue: 455 nm; Green: 530 nm; and Red: 630 nm) of the micro-focused beam on wild type mice and pigs as well as animals with photoreceptor degeneration caused by gene mutation or laser-injury. Micro-focal ERG from multiple strobe light flashes were averaged and filtered to obtain the final waveform.

Results: Functional deficits in mice and pigs with photoreceptor degeneration was observed via micro-focal ERG measurements. Further, μ fERG recordings from different types of cones produced unique characteristic responses when stimulated by blue, green, or red micro-focused beam at targeted locations. No micro-focal cone ERG response was observed with red light stimulation (since mice and pigs lack red sensitive-cones). Using low intensity stimulation, μ fERG measurements from rod photoreceptors could be detected and isolated from cone response.

Conclusions: Our results show that OCT guided μ fERG allows functional evaluation of retinal degeneration. Micro-focal ERG is able to not only characterize differences in rod and cone function but also distinguish different cones with selected stimulation wavelengths. Control of light adaptation and stimulation parameters in the OCT guided μ fERG such as intensity, wavelength, and pulsing allow distinguishing differences in functioning of different photoreceptors and cell types.

CONTROL ID: 3547502

SUBMITTER (NAME ONLY): Jesse Jung

TITLE: Quantitative Analysis of Quadrant Asymmetry of OCTA Metrics in Central Retinal Vein Occlusion Eyes

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Central retinal vein occlusion (CRVO) is a common cause of visual loss. Asymmetry among the 4 ETDRS quadrants (superior [SUP], nasal [NAS], inferior [INF] temporal [TEMP]) in terms of optical coherence tomography angiography (OCTA) metrics (e.g., superficial retinal layer [SRL] perfusion density [PD, total area of perfused vasculature/unit area], vessel density [VD, total length of perfused vasculature/unit area] inner thickness [IT] and outer thickness [OT]) exists in control eyes. Herein, we assess if the insult of a non-ischemic versus ischemic CRVO affects the quadrant asymmetry (QA) differentially.

Methods: 28 control eyes, 6 non-ischemic and 7 ischemic CRVO eyes underwent 3x3 mm OCTA scans with signal strength >7. Automated segmented scans with registration for the SRL. QA was defined as the maximum value among the 4 ETDRS quadrants minus the minimum value for a given eye. OCTA parameters were assessed by multivariate linear regression analysis including fixed effects for each individual-by-eye.

Results: There was no significant QA for the 4 OCTA metrics when comparing non-ischemic CRVO with control eyes ($p>0.05$). However, ischemic CRVO eyes had greater PD QA (+0.014, $p=0.006$), IT QA (+20.7, $p<0.001$) and OT QA (+6.3, $p<0.001$) than control eyes. Ischemic CRVO eyes had greater VD QA (+1.48, $p<0.001$), PD QA (+0.030, $p=0.003$), IT QA (+43.3, $p<0.001$) and OT QA (+17.6, $p<0.001$) than non-ischemic CRVO eyes. Within control eyes, OCTA metrics tended to be greatest in NAS, with INF and SUP having lower VD (2.55, $p=0.001$; 1.54, $p=0.002$), PD (0.04, $p=0.001$; 0.02, $p=0.011$), IT (10, $p<0.001$; 14.8, $p<0.001$) and OT (29.6, $p<0.001$; 32.0, $p<0.001$), and TEMP having lower IT (5.2, $p=0.008$) and OT (17.7, $p<0.001$). In contrast, in CRVO eyes, the max quadrant was not consistent ($p>0.05$) aside from NAS IT in non-ischemic CRVO eyes higher than INF (6.8, $p=0.041$) and SUP (10.3, $p=0.015$) and NAS OT in ischemic CRVO eyes higher than INF (30, $p=0.008$) and SUP (39.1, $p=0.003$).

Conclusions: Although QA does not differ between nonischemic CRVO and control eyes, ischemic CRVO affects PD, VD, IT and OT more asymmetrically across the 4 ETDRS quadrants when compared to non-ischemic CRVO eyes, and affects PD, IT and OT more asymmetrically than control eyes. QA of OCTA metrics in control eyes tended to be driven by the largest values found in the nasal quadrant, but were more evenly distributed in CRVO eyes.

CONTROL ID: 3547506

SUBMITTER (NAME ONLY): Alexandra Warter

TITLE: Simultaneous combination steroid anti-VEGF therapy for monotherapy resistant macular disease

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Warter, M. Cavichini Cordeiro, D.G. Bartsch, S.R. Singh, D.R. Freeman, Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our purpose was to analyze the safety and efficacy of the use of combined anti-VEGF and long-acting steroid IV therapeutic agents in resistant macular fluid after conventional monotherapy. We performed a retrospective observational clinical study to assess anatomical and visual changes in a consecutive cohort of patients resistant to aggressive monotherapy in retinovascular (RVD) induced edema (ME) and choroidal vascular induced edema (CNV) in Wet-AMD.

Methods: This study included a total of 28 eyes (56 injections) with nonresponsive macular fluid after a standardized protocol consisting in escalation treatment with varied doses of alternating anti-VEGF or steroid injections. Resistance was defined as persistent fluid after escalation of anti-VEGF to 1mg Aflibercept every 4 weeks and additional monotherapy resistance to IV Triamcinolone Acetonide (TCA) or Dexamethasone in RVD. A prior mean of injections was 36.45[18-67] in Wet-AMD and 9.17[3-17] in RVD. Combination therapy consisted in the simultaneous administration of IV anti-VEGF and steroid. Slit lamp evaluation, VA, IOP, and Optical Coherence Tomography (Heidelberg Spectralis) measurements of central retinal thickness (CRT) were recorded every 4 weeks post injection. All eyes received prophylactic topical anti-glaucoma medication for 2 weeks (Timolol 0.5%/Dorzolamide 2%). Outcomes included reduction in CRT, VA, and IOP changes.

Results: Our initial analysis was performed post first injection of combined therapy in one eye of each patient. Safety data showed no evidence of infection. 14% of patients reported transient visual obscuration due to TCA particles. There was a modest rise in IOP in 19% of patients; no eyes required glaucoma surgery or showed vascular occlusions. Anatomic outcomes showed a statistically significant reduction in CRT in both groups; paired analysis showed an average CRT reduction of $45.55\mu\text{m}\pm\text{SD}20.656$ ($p<0.05$) in CNV and $145\mu\text{m}\pm\text{SD}31.651$ ($p<0.0003$) in RVD. There was a non-significant trend of VA improvement ($p=0.712$).

Conclusions: We found that combination of IV steroids and anti-VEGF produces clear anatomic improvement in CNV. Other studies have evaluated combination therapy in RVD and found vision improvement, but not in eyes resistant to monotherapy with both anti-VEGF and steroids. In such eyes, we found overall disease improvement. Combination therapy therefore may be useful in treating resistant Wet-AMD CNV and RVD ME.

CONTROL ID: 3547508

SUBMITTER (NAME ONLY): Luz Giorgi-Sandoval

TITLE: Comparative Benefit of Two Concentrations of Autologous Serum Eyedrops in Patients with Ocular Surface Disease Associated to Topical Preserved Glaucoma Therapy

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Ocular surface disease (OSD) is a defying condition affecting patients under preserved topical glaucoma therapy. Even when the safety and effectiveness of both short-term and long-term use of autologous serum (AS) eyedrops has been studied in a myriad of diseases affecting the ocular surface, there is scarce information regarding AS benefit on OSD derived from preserved topical glaucoma therapy. The aim of this study is to compare effectiveness and safety AS eyedrops (comparing 30%AS vs 50%AS concentrations) in glaucoma patients with severe/persistent OSD using topical hypotensive treatment.

Methods: A retrospective assessment of all consecutive patients under glaucoma treatment in a specialized center was performed. A total of 396 patients with severe OSD under glaucoma treatment were identified. Twenty-nine cases had AS eyedrops in concentrations 30%AS and 50%AS, as well as other treatment regimes. Variables included BCVA, TBUT, ocular surface staining (OSS) percentage, presence of Meibomian gland dysfunction and ocular-surface disease index (OSDI). A p value ≤ 0.05 was considered as statistically significant.

Results: Fifty-eight eyes from 29 patients were included in the study (22 females, 7 males) had a mean age of 67.0 ± 16.1 years. According to AS concentration, 56% of the eyes were treated with a 30%AS and 44% with 50%AS. Mean time of preserved topical treatment was 1.6 ± 1.0 years. Baseline IOP (RE, 19.2 ± 5.9 mmHg; LE, 19.1 ± 8.8 mmHg) was not different as compared to the measurements at the last visit (RE, 18.9 ± 6.1 mmHg; LE, 19.4 ± 7.3 mmHg; $p \geq 0.05$). Mean time of AS administration (RE, 8.9 ± 7.5 weeks; LE, 9.7 ± 8.3 weeks; $p = 0.5$). Overall, a comparative improvement was significant in regards of BCVA (RE, $p = 0.001$; LE, $p = 0.007$), OSS (RE, $p = 0.045$; LE, $p = 0.035$), OSDI (RE, $p = 0.04$; LE, $p = 0.03$). No significant change was demonstrated in TBUT (RE, $p = 0.12$; LE, $p = 0.08$). Comparative success rate between groups are not significantly different (30%AS, 84%; 50%AS, 86%). One non-infectious ulcer was present in the group treated with 30%AS eyedrops but it healed without further complication.

Conclusions: Current study results suggest that ASE of either concentration is effective and safe for treating severe ocular surface diseases caused by glaucoma eyedrops containing preservatives.

CONTROL ID: 3547509

SUBMITTER (NAME ONLY): Kathleen Heng

TITLE: Intravitreal delivery of AAV2 transduces porcine retinal ganglion cells.

SESSION TITLE: Drug delivery and Gene Therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: K. Heng, B. Li, A. Singh, R. Wen, A.Y. Wu, J.L. Goldberg, Department of Ophthalmology, Stanford University, Stanford, California, UNITED STATES|K. Heng, B. Li, A. Singh, R. Wen, A.Y. Wu, J.L. Goldberg, Byers Eye Institute, Spencer Center for Vision Research, Palo Alto, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Adeno-associated virus serotype 2 (AAV2) is a promising gene therapy platform for glaucoma and other retinal ganglion cell (RGC) degenerative diseases. Although pro-survival and pro-regenerative AAV2 gene therapies have been identified in mouse, advancement towards human therapeutics has been limited due to a lack of data in a large animal model. Here we test transduction of porcine RGCs with AAV2 in vivo while evaluating vector promoters and optimizing injection technique.

Methods: Yucatan minipigs (5.5-6 months old) were intravitreally co-injected with AAV2-UBC-eGFP and AAV2-CAG-TdTomato to compare promoter strength. In order to optimize vector delivery, three injection strategies were evaluated: (1) 1-point injection at the temporal aspect of the eye 4 mm posterior to the limbus, (2) 2-point injection at the temporal and nasal aspects, and (3) 4-point injection at the temporal, nasal, superior, and inferior aspects. Four weeks after injection, retinas were harvested, stained by immunofluorescence for Brn3a (RGC marker), flat-mounted, and imaged by confocal microscopy. Fluorescent cells were quantified on ImageJ, and transduction efficiency was determined by calculating the percentage of Brn3a+ cells that were eGFP+ or TdTomato+. All research was conducted in compliance with IACUC approval and the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Results: Both UBC and CAG promoters drove high fluorophore expression in RGCs (75% and 74% transduction efficiency, respectively). The 2-point injection strategy resulted in high transduction efficiency across the retina, whereas 1-point injection resulted in high transduction in the temporal retina but moderate or low transduction elsewhere, and 4-point injection resulted in minimal transduction across the retina.

Conclusions: AAV2 is a viable technology for gene delivery in porcine RGCs in vivo. Both UBC and CAG promoters strongly promote transduced gene expression in porcine RGCs, and a 2-point injection method yielded optimal delivery efficiency.

CONTROL ID: 3547510

SUBMITTER (NAME ONLY): Wonkyu Ju

TITLE: AIBP promotes mitochondrial bioenergetics in Müller glia in response to elevated pressure

SESSION TITLE: Pharmacological intervention and cellular mechanisms

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The goal of this study is to investigate the effect of Apolipoprotein A-I binding protein (AIBP; gene name APOAIBP) on mitochondrial structure and function in Müller glia in response to elevated pressure.

Methods: Retina tissues were prepared from wild-type (WT, C57BL/6J) and AIBP knockout (Apoa1bp^{-/-}) mice. Mitochondrial morphology and ATP production were assessed by serial block-face scanning electron microscopy (SBEM) and electron microscope (EM) tomography. Rat Müller glia cell line (rMC-1) cultures were pretreated with BSA or recombinant human AIBP (0.2 µg/ml) at 2 hours before exposure to elevated hydrostatic pressure (HP, 30 mmHg) for 2 hours. Mitochondrial respiration in rMC-1 cells was assessed by measuring oxygen consumption rate using a Seahorse XF24 analyzer. Mitochondrial activity and cell viability were measured by MTT and CellTiter-GloTM luminescent assays.

Results: Apoa1bp^{-/-} mice showed mitochondrial fragmentation and reduction of ATP production in Müller glia mitochondria. Quantitative analyses showed that there were no significant changes in mitochondrial volume, volume density, or mitochondrial number in the Apoa1bp^{-/-} Müller glia endfeet. The form factor for the Apoa1bp^{-/-} mitochondria was significantly lower than for the WT, meaning more mitochondrial rounding in the Apoa1bp^{-/-}. Mitochondrial length was significantly decreased in Apoa1bp^{-/-}. Similarly, the crista density and the modeled rate of ATP production per mitochondrial volume were lower in the Apoa1bp^{-/-}. In contrast, the modeled rate of ATP production per mitochondrion was not lower in the Apoa1bp^{-/-}, yet there was a significant decrease in cellular ATP production via mitochondria in the Apoa1bp^{-/-}. AIBP treatment promoted basal and maximal respiration along with an increase of ATP production and spare respiratory capacity, as well as mitochondrial activity in rMC-1 cells exposed to normal pressure compared to BSA treatment. In BSA treatment, elevated HP significantly reduced maximal respiration and spare respiratory capacity in rMC-1 cells compared to cells exposed to normal pressure. In addition, AIBP treatment enhanced basal and maximal respiration, as well as mitochondrial activity and cell viability in rMC-1 cells exposed to elevated HP.

Conclusions: These findings suggest that AIBP may protect retinal ganglion cells by promoting mitochondrial bioenergetics of Müller glia during glaucomatous neurodegeneration.

CONTROL ID: 3547514

SUBMITTER (NAME ONLY): Gavin Tan

TITLE: Evaluation of an ophthalmic grader led virtual imaging clinic pathway in the management of patients with retina diseases.

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G. Tan, A. Tsai, Surgical Retina, Singapore National Eye Center Vitreoretinal Division, Singapore, SINGAPORE|G. Tan, K. Teo, A. Tsai, Ophthalmology, Duke-NUS Medical School, Singapore, SINGAPORE|K. Teo, Medical Retina, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|L. Lee, A. Juhari, H. Hamzah, SNEC Ocular Reading Centre, Singapore National Eye Centre, Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: To evaluate the diagnostic accuracy of a Retinal virtual multimodal-imaging clinic led by ophthalmic graders in the management of patients with retina diseases

Methods: Prospective comparative observational study. Patients who were known to have retinal diseases (including diabetic retinopathy (DR), age-related macular degeneration(AMD) or other retina conditions) were recruited from the Singapore National Eye Centre Retina Clinic, and underwent a clinical pathway, involving optical coherence tomography(OCT) [Cirrus Photo, Zeiss, Germany] and ultrawide wide field fundus image(UWF) [Clarus, Zeiss, Germany] which are reviewed by trained non-physician graders (Ophthalmic graders) to detect for active retinal disease that require treatment or further evaluation by ophthalmologist. Patients were subsequently reviewed on the same day in standard of care retina clinics by an ophthalmologist (resident to consultant level) blinded to the grader outcome with OCT performed as clinically indicated. The reference standard was evaluation of the clinical notes and multimodal imaging (OCT + UWF) by a masked Retina specialist. A composite outcome of active retinal disease was defined as the presence of either: 1)vision threatening diabetic retinopathy(VTDR) [severe non proliferative DR or active proliferative DR], 2) Centre involving diabetic macular edema, 3) Active neovascular AMD. The sensitivity and specificity of the new clinical pathway in identifying treatment requiring retinal disease was evaluated against the reference standard.

Results: There were 494 participants of which 38 (8.3%) patients had active retinal disease identified. The new clinical pathway had a sensitivity of 95.1 % (95% confidence interval [CI] 88.5-100%) and a specificity of 97.4% (95% CI 95.9-98.8%) to detect active retinal disease. The positive predictive value was 76.5% and the negative predictive value was 99.6% There were 2 cases of active retinal disease misclassified by the grader pathway as stable, and both had severe non-proliferative DR with no macular disease.

Conclusions: The new ophthalmic grader led multimodal imaging based clinical pathway had good sensitivity and specific for identifying active retinal disease that may require treatment. This pathway may be able to replace standard specialist outpatient clinic for the management of selected patients with retinal diseases.

CONTROL ID: 3547515

SUBMITTER (NAME ONLY): Anya de Leeuw

TITLE: Comparison and Correlation of Schirmer's Tests Results in Patients with Neuropathic Corneal Pain and Dry Eye Disease

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Neuropathic corneal pain NCP is commonly thought to present with discordant signs and symptoms with minimal to no ocular surface staining. However, the Schirmer's test result in patients with NCP have previously not been compared to patient with conventional dry eye disease DED. Thus, the purpose of the current study was to compare Schirmer's test results between patients with NCP as compared to DED.

Methods: This is a comparative, retrospective case-control study of age and sex matched NCP and DED patients, who were seen at the New England Eye Center between August 2018 and November 2020. NCP was diagnosed clinically and confirmed by in vivo confocal microscopy and the proparacaine challenge. Demographics, Schirmer's test results with anesthesia, tear-break-up time TBUT, corneal staining CFS, ocular pain scores, ocular and systemic comorbidities were recorded. Patients were included in the DED group, based on the inclusion criteria of CFS staining ≥ 4 and TBUT ≤ 7 .

Results: The mean age of patients with NCP was 45.7 ± 4.9 with $n=4$ males and $n=19$ females, and 63.1 ± 3.9 for the DED group with $n=5$ males, and $n=14$ females $p=0.199$ for age $p=0.707$ for gender. The mean Schirmer's tests results for the NCP group were $9.8\text{mm} \pm 1.8$ and $7.1\text{mm} \pm 1.1$ for the DED group, respectively with a p value of $p=0.450$. This indicated no significant difference in Schirmer's results between the DED and NCP patients, with both groups demonstrating decreased results compared to healthy subjects. There was no difference in Schirmer's results in the NCP group regardless of breakdown into peripheral $n=3$ mean 8.67 ± 5.78 , mixed $n=9$ mean 12.33 ± 2.73 and central $n=3$ mean 5.00 ± 1.16 $p=0.383$. The mean TBUT for the DED group was $4.0\text{sec} \pm 0.4$ and $10.2\text{sec} \pm 0.5$ for the NCP group $p= <.001$. The mean CFS was 4.1 ± 1.0 for DED, and 0.4 ± 0.2 for the NCP group $p=.011$. DED patients reported a mean pain level of 1.9 ± 0.7 on VAS, while NCP patients reported VAS of 4.5 ± 0.3 $p=.002$. DED patients reported a mean of 1.8 ± 0.7 on OPAS questions 5-7 indicating pain over the previous 24hr period, while NCP patients reported 5.0 ± 0.7 $p=.001$.

Conclusions: The results of this study shows that NCP patients may present with low values on Schirmer's tests in the absence of clinical signs of DED. The data suggests that abnormal Schirmer's test results may be due to nerve dysfunction and that abnormal Schirmer's tests results should not be used to exclude NCP.

CONTROL ID: 3547518

SUBMITTER (NAME ONLY): Miguel Amaro

TITLE: Subretinal Hyperreflective Material on Structural OCT in nAMD

SESSION TITLE: Diabetic retinopathy/retinal pharmacology/physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: To assess the importance of subretinal hyperreflective material in nAMD visualized on structural OCT and its response to anti-VEGF treatment.

Methods: We analyzed eighteen eyes from twenty five subjects with nAMD. These were nAMD consecutive cases and we followed them for up to five years to investigate the incidence of subretinal hyperreflective material during nAMD treatment with ranibizumab and bevacizumab. The best visual acuity before treatment ranged from 20/40 to 20/100

Results: We found four cases of subretinal hyperreflective material (SHM) on the follow up of the treated subjects. Visual acuity had no improvement during the treatment of the the patients affected by the SHM. Two of the subjects presenting SHM had a initial improvement of visual acuity, developing retrogression after the development of the pathology.

Conclusions: The appearance of subretinal hyperreflective material on OCT during treatment with anti-vegf for nAMD is possible and suggests worse visual prognosis when compared to patients with no hyperreflective material

CONTROL ID: 3547522

SUBMITTER (NAME ONLY): Samuel Fowler

TITLE: Genome-wide Association Study Finds Multiple Loci Associated with Intraocular Pressure In HS Rats

SESSION TITLE: Genetics of Glaucoma

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Fowler, T. Hollingsworth, M.M. Jablonski, Department of Ophthalmology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|T. Wang, A.G. Martinez, J. Ni, H. Chen, Department of Pharmacology, Addiction Science, and Toxicology, The University of Tennessee Health Science Center, Memphis, Tennessee, UNITED STATES|D. Munro, A. Palmer, O. Polesskaya, Department of Psychiatry, and Institute for Genomic Medicine, University of California San Diego, La Jolla, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Elevated intraocular pressure (IOP) is influenced by environmental and genetic factors. It is associated with multiple disease processes with primary open angle glaucoma (POAG) being the most prevalent. Due to its complex, multifactorial nature, genetic predisposition is not completely understood, and a standardized animal model has yet to be developed for POAG. Heterogenous stock (HS) outbred rats is a multigenerational outbred population derived from eight fully sequenced founder strains. This population is ideal for genome-wide association studies (GWAS) due to most genetic variants being common, access to a large collection of tissue samples, and the large allelic effect size compared to human studies. The purpose of this study was to use HS rats to identify genetic loci underlying elevated IOP.

Methods: Both male and female HS rats (N=1812) were used in the study with genotyping by sequencing conducted on all subjects. We mapped quantitative trait loci (QTLs) for IOP phenotypes and SNP heritabilities were estimated. We used permutation to determine the threshold for significance using an empirical p value of 0.05. Linear mixed model was used to control for the complex family relationships of the HS rats.

Results: GWAS identified three genome wide significant loci for elevated IOP located on chromosomes 1, 5, and 16. The QTLs contained 18 genes in total. Only one of these genes has been previously associated with human POAG.

Conclusions: This study highlights the efficacy of HS rats for investigating the genetics of elevated IOP and identifying potential candidate genes for future functional testing. GWAS is a powerful method for identifying genome regions which harbor variants responsible for the variation in quantitative traits, such as IOP. The identification of three independent QTLs in a relatively small sample size is promising for continued future findings as the sample population grows. Additional studies are ongoing to narrow the list of candidate genes in these intervals.

CONTROL ID: 3547523

SUBMITTER (NAME ONLY): Paul Cullen

TITLE: A novel enrichment method reveals transcriptional changes in retinal astrocytes exposed to elevated IOP

SESSION TITLE: Glial Cells, Retina Development and In vitro Models

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Cullen, Y. Yang, S. Muroy, L. Chen, J.G. Flanagan, Optometry & Vision Science, University of California Berkeley, Berkeley, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: The neuroprotective role of glial cells is a growing research focus in nervous system pathologies including glaucoma, which is one of the most common neurodegenerative disorders and the leading cause of irreversible blindness worldwide. Retinal astrocytes, along with those of the optic nerve, have been shown to play key roles in the survival of retinal ganglion cells, particularly in response to glaucomatous stress. The mechanisms regulating this protection, however, are poorly understood, as these cells populate the retina sparsely and are difficult to isolate acutely. By utilizing a novel isolation method and examining the transcriptomic data from retinal astrocytes exposed to elevated intraocular pressure (IOP), we aim to understand the response of these cells to glaucomatous stress.

Methods: Adult male C57/B6 mice underwent laser-induced episcleral vein cauterization, resulting in an elevation in IOP. After one week, treated animals and age-matched controls were euthanized and highly enriched populations of retinal astrocytes were isolated by a combination of enzymatic dissociation and mechanical separation. Purified RNA from these samples was used to generate cDNA libraries for next generation sequencing, and differential gene expression was analyzed after bioinformatic cleanup.

Results: After applying thresholds of 2-fold change in expression and $< .05$ for false discovery rate, 335 upregulated genes were identified in samples from experimental animals relative to those from controls. The most strongly correlated gene ontology category was 'GO:0006954: inflammatory response', with a $-\log_{10}(P)$ of 27.8. Furthermore, a number of these upregulated genes have been previously implicated as markers of astrocyte reactivity. The second most strongly correlated GO category was 0001568: blood vessel development, with a $-\log_{10}(P)$ of 25.1, likely reflecting the close association of astrocytes with the superficial retinal vasculature.

Conclusions: Our results are broadly consistent with studies of reactive astrocytes in the brain, while delivering new insight into the behavior of these cells in the retina; this may illuminate future directions for research into retinal neuroprotection. This outcome also demonstrates the utility of our approach to retinal astrocyte isolation, which requires little in the way of specialized equipment and benefits from a post-mortem interval of less than one hour.

CONTROL ID: 3547524

SUBMITTER (NAME ONLY): Jibril Hirbo

TITLE: Predicting gene expression analysis of PACG implicates unique inflammatory and blood pressure pathways in across-ancestry disease etiology

SESSION TITLE: Functional Genomics and Transcriptomics of inherited ophthalmic disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: J. Hirbo, D. Zhou, E. Gamazon, N. Cox, Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|P. Pawar, M.A. Brantley, K.M. Joos, Vanderbilt Eye Institute, Nashville, Tennessee, UNITED STATES|C. Khor, Genome Institute of Singapore, Singapore, SINGAPORE|

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ABSTRACT BODY:

Purpose: Primary-angle closure glaucoma (PACG) is the second most common form of glaucoma with over 23 million affected in 2020 globally. It is more common in Asian populations and may manifest sudden extreme IOP elevations with rapid optic nerve damage. However, identifying individuals who are at risk to provide appropriate clinical management is challenging. Given the disparity in prevalence across global populations, there is potentially a complex interplay among risk factors in inter-racial predisposition towards PACG. Two major Genome-Wide Association (GWAS) meta-analyses of PACG across global populations identified 17 variants in eight loci to be potentially causal. It is not clear how these variants mechanistically contribute to manifestation of the disease. We hypothesize that there are unique molecular factors that contribute to disparity observed for PACG based on ancestry.

Methods: Transcriptome-based predicted gene expression associations (TWAS) of PACG could provide powerful methods to prioritize genes involved in the etiology of the disease. We used three recently developed TWAS methods that provide a framework for directly estimating gene expression using GWAS summary data. We performed TWAS on global-multiethnic (n=40,070) and South-East Asian (SEA, n=12,743) summary PACG data across 49 GTEx tissues.

Results: We identified 78 genes in 42 loci associated with PACG, including genes in GWAS loci with subgenome-wide signals. Three prominent loci with multiple gene signals: GWAS PLEKHA7 locus (eight genes), and novel CYP2C9 (four genes) and ECM2 (eight genes) loci that were unique to SEA, we performed sequential conditional analysis in each tissue. We further rebuilt prediction models excluding variants in models of other genes in the loci that were in LD with any variants of the strongest signal. The strongest signals in these loci were NCR3LG1 ($p=4.4e-14$), CYP2C9 ($p=3.3e-15$) and ECM2 ($p=2.4e-26$), respectively, and all the other 17 gene signals were not independent of these signals. Multigenic score and comorbidity analyses in a large EHR-linked BioVU data (n=100,262) implicated dysregulation in inflammatory and blood pressure processes in PACG. Moreover, our results point to unique genetic factors and pathways in across-ancestry risk to PACG.

Conclusions: Unique inflammatory and blood pressure processes are involved in across-ancestry PACG etiology

CONTROL ID: 3547525

SUBMITTER (NAME ONLY): Erin Hennessey

TITLE: Assessing the Pathogenicity and Pharmacogenetic Properties of Rhodopsin Variants Using Functional Genomics

SESSION TITLE: Ocular transcriptomics, epigenomics, computational biology and beyond

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: E. Hennessey, J. Comander, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, UNITED STATES|E. Hennessey, J. Comander, Department of Ophthalmology, Harvard Medical School, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: The diverse DNA variants found in human patients can differ not only in their pathogenicity but also in their response to therapeutic compounds. Both of these issues can prevent inherited retinal disease patients from receiving treatment. Our goal is to create high-throughput cell-based assays to categorize variants and their differential sensitivity to potential therapeutic compounds. For example, 9-cis retinal, a form of vitamin A, is a known molecular chaperone for misfolded mutant rhodopsin (RHO), and mutations in RHO are a major cause of autosomal dominant retinitis pigmentosa.

Methods: A library of 211 rhodopsin variants was created and transfected into HEK293 cells. After transfection, all variant-expressing cells were pooled. Cells were treated with 5 different doses of 9-cis retinal for 24 hours. The cells were fixed and stained with a monoclonal anti-rhodopsin antibody to detect rhodopsin that was successfully folded and transported to the cell surface. Using FACS, cells from each dose were sorted according to their rhodopsin surface expression. Residual transfected DNA inside the cells was extracted and the RHO amplicon amplified via PCR. The relative rhodopsin expression of each library variant for each dose was quantified by next-generation sequencing. Clustering algorithms partitioned the variants into clusters which behaved similarly across the experimental conditions.

Results: Sorted cells from 3 biological replicates were sequenced across 7 conditions using 4×10^6 total sequencing reads. Library coverage was 99-100%. Replicate experimental conditions showed low dispersion within clusters. Biologically, previously unclassified RHO mutations partitioned into either retinal responsive groups containing class II and III mutants, or a non-retinal responsive groups containing class I, IV, and VI mutants.

Conclusions: Functional genomics approaches can be used to classify the pathogenicity and the response to potential therapeutic compounds of a large number of RHO variants. Multiple mutations with no previously-known mechanism were identified that could be particularly amenable to chaperone treatment. This pharmacogenomic approach helps to better understand therapeutic options in RHO, and can also be applied to mutations in other genes.

CONTROL ID: 3547526

SUBMITTER (NAME ONLY): Joseph Pecha

TITLE: Characterization of pediatric ocular trauma during the Covid-19 quarantine

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Pecha, K. Matharu, K. Yen, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|H. Zhu, K. Yen, Texas Children's Hospital, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Eye injuries are the leading cause of vision loss for children in the US. Many of these injuries are preventable. We aim to determine whether the COVID-19 associated quarantine resulted in fewer and less severe pediatric ocular injuries.

Methods: We conducted a retrospective review of patients with adnexal, anterior segment, posterior segment, and penetrating ocular injuries requiring surgical repair presenting between March 1- June 1, 2019 and March 1-June 1, 2020 to a tertiary referral pediatric emergency center.

Results: 17 patients in 2019 compared to 15 in 2020 required surgery for ocular trauma during this time period. Average age was 7.27 (2019) and 9.58 (2020), and 15/17 (2019) and 11/15 (2020) were males. In both 2019 and 2020, the majority of cases were adnexal (88% and 53% respectively), most injuries were related to sharp objects (65% and 93%) and the most common etiology was animal related (35% and 53%, respectively). While not statistically significant, there was a trend toward a higher number of animal- and pencil-related injuries in 2020 compared to 2019. There was no significant difference in patient race/ethnicity, Medicaid status, age, or gender between 2019 and 2020, and, although there were fewer surgeries in 2020, the difference was not significant. However, there was a significant increase in number of patients in 2020 having last-recorded visual acuities worse than 20/40 in the injured eye with no patients in 2019, and 5 (33%) in 2020 having worse visual acuity.

Conclusions: Quarantine restrictions, with a decrease in organized sports and in-person school, did not significantly change characteristics of pediatric ocular injuries requiring surgical repair in our patient population, although a trend toward increased animal- and pencil-related injuries could be related to more indoor activity. Substantial risk of vision-threatening injury occurs even with the absence of in-person school and organized sporting activity which may be associated with increased eye injury severity.

CONTROL ID: 3547527

SUBMITTER (NAME ONLY): Francesca BARONE

TITLE: Optical Coherence Tomography Angiography (OCTA) characterization of the choriocapillaris in a laser pig model of retinal degeneration

SESSION TITLE: Animal imaging

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: F. BARONE, R. Gupta, R. Sharma, J. Amaral, I. Bunea, A. Maminishkis, K. Bharti, National Eye Institute, National Institutes of Health, Bethesda, Maryland, UNITED STATES|J. Phillips, D. Gamm, Dept of Ophthalmology and Visual Sciences and McPherson Eye Research Institute, University of Wisconsin System, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Choroideremia (CHM) is a disorder affecting the retinal pigment epithelium (RPE), photoreceptors (PR), and the outermost vascular layer, choroid (more specifically the choriocapillaris CC) [1]. OCTA technology uses laser light reflectance of the surface of moving red blood cells to depict vessels through different segmented areas of the eye, allowing non-invasive detailed imaging of the retina microvasculature that is not possible with conventional angiography [2]. We recently showed that micropulse laser of 1% and 3% duty cycle (DC) damages the RPE of Yucatan minipigs [3]. Here we extend this work to evaluate the effect of micropulse laser on pig CC and larger choroidal vessels using OCTA with conventional angiography, to develop an induced choroidal degeneration (choroideremia) pig model

Methods: A micropulse laser of 532 nm with 330 msec pulses was used with different DC (1, 1.5, 2, and 3%) in 8 eyes of Yucatan minipigs. Animals were evaluated every week for up to 12 weeks with Optical Coherence Tomography OCT, OCTA and conventional angiography (fluorescein angiography FA and indocyanine green-angiography ICGA)

Results: Data acquired with the different techniques are consistent and show that CC degeneration is visible 7 days post laser treatment for all DC, and the severity of degeneration is directly proportional to the laser power. The CC appear to progressively recover from the edges of the lesion for lower DC laser (1, 1.5, and 2%), leading to almost complete recovery in 1% DC in 12 weeks. Laser power of 1 and 1.5% DC leaves INL intact and ONL partially preserved; 2% DC laser more severely damaged the ONL, and mildly the INL; 3% DC leads to complete degeneration of ONL and INL. Our results indicate that lower power laser (1, 1.5, and 2% DC) induces CC and PR degeneration likely as a secondary effect of RPE loss. In comparison, higher power laser (3% DC) severely damages retinal and choroid structure causing complete CC, RPE, ONL, and INL loss

Conclusions: Our data suggest that laser power of 1.5% and 2% DC leads to RPE, PR, and CC damage in the Yucatan minipig retina comparable to late stage of CHM. The OCTA, combined with other imaging techniques (OCT, FA, and ICGA) allows for an accurate in vivo follow-up of the CC and the retinal layers and therefore a direct translation of the efficacy of potential therapy from the pig model to the patients

CONTROL ID: 3547528

SUBMITTER (NAME ONLY): zeshan tariq

TITLE: Baltimore Homeless Eye Disease Study

SESSION TITLE: Aging, social and environmental determinants and the eye

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Z. tariq, A. Vinnett, L. Andrews, M.R. Levin, M. Kaleem, Department of Ophthalmology and Visual Sciences, University of Maryland School of Medicine, Baltimore, Maryland, UNITED STATES|J. Alvarez, Sinai Hospital, Baltimore, Maryland, UNITED STATES|M. Kaleem, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|N. Okezie, University of Maryland Baltimore, Baltimore, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Homelessness currently impacts 3.5 million Americans and costs the U.S. economy two trillion dollars annually. Homelessness is strongly associated with various comorbidities including cardiovascular disease, diabetes mellitus, and depression. However, our understanding of homelessness' impact on vision is limited. Vision is of specific importance due to its central role in maintaining individuals' quality of life and day-to-day functioning. In this study, we survey and record exam findings from over 150 homeless participants who presented to the Healthcare for the Homeless Eye Clinic in Baltimore, Maryland.

Methods: We surveyed over 150 homeless participants who presented for general ophthalmic examinations at Health Care for the Homeless in Baltimore, Maryland. Surveys collected information regarding vision related quality of life, past medical history, living conditions, and medical diagnoses. Surveys were offered in both Spanish and English.

Results: Our captured population was mostly composed of Blacks (49%) or Hispanics/Latinos (38%). We also captured a small number of Caucasians (10%). The most common self-reported vision problems were blurry vision (70%), wanting glasses (51%), eye pain (27%), and dryness (27%). The most frequent ocular diagnoses were refractive error (77%), cataracts (36%), glaucoma/glaucoma suspect (24%), and dry eye (23%). Forty-four% of participants were referred for further subspecialty ophthalmic care. Black patients were significantly older than Hispanic/Latino patients, predominantly male (63%), and had greater incidence of glaucoma and cataracts. In contrast, Hispanic/Latino patients were younger, predominantly female (66%), and more likely to be diagnosed with dry eye, allergies, and other corneal diseases.

Conclusions: In this study, we characterized the ophthalmic needs of a homeless population in Baltimore, Maryland. Within this population, we identified differences between the demographic characterization and ophthalmic needs of Black and Hispanic/Latino subpopulations experiencing homelessness. Overall, our data emphasizes that homelessness is a complex social factor with various subpopulations requiring unique ophthalmic considerations.

CONTROL ID: 3547529

SUBMITTER (NAME ONLY): Selwyn Prea

TITLE: Survey of long-term home monitoring of visual field in patients with chronic eye disease.

SESSION TITLE: Aspects of Visual Function

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.H. Guymer, Ophthalmology, Department of Surgery, The University of Melbourne, Melbourne, Victoria, AUSTRALIA|S. Prea, A.J. Vingrys, Optometry & Vision Sciences, The University of Melbourne Faculty of Medicine Dentistry and Health Sciences, Melbourne, Victoria, AUSTRALIA|S. Prea, Y. Kong, Royal Victorian Eye and Ear Hospital, East Melbourne, Victoria, AUSTRALIA|E.K. Baglin, P. Sivarajah, R.H. Guymer, Centre for Eye Research Australia Ltd, East Melbourne, Victoria, AUSTRALIA|

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ABSTRACT BODY:

Purpose: To survey participant perceptions on the use of a tablet device for weekly home-monitoring of visual field (VF) by glaucoma and age-related macular degeneration (AMD) patients.

Methods: We recruited participants with either stable glaucoma in at least one eye, or intermediate AMD at a routine clinical review. Baseline perimetric examination was conducted with the Humphrey Field Analyzer (HFA, glaucoma) or Macular Integrity Assessment perimeter (MaIA, AMD). Test subjects were trained on how to undertake a home VF test facilitated by the Melbourne Rapid Fields (MRF) iPad application. They were tasked with performing weekly home examinations using the MRF for 12-months, assisted by a 'voice-over' that guided the testing process. At the completion of the study, participants were surveyed on the ease of use of the tablet device for home monitoring of vision, factors that would ensure the success of home monitoring, and their preference for using the iPad in assessing the visual field. Responses were scored using a 5-point Likert scale and the mean score [\pm SEM] was determined to gauge significance in preference.

Results: Eighty-seven participants were recruited to the survey (n=37 glaucoma, n=50 AMD, mean age 66.9 [range: 29-84]). Participants found the MRF app very easy to use (mean 4.4 [0.08]) and the 'voice-over' feature helpful in guiding them through the exam (mean 3.7 [0.13]). Previous experience using an iPad, as well as an information pamphlet provided at the training session were seen as most useful in enabling participants to use the iPad for visual field testing. A text message was the preferred method for reminding patients to perform their test. Undertaking a visual field examination with the iPad was much preferred over standard clinical devices (HFA/MaIA, mean 4.64 [0.08]). Those with a chronic eye disease favoured home monitoring their vision at either weekly (mean 3.80 [0.13]) or monthly (mean 3.92 [0.11]) intervals over the long term (weekly versus monthly, $p > 0.05$). A sub-analysis of different age groups found no significant difference in survey preferences from younger (< 70 yo) or older (≥ 70 yo) participants.

Conclusions: Home monitoring of the visual field under the guidance of tablet generated voice prompts was a positive experience for most participants with chronic eye disease. Participants were receptive to undertaking either weekly or monthly home monitoring in the long term.

CONTROL ID: 3547530

SUBMITTER (NAME ONLY): Michael Puente, Jr.

TITLE: Ocular Manifestations of Ruptured Arachnoid Cysts in Pediatric Patients

SESSION TITLE: Neuro-ophthalmology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Puente, Jr., J.L. Jung, Ophthalmology, University of Colorado Denver School of Medicine, Aurora, Colorado, UNITED STATES|M.A. Puente, Jr., J.L. Jung, Ophthalmology, Children's Hospital Colorado, Aurora, Colorado, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Michael Puente, Jr.: Commercial Relationship: Code N (No Commercial Relationship) | Jennifer Jung: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Arachnoid cysts are intra-arachnoidal collections of cerebrospinal fluid, which may be congenital or secondary to head injuries, intracranial hemorrhage, or infection. Occasionally these cysts can rupture spontaneously or secondary to trauma, resulting in subdural hemorrhage or, more rarely, a subdural cerebrospinal fluid collection without hemorrhage. While the neurologic manifestations of ruptured arachnoid cysts have been well described, there is little published data examining the ocular manifestations in the setting of ruptured arachnoid cysts, particularly among patients with associated subdural hemorrhage or fluid collection. By examining the records of pediatric patients with documented radiographic evidence of ruptured arachnoid cysts as well as a formal ophthalmologic exam, we sought to better characterize the ocular findings associated with ruptured arachnoid cysts.

Methods: We performed a retrospective chart review of all patients treated for ruptured arachnoid cysts at Children's Hospital Colorado from 1 January 2006 to 1 August 2018 and recorded the findings of ophthalmology exams in these patients. Children who did not receive an eye exam during their initial admission were excluded.

Results: A total of 23 children were treated for ruptured arachnoid cysts at our institution during the study period, 17 of whom were eligible for this study due to receiving an eye exam during their admission. Age at time of rupture ranged from 9 months to 17 years (median age 5 years). Eleven children experienced spontaneous rupture of their arachnoid cyst, while the etiology was traumatic in the remaining six. Subdural hemorrhage or fluid was noted in 16 of the 17 patients on MRI. Funduscopic exams revealed papilledema in 10 patients, but no papilledema was noted in any of the 5 patients under 3 years old. Retinal hemorrhages were found only in the 2 patients who were under 2 years old, with non-accidental trauma highly suspected in one case. Best corrected visual acuity in verbal children ranged from 20/20 to 20/30.

Conclusions: Children with ruptured arachnoid cysts commonly develop papilledema, though this may be less likely in younger children. Retinal hemorrhages are less likely to develop but may be seen in especially young patients. Ophthalmology should be consulted in all cases of ruptured arachnoid cysts in children due to the likelihood of ocular manifestations, though the visual prognosis is generally good.

CONTROL ID: 3547532

SUBMITTER (NAME ONLY): Lalit Ahirwar

TITLE: Bioinformatically predicted, stress-associated mitogen-activated protein kinase 7 (PsMPK7) of *Pythium insidiosum* is significantly associated with infection progression in human cadaveric cornea

SESSION TITLE: Immunity and Host Defense

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.K. Ahirwar, S. Sharma, Jhaveri Microbiology Centre, LV Prasad Eye Institute, Hyderabad, Telangana, INDIA|L.K. Ahirwar, Manipal Academy of Higher Education, Manipal, Karnataka, INDIA|

Commercial Relationships Disclosure (Abstract): Lalit Ahirwar: Commercial Relationship: Code N (No Commercial Relationship) | Savitri Sharma: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Keratitis caused by *Pythium insidiosum* is rare but severe and can lead to vision loss. To study its pathogenicity and determine its putative virulence genes, we investigated the genome of ocular *P. insidiosum* isolate using bioinformatics tools. The selected virulence genes of *P. insidiosum* were studied for mRNA expression in infected human cadaveric cornea (HCC)

Methods: The whole genome sequencing of *P. insidiosum* obtained from a patient with keratitis was performed for gene prediction (GeneMark-ES) and virulence genes identification (PHI base). Primers were designed for the identified genes [Aspartate aminotransferase 3 (PsAAT3), Stress associated mitogen activated protein kinase 7 (PsMPK7), ADP-ribosylation factor 2 (ARF2)] and a housekeeping gene (GAPDH) using Primer3. Ex-vivo cultures (n=6) of HCC were infected (intrastromal injection) with zoospores of a clinical isolate from a patient with severe *P. insidiosum* keratitis. Postinfection (PI) the HCC were incubated at 37°C, harvested (PI- 24hrs, n=3; 48hrs n=3) and preserved in RNAlater. The culture of *P. insidiosum* was used as control. RNA extraction, cDNA synthesis and RT-qPCR (QuantStudio 3) were performed for gene expression analysis. Data was analyzed using one-way ANOVA with Post-Hoc Tukey HSD test (p-value ≤0.05-significant).

Results: The gene prediction in *P. insidiosum* genome resulted in the identification of 27706 coding sequences. These coding sequences showed a total of 6812 distinct virulence genes. Among these, we selected 3 genes based on the least e-value (0 to 3.5e-56), >90% similarity matches and their function. The mRNA analysis, showed significant elevation of PsMPK7 expression after 48hrs PI [mean±SD (9.09±2.29)] compared to 24hrs (1.66±1.32), p-value ≤0.008. Although, the expressions of PsAAT3 [24hrs vs 48hrs (0.42±0.063 vs 0.55±0.26, p-value≤ 0.42)] and ARF2 (0.34±0.09 vs 0.74±0.31, p-value≤ 0.10) were not significantly different they were higher at 48 hrs.

Conclusions: This study demonstrates the expression of PsMPK7 gene in *P. insidiosum* in ex-vivo human corneal culture. This gene, known to play a crucial role in response to various stresses and reactive oxygen species detoxification, seems to play an important role in the pathogenicity of severe *P. insidiosum* keratitis.

CONTROL ID: 3547539

SUBMITTER (NAME ONLY): Alexander Baten-Tschan

TITLE: Optimal Follow-up and Medication Management for Traumatic Hyphema

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Baten-Tschan, C. Callahan, M.C. Chen, Ophthalmology, Penn State College of Medicine, Hershey, Pennsylvania, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Alexander Baten-Tschan: Commercial Relationship: Code N (No Commercial Relationship) | Christine Callahan: Commercial Relationship: Code N (No Commercial Relationship) | Michael Chen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Acute hyphema is one of the most common ocular injuries that results in emergent ophthalmologic consultation. Associated complications, such as severely elevated intraocular pressure (IOP) and corneal blood staining, can cause vision loss. At our institution, patients are followed daily for a period of 5-7 days to ensure that re-bleeding and IOP elevations do not occur. As management strategies often vary by provider or institution, the purpose of this study is to determine at what point certain complications are most likely to occur to inform optimal management strategies.

Methods: Retrospective chart review of all traumatic hyphemas treated at Penn State Eye Center between January 2015 and October 2020 was performed. Data collected included age, injury mechanism, initial hyphema level, baseline IOP, maximum IOP, and re-bleed date. Hyphema associated with open globes, post-operative, and spontaneous hyphemas were excluded. IOP elevations were defined as a >5 mmHg elevated in IOP from initial examination or presenting IOP of >21 mmHg. The Penn State College of Medicine Institutional Review Board reviewed the study protocol and determined it exempt from further review.

Results: 100 eyes of 100 patients met the inclusion criteria. The mean age was 27.01 ± 20.4 (range 2-92) years and 75% were male. The most common mechanisms were high velocity projectiles (73%), blunt trauma (17%), and motor vehicle accidents (5%). The average presenting level of hyphema was 1.55 ± 1.94 (range 0-9.7) mm. Of the 78 patients were tested for sickle cell trait, two were positive. The mean presenting IOP was 19.65 ± 8.35 (range 7-52) mmHg and maximum IOP during the follow up period was 25.96 ± 10.92 (range 10-64) mmHg. IOP elevations were found to occur in 26 eyes and occurred from 1 to 15 days. 38 eyes required intervention for IOP during their clinical course. Re-bleeds were found to occur in 6 eyes and occurred from 2 to 8 days.

Conclusions: The clinical course of traumatic hyphemas is highly variable. As such, daily follow up should continue in order to diagnose re-bleeds and IOP elevations in a timely manner.

CONTROL ID: 3547540

SUBMITTER (NAME ONLY): Barbara Rangel

TITLE: Increased Cx43 and VEGF expression in acute nonarteritic anterior ischemic optic neuropathy induced with 577nm laser

SESSION TITLE: Central Vision and ERG

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B.R. Rangel, L.A. Mesentier-Louro, A. Shariati, R. Dalal, Y.J. Liao, Ophthalmology, Stanford Medicine, Stanford, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Cx43, a gap junction protein expressed in astrocytes, is known to play an important role in modulating the response to CNS injury. Blocking Cx43 hemichannel opening in ischemia/reperfusion models has been shown to rescue RGCs by preventing secondary damage spread. Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in those older than 50 years old and it presents as sudden, painless visual field loss. Here, we introduced and validated a novel photochemical thrombosis NAION animal model and investigated changes in Cx43 expression in retinal astrocytes.

Methods: We induced photochemical thrombosis NAION model in adult C57BL/6 mice using a 577nm laser (200µm spot size, 50mW power, 500ms, 15 spots). We assessed retinal and optic nerve in vivo imaging using spectral-domain optical coherence tomography (OCT) at baseline, day 1, 3 and 21 after NAION induction and used immunohistochemistry examine changes in Cx43, VEGF and Brn3a expression.

Results: One day after NAION induction, there was significant thickening of the peripapillary ganglion cell complex (GCC) (RNFL+GCL+IPL) compared with baseline (baseline: $80 \pm 1\text{mm}$, $n=10$; day-1: $88 \pm 3\text{mm}$, $n=10$, $p<0.05$). Immunohistochemistry showed that NAION also led to the increase in the levels of VEGF (Ctrl: 2319 ± 195 , $n=5$; day-1: 4549 ± 683 gray mean value, $n=5$, $p<0.05$) which correlates with retinal edema ($r=0.89$, $p=0.045$). NAION induced a significant increase in Cx43 expression (Ctrl: 1351 ± 80 , $n=4$; NAION day-1: 1791 ± 55 , $n=5$, $p<0.05$; NAION day-3: 2844 ± 148 puncta/ mm^2 , $n=4$, $p<0.0001$), which normalized within 3 weeks (NAION day-21: 1639 ± 100 puncta/ mm^2 , $n=4$). Twenty one days after NAION, OCT imaging showed a significant thinning of the GCC (69 ± 1 , $n=9$, $p<0.01$) indicating loss in RGCs, confirmed by a 30% decrease in Brn3a⁺ cells (Ctrl: 3131 ± 44 cells/ mm^2 , $n=4$; NAION: 2180 ± 217 , $n=8$, $p<0.01$).

Conclusions: A novel protocol of photochemical thrombosis using a 577nm laser induced elevation of VEGF positively correlated to GCC swelling and also led to significant RGCs loss at 21 days, reproducing the expected phenotype of a NAION model. The focal ischemia also led to an increase in Cx43 one day after NAION which was 1.5x more elevated by day 3. Early astrocytic changes in Cx43 expression could be relevant mechanism involved in NAION pathology and therefore a potential therapeutic target.

CONTROL ID: 3547541

SUBMITTER (NAME ONLY): Arthur Nassaralla

TITLE: Predominantly hemorrhagic lesion in nAMD and response to Anti-VEGF treatment

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Nassaralla, J.J. Nassaralla, Retina, Instituto de Olhos de Goiânia, Goiânia, Goiás, BRAZIL|M.H. Amaro, Retina, Eye and Laser Institute of Belém, Belém, Pará, BRAZIL|C. Muccioli, Instituto da Visao da Paulista, Sao Paulo, São Paulo, BRAZIL|T. Aihara, Faculdade de Ciencias Medicas da Santa Casa de Sao Paulo, Sao Paulo, São Paulo, BRAZIL|

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ABSTRACT BODY:

Purpose: To assess the prognosis of nAMD with hemorrhagic choroidal neovascularization treated with ranibizumab, bevacizumab and aflibercept

Methods: We investigated twelve nonconsecutive cases of nAMD with predominantly hemorrhagic neovascularization over the course of six years. During the investigation, we looked for signs of worsening or improvement in patient's vision and for difference between the chose drugs results

Results: During the treatment, we found a satisfactory response of the eyes suffering from nAMD with hemorrhagic choroidal neovascularization when treated with anti VEGF drugs. The first signs of improvement were noticed three months following the initial therapy and the patient who took the longest to show improvement after the begining of the treatment did so after eight months. No patient showed imediate response to the treatment and no difference between the drugs were noticed during the treatment.

Conclusions: These cases of nAMD with hemorrhagic choroidal neovascularization benefited from the treatment with anti VEGF, despite its first responses being held after three months of treatment. No difference in the result between drugs was noticed. 70% of the eyes treated showed improvement in the visual acuity. Two of the cases evolved to subretinal fibrosis. nAMD is still an important therapy in patients of nAMD

CONTROL ID: 3547542

SUBMITTER (NAME ONLY): Sergio Guevara-Quintanilla

TITLE: Correlation of Two Methods to Evaluate Dry Eye in the Office

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S.E. Guevara-Quintanilla, M. Herrera-Rodriguez, S. Garza, M.A. Hernandez-Delgado, M. Salan-Gomez, J. Valdez-Garcia, Tecnológico de Monterrey, Instituto Tecnológico y de Estudios Superiores de Monterrey, Monterrey, Nuevo Leon, MX, academic, MEXICO|

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ABSTRACT BODY:

Purpose: To compare results obtained through the standard slit-eye examination of tear breakup time (TBUT) and Schirmer's test with the JENVIS Dry Eye Report software values in the diagnosis of dry eye.

Methods: Retrospective observational study. We used a random sample of 20 patients at Zambrano Hellion Medical Center, Tecnológico de Monterrey. All patients were diagnosed with dry eye syndrome between January and December 2020. Their TBUT was measured through slit-lamp examination and with the JENVIS software installed in the OCULUS Keratograph 5M. Three JENVIS values were compared with slit-lamp results (which acted as control): the total breakup time (NIK BUT, noninvasive breakup time), the time to first rupture (NIK BUT_f), and the average time of rupture (NIK BUT_{av}). Schirmer's test results were also compared with tear meniscus height (TMH) values given by the JENVIS software. A statistical analysis between values followed.

Results: Twelve patients were female (60%), and eight patients were male (40%). The age range was of 26 - 69 years with a mean of 45 years. Eight patients (40%) had a previous refractive surgery (LASIK). TBUT results obtained through slit-lamp had a mean of 5.89 seconds (range 3-9 seconds). The NIK BUT results had a mean of 10.53 seconds (range 1.53-24.98 seconds). The correlation between this value and slit-lamp TBUT was found to be moderately positive ($r=0.34$), statistically significant ($p=0.03$). The NIK BUT_f results had a mean of 6.74 seconds (range 2.17-17.21 seconds). A statistically significant ($p=0.04$), moderately positive ($r=0.38$) relation was also found. The third value was the NIK BUT_{av} with a mean of 8.52 seconds (range 3.39-21.58 seconds). The correlation between both of these values was not found to be statistically significant ($p=0.09$). TMH had a mean of 0.18 mm (range 0.1-0.34 mm). Its relation to Schirmer's test values was also not found to be significant ($p=0.8$).

Conclusions: We found that at least 2 values given by the JENVIS software had a significant correlation with slit-lamp examination values. This suggests that the software may be used as an automatic, more systemized way of measuring TBUT that is easier, faster and less prone to subjective interpretation for those who possess an OCULUS Keratograph 5M. Schirmer's test and TMH results should still be analyzed separately. The main disadvantage of this study is its small sample size, so repeating the study with a larger sample is warranted.

CONTROL ID: 3547543

SUBMITTER (NAME ONLY): Pulak Nath

TITLE: Elucidating the immune-regulatory mechanisms in non-infections uveitis patients

SESSION TITLE: Innate and Adaptive Immune Cells in Humans and Animal Models of Immune Disease

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P.R. Nath, M. Maclean, K.D. Kaya, A. Kumar, V.V. Agashe, J.W. Lee, M. Yakin, H. Sen, Clinical and Translational Immunology Unit, Laboratory of Immunology, National Eye Institute, Bethesda, Maryland, UNITED STATES|

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ABSTRACT BODY:

Purpose: Uveitis is a significant cause of severe visual handicap. Evidence links induction of experimental autoimmune uveitis to T cell mediated pathogenesis which is broadly regulated by the crosstalk between natural killer (NK) cells and dendritic cells (DC). Blockade of IL2Ra in uveitis patients lead to expansion of CD56^{bright} NK cells whose immunomodulatory effects inhibit activated T cell survival. The role of NK cells as however, as modulators of autoimmune responses in uveitis patients, has not been extensively explored. The purpose of this study is to present the analysis of major immune cell populations in the peripheral blood lymphocytes (PBMCs) of a large cohort of non-infectious uveitis patients with a focus on NK cell, DC and T cell crosstalk.

Methods: Bulk-RNA from PBMCs of 153 non-infectious uveitis patients and 51 age-, sex- and race-matched healthy individuals from a prospective clinical study (NCT02656381) were sequenced using Illumina NovaSeq 6000 platform. Multicolor flow panels were designed to interrogate subsets of T cells, NK cells and monocyte/DCs in freshly isolated peripheral blood and acquired on a BD LSR Fortessa cytometer.

Results: A clear distinction of transcriptome was observed between healthy donors and uveitis patients while analyzing their corresponding PBMCs. Introducing a cutoff of 1.2 folds and FDR 0.05 separated intermediate uveitis from posterior and pan uveitis based on their transcriptome signatures. High dimensional flow cytometric analysis revealed a significant upregulation of NK cells subsets ($p = 0.0023$) and a concomitant downregulation of DC subsets ($p = 0.003$) in PBMCs of uveitis patients. T cell subset analysis revealed a significant expansion of CD4⁺ T cells ($p = 0.0142$) as well as CD8⁺ T effector memory CD45RA⁺ cells ($p = 0.0183$) in uveitis patients.

Conclusions: Our observation indicates basal expansion of CD4⁺ T cells and NK cells in uveitis patients. Concomitant decrease of DCs and increase of terminally differentiated CD8⁺ T cells suggest both cytotoxic and regulatory roles of NK cells in uveitis patients, which need to be further examined.

CONTROL ID: 3547547

SUBMITTER (NAME ONLY): Marco Beccarini

TITLE: Correlating Optical and Electromagnetic Tracking Methodologies for Surgical Guidance in Vitrectomy Surgery

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: M. Beccarini, C. Luciano, Y. Leiderman, University of Illinois at Chicago, Chicago, Illinois, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Marco Beccarini: Commercial Relationship: Code N (No Commercial Relationship) | Cristian Luciano: Commercial Relationship: Code N (No Commercial Relationship) | Yannek Leiderman: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: In vitreoretinal surgery, surgeons manipulate sharp surgical instruments in close proximity to the retina, with the potential for unintentional tissue-instrument interactions causing tissue damage. The principles of collision avoidance may be applied to ophthalmic surgery in order to minimize the potential for tissue damage. Accurate assessment of the position of the surgical instruments and intraocular tissues is requisite.

Methods: Tracking of surgical instruments and intraocular tissues may be performed via two approaches; optical tracking via surgical stereo cameras to track the retina, and electromagnetic sensing to track the surgical instrument. A rigid registration of the two reference systems allows for the determination of the distance between the tip of the instrument and the retina. We created a virtual and navigable three-dimensional environment, generated in real time, for the visualization of distances. We assessed the accuracy of a registered optical-electromagnetic tracking system in measuring distance in real time. The evaluation of the algorithm has been performed at the macroscale with a tracking volume size of 46x56x30 cm.

Results: With an exemplar chosen ground truth distance of 15cm, the optical tracker detected distances with an average accuracy of 97.15%, with a mean absolute error of 4.28mm and a standard deviation of 1.5mm. The registered camera-sensor system showed an average distance detection accuracy of 92.84%, with a mean absolute error of 1.07 cm and a standard deviation of 1.068cm.

Conclusions: These data indicate that this approach has the potential to provide reliable real-time surgical guidance by assessing surgical instrument positional data relative to intraocular tissues. Experiments at the microscale using a surgical microscope will yield additional data on the potential utility of this approach in the microsurgical environment.

CONTROL ID: 3547548

SUBMITTER (NAME ONLY): Umangi Patel

TITLE: The Presence of SARS-CoV-2 in Human Corneal Tissue

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: U. Patel, Y. LIU, D. Miller, A. Naranjo, X. Liu, J. Maestre-Mesa, R.K. Lee, S.R. Dubovy, Bascom Palmer Eye Institute, University of Miami Health System, Miami, Florida, UNITED STATES|U. Patel, A. Naranjo, E. Fout, S.R. Dubovy, Florida Lions Ocular Pathology Laboratory, Bascom Palmer Eye Institute, University of Miami Health System, Miami, Florida, UNITED STATES|D. Miller, J. Maestre-Mesa, Microbiology, Bascom Palmer Eye Institute, University of Miami Health System, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: The involvement of severe acute respiratory syndrome related coronavirus 2 (SARS-CoV-2) in ocular tissue is currently poorly understood. This study examines the presence of SARS-CoV-2 in cornea tissue from postmortem donors with confirmed SARS-CoV-2 infection

Methods: We conducted a retrospective analysis of human cornea tissue from nine postmortem SARS-CoV-2 positive donors to examine for the presence of SARS-CoV-2 RNA and protein. All tissue donors were confirmed positive for SARS-CoV-2 via nasopharyngeal swab during tissue recovery. Real-time polymerase chain reaction (RT-PCR), immunofluorescence, and histopathologic evaluations were performed to examine for the presence of SARS-CoV-2 structural proteins (spike, nucleocapsid) and human viral ligands, angiotensin converting enzyme 2 (ACE2) and transmembrane protease serine type 2 (TMPRSS2).

Results: RT-PCR analysis of cornea tissue demonstrated 100% (9 of 9) positivity for SARS-CoV-2 RNA in right corneal tissue and 77.8% (7 of 9) positivity in left corneal tissue. Immunofluorescence demonstrated the presence of ACE2 and TMPRSS2 within the corneal epithelium and endothelium. SARS-CoV-2 spike and nucleocapsid proteins were present in 77.8% and 88.9% of corneal epithelial tissue and in 88.9% and 66.7% of corneal endothelial tissue, right and left respectively. ACE2 and TMPRSS2 expression co-localized with SARS-CoV-2 spike and nucleocapsid proteins. Histopathologic evaluation was unremarkable for all nine pairs of specimens.

Conclusions: This retrospective case series demonstrates the presence of SARS-CoV-2 RNA within cornea tissue using RT-PCR. Furthermore, we show by immunofluorescence that spike and nucleocapsid SARS-CoV-2 proteins within the cornea colocalized native ligands in the epithelium and endothelium. Further investigation is warranted for the possibility of SARS-CoV-2 transmission and the utilization of SARS-CoV-2 positive tissue in corneal transplant surgeries

CONTROL ID: 3547550

SUBMITTER (NAME ONLY): Xianjun Zhu

TITLE: The ER membrane protein complex subunit Emc3 controls angiogenesis via the FZD4/WNT signaling axis

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Zhu, Sichuan Provincial People's Hospital, Chengdu, CHINA|

Commercial Relationships Disclosure (Abstract): Xianjun Zhu: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The ER membrane protein complex (EMC) regulates the synthesis and quality control of membrane proteins with multiple transmembrane domains and has been implicated in several disease conditions. However, the role of EMC in angiogenesis remains elusive. The purpose of this study is to investigate the role of Emc3 in retinal angiogenesis using genetic knockout mouse models.

Methods: Endothelial specific knockout model of Emc3 was generated by crossing conditional allele of Emc3 with Pdgfb-Cre ER line. Retinal vascular development was assessed using retinal whole mount staining. Tube formation and cell proliferation was analyzed in primary human retinal endothelial cells (HRECs) with EMC3 knockdown mediated by shRNA lenti-virus. Downstream target genes were assessed by transcriptome analysis.

Results: We show that the EMC subunit Emc3 plays critical roles in retinal vascular angiogenesis by regulating Norrin/Wnt signaling. Postnatal endothelial cell (EC)-specific deletion of Emc3 led to retarded retinal vascular development with a hyperpruned vascular network, the appearance of blunt-ended, aneurysm-like tip endothelial cells (ECs) with reduced numbers of filopodia at the vascular front and reduced numbers of tip cells. Leakage of erythrocytes was also prominent. Knockdown of EMC3 in primary human retinal endothelial cells (HRECs) impaired tube formation and diminished cell proliferation. Mechanistically, deletion of Emc3 reduced EC proliferation by reducing the expression level of the Wnt receptor FZD4. Knockdown of Emc3 decreased FZD4 expression and reduced β -catenin signaling, as revealed by luciferase reporter assay. Moreover, augmentation of Wnt activity via lithium chloride treatment partially reversed the angiogenesis defects in Emc3-cKO mice.

Conclusions: Our data reveal that Emc3 plays essential roles in angiogenesis through direct control of FZD4 expression and Norrin/ β -catenin signaling and provide a potential therapeutic target.

CONTROL ID: 3547551

SUBMITTER (NAME ONLY): Sunil Bellur

TITLE: Identification of Common Systemic Comorbidities in Patients with Panuveitis

SESSION TITLE: Epidemiology, Prognosis and Burden of Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Bellur, M. Asahi, C.T. Khoo, Ophthalmology, George Washington University Medical Faculty Associates, Washington, District of Columbia, UNITED STATES|R. Raiker, West Virginia University Health Sciences Center, Morgantown, West Virginia, UNITED STATES|H. Pakhchanian, The George Washington University, Washington, District of Columbia, UNITED STATES|H. Sen, National Eye Institute, Bethesda, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Sunil Bellur: Commercial Relationship: Code N (No Commercial Relationship) | Haig Pakhchanian: Commercial Relationship: Code N (No Commercial Relationship) | Rahul Raiker: Commercial Relationship: Code N (No Commercial Relationship) | Masumi Asahi: Commercial Relationship: Code N (No Commercial Relationship) | Chloe Khoo: Commercial Relationship: Code N (No Commercial Relationship) | H Nida Sen: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: While the ocular comorbidities of panuveitis are well documented, there is a dearth of literature analyzing the general health of these patients as represented by other systemic comorbidities. This investigation identifies the fifteen most common non-ocular comorbidities in patients with panuveitis.

Methods: TriNetX (Cambridge, MA, USA) is a real-time, federated healthcare database that was used in this study. At the time of the study, the database included 60 million unique electronic medical records (EMR) of patients from 41 healthcare organizations (HCOs). The TriNetX platform mostly receives EMR data from HCO's that are large academic centers across the USA. All data, when appropriate, were queried based on the International Classification of Diseases codes. The goal of this study was to analyze the prevalence of non-ocular comorbidities amongst panuveitis patients in this cohort. Inclusion criteria included patients with ICD-10 codes corresponding to panuveitis (H44.11) and the fifteen most prevalent ICD-10 codes associated with a disease diagnosis. Patients aged 18 years and older were included.

Results: 6126 patients with panuveitis were identified in the cohort. The mean age +/- standard deviation was 52.7 +/- 18.4 years old. 57% of the cohort was female (n=3490) and 43% male (n=2633). 52% of the study population identified as white (n=3219), 27% black or African American (n=1647), and 3% as Asian (n=158). The fifteen most common systemic comorbidities included essential hypertension 14% (n=1141), disorders of lipoprotein metabolism and other lipidemias 11.6% (n=712), diabetes mellitus 10.5% (n=647), other diseases of intestines 9.5% (n=584), gastroesophageal reflux disease 8.7% (n=535), benign neoplasms 7.7% (n=476), osteoarthritis 7.5% (n=464), nicotine dependence 7.3% (n=448), other headache syndromes 7.3% (n=445), major depressive disorder 7.1% (n=437), obesity 6.9% (n=428), anemia unspecified 6.6% (n=407), inflammatory polyarthropathies 6.5% (n=309), sleep disorders 6.3% (n=384), and other anxiety disorders 6.1% (n=374).

Conclusions: To our knowledge this is the first study looking at the prevalence of non-ocular comorbidities in panuveitis patients. Further research is necessary to determine which comorbidities are more prevalent than in the general population and which are possible secondary effects from therapies.

CONTROL ID: 3547552

SUBMITTER (NAME ONLY): Mustafa Arikan

TITLE: Uncertainty-based Deep Active Learning for Retinal Layer Segmentation

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Arikan, H.M. Ahmed, A.M. Hagag, A. Dubis, UCL Institute of Ophthalmology, UCL, University College London, London, London, GB, academic, London, UNITED KINGDOM|F. Sallo, A. Montesel, Hopital ophtalmique Jules-Gonin, Lausanne, Vaud, SWITZERLAND|M. Book, H. Faatz, St Franziskus-Hospital Munster GmbH, Munster, Nordrhein-Westfalen, GERMANY|M. Cicinelli, Northwestern University, Evanston, Illinois, UNITED STATES|W. Lilaonitkul, UCL Institute of Health Informatics, University College London, London, London, UNITED KINGDOM|A.M. Hagag, A. Dubis, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|W. Lilaonitkul, Health Data Research UK (HDRUK), London, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: Progress of deep learning (DL) research in medicine is often hampered by the time required to generate the large amounts of labelled data for model training. To address this, we propose an active learning method to optimize training efficiencies while minimizing labelling efforts. We employed model uncertainty as an objective metric for prioritizing the candidate training images. Intuitively, images giving rise to higher levels of model uncertainty during prediction would contain more informative features that could help accelerate the rate at which a DL model can learn. We evidence the benefit of active learning on retinal-layer segmentation in optical coherence tomography (OCT) images.

Methods: 20 AMD, 20 DME and 20 normal OCT volumes (16-61 scans/volume) were obtained using the Heidelberg Spectralis device. We used a 12-12-36 split over the volumes for training, validation and testing. We quantified gains from active learning by comparing segmentation performance (intersection-over-union (IoU)) of a DL model trained with images selected by high uncertainty against a baseline where training samples were selected at random. Starting with a DL model trained on a prior subset of training images, we employed the Bayesian Dropout method to estimate the trained model's uncertainty when deployed on the remaining candidates of unseen training images. We select an increment of additional images based on high uncertainty values for model retraining. In the baseline experiment, additional images were selected at random. We continue to iterate the process and record the test performance over 4 increments and over 3 experimental repeats.

Results: Active learning produce higher IoU at the lower training sets sizes. This trend was greatest for DME scans.

Conclusions: In general, active learning is a principled method that can help minimize the burden of expensive and time-consuming data labelling and, in the process, can help accelerate deep learning research in medicine. In our results, while active learning provides trends of efficiency, more experimental repeats are needed to determine significance.

CONTROL ID: 3547554

SUBMITTER (NAME ONLY): Meraf Wolle

TITLE: The association between the severity of eyelid margin conjunctivization and trichomatous trichiasis severity in surgical patients in Tanzania

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.A. Wolle, B. Munoz, S.K. West, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|H. Mkocha, Kongwa trachoma project, TANZANIA, UNITED REPUBLIC OF

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ABSTRACT BODY:

Purpose: To determine the association between the severity of upper eyelid margin conjunctivization (CM) and trichomatous trichiasis (TT) severity as well as to evaluate the association between CM and entropion in TT surgical patients.

Methods: A cross-sectional study was conducted amongst adults with TT who were referred to surgical camps in Bahi District, Tanzania, for TT surgery. Participants underwent ocular examination. The presence and severity of CM was evaluated in photographs of the everted upper eyelid and the presence of entropion was evaluated in a subset of these photographs. TT severity was assessed at the time of the ocular exam based on the number of lashes touching the globe and/or evidence and extent of epilation. Ordinal logistic models were used to examine the association between the severity of CM and TT severity.

Results: A total of 627 eyes of 388 subjects were included. The participant's mean age was 64.6 years, 81% were females, and 62% had bilateral TT. 75.2% of the eyes had severe conjunctivization of the lid margin and 42% of the eyes had severe trichiasis. An increase in the severity of CM was associated with an increase in TT severity. Using as a reference eyes with none to mild CM, the odds of increased TT severity per one level increase in CM severity was 2.12 (95% CI: 1.56, 2.88).

Conclusions: In cases of trichomatous trichiasis presenting for surgery, TT severity was significantly associated with the severity of CM. Almost all cases of TT had moderate or severe CM. CM could be a useful adjunct in helping determine who needs trichiasis surgery.

CONTROL ID: 3547556

SUBMITTER (NAME ONLY): Deven Deonarain

TITLE: Supplemental scleral buckle for the management of rhegmatogenous retinal detachment by pars plana vitrectomy: A systematic review and meta-analysis of randomized controlled trials

SESSION TITLE: Retinal detachment

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Deonarain, V. Chaudhary, St. Joseph's Healthcare Hamilton, Hamilton, Ontario, CANADA|D. Rosenberg, Michael G. DeGroote School of Medicine, McMaster University, Hamilton, Ontario, CANADA|H.S. Ghayur, M. Phillips, Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, CANADA|V. Chaudhary, Department of Surgery, McMaster University, Hamilton, Ontario, CANADA|

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ABSTRACT BODY:

Purpose: Recent advancements in surgical instrumentation have shifted physician preference toward use of PPV for treatment of primary RRD. Placement of a supplemental buckle, however, remains the subject of intense debate. The present review aims to synthesize evidence from randomized controlled trials (RCTs) that compared efficacy and safety of pars plana vitrectomy (PPV) with and without application of a supplementary scleral buckle (SB) for management of rhegmatogenous retinal detachment (RRD).

Methods: The authors searched MEDLINE, EMBASE, and CENTRAL on July 2, 2020 from their inception to identify RCTs published in English that compared safety and efficacy of PPV with and without supplemental SB. Risk of bias was assessed according to Cochrane Risk of Bias 2 tool. We present risk ratios (RRs), mean differences (MDs), and 95% confidence intervals (CIs) estimated using random effects meta-analyses.

Results: We identified six eligible RCTs (705 eyes). Primary reattachment (6 studies, 345 eyes PPV, 324 eyes PPV+SB; RR 0.99, 95% CI 0.93-1.06, I² = 0%, p = 0.78) and final anatomic success rates (4 studies, 272 eyes PPV, 267 eyes PPV+SB; RR 1.00, 95% CI 0.98-1.02, I² = 0%, p = 0.89) were similar between groups. Postoperative improvement in visual acuity (5 studies, 244 eyes PPV, 222 eyes PPV+SB; MD 6.09 letters, 95% CI -0.47-12.64, I² = 69%, p = 0.07) and frequency of adverse events (6 studies, 1294 observations PPV, 1221 observations PPV+SB; RR 0.76, 95% CI 0.57-1.01, I² = 25%, p = 0.06) likewise were not found to differ significantly between treatment arms.

Conclusions: Low-certainty evidence from RCTs did not demonstrate a benefit in placement of a supplemental scleral buckle during vitrectomy for management of RRD. Additional high-quality trials are needed to provide more precise estimates of effect.

CONTROL ID: 3547558

SUBMITTER (NAME ONLY): Charles DeBoer

TITLE: Innovative Solutions to Improve Protection from Airborne Pathogens During Retinal Imaging and Examination

SESSION TITLE: Imaging of posterior segment II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. DeBoer, D. Lee, L. Lam, S. Zhang-Nunes, Roski Eye Institute, University of Southern California, Los Angeles, California, UNITED STATES|D. Stemen, D. Hwang, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: To develop and evaluate custom solutions for ophthalmologists when performing retinal examination on patients with airborne communicable disease.

Methods: Two solutions were developed for viewing and imaging patients with airborne communicable disease. The first solution was a custom indirect ophthalmoscope barrier shield consisting of a 3D printed bracket and laser cut shield. The shields were mounted using a rubber band fastening device to allow easy removal and cleaning. The bracket spaced the shield from the user to prevent fogging and heat generation. The central aperture allowed an unobstructed view of the retina. The second solution was a hand-held off the shelf portable fundus camera used with a Controlled Air-Purifying Respirator (CAPR) for providers examining patients in negative pressure rooms. Clinical viability was assessed with a survey completed by providers.

Results: Providers completed the survey after use. No fogging obscured view of the retina. Ergonomically, the provider was able to maneuver and perform indirect ophthalmoscopy to the periphery. Spacing of the shield allowed use with a N95 and prevented heat buildup. The portable fundus camera was used with a CAPR successfully allowing the user to maintain full PPE while taking fundus photos of patients on airborne precautions. It was possible to use an N95 mask with the CAPR to prevent transmission of airborne particles from the user.

Conclusions: There is a need for improved personal protective equipment due to the spread of COVID-19. Both solutions allowed ophthalmologists to maintain airborne precautions when examining patients. The first solution was compatible with a N95 mask and provided an additional face shield. This solution allowed viewing of the macula as well as far periphery. The second solution allowed use of a CAPR, making it suitable for providers who do not fit N95 masks. Photographs of the macula and mid-peripheral retina were possible with this option and dilation was not needed for examination. However, peripheral retinal viewing was more limited compared with the first option.

CONTROL ID: 3547559

SUBMITTER (NAME ONLY): Parthasarathi Kalaiselvan

TITLE: Antimicrobial activity of a peptide mimic against *Pseudomonas aeruginosa* in solution and when immobilised onto contact lenses.

SESSION TITLE: Antimicrobials and Immunomodulators

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Kalaiselvan, R. Kuppusamy, M. Willcox, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|R. Kuppusamy, N. Kumar, School of Chemistry, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The purpose of this study was to evaluate the antimicrobial activity of peptide mimic 758 against a drug-resistant and biofilm-producing strain of *Pseudomonas aeruginosa* in solution and when surface immobilised onto contact lenses.

Methods: Minimal inhibitory concentration (MIC) and Minimum bactericidal concentration (MBC) of 758 was measured against the *P. aeruginosa* strain 6294. 758 was covalently attached to etafilcon A contact lenses via EDC (1-ethyl-3-[3-dimethylaminopropyl] carbodiimide hydrochloride) and NHS (N-hydroxysuccinimide) coupling. High salt (10% NaCl) treatment was carried out to extract any adsorbed peptide to ensure that the activity was only due to 758 peptide mimic attached to the lens surface. The antimicrobial activity of 758 was evaluated against *P. aeruginosa* by measuring the amount of cell death compared to control uncoated lenses.

Results: MIC and MBC of 758 against *P. aeruginosa* was $45.5 \mu\text{g ml}^{-1}$ and $91 \mu\text{g ml}^{-1}$ respectively. When allowed to adhere to contact lenses coated with 1mg ml^{-1} 758 *P. aeruginosa* adhered to $0.15 \log_{10}$ colony forming units (cfu/lens) whereas *P. aeruginosa* adhered to control lenses to $\geq 3. \log_{10}$ cfu/lens. Therefore, covalently attached 758 was active against drug-resistant and biofilm-producing strain of *P. aeruginosa*, giving $\geq 2.9 \log_{10}$ reduction in bacterial counts compared to control lenses.

Conclusions: The peptide mimic 758 showed excellent antimicrobial activity against *P. aeruginosa*. Future research will examine the activity of 758 against drug-resistant Gram-positive bacteria, to see the potential for development as a broad-spectrum antimicrobial coating for contact lenses.

CONTROL ID: 3547563

SUBMITTER (NAME ONLY): Michael Ward

TITLE: Retinal Artery Occlusions and Risk Factors in the Young

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Ward, J. Etzel, S. Sauerzopf, G. Crabtree, Ophthalmology, Geisinger Medical Center, Danville, Pennsylvania, UNITED STATES|G. Crabtree, Ophthalmology, University of Wisconsin-Madison, Madison, Wisconsin, UNITED STATES|

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ABSTRACT BODY:

Purpose: Retinal artery occlusions (RAOs) are rare and understudied in young patients, and the etiology of these events are thought to differ from older adults. We performed a retrospective, observational study to investigate risk factors associated with RAOs in young adults.

Methods: A retrospective chart review of patients under 40 was conducted of the medical record from 1/1/2003 through 10/28/2019. Patients were identified by the ICD-9/ICD-10 codes for central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), and partial retinal artery occlusion. Clinical data was obtained by manual chart review.

Results: 30 eyes from 28 patients were identified with a RAO. 8 patients were found to have CRAO, 19 had BRAO, and two patients had a hemiretinal artery occlusion. The average age at onset was 33.14 years. 71.4% of patients were female, and only 10.7% were non-White.

Systemic risk factors were discovered in 25 patients (89.3%), with 12 patients (42.9%) having a hypercoagulable state, 4 patients (14.3%) having a rheumatologic condition without hypercoagulability, 3 patients (10.7%) with significant cardiac risk factors, and 2 patients (7.1%) whose only risk factor was hormonal contraceptive use. One traumatic and one post-operative RAO were identified. One patient was diagnosed with Susac Syndrome.

6 patients (21.4%) were smokers at onset of the RAO. A large percentage of affected patients were overweight, with 14 patients (50%) having BMI >25, and 11 (39.3%) with BMI >30.

Two patients (7.14%) died within 1 year of RAO onset, and a third patient passed approximately 8 years after RAO onset.

Conclusions: Retinal artery occlusion in young adults is rare. Unlike the embolic nature in older adults, hypercoagulable conditions, such as Lupus, are frequently found in younger patients and is the most common etiology in this study. Conditions associated with vaso-occlusive events such as smoking, hormonal contraceptive use, and cardiovascular disease were less common.

A third of the patients were obese/morbidly obese, hinting at a possible association with RAO. Additionally, clinically significant vaso-occlusive events leading to death occurred in several patients after RAO. This may suggest that RAO in young adults may be a harbinger of poor outcomes. However, due to the extreme rarity of this disease entity, further study is required to draw definitive conclusions.

CONTROL ID: 3547567

SUBMITTER (NAME ONLY): Minh Nguyen

TITLE: Photodynamic therapy for the treatment of choroidal metastases: A case series and meta-analysis

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M.T. Nguyen, A.W. Stacey, Department of Ophthalmology, University of Washington, Seattle, Washington, UNITED STATES|

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ABSTRACT BODY:

Purpose: Choroidal metastasis remains the most common type of ocular malignancy, affecting quality of life of patients who already carry poor prognosis from their primary cancers. Among the local treatment modalities for choroidal metastasis, photodynamic therapy (PDT) is an effective option and requires little time commitment. This study is a systematic review and meta-analysis aiming to investigate the efficacy and safety of photodynamic therapy in the treatment of choroidal metastasis.

Methods: We compiled all cases of choroidal metastases treated with PDT in literature, and included the unreported cases seen at our institution, a tertiary referral center, for a comprehensive meta-analysis.

Results: 50 tumors in 40 eyes of 34 patients were identified from the choroidal metastases treated with PDT at our institution and from 12 case reports in literature since 2004. Tumors became significantly flatter after an average of 1.4 PDT treatments (mean thickness was 1.9mm pre-operatively vs 1.0mm post-operatively, $p < 0.0001$). Similarly, there was a significant decrease in central macular thickness (CMT) post-operatively (mean CMT of 289 μ m vs 454 μ m, $p = 0.03$). After PDT, the majority of tumors completely flattened, had reduced thickness or stayed flat (82% of the tumors) and no longer had sub-retinal fluid (75% of the eyes). PDT also resulted in visual protection (stable or improved vision) in 77.5% of treated eyes, but there was no significant difference in vision between pre-PDT and post-PDT eyes ($P = 0.54$). There were no adverse events reported, and PDT was shown to be safe and effective in treating fovea and optic nerve involving tumors (tumor control efficacy of 86% and 75%, respectively), as well as metastases originating from the most common primary sites (tumor control efficacy of 94% in lung adenocarcinoma and 92% in breast carcinoma).

Conclusions: Although PDT requires less time consumption than other local treatment methods for choroidal metastasis, it showed effective tumor control and vision protection in our meta-analysis.

CONTROL ID: 3547570

SUBMITTER (NAME ONLY): Mariam Hamid

TITLE: Characteristics of Ophthalmology Procedural Care during the COVID-19 Pandemic

SESSION TITLE: Healthcare Delivery during Covid Pandemic

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: M. Hamid, S. Rezaei, D. Goldman, R. Levine, P.A. Edwards, Henry Ford Hospital, Detroit, Michigan, UNITED STATES|

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ABSTRACT BODY:

Purpose: Describing the procedures conducted during the peak of the COVID-19 pandemic in the department of ophthalmology at Henry Ford Hospital in Detroit, MI and understanding how the demographics of these patients compared to preceding years

Methods: Electronic medical record data at Henry Ford Hospital in Detroit, MI was queried for all operative procedures. The procedures must have met three criteria: 1) scheduled from March 15th to May 19th, 2020, 2) A staff ophthalmologist as the primary surgeon, 3) The procedure status was "completed." Parallel dates in the preceding three years 2017-2019 were queried to use as controls. Information obtained for each procedure included: date, procedure completed, age, race, sex, primary insurer, class of procedure (inpatient vs. outpatient). 2-tailed equal proportions tests and 2-tailed T tests were used to determine statistical significance of 2020 vs. preceding years 2017-2019.

Results: On average, there was a 94% decline in the number of procedures in 2020 compared to the average of the three preceding years. Over 800 surgical procedures were postponed during the pandemic. Retina procedures were most prevalent in 2020. Significantly younger patients were seen in 2020. There were no significant difference in race distributions by year. There was a significantly higher proportion of males who underwent operative procedures in 2020. Significantly more procedures were done with inpatient status compared to outpatient compared to preceding years

Conclusions: It is estimated that there is a 80-100% reduction in ophthalmologic surgical cases during COVID, which was consistent with our study of 94% decrease. The younger age group seen in 2020 was likely multifactorial, partially thought to be secondary to cancelling routine cataract and lens procedures on a largely older population skews the average age of procedures to the right, as well as a higher incidence of trauma requiring emergent procedural intervention in younger individuals such as for orbital floor fractures. Regarding a higher proportion of men, retinal procedures more commonly occur in men, and ambulatory procedures like cataract extraction which were cancelled during the pandemic are more commonly occur in women. We found no differences by race, which requires further study, and may possibly related to differences in baseline characteristics.

CONTROL ID: 3547573

SUBMITTER (NAME ONLY): Natela Shanidze

TITLE: Saccades during smooth pursuit in macular degeneration

SESSION TITLE: Visual Impairment - Assessment and Measurement

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N.M. Shanidze, Z. Lively, R. Lee, A. Velisar, P. Verghese, The Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Saccades and smooth pursuit are inextricably linked, particularly in cases of low gain, where saccades can help bring the fovea back on target. Individuals with macular degeneration (MD) have compromised foveas due to central field loss, which impacts both fixation stability and saccades, as well as the interaction between the saccade and pursuit systems. To investigate how saccades associated with pursuit are affected, we conducted a quantitative analysis of binocular smooth pursuit eye movement data collected for a prior study (Shanidze et al., 2016) of smooth pursuit in MD. Here we extend that work by characterizing saccadic intrusions in MD participants during pursuit and pre-pursuit fixation.

Methods: We examined saccade frequency, magnitude, and direction across viewing conditions for MD (7, 4F) and control participants (4, 1F). Participants were asked to pursue a 1° annular target, moving in a step ramp (6° step, 12° ramp) in one of 6 directions (4 cardinal & 2 oblique). Saccades were detected offline when eye velocity exceeded 40°/s, or acceleration exceeded 150 (°/s²) and confirmed manually by an experimenter during the fixation and pursuit portions of each trial.

Results: Individuals with MD made significantly more saccades during fixation and pursuit than controls (Fig F). During pursuit, both control and MD participants made saccades aligned with the target direction. However, MD participants also made saccades in non-target directions (Fig A-D). To quantify this difference, we computed the anisotropy index (a comparison of saccades aligned with and orthogonal to the target, Fig E). We found controls had a significantly higher anisotropy index than MDs, indicating greater alignment with target direction.

Conclusions: Our analysis suggests that despite higher frequency, a large number of saccades during pursuit in MD participants are not in the target direction, and thus are not catch-up saccades that serve to keep the eye on the target. The saccades in non-target directions appear to be associated with the significant increase in saccades during fixation. Thus, MD participants do not effectively use saccades to compensate for the lower pursuit gains reported previously.

CONTROL ID: 3547574

SUBMITTER (NAME ONLY): PEI-YIN SU

TITLE: Characterization of Stargardt disease patient-derived human retinal organoids harboring the p.Gly1961Glu mutation in the ABCA4 gene

SESSION TITLE: Ocular Development and Regeneration

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: P. SU, W. Lee, J. Zernant, S.H. Tsang, T. Nagasaki, R. Allikmets, Department of Ophthalmology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|S.H. Tsang, R. Allikmets, Department of Pathology & Cell Biology, Columbia University Irving Medical Center, New York, New York, UNITED STATES|J. Chuang, C. Sung, Department of Ophthalmology, Weill Cornell Medicine, New York, New York, UNITED STATES|C. Sung, Department of Cell and Developmental Biology, Weill Cornell Medicine, New York, New York, UNITED STATES|W. Lee, Department of Genetics & Development, Columbia University Irving Medical Center, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: To investigate the cellular pathophysiology of Stargardt disease caused by the c.5882G>A p.(Gly1961Glu) in a patient-derived retinal organoid model system.

Methods: Human induced pluripotent stem cells (iPSCs) were reprogrammed from peripheral blood lymphocytes from 4 STGD1 patients and 2 two unaffected control subjects. One patient was homozygous for the p.Gly1961Glu variant, two were compound heterozygous, and one patient harbored two deleterious ABCA4 alleles. Mycoplasma testing and karyotyping was performed before differentiation, and pluripotent markers, LIN28, NANOG, OCT4, and SOX2 expression were confirmed by PCR. To begin differentiation, hiPSCs were cultured in neuron-inducing medium for 16 days and then switched to retina-inducing medium. At day 42, 10% FBS and 100uM taurine were added to the medium for long-term differentiation. Developing organoids were manually picked between days 25 and 30, and cultured in suspension. Cryosectioning and immunofluorescence (IF) microscopy were performed at days 90, 120, 150, and 230, followed by transmission electron microscopy (TEM) at day 260.

Results: At day 230, organoids from one compound heterozygous patient for the p.(Gly1961Glu) and c.4947del p.(Glu1650fs) variants, exhibited round contours with visible lamination of the neural retina. Rudimentary subcellular compartments of photoreceptors along the outer edge were discernible on IF by Hoeschst (nuclei), RHO (rods) and Opsin (Blue, Red/Green cones) staining. These distal structures were visualized by TEM and are consistent with short, nascent outer segments. Mutant ABCA4 protein was detected using two separate antibodies--ABCA4 RIM3F4 and RIM5B4, and co-localized with Opsin Blue, or Opsin Red/Green in photoreceptors.

Conclusions: Patient-derived retinal organoids recapitulate complex cellular features of the human retina and express mutant ABCA4 protein in the distal portions of developing photoreceptors. These findings provide a functional model system to characterize the physiological consequences of ABCA4 mutations in individual patients and simultaneously offers a broad window for understanding the mechanism of retinal degenerative diseases.

CONTROL ID: 3547575

SUBMITTER (NAME ONLY): Brian Leonard

TITLE: Dose dependent induction and kinetics of human beta-defensin 3 peptide expression after treatment with herbal compounds

SESSION TITLE: Corneal immunology and neovascularization II

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: B. Leonard, T. Aung, M. Quan, A. Shannon, S.M. Thomasy, C.J. Murphy, University of California Davis, Davis, California, UNITED STATES|V. Raghunathan, University of Houston, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: Antimicrobial peptides (AMPs), including defensins, are key effector molecules of innate immunity expressed and secreted by corneal epithelial cells. Previous studies from our lab demonstrate a marked upregulation of human beta-defensin 3 mRNA (DEFB103) expression in corneal epithelial cells treated with herbal compounds andrographolide, oridonin, isoliquiritigenin. The current study focused on quantification of human beta-defensin 3 peptide (hBD3) after induction with the herbal compounds and determination of the induction kinetics.

Methods: hTCEpi cells were treated with increasing concentrations of andrographolide (10-100 μ M), oridonin (1-15 μ M), isoliquiritigenin (5-50 μ M) or negative control (vehicle: DMSO or EtOH) for 48 hours. After treatment, the supernatant was collected and 100 μ l was used to quantify hBD3 peptide concentration and performed in duplicate for each treatment. To determine kinetics of DEFB103 mRNA upregulation, hTCEpi cells were treated with andrographolide (75 μ M), oridonin (10 μ M), or isoliquiritigenin (25 μ M) for 2, 6, 12, and 24 hours prior to mRNA isolation and compared with vehicle control. Statistical significance was determined based on an ANOVA and appropriate post-hoc test.

Results: The level of hBD3 peptide was below the threshold of detection when hTCEpi cells were treated with vehicle, 10, 25 and 50 μ M of andrographolide, yet resulted in detectable levels of hBD3 peptide of 260 pg/ml and 488 pg/ml with 75 and 100 mM, respectively. Additionally, hBD3 peptide levels were below the level of detection in supernatants from hTCEpi cells treated with oridonin and isoliquiritigenin at all doses. Both isoliquiritigenin and oridonin had an initial upregulation of DEFB103 mRNA expression within 6 hours, peaking by 12 hours and returning to baseline levels by 24 hours post-treatment. Andrographolide had an initial upregulation of DEFB103 mRNA expression by 6 hours that continued to increase at 24 hours post-treatment.

Conclusions: Modulation of AMP expression with herbal compounds (andrographolide, oridonin, isoliquiritigenin) represent a novel approach to treating patients with resistant bacterial infections of the ocular surface. The kinetics of DEFB103 induction with each compound provides insight as to the frequency of application that may be required to sustain antimicrobial activity.

CONTROL ID: 3547576

SUBMITTER (NAME ONLY): Rebecca Lian

TITLE: A simplified nomogram for approximating intraocular lens (IOL) power in post-LASIK patients

SESSION TITLE: Cataract Surgery/Epidemiology

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Lian, F. Malé, R. Sella, H. Gali, A. Chayet, N.A. Afshari, Viterbi Family Department of Ophthalmology, University of California San Diego, La Jolla, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Rebecca Lian: Commercial Relationship: Code N (No Commercial Relationship) | Francisco Malé: Commercial Relationship: Code N (No Commercial Relationship) | Ruti Sella: Commercial Relationship: Code N (No Commercial Relationship) | Helena Gali: Commercial Relationship: Code N (No Commercial Relationship) | Arturo Chayet: Commercial Relationship: Code N (No Commercial Relationship) | Natalie Afshari: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To study the ability of a simplified nomogram, that can be used as a mental calculation, to approximate IOL power in myopic eyes post LASIK.

Methods: Nomogram predictions were calculated by adding a set number of diopters to the pre- operative SRK/T (5 for KM 25-30, 4 for KM 30.01-35, 2.5 for KM 35.01-40, 1.5 for KM 40.01-42.99, 1 for KM 43-45). Records of 64 eyes of 51 myopic patients who underwent cataract surgery after LASIK were reviewed. The percentage of eyes with post-operative spherical equivalent (SE) within 0.5 D and 1D of preoperative target was calculated. The proportion of predictions within 0.5 D and 1 D of Optiwave Refractive Analysis (ORA) and Barrett True K (BTK) IOL values were calculated.

Results: Refractive outcomes showed 71.9% and 93.75% of eyes with post-operative SE within 0.5 D of target refraction respectively. The nomogram IOL prediction fell within 0.5 D of BTK value in 85.94% (n=55) of eyes and within 1 D in 93.75% (n=60) of eyes. The nomogram output fell within 0.5 D of ORA prediction in 68.75% (n=44) of eyes and within 1 D in 92.19% (n=59) of eyes. There were no significant differences between the nomogram and ORA IOL predictions (mean difference 0.07 D, p=0.86) or between the nomogram and BTK IOL predictions (mean difference 0.04 D, p=0.92).

Conclusions: This nomogram approximates IOL power in myopic eyes post LASIK and can be used for mental calculation of IOL power.

CONTROL ID: 3547577

SUBMITTER (NAME ONLY): Blanka Golebiowski

TITLE: TESTOSTERONE AND PROGESTERONE IN HUMAN MEIBOMIAN GLAND EPITHELIAL CELLS DETECTED USING LC-MS

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Golebiowski, M. Phan, M. Bucknall, M.C. Madigan, M. Willcox, F. Stapleton, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA]

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ABSTRACT BODY:

Purpose: Sex hormones may regulate lipid production in the meibomian glands. Sex hormone receptors and mRNAs of key steroidogenic enzymes are present in human meibomian glands and in meibomian gland cells, suggesting these hormones are locally synthesised and metabolised. However, the presence of sex hormones in meibomian gland cells or tissue has not yet been reported. This study aimed to determine whether androgens or estrogens can be synthesized in immortalised human meibomian gland cells (iHMGEc) from the precursor dehydroepiandrosterone (DHEA).

Methods: Undifferentiated and PPAR γ -agonist-differentiated iHMGEc were cultured in serum-free media and treated for 3 days with DHEA (0.1 and 1 μ M). Culture supernatant and cell lysates were extracted with tert-butyl methyl ether. Detection of sex hormones in the extracts was carried out by liquid chromatography-mass spectrometry on a Thermo QExactive Plus quadrupole-orbitrap MS. The extracts were examined for the presence of testosterone, dihydrotestosterone, estrone, estradiol, estriol, androstenedione, progesterone and DHEA. All experiments and analyses were run in duplicate.

Results: Testosterone, androstenedione and DHEA were detected in cell lysates of DHEA-treated cells cultured with and without PPAR γ -agonist (rosiglitazone) and in the culture supernatants, whereas progesterone was detected in cell lysates only. When cells were cultured without DHEA, testosterone, androstenedione, progesterone and DHEA were detected in the cell lysates only, but not the supernatant. Signal intensity (ion counts) indicated that the detected sex hormones were present in much greater abundance in the supernatant than in cell lysate. Dihydrotestosterone and estrogens were not detectable in any of the samples using our current methods.

Conclusions: iHMGEc synthesize the androgens testosterone and androstenedione from the precursor DHEA, followed by the release of these sex hormones from cells into the culture medium. The synthesis of dihydrotestosterone and the estrogens will be confirmed using a more sensitive MS approach.

CONTROL ID: 3547581

SUBMITTER (NAME ONLY): Daniel Bigley

TITLE: Characterizing Corneoscleral Permeability in Microgravity: A Novel Model for Testing Topical Ophthalmic Medication For Spaceflight

SESSION TITLE: Cornea, Conjunctiva, Lacrimal gland and Meibomian gland

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D. Bigley, J. Ong, A. Chaudhry, M.V. Fedorchak, Ophthalmology, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, UNITED STATES|

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ABSTRACT BODY:

Purpose: During spaceflight, astronauts may use topical ophthalmic medication for conditions such as inflammation and Spaceflight Associated Neuro-Ocular Syndrome (SANS). We sought to construct a microgravity-proof model for determining corneal permeability, which will be employed on a parabolic flight to test the hypothesis that corneoscleral permeability in microgravity differs from that of terrestrial gravity. The present study seeks to prove the corneoscleral permeability modeling capability of the novel microgravity-proof experimental set-up.

Methods: Corneas were dissected from freshly enucleated bovine eyes and tightly secured in Corning™ Costar™ Netwell™ Inserts (N=6) using rubber gaskets fit to the diameter of the inserts. 3 mL Milli-Q water was pipetted into wells to allow for interfacing with the cornea-insert system. 1 mL 10% fluorescein solution was applied to corneal surfaces and allowed to diffuse into well water. Samples were taken from individual wells at assigned time intervals. Diffusion was characterized by absorption spectroscopy (480 nm). Average sample absorptions were adjusted for absorption of Milli-Q control by subtracting the average control absorption.

Results: Average adjusted sample absorption (AU) and time (min) displayed a strong positive linear correlation ($r=0.90$, $r^2=0.82$, $p=0.013$). Interestingly, a lag in diffusion of fluorescein across the corneal membrane resulted in earlier time intervals (0.5 min to 2.5 min) having adjusted absorbances that were essentially 0 AU, causing large standard error (SEM=3377). Nevertheless, the data set highlights that the model can demonstrate relatively low and high concentrations of diffused molecules via absorbance values.

Conclusions: The novel set-up has the capacity to model corneoscleral permeability, demonstrating a successful proof of concept for investigation of permeability variation due to microgravity. Successful trialing with fluorescein indicates that "lag time," the time it takes before any significant absorbance is measured, must be considered when investigating permeability of ophthalmic medications and constructing time intervals for sampling.

CONTROL ID: 3547583

SUBMITTER (NAME ONLY): Roshun Sangani

TITLE: Characteristics of traumatic retinal detachments after open globe injury

SESSION TITLE: Vitreoretinal surgery

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Sangani, M.A. Zarbin, N. Bhagat, IOVS-New Jersey Med School, Rutgers New Jersey Medical School, Newark, New Jersey, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Roshun Sangani: Commercial Relationship: Code N (No Commercial Relationship) | Marco Zarbin: Commercial Relationship: Code N (No Commercial Relationship) | Neelakshi Bhagat: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Retinal detachments (RD) related to open globe injuries (OGIs) have poor visual and anatomic prognosis. This study attempts to determine the characteristics of open globes at-risk of recurrent RDs.

Methods: We retrospectively analyzed all cases of traumatic RDRs after OGI performed at a single tertiary care center over a 3-year duration. The eyes with recurrent RDs were labeled group 1 and the remaining eyes that underwent successful primary RD repair were labeled group 2. Variables recorded included age, gender, duration between OGI and primary RDR, duration between primary RDR and additional RDR, zone of injury, use of silicone oil, presence of choroidal detachment (CD), and presence of intraocular foreign body (IOFB).

Results: Of the 19 cases of traumatic RDR identified, 6 (32%) had recurrent RD and underwent further surgical repairs. The average follow-up duration of the study was 12 months. The average time between initial OGI and RDR in cases with and without recurrent RD (group 1 and 2) was 18 days and 8 days respectively. Furthermore, the average time of initial RDR and recurrent RDR repair (group 2) was 84 days. The average age of both groups was 41 years old. Males comprised 100% of group 1, and 92% of group 2. Moreover, the zones of OGI (Z1, Z2, Z3) was (33%, 50%, 17%) and 61%, 8%, 31% in Groups 1 and 2 respectively. Also, presence of proliferative vitreoretinopathy (PVR) was noted in 100% of eyes in group 1 and 38.5% of eyes in group 2. Silicone oil was used for tamponade in 100% of group 1 eyes and 70% of group 2 eyes. Half (50%) of the patients in group 1 had CDs, compared to 13% of patients in group 2. The presence of an IOFB was noted to be 50% and 46% of cases in groups 1 and 2 respectively.

Conclusions: Recurrent RDs were seen in 32% of OGIs in this study. Two-thirds of these eyes had Zone 2 or 3 injuries, and 50% cases had CDs with PVR diagnosed in all subjects. Interestingly both groups had a high incidence of IOFBs.

CONTROL ID: 3547584

SUBMITTER (NAME ONLY): Aiyin Chen

TITLE: Accuracy of electronic health records for systemic risk factors of ophthalmology patients

SESSION TITLE: Data science, machine learning, and artificial intelligence

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Chen, C. Yee, M. Hribar, Oregon Health & Science University, Portland, Oregon, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Aiyin Chen: Commercial Relationship: Code N (No Commercial Relationship) | Claudine Yee: Commercial Relationship: Code N (No Commercial Relationship) | Michelle Hribar: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Systemic conditions such as hypertension (HTN) is a risk factor for ocular diseases. Electronic health records (EHRs) contain extensive data on systemic conditions that can help identify risk factors for eye disease, but the quality of EHR data is unclear. This project assesses the readiness of EHRs for large scale ophthalmic epidemiology research by examining data accuracy in EHRs of an ophthalmology practice for providing a definitive diagnosis of HTN.

Methods: Retrospective chart review of randomly selected cataract surgery patients at Oregon Health & Science University (OHSU) was conducted in OHSU's EHR (Epic) and a combined EHR database outside our institution (Care Everywhere). Charts were reviewed for evidence of a primary care provider (PCP) at OHSU, while progress notes, problem lists, and medication lists were examined for evidence of a HTN diagnosis. Diagnosis of HTN was established when HTN was documented in any progress note or problem list, and anti-HTN medications appeared in medication list. The absence of HTN was established when there was no documentation of HTN and anti-HTN medications. Cases that did not fit into either category were deemed uncertain. Documentation in medication lists was compared for consistency between our institution's EHR and outside EHRs.

Results: Of 134 patients reviewed, 69 (51%) had a PCP at OHSU, and 65 (48%) did not. Further, 87 patients (65%) had a certain diagnosis of HTN, 37(28%) did not have HTN, and 10(7%) were uncertain. There was no difference in frequency of uncertain cases between patients who had PCPs at OHSU vs those at outside institutions ($P = 0.52$). Patients were more likely to have an accurate HTN diagnosis in the problem list if they had OHSU PCPs (81%) than those without (61%; $P = 0.01$). Discrepancies between anti-HTN medications listed in the OHSU EHR and outside EHRs were present in 32% of patients; of these, 56% had PCPs at OHSU and 44% had outside PCPs ($P = 0.25$).

Conclusions: EHRs provide a valid diagnosis of HTN in most cases. Accuracy of the HTN diagnosis, particularly in problem lists, increases when the patient's PCP is affiliated with the same institution. Inconsistencies exist in documentation of medications across different EHRs. Analysis of EHR data reliability is necessary before conducting large scale ophthalmic research.

CONTROL ID: 3547585

SUBMITTER (NAME ONLY): Jingyuan Zhu

TITLE: Oral scutellarin treatment preserves retinal structure and visual function in glaucomatous neurodegeneration

SESSION TITLE: Neurodegeneration and neuroprotection

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Zhu, A. Sainulabdeen, K. Akers, V. Adi, J.R. Sims, E. Yarsky, Y. Yan, H. Ishikawa, G. Wollstein, J.S. Schuman, K. Chan, Department of Ophthalmology, NYU Langone Health, New York, New York, UNITED STATES|J. Zhu, W. Wei, Department of Ophthalmology, Beijing Tongren Hospital, Beijing, Beijing, CHINA|A. Sainulabdeen, Department of Surgery and Radiology, College of Veterinary and Animal Sciences, Kerala Veterinary and Animal Sciences University, Thrissur, INDIA|Y. Yu, Pleryon Therapeutics Limited, Shenzhen, CHINA|C.K. Leung, University Eye Center, Hong Kong Eye Hospital, Hong Kong, CHINA|C.K. Leung, Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong, CHINA|J.S. Schuman, Department of Biomedical Engineering, New York University Tandon School of Engineering, Brooklyn, New York, UNITED STATES|K. Chan, Department of Radiology, NYU Langone Health, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Intraocular pressure (IOP) is currently the only modifiable risk factor for glaucoma, yet glaucoma can continue to progress despite controlled IOP. Thus, development of glaucoma neurotherapeutics remains an unmet need. Scutellarin is a flavonoid that exhibits a number of neuroprotective effects on the brain and the eye. Here, we investigated the neurobehavioral effects of oral scutellarin treatment in a novel experimental model of chronic glaucoma.

Methods: Ten adult C57BL/6J mice (Group 1) were unilaterally injected with an optically clear hydrogel into the anterior chamber to obstruct aqueous outflow and induce chronic IOP elevation. Eight other mice (Group 2) received a unilateral intracameral injection of phosphate-buffered saline only. Another eight mice (Group 3) with hydrogel-induced unilateral chronic IOP elevation also received daily oral gavage of 300 mg/kg scutellarin from 1 week before to 2 weeks after hydrogel injection. Tonometry, optical coherence tomography, and optokinetic visuobehavioral testing were performed longitudinally to monitor the IOP, total retinal thickness, visual acuity, and contrast threshold of bilateral eyes in all three groups.

Results: Intracameral hydrogel injection resulted in unilateral chronic IOP elevation with no significant IOP difference between scutellarin treatment and untreated groups (Figure 1). With scutellarin treatment, the hydrogel-injected eyes showed less retinal thinning and reduced visual behavioral deficits when compared to the untreated, hydrogel-injected eyes (Figure 2). No significant difference in retinal thickness or optokinetic measures was found in the non-injected eyes over time or between all groups.

Conclusions: Oral scutellarin treatment appeared to preserve retinal structure and visual function in experimental glaucoma induced by chronic IOP elevation. Scutellarin may be a possible candidate as a novel neurotherapeutic agent for glaucoma treatment.

CONTROL ID: 3547587

SUBMITTER (NAME ONLY): Jacob Heng

TITLE: Visual acuity outcomes following cataract surgery in Macular Telangiectasia Type 2 patients

SESSION TITLE: Macular diseases/ macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.S. Heng, Ophthalmology and Visual Science, Yale University School of Medicine, New Haven, Connecticut, UNITED STATES|J.S. Heng, J.T. Handa, Johns Hopkins Medicine Wilmer Eye Institute, Baltimore, Maryland, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Jacob Heng: Commercial Relationship: Code N (No Commercial Relationship) | James Handa: Commercial Relationship(s);Bayer Pharmaceuticals:Code F (Financial Support);Clover Therapeutics:Code F (Financial Support)

ABSTRACT BODY:

Purpose: To evaluate visual acuity outcomes following cataract surgery in eyes with Macular Telangiectasia (MacTel) Type 2.

Methods: Retrospective single-center cohort study of patients who underwent cataract surgery and were followed up at the same institution. Pre-operative evaluation included examination by a retinal specialist and macular optical coherence tomography (OCT). Primary outcome measure was post-operative change in best-corrected visual acuity (BCVA). Secondary study outcomes were achieving post-operative BCVA better than Snellen acuity of 20/40 and time to loss of visual acuity by 2 lines or more. Multivariate analyses were carried out using regression methods with generalized estimating equations.

Results: 20 eyes of 11 patients underwent cataract surgery and were followed for a median of 25.5 months (IQR 17.5 – 44.2 months). The median improvement in BCVA post cataract surgery was 10.5 letters (IQR 3.50 – 20.25). In a multivariate generalized linear model, only nuclear sclerosis grade ($p=0.00177$) was significantly associated with post-operative change in BCVA. The presence of foveal ellipsoid zone (EZ) breaks ($p < 0.001$) on OCT was inversely correlated with post-operative BCVA better than 20/40 in a multivariate logistic regression model. In addition, the presence of foveal EZ breaks ($p < 0.001$) and MacTel Type 2 disease stage ($p=0.027$) were independently associated with shorter time to vision loss of two lines or more in a multivariate Cox regression model.

Conclusions: There was a modest but significant improvement in visual acuity after cataract surgery in eyes with MacTel Type 2. This improvement was correlated with the severity of the cataract. The presence of central foveal EZ breaks was associated with poorer post-operative visual acuity and subsequent vision loss from disease progression.

CONTROL ID: 3547589

SUBMITTER (NAME ONLY): Esteban Peralta

TITLE: Outcomes of Outreach Surgery in the Navajo Nation, a retrospective study

SESSION TITLE: Healthcare Delivery and Quality of Care

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Peralta, The University of Utah School of Medicine, Salt Lake City, Utah, UNITED STATES|R.T. Wallace, University of Washington School of Medicine, Seattle, Washington, UNITED STATES|M. Murri, J.H. Pettay, University of Utah Health John A Moran Eye Center, Salt Lake City, Utah, UNITED STATES|

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ABSTRACT BODY:

Purpose: There is a dearth of medical literature on the status of eyecare in Native American Populations. We performed a retrospective, observational clinical study to assess outcomes of ophthalmic surgical interventions among the Navajo Nation population in the Four Corners region of the United States.

Methods: We analyzed 8 years of longitudinal data from the Moran Eye Center Global Outreach Division database (2013-2020). Records from Navajo patients (n=147) who underwent cataract, glaucoma, and pterygium excision surgery as part of the Navajo Nation Eye Care Initiative were reviewed for surgical outcomes and complications. Intraoperative and postoperative complication rates were calculated, and the nature of complications were evaluated. Surgical techniques, medical comorbidities, and mitigating efforts were reviewed on a case-by-case basis.

Results: The vast majority of surgical interventions studied were cataract extraction with IOL implantation. Over the 8 years (n=200 surgeries, 147 patients), 12 patients (7.5%) experienced intraoperative or postoperative complications. Ten patients were noted to have complications of cataract surgery, including hyphema with permanent MVL in the setting of uncontrolled T2DM, Descemet's detachment, IOL dislocation, residual cortical material, and posterior capsule tears. There were also two cases of pterygium graft maladherence.

Conclusions: This is the first analysis of surgical outcomes in the Navajo tribe of the Intermountain West. In a population with known high rates of diagnosed T2DM and likely high rates of undiagnosed HTN, a rate of 92.5% uncomplicated surgeries is remarkable. Critically, this study speaks to the need for surgical capacitation and training of skilled ophthalmologists deployed in geographical proximity to Native American Indian territories. The results we describe help provide a justification for outreach surgeries and a framework for quality improvement in the delivery of eye care in the Navajo Nation.

CONTROL ID: 3547594

SUBMITTER (NAME ONLY): Charles Dale

TITLE: Interrater agreement of meibomian gland loss quantified by IR meibography software within a multi-functional corneal topographer

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: C. Dale, A. Ravikumar, E. Ritchey, University of Houston College of Optometry, Houston, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Charles Dale: Commercial Relationship: Code N (No Commercial Relationship) | Ayeswarya Ravikumar: Commercial Relationship: Code N (No Commercial Relationship) | Eric Ritchey: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Meibomian gland loss is a significant predictor for dry eye disease. Non-contact infrared meibography is a popular imaging technique integrated into multi-functional corneal topographers, and can be used clinically to grade the degree of meibomian gland loss in patients. In this study, we examined the inter-observer reliability of the CSO Antares, a multi-functional corneal topographer and infrared meibographer with integrated analysis software, in quantifying meibomian gland loss in upper and lower eyelids.

Methods: Ninety-six images were taken of the meibomian glands for the upper and lower eyelids in both eyes for 24 subjects. Images were analyzed by two independent graders using the directions provided with the Antares integrated analysis software. Interrater reliability was compared for the calculated percent area loss using Bland-Altman limits of agreement, as well as categorically by a displayed 5-point Likert clinical grading scale (grade 0 as <10% loss; grade 1 as <25% loss; grade 2 as <50% loss; grade 3 as <75% loss; and grade 4 as $\geq 75\%$ loss) using a weighted Cohen's kappa statistic.

Results: Subjects ranged in age from 8-24 years old, with a mean age of 14.8 years old. When comparing the calculated percent area meibomian gland loss between graders, a mean difference of 0.856% (SD=4.117%) was observed for upper eyelids, and a mean difference of 21.41% (SD=12.56%) was observed for lower eyelids. Categorical meibomian gland loss scores using a 5-point Likert clinical grading scale displayed strong agreement between the 2 observers for grading meibomian gland loss for the upper eyelids ($\kappa = 0.722$, $p < .0005$), and fair agreement for grading meibomian gland loss for lower eyelids ($\kappa = 0.557$, $p < .0005$).

Conclusions: Inter-observer grading repeatability for meibomian gland loss with the integrated analysis software of CSO Antares topographer displayed stronger limits of agreement between observers for both the continuous percent area loss metric and the 5-point Likert clinical grading scale when examining upper eyelids. For lower eyelids, more inter-observer variability was observed in the analysis of meibomian gland loss for both metrics. These findings suggest that the grading approach with the integrated analysis software of the Antares is better suited for consistent evaluation of meibomian gland loss for upper eyelids between eye care practitioners.

CONTROL ID: 3547596

SUBMITTER (NAME ONLY): Tej Kalakuntla

TITLE: Comparing Clinic Cycle Time and Patient Follow Up with Same-Day Visual Field Visits versus Separate Day Visual Field Visits in Glaucoma Patients in a County Hospital System

SESSION TITLE: Glaucoma Epidemiology and Care Management

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: T. Kalakuntla, E. Jung, B. Wong, Ophthalmology, Keck Hospital of USC, Los Angeles, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Tej Kalakuntla: Commercial Relationship: Code N (No Commercial Relationship) | Eric Jung: Commercial Relationship: Code N (No Commercial Relationship) | Brandon Wong: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Automated Humphrey visual field (HVF) testing is critical in diagnosing and monitoring glaucoma, but obtaining testing is a time-intensive process that may lead to extended clinic visit times for patients. Visual field testing is often scheduled as stand-alone appointments separate from the date of provider examination, but it is not currently known whether this strategy improves clinic efficiency or patient compliance with visits.

Methods: Retrospective analysis was performed on LAC+USC ophthalmology patients with an ICD-10 coding (diagnosis of glaucoma) who were scheduled for HVF on the same day as the provider or on separate day from provider visit between 1/2/2019 and 7/28/2019. Clinic cycle time, appointment no-show rates, and patient demographics were calculated and compared for visits. An unpaired two-tailed t-test was used to compare cycle times between groups.

Results: There were 371 same-day HVF and provider visits and 409 HVF visits scheduled separately from the provider visits. Glaucoma patients attended 195 (52.3%) of the same-day HVF and provider visits and missed 173 (46.4%) of them in their entirety. In four visits (1.08%), patients attended their HVF visit but left prior to being seen by the provider. Of the separately scheduled HVF and provider appointments, only 9 patients (2.2%) successfully attended both visits. For 328 (80.2%) of the separate visits, patients missed both visits entirely. 69 separate day visit pairs (16.87%) resulted in patients attending their provider visit only and missing their HVF visit, while 3 different day visit pairs (0.73%) resulted in patients attending only their HVF visit and missing their provider visit. Mean cycle time for patients with same day HVF and provider appointment was 4.83 hours, while combined average time spent at the clinic when HVF was separately scheduled from a provider visit was 5.81 hours. There was no statistically significant difference in combined cycle time when scheduling a separate HVF appointment (p-value = 0.30).

Conclusions: Compared to same day HVF and provider visits, separate day HVF testing does not improve clinic cycle time and may lead to increased no-show rates in glaucoma patients in a county hospital setting.

CONTROL ID: 3547598

SUBMITTER (NAME ONLY): Saoul Mancha

TITLE: Foggy Phoropters: A Solution to Mask-Related Lens Fogging in the COVID-19 Era

SESSION TITLE: Psychophysics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Mancha, W.E. Sponsel, WESMDPA, Texas, UNITED STATES|G. Slagle, Clinical Research, Sponsel Foundation, San Antonio, Texas, UNITED STATES|W.E. Sponsel, Visual sciences, University of the Incarnate Word, San Antonio, Texas, UNITED STATES|F. Trujillo, 3C Vision Specialist, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: The emergence of COVID-19 has introduced new challenges to eye care practitioners, not the least of which is mask-related fog on slit lamps, condensing lenses, phoropters, and perimeters. In this case series, we examine the effect that phoropter lens condensation has on visual acuity and contrast sensitivity and evaluate the efficacy of an anti-fog device at preventing condensation on a phoropter lens.

Methods: Snellen visual acuity (VA) and contrast sensitivity (CS) measured across four spatial frequencies (3, 6, 12, 18 cycles/degree) with Vector Vision (Guardion Health Sciences, San Diego, CA) were examined. Both VA and CS were evaluated monocularly in healthy subjects wearing KN95 masks, first while viewing through a Lorgnette occluder as a control (no lens), then through a phoropter. When using the phoropter the +0.125 lens was deployed bilaterally to emulate lens presence during refraction while minimally affecting refractive error. During testing the right lens of the phoropter was room temperature (20°C) and the left lens was heated to 37-40°C using a flexible electric heating strip. Subjects were not masked to which side was heated.

Results: Ten eyes of 5 subjects (2 female, 3 Male, mean age 32.4yr) were evaluated. Baseline mean LogMAR VA (\pm SD) was 0.00 \pm 0.12 in the right eye (OD) and 0.04 \pm 0.16 in the left eye (OS). Mean CS area under the curve (AUC) was 6.7 \pm 0.4 OD, and 6.7 \pm 0.5 OS. There was no difference in baseline VA or CS between left and right eyes (both $P>0.3$). Eyes re-tested through the heated phoropter lens had mean LogMAR VA of 0.02 \pm 0.1 and CS AUC of 6.8 \pm 0.7 and were not different from baseline (both $P>0.2$). However, eyes re-tested through the unheated phoropter lens (control) showed mean LogMAR VA of 0.09 \pm 0.1, and CS AUC of 5.0 \pm 1, both of which were significantly worse than baseline (both $P<0.05$). All subjects reported various amounts of condensation on the room temperature lens and no condensation on the heated lens.

Conclusions: An electrically heated adhesive fabric eliminated mask-related fog on the phoropter lens and prevented fog-associated deficits in VA and CS. The utilization of lens heating devices on microscopes, perimeters, and phoropters will alleviate fogging introduced by measures intended to limit the spread of COVID-19.

CONTROL ID: 3547599

SUBMITTER (NAME ONLY): Luz Paczka-Giorgi

TITLE: Awareness, Knowledge, and Attitude of Telemedicine among Lay Persons in Western Mexico

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L.A. Paczka-Giorgi, Research & Development, Telemedicine LATAM, Toronto, Ontario, CANADA|G. Velasco Gutiérrez, Business School, Instituto Tecnológico y de Estudios Superiores de Monterrey Campus Guadalajara, Zapopan, Jalisco, MEXICO|L.A. Giorgi-Sandoval, J.A. Paczka, Research, Telemedicine LATAM, Guadalajara, Jalisco, MEXICO|J.A. Paczka, Instituto de Oftalmología y Ciencias Visuales, Universidad de Guadalajara, Guadalajara, Jalisco, MEXICO|

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ABSTRACT BODY:

Purpose: Telemedicine is an emerging technology in the health sector in Mexico. The success of any new technology depends on many factors including the knowledge and understanding of the concept and attitude towards technology and working environment by the potential users. The objective of this study was to assess the awareness, knowledge, and attitude toward telemedicine among adults living in Guadalajara western Mexico.

Methods: A cross-sectional survey was carried out among adults assisting to three commercial malls. A total of 143 non-health personnel were included in the study. A pre-validated self-administered questionnaire was used for the survey to assess the awareness, knowledge, and attitude toward concepts of telehealth, telemedicine and teleophthalmology. The questionnaires were administered by an interviewer in a face-to-face format. Completed questionnaires were analyzed as per the study objectives using descriptive statistics for the quantitative data and content analysis considering a p value equal or less than 0.05 as statistically significant.

Results: A total of 148 patients completed the survey (78 females and 70 male) with a mean age of 43.2 ± 15.5 years.. Overall, 78.4% of participants had used the Internet for a variety of reasons including some health-related issues and 74.3% had finished high school. The knowledge level of the respondents was found to be moderate (47.5%) regarding telemedicine and low (36.5%). To most of the respondents, self-care regarding health is relevant (84.4%), especially eye health care (91.9%). With regard to the attitude towards telemedicine 62% of the respondents possess high attitude, 21% possess moderate attitude and 17% possess low level of attitude toward telemedicine and telehealth programs.

Conclusions: The current results suggest that although the respondents' knowledge is very limited in telemedicine, a large proportion of them have positive attitude towards telemedicine and teleophthalmology. Education on new technology applied to health seems to be relevant to impulse lay-persons to use telemedicine facilities when they are available.

CONTROL ID: 3547600

SUBMITTER (NAME ONLY): Pablo Ortiz

TITLE: Autofocusing and Autoaligning Robotic Optical Coherence Tomography

SESSION TITLE: OCT/OCTA - New biomarkers and technical improvements II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Ortiz, M. Draelos, R.P. McNabb, A.N. Kuo, J. Izatt, Duke University, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Optical Coherence Tomography (OCT) is an important imaging technique in ophthalmology. Traditionally, clinical OCT requires an operator and patient cooperation to both align and correct for refractive errors. Automating the tasks of alignment and focusing can increase the accessibility of OCT and make it available outside of specialty clinics. In order to automate these tasks, we developed a robotically-aligned OCT scanner that automatically aligns and corrects defocus refractive error.

Methods: We built a 100kHz swept-source retinal OCT scanner designed for 16-degree field of view imaging. This scanner was mounted on a 7 degree-of-freedom robot (Fig. 1) along with 3 pupil cameras and 4 IR LEDs for eye tracking. The pupil cameras capture real-time images of the eye, which are then utilized to extract location—through linear triangulation—and orientation—through pupil-center and corneal-reflection segmentation analysis. Using the tracking information as input, the robotic arm is controlled in real-time to orient the scanner relative to the eye's optical axis as well as position it to correct for misalignment error. Once aligned, the system triggers automatic focusing to correct any refractive errors. Dynamically switching from regular dense volumes (160,000 AScans) to a sparse scan (400 AScans) in real-time allowed for faster focusing compared to traditional approaches. We demonstrated the automatic focusing of the system by imaging a retinal model eye (Rowe Tech. Design) through varying trial lenses to evaluate the time to regain focus and the dioptric correction range (Fig. 2).

Results: Focusing was obtained in <3s over a Diopter range of -12D to 12D. Gaze tracking tests demonstrate 0.337° accuracy and 0.236° precision within a 28° range. Pupil tracking tests demonstrate 19.5µm lateral and 34.2µm axial accuracy along with 5.9µm lateral and 6.1µm axial precision within a 300mm lateral and 150mm axial range. Freestanding human imaging without a fixation target demonstrated successful automatic alignment.

Conclusions: We demonstrate an autonomous system that can image freestanding subjects as well as quickly correct for ocular defocus.

CONTROL ID: 3547604

SUBMITTER (NAME ONLY): Sarah Naguib

TITLE: Investigating the role of neuronal Nrf2 in glaucoma

SESSION TITLE: Neuroprotection

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Naguib, T.S. Rex, M. Gil, Neuroscience, Vanderbilt University, Nashville, Tennessee, UNITED STATES|T.S. Rex, J.R. Backstrom, Vanderbilt University Medical Center, Nashville, Tennessee, UNITED STATES|

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ABSTRACT BODY:

Purpose: Our goal is to study the role of neuronal Nrf2 in early glaucomatous pathogenesis by removing and/or overexpressing Nrf2 in the neurons of the ganglion cell layer in ocular hypertensive and control mice.

Methods: We intravitreally injected AAV2/2.CMV.Nrf2 or AAV2/2.CMV.eGFP into 2-3 month old male and female C57Bl/6 or Nrf2 KO mice. After 2 weeks, we bilaterally injected polystyrene beads into the anterior chamber of both C57Bl/6 mice or Nrf2 KO mice to induce ocular hypertension. We quantified superoxide levels in vivo using dihydroethidium. We measured visual function using flash ERG, VEP and the photopic negative response (PhNR).

Results: In AAV2/2.CMV.eGFP injected C57 mice, there was a 3-fold increase in DHE fluorescence in the microbead group in comparison to the saline-injected controls. This increase was absent in microbead injected C57 mice injected with AAV.Nrf2 ($p=0.27$). The PhNR was decreased in microbead injected C57 mice injected with AAV2/2.CMV.eGFP at $26.91\text{mV} \pm 5.10$ as compared to controls at $41.98\text{mV} \pm 3.56$; $p=0.0043$. This decrease was prevented by overexpression of Nrf2, with a PhNR of $40.6\text{ mV} \pm 5.37$. DHE fluorescence was further increased in ocular hypertensive Nrf2 KO as compared to C57 mice. Treating the Nrf2 KO mice with AAV.Nrf2 prevented the increase in DHE fluorescence. The average amplitude of the PhNR in Nrf2 KO mice (saline and microbead) was significantly reduced in comparison to C57 controls. Treatment with AAV.Nrf2-treated Nrf2 KO groups preserved the mean amplitude of the PhNR as compared to Nrf2 KO mice that received AAV.eGFP.

Conclusions: Overexpression of Nrf2 in ganglion cell layer neurons via intravitreal injection of AAV2/2.CMV.Nrf2 reduced ROS levels and preserved the PhNR after microbead occlusion and in the Nrf2 KO mouse. This suggests that much of the oxidative stress and susceptibility in the Nrf2 KO derives from the retinal ganglion cells. This data also suggests that AAV2/2.CMV.Nrf2 may be an effective gene therapy for the treatment of glaucoma and should be explored further.

CONTROL ID: 3547605

SUBMITTER (NAME ONLY): Edward Korot

TITLE: Democratizing AI for DR: Automated Self-Training to Address Label Scarcity for Deep Learning in Diabetic Retinopathy Classification

SESSION TITLE: Machine learning I

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Korot, Ophthalmology, Stanford University School of Medicine, Stanford, California, UNITED STATES|E. Korot, M.B. Goncalves, J.C. Huemer, H. Khalid, S. Wagner, L. Faes, P. Keane, Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|X. Liu, A.K. Denniston, University of Birmingham, Birmingham, Birmingham, UNITED KINGDOM|

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ABSTRACT BODY:

Purpose: To address the scarcity of high quality adjudicated labels for training supervised deep learning models. We used an automated sans-coding approach, developing a teacher model from a small high quality labeled dataset to subsequently assign diabetic retinopathy (DR) referral pseudolabels to a large unlabeled dataset. A student model was then trained from the combined dataset.

Methods: We utilized two publicly available fundus photo DR datasets. High quality adjudicated DR severity labels were applied to the first dataset of fundus photos (n=1744). Google Cloud Automated Machine Learning (AutoML) was next used to train a deep learning image classification model sans-coding, termed the teacher model for referable and nonreferable DR. The resulting algorithm was deployed in Google Cloud platform and made available for inference. The teacher model was used to generate DR referral predictions for an unlabeled public fundus photo dataset (n=58,689). The resulting image-label pairs were combined with the high quality teacher model's training dataset, and a student deep learning model was trained.

Results: The teacher model area under the precision-recall curve (AUPRC), accuracy, sensitivity, specificity was 0.964, 92.0%, 73.9, 98.4 respectively, while the student model metrics improved to 0.976, 92.5%, 87.0%, 94.5% on the internal validation dataset. Teacher model external validation accuracy, sensitivity and specificity was 93.3%, 94.4%, 75.0%, while student model external validation metrics improved to 97.6%, 99.5%, 66.7% respectively.

Conclusions:

We demonstrate a sans-coding framework, which utilizes AutoML to address label scarcity for deep learning in DR. We show that self-training is an effective method to increase performance and decrease overfitting, which may simultaneously save time on expensive yet high-quality expert labeling. While the student model external validation dataset had 1 more false positive than the teacher model, clinically costly false negatives decreased by 10 as compared to the teacher model. As the tools for machine learning continue to be democratized, our methodology has potential to address the remaining disparity of expensive clinical labeling which bottlenecks small scale clinicians and researchers.

CONTROL ID: 3547607

SUBMITTER (NAME ONLY): Jiaying Chen

TITLE: Real-life in situ measurement of blinking using a wearable device: establishing a gold standard for spontaneous blinking

SESSION TITLE: Dry eye and ocular surface microbiome clinical

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J. Chen, N.C. Chidi-Egboka, I. Jalbert, P. Wagner, B. Golebiowski, School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, AUSTRALIA|

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ABSTRACT BODY:

Purpose: The study of blinking has been hampered in part by the lack of a gold standard condition for measurement. This study measured blinking in situ in a real-life setting during various reading and non-reading tasks and also examined repeatability.

Methods: Ten healthy adults (30.7 ± 3.6 years; 4M:6F) completed a randomised cross-over intervention study. Participants wore an eye-tracking headset (Pupil Labs GmbH) during 8 tasks (15 min each): A) conversation, B) reading from printed text, C) laptop screen, D) smart TV at 6 m, E) smartphone, F) smartphone at 50% brightness, G) smartphone (more complex text), H) walking indoors. To determine repeatability, task E was completed twice. Symptoms (Instant Ocular Symptom Survey) were measured before and after each task. Spontaneous blink rate and interblink interval were recorded using the headset. Blink parameters were compared between tasks using repeated measures ANOVA and post hoc comparisons with Bonferroni correction. Ocular symptoms pre- and post-task were compared using the Paired t-test. Repeatability was examined using the Bland & Altman method (Coefficient of Repeatability, CoR).

Results: Blink rate was reduced during all reading tasks (B to G) compared to conversation ($p \leq 0.003$) and walking ($p \leq 0.04$). There was no significant difference in blink rate between conversation and walking, nor between any of the reading tasks. There were no significant differences in interblink interval between tasks. Ocular symptoms worsened after reading from a smartphone at reduced brightness ($p = 0.02$), more complex text ($p = 0.04$) and from a distant TV screen ($p = 0.01$). CoR was ± 14.5 blinks/min for blink rate and ± 22.4 s for interblink interval while reading from a smartphone.

Conclusions: The wearable eye tracker can reliably measure blink rate and interblink interval in situ. In a real-life setting, blink rate was reduced during reading compared to conversation or walking, irrespective of reading task complexity, working distance or device used.

CONTROL ID: 3547610

SUBMITTER (NAME ONLY): Benjamin King

TITLE: Intravitreal Carboplatin as Salvage Treatment for Progressive Vitreous Disease in Retinoblastoma: a Phase I Clinical Trial

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. King, M.W. Wilson, R. Brennan, Surgery, St. Jude Children's Research Hospital, Memphis, Tennessee, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Benjamin King: Commercial Relationship: Code N (No Commercial Relationship) | Matthew Wilson: Commercial Relationship: Code N (No Commercial Relationship) | Rachel Brennan: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: Intravitreal chemotherapy is an increasingly popular treatment modality for vitreous seeding in intraocular retinoblastoma. The most commonly used agent – melphalan – is associated with multiple reports of retinal toxicity. Other chemotherapeutic agents may offer similar efficacy with a more favorable safety profile

Methods: The iRET protocol was a prospectively enrolled phase I clinical trial testing the safety and efficacy of intravitreal carboplatin in the treatment of progressive vitreous disease in intraocular retinoblastoma. Children who developed new vitreous seeds after completing primary treatment were eligible to receive an intravitreal injection of 0.3 mg carboplatin every 2 weeks. A serious adverse event prompted dose reduction to 3 µg.

Results: Four patients were enrolled at an initial dose of 0.3 mg. Complete regression of vitreous seeds was noted in all patients following 5, 2, 2 and 1 injections. Two patients developed recurrent vitreous disease at 3 months and 25 months after complete regression. All four patients are long term survivors, but those with recurrence ultimately required enucleation. A serious adverse event occurred in one patient who developed acute vision loss with extinguished electroretinography response 72 hours after the second injection. The protocol was temporarily suspended pending dose recalculation. Two additional adverse events were noted including cataract (previously therapy included subconjunctival carboplatin exposure) and grade 3 neutropenia. Three patients were enrolled at an injection dose of 3 µg and treated with a total of 5, 2 and 1 injections respectively, with close monitoring of ERG in all cases. Complete regression of vitreous disease was not achieved in any patient at the 3 µg dose, as well as no change in ERG, but all three showed immediate clinical response to intravitreal melphalan (ocular salvage x / 3). Therefore the protocol was terminated due to lack of efficacy rather than pursue dose escalation.

Conclusions: Intravitreal carboplatin may be effective in treating progressive vitreous seeding at higher doses. Given the occurrence of permanent retinal toxicity however, its overall therapeutic ratio appears to be unacceptably low. Other alternative agents should be investigated.

CONTROL ID: 3547617

SUBMITTER (NAME ONLY): Riley Short

TITLE: Comparison of outcomes of urgent ophthalmic surgeries performed after-hours at inpatient and outpatient operating locations at a tertiary care center

SESSION TITLE: Ocular Trauma and corneal disease

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Short, J. Cho, J. Landreneau, E. Mellencamp, E. Pratte, C. Petris, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate perioperative management and outcomes of after-hours urgent ophthalmic surgery performed at inpatient versus outpatient hospital-based operating venues at a single institution in an effort to minimize insufficiencies, waste, and patient-centered complications.

Methods: A retrospective chart review was performed for all patients who underwent urgent or emergent ophthalmic surgery outside of normal operative block times between January 2018 -April 2020. Primary outcomes measures included length of time to first incision, duration of surgery, improvement in visual acuity, and post-operative complications. Comparisons of each outcome measure were made based on the location where the surgery was performed which were designated as main in-patient operating room (MOR) or a hospital-based outpatient surgical center (OSC) where most routine outpatient ophthalmic surgery is performed.

Results: 73 patients were included. 24 patients (32.9%) involved open globe injuries while the remainder underwent urgent surgical intervention for other peri-ocular or orbital reasons that were not associated with a penetrating or perforating globe injuries. There were two locations designated as MOR and two locations denoted as OSC. 32 surgeries were performed at the MORs and 41 cases were performed at the OSCs. Average duration from admission to surgery was 5.29 ± 2.64 hours for open globes versus 17.64 ± 30.46 for non-open globes ($p=0.01$). The average length of surgery was 2.16 ± 1.19 hours for open-globe procedures versus 1.78 ± 0.84 for non-globe cases ($p>0.05$). Duration between admission and surgery was 24.1 ± 35.95 hours for the MORs versus 5.4 ± 4.34 prior to surgery at the OSCs ($p=0.01$). Average length of surgery was 2.14 ± 0.94 hours for MOR versus 1.72 ± 0.98 for OSC ($p=0.06$). OSCs were 11 times more likely to have cases start within 12 hours of admission ($p<0.001$). 11 patients (34.4%) who underwent surgery at the MOR locations experienced post-operative complications compared to 15 patients (36.6%) at OSCs ($p=0.85$).

Conclusions: This study did not find that improvement in visual acuity or complications rates were significantly impacted by the surgery location; however, less ideal peri-surgical circumstances were encountered with utilization of the MOR including longer hospitalizations and greater intra-operative duration.

CONTROL ID: 3547622

SUBMITTER (NAME ONLY): Chuan Hou

TITLE: Perceptual learning with attention tasks improves contrast sensitivity in V1 of human adults with amblyopia

SESSION TITLE: Amblyopia: Translational Studies and Trials

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: C. Hou, G. Acevedo Munares, The Smith-Kettlewell Eye Research Institute, San Francisco, California, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Chuan Hou: Commercial Relationship: Code N (No Commercial Relationship) | Gabriela Acevedo Munares: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: The neural correlates of perceptual learning in amblyopia remain unclear. The specificity of task orientation in behavioral studies is commonly interpreted as evidence that perceptual learning reflects plasticity in the primary visual cortex (V1). However, physiological evidence for this assumption is modest or controversial. To reveal neural correlates of perceptual learning, we measured contrast sensitivity in V1 of human adults with amblyopia using fMRI-informed EEG source imaging before and after perceptual learning.

Methods: A group of adults with amblyopia was trained using dichoptic attention tasks for about 2 visits/week for 2 months. The training task was to quickly search for and count the number of Targets presented in the trained eye while simultaneously being presented with Distractors in the untrained eye through a mirror stereoscope. We arranged 90% of trials with Targets in the amblyopic eye and only 10% of trials with Targets in the non-amblyopic fellow eye in each training session. We expected to improve attentional deployment considerably in the amblyopic eye. Contrast response function in each eye was measured by 128-channel swept parameter visual evoked potential (sVEP) before and after training. Contrast threshold was defined by using the regression to zero amplitude approach. V1 was defined by structure and fMRI in a separate session from EEG recordings. Contrast sensitivity ($1/\text{threshold}$) in V1 was compared in each participant pre and post training.

Results: Contrast sensitivity in V1 improved for both the amblyopic and the fellow eye of adults with amblyopia after perceptual learning with attention tasks. The improvement was greater in the amblyopic eye than that in the fellow eye. We did not find significant difference in improvement between anisometropic and strabismic subgroups. Contrast sensitivity improvement in V1 indicates learning effect by enhancing attentional deployment in the amblyopic brain.

Conclusions: Perceptual learning with attention tasks improves contrast sensitivity in V1 of human adults with amblyopia. Our results suggest that top-down mechanisms play an important role in perceptual learning-induced plasticity in early visual cortex.

CONTROL ID: 3547623

SUBMITTER (NAME ONLY): Shruti Singh Kakan

TITLE: Identification of miRNAs in tears of a murine model of Sjögren's syndrome that may represent putative diagnostic biomarkers

SESSION TITLE: Translational Immunology and Ocular Inflammatory Disorders

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: S. Singh Kakan, M. Edman, S.F. Hamm-Alvarez, Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|S. Singh Kakan, B.E. Hjelm, Trnslational Genomics, University of Southern California Keck School of Medicine, Los Angeles, California, UNITED STATES|C.T. Okamoto, S.F. Hamm-Alvarez, School of Pharmacy, University of Southern California, Los Angeles, California, UNITED STATES|

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ABSTRACT BODY:

Purpose: Sjögren's Syndrome (SS) is an autoimmune disease exhibiting inflammation and loss of function of exocrine glands including lacrimal gland (LG). Diagnosis of SS is lengthy and cumbersome. The male NOD mouse exhibits many symptoms of the autoimmune-mediated dry eye seen in SS patients. To identify tear biomarkers that might aid in diagnosis of SS-associated dry eye, we investigated the miRNA composition of tears from male NOD mice. miRNAs are 19-26 nucleotide long, highly-conserved, RNAs that regulate mRNA transcription and are altered in disease. Relative to proteins, miRNAs have less sequence heterogeneity and inter-individual variance, and have shown high sensitivity as biomarkers.

Methods: Tears were collected with topical stimulation of LG with carbachol from male NOD (disease model), BALB/c (healthy control) and female NOD mice (strain control lacking LG inflammation) aged 12-14 weeks. Tear RNA was isolated from pools of 5 mice per sample with 5 samples of male NOD and BALB/c mice and 3 samples of female NOD. RNA quality was determined using Tapestation, then a small-RNA library was prepared using the Illumina TruSeq Small RNA library prep kit and sequenced on an Illumina HiSeq system. Following bioinformatics data analysis, miRNA hits were identified and validated using qRT-PCR. Hits were considered significant if they were up or downregulated in NOD tears with a \log_2 FC of ± 0.5 in the same direction when compared to both male BALB/c and female NOD, and had a p value < 0.05 (DESeq2).

Results: In comparison to both male BALB/c and female NOD mice, 8 tear miRNAs (miR-107-3p, miR-181a-5p, miR-181b-5p, miR-3572-3p, miR-3572-5p, miR-3963, miR-3076-3p) were upregulated whereas another 8 (miR-322-3p, miR-322-5p, miR-146b-5p, miR-146a-5p, miR-147-3p, miR-421-3p, miR-542-3p, miR-503-5p) were downregulated in male NOD. miRNAs 146a/b-5p which was significantly downregulated in male NOD mouse tears, and miR-155-5p, which was slightly but not significantly upregulated in male NOD mouse tears, have been implicated in autoimmune inflammation. The remaining miRNAs represent novel hits with their functional relevance under investigation.

Conclusions: We have identified a panel of differentially expressed miRNA in male NOD mouse tears that may serve as novel biomarkers for early detection of SS.

CONTROL ID: 3547625

SUBMITTER (NAME ONLY): William Binotti

TITLE: Novel En Face Optical Coherence Tomography Parameters for the Assessment of Palisades of Vogt Complex in Patients with Limbal Stem Cell Deficiency

SESSION TITLE: Corneal epithelium and Corneal tissue engineering and regenerative medicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: W. Binotti, A. de Leeuw, D. Saukkonen, B. Bayraktutar, M. Ozmen, P. Hamrah, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

Commercial Relationships Disclosure (Abstract): William Binotti: Commercial Relationship: Code N (No Commercial Relationship) | Anya de Leeuw: Commercial Relationship: Code N (No Commercial Relationship) | Daniel Saukkonen: Commercial Relationship: Code N (No Commercial Relationship) | Betul Bayraktutar: Commercial Relationship: Code N (No Commercial Relationship) | M. Cuneyt Ozmen: Commercial Relationship: Code N (No Commercial Relationship) | Pedram Hamrah: Commercial Relationship(s);Heidelberg Engineering:Code C (Consultant)

ABSTRACT BODY:

Purpose: To explore the diagnostic value of quantitative limbal palisades of Vogt complex (PVC) parameters by en face optical coherence tomography (OCT) for limbal stem cell deficiency (LSCD).

Methods: Retrospective analysis of limbal en face OCT images of 11 eyes of 11 patients with LSCD and 10 eyes of 10 healthy controls. PVC was defined as the hyporeflective tissue within the anatomical limbus, including the palisades of Vogt and the surrounding limbal epithelium. Three-dimensional en face scans through the PVC, of 9µm depth each, were assessed to determine the anterior and superficial borders (end of Bowman's layer) and the posterior and deep borders (transition of hyper-hyporeflective sclera-limbus). The area and volume of each scan were measured manually with ImageJ. Minimum and maximum depth were determined as the first and last appearance of the PVC on the OCT device, respectively. Statistical models were performed to account for different limbal scans of the same eye and age. Slit-lamp grading (0: no loss, 1: <50% loss and 2: ≥50% loss of palisades of Vogt) were correlated to en face OCT parameters.

Results: Mean age was 54.1±19.9 and 39.5±13.6 years in the LSCD and control groups, respectively (p>0.05). There was no statistically significant difference between gender and limbus location (nasal, temporal, superior, inferior) within groups (p=0.61 and p=0.11, respectively). Compared to controls, the LSCD group showed an overall decreased PVC area (0.41±0.04 and 0.86±0.05 mm², p=0.001), maximum area (1.27±0.29 and 2.27±0.19 mm², p=0.013) and volume (0.06±0.01 and 0.09±0.01 mm³, p=0.001) on en face OCT. The comparison for each limbal location is shown in Figure 1. PVC area, maximum area and volume showed a strong inverse correlation with slit-lamp grading (r=-0.586, r=-0.519 and r=-0.586, respectively; p<0.001).

Conclusions: PVC parameters were significantly decreased in LSCD patients compared to healthy controls. All limbal locations with LSCD showed significant PVC changes compared to their respective control regions. En face OCT is a promising non-invasive and quantitative tool for the diagnosis of LSCD.

CONTROL ID: 3547628

SUBMITTER (NAME ONLY): Jorey Cohen

TITLE: Pleiotropic Loci Exist for Advanced AMD and Celiac Disease

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: J.E. Cohen, D.L. Geiser, J. SanGiovanni, The University of Arizona BIO5 Institute, Tucson, Arizona, UNITED STATES|

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ABSTRACT BODY:

Purpose: Nutrient-based interventions are used for tertiary prevention of advanced AMD. Pleiotropic loci exist for AMD and health conditions characterized by altered nutrient absorption.

Methods: We examined advanced AMD (AAMD)-associated missense DNA variants from the IAMDC|GWAS Catalog|PheWeb for pleiotropy with Celiac Disease (CD), a condition characterized by malabsorption of zinc (a key constituent of the AREDS formulation) and other minerals linked to diet-associated reductions in likelihood of having or progressing to AAMD. The genetic architecture of co-inherited SNPs in people of western-European ancestry ($r^2 > 0.80$, LDLink-NCI and HaploReg 4.1) was also analyzed.

Results: Analysis of IAMDC, GWAS Catalog and PheWeb data showed that 13 genes containing AAMD-related ($P < 1.0E-7$) exonic SNPs also carry CD-associated DNA variants. Analysis of all concordant genes (those containing any form of genome-wide AAMD- and CD-related variation) yielded a CD enrichment Q-value of $2.3E-18$. We filtered IAMDC results for AAMD by genome-wide CD-associated loci ($P < 1.0E-7$) that were identified in a fine-mapping study on $> 24,000$ people (PMID: 22057235). Within the 6p21 locus, 58 SNPs in 25 LD-independent ($r^2 < 0.60$) loci were both associated with AAMD and CD. These loci include SNPs in complete LD ($r^2 > 1.0$) with 6 missense DNA sequence variants (in CCHCR1, MSH5, C2, CFB, TNXB, PSMB9).

Conclusions: Our findings provide a reasonable basis for investigating the possibility of a common underlying biology and therapeutic options for AAMD and Celiac Disease through processes driven by proteins encoded by genes in the 6p21 locus.

CONTROL ID: 3547636

SUBMITTER (NAME ONLY): Aarushi Kumar

TITLE: Telegenetics for Inherited Retinal Diseases during the COVID-19 pandemic

SESSION TITLE: Genetics of Retinal dystrophies and Functional Genomics

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Kumar, A. Al Moujahed, T. Chemudupati, V.B. Mahajan, Molecular Surgery Program, Department of Ophthalmology, Stanford University, Stanford, California, UNITED STATES|S. Tsang, Columbia University, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: Inherited Retinal Diseases (IRDs) are a group of rare genetic disorders that require a detailed approach and workflow for diagnosis. To facilitate optimal patient care while minimizing the hazard of direct person-to-person exposure during the COVID-19 pandemic, we developed a telehealth management protocol, or telegenetics, for complete or hybrid virtual visits.

Methods: Our telegenetics protocol comprised of three key components: (1) Digitization of diagnostic imaging and electrophysiological testing for review by physicians remotely; (2) Telemedicine video visits performed using MyHealth, a Health Insurance Portability and Accountability Act (HIPAA) compliant platform. (3) Complete shift to remote genetic testing using IRB-approved e-consents (electronic consent forms) and remote genetic testing saliva kits.

Results: Telegenetic care was provided for 113 patients, including 3 international patients (age range: 5-99 years). During the first eight months of this program, 25 return and 28 new patient evaluations were completed virtually. Sixty patients were seen in a hybrid manner (45 new and 15 return), where an in-person clinic visit was performed followed by remote consenting, and saliva collection, genetic testing, and genetic counseling. A spectrum of retinal dystrophies were diagnosed and pathogenic mutations were detected in several genes, including genes approved or under-investigation for gene therapy like RPE65, CHM, and RPGR. Four patients with cystoid macular edema were successfully treated with topical dorzolamide, and 26 were referred for low-vision rehabilitation

Conclusions: Telegenetic services have proved to be a useful tool during the COVID pandemic. They provide a safer alternative by limiting the exposure of patients and staff to the virus while maintaining the same high quality of care that was provided to patients before the pandemic. With the added efficiency and convenience of virtual patient care, we expect that telegenetics will continue and expand into other medical genetic conditions long after the pandemic.

CONTROL ID: 3547643

SUBMITTER (NAME ONLY): Sejiro Littleton

TITLE: Single Cell RNA-Sequencing Points to an Inter-relationship between Corneal Macrophages and Dendritic Cells

SESSION TITLE: Corneal Immunology and T cell Responses

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: S. Littleton, D.R. Saban, Immunology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|S. Littleton, C. Yu, R. Mathew, J. Kalnitsky, D.R. Saban, Ophthalmology, Duke University School of Medicine, Durham, North Carolina, UNITED STATES|

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ABSTRACT BODY:

Purpose: Macrophages (MF) and dendritic cells (DC) are categorized as two separate cell types with distinct roles in innate immunity, but also can have overlapping functions given their highly complex and plastic nature. In the cornea, current classifications for these two population of mononuclear phagocytes are still limited to only several markers or genes. Thus, a better accounting of the full range and dynamics of their cell states is needed to more completely understand the distinct roles of these cells and how they fulfill their functions. We addressed this knowledge gap here at the transcriptome level, by applying single cell RNA-seq of mononuclear phagocytes from the cornea and their precursors from the blood in normal adult mice.

Methods: Corneas from n=25 male and n=25 female eight-week-old C57BL/6 mice were harvested, prepared as single cell suspensions, and FACS sorted for live CD45+ populations. Additionally, the peripheral blood of n=5 male and n=5 female mice were FACS sorted for live CD45+, CD11b+, CD115+, Ly6G- cells to enrich for circulating monocytes and precursor DCs. FACS sorted cornea and blood were pooled by sex before sequencing.

Results: Our dataset included n=3,237 viable cells and n=15,831 genes. Unbiased cluster analysis at a resolution of 1.5 via Seurat resulted in n=25 clusters. To understand the potential relationships between these clusters we conducted a pseudotime analysis. Any clusters with lymphoid or granulocyte signatures were excluded. Langerhan's cells were also excluded given their fetal origins. Our results revealed two main trajectory branches. One branch transitioned through a DC-like state, while the other did not. Interestingly, both branches converged into several closely related clusters dominated primarily by a MF gene signature, with genes related to DC function.

Conclusions: Collectively, our results suggest that corneal mononuclear phagocytes derived from adult blood precursors represent MFs of which had either transitioned through a DC-like state or did not, yet retained DC features. Hence, rather than a two-cell type model for DCs and MFs, our findings suggest that they exist in a continuum of cell states and expressed gene programs in the cornea. These implications may better explain how mononuclear phagocytes maintain such a diverse functional repertoire with efficient on-demand responses involved in corneal homeostasis and disease.

CONTROL ID: 3547660

SUBMITTER (NAME ONLY): YOSUKE TAKI

TITLE: FAZ alterations after ILM peeling for ERM

SESSION TITLE: OCT Angiography - Clinical applications

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: Y. TAKI, Y. Ito, J. TAKEUCHI, Y. NAKANO, E. HORIGUCHI, O. HIKARU, H. Kaneko, S. Ueno, H. Terasaki, K. kataoka, Nagoya Daigaku, Nagoya, Aichi, JAPAN|

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ABSTRACT BODY:

Purpose: We investigated the changes in foveal avascular zone (FAZ) area after vitrectomy with internal limiting membrane (ILM) peeling for epiretinal membrane (ERM).

Methods: This retrospective observational case series included 21 eyes of 21 patients (age: 68.4 ± 6.5 years) who underwent vitrectomy with ILM peeling for ERM. Pre- and post-operative FAZ areas were measured using 3×3 mm superficial optical coherence tomography (OCT) angiography, and the relationship was investigated. In addition, the displacement distance of the centroid of FAZ was measured in OCT angiography images, and the association of the changes in FAZ area with pre-operative FAZ area, pre-operative foveal thickness, axial length, and the displacement distance of the centroid of FAZ were also investigated.

Results: Pre- and post-operative FAZ areas correlated significantly ($p < 0.001$). Preoperative FAZ areas larger than 0.10 mm^2 , were reduced after surgery and vice versa. The multivariate analysis showed that the changes in FAZ area were only associated with pre-operative FAZ area ($p = 0.001$), and were not associated with other factors (all $p > 0.05$).

Conclusions: Postoperative changes in FAZ area after ILM peeling only depended on baseline FAZ area. Because FAZ area of 0.10 mm^2 is much smaller than normal FAZ area, ILM may have centrifugal tractional forces on the fovea, and the FAZ area without the centrifugal tractional force of the ILM may be about 0.10 mm^2 .

CONTROL ID: 3547674

SUBMITTER (NAME ONLY): Xiaolin Xu

TITLE: High-risk Histopathologic Features of Primarily Enucleated Retinoblastoma

SESSION TITLE: Recent Advances in Retinoblastomas, Intra and Extra Ocular Pathologies

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: X. Xu, X. Zhang, F. Gao, Z. Zhang, Beijing Institute of Ophthalmology, Beijing Tongren Hospital, CHINA|

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ABSTRACT BODY:

Purpose: To evaluate the high-risk histopathologic features (HRFs) of retinoblastoma (RB) eyes enucleated as the primary treatment strategy.

Methods: A retrospective histopathological analysis of HRFs was performed. A total of 950 primarily enucleated RB eyes from Beijing Tongren Hospital were analyzed.

Results: Of the 950 primarily enucleated RB eyes, 362(38.1%) were classified as HRFs, of which 287 (30.2%) had post lamina cribrosa optic nerve invasion (including 32 (3.4%) with optic nerve transection invasion), 133 (14.0%) with massive choroidal invasion, 58 (6.1%) with anterior segment invasion, and 12(1.3%) with extraocular invasion. NVI was identified in 508 patients (53.5%) and was significantly correlated with HRFs. The proportion of HRFs was significantly higher in the NVI-positive group (50.6%) compared to the NVI-negative group (23.8%) ($P < 0.001$). The proportion of post lamina cribrosa optic nerve invasion was significantly higher in the NVI-positive group (44.1%) compared to the NVI-negative group (14.3%) ($P < 0.001$). The proportion of massive choroidal invasion was significantly higher in the NVI-positive group (18.9%) compared to the NVI-negative group (10.6%) ($P < 0.001$).

Conclusions: HRFs occurred in slightly more than one-third of RB cases, which was similar to HRFs incidence in developing countries and higher than that in developed countries. To a certain degree NVI is a predictor of HRFs. When considering primary treatment, especially intra-artery chemotherapy (IAC), the facts that more than one-third of RB eyes have HRFs and a little more than half of NVI-positive RB eyes have HRFs should be carefully thought out.

CONTROL ID: 3547701

SUBMITTER (NAME ONLY): Ana MIGUEL

TITLE: Artificial Intelligence to detect glaucoma through OCT Angiography– a pilot study

SESSION TITLE: Machine learning II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. MIGUEL, B. Silva, Ophthalmology, Polyclinique de la Baie, Saint-Martin-des-Champs, FRANCE|

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ABSTRACT BODY:

Purpose: Artificial intelligence (AI) has been used successfully to diagnose several eye conditions, including glaucoma. OCT-Angiography (OCTA) is a non-invasive technology useful for glaucoma diagnosis and follow-up. To our knowledge, no study has applied AI in OCTA scans to increase the diagnostic capacity in glaucoma. Our purpose was to develop an AI tool to assist in glaucoma diagnosis using OCTA scans. We also intended to measure its performance using the area under the curve (AUROC), as done for diagnostic studies.

Methods: We performed an observational retrospective study from 2020 to 2015. We had local Ethics Committee approval and followed the tenets of the Helsinki declaration. Patients with retinographies, OCT, OCTA, visual fields, intraocular pressure (IOP) measurement, and complete ophthalmology records were included. A glaucoma expert reviewed the medical records to classify patients with glaucoma and those without glaucoma. Patients with systemic or other ophthalmologic pathologies and glaucoma-suspects were excluded, as well as incomplete records. Low-quality OCTA images were excluded (with strength signal index ≤ 50 , media opacities, or fixation artifacts). We built a deep-learning software using the OCTA scans, using 90% of them to train its neural network to distinguish the images between glaucoma and non-glaucoma. The remaining ten percent were used for validation. We used the TensorFlow (v.1.15.2) encoder library, followed by several layers of mathematical operations and the RMSProp optimizer, and a learning rate of 0.001.

Results: We included 262 patients, from which 40 were healthy controls, and 222 were glaucomatous patients. The AI system successfully discriminated glaucoma from healthy eyes from OCTA scans, with a sensitivity of 99.55%, a specificity of 92.5%, and an AUROC of 85%.

Conclusions: Despite a small database, the AI discriminating results were promising in this pilot study. Associating OCTA scans to AI may be an effective strategy to help ophthalmologists diagnose glaucoma. More extensive multi-centric studies are needed to improve deep learning algorithms and detect glaucoma better.

CONTROL ID: 3547713

SUBMITTER (NAME ONLY): Renata Puertas

TITLE: Long-term follow-up of Glaucoma Drainage Implants (Tubes) in Paediatric Glaucoma Patients

SESSION TITLE: Surgery and Wound Healing I and II

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R.A. Puertas, S. Koenig, Glaucoma Department, Moorfields Eye Hospital NHS Foundation Trust, London, London, UNITED KINGDOM|

Commercial Relationships Disclosure (Abstract): Renata Puertas: Commercial Relationship: Code N (No Commercial Relationship) | Susanna Koenig: Commercial Relationship: Code N (No Commercial Relationship)

ABSTRACT BODY:

Purpose: To evaluate the long-term outcomes and safety profile of tube implants in primary and secondary paediatric glaucoma patients (≤ 16 years of age) at a tertiary centre.

Methods: Between January 2005 and August 2020, 361 paediatric glaucoma patients had a tube implant. Of these, 121 were analysed and 83 eyes were included as a first tube implant with sufficient follow-up of at least 12 ± 2 months. This is a retrospective data collection. Failure was defined as loss of light perception (PL) vision, tube explantation, need for oral Acetazolamide or further glaucoma surgery. Eyes that did not fail by the above criteria, but were on supplemental topical medical therapy were considered qualified successes. Eyes that did not fail and were not on any medical therapy were considered complete successes.

Results: The mean age at surgery was 8.1 ± 5.3 years (55.4% female). The average intraocular pressure (IOP) at listing was 28.1 ± 7.2 mmHg, on 3.1 ± 0.9 medications with 27 (32.5%) patients taking oral Acetazolamide. The mean follow-up time was 3.4 ± 2.0 years. One year after tube implant [7 Ahmed valves (8.4%), 1 Molteno tube (1.2%), 75 Baerveldt tubes (90.4%) $n=79$], the IOP decreased to 14.8 ± 4.2 mmHg on 2.6 ± 1.0 medications. The average IOP was 15.7 ± 4.7 mmHg on 2.4 ± 0.8 medications after 3 years ($n = 46$) and 15.1 ± 5.5 mmHg on 2.6 ± 0.7 agents after 5 years ($n = 26$).

The average visual acuity (VA) was 0.6 ± 0.51 logMAR at listing. At one year follow up, VA was 0.6 ± 0.6 logMAR; at three years VA was 0.6 ± 0.6 logMAR and at 5 years, VA was 0.7 ± 0.5 logMAR ($p > .05$).

Altogether, one patient lost PL (1.2%) four years post-op, one tube was explanted and replaced with another tube due to poor IOP control (1.2%) and further eight (10%) patients needed additional glaucoma surgery.

Conclusions: Despite the inherent risk in the paediatric population, tube implants appear to be an effective procedure driving drastic reduction in pressure ($p < .00001$ at all times) as well as in use of medication in long-term ($p < .00001$ at all times). This study provides information about the safety profile of tube implants in a paediatric glaucoma population of a single hospital. New evidence of tube implant in glaucoma has changed adult glaucoma management in the last decade. We hope our study can show tube implants as a safe procedure and one more option for children who will need follow up and treatment for a lifetime.

CONTROL ID: 3547742

SUBMITTER (NAME ONLY): Arjun Watane

TITLE: The Effect of Market Competition on the Price of Topical Eye Drops

SESSION TITLE: Ophthalmology Training/Careers, Health Economics and Telemedicine

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Watane, M. Kalavar, J. Reyes, N.A. Yannuzzi, J. Sridhar, University of Miami Health System Bascom Palmer Eye Institute, Miami, Florida, UNITED STATES|

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ABSTRACT BODY:

Purpose: To describe the relationship between the number of Federal Drug Administration (FDA)-approved manufacturers and the price change of generic and branded topical eye drops.

Methods: Retrospective analysis of topical eye drop medications with formulations listed in the Federal Drug Administration's (FDA) Orange Book and the National Average Drug Acquisition Cost database from 2013 to 2017.

Results: The most frequently prescribed generic topical drugs were glaucoma medications (34%), antimicrobials (32%), anti-inflammatories (24%), mydriatics (5%), and anesthetics (5%). The most frequently prescribed branded topical drugs were anti-inflammatories (45%), glaucoma medications (32%), antimicrobials (21%) and dry eye medications (3%). From 2013 to 2017, generic eye drops had a median price decrease of 20% (IQR 32%) while branded eye drops had a median price increase of 44% (IQR 28%) ($P < .001$). A significant inverse association was identified between the price change of generic eye drops and the total number of all manufacturers ($r = -.41$, $P = .010$), generic drug manufacturers ($r = -.32$, $P = .0496$), and alternative branded drug manufacturers ($r = -.57$, $P = .002$). There was no significant association between the price change of branded eye drops and number of manufacturers. Glaucoma ($r = -.58$, $P = .039$) and anti-inflammatory ($r = -.69$, $P = .047$) eye drops also had significant inverse associations with the number of generic manufacturers.

Conclusions: From 2013 to 2017, the price of generic eye drops decreased whereas the price of branded eye drops increased. Market competition was significantly inversely associated with price changes of generic eye drops but not branded eye drops.

CONTROL ID: 3547750

SUBMITTER (NAME ONLY): Eli Pratte

TITLE: Lacrimal stenting with Nunchaku versus Crawford tubes for Congenital or Partial Acquired Nasolacrimal Duct System Obstruction

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Pratte, J. Cho, R. Short, E. Mellencamp, School of Medicine, University of Missouri System, Columbia, Missouri, UNITED STATES|C. Petris, Department of Ophthalmology, University of Missouri System, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To compare Nunchaku or Crawford stent placement during probing for the treatment of congenital or acquired nasolacrimal duct obstruction.

Methods: A retrospective chart analysis was undertaken for patients that underwent lacrimal stenting with Nunchaku-style tubes (19 patients, 27 eyes) and Crawford tube placement (37 patients, 40 eyes) at the same institution from 2017-2018 by one of two oculoplastic surgeons. With the exception of lacrimal balloon dilation, cases performed in conjunction with other surgical procedures, such as ectropion repair or dacryocystorhinostomy (DCR), were excluded. The primary outcome measure was resolution of daily epiphora.

Results: Outcomes were recorded in the early (<1 month) or late (1-3 months) post-operative period or long-term (>3 months) follow-up (Table 1). In the early post-operative period, the Nunchaku cohort 15 eyes (57.7%) had resolution of epiphora (9 ± 5.2 days) compared to 21 eyes (75.0%) of those that received a Crawford stent reported achieving success at 17.2 ± 7.6 days ($p=0.18$). In the late post-operative period, average time of follow-up for the Nunchaku cohort was 46.5 ± 10.5 days with 14 eyes (87.5%) reporting success compared to 61.3 ± 19.3 days with 3 eyes (75%) achieving success ($p=0.51$). In long-term follow-up, average duration was 118.4 ± 18.4 days with 5 eyes (100%) achieving success compared to average duration of 336.9 ± 241.2 days with 14 eyes (87.5%) reporting success ($p=0.99$).

We also analyzed success rates for patients receiving stents for congenital and acquired NLDO (Table 2). Average age of patients receiving Nunchaku stent for congenital NLDO was 3.5 ± 3.2 years compared to 70.6 ± 11.8 for acquired NLDO. For the Crawford stents, average age for congenital NLDO 2.1 ± 1 years and 53.7 ± 12.3 years for acquired NLDO. Success rates at every post-operative interval for both congenital and acquired NLDO was comparable between Nunchaku and Crawford stents.

Conclusions: The short and long-term follow-up visits demonstrated comparable rates of improvement in epiphora for both the Crawford and Nunchaku style lacrimal stents. The Nunchaku lacrimal stent is a "push-style" stent that does not require intranasal retrieval or tying/securing of the distal ends of the tubes. In instances where the Nunchaku style stent is appropriately utilized, there may be benefits of improved surgical efficiency.

CONTROL ID: 3547754

SUBMITTER (NAME ONLY): John Paul SanGiovanni

TITLE: Differential Expression Patterns of Genes Encoding Monoamine Pathway Constituents Exist in Retinal Specimens of People with Neovascular AMD

SESSION TITLE: Genetics of corneal dystrophy, glaucoma, lens and AMD

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: D.Q. SanGiovanni, Emory University, Atlanta, Georgia, UNITED STATES|R.W. Snyder, Biomedical Engineering, University of Arizona, Tucson, Arizona, UNITED STATES|J. SanGiovanni, BIO5 Institute, University of Arizona, Tucson, Arizona, UNITED STATES|D.L. Geiser, Nutritional Sciences, University of Arizona, Tucson, Arizona, UNITED STATES|B.S. McKay, Ophthalmology and Vision Science, University of Arizona, Tucson, Arizona, UNITED STATES|

Commercial Relationships Disclosure (Abstract): John Paul SanGiovanni: Commercial Relationship: Code N (No Commercial Relationship) | Daniel SanGiovanni: Commercial Relationship: Code N (No Commercial Relationship) | Robert Snyder: Commercial Relationship(s);Snyder Biomedical:Code I (Personal Financial Interest);Snyder Biomedical:Code E (Employment);Snyder Biomedical (WO/2020/160256):Code P (Patent) | Dawn Geiser: Commercial Relationship: Code N (No Commercial Relationship) | Brian McKay: Commercial Relationship(s);Snyder Biomedical:Code P (Patent)

ABSTRACT BODY:

Purpose: We have previously applied methods in genomics, structural chemistry, ophthalmic epidemiology and clinical trials to demonstrate associations of L-DOPA, dopamine (DA) and monoaminergic receptors with advanced AMD. In this work we report findings on human retinal transcriptomes to extend our investigations.

Methods: We used QC-validated and normalized RNA-seq data collected with Illumina HiSeq 2500 from a public-access NCBI GEO database (GSE115828) of retinal specimens in order to identify differential gene expression profiles in seven people with neovascular AMD (NV AMD), relative to twelve age-matched AMD-free peers. We conducted gene ontology and pathway analysis with Gene Set Enrichment Analysis (GSEA) software.

Results: RNA levels of DBH-like monooxygenase protein 1 (MOXD1), an enzyme implicated in dopamine catabolism, were 3.3-fold higher in retinal specimens of people with NV AMD ($P < 9.91E-5$; FDR Q = 0.095) – these findings were concordant with a published work reporting a 2.8-fold increase in MOXD1 expression within macular specimens of people with NV AMD (PMID: 22364233). Gene Ontology Enrichment Analysis on the full set of 17910 transcripts yielded strongest relationships for down regulation of chemical synaptic transmission (GO: 0007268; FDR Q = 6.3E-13) in the NV AMD cohort – subsequent Pathway Enrichment Analysis showed significant NV AMD-associated retinal down regulation of 14 genes in the KEGG Dopamine Synapse Pathway (hsa04728; FDR Q = 1.4E-4) and 4 genes in the WikiPathways Nicotine Effect on Dopaminergic Neurons Pathway (WP1602; FDR = 0.048). Gene sets from the Reactome Dopamine Release Cycle (FDR Q = 0.14) and Gene Ontology Regulation of Dopamine Secretion (FDR Q = 0.17) also showed significantly lower expression values in people with NV AMD.

Conclusions: Our findings strengthen inferences on AMD-associated alterations in function of monoaminergic signaling pathways.

CONTROL ID: 3547775

SUBMITTER (NAME ONLY): Ashkan Abbey

TITLE: The Use of a Combination of Ozurdex (dexamethasone intravitreal implant) and Eylea (afibercept) versus Eylea Monotherapy for Diabetic Macular Edema: Preliminary Data from a Prospective, Comparative Trial (COED Trial)

SESSION TITLE: Diabetic macular edema

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: A. Abbey, Texas Retina Associates, Dallas, Texas, UNITED STATES|

Commercial Relationships Disclosure (Abstract): Ashkan Abbey: Commercial Relationship(s);Allergan:Code F (Financial Support);Allergan:Code C (Consultant);Allergan:Code R (Recipient);Regeneron:Code C (Consultant);Regeneron:Code R (Recipient);Genentech:Code C (Consultant);Genentech:Code R (Recipient);Alimera Sciences:Code C (Consultant);Alimera Sciences:Code R (Recipient);Spark Therapeutics:Code R (Recipient);Novartis:Code C (Consultant);Novartis:Code R (Recipient)

ABSTRACT BODY:

Purpose: This study evaluated the safety, efficacy, and durability advantages of Ozurdex (OZ) in conjunction with intravitreal aflibercept (AF) compared with AF monotherapy for treatment of diabetic macular edema (DME). We expect reduced time to resolution of DME on OCT and fewer total injections with the use of combination therapy.

Methods: COED is a prospective, randomized, open-label, multicenter collaborative study. Patients were randomized 1:1 to OZ and AF (active) or AF monotherapy (control), and assessed over 48 weeks. Treatment-naïve eyes with DME (or eyes previously treated with anti-VEGF after a 3-month washout period) with best-corrected visual acuity (BCVA) of 25 to 73 letters and central subfield retinal thickness (CST) of more than 300 µm were included. Patients that have completed 24 weeks of the trial were included in this preliminary analysis. The active group (AG) (n = 13) received OZ and AF at baseline. They would then receive monthly injections of AF, and treatment with OZ would be performed every 3 months PRN. Patients in the control group (CG) (n = 10) received AF at baseline. These patients would subsequently receive monthly injections of aflibercept PRN. At each visit, the following criteria were assessed to determine whether to treat:

- Macular Edema, defined as intraretinal or subretinal fluid (new or persistent), in conjunction with a CST \geq 300 µm as measured by SD-OCT.
- A decrease in BCVA of 6 letters or greater between the current visit and the BCVA reading from the previous visit with an increase in CST of $>$ 50 µm from the previous visit, associated with new fluid.
- A decrease in BCVA of 10 letters or greater from the best measurement (during the study) with an increase in CST of $>$ 50 µm from the previous visit, associated with new fluid.

Results: At week 24, the difference in mean BCVA (AG – CG) was -4.59 ± 5.33 (p = 0.40). The difference in mean CST was -37.88 ± 73.87 (p = 0.61). Eyes in AG received fewer treatments (mean 4.23 vs. 5.4).

Conclusions: OZ administered in conjunction with intravitreal AF for treatment of DME provides similar visual benefit at 24 weeks' follow-up compared with AF monotherapy and shows anatomic benefit with potential to reduce treatment burden.

CONTROL ID: 3547786

SUBMITTER (NAME ONLY): Laura Schaefer

TITLE: Gut microbiota from Sjögren Syndrome patients causes decreased T regulatory cells in the lymphoid organs and ocular barrier disruption in mice.

SESSION TITLE: Dry eye and Tear film

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: L. Schaefer, R. Britton, Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas, UNITED STATES|C. Trujillo-Vargas, S.C. Pflugfelder, C.S. De Paiva, Ophthalmology, Baylor College of Medicine, Houston, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: We are investigating the effects of the gut microbiota on immune homeostasis at the ocular surface and on ocular pathophysiology in Sjogren Syndrome.

Methods: 4-week-old female germ-free C57BL/6 mice were individually humanized with stools from either healthy donors or SS patients (n = 5 donors per group). Flow cytometry analysis investigated the frequency of CD4⁺FoxP3⁺ cells in ocular draining nodes, spleens, intestinal lamina propria and mesenteric lymph nodes 4 weeks post-humanization. A separate group of germ-free mice after humanization with SS and healthy donors were mated to established humanized colonies. Humanized mice (n = 3 different donors per group) were subjected to the standard desiccating stress for 5 days. Uptake of Oregon-Green-Dextran (OGD) dye was used to evaluate corneal barrier function after desiccating stress. Data analysis was performed after combining the results from individual subjects.

Results: We observed a consistent decrease in the percentages of CD4⁺FoxP3⁺ lymphocytes in the eye draining lymph nodes in the SS humanized mice compared to healthy donors (11.6±5 vs 15.8±4.6% of the total leukocytes, n=19 mice/group, p=0.01 unpaired t test). This finding was recapitulated in the offspring of the humanized colonies, in which we also observed the same phenomenon in the spleen and mediastinal lymph nodes, indicating that this effect has vertical transmission. Following exposure to desiccating stress for 5 days, we observed significant disruption of corneal barrier function in SS-humanized mice compared to healthy donors.

Conclusions: These findings suggest that the gut microbiota influences the proper development of T regulatory cells in draining lymph nodes of mucosal surfaces, such as the eye. They also suggest that the bacterial communities from Sjogren Syndrome patients are less protective of the ocular surface against desiccating environmental stress, as SS-humanized mice had worse corneal barrier function.

CONTROL ID: 3547789

SUBMITTER (NAME ONLY): clark tedford

TITLE: Improvement of Visual Function following Multi-wavelength Photobiomodulation with the Valeda Light Delivery System on Electroretinography (ERG) and Best Corrected Visual Acuity (BCVA) in Dry Age-related Macular Degeneration in the ELECTROLIGHT Study (Interim Analysis)

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: Electroretinography is a quantitative and functional indicator of visual function and is an important tool for the diagnosis and management of retinal function in ocular disease. Dry age-related macular degeneration (AMD) demonstrates underlying mitochondrial dysfunction. The Valeda multi-wavelength photobiomodulation (PBM) device, and the Diopsys NOVA ERG device were used to investigate the effects on multiple parameters of visual function in the ELECTROLIGHT dry AMD study.

Methods: A total of 23 eyes from 15 subjects with intermediate Dry AMD were enrolled into the prospective clinical study and treated with one series of PBM treatment using the Valeda (3x per week for 3 weeks). PBM therapy consists of low-level light exposure to selected tissues resulting in positive effects on mitochondrial Cytochrome C Oxidase output and improvement in metabolic activity. Subjects were assessed for clinical and safety outcomes (i.e., visual acuity, contrast sensitivity, color vision, amsler grid test, perimetry, and ERG). Independent OCT outcomes at 3- and 6-months post-treatment were analyzed by a masked imaging center. An interim analysis was performed following the month 1 study visit.

Results: Subjects showed approximately 12.6 ± 1.25 letter improvement in BCVA at Month 1 compared to BL scores. Mars Contrast Sensitivity (CS) also showed improvement from BL to 1 month at 40 cm ($0.165 \log + 0.25$), 80 cm ($0.134 \log + 0.20$) and 120 cm ($0.22 \log + 0.37$). A positive correlation between multiluminance ERG and BCVA was seen and strong positive correlations between multiluminance ERG and fixed luminance ($R = 0.852$) and Chromatic ERG outcomes. Reductions in drusen were seen in select patients. Multiluminance ERG Magnitude AUC improved by 14.4% from baseline to the fourth test after completion of the 1-month treatment, and this difference was determined to be significant ($p = 0.001$).

Conclusions: Valeda provided statistically significant improvements in BCVA, CS and multiluminance ERG function from baseline at the 1-month time point following 9 PBM treatments. PBM therapy represents a novel approach to treat patients with dry AMD. Diopsys multiluminance ERG may be used as an early and sensitive measure of visual dysfunction in dry AMD patients.

CONTROL ID: 3547791

SUBMITTER (NAME ONLY): Elizabeth Mellencamp

TITLE: Utilization and success rates of various lacrimal surgeries with a Nunchaku-style lacrimal stent

SESSION TITLE: Strabismus

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: E. Mellencamp, J. Cho, R. Short, E. Pratte, School of Medicine, University of Missouri, Columbia, Missouri, UNITED STATES|C. Petris, Ophthalmology, University of Missouri, Columbia, Missouri, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the utility of a Nunchaku-style stents in various lacrimal surgeries.

Methods: Charts were reviewed for patients who underwent placement of the Nunchaku (FCI Ophthalmics, Pembroke, MA) stent placement between (2017-2018) an oculoplastic surgeon at a single institution. The primary outcome measures were recorded as the rate of resolution of daily epiphora or absence of daily tearing symptoms at the early (<30 days) and late post-operative visits (>30 days). Patient demographics, type of surgery, use of a lacrimal balloon dacryoplasty or canaliculoplasty, concomitant procedures, level of obstruction, size of tube and post-operative complications were recorded.

Results: 40 patients (51 eyes) were included. 27 underwent probing for congenital or acquired NLDO, 18 had dacryocystorhinostomy (DCR), 4 had canalicular laceration repair, and 2 had canalicular reconstruction following Mohs surgery. Rates of epiphora were evaluated at early (10.8 ± 8.13 days) and late (57.7 ± 50.41 days) post-operative timepoints. At early post-op follow-up 15 eyes (54.9%) of patients undergoing probing with silicone intubation had resolution compared to 17 eyes (94.4%) who underwent endoDCR. At late follow-up 24 eyes (88.9%) who underwent probing with silicone intubation had resolution compared to 17 eyes (94.4%) who underwent endoDCR. Eyes who received stents for canalicular reconstruction after Mohs or canalicular laceration repair didn't exhibit occurrence of epiphora at any time points after surgery (table 1).

Conclusions: Traditionally Crawford style stents have been used in oculoplastic lacrimal surgery. The Nunchaku lacrimal stent - a self-retaining, push-style stent - circumvents the need for intranasal retrieval, securing, and is easier to remove. Overall, our results show that Nunchaku stenting with probing and endoDCR had high rates of success in the late post-operative period. In addition, low rates of new-onset epiphora after canalicular lacerations or canalicular repair after Mohs defects were seen. Higher rates of epiphora in the early post-operative period had improved at the later timepoints, which is likely attributable to post-operative swelling. This study provides further evidence that Nunchaku stents should be used with high confidence in treatment for patients with various lacrimal pathologies. Further studies directly comparing Nunchaku-style and Crawford tubes may be beneficial.

CONTROL ID: 3547909

SUBMITTER (NAME ONLY): Shabnam Majidi

TITLE: Spatiotemporal mapping of neurogenic gene expression during mammalian retinal development

SESSION TITLE: AMD and retinal physiology

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: The prevalence of blindness due to retinal injury has inspired widespread efforts to develop new treatments. Despite significant advances made in retinal cell transplantation, achieving proper repair of existing retinal tissue remains a significant obstacle. A new and exciting alternative strategy involves the stimulation of retinal regeneration from a patient's own stem-like cells. Müller glia are the only retinal cell type to express the orphan nuclear receptor TLX, a master regulator of neuronal stemness. Due to its enriched expression in Müller glia and the potential for pharmacologic manipulation, we hypothesize that TLX may serve as an ideal therapeutic target for stimulating repair and regeneration in the mammalian retina.

Methods: A transgenic mouse model was developed wherein Müller glia express a YFP reporter transgene, allowing us to effectively track Müller glia through 8 key stages of retinal development that coincide with available single cell RNA-sequencing (scRNA) datasets. Freshly enucleated eye cups were harvested from wild type and transgenic mice at each key developmental stage. All eyecups were fixed with 4% paraformaldehyde, washed with PBS and stored in 30% sucrose/PBS solution. Eyecups were cryopreserved and 12 um cryosections obtained for immunofluorescence detecting TLX and markers of Müller glia and other retinal cell types. Imaging was performed via confocal microscopy.

Results: TLX is highly expressed in the embryonic retinal progenitor cells during mouse retinal development via scRNA sequencing data. Müller glia start expressing TLX mRNA and protein at postnatal day 5 (P5) in mouse retina. By P8, TLX mRNA and protein are solely expressed by Müller glial cells in the retina.

Conclusions: Overall, we have temporospatially mapped the expression of TLX from embryonic retinal progenitor cells to fully differentiated retinal cell types of the adult retina. We find that TLX expression becomes restricted to Muller glia over the course of mouse retinal development. Collectively, these studies provide a foundation of understanding for the potential molecular mechanisms implicated in the retinal regenerative capacity of mammalian Müller glia and provide further basis for the study of TLX as a candidate target for retinal regeneration.

CONTROL ID: 3548072

SUBMITTER (NAME ONLY): Daniel Saukkonen

TITLE: Regional Differences of Novel Limbal Palisade of Vogt Complex Parameters using En Face Optical Coherence Tomography in Healthy Subjects

SESSION TITLE: Corneal epithelium

SESSION TYPE: Paper Session

AUTHORS/INSTITUTIONS: D. Saukkonen, W. Binotti, A. de Leeuw, B. Bayraktutar, M. Ozmen, P. Hamrah, Ophthalmology, Tufts Medical Center, Boston, Massachusetts, UNITED STATES|

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ABSTRACT BODY:

Purpose: To explore the capability of en face optical coherence tomography (OCT) in measuring the dimensions of the limbal palisades of Vogt complex (PVC) and describe the regional differences in healthy subjects.

Methods: Retrospective analysis of limbal en face OCT images from 10 eyes of 10 healthy individuals. The best quality image from all available regions (nasal, temporal, superior, inferior) were selected for each subject. PVC was defined as the hyporeflective tissue within the anatomical limbus, including the palisades of Vogt and the surrounding limbal epithelium. Three-dimensional en face scans through the PVC, of 9µm depth each, were assessed to determine the anterior and superficial borders (end of Bowman's layer) and the posterior and deep borders (transition of hyper-hyporeflective sclera-limbus). The area and volume of each scan were measured manually with ImageJ (Figure 1). Minimum and maximum depth were determined as the first and last appearance of the PVC on the OCT device, respectively. Statistical models were performed to account for different scans of the same eye and age.

Results: A total of 10 nasal, 10 temporal, 5 superior and 5 inferior en face OCTs regions were assessed. Mean age was 39.5±13.6 years [26-77] with equal male-to-female ratio. En face OCT PVC was detected in all regions. PVC area, volume, maximum area, maximum depth and thickness were greater in the superior and inferior limbus compared to the nasal and temporal (1.18 ± 0.10 and $0.68\pm0.05\text{mm}^2$, $p=0.003$; 3.15 ± 0.24 and $1.90\pm0.19\text{mm}^2$, $p<0.001$; 0.17 ± 0.02 and $0.06\pm0.01\text{mm}^3$, $p<0.001$; 129.4 ± 5.0 and $107.7\pm3.4\mu\text{m}$, $p=0.002$; and 63.4 ± 3.8 and $44.7\pm4.2\mu\text{m}$, $p<0.001$; respectively). PVC minimum depth was not statistically significant between the regions (62.5 ± 3.1 and $69.0\pm12.2\mu\text{m}$, $p=0.116$; respectively). Age was not a significant covariate in this study.

Conclusions: Superior and inferior PVC area, maximum area, volume, maximum depth and thickness were greater than nasal and temporal PVC, in accordance to previous histopathological reports on regional stem cell density. En face OCT can provide novel and potentially clinical useful quantitative measurements to assess PVC health.

CONTROL ID: 3548104

SUBMITTER (NAME ONLY): Rabia Karani

TITLE: Analysis of COVID-19 Virus Particles on Surfaces in New York City

SESSION TITLE: Impacts of Covid on patients and practice

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: R. Karani, Q. Zeng, A. Abdelhakim, V. Diaconita, O. Moussa, T. Sharma, S. Chang, J.D. Horowitz, L. Park, D. Trief, T.H. Tezel, Edward S. Harkness Eye Institute, Columbia University Irving Medical Center, New York, New York, UNITED STATES|H. Zhou, Z. Snow, A. Kassotis, M. Sohail, A.Y. Chang, Columbia University Vagelos College of Physicians and Surgeons, New York, New York, UNITED STATES|

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ABSTRACT BODY:

Purpose: SARS-CoV-2 virus can remain stable on surfaces for several days. This cross-sectional analysis sought to determine the presence of SARS-CoV-2 virus on various surfaces that trainees and faculty of an academic eye clinic routinely came into contact with during the pandemic in New York City.

Methods: Samples were collected by faculty and trainees from surfaces encountered during daily life. On 4 different days, teams collected at least two samples using sterile swabs (Puritan HydraFlock). Prior to collection, nasal swabs were obtained from all individuals to check for SARS-CoV-2. Collection sites were grouped into four zones depending on proximity and the amount of the time personnel spent there. Zones included: (1) Work microenvironment: Slit lamp; door handles; computers; waiting room; reception; bathrooms (2) Work macroenvironment: ICU, ED, inpatient units; elevators, bathrooms; cafeteria (3) Living microenvironment: Home doorknob; kitchen; car; sitting area (4) Living macroenvironment: Subway station; subway cars; car services; restaurants; bike stations; grocery stores. Samples were transported to the lab in transport medium and RNA extraction was conducted using the QIAamp DSP Viral RNA Mini Kit. Presence of viral RNA was investigated using Luna Universal Probe One-step RT-qPCR.

Results: A total of 816 swabs were submitted. Only 2 (0.25%) samples were positive. The first was a sample from a patient bathroom sink handle in the main emergency room and the second was a nasal swab from a staff member who had been assigned to collect samples. Prior to this positive swab result, this staff member had tested positive for COVID-19, quarantined for two weeks, and had then received one prior negative test.

Conclusions: Though COVID-19 is currently widespread in the United States, this study shows that the healthcare personnel working in New York City at Edward S. Harkness Eye Institute at the Columbia University Irving Medical Center have a low chance of encountering viral RNA on surfaces they are in close contact with during their daily life. Considering the 1.77-2.39% citywide test positivity during the time this study was conducted, the likelihood of faculty and trainees getting infected from contaminated surfaces is 100 times less likely than acquiring COVID-19 from an infected individual. This result may be a reflection of the efficacy of disinfection protocols or the limited viability of the virus on inorganic surfaces.

CONTROL ID: 3548189

SUBMITTER (NAME ONLY): Paulina Garcia de Alba Graue

TITLE: CYSLTR1 Inverse agonist, MK571, induces apoptosis in primary and metastatic uveal melanoma cell lines

SESSION TITLE: Recent Advances in Uveal Melanoma

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: P. Garcia de Alba Graue, M. Abdouh, A.A. Goyeneche, A.B. Dias, T. Ferrier, Pathology, McGill University Health Centre, Montreal, Quebec, CANADA|P. Garcia de Alba Graue, M. Abdouh, A.A. Goyeneche, A.B. Dias, T. Ferrier, M.N. Burnier, McGill University Faculty of Medicine, Montreal, Quebec, CANADA|

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ABSTRACT BODY:

Purpose: Uveal Melanoma (UM) is the most common primary intraocular malignancy in adults. It is characterized by developing early gain-of-function mutations (~98%) within GPCR components such as GNAQ and GNA11. Cysteinyl leukotriene receptor 1 (CYSLTR1) is another component in the structure of the G-protein coupled receptor (GPCR), which activates GNAQ/GNA11 and induces the MAPK/MEK/ERK signaling pathway. We previously identified CYSLTR1 expression in three primary and one metastatic UM cell lines as well as in the majority of UM enucleated specimens. Here, we investigated the biological effects of MK571, an inverse agonist of CYSLTR1, on UM cancer cells in an in vitro model.

Methods: In this study we used normal uveal melanocytes, CYSLTR1 negative, and four UM cell lines (MP41, MP46, MEL270, OMM2.5), CYSLTR1 positive. We determined the expression of CYSLTR1 receptor by immunocytochemistry. Cells were then treated with increasing concentrations of MK571 (25, 50, 75, 87.5µM) and our control were untreated cells. Afterwards, cell apoptosis was assessed using Annexin V/PI staining and flow cytometry. Statistical analysis was determined using two-way ANOVA; P<0.05 was considered significant.

Results: We found that inverse agonist, MK571, significantly increased the percentage of apoptotic cells (Annexin V positive cells) in a dose-dependent manner, including early and late apoptotic cell populations in all four cell lines treated ($p < 0.05$). Additionally, we found that after 48 hours of MK571 treatment, cells had ruptured, fragmented and nuclei shrinkage could be widely observed, furthermore, suggesting that this treatment could be responsible for inducing an apoptotic cell death in UM cells.

Conclusions: Inverse agonist, MK571, was proven to be effective as a single agent in inducing the apoptosis of four UM cell lines. It markedly reduced cell proliferation via induction of apoptosis. As such, it may serve as a novel therapeutic agent for uveal melanoma.

CONTROL ID: 3548267

SUBMITTER (NAME ONLY): Nikisha Kothari

TITLE: Fluticasone Intravitreal Implant in Patients with Macular Edema Due to Retinal Vein Occlusion

SESSION TITLE: Stem cells / gene therapy/ transplantation/ laser/ local therapy

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: N. Kothari, D. Chong, R. Wang, C. Fuller, A. Abbey, Retina, Texas Retina Associates, Arlington, Texas, UNITED STATES|

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ABSTRACT BODY:

Purpose: To evaluate the outcomes of use of the fluticasone acetate implant in eyes with macular edema from retinal vein occlusion.

Methods: We retrospectively reviewed 13 eyes with macular edema from retinal vein occlusion who received an injection with the fluticasone implant. We evaluated visual acuity and central retinal thickness outcomes and documented complications including cataract progression and increased intraocular pressure (IOP).

Results: Visual acuity improved following injection with the fluticasone implant at final follow up (0.39 vs 0.26, $p=0.02$). In addition, central retinal thickness improved by 6 months, but then increased by final follow up (412mm, 302mm $p=0.01$, 345mm $p=0.3$). In all phakic patients, cataract progression was seen and required phacoemulsification surgery. Seven (53%) patients required IOP lowering medications and two (15%) required glaucoma filtration surgery.

Conclusions: Our study found the use of the fluticasone implant to be safe and effective for the management of macular edema from retinal vein occlusion. Further larger, randomized controlled studies are required to further evaluate their efficacy.

CONTROL ID: 3548299

SUBMITTER (NAME ONLY): Aleksandra Rachitskaya

TITLE: Retinal vein occlusion randomized control trials' demographics compared to the US census data

SESSION TITLE: Retinal vascular diseases

SESSION TYPE: Poster Session

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ABSTRACT BODY:

Purpose: It is important that randomized control trials (RCTs) represent real world patient populations. The purpose of this study was to compare the distribution of race in retinal vein occlusion (RVO) RCTs to the United States population.

Methods: We performed a cross-sectional study of the racial demographics of 8 RCTs for RVO and compared them to the United States 2019 census data. The number and percent of White, Black, Hispanic, Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander participants was recorded. Chi-square test and one-sample z-test were used. Over- or underrepresentation of each race in every RCT was denoted.

Results: In the 8 RVO RCTs the white patient cohort was overrepresented in 5 RCTs. The difference was not statistically significant in 3. Of note, one study described the study participants only as white and non-white. The black patient cohort was underrepresented in 5, and not statistically different in 2. The Hispanic patient cohort was underrepresented in 6 and not statistically different in 1. The Asian patient cohort was overrepresented in 2 RCT, underrepresented in 1, and not statistically different in 4. The American Indian/Alaska Native and Hawaiian/Pacific Islander patient cohort was underrepresented in 6 RCT and not statistically different in 1.

Conclusions: The current study finds that that racial demographic data of subjects in majority of randomized control trials for treatment of retinal vein occlusion does not reflect that of the United States population, according to the 2019 US Census. Subjects identified as white tend to be overrepresented in randomized control trials. More efforts should be made to recruit underrepresented minorities to improve trial external validity and better serve these subpopulations.

CONTROL ID: 3548335

SUBMITTER (NAME ONLY): Brecken Blackburn

TITLE: Depth-dependent effects of intraocular pressure on phase-decorrelation OCT measurements

SESSION TITLE: Corneal Biomechanics, Keratoconus and Collagen Crosslinking

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: B. Blackburn, M. McPheeters, M.W. Jenkins, A.M. Rollins, Case Western Reserve University, Cleveland, Ohio, UNITED STATES|W.J. Dupps, Cleveland Clinic, Cleveland, Ohio, UNITED STATES|

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ABSTRACT BODY:

Purpose: Decorrelation-based OCT is of interest for cornea biomechanics because it can provide spatially-resolved mechanical contrast based on the microstructural dynamics of the corneal tissue in a wholly non-perturbing manner. Previously, it was found that there was no significant relationship between intraocular pressure (IOP) within normal limits and decorrelation coefficient of the cornea averaged in depth. However, it was suspected that there may be a depth-dependent effect wherein the anterior half of the cornea experiences negative strain and the posterior half of the cornea experiences positive strain, and exhibits, respectively, a relative increase and decrease in decorrelation coefficient.

Methods: Whole porcine globes, obtained fresh from the abattoir, were used in this study with externally-controlled intraocular pressure. IOP was varied from 15 to 25 mmHg while the corneas were imaged with a spectral domain OCT system with a central wavelength of 1310nm. Scans were acquired using an M-B scan pattern with 2ms M-scans. Decorrelation coefficients were calculated using custom MATLAB software, pixelwise with a maximum of 0.06ms of lag.

Results:

It was found that there was a depth-dependent change in decorrelation coefficient as a function of IOP. (Figure 1). It is hypothesized that the change in decorrelation coefficient is due to changing internal stresses in the cornea as a result of IOP. This corresponds well with recently published literature regarding the distribution of strain within the cornea with increasing IOP.

Conclusions: As decorrelation-based OCT is used to study the depth-dependent mechanical properties of the cornea, for instance, in disease detection and treatment monitoring, the possible depth-dependent effect of IOP should be considered.

CONTROL ID: 3548611

SUBMITTER (NAME ONLY): Gerd Auffarth

TITLE: Repeatability of essential tomographic and aberrometric parameters of the Pentacam

SESSION TITLE: Imaging and optical aberrations

SESSION TYPE: Poster Session

AUTHORS/INSTITUTIONS: G.U. Auffarth, M. Koeppel, A.L. Stengele, T. Naujokaitis, Dept. of Ophthalmology, Ruprecht Karls Universität Heidelberg, Heidelberg, Baden-Württemberg, GERMANY|

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ABSTRACT BODY:

Purpose: To establish the degree of repeatability for numerous tomographic and aberrometric parameters for the Pentacam AXL and AXL Wave.

Methods: Retrospective study with three consecutive measurements per eye, all with good quality scores of the respective parameters. Tomography was measured by the Pentacam AXL and AXL Wave, aberrometry data originated exclusively from the AXL Wave (hence, was a subgroup of the entire measurements).

The following tomographic parameters were analysed: Chord μ , Chord α , HWTW, B/F Ratio; Pachymetry (apex, thinnest and their difference), anterior chamber depth (ext and int), corneal optical densitometry and pupil dia. (photopic).

The following aberrometric parameters (total eye) were analysed: RMS HOA, Spherical Aberration, Coma and pupil dia. (mesopic). Repeatability was assessed with the standard deviation and the coefficient of variation (CV [%])

Results: The study includes 97 patients (96 OD and 92 OS) with a mean age of $37 \pm 13,8$ years (the subgroup comprises 59 OD and 56 OS). The examined eyes were all phakic and without any known ocular pathologies. Tomographic parameters. Chord μ : mean=0,22 μ m, SD=0,02, CV=11,2; Chord α : mean=0,45 μ m, SD=0,04, CV=8,2; HWTW: mean=12,1mm, SD=0,05, CV=0,4; B/F Ratio: mean=82%, SD=0,31, CV=0,4; Pachy_{apex}: mean=540 μ m, SD=1,8, CV=0,3; Pachy_{thinnest}: mean=535 μ m, SD=2,1, CV=0,4; Pachy_{Diff}: mean=4,9 μ m, SD=1,2, CV=24,4; ACD_{ext}: mean=3,50mm, SD=0,02, CV=0,6; ACD_{int}: mean=2,97mm, SD=0,02, CV=0,7; COD: mean=13,2%, SD=0,65, CV=4,9; pupil dia_{photopic}: mean=2,7mm, SD=0,13, CV=4,9.

Aberrometric parameters. RMS HOA mean=0,126 μ m, SD=0,023, CV=18,3; spherical aberration: mean=0,046 μ m, SD=0,014, CV=30,1; coma: mean=0,066 μ m, SD=0,023, CV=34,2; pupil dia_{mesopic}: mean=5,1mm, SD=0,4, CV=7,0.

Conclusions: The analysis showed very good repeatability for all tomographic parameters. Standard deviations confirmed values clearly below clinical relevant deviations. CVs were excellent for six parameters and still good for further four. The standard deviations of the aberrometric parameters also revealed good repeatability. The slightly higher values for the coefficient of variations can be explained with the low mean value of the aberrations. The comparison of the repeatability for the mesopic and photopic pupil diameters showed a better repeatability under photopic conditions.

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TITLE: Automated detection of genetic relatedness from fundus photographs using Convolutional Siamese Neural Networks

SESSION TITLE: Deep learning for classification and segmentation

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ABSTRACT BODY:

Purpose: To develop an automated algorithm for detection of genetic relatedness from color fundus photographs (FPs)

Methods: The degree of shared ancestry among pairs of UK Biobank participants (identity by descent, IBD) was estimated genome-wide using PLINK software. Pairs with $IBD > 0.1875$ (halfway between the expected IBD for third- and second-degree relatives) but < 0.98 (presumed duplicates) were considered related, while those with non-calculable IBD were considered unrelated. Unrelated FP pairs were generated using a combination of FPs from the related pairs and FPs randomly sampled from the rest of the data. FP pairs were divided into training and testing sets in an 80:20 ratio. A convolutional Siamese neural network-based algorithm composed of two Densenet-121 networks each pretrained on imageNet was trained to output a measure of genetic relatedness using 5620 pairs (2810 related and 2810 unrelated) of fundus images.

Results: Among the 1380 pairs of FPs in our test set, the model trained assigned each pair of images a Euclidean distance (ED), a measure of genetic relatedness. The average ED was 19.78 ± 10.06 among related pairs and 36.36 ± 12.29 among unrelated pairs, Fig 1. After normalization of EDs and using an optimal threshold for $ED=27.95$ (Youden's Y point), the sensitivity and specificity of our model were 78.7% and 74.7% respectively. When the computed EDs were used to determine probability of relatedness, the area under receiver operating curve for identifying related vs unrelated FP pairs reached 0.843. The ROC curve along with the associated confusion matrix using the computed threshold is shown in Fig 2.

Conclusions: A Siamese neural network based Euclidean distance obtained from pairs of FPs is able to accurately predict genetic relatedness.